

Marijuana Induced State-Dependent Verbal Learning

William H. Rickles, Jr., Michael J. Cohen, Charlotte A. Whitaker, and
Keren E. McIntyre

Department of Psychiatry, UCLA School of Medicine, Los Angeles, California 90024

Received December 18, 1972; Final Version March 21, 1973

Abstract. Human, male subjects from our light marijuana usage category were given paired associate learning under either placebo or marijuana intoxication. A 2×2 experimental design was used to test for dissociation effects. Marijuana intoxicated subjects needed significantly more trials to reach criterion learning than subjects under placebo. Testing of recall, ten days later, demonstrated a significant state-dependent effect. The results were discussed in terms of state-dependent theory and the effects of central nervous system active drugs on learning models.

Key words: Marijuana — State-Dependent — Dissociation — Verbal Learning.

A popular justification for marijuana is that marijuana intoxication provides an altered state of consciousness considered to be pleasurable and beneficial (Tart, 1971). Concern has been expressed, however, that indulgence in this pharmaceutically induced state may actually interfere with the functioning of thought processes (National Commission on Marijuana and Drug Abuse, 1972; West, 1970). Marijuana has been documented as altering time sense and immediate memory (Melges, Tinklenberg, Hollister and Gillespie, 1970; Hollister, 1971); and Abel (1971a, 1971b, 1971c) has found that marijuana interfered with the initial encoding process and long term storage of information. We have undertaken a series of experiments to further characterize the cognitive and physiological concomitants of the marijuana induced state of consciousness. Subjects (Ss) with varying past histories of marijuana usage are being studied. Part of these experiments which explore acquisition and retrieval of paired associates, using a 2×2 drug design, are reported below.

Method

Subjects. Thirty-two Ss from our light usage category were selected. Light users were operationally defined as Ss who smoked marijuana not more than three times per week, and not less than once per month during the preceding year. We consider this group to be "social" users. All Ss were paid volunteers ranging in age from 18 to 27 years with an average of 22 years. The Ss were initially screened with the Minnesota Multiphasic Personality Inventory (MMPI) and the Wechsler Adult

Intelligence Scale (WAIS). Present norms for college students were used for the MMPI and *Ss* were selected for scores between 110 and 140 on the verbal scale of the WAIS. Aside from hashish, no other drugs were used with regularity.

Design and Procedure. Each *S* was observed on two occasions, ten days apart. Testing was performed under both marijuana (M) and placebo (P) conditions. The *Ss* were randomly assigned to four groups, tested respectively, under conditions P-P, P-M, M-P, and M-M. During each experimental session, *S* was comfortably seated in a small subject room facing a projection screen. Electrodes were attached for recording physiological reactions on a polygraph located in an adjoining room (results to be reported elsewhere). After obtaining 5 min of baseline physiology *S* smoked two 1 g "marijuana" cigarettes. On P days, each cigarette contained 1000 mg of exhaustively, alcohol-extracted marijuana. On M days, each cigarette contained 500 mg of marijuana, assayed to contain 1.4% Δ^9 -THC, which was sandwiched between 250 mg of placebo placed at each end of the cigarette. Therefore on M days, 14 mg of Δ^9 -THC was available to the *S*. The *S* smoked in his usual fashion for marijuana cigarettes (deep inhalation and hold) and was asked to finish both cigarettes in 20 min. The usual smoking time was 25 min and each cigarette was smoked as completely as the *S* could. A hemostat was provided for holding the short butt. Double blind conditions were maintained throughout.

Following smoking, 5 min of physiology were recorded. A habituation sequence of ten 500 Hz, 75 db tones of one second duration then ensued. The tones were accompanied by a one second presentation of a blank, white slide. During the habituation sequence, the tone-slide compound stimulus was programmed on a variable interval schedule (range 15–25 sec, average 20 sec). Subjects next received instructions for learning a list of nine paired associates. Each paired associate consisted of a nonsense syllable (CVC trigram) and a common English word. The nonsense syllable was presented for 1.0 sec followed by the common English word for 1.0 sec. Interpolated between the nonsense syllable and the word was 0.5 sec blank screen time while the projector changed slides. Thus, there was a total of 1.5 sec from the onset of the nonsense syllable to the onset of the word. The 75 db tone accompanied the nonsense syllable and acted as a cue for the beginning of a pair. The tone also served to mask the sound of the Kodak 850 Carousel slide projector. The projector was located in the adjoining room with the polygraph and projected through one-way glass into the subject room. A 20 sec fixed intertrial interval separated the paired associates to allow for recovery of phasic physiological responses. During this period, the projection screen was blank.

