MARIJUANA: ACUTE EFFECTS ON HUMAN MEMORY

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I. INTRODUCTION

The single, most consistently reported, behavioral effect of cannabinoids in humans is an alteration in memory functioning (1). Interest in the effects of cannabis on memory stemmed from anecdotal reports of the effects of cannabis on mood and thinking. In 1845, the French psychiatrist de Tours Moreau (2) provided an elegant characterization of the effects of hashish on human mental functioning. Moreau stated that one of the more prominent effects of hashish was a "gradual weakening of the power to direct thoughts at will". Ideas extraneous to the focus of an individual's attention appeared to enter the mind producing a loosening of associations. Other early investigators such as Bromberg (3) and Ames (4) employing less potent cannabis preparations than those used by Moreau and his followers also noted fragmentation of thought and confusion on attempting to remember recent occurrences.

Objective substantiation of some of these observations has been gained in studies employing known doses of delta-9-tetrahydrocannabinol (THC). Tinklenberg et al. (5) found that orally administered THC (20, 40, 60 mg) impaired immediate memory for digits recalled in forward or reverse order with peak impairment at 1.5 and 3.5 hours, respectively. Memory impairment was intermittent and not dependent on dose. The transient nature of the memory loss was reminiscent of the waxing and waning effect following marijuana intoxication described by Clark et al. (6). Oral THC has also been found to induce "temporal disintegration," which is defined as a difficulty in retaining, coordinating and serially indexing those memories, perceptions, and expectations that are rele-

vant to the attainment of some goal (7,8). The measure of temporal disintegration was the Goal Directed Serial Alternation Test (GDSA) that required a subject to subtract and add numbers from each other until some specified number was reached. The dose-related disruption found on this task was thought to be related to impaired time perception. Also, the inability to temporally coordinate recent memories with intentions might account for disorganized speech patterns found by Weil and Zinberg (9) following marijuana intoxication. Since words and phrases are hierarchically ordered in a goal directed fashion, speech may become disorganized under the drug and a person is likely to lose his train of thought. While the GDSA has proven to be an interesting measure with which to assess the effects of cannabinoids, Abel (10) has questioned its reliability. Studies by Rafaelsen et al. (11) and Tinklenberg et al. (12) have found some difficulty in replicating their original findings with the GDSA. This lack of replicability appears to be due in part to limited within drug session employment of the GDSA task that resulted in an abbreviated sampling of the behavior in question.

In order to determine a specific locus of action of marijuana on memory, it has been suggested that testable models of human memory be employed so that any selective impairment due to intoxication might be determined (1,13). One such model has been proposed by Shiffrin and Atkinson (14). The model is based on psychological evidence as well as neurophysiological and anatomical observations which suggest that memory might be best conceptualized as a two component process containing a short-term and long-term storage component. The model illustrated in Figure 1 consists of three basic aspects: a sensory information in an unaltered form for a few milliseconds while analysis, identification, and encoding take place. The short-term memory store is an individual's working memory. It is responsible for holding the trace of the external stimulus and at the same time matching the memory trace of the stimulus with a previously encoded representative of the stimulus from the long-term storage component. The short-term store and long-term store differ in terms of both information capacity and duration. Only a small number of items can be maintained in the short-term store at any given time. Maintenance of memory can be achieved by various control processes including rehearsal, imagery, or use of mnemonics. When information resides in short-term storage for a reasonable period of time, it is automatically transferred to long-term memory. The long-term store is a permanent repository for information.

A number of studies have investigated the actions of marijuana on different stages of memory employing this model. The experimental paradigm usually consists of a free recall task involving lists of words. The dependent variable is the prob-

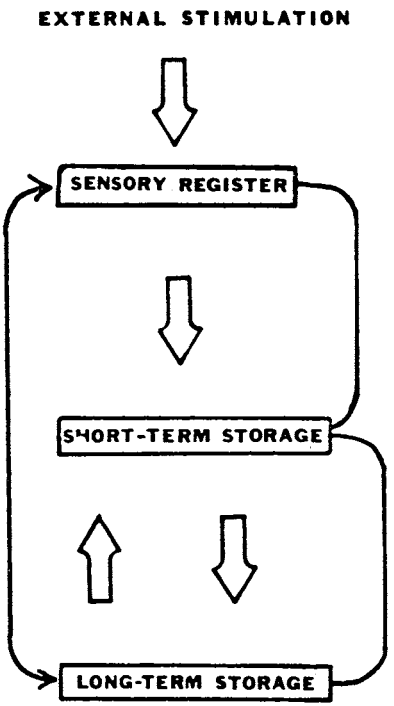

FIGURE 1. Structure of the memory system.

ability of recall or number of words recalled as a function of position of word in a list or its "serial position". A bimodal U-shaped function relating probability of recall to serial position of an item can be plotted. Since the beginning and end of the serial position curve respond differently to a range of experimental variables, the positions are thought to represent output from different storage mechanisms. The probability of recall for both early and late items is higher than for middle items. These two effects are termed, respectively, the primacy and recency effects.

A study by Darley et al. (15) demonstrated the effects of orally administered THC (20 mg) on the different stages of memory proposed by this model. Subjects were presented with 10 lists of 20 words, each of which was followed by an immediate recall test. Immediately following the last list, half the subjects ingested a 20 mg dose of THC, the other half placebo. One hour later, subjects were given a delayed recall and recognition test. Then, the whole sequence of list presentation, immediated, delayed recall, and recognition was repeated. The results indicated that if THC was administered after list presentation but before delayed recall, no effects

were noted which were different from placebo, suggesting that retrieval processes were not influenced (see Figure 2).

