Psychopharmacology (1993) 110:219–228

Psychopharmacology

Effects of chronic marijuana use on human cognition

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Received April 23, 1991 / Final version June 15, 1992

Abstract. Impairments of human cognition and learning following chronic marijuana use are of serious concern, but have not been clearly demonstrated. To determine whether such impairments occurred, this study compared performance of adult marijuana users and non-users ($N = 144$ and $N = 72$, respectively) matched on intellectual functioning before the onset of drug use, i.e., on scores from standardized tests administered during the fourth grade of grammar school (Iowa Tests of Basic Skills). Subjects were given the twelfth grade versions of these tests (Iowa Tests of Educational Development) and other, computerized cognitive tests in successive test sessions. "Heavy" marijuana use (defined by use seven or more times weekly) was associated with deficits in mathematical skills and verbal expression in the Iowa Tests of Educational Development and selective impairments in memory retrieval processes in Buschke's Test. The retrieval impairments were restricted to words that were easy to visualize. Impairments depended on the frequency of chronic marijuana use, i.e., "light" and "intermediate" marijuana use (defined by use one to four and five to six times weekly, respectively) were not associated with deficits. Intermediate use was associated with superior performance in one condition ("fuzzy" concepts) of a Concept Formation test.

Key words: Marijuana – Chronic drug use – Cognition – Iowa Tests – Memory – Learning – Imagery – Abstraction

Adverse effects of chronic marijuana use on cognition are of serious concern, since marijuana is the most widely used illicit drug. Clinical impressions of many observers suggest that chronic marijuana use impairs cognitive function (National Institute on Drug Abuse 1982), but experimental studies of this issue have frequently been methodologically weak, ambiguous in outcome, or both. Of about a dozen studies conducted in the United States and Canada and a similar number elsewhere, a minority of studies have reported some cognitive impairments from chronic marijuana use (Soueif 1971, 1975, 1976; Entin and Goldzung 1973; Page et al. 1988; Schwartz et al. 1989), while the majority have found that impairments were absent or negligible (Bowman and Pihl 1973; Weckowicz and Janssen 1973; Rubin and Comitas 1975; Carlin and Trupin 1977). Both studies reporting impairments from marijuana use and those reporting no change suffer from a serious methodological shortcoming: a crucial requirement for evaluating performance of chronic marijuana users is comparison with a group of non-using subjects who are matched on relevant demographic characteristics and, most importantly, on some measure of intellectual functioning obtained before the onset of drug use. Yet only one past study matched the marijuana users and non-users on intellectual functioning before the onset of drug use and this study found no impairments in the users, possibly due to the minimal inclusion criteria stipulated for marijuana use, i.e., use at least twice a month for one year (Culver and King 1974).

We examined cognitive effects of chronic marijuana use by comparing the performance of marijuana users and non-users who were matched on intellectual functioning before the onset of drug use, i.e., on their scores during the fourth grade of grammar school on the Iowa Tests of Basic Skills (Hieronymus et al. 1982), standardized tests that have been administered to almost all grammar school children in Iowa for several decades. The twelfth grade versions of the Iowa Tests and other, computerized cognitive tests were administered to determine if chronic marijuana users were impaired and, if so, whether impairments depended on the frequency of their marijuana use.

Materials and methods

Screening

Volunteers were recruited through advertisements. During preliminary screening visits, informed consents were obtained after the nature and possible consequences of the study were explained. Volunteers then provided a urine sample for drug screening and information about their medical history, demographic character-

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istics, and use of marijuana and other drugs. They classified their average weekly frequency of using marijuana or other cannabis products as "not at all", "less than once", one to four times ("light" users), five to six times ("intermediate" users), or seven or more times ("heavy" users) and indicated the duration of their use at this frequency. In addition, they completed a questionnaire (derived with modifications from Johnston et al. 1981) concerning the number of occasions on which they had used various drugs in their lifetime, during the last 12 months, and during the last 30 days. Portions of the Diagnostic Interview Schedule (DIS) Version III-A (Robins and Helzer 1985), a structured psychiatric screening interview for use by research staff, were administered.

So that their scores on the Iowa Tests could be retrieved, subjects were restricted to adults (age range, 18–42 years) who had attended the fourth grade of grammar school in Iowa. Marijuana users were restricted to individuals who had used marijuana at least weekly for the last 2 years or more. Non-users were restricted to individuals who had not used marijuana more than twice in their lives.

So that test performance would not be influenced by acute effects of drugs, subjects had to promise to abstain from alcohol on the day of each subsequent session and after 6 p.m. on the preceding evening; and to abstain from marijuana and other drugs for 24 h before each subsequent session. Subjects were questioned about compliance with these promises before each session.

