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Effect of Subject Expectancy on the THC Intoxication and Disposition From Smoked Hashish Cigarettes[1,2]

J. CAMÍ,[3] D. GUERRA, B. UGENA, J. SEGURA AND R. DE LA TORRE

Department of Pharmacology and Toxicology, Instituto Municipal de Investigación Médica, Barcelona, Spain

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CAMÍ, J., D. GUERRA, B. UGENA, J. SEGURA AND R. DE LA TORRE. *Effect of subject expectancy on THC intoxication and disposition from smoked hashish cigarettes*. PHARMACOL BIOCHEM BEHAV **40**(1) 115–119, 1991.—Subject expectancy on cannabis effects was assessed in a balanced-placebo study in experienced consumers who smoked cigarettes containing hashish (200 mg hashish with 11.5% THC per 1 g tobacco cigarette) (n=24) or placebo (n=24). Although statistically significant differences were not found between subjects who received the drug with positive or negative expectancy, a tendency toward more marked subjective effects was shown in subjects who expected and received the drug. This trend was supported by the significant difference observed in the mean AUC_{0-25} of the heart rate between subjects who smoked hashish with positive or negative expectancies. In subjects who received hashish, the sum AUC_{0-205} of THC and COOH-THC of those who expected the drug was greater than in those who did not expect it ($p<0.05$). The ratio THC/COOH-THC AUC_{0-205} was lower in those with positive expectancy than in those with negative expectancy ($p<0.02$). An increased metabolism of THC was shown in subjects with positive expectancy. Positive expectancy induced powerful subjective effects in the absence of active THC. Expectancy appeared to influence smoking behavior, as seen in higher plasma levels of cannabinoids for the group who received the drug.

Tetrahydrocannabinol Hashish smoking behavior Cognitive expectancies Subjective effects Balanced-placebo design

THE influence of set and setting in interpreting the results of marijuana behavioral effects has been systematically stressed (4, 8, 12, 14, 27). Results of clinical trials revealed that changes in mood following marijuana use could be attributed to a number of variables, such as personality, previous marijuana experience, and expectations (11, 22, 28, 30).

It has been observed that the subjective effects experienced by many marijuana smokers were more influenced by psychological factors than by the tetrahydrocannabinol (THC) content of the cigarettes smoked. At the same dose of THC, the subjective response was different depending upon the companions. Subjects tested individually showed the relaxed, slightly drowsy, and undramatic state usually seen in the laboratory, whereas those in a group setting showed elation, euphoria, uncontrolled laughter, and a marked lack of sedation (14). It has been also shown that the subject's mood following marijuana use was significantly related to the prevailing moods of other subjects in the group (24) and that low doses of cannabis can have different effects when smoked in the company of friends or strangers (18).

The effect of expectancy on cannabis effects has not been fully described. It has been reported that self-ratings of intoxication obtained from experienced marijuana users interact with subject's expectancy and behavior at a moderate dose of marijuana (5). Whereas some studies showed that subjects adjusted their smoking of marijuana cigarettes differing in THC content (9,10), other studies demonstrated that the pattern of smoking marijuana is not immediately adjusted to titrate the inhaled dose of THC (3, 21, 29), thus suggesting that smoking marijuana probably represents, to a larger extent, a learned technique based on previous experience and interaction with other smokers.

Alcohol studies using a balanced-placebo design (23) revealed that cognitive expectancies on subjective effects clearly increased craving for alcohol consumption, sexual arousal and aggression, and may disturb mood, motor skills and memory (13, 16, 19, 26). In addition, subjects who expected alcohol estimated greater amounts of alcohol in their drinks that those who expected nonalcohol beverage, especially when low doses were used (15). We used the balanced-placebo design to test the relevance of expectancy on cannabis effects of hashish cigarettes in healthy experienced cannabis smokers.

METHOD

A balanced-placebo, double-blind clinical trial was designed to examine the pharmacological interaction between alcohol and

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[3]Requests for reprints should be addressed to Dr. Jordi Camí, Instituto Municipal de Investigación Médica, Paseo Marítimo 25, 08003 Barcelona, Spain.

hashish and the relevance of the subjects' induced expectancy (1).