When THC was administered prior to list presentation, performance during immediate recall testing was depressed except for those items in the terminal list positions, suggesting that some aspect of long-term storage was disrupted. However, items appeared to enter the sensory register and short-term store equally well (see Figure 2). Since the memory of THC-treated subjects was lower for both delayed recall and recognition, it was suggested that transfer of information from short-term to long-term memory did not take place. One possible reason for the lack of transfer is that subjects did not rehearse incoming information, a process necessary for transfer to occur (16). However, Darley and Tinklenberg (13) found that drugged subjects still displayed impaired recall when amount of rehearsal was fixed in both groups. It was felt

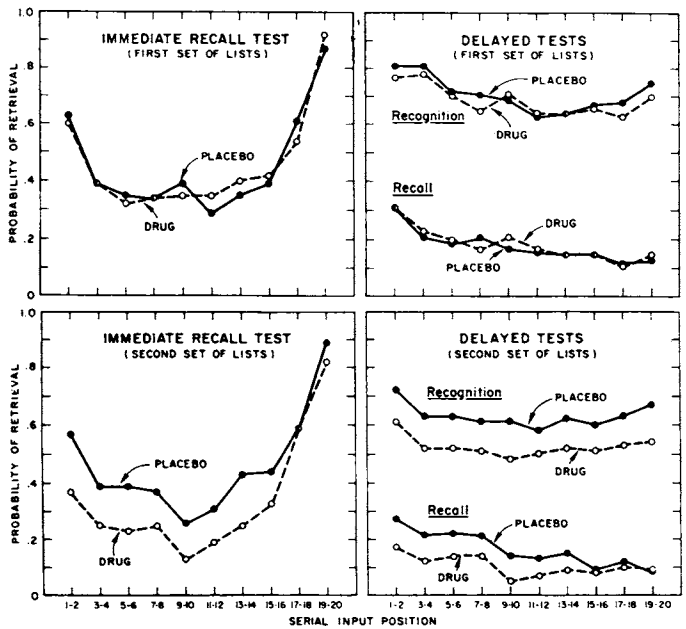

FIGURE 2. The probability of immediate recall (left panel) and delayed recall and recognition (right panel) as a function of the serial input position of items. Separate functions are plotted for drug and placebo groups. The top panel comprises free recall and recognition data when encoding took place prior to drug ingestion, the bottom panel following drug ingestion.

that there was a reduced level of attention to list items probably because of increased competition during the intoxicated state from the subjects' own thoughts, which might have accounted for the inadequate transfer. Another possibility was that items residing in the short-term store were lost more quickly and this resulted in the transfer deficit.

Although the results of the Darley et al. study suggested that storage of information rather than retrieval of information was affected by THC or marijuana intoxication, this view is still open to speculation. The lack of definitiveness has arisen because of methodological and theoretical considerations. These issues are discussed in a later portion of this paper.

Research efforts in our laboratory concerning the effects of marijuana on memory have centered mainly on assessing the actions of the drug on free recall. This paradigm was employed because of its strong theoretical underpinnings and because of the consistency with which marijuana produces reliable effects across studies using this technique. The research to be described took place over a period of 4 years in an effort to define and analyze the effects of marijuana on human memory.

II. METHODS AND RESULTS

A. Smoking Technique and Volunteer Characteristics

Recruitment of volunteers took place mainly in a large university community. Most were upper level undergraduates along with some medical, dental and graduate students; all were males. Other volunteers were also recruited who were not students at the time of study, but all had at least one year of college. All participants were run through ascreening battery including a physical examination, psychiatric interview, MMPI, medical history and laboratory tests including liver function tests, urinalysis and EKG. We found we rejected about 25-30% of our interviewees on the basis of laboratory tests or physical examinations and very few on psychological bases. The medical history included a drug taking inventory in which volunteers were required togivea detailed history of drug use. At the time of the inventory all volunteers were made aware of federal confidentiality requirements and that no names would appear on any hospital records. We found that almost all had some experience with harder drugs especially amphetamines and hallucinogens at some time or another. We attempted to recruit moderate users of marijuana whose use ranged from a few times a week to a few times per month. Most fell into this category because most

were in school. Our choices were also limited to those not currently using other drugs except for tobacco and occasional alcohol use. Very heavy marijuana users were also excluded. The volunteers who were eventually selected were used in repeated studies. All had extensive practice with a variety of cognitive tasks during the course of our research. This eliminated a lot of novelty from the situation and they knew what to expect as soon as they entered the experimental situation.

All of our studies were conducted with smoked marijuana. The cigarettes were obtained from the National Institute on Drug Abuse (NIDA) and varied in THC content. We originally employed a standardized procedure. Volunteers were presented with a single cigarette, instructed to inhale deeply, hold the smoke in their lungs for 10-15 sec. before taking the next puff. Puff inspiration was supervised and timed by an observer. Smoking took between 7 and 10 min. and volunteers were required to smoke as much of the butt as possible. Volunteers were run individually and testing was performed in a quiet comfortable room.

The smoking procedure was altered after an initial study when it was discovered that the standardized procedure was not to the liking of our participants. It was considered to be overly regimented, less enjoyable and somewhat irritating to the throat. Also, participants did not like to smoke alone. Again, it was deemed less enjoyable. All enjoyed the social aspects of smoking. So we opted to smoke in small groups of 3-6 and employed an ad lib smoking procedure. Approximately half the volunteers were assigned to placebo and half to a marijuana condition. Volunteers were instructed to smoke in any manner they desired but again told to consume as much of the cigarette as possible. These changes in procedure proved effective in keeping them motivated, coming to experiments, and made for a more enjoyable experience especially since a number of experimental procedures were considered tedious.