Matching of the groups

Early in the study, excessive numbers of female non-users were tested before it became clear that the marijuana users were mostly men. For this reason, the most efficient method to subsequently obtain matched groups of marijuana users ($N = 144$) and non-users ($N = 72$) was to select only a fraction of the female non-users ($N = 15$ of 63) for analysis. Using propensity (P) score techniques (Rosenbaum and Rubin 1985), a subset of female non-users was chosen with the goal of matching users and non-users on age, education, and the five subtest scores of the fourth grade Iowa Tests. Rather than attempting to match on these seven characteristics individually, they were transformed into a single variable, the P score, which was calculated from a logistic multiple regression in which the seven characteristics were independent variables and the user/non-user dichotomy was the dependent variable. The P score represented the estimated conditional probability that a subject was a marijuana user, based solely on these seven characteristics. Selection of the subset of female non-users was based on these P scores, with the hope that matching users and non-users on P scores would produce matching on all seven characteristics. Selections were subjected to an additional constraint to avoid disrupting planned counterbalancing, i.e., female non-users were chosen such that equal numbers of non-users (male and female combined) came from each of eight test conditions differing in the orders and alternate forms of the tests. Selections were made without reference to individuals' scores on the twelfth grade Iowa Tests and computerized tests.

Testing

In one session, which lasted about 3 h, four tests from the Iowa Tests of Educational Development (level II) were administered along with the Short Test of Educational Ability (level 5), a test of general academic ability standardized with the Iowa Tests (Science Research Associates 1981). The tests were administered according to procedures specified in the test manuals (Science Research Associates 1974; Iowa Testing Programs 1987a). All were pencil-and-paper tests in multiple-choice format. In a second session, which lasted about 2.5 h, cognitive and psychomotor tests were administered by an Apple II Plus computer system. Subjects responded orally or by pressing buttons.

Two different orders of the tests within each session were used for different subjects, as were two alternate forms of each test except the Short Test of Educational Ability and two computerized psychomotor assessments. The alternate forms were each given to half the subjects within each user group, except that this counterbalancing was off by one subject among the heavy users.

Details of the functions assessed by the tests given in the first session were as follows:

1. *Ability to do quantitative thinking.* Solving mathematical word problems and answering questions assessing understanding of basic mathematical concepts.
2. *Correctness and appropriateness of expression.* Recognizing misspelled words and deciding which of alternative versions of a specified portion of text best expressed the idea, made the statement grammatically correct or most precise, or was correctly punctuated or capitalized.
3. *Vocabulary.* Picking which of several words was the closest synonym for a specified word.
4. *Ability to interpret literary materials.* Answering questions assessing comprehension of a text.
5. *Short test of educational ability.* Answering four types of questions involving vocabulary, arithmetic computation, letter series (recognizing patterns in series of letters), and symbol manipulation (recognizing symbolic quantitative relations).

Details of the tests given in the second session were as follows:

1. *Buschke's test.* A list of 16 nouns, half "high imagery" words that were easy to visualize (e.g., "bouquet") and the remainder "low imagery" words that were difficult to visualize (e.g., "replacement") (Paivio et al. 1968), was presented on the monitor at a rate of 3 s per word. The subject tried to recall as many words as possible. Seven learning and test trials were given consecutively. The subject tried to recall the whole list on each test trial, but on learning trials after the first, he or she was reminded only of the words missed on the immediately preceding test trial. This procedure allowed scoring several aspects of memory in addition to total recall (Buschke 1973): in essence, recall of a word without an immediately preceding reminder (i.e., recall on two successive trials) indicated that the word had entered (and presumably remained in) long-term storage. Recall of the word before this occurrence was attributed to short-term retrieval; after it, to long-term retrieval. Long-term retrieval was designated "consistent" when the word was never subsequently omitted.

2. *Concept formation.* The stimuli for this test of abstraction were schematic faces (Reed 1972; Martin and Caramazza 1980) with seven varying features, each having three possible values, e.g., eyes facing left, right, or center. The subject studied a card picturing five members of each of two "families" for 1 min. Then 20 new faces, half from each family, were shown at a 10 s rate on the monitor. The subject indicated to which family each belonged. The card remained present only while the subject classified the first ten new faces. The entire procedure was then repeated with a different card defining the families. One card portrayed a "clear" concept: each family had two distinguishing features, e.g., one had large beards and round noses; the other, smiling faces and no hair. The other card portrayed a "fuzzy" concept (Rosch and Mervis 1975) following a similar pattern, but with some exceptions, e.g., in one family, 80% had small beards; in the other, 80% had frowning faces. Every member of one family bore more resemblance to its family than the other, but the families had no uniformly distinguishing features.

3. *Text learning.* The subject read a paragraph from a magazine article on the monitor at his or her own pace and then recalled as much as possible in three minutes. The subject then reread the paragraph and recalled it again. Following this, the entire procedure was repeated with a different paragraph. The subject's recall was tape-recorded for later scoring of the propositions recalled (Miller and Kintsch 1980).

4. *Free and constrained associations.* For each of 100 words presented at a 10 s rate on the monitor, the subject gave a single word as an association. For 50 words, the subject was cued to provide a "free association", i.e., any kind of association that came to mind; for 10 words each, the subject was to provide one of five types of "constrained associations", i.e., his or her response was to relate to the stimulus in a specified way, cued by the words "another",

"category", "example", "opposite", or "property". The words were drawn from those used in a pilot study (Block et al. 1989) involving introductory psychology students, so that for each response in the present study, the number of pilot subjects giving that response ("dominance") could be scored, e.g., eight pilot subjects gave "sandal" in response to "shoe".