To prevent serial learning, three random sequences of the nine word list were used. Presentation of one complete sequence was defined as a learning trial, and the three sequences were presented in rotation until criterion learning was reached. Criterion learning consisted of correctly anticipating all nine words within one sequence of a list. Anticipation of the correct word had to occur during the 1.5 sec inter-pair interval. Attainment of criterion was followed by 100% overlearning. As an example, if the *S* needed five trials to reach criterion this was immediately followed by five additional trials. On day two, after testing for retention of day one learning, *Ss* were required to learn another paired associate list of equal difficulty in pronunciation, learnability, and meaningfulness (Thorndike and Lorge, 1944; Underwood and Schultz, 1960). On either day, if *S* failed to reach criterion within 15 trials he was dropped from the study. This was done to insure that learning took place under a state of acute intoxication.

On day two, immediately preceding the learning phase, *S* was tested for recall of list one learning. List one nonsense syllables were presented, along with the tone, for one trial and *S* was asked to recall the word that had been associated with a

particular nonsense syllable. The nonsense syllable was presented for one second followed by 20 sec of blank screen time. The *S* was given the full amount of time to respond.

Results

On day one, eight *Ss* failed to reach criterion learning, seven under the drug condition and one under placebo. On the second day, two *Ss* did not reach criterion: both were marijuana intoxicated. Two *Ss* failed to follow experimental protocol; both had received marijuana. If a *S* was dropped, the next *S* arriving at the laboratory was assigned the same double blind condition. Therefore, the remaining 20 *Ss* were equally divided among the four groups.

The results reported below concern learning on days one and two and recall of day one learning. Between groups comparisons were calculated on day one trials to criterion for the two groups receiving placebo and the two groups receiving marijuana. In both cases, the difference between the means was not significant. The same comparisons were performed for the marijuana and placebo groups on day two trials to criterion. Again, no differences were found. When possible, subsequent analyses were, therefore, conducted on the pooled data from the ten *Ss* receiving like drug conditions. Means and standard deviations based on trials to criterion for the individual groups are presented in Table 1.

On day one, *Ss* intoxicated with marijuana needed significantly more trials to reach criterion than placebo *Ss*, $F(1, 18) = 4.92, p < 0.05$. The average trials to criterion for *M* and *P* groups were 8.6 and 5.6 respectively. The same phenomenon was observed on day two trials to criterion $F(1, 18) = 4.71, p < 0.05$. Placebo *Ss* required 5.1 and marijuana *Ss* needed an average of 7.7 trials to attain criterion. The data from the recall of list one learning were subjected to a 2×2 analysis of variance. Table 2 summarizes the experimental design, cell means, and standard deviations for recall.

The only significant finding for the recall section was the Day One Drug \times Day Two Drug interaction, $F(1, 16) = 5.36, p < 0.05$, indicating that recall was significantly influenced by drug state.

Table 1. Means and standard deviations for trials to criterion. Standard deviations calculated using $n-1$. P = placebo, M = marijuana

Group	Day 1		Day 2	
	Mean	S.D.	Mean	S.D.
P-P	5.6	2.5	5.4	1.3
P-M	5.6	2.9	6.4	2.4
M-M	10.0	3.2	9.0	4.2
M-P	7.2	3.3	4.8	1.6

Table 2. Drug rotation and average recall for groups, P = placebo, M = marijuana. Standard deviation calculated using $n-1$

		Day two drug	
		P	M
Day one drug	P	Group P-P, Recall = 8.0 S.D. = 1.0	Group P-M, Recall = 5.8 S.D. = 3.6
	M	Group M-P, Recall = 6.8 S.D. = 1.9	Group M-M, Recall = 8.2 S.D. = 0.8

Discussion

The results suggested that in a group of "social" marijuana users, a moderately high dose of marijuana interfered with learning new material. Not only did marijuana intoxicated *Ss* require more trials to reach criterion on both days, nine of the ten *Ss* failing to attain criterion were marijuana intoxicated. Abel (1971 a, 1971 b, 1971 c) concluded marijuana causes an impairment in the function of attention and this interferes with the rehearsal of the information. Thus, information cannot enter long term storage. An alternate hypothesis is that the transfer mechanism from the sensory register into short term memory is interrupted and *S* has nothing in short term memory to rehearse. This, however, does not appear to be the case, for marijuana does not produce a complete amnesia. Information does get through, but apparently is inefficiently processed.

Once information was learned, recall of items stored in long term memory was superior when performed in the same drug state that learning took place. These results are in accord with animal studies demonstrating state-dependent effects of THC (Barry and Kubena, 1972; Henriksson and Jarbe, 1971, 1972). The similarity between the no change groups (P-P and M-M) is further substantiated by the lower within-group variance as opposed to the change groups (P-M and M-P). A state-dependent theory might postulate that a CNS active drug gives rise to a unique, discernible pattern of internal cues. When a task is learned under the influence of one of these drugs, the internal cues become part and parcel of the learning process. If subsequently *S* performs the task in a non-intoxicated state, the stimulus configuration is somewhat different from the original learning situation. Performance should then decrease along a generalization gradient based on a dose response relationship. Dose response relationships have been reported for state-dependent learning with animals (Overton, 1971 a).