B. Experiments on Memory

In most of the memory studies to be described, three basic measures were usually employed. These included (1) subjective measures of intoxication consisting of ratings of potency of marijuana and the pleasantness of theexperience witheach being rated on a 1-100 point scale, (2) a physiological measure, pulse rate, which was expressed in terms of beats per minute (BPM) and (3) memory measures which usually consisted of number of words correctly recalled on a free recall test and hit and false alarm rates on a recognition memory task. A recognition memory task differs from free recall in that

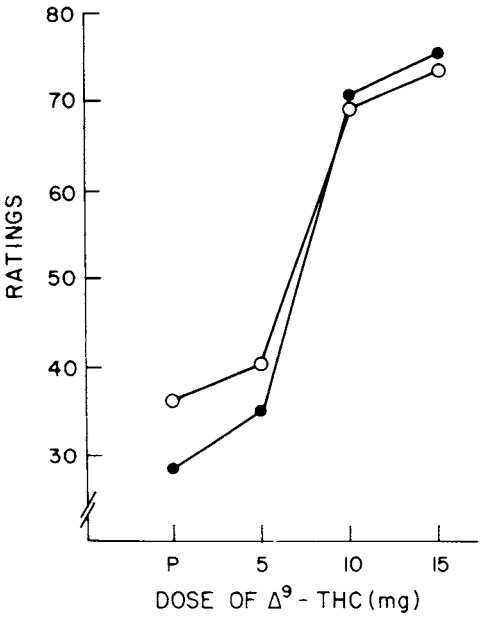

FIGURE 3. Mean potency (open circles) and pleasantness (closed circles) ratings as a function of dosage of THC contained in marijuana. P = placebo.

recognition simply involves the identification of previously presented information which is presented in the context of old material (i.e., a subject is given a list of words, some of which he was presented with and some which are new, or "distractors", and told to pick out the items he remembers having seen on the original recall list). In free recall previously presented information must be reproduced.

In an initial study (17), dose-response data for each of these measures was obtained. The design was performed with each volunteer being run as his own control under 4 drug conditions, 0, 5, 10 and 14 mg THC contained in the marijuana cigarettes. A total of 16 volunteers were run on four different occasions. Although the design was not a complete Latin square, both dosage and word lists were counterbalanced across sessions. In any session, four subjects were allowed to hear 8 different word lists 40 items in length. Four of the word lists were presented at a 2 sec rate and four at a 4 sec rate. Immediate and delayed recall tests (delayed recall occurred 20 minutes after the last list) were given. New word lists were employed in each session. Each of the four volunteers

received one of the above doses of marijuana in any session. Potency, pleasantness ratings and pulse rate were also measured 10-15 minutes following smoking. The results are presented in Figures 3,4,5, and 6. Potency and pleasantness ratings rose with dosage of THC contained inthe marijuana with the biggest jump in ratings occuring at the 10 mg dose. Pulse rate was also elevated following intoxication with both the peak effect of the drug and duration of action varying directly with dosage.

Both immediate and delayed free recall were reduced in a dose-related manner following intoxication with marijuana for both presentation rates. Delayed recognition tests indicated that the distribution of hit and false alarm rates did not vary as a function of dosage. These results indicated that although recall was reduced following intoxication, subjects were familiar enough with previously presented items so that recognition was accurate. The recognition data did not support those of Darley and Tinklenberg (13) or Zeidenberg et al. (18) but paralleled results reported by Dornbush (19).

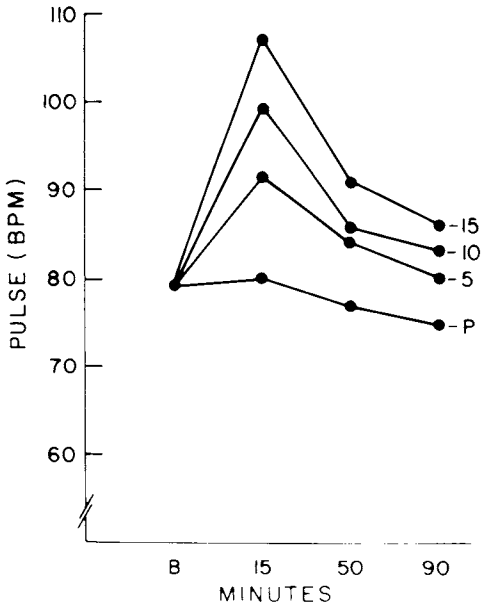

FIGURE 4. Mean pulse rate changes over time as a function of dosage of THC contained in marijuana. P = placebo; B = baseline.

In a number of studies determining the effects of marijuana on recall/recognition, recognition memory has been little influenced whereas recall deficits are universally reported following marijuana intoxication. In those cases where some recognition changes are noted, it is usually the result of an increase in false alarm rates (identifying a newly presented item as being previously seen). Hit rates (identifying an old item correctly) are usually unaffected by marijuana. These false alarm rates rather than reflecting a true memory loss may be considered intrusive type errors. Marijuana has been found in several studies to increase intrusion errors (1). In a free recall task, this usually involves the introduction of intra or extra list word associations during the free recall of words, or the introduction of unrelated extraneous material during prose recall. Thus, some of the memory loss produced by cannabinoids may be a result of increased imagery or thought flow due to the intrusion of irrelevant associations.

Intrusions are often reflected in conversational speech following intoxication. An analysis of speech samples indicates that marijuana produces more free verbalizations and associations, vivid imagery and a decreased awareness of a listener (9). The distortions in speech do not appear to

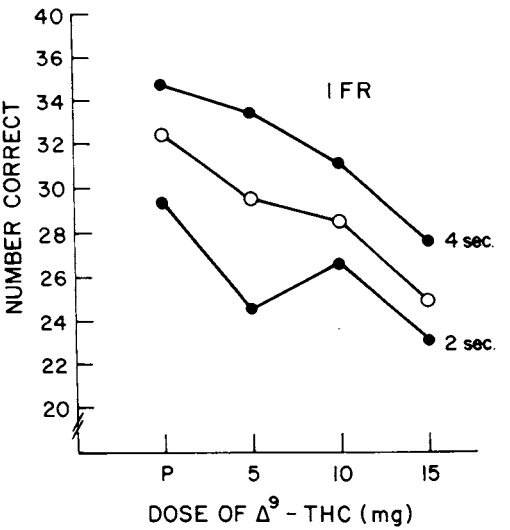

FIGURE 5. Mean number of words correctly recalled on the immediate free recall test (IFR) as a function of dosage of THC contained in marijuana and presentation rate. P = placebo. Open circles represent the combined means.

occur at a syntaxical level. However, the intoxicated subject displays lapses in memory for what was said as well as a tendency to be tangential. Other studies have shown that marijuana intoxication resulted in increased latency of verbal response, produced fewer syllables per phrase and a prolongation of syllables suggesting a deficit in information processing and a decreased ability to focus verbal communication (18,20). Intrusions as a consequence of marijuana intoxication are a robust phenomena when measured.