5. *Paired associate learning.* A list of 30 pairs of words was presented at a 3 s rate on the monitor. Then the initial word from each pair was presented at a 5 s rate and the subject tried to respond with the second word from each pair. These learning and test trials were then repeated. Following this, the entire procedure was repeated with a different list of pairs of words. The pairs represented eight types of free and constrained associations (e.g., "carpet-laughter", "horse-tail").

6. *Psychomotor tests*: (a) Critical flicker fusion: the subject viewed two light-emitting diodes. One was flickering and the other remained constantly illuminated. During the 2 s period of flickering or the following 3 s interstimulus interval, the subject indicated which diode was flickering. The computer determined the flicker fusion threshold by increasing or decreasing the rate of flickering depending on the correctness of the subject's responses. The task was repeated twice, with two threshold estimates produced each time. (b) Discriminant reaction time: the subject viewed a series of digits flashed for 100 ms each and pressed a button as fast as possible following each "4". The interstimulus interval, initially 400 ms, was increased or decreased by the computer depending on the correctness of the subject's responses to determine the most rapid rate at which accuracy could be maintained (Berchou and Block 1983). Digits were presented for 50 s. The task was repeated four times.

Statistical analyses

To check that matching of users and non-users was adequate, the scores on the fourth grade Iowa Tests, age, and education were submitted to analyses of variance involving user group (heavy, intermediate, light, and non-users) and sex as between-subjects factors. Categorical demographic characteristics of users and non-users such as work status were compared by chi-square tests. Fisher's exact tests were done to compare pairs of user groups with decreasing intensities of marijuana use (heavy versus intermediate, intermediate versus light, and light versus non-users) on lifetime prevalence of trying the drugs other than marijuana included on the drug questionnaire.

To assess effects of chronic marijuana use while controlling for any residual differences in fourth grade Iowa Test scores, the twelfth grade Iowa Tests and computerized tests were submitted to analyses of covariance in which the log-transformed P score LOG((1-P) /P) served as a covariate. These analyses included between-subjects factors representing user group, sex, the orders in which the tests were given, and the two alternate forms of tests. From one to three additional within-subjects factors representing test manipulations appropriate for the individual computerized tests were included in the analyses, as follows: in Buschke's Test, seven trials and two imagery levels of the words (high versus low imagery words); in Concept Formation, two types of concepts (clear versus fuzzy concepts) and two test conditions (example card present versus absent); in Text Learning, two paragraphs and two trials per paragraph; in Free and Constrained Associations, two classes of associations (free versus constrained associations) and five types of associative relations (e.g., "example", "property"); in Paired Associate Learning, two lists, two trials per list, and eight types of associative relations between pairs of words (e.g., "example", "property"); in the Psychomotor Tests, two trials and two threshold estimates per trial for Critical Flicker Fusion and four trials for Discriminant Reaction Time. Tests for within-subjects effects and interactions involving these effects were adjusted using the Greenhouse-Geisser procedure (Winer 1971, p 523).

Adjusted means were computed and Dunnett's tests were done to compare performance of the heavy, intermediate, and light marijuana users with the non-user control group. The significance level was $P < 0.05$, adjusted for the number of comparisons made. When an interaction of user group with another factor was detected in an analysis of covariance, similar follow-up Dunnett's tests were done separately for each level of the factor interacting with user group.

Results

Marijuana use

Among the marijuana users, the reported frequency of using marijuana was seven or more times weekly for 52 users, five to six times weekly for 28 users, and one to four times weekly for 64 users. These heavy, intermediate, and light users reported using marijuana at their indicated frequencies for means ($\pm$ SEs) of 6.2 ± 0.6, 5.8 ± 0.7, and 5.5 ± 0.5 years, respectively. They started in similar grades: 9.5, 10.1, and 10.5, respectively. In the last 30 days, the median frequency of marijuana use for the heavy users was 20–39 times and the upper quartile (75th percentile) was 40–99 times. For each of the other groups, the median and upper quartile were identical, being 20–39, 10–19, and zero times for the intermediate, light, and non-users, respectively. Twelve percent of the heavy users reported using marijuana 100 or more times in the last 30 days.

Lifetime use of drugs other than marijuana

Apart from marijuana, alcohol was the only drug included on the drug questionnaire that all heavy marijuana users had tried at least once in their life. The heavy marijuana users' lifetime prevalences of having tried the other drugs showed the following ordering: cocaine, 90%; psychedelics other than lysergic acid diethylamide (LSD), 88%; LSD, 79%; amphetamines, 79%; narcotics other than heroin, 54%; tranquilizers, 52%; amyl or butyl nitrites, 42%; barbiturates, 31%; methaqualone (Quaalude®), 27%; phencyclidine, 12%; and heroin, 12%. The heavy and intermediate users did not differ in lifetime prevalence of having tried any of the drugs. The intermediate and light users differed only for narcotics other than heroin, which had been tried by more intermediate than light users, $P < 0.01$. In contrast, the light marijuana users had tried every drug more often than the non-users, Ps < 0.05–0.001, except for alcohol and heroin, which had been tried by almost all and almost none in both groups, respectively. The non-users had almost no experience with drugs other than alcohol.