Subjects (n = 96) were recruited from contacts in the student community. Sufficient alcohol experience (monthly consumption, from 700 to 4000 ml) and personal experience with hashish (at least 12 times per year but a maximum of two times per day) were requirements for inclusion as well as absence of signs of disease as judged from physical examination and routine laboratory parameters before the study, and written informed consent according to the authorized protocol ("Dirección General de Farmacia y Productos Sanitarios," 85/27). Subjects with medical and psychiatric pathologic antecedents, particularly those who fulfilled criteria of drug dependence, except tobacco smoking, were excluded.

Subjects were informed of the purposes of the investigation and that they would receive either alcohol, hashish, both drugs together, or their corresponding placebos. They were told that the final selection of drug administration would be determined by lot immediately before the start of the experiment. This was, however, a false lot that induced the required expectancy, independently of how drug administration was randomly selected, and this belief was reinforced throughout the experiment. The efficacy of deception was assessed at the end of the experiment by an external investigator. The participants were randomly assigned to treatment groups of six subjects each in a factorial $2 \times 2 \times 2 \times 2$ basis (combination of the two drugs, their respective placebos and the expectancy towards the consumption of each drug). Subjects were assigned to one of four drug conditions: active alcohol, placebo alcohol, active hashish or placebo hashish. Within each of these groups expectancy was independently manipulated for alcohol (expected/not expected) and hashish (expected/not expected). Thus some subjects expected to receive drug combinations, although these were not actually given.

Subjects were fasted overnight and required to abstain from alcohol and hashish use for 48 hours before each experiment. This was confirmed by chemical analysis of blood samples taken prior to drug and placebo administration. Before the beginning of the experiments, subjects filled out a set of questionnaires about previous drug experience, self-estimated level of performance while under the effects of alcohol and hashish (20) and the Eysenck Personality Questionnaire (6).

The experiments were performed in groups of two subjects and began at 10 a.m. The false lot did not permit the same experimental condition to be assigned to the two subjects who participated on the same day. Alcohol was administered in long cold alcoholic drinks based on vodka and tonic water containing a total dose of ethanol of 0.5 g per kg. Several drops of bitters and lemon juice were added to this mixture to successfully mask the placebo drink. The ingestion of alcohol or placebo beverage accounted for a period of 30 min.

Hashish cigarettes containing 23 mg of THC or its placebo were administered by smoking for a period of 10 min, starting 5 min after the end of beverage consumption (minute 0 to 10 in the present study). Cigarettes consisted of a mixture of 600 mg Virginia tobacco, 200 mg of aromatic smokable herbs (Honeyrose®) with or without 200 mg of hashish. A filter was adapted to avoid the formation of a roach and to ensure smoking of the entire cigarette. The hashish material contained 11.5% of THC as determined by gas-liquid chromatography and was provided by the "Servicio de Control de Estupefacientes," Spanish Ministry of Health.

Throughout the experiment the subjects self-rated their degree of alcohol intoxication or hashish high by means of two independent 0–100 vertical scales. Zero was defined as sober and 100 as the most drunk or most "stoned" they had ever been in any social situation. Heart rate was recorded simultaneously at predose and at 10, 25, 40, 55, 85, 145, 205, and 325 min after the beginning of cigarette smoking.

Blood samples were taken in basal conditions and at 3, 5, 7, 10, 15, 20, 25, 40, 55, 85, 145, 205, and 325 min after the beginning of cigarette smoking. Plasma levels of delta-9-THC (THC) and 11 nor-9 COOH-delta-9-THC (COOH-THC) were measured by RIA (Research Triangle Institute, NC). The coefficient of variation for THC at 8 ng/ml was 6.6% (8.23 ± 0.55, n = 6), at 30 ng/ml 3.5% (32.86 ± 1.15, n = 6), and at 80 ng/ml 11.9% (85.42 ± 10.19, n = 6). The corresponding values for COOH-THC at 8 and 30 ng/ml were 10.9% (8.02 ± 0.88, n = 12) and 12.6% (31.84 ± 4.01, n = 12), respectively.