The next study we initiated was similar in scope to the previous study except that we employed a single marijuana dose (14 mg THC and a between subjects design). Thirty-four volunteers were randomly assigned to either a placebo or marijuana condition and were presented with 20 fifteen item word lists. After each list a recall test was given and following lists 10 and 20 a delayed recall test was administered which consisted of having subjects write down all the words they could remember from the previous lists. One of the lists was repeated at positions 1, 6, 11 and 16, but subjects were not informed of this prior to testing. This latter procedure was originally employed by Hebb (21) in studies of the human memory trace.

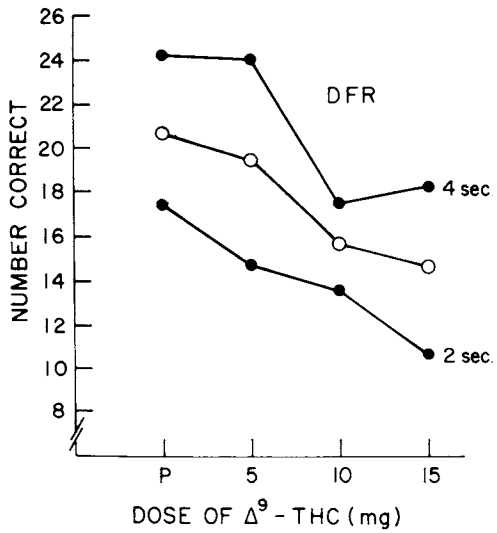

FIGURE 6. Mean number of words correctly recalled on the delayed free recall test (DFR) as a function of dosage of THC contained in marijuana and presentation rate. P = placebo. Open circles represent the combined means.

Repeating the same list allowed us to assess the effect of marijuana on memory consolidation over trials while presentation of the different lists enabled us to determine whether practice on lists within a session would produce an attenuation of the effect of marijuana over time. A recognition memory test was also presented following the second delayed free recall test. The basic results are presented in Figures 7 and 8. In the first graph, it should be noted that marijuana reduced recall on each of the non-repeated lists and practice over 16 lists did not attenuate the effect of the drug. Recall on the repeated lists was also reduced following drug, but the number of items gained on each presentation trial was about the same. This suggests one major effect of the drug is on initial formation of a memory trace, but with repeated presentation the amount of information gained on subsequent trials is similar. The serial position curves which reflect number of words recalled as a function of input serial position are presented in Figure 8. For immediate free recall (IFR), a U-shaped serial position curve was found for both drug and placebo conditions. The marijuana group displayed a deficit in recall at all positions with a greater reduction occurring in the middle portion of all positions with a greater reduction occurring in the middle portion of the list. The serial position results departed slightly from those reported by Abel (16) and Darley et al. (13) in that little effect of marijuana on terminal list items was shown in their

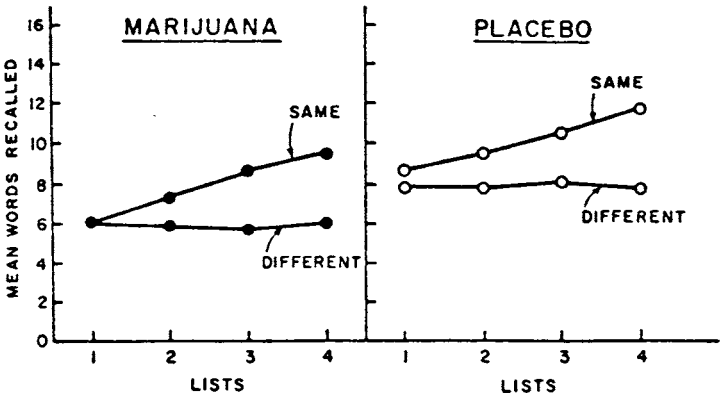

FIGURE 7. Mean number of words recalled over repeated (same) and nonrepeated (different) lists. Recall for 16 nonrepeated lists is presented in blocks of four lists.

studies. On the delayed free recall test (DFR), differences between the two groups still existed although floor effects appeared to occur. A negative recency effect was also noted. This refers to the inferior recall of terminal list items which were recalled well on the immediate free recall test (22).

On the recognition memory test, false alarm rates were moderately elevated while hit rates were relatively equal in both groups. A signal detection analysis applied to this data indicated that neither 'd', an unbiased indicator of memory strength nor B, a measure of the criterion which an individual chooses to make a response, were affected by marijuana. Again, memory trace strength as measured by a recognition memory test was not altered.

Intrusion errors were elevated on both the IFR and DFR tests. On the immediate free recall test, internal intrusions, which consisted of the introduction of words during recall that were contained in lists presented prior to a given IFR, were not significantly elevated in the marijuana condition in comparison to the placebo condition. However, more external intrusions consisting of words not presented in any list occurred following marijuana intoxication.

Long term retention was estimated by determining whether items recalled on the IFR test would also be recalled on the DFR test. Two conditional probability scores were calculated for each subject. The first score consisted of the proportion of items recalled on the DFR test given correct recall on the IFR test (R2/R1). A second probability score consisting of the proportion of items recalled on the DFR test given that recall did <u>not</u> occur on the IFR test (R2/R1). Items on the repeated lists were not included in this analysis. No differences were found between marijuana and placebo groups in the magnitude of these two scores. R2/R1 was higher than R2/N1 for both groups indicating that if an item was recalled on the IFR test it was more likely to be recalled in the DFR than if it was not recalled on the IFR test. However, the R2/R1 probability was quite low, 0.26 for the placebo group and 0.23 for the marijuana group. If a high proportion of items recalled in the IFR test were being retained, the R2/R1 score would be closer to 1. The R2/N1 scores were approximately 0.03 for both groups indicating that if an item was not recalled initially it was very unlikely to occur on the DFR test.