Among the heavy marijuana users, the only drugs other than marijuana that any subjects had used 100 or more times in their life were: alcohol, 88% of subjects; cocaine, 12%; amphetamines, 12%; psychedelics other than LSD, 6%; LSD, 6%; and tranquilizers, 4%. Histories of dependence (Robins and Helzer 1985) on drugs other than marijuana were obtained from one heavy marijuana user (2%, amphetamines) and one intermediate marijuana user (4%, heroin and other opiates).

Use of drugs other than marijuana in the last 30 days

In the last 30 days, the median frequency of alcohol use for the heavy marijuana users was 6–9 times and the upper

quartile was 10–19 times. Corresponding frequencies for the other marijuana user groups were 10–19 and 20-39 times for both the intermediate and light users; and 3–5 and 6–9 times for the non-users. More of the light marijuana users had used alcohol at least once in the last 30 days than the non-users of marijuana, $P < 0.001$, but the light and intermediate users did not differ in this respect, nor did the intermediate and heavy users. The same pattern held when frequencies of alcohol use in the last 30 days were analyzed, the only difference being that between light and non-users, $P < 0.001$.

Eight heavy marijuana users (15%) and one intermediate user (4%) reported using illicit drugs other than marijuana more than twice in the last 30 days—two LSD, one psychedelics other than LSD, three amphetamines, two cocaine, and one both cocaine and narcotics other than heroin. In the urine screening, one heavy user (2%) showed codeine, and four heavy users (8%) and three intermediate users (11%) showed cocaine. One of the latter intermediate users was the individual with a history of dependence on heroin and other opiates mentioned above.

Comparability of the groups

Figure 1(A) shows the subjects' fourth grade Iowa Test scores. Before the onset of drug use, the groups were well matched, i.e., they showed no significant differences on test scores. Table 1 gives information about demographic characteristics of the subjects. The groups showed no significant differences with respect to age, education, work status, annual income, Hollingshead Occupational Scale Score (Hollingshead 1949), sex, or race.

Performance in test sessions

Figure 1(B) shows performance in the twelfth grade Iowa Tests. Two of these tests, those dealing with mathematics (Ability to Do Quantitative Thinking) and verbal expression (Correctness and Appropriateness of Expression), showed impairments in heavy users relative to non-users (significant Dunnett's tests, $P < 0.05$). Heavy users were unimpaired on the other three tests, i.e., Vocabulary, Ability to Interpret Literary Materials, and Short Test of Educational Ability.

One computerized test, Buschke's Test, showed interactions indicating impairments in heavy users. In this test, which compared memory for high and low imagery words, heavy users showed impairment relative to non-users in long-term retrieval for high but not low imagery words (Fig. 2, center; significant user group × imagery interaction, $F_{3,183} = 3.1$, $P < 0.05$, and Dunnett's test). Consistent long-term retrieval, which measured the numbers of words reliably recalled from trial to trial without omission, showed a similar pattern, i.e., impairment in heavy users relative to non-users for high but not low imagery words (Fig. 2, left; significant user group × imagery interaction, $F_{3,183} = 3.4$, $P < 0.05$, and Dunnett's test). The data for short-term retrieval suggested a slight, opposite, compensatory tendency, but were equivocal