The experimental parameters (C_{max}, maximum blood concentration; E_{max}, maximum effect; T_{max}, time to either maximum blood concentration or maximum effect; AUC, area under the curve) for plasma levels of THC and COOH-THC and self-rated effects were evaluated. The area under the curve was calculated by the trapezoidal method. The sum of and the ratio between AUC_{0-205} for plasma levels of drug and metabolite were used as tentative indicators of the global ingestion of cannabinoids and the degree of metabolism.

All comparisons were made by ANOVA test using SPSSx® software, version 3.12. The compare between AUC of self-rated effects, Mann-Whitney test was used. Data are presented as mean ± SD.

RESULTS

From 207 eligible subjects, 96 male paid volunteers aged 21 to 30 years were selected. Eighty-seven percent were students and 88% smoked cigarettes on a regular basis. Data presented here refers only to half of the 96 participants who did not receive the alcohol beverage, but who did smoke cigarettes containing hashish (n = 24) or placebo (n = 24). Data were analyzed according to four experimental groups of 12 subjects who, independently of alcohol expectancy, received hashish or placebo cigarettes and were told they would or would not smoke the drug; each of these groups included a pure-hashish deceived experimental subgroup of six subjects who also received hashish or placebo cigarettes, did not expect alcohol, and were told they would or would not smoke the drug (R/E, received/expected; R/NE, received/did not expect; NR/E, did not receive/expected; NR/NE, did not receive/did not expect).

Eighteen (33.8%) of the 48 participants were heavy hashish smokers (between once or twice a day and two to six times a week), 13 (27%) declared consumption of hashish once a week, and 13 (27%) from one to three times a month.

No significant differences were found between the treatment groups concerning previous drug experience, dimensions of Eysenck Personality Questionnaire (EPQ), and self-estimated level of performance while under the effects of hashish (SEPH). Mean scores for extraversion (14.7 ± 3.3), neuroticism (8.8 ± 4.3), psychoticism (6.0 ± 2.9), and lie (13.8 ± 3.7) were no different from scores for healthy volunteers participating in clinical trials (2). The mean SEPH score was 14.2 ± 9.3 (maximum score, 60). An inverse relationship between SEPH and previous drug experience was found ($r = .160$, $p < 0.05$).

Deception was achieved in 42 (87.5%) of the 48 subjects as determined by interrogation. Of the six subjects who were not deceived, three received hashish but were told that they would not receive the drug and the other three smoked placebo but were told they would receive hashish. Dimensions of the EPQ and SEPH values of subjects deceived were not statistically dif-

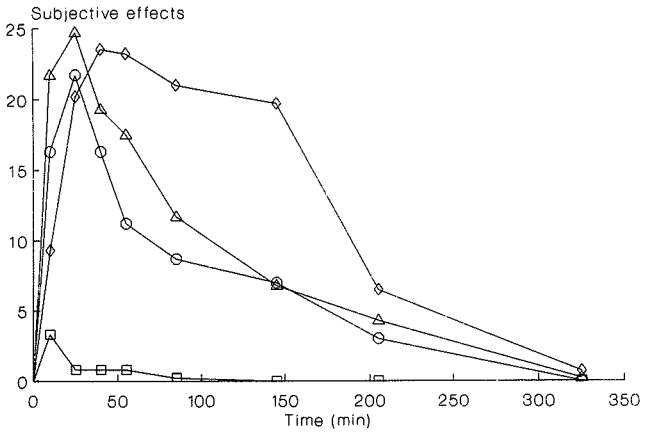

FIG. 1. Time course of ratings of self-reported overall hashish high (mean values) (diamonds: R/E, received/expected; triangles: R/NE, received/did not expect; circles: NR/E, did not receive/expected; squares: NR/NE, did not receive/did not expect). Data referred to the pure hashish-deceived experimental group of six subjects.

ferent from subjects not deceived.