Summarizing our memory results to this point, it was found that (1) recall but not recognition memory was reduced following intoxication with marijuana, (2) the recall deficit was dose related, (3) the incidence of intrusion errors increased following intoxication, and (4) long-term retention levels under drug are equivalent to those found for placebo when levels of initial recall are taken into account.

In another study, (23,24) the effect of marijuana on the recall of prose material was investigated. This was of particular interest since an earlier study suggested that memory for narrative material was particularly sensitive to the effects of marijuana (25). This study also sought to determine the effect of cueing on memory impairments produced by the drug, or more specifically, whether the use of retrieval cues would reverse the recall deficits. Failure to recall an item during intoxication does not necessarily mean that an item is no longer available in memory, but may simply mean that an item is not accessible (26). Finally, the effect of marijuana on possible state dependent learning was measured.

The design was conducted in two phases. On day 1, volunteers (n = 40) smoked a single one gram cigarette containing 0.94% THC or a placebo cigarette. Following smoking each volunteer heard and at the same time read a brief narrative of approximately 200 words. The narrative was presented twice. It contained a total of 24 basic facts and volunteers were instructed to recall as many of the facts as possible. On day 2, half of the volunteers in the drug group were switched to placebo while the other half continued on drug. The placebo group was also split with half volunteers continuing on placebo and half on drug. The drug dosage remained the same on both days. Following treatment on day 2, volunteers performed the following tasks: (1) recalled the story presented on day 1, (2) were presented with 24 questions concerning the story each of which could be answered with a simple phrase from the

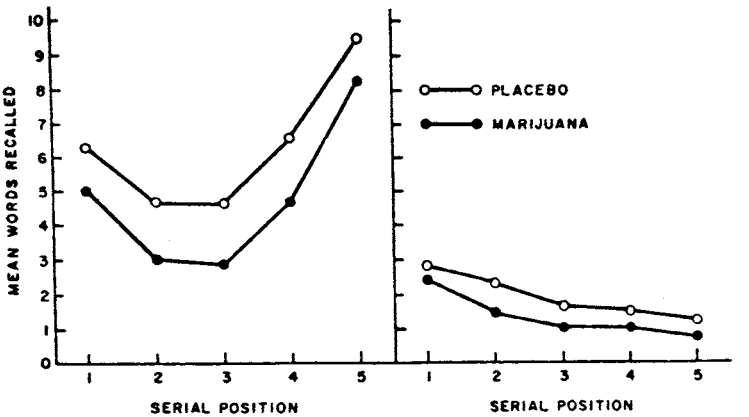

FIGURE 8. Mean number of words recalled for immediate free recall (left panel) and delayed free recall (right panel) as a function of serial input position of items on nonrepeated lists.

story (these questions served as retrieval cues), (3) were presented with a new story which had to be recalled, and (4) presented with 24 questions concerning the new story. The basic dependent variables in this study were number of memory units recalled during free and cued recall on both days, serial position curves, and recall as a function of change in drug state.

The recall results were presented on Table I and in Figures 9 and 10. It can be seen from Table I that on day 1 free recall was significantly reduced following intoxication. Statistically the results were overpowering. Of the 20 subjects in the marijuana group only one did as well as any individual in the placebo group. Serial position curves also developed for free recall on day 1 and these are presented in the left half of Figure 9. A significant primacy effect was found (recall is higher for initially presented items) but the recency effect was not as pronounced as is usually found in the recall of word lists.

On day 2, recall of the old story remained low in groups receiving marijuana on day 1, but retention deficits from day 1 to day 2 were low. Retrieval cues did reverse the recall deficits in all groups but no cued recall advantage was found for the marijuana groups receiving drug on day 1 or day 2. Marijuana was also found to affect retrieval on day 2 of information encoded in either the placebo or drug state on day 1. This was determined by calculating the two conditional probability scores discussed previously. The first consisted of the proportion of correct items recalled on the retention test given correct recall on the immediate test on day 1 (R2/R1). The second consisted of the proportion of items recalled on the retention test given that recall did not occur on day 1 (R2/N1). It was found that R2/R1 probability was

TABLE I. Mean Number of Prose Units Recalled Under Each Recall Condition (+/- S.E.M.)

Group	Day 1	Day 2 (old story)		Day 2 (new story)	
	FR	FR	CR	FR	CR
M-P	6.8 (4.4)	6.3 (3.3)	9.2 (4.0)	12.1 (3.3)	14.8 (3.6)
M-M	7.3 (2.3)	5.8 (2.4)	8.6 (2.0)	9.6 (3.0)	12.8 (3.1)
P-M	11.6 (3.0)	8.5 (3.3)	12.0 (3.1)	9.6 (4.3)	12.9 (4.5)
P-P	12.4 (4.3)	11.5 (3.2)	14.5 (3.6)	15.5 (4.6)	17.5 (4.9)

significantly reduced following intoxication on day 2, meaning that the recall of items on day 2 which were originally recalled on day 1 was significantly reduced by marijuana. The R2/N1 probability was not affected. Thus, retrieval of initially recalled items was reduced by marijuana but not by placebo.

Another interesting finding concerned the effect of marijuana on state dependent learning (see Figure 10). On day 2, recall of the story presented on day 1 was not related to the change in drug state which occurred on day 2. However, recall of the new story was subject to some transfer deficit and this was related to the serial position of items. It appears from Figure 10 that the P-P group displays a significant amount of positive transfer or learning to learn going from recall of story 1 to recall of story 2. However, the M-P group displays a significant reduction in recall in comparison to group P-P, although the two placebo groups should display equivalent recall of the new story.