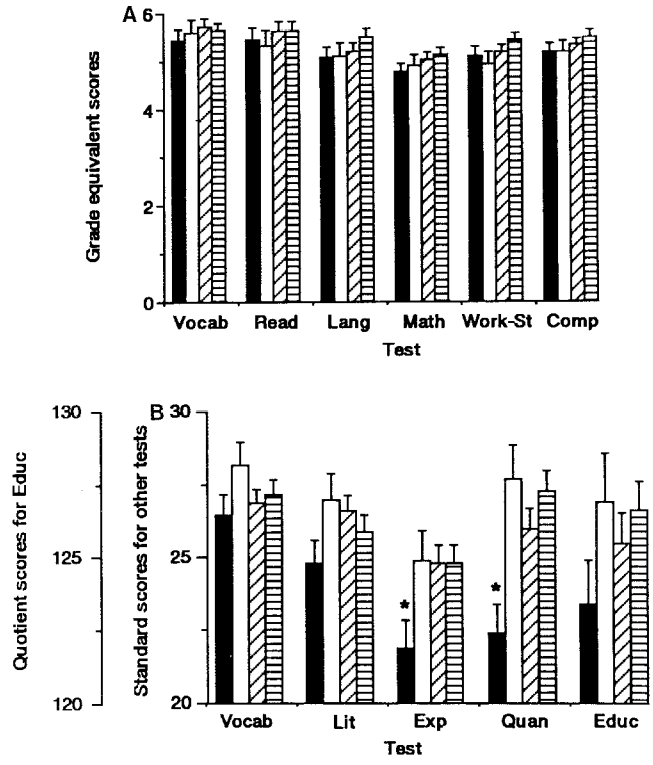

Fig. 1. A, B Scores on the Iowa Tests and the Short Test of Educational Ability. The bars indicate standard errors. **A** Performance of subjects on the Iowa Tests of Basic Skills during the fourth grade of grammar school. The scores are grade equivalents, i.e., *4* = fourth grade, *5* = fifth grade, etc. *Vocab* = Vocabulary, *Read* = Reading Comprehension, *Lang* = Language Skills, *Math* = Mathematics Skills, *Work-St* = Work-Study Skills, *Comp* = Composite Score. **B** Performance of subjects on the twelfth grade versions of the Iowa Tests of Educational Development (right ordinate axis, standard scores) and the Short Test of Educational Ability (left ordinate axis, quotient scores). *Vocab* = Vocabulary, *Lit* = Ability to Interpret Literary Materials, *Exp* = Correctness and Appropriateness of Expression, *Quan* = Ability to Do Quantitative Thinking, *Educ* = Short Test of Educational Ability. The fourth grade tests most comparable to Vocab, Lit, Exp, and Quan are Vocabulary, Reading Comprehension, Language Skills, and Mathematics Skills, respectively. Significance is indicated as follows: * heavy marijuana users differ from non-users by Dunnett's test, $P < 0.05$. (■) Heavy users, $n = 52$; (□) intermediate users, $n = 28$; (▨) light users, $n = 64$, except that $n = 63$ for fourth grade Language Skills, Work-Study Skills, and Composite Score; (▤) non-users, $n = 72$

(Fig. 2, right); although the user group × imagery interaction was significant, $F_{3,183} = 3.2$, $P < 0.05$, non-users did not differ from heavy users (or from intermediate or light users).

Subjects went through seven successive trials, and the impairment of heavy users relative to non-users in consistent long-term retrieval tended to be greater on initial trials than subsequent trials; this user group × trial interaction was significant by the usual F test, $F_{18,1098} = 1.7$, $P < 0.05$, but only marginal after adjustment using the Greenhouse-Geisser procedure, $P < 0.10$. Table 2 shows the adjusted mean scores in Buschke's Test by user group.

One other computerized test, the one that assessed abstraction (Concept Formation), showed an interaction

Table 1. Demographic characteristics of user groups

	User group			
	Heavy ($n = 52$) [a]	Intermediate ($n = 28$) [a]	Light ($n = 64$) [a]	Non ($n = 72$) [a]
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
Age (years)	23.4 ± 0.7	23.4 ± 0.7	23.2 ± 0.6	23.3 ± 0.7
Education (years)	14.0 ± 0.2	14.6 ± 0.2	14.2 ± 0.2	14.3 ± 0.2
	Frequency distributions (%)			
Work status				
Employed (non-students)	29	14	22	18
Employed (students)	37	61	41	50
Unemployed[b]	35	25	38	32
Annual income				
Under $15, 000	87	89	88	76
$15, 000 to $35, 000	13	11	13	24
Hollingshead Occupational Scale Score[c]				
1, 2, or 3	41	52	29	33
4 or 5	35	33	34	41
6, 7, 8, or 9	24	14	37	26
Sex				
Men	81	79	75	79
Women	19	21	25	21
Race				
White	100	100	97	97
Non-white	0	0	3	3

Note: Percentages may not add to 100 within each user group due to rounding error

[a] One light marijuana user did not provide information on education. For the Hollingshead Occupational Scale Score, the unemployed and eight employed students who did not indicate their occupations were excluded

[b] All the unemployed subjects were students except for four heavy users, two light users, and one non-user

[c] Occupations were scored on a nine-point scale where lower scores indicated less status (Hollingshead 1949)

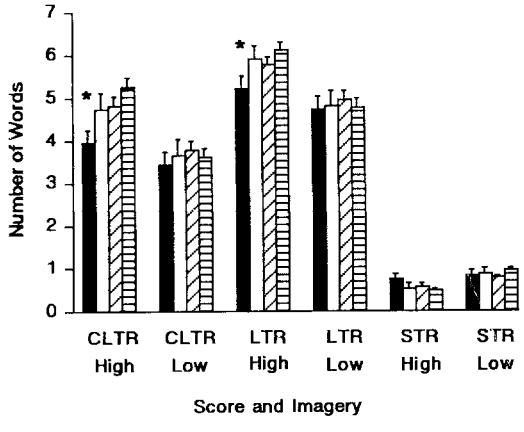

Fig. 2. Significant interactions of user group and imagery for consistent long-term retrieval (*CLTR*), long-term retrieval (*LTR*), and short-term retrieval (*STR*) scores in Buschke's Test. The scores, which are averaged over trials, are based on eight high imagery words (*High*) and eight low imagery words (*Low*). The bars indicate standard errors. The performance of the heavy users is primarily responsible for the interactions for the consistent long-term retrieval score and the long-term retrieval score. Significance is indicated as follows: * heavy marijuana users differ from non-users by Dunnett's test, $P < 0.05$. (■) Heavy users, $n = 52$; (□) intermediate users, $n = 28$; (▨) light users, $n = 64$; (⊟) non-users, $n = 72$

of a within-test manipulation with marijuana use. Intermediate users achieved a higher percentage of correct responses than non-users on fuzzy concepts, for which the families of faces had no uniformly distinguishing features, whereas non-users did not differ from heavy, intermediate, or light users on clear concepts, for which there were uniformly distinguishing features (significant user group × concept interaction, $F_{3,183} = 2.9$, $P < 0.05$, and Dunnett's test). The presence versus absence of the original card picturing faces of five members of each family, which was removed after half the testing on new faces had been completed, did not influence the effect of marijuana use. Table 2 shows the adjusted mean percentages of correct responses by user group for fuzzy and clear concepts. Apart from this one interaction attributable mainly to intermediate users, intermediate and light users never differed from non-users on any test.