In R/E subjects, self-rated hashish high reached a peak at 41.2 ± 34.3 min (T_{max}). The peak effect of R/NE subjects and NR/E, appeared at the same time (22.7 ± 17.5 and 20.5 ± 9.6 min, respectively). The peak value of the self-reported high on the scale (E_{max}) was different between the groups: 33.6 ± 17.1 for R/E, 25.0 ± 20.1 for R/NE, and 24.1 ± 16.3 for those NR/E. The control group (NR/NE) rated only basal values. Time course ratings of self-reported overall hashish high (mean values) are shown in Fig. 1.

The overall high (AUC_{0-325}) of the groups that received the drug (R/E, mean AUC_{0-325} 4,925; and R/NE, mean AUC_{0-325} 3,339) and of the group that expected the drug (NR/E, mean AUC_{0-325} 2,036) was significantly higher than the overall basal rate of the control group (mean AUC_{0-325} 111) (R/E vs. NR/NE, $Z = 0.004$; R/NE vs. NR/NE, $Z = 0.004$; NR/E vs. NR/NE, $Z = 0.025$); R/E subjects rated higher than, but not statistically different from R/NE subjects ($Z = 0.37$).

In the group of subjects who received and expected hashish (R/E) and received and did not expect hashish (R/NE), the heart rate reached a peak (T_{max}) at 11.3 ± 3.3 and 13.9 ± 4.3 min, respectively. Both values were significantly different from those of subjects who did not receive and expected hashish (NR/E) (6.6 ± 5.2 min, $p<0.02$), and subjects who did not receive and did not expect hashish (NR/NE) (6 ± 4.5 min, $p<0.0004$).

The mean of maximum heart rate (E_{max}) observed in the above-mentioned four groups were 119.1 ± 17.6, 106.2 ± 19.5, 102.9 ± 15.5, and 94.4 ± 18.8 for R/E, R/NE, NR/E and NR/NE, respectively. Statistically significant differences were only observed between subjects that received and expected hashish and subjects who did not receive the drug (R/E vs. NR/E, $p<0.03$; R/E vs. NR/NE, $p<0.0004$).

The mean AUC of the heart rate recorded for the groups that received hashish was calculated between the time interval 0–25 which was the moment when most subjective effects occurred. The mean AUC_{0-25} of the heart rate recorded for the group that expected hashish (NR/E) ($2,741 \pm 348$, $n = 10$) was higher, although not significantly different from that of the control group (NR/NE) ($2,573 \pm 526$, $n = 12$), nor was it significantly different from that of subjects who received hashish although they did not expect it (R/NE) ($2,459 \pm 377$, $n = 9$). Only the heart rate recorded in the group that received and expected the drug (R/E) (AUC_{0-25} $2,998 \pm 397$, $n = 10$) was significantly higher than that of the group that received and did not expect the drug (R/NE) ($p<0.007$) and the control group ($p<0.04$) (Fig. 2).

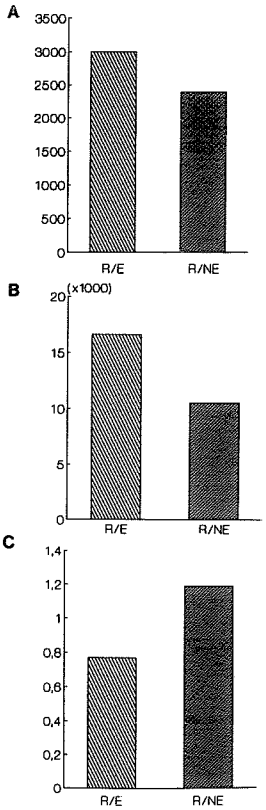

FIG. 2. Comparison between the group that received hashish and expected the drug (R/E) and the group that received hashish and did not expect the drug (R/NE) with regard to (A) the mean AUC_{0-25} of heart rate, (B) sum of AUC_{0-205} of THC and COOH-THC, and (C) ratio of AUC_{0-205} between THC and COOH-THC. Data referred to the group of 12 subjects.