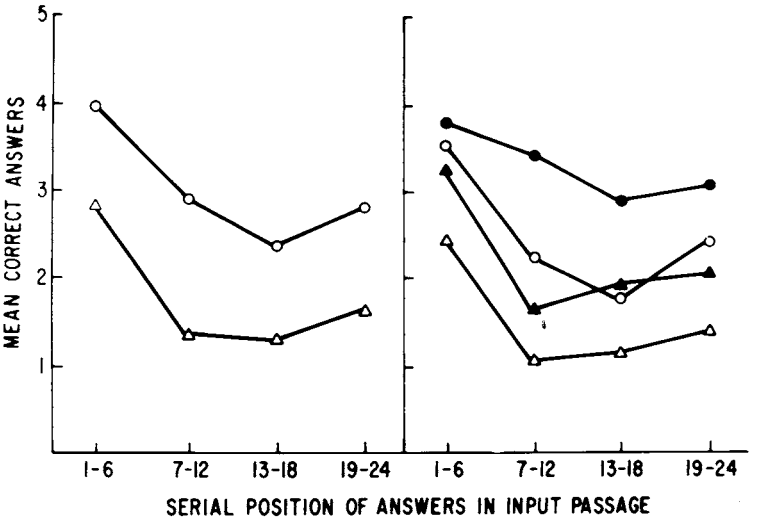

FIGURE 9. Mean number of correct answers as a function of serial position of answers in the input passage (old story). Circles = placebo; triangles = marijuana; closed = cued; open = uncued. The left side of the figure represents immediate free recall by marijuana and placebo groups on day 1. The right side of the figure represents cued and uncued recall of the old story as a function of drug state on day 1.

The mechanism by which marijuana reduces free recall remains elusive. We thought that one way in which the drug altered recall was to interfere with a volunteer's ability to organize the material prior to the recall test. By organization is meant that volunteers recalling word lists tend to develop word groups in a list and as recall trials continue, words are added to these groupings. The question was whether marijuana reduced recall by interfering with subjective organization. The next study addressed this question.

Another purpose of this study was to compare the effect of marijuana on the recall of verbal and pictorial memory. Marijuana has been reported to facilitate both visual and mental imagery (4,27). Since imagery has been posited to be an important component in the encoding of certain types of visual materials especially pictures, it was of interest to test the effect of marijuana on memory for material which might be encoded differently from words.

In this study, 28 volunteers were recruited with each being run as his own drug control in two phases with each being separated by a week. A single one gram cigarette containing 14 mg THC was smoked. Two lists of common objects

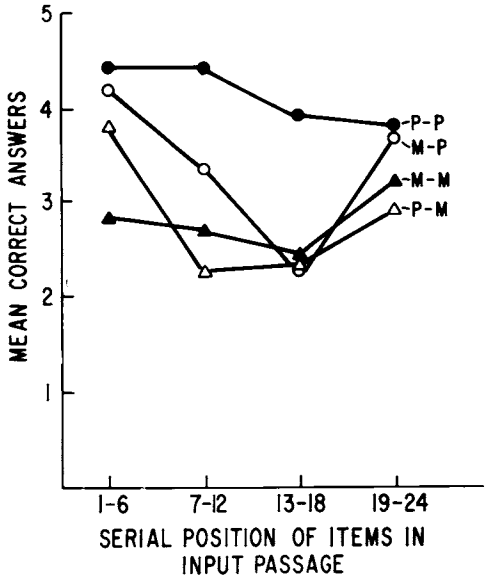

FIGURE 10. Mean number of correct answers as a function of serial position of answers in the input passage (new story) and change in drug state. Cued and uncued recall scores are combined.

were constructed. One list consisted of words typed on slides while the other consisted of simple black line drawings. During the initial session half of the volunteers received placebo and half marijuana. Following smoking half the volunteers were presented with words at a 3 second rate for 5 trials. An immediate free recall test following each trial. Then, the pictures were presented for five trials with a recall test following each trial. The other half of the volunteers experienced pictures first followed by words. One week after the initial session, another session was run with volunteers receiving drug in the first session now receiving placebo and vice versa. Pulse rate measures and potency and pleasantness ratings were also taken.

The results are presented in the Figures 11 and 12. First, there was little overall difference in the recall of pictures and words except on trial 1 where pictures were superior. Marijuana reduced the recall of both, but there was a differential effect of drug on words and pictures as a function of recall trials. Recall of words was initially reduced under drug but as training continued improvement in recall occurred

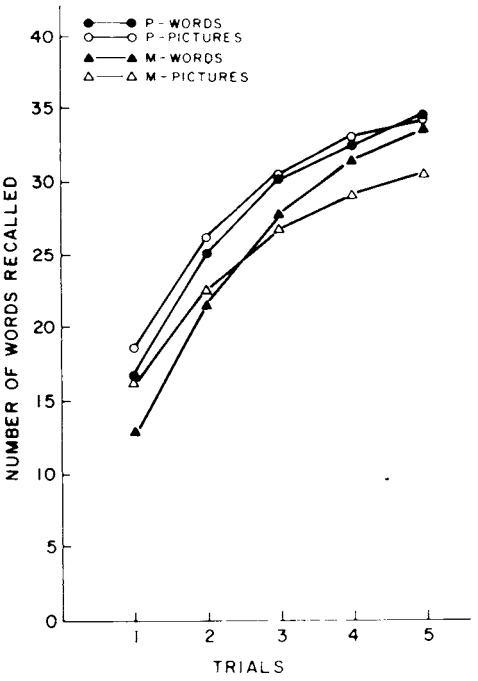

FIGURE 11. Mean number of pictures and words recalled as a function of trials.

so that by trial 5, both treatment conditions were equal. With pictures, however, a divergence in performance took place so that under marijuana performance remained inferior throughout acquisition in comparison to placebo.