No effects of marijuana use were shown by the other computerized tests, i.e., the tests assessing learning of paragraphs of text (Text Learning) and associations between pairs of words (Paired Associate Learning), the test in which the subject gave various types of associations to words (Free and Constrained Associations), and the psychomotor tests (Critical Flicker Fusion and Discrim-

Table 2. Adjusted scores on computerized tests by user group (mean ± SE)

Test and dependent variable	User group			
	Heavy	Intermediate	Light	Non
Buschke's Test				
Number of words[a]				
Total recall	5.8 ± 0.2	6.1 ± 0.2	6.0 ± 0.1	6.2 ± 0.1
Long-term retrieval	5.0 ± 0.2	5.4 ± 0.3	5.4 ± 0.2	5.5 ± 0.2
Long-term storage	5.5 ± 0.2	5.8 ± 0.3	5.8 ± 0.2	5.8 ± 0.2
Short-term retrieval	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1
Consistent long-term retrieval	3.7 ± 0.3	4.2 ± 0.3	4.3 ± 0.2	4.4 ± 0.2
Concept formation				
Percentage correct				
Fuzzy concepts	64.5 ± 2.6	77.0 ± 3.0	72.4 ± 1.8	68.5 ± 1.8
Clear concepts	83.6 ± 2.4	85.3 ± 2.8	84.0 ± 1.6	86.4 ± 1.7
Text Learning				
Number of propositions recalled	12.4 ± 0.8	11.9 ± 0.9	13.4 ± 0.5	13.4 ± 0.5
Paired Associate Learning				
Percentage correct	74.7 ± 2.1	76.7 ± 2.5	79.3 ± 1.5	76.6 ± 1.5
Free and Constrained Associations				
Dominance of responses	43.3 ± 1.2	44.9 ± 1.4	46.5 ± 0.8	46.7 ± 0.8
Psychomotor Tests				
Critical flicker fusion threshold (Hz)	37.0 ± 0.6	35.8 ± 0.8	36.7 ± 0.4	35.9 ± 0.4
Discriminant reaction time (s/100)	37.9 ± 0.4	37.4 ± 0.5	37.8 ± 0.3	38.2 ± 0.3

[a] The scores, which are averaged over trials and types of imagery, are based on eight words

inant Reaction Time). The adjusted mean scores by user group are given in Table 2.

Controlling for use of other drugs

Lifetime use of other drugs. Between-subjects comparisons indicated overall impairments of the heavy users relative to the non-users in two tests, the twelfth grade Iowa Tests dealing with mathematics and verbal expression. Attributing these impairments to marijuana might not be justified, however, as the heavy users also had more experience with other drugs. This possibility was examined by repeating the analyses of these tests with 12 additional covariates representing lifetime frequencies of use of alcohol, cocaine, amphetamines, LSD, psychedelics other than LSD, heroin, narcotics other than heroin, tranquilizers, amyl or butyl nitrites, barbiturates, methaqualone, and phencyclidine. The possible values for each covariate were the frequencies of use (0, 1–2, 3–39, 40–99, and 100 or more times). Four intermediate frequency categories on the drug questionnaire (3–5, 6–9, 10–19, and 20–39 times) were pooled into a single category for these analyses, because adjusted means were otherwise non-estimable (Freund and Little 1985, pp 176–180). The impairments of the heavy users relative to the non-users in these tests remained significant while controlling for lifetime use of other drugs (significant Dunnett's tests, Ps < 0.05).

Use of other illicit drugs in the last 30 days. Some of the marijuana users had used illicit drugs other than marijuana in the last 30 days. This might have affected their performance, making it unjustifiable to attribute the impairments of the heavy users in the tests dealing with mathematics and verbal expression to marijuana. This possibility was examined by repeating the analyses described in the previous section after excluding all subjects who had used any illicit drug other than marijuana more than twice in the last 30 days or who showed any in their urine. The impairments of the heavy users relative to the non-users in these tests remained significant while simultaneously controlling for use of other illicit drugs in the past 30 days and lifetime drug use (significant Dunnett's tests, Ps < 0.05).

History of alcohol dependence. Attributing the impairments of the heavy users in the tests dealing with mathematics and verbal expression to marijuana might not be justified, as 88% of the heavy users, compared to only 49% of the non-users, had used alcohol 100 or more times in their lifetime, raising concerns about the possible influence of alcohol on performance in these tests. No quantitative measure of heavy, long-term alcohol use was available, since frequencies of lifetime alcohol use greater than 100 times were not quantified in further detail. However, the influence of alcohol could be examined by comparing performance of the heavy marijuana users in the study, none of whom had a history of alcohol dependence, with performance of nine additional heavy marijuana users having a history of alcohol dependence who were tested. These analyses indicated that performance in the tests dealing with mathematics and verbal expression did not differ for heavy marijuana users with and without a history of alcohol dependence, Ps > 0.05.