Figure 3 shows the mean time-course of THC and COOH-THC of subjects who smoked hashish cigarettes with different expectancies. In the group that expected the drug, the THC C_{max} was 172.2 ng/ml, T_{max} 19.9 min and COOH-THC C_{max} 64.7 ng/ml, T_{max} 30 min. In the group that did not expect the drug, the THC C_{max} was 165 ng/ml, T_{max} 11.4 min and COOH-THC C_{max} 33.5 ng/ml, T_{max} 29.6 min. As shown in Fig. 2 the sum of AUC_{0-205} of THC and COOH-THC in the group that expected to smoke hashish was higher than that of the group that did not expect to receive the drug (Z AUC_{0-205} $16,604 \pm 12,722$, $n = 12$ vs. $10,521 \pm 6,491$, $n = 10$, $p<0.05$). The ratio of AUC_{0-205} between THC and COOH-THC also varied in accordance with the expectancy of the groups (ratio AUC_{0-205} 0.77 ± 0.32 vs. 1.2 ± 0.41, $p<0.02$).

Statistical analyses of all data showed that the groups which differed only with respect to alcohol expectancy were not different. Therefore, the heart rate of THC and COOH-THC levels recorded were always independent of alcohol consumption and the effects of alcohol expectancies.

DISCUSSION

In this study, the random allocation of participants in the different experimental groups gave rise to homogeneity within each

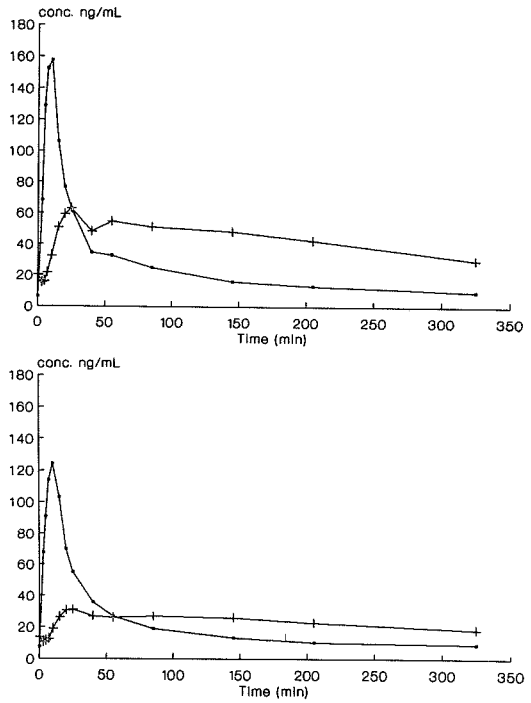

FIG. 3. Time-course of THC (−) and COOH-THC (x-x) plasma concentrations (mean values) in subjects who smoked hashish cigarettes and expected the drug (R/E) (top) and who smoked hashish and did not expect the drug (R/NE) (bottom). Data referred to the group of 12 subjects.

group and between the groups as far as personality, previous drug experience, and SEPH. It has been reported that toxicologic history has a significant influence on the subject's expectancy of the effects of alcohol. An inverse relationship was found between SEPH and previous hashish experience. Subjects with less hashish experience estimated that their performance would be more greatly affected than performance estimated by subjects with greater hashish consumption. This coincides with findings reported in alcohol studies (20,25).

The use of a balanced-placebo design has proven that it is possible to deceive subjects receiving low doses of hashish and to make them believe that they have not receive the drug, or that thay have done so. Subjects who received the drug (R/E and R/NE) showed subjective effects that were sufficiently marked and significantly different than those experienced by subjects in the control group (NR/NE). Although statistically significant differences were not found between subjects who received the drug with positive or negative expectancy, a tendency toward a more marked subjective effect was shown in R/E subjects. This trend is supported by the significant difference observed in the mean AUC_{0-25} of the heart rate between subjects who smoked hashish with positive or negative expectancies.