In this study, a volunteer's ability to organize material for recall was measured. Previous studies have shown that as recall increases over trials, organization becomes more consistent. Four different measures of subjective organization were calculated. 1) Tulvings (26) - subjective organization measure (SO). This measure is an index of the frequency with which pairs of words recalled on trial N are also recalled together and in the same order on trial N + 1 (an intertrial repetition). 2) SO_2 - Tulvings SO measure was modified so that items recalled together on trial N and N + 1 were considered to be intertrial repetitions regardless of order. 3) SO-OR - this measure considered only those items which were adjacent to each other during list presentation and recall and represents to the extent to which a volunteer reproduced the serial organization of the list as presented for learning. 4) Deviation Ratio - this measure consists of the number of intertrial repetitions minus chance performance divided by the total number of intertrial repetitions possible. This measure corrects for chance occurrence of clustering. The results of these analyses are presented in Figure 12. They indicated (1) as recall improved, all measures of subjective organization increased and were highly correllated with recall, (2) subjective organization did not differ for pictures and words, and (3) although recall was significantly reduced following intoxication, measures of subjective organization were not affected by marijuana. Thus, recall was reduced by the drug but evidently this effect was not mediated by any alteration in organizational capacity as measured by consistency in recall from trial to trial. However, it should be noted that subjective organization measures do not tap into qualitative aspects of organization and that other measures of organization could still be affected by the drug.

One findings of the study which proved to be rather revealing occurred when a factor analysis was applied to the difference scores (placebo-marijuana) for pulse rate, memory and subjective ratings. Three different factors emerged from this analysis, Factor1, labeled pulse rate accounted for 40.02% of the variance of the factor matrix while two other factors, memory and subjective ratings accounted for 34.70% and 25.28% of the variance, respectively. This means that the effects of marijuana on measures of pulse rate, memory, and subjective ratings are statistically independent of each other. If changes in subjective ratings, pulse rate and memory were related to each other, they would load on the same factor. These results pose some difficulty for attempting to

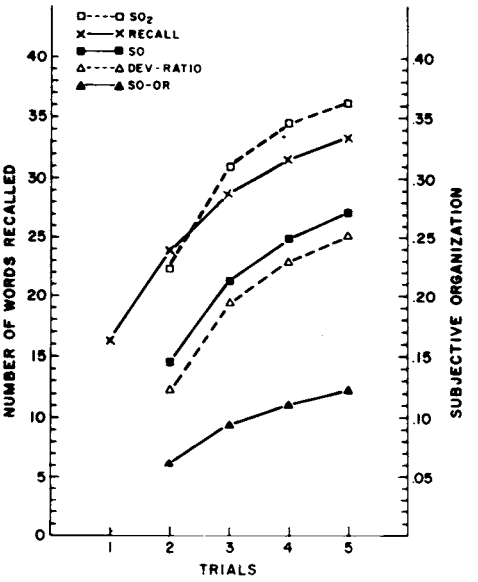

FIGURE 12. Mean number of items recalled (collapsed across recall and treatment conditions) and measures of subjective organization as a function of trials. See text for explanation of various measures of subjective organization.

predict on the basis of either physiological changes or subjective estimates of how "high" an individual describes himself as being, changes in recall ability. Whether this is generalizable to other types of drug-induced behavioral change remains to be seen.

While the studies conducted to date in our laboratory indicate that a persistent effect of marijuana is to reduce the free recall of variety of stimulus materials, the mechanism by which the drug produces its effect on storage and retrieval processes is not as yet apparent. The finding that recall rather than recognition is reduced may suggest that while the intoxicated subject's ability to retrieve information from memory is impaired, material appears to be encoded well enough for recognition to occur. However, recall may be more difficult for the intoxicated individual than recognition, not because these tasks involve different types of memory processing, but because of the way in which these two type of tasks are set up. Recall involves a large or open ended set of alternatives while recognition usually involves a binary choice. Since marijuana has been reported to distort

temporal judgment, recall may be difficult for the intoxicated individual because of an inability to restrict his search set to temporally recent items. This may account in part for the increase in intrusion errors found under the drug. Recognition automatically restricts this search set. Thus, the intoxicated subject may be deficient in retrieving unique items of information on the basis of contextual cues which would normally permit a differentiation between items searched for and competing irrelevant items. However, with continued practice, intoxicated subjects do encode and retrieve repeatedly presented material although retrieval of unique information from episodic memory remains impaired.

It has been assumed in the literature on marijuana and memory, based mainly on the serial position curve results, that storage rather than retrieval is influenced by the drug. However, theoretical and methodological difficulties suggest that the hypothesis is open to speculation.

First, the results of our studies suggest that recognition memory is little affected by cannabinoids. Two factor memory theory postulates that recognition memory is a measure of storage while recall is a measure of both storage and retrieval (28). According to Kintsch (29), recognition involves "checking the familiarity or response strength of an item, but recall involves an additional process of search and retrieval." Whereas deficits in recall and recognition could be interpreted as being due to a storage problem, a deficit in recall but not recognition could be interpreted as a retrieval failure. Tulving and Pearlstone (30) have drawn a distinction between what is in memory and what can be retrieved -- i.e., availability vs. accessibility. Recall is an insensitive indicator of what is available in memory (31), whereas a recognition test can often detect the availability of previously learned information when recall (accessibility) fails to do so (32). Viewed in the above context, a plausible interpretation of cannabinoid disruption of recall but not recognition is that cannabinoids disrupt accessibility of information acquired during cannabinoid intoxication.

On a methodological level, one possible reason retrieval deficits have not been shown is that a retrieval deficit is measured usually in terms of a delayed recall test. Ona delayed recall test, the amount of information remaining in the memory is reduced substantially in comparison to an immediate free recall test. Therefore, the amount of information available for recall is lessened and recall levels are generally very low -- "the floor effect" (see the right panel in Figure 8). The assessment of drug-induced recall deficits is difficult when the baseline level of recall is very low. On the other hand, the Miller et al. (23) prose study indicated that recall of prose was reduced 24 hours following intoxica-

tion. In that particular study, recall level was 90% of baseline prior to the delayed recall test.

III. MARIJUANA AND MEMORY - AN INTEGRATIVE ASSESSMENT

Recently, a method for analyzing impaired memory, termed the "restricted reminding technique", has been developed (33). This method provides for the assessment and simultaneous analysis of storage, retention and retrieval during a verbal memory task. In the restricted reminding task, an individual must recall information spontaneously without presentation. The usual free recall paradigm analysis of memory is confounded because of interference produced by the immediate recall of items which were recently presented. According to Bushke and Fuld (33), an item can be considered to be in long-term memory only when it is recalled without repeated presentation. Recall is assessed independently of confounding due to continued presentation of stimuli on each trial.