Discussion

Overall impairments associated with heavy marijuana use

On the twelfth grade Iowa Tests assessing mathematics and verbal expression, heavy users showed overall impairments relative to non-users who were matched on in-

tellectual functioning before the onset of drug use. No overall impairments were detected in other capabilities including reading comprehension, vocabulary, psychomotor performance, concept formation, associative processes, and memory. The impairments in performance observed in the heavy users could indicate that use of marijuana seven or more times weekly for extended periods produces impairments in CNS function that outlast the drug's acute effects. However, possible criticisms of our methodology and alternative explanations of the findings must be considered.

Reliability, validity, and intercorrelations of tests. Parrott (1991a, b, c) has recently criticized much human psychopharmacology research for limited use of complex tests of higher cognitive function and reliance on performance tests with little or no evidence of validity and undocumented reliability, making the interpretation of findings difficult and ambiguous. Interpretation of the impairments of the heavy users in mathematics and verbal expression is not susceptible to these criticisms. The twelfth grade Iowa Tests, as well as the fourth grade Iowa Tests and the Short Test of Educational Ability, assess higher cognitive functions and their developers have accumulated extensive evidence of validity and reliability (Science Research Associates 1972, 1981; Hieronymus et al. 1982; Iowa Testing Programs 1987b).

The value of matching groups of marijuana users and non-users on fourth grade Iowa Test scores might also be questioned. Would these scores really predict intellectual capabilities many years later? This question was examined using data of the non-users, and an affirmative answer was indicated by substantial Pearson product-moment correlations of the twelfth grade Iowa Tests with corresponding fourth grade Iowa Tests, $Ps < 0.001$ for all: Vocabulary with Vocabulary, $r = 0.59$; Correctness and Appropriateness of Expression with Language Skills, $r = 0.56$; Ability to Interpret Literary Materials with Reading Comprehension, $r = 0.52$; Ability to Do Quantitative Thinking with Mathematics Skills, $r = 0.44$.

Long-lasting acute effects of marijuana. So that acute effects of marijuana smoking would not influence test performance, subjects had to abstain for 24 h before testing. We considered this period of abstention sufficient to avoid acute effects of marijuana smoking on performance and did not ask subjects to abstain longer because we thought that doing so would decrease recruitment, compliance, and truthfulness among the heavy users. However, the possibility that the impairments observed in the heavy users were due to long-lasting acute effects must be considered.

There have been a few reports of such effects. In a preliminary, open study of simulated flying without placebo controls, Yesavage et al. (1985) found that pilots performed poorer 24 h after smoking marijuana than before smoking. In the first of two subsequent studies with placebo controls, they failed to replicate these results (Leirer et al. 1989). In the second, they reported a significant impairment 24 h after smoking marijuana based on analyses utilizing multiple, one-tailed t tests (Leirer et al. 1991). With more conventional, two-tailed analyses, the impairment would not have been significant for more than 4 h after smoking. This duration of effect would be somewhat more consistent with another group's findings regarding marijuana's effect on simulated flying (Janowsky et al. 1976).

Three other reports of long-lasting acute effects of marijuana have been even more equivocal. In two studies, Chait and colleagues (Chait et al. 1985; Chait 1990) found only weak evidence that test performance or subjective state in the morning was affected by marijuana smoking on the preceding day, and there were discrepancies between studies in the effects that were observed. Heishman et al. (1990) found small residual effects on the day after marijuana smoking on certain tests in some of the three individuals they studied, but provided no statistical analyses of the results.

Other studies have looked for long-lasting acute effects of marijuana (Barnett et al. 1985) or cannabis resin (L. Rafaelsen et al. 1973; O.J. Rafaelsen et al. 1973), but found none. These negative findings, combined with the equivocal findings in studies reporting long-lasting acute effects of marijuana, make it seem unlikely that such effects could account for the impairments that we observed in the present study among the heavy users.

Use of other drugs. Were the overall impairments of the heavy users relative to the non-users in mathematics and verbal expression artifacts resulting from differences between groups in use of other drugs? The fact that the heavy and intermediate users did not differ in lifetime prevalence of trying any drugs other than marijuana, together with the fact that the heavy users showed impairments and the intermediate users did not, argue against this interpretation. Additional evidence that the impairments associated with heavy marijuana use were not artifacts derives from the findings that: (1) They remained significant while controlling for use of other illicit drugs in the past 30 days and lifetime frequencies of use of other drugs. (2) Heavy marijuana users with a history of alcohol dependence were not impaired on these tests relative to heavy marijuana users without such a history. Thus, heavy marijuana use seems to be associated with impairments even while controlling for use of other drugs. (The results do not indicate if marijuana use is associated with larger or smaller impairments than use of other illicit drugs, as we sought subjects who had limited experience with such drugs.)

Did heavy marijuana use impair CNS function? If heavy marijuana use was associated with cognitive impairments even after controlling for use of other drugs, and if these impairments were not due to long-lasting acute effects of marijuana, can we conclude that heavy use produces impairments in CNS function that outlast marijuana's acute effects? We cannot confidently draw this conclusion; our findings are susceptible to other, plausible interpretations. Since our study was not a controlled experiment in which individuals were assigned randomly to groups of users and non-users, the linkage between heavy use and impairments was correlational rather than causal. Though the groups of users and non-users were balanced on intellectual functioning before onset of drug use, educa-

tion, income, occupational status, and other demographic characteristics, they may still have differed in characteristics of their educational, socioeconomic, medical, or other history—predictors or concomitants of marijuana use or non-use—that we did not assess. Such hypothetical differences, rather than heavy marijuana use, may have produced the observed impairments.