The subjects with positive expectancy seem to inhale larger quantities of cannabinoids from the cigarettes. Although it is not possible to determine the exact bioavailability of these cigarettes, differences between the AUC obtained for THC and COOH-THC varied according to the expectancy created. In studies on the smoking of cigarettes containing marijuana, it has been suggested that approximately 50% of THC originally contained is released in the smoke assuming that the whole cigarette is smoked. It would appear that the amount of THC released in the smoke is relatively independent of the volume inhaled or the length of inspiration (7,17). It has been shown that in the second half of a cigarette less smoke is inhaled than in the first half. The smoker adjusted the puff volume of smoke to deliver an amount of THC to the mouth that would achieve a desired level of intoxication (29); this might explain, in part, the declining plasma levels of THC that have been recorded during the latter portion of a marijuana cigarette (21). Results are contradictory when explored if smokers adjust the dynamics of smoking to the potency of the cigarette (10,29). Assuming that the pattern of smoking is not immediately adjusted to titrate the inhaled dose of THC, the differences observed in the AUC_{0-205} of THC and COOH-THC could be attributed to a higher intake of cannabinoids in subjects who expected the drug, compared to the group that did not expect hashish.

The differences shown in the ratio AUC_{0-205} THC/COOH-THC could indicate that in the group with positive expectancy there was a greater metabolism of THC to COOH-THC in the same period of time. A possible reason for this would be that in this group of subjects the heart rate was higher, which could have increase the metabolic extraction of THC to COOH-THC through an increased liver blood flow. A comparison of these pharmacokinetic data should be interpreted with caution because cognitive expectancies were not subjected to a crossover design study, because the balanced-placebo design prevented subjects who were suitable candidates from repeating a study that they were already conversant with.

In conclusion, positive expectancy to hashish after placebo consumption may induce subjective effects similar to those produced by low doses of the drug. Subjects who are invited to smoke a cigarette containing hashish, if they are induced with positive expectancy of the drug, can obtain a larger amount of THC from the cigarette compared with when they do not believe they are smoking hashish. Positive expectancy induced powerful subjective effects in the absence of active THC. Expectancy appeared to influence smoking behavior, as seen in higher plasma levels of cannabinoids for the group who received the drug.

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REFERENCES

1. Camí, J.; de la Torre, R.; Guerra, D.; Ortuño, J.; Segura, J. Pharmacokinetic interaction between low doses of alcohol and hashish. Eur. J. Clin. Pharmacol. (Suppl.) 36:A312; 1989.
2. Camí, J.; Llorente, M.; Farré, M.; Badenas, J. M.; Ugena, B. Personality of healthy volunteers participating in phase I clinical trials. Person. Indiv. Diff. 10:1199–1200; 1989.
3. Cappell, H.; Kuchar, E.; Webster, C. D. Some correlates of marihuana self-administration in man: A study of titration of intake as a function of drug potency. Psychopharmacologia 29:177–184; 1973.
4. Cappell, H.; Pliner, P. Cannabis intoxication: The role of pharmacological and psychological variables. In: Miller, L. L., ed. Marijuana: Effects on behavior. New York: Academic Press; 1974:233–263.
5. Carlin, A. S.; Bukker, C. B.; Halpern, L.; DeePost, R. Social fa-