The data to be described are strikingly similar (in pattern of effects on memory but not magnitude) to those found with patients experiencing amnesia due to herpes simplex encephalitis (34), Korsakoff syndrome (35,36), or Alzheimer's disease (37). Herpes simplex and Alzheimer's disease are thought to affect the limbic system via disruption of muscarinic limbic pathways (34, 38,39), while Korsakoff syndrome may be due to lesions in the hippocampus, mamilliary bodies and/or dorsalmedial nucleus of the thalamus (40).

The task employed was a free recall task in which words in a list are presented individually until recall of the word occurs once. Following initial recall, words are not presented again so that eventually recall trials occur without any further presentation of items. All words are recalled on each trial. Buschke has argued that storage and retrieval of items in memory cannot be evaluated when all items are presented before every recall attempt because immediate recall of items does not demonstrate that an item resides in long-term memory (33). The dependent variables in this paradigm are long-term storage, which consists of the number of items encoded on a given trial, while retrieval consists of the number of items recalled on each trial that are considered to be in long-term storage.

Miller et al.(41), employing the restricted reminding technique, ran 16 male volunteers in a crossover design with each receiving both smoked marijuana (10.5 mg THC) or placebo in successive sessions separated by one week. In each session, a different 30-item word list was employed with words being presented at a 3-second rate. Recall testing occurred

for 12 trials. The results of this study are presented in Figures 13 and 14. Only the most salient features will be emphasized.

In Fig. 13, it can be seen that the number of items eventually encoded under marijuana and placebo were essentially the same although it took more recall trials for the same number of items to be encoded under drug. However, retrieval of items from long-term storage was significantly impaired under drug and this was due to the fact that more memory lapses or recall failures took place following intoxication. That is, intoxicated subjects displayed an inconsistency in recall. For example, under marijuana an encoded word might be retrieved on a given trial following which a 3 to 4 trial lapse in recall would occur before the word would be recalled again. In Fig. 14, it can be seen that intrusion error rates were significantly elevated in the drug condition in comparison to placebo. Intrusions consisted of the number of different extra list words which were emitted. What intoxicated subjects tended to do was commit an intrusion error, encode the word and repeat it on the majority of recall trials or if they committed one error, they might drop that word and substitute another. Thus, extraneous words from long-term memory were introduced which may have interfered with recall.

These data suggest that the mechanism of impaired recall in the intoxicated individual may be in his capacity to integrate material in some meaningful fashion for recall to occur. Buschke suggests that when items of information are consis-

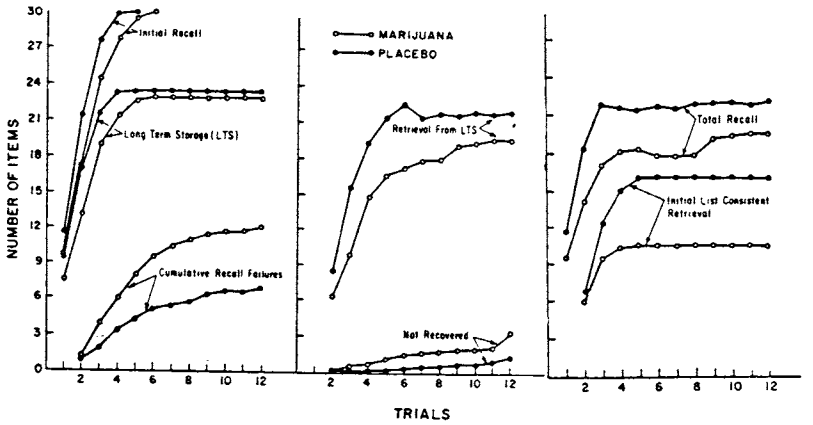

FIGURE 13. Analysis of free recall by restricted reminding for placebo and marijuana.

tently retrieved in memory they are integrated with the retrieval of other items in the list. Thus, items in memory are encoded within a given context. Information about a target item and its relationship to other words in the semantic system provides a basis of organization. That is, the learner imposes structure on information already in long-term memory. Marijuana may affect an individual's capacity to make use of information in his semantic memory to employ efficient recall strategies. Thus, the depth to which information is processed following cannabis intoxication may be an important mechanism by which recall is impaired. Intrusion errors may be seen as being secondary to organizing and integrating deficiencies since information from long-term memory which is the basis for semantic organization intrudes on the recall process.

These data are consistent with the interpretation of Adam (42) for the effect of anesthetic gases on memory processes. These agents may make memory traces temporarily inaccessible, a form of anterograde amnesia. Impaired retrieval of information occurs because encoding processes are not consistent with efficient retrieval.

In conclusion, the deleterious effect of cannabis on free recall memory are a reliable and consistent finding. The pattern of memory deficits are similar to those found in neurally compromised patients with memory disorders thought to be mediated by cholinergic limbic dysfunction. These memory deficiencies are characterized by: 1) lapses in recall, 2) inconsistent retrieval of information, and 3) memory intrusions.

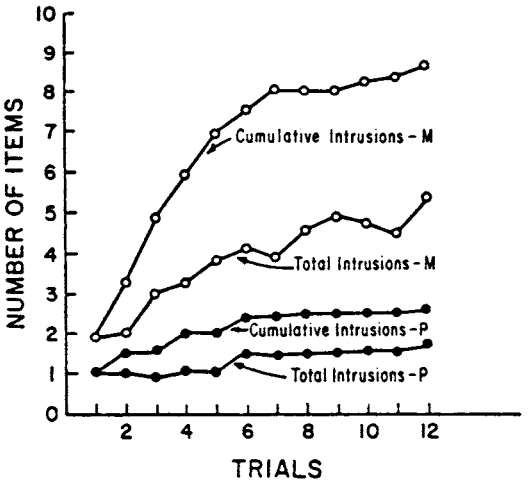

FIGURE 14. Total number of intrusion errors and cumulative intrusion errors for placebo and marijuana conditions.

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