For example, we did not ask subjects how often they attended school while under the influence of marijuana's acute effects. It is possible that the heavy users did so frequently and, consequently, learned less than the non-users, which could help explain their impairments relative to the non-users on the tests of mathematics and verbal expression. Overall impairments of the heavy users were clearer in these tests, which assessed utilization of pre-experimentally acquired information, than in tests involving learning of new information. Since these two types of tests were not matched in content, this difference cannot be interpreted with certainty; but one intriguing interpretation is that effects of chronic marijuana use may be most observable in measures reflecting an individual's cumulative learning history over a period of years.

Qualitative changes in performance associated with chronic marijuana use

In two tests, chronic marijuana use was associated with changes in performance in certain testing conditions, but not with overall impairments.

Effects on memory. Heavy use was associated with selective impairments in memory retrieval processes in Buschke's Test, which were restricted to high imagery words. Consistent long-term retrieval, which was particularly sensitive to marijuana's effects, is presumed to reflect development of organized, elaborated semantic representations mediating consistent recall. Heavy marijuana use was associated with a decrease in the size of the normal imagery effect in retrieval, i.e., the superiority in performance for high imagery relative to low imagery words. The decreased imagery effect could also reflect decreased or slowed development of elaborated representations among the heavy users. This effect is similar to the acute effects we observed with the benzodiazepines (Block and Berchou 1984). It is interesting in view of the subjectively reported increase in imagery following marijuana smoking (Tart 1971), together with our inability in past work to detect any corresponding objective changes in performance following marijuana smoking (Block and Wittenborn 1984). The absence of specific measures of retrieval in the other memory tests may have rendered them less sensitive than Buschke's Test to marijuana's effects. The more structured materials used in these other tests, i.e., text and pairs of words, may also have contributed to their lesser sensitivity.

Concept formation. In the Concept Formation test, intermediate users showed a selective improvement relative to non-users in the percentage of correct responses for fuzzy concepts. Research with fuzzy categories has suggested that people may often develop "prototypes" for each category representing the most typical examples and then classify new instances by evaluating their similarity to these prototypes (Reed 1972). Perhaps intermediate users relied more on such a global, "gestalt", perceptually mediated approach than on a focussed, logical, systematic search for distinguishing features of categories. This seems compatible with subjectively reported shifts in thought processes following marijuana smoking (Tart 1971). However, heavy users did not show the same pattern as intermediate users, tending instead to have the lowest percentage correct of any group. The non-monotonic relation between frequency of chronic marijuana use and percentage correct for fuzzy concepts mandates caution in interpreting this relation, which should be considered tentative until future verification.

Relation to other studies of chronic cannabis use

The most important findings of our study, the overall impairments in mathematics and verbal expression associated with heavy use, cannot be compared to past studies of chronic use of marijuana (or, more broadly, cannabis), since none have included achievement tests among their assessments. There have been reports of impairments on intelligence tests or subtests among chronic cannabis users in Greece and India (Stefanis et al 1976; Wig and Varma 1977), but many other studies have found no impairments on intelligence tests (e.g., Culver and King 1974; Carlin and Trupin 1977). The impairments that we observed in mathematics and verbal expression should not be interpreted as evidence of impaired intelligence.

Our finding that heavy marijuana use was associated with selective impairments in memory retrieval processes in Buschke's Test accords with a previous report of retrieval impairment in Buschke's Test among chronic cannabis users in Costa Rica (Page et al. 1988). Retrieval impairment in Buschke's Test has also been observed as an acute effect of marijuana smoking (Miller et al. 1978; Block et al. 1992). Impairments among chronic marijuana users in the United States and Canada have been detected primarily by memory tests. Three groups have reported memory impairment in different tests (Entin and Goldzung 1973; Gianutsos and Litwack 1976; Schwartz et al. 1989), whereas only single, isolated reports have suggested impairment of other cognitive functions (Grant et al. 1973; Weckowicz et al. 1977). Outside the United States and Canada, memory impairments among chronic cannabis users have also been reported in several studies, as have impairments of psychomotor performance and time perception (Soueif 1971, 1975, 1976; Wig and Varma 1977; Mendhiratta et al. 1978; Page et al. 1988; Varma et al. 1988). The relative sensitivities of memory and other capabilities to impairments associated with chronic cannabis use are not yet clear.

None of these studies reporting impairments associated with chronic cannabis use matched users and non-users on measures of intellectual function obtained before the onset of drug use, as we did. Thus, none controlled for the possibility that individuals who became chronic cannabis users might have been poorer in intellectual function initially. To keep these numerous reports of cognitive

impairments in perspective, moreover, it should be noted that: (1) they are a minority, since most studies of effects of chronic cannabis use on cognition, memory, or psychomotor performance have not found impairments, e.g., Bowman and Pihl (1973); (2) even in studies reporting some impairment, cumulatively, many more tests have been found unimpaired than impaired; (3) sometimes, specific tests showing impairment in one study have not shown impairment in others; (4) studies have varied widely in methodological soundness; (