cilitation of marijuana intoxication: Impact of social set and pharmacological activity. J. Abnorm. Psychol. 60:132–140; 1972.
6. Eysenck, S.; Eysenck, H. J. Manual of the Eysenck Personality Questionnaire (adult and junior). London: Hoder and Stoughton; 1975.
7. Kinzer, G. W.; Foltz, R. L.; Mitchell, R. L.; Truitt, E. B., Jr. The fate of cannabinoid components of marijuana during smoking. Bull. Narc. 26:41–54; 1974.
8. Galanter, M.; Stillman, R.; Wyatt, R. J.; Vaughan, T. B.; Weingartner, H.; Nrunberg, F. L. Marijuana and social behavior. Arch. Gen. Psychiatry 30:518–521; 1974.
9. Heishman, S. J.; Stitzer, M. L.; Yingling, J. E. Effects of tetrahydrocannabinol content on marijuana smoking behavior, subjective reports, and performance. Pharmacol. Biochem. Behav. 34:173–179; 1989.
10. Herning, R. I.; Hooker, W. D.; Jones, R. T. Tetrahydrocannabinol content and differences in marijuana smoking behavior. Psychopharmacology (Berlin) 90:160–162; 1986.
11. Hollister, L. E. Marijuana in man: Three years later. Science 172: 21–29; 1971.
12. Hollister, L. E.; Overall, J. E.; Gerber M. L. Marijuana and setting. Arch. Gen. Psychiatry 32:798–801; 1975.
13. Hull, J. G.; Bond, C. F. The social and behavioral consequences of alcohol consumption and expectancy. Psychol. Bull. 99:347–360; 1986.
14. Jones, R. T. Tetrahydrocannabinol and the marihuana-induced social "high," or the effects of the mind on marihuana. Ann. NY Acad. Sci. 191:155–165; 1971.
15. Knight, L. J.; Barbaree, H. E.; Boland, F. J. Alcohol and the balanced-placebo design: the role of experimenter demands in expectancy. J. Abnorm. Psychol. 95:335–340; 1986.
16. Lang, A. R.; Goeckner, D. T.; Adesso, V. J.; Marlatt, G. A. Effects of alcohol on aggression in male social drinkers. J. Abnorm. Psychol. 84:508–518; 1975.
17. Manno, J. E.; Kiplinger, G. F.; Bennet, I. F.; Haine, S.; Forney, R. B. Comparative effects of smoking marijuana or placebo on human motor and mental performance. Clin. Pharmacol. Ther. 11: 808–815; 1970.
18. Marks, D. F.; Pow, G. M. Cannabis and human social behavior. Hum. Psychopharmacol. 4:283–290; 1989.
19. Marlatt, G.; Rohsenow, D. J. Cognitive processes in alcohol use: Expectancy and the balanced placebo design. In: Mello, N. K., ed. Advances in substance abuse: Behavioral and biological research, vol. 1. Greenwich, CT: JAI Press Inc.; 1980:159–199.
20. Mills, K. C.; Bisgrove, E. Z. Cognitive impairment and perceived risk from alcohol. J. Stud. Alcohol 44:26–46; 1983.
21. Pérez-Reyes, M.; DiGuiseppi, S.; Davis, K. H.; Schnidler, V. H.; Cook, C. E. Comparison of effects of marijuana cigarettes of three different potencies. Clin. Pharmacol. Ther. 31:617–624; 1982.
22. Pillard, R. C.; McNair, D. M.; Fisher, S. Does marijuana enhance experimentaly induced anxiety? Psychopharmacologia 40:205–210; 1974.
23. Ross, S.; Krugman, A. D.; Lyerly, S. B.; Clyde, D. J. Drugs and placebos: a model design. Psychol. Rep. 10:383–392; 1962.
24. Rossi, A. M.; Kuehnle, J. C.; Mendelson, J. H. Marijuana and mood in human volunteers. Pharmacol. Biochem. Behav. 8:447–453; 1978.
25. Southwick, L.; Steele, C.; Marlatt, A.; Lindell, M. Alcohol related expectancies defined by phase of intoxication and drinking experience. J. Consult. Clin. Psychol. 49:713–721; 1981.
26. Vuchinich, R. E.; Sobell, M. B. Empirical separation of physiological and expected effects of alcohol on complex perceptual motor performance. Psychopharmacology (Berlin) 60:81–85; 1978.
27. Waskow, I. E.; Olsson, J. E.; Salzman, C.; Katz, M. M. Psychological effects of tetrahydrocannabinol. Arch. Gen. Psychiatry 22: 97–107; 1970.
28. Weil, A. T.; Zinberg, N. E.; Nelsen, J. M. Clinical and psychological effects of marijuana in man. Science 162:1234–1242; 1968.
29. Wu, T.; Tashkin, D. P.; Rose, J. E.; Djahed, B. Influence of marijuana potency and amount of cigarette consumed on marijuana smoking pattern. J. Psychoactive Drugs 2:43–46; 1988.
30. Zinberg, N. E. Drugs, set, setting. New Haven: Yale University Press; 1984.