Human verbal learning is probably more complicated. Mechanisms such as rehearsal and the formation of mnemonics come into consideration. Only a few studies have been carried out with regard to drug

induced state-dependent learning. Such drug effects have been reported for alcohol and amytal (Storm and Caird, 1967; Bustamente, Rosello, Pradere, and Martinez, 1969; Overton, 1971 b). Though the number of experimental subjects in this study was small, we suggest that the state-dependent marijuana effect is reliable. Procedural variables were present which are known to attenuate the state-dependent effect. These include 100% overlearning and practice while the drug effect is diminishing (Bliss, 1968; Overton, 1971 a). Thus, significant results were obtained under conditions considerably less than optimum for demonstrating state dependency. Prior experience with marijuana, high verbal I.Q., and the opportunity for Ss to form mnemonics during the experiment are other variables which probably interact with state-dependent effects in as yet an indeterminate way. To test the extent to which prior drug experience is a meaningful variable, we have run chronic marijuana users through the verbal learning task. The results will be available shortly.

This study was supported by NIMH Grant 5 ROI MH 19488-02. Computing assistance was obtained from the Health Sciences Computing Facility, UCLA, sponsored by NIH Special Resources Grant RR-3.

References

- Abel, E. L.: Marijuana and memory: acquisition or retrieval? *Science* **173**, 1038-1040 (1971 a).
- Abel, E. L.: Retrieval of information after use of marijuana. *Nature (Lond.)* **231**, 58 (1971 b).
- Abel, E. L.: Effects of marijuana on the solution of anagrams, memory, and appetite. *Nature (Lond.)* **231**, 260-261 (1971 c).
- Barry, H., Kubena, R. K.: Discriminative stimulus characteristics of alcohol, marijuana, and atropine. In: *Drug addiction: experimental pharmacology*. J. M. Singh, L. Miller and H. Lal, eds., vol. 1, pp. 3-16. Mount Kisco-New York: Futura Publishing Co. 1972.
- Bliss, D. K.: Behavioral and electrographic indices of drug dissociated learning. Unpublished doctoral dissertation, University of California, Berkeley 1968.
- Bustamente, J. A., Rosello, A., Pradere, E., Martinez, H.: Learning and drugs. *International Congress of Psychology, 18th Proceedings*, vol. 8, pp. 69-70 (1966).
- Henriksson, B. G., Jarbe, T.: The effect of two tetrahydrocannabinols (Δ^9 -THC and Δ^8 -THC) on conditioned avoidance learning in rats and transfer to normal state conditions. *Psychopharmacologia (Berl.)* **22**, 23-30 (1971).
- Henriksson, B. G., Jarbe, T.: Δ^9 Tetrahydrocannabinol used as discriminative stimulus for rats in position learning a T-shaped water maze. *Psychonom. Sci.* **27**, 25-26 (1972).
- Hollister, L. E.: Marijuana in man: three years later. *Science* **172**, 21-28 (1971).
- Marijuana: a signal of misunderstanding. Washington: National Commission on Marijuana and Drug Abuse 1972.
- Melges, F. T., Tinklenberg, J. R., Hollister, L. E., Gillespie, H. K.: Temporal disintegration and depersonalization during marijuana intoxication. *Arch. gen. Psychiat.* **23**, 204-210 (1970).

- Overton, D. A.: Discriminative control of behavior by drug states. In: Stimulus properties of drugs, T. Thompson and I. Pickens, eds., pp. 85—110. New York: Appleton-Century-Crofts 1971 a.
- Overton, D. A.: State-dependent learning produced by alcohol and its relevance to alcoholism. In: The biology of alcoholism. B. Kissin and H. Begleiter, eds., Vol. II, pp. 193—218. New York: Plenum Press 1971 b.
- Storm, T., Caird, W. K.: The effects of alcohol on serial verbal learning in chronic alcoholics. *Psychonom. Sci.* 9, 43—44 (1967).
- Tart, C. T.: On being stoned, a psychological study of marijuana intoxication. Palo Alto: Science and Behavior Books 1971.
- Thorndike, E. L., Lorge, I.: The teacher's word book of 30,000 words. New York: Columbia University Press 1944.
- Underwood, B. J., Schultz, R. W.: Meaningfulness and verbal learning. Philadelphia: Lippincott 1960.
- West, L. J.: On the marijuana problem. In: Psychotomimetic drugs. D. Efron, ed., pp. 327—328. New York: Raven Press 1970.

William H. Rickles, Jr.
Department of Psychiatry
UCLA School of Medicine
Los Angeles, California 90024
U.S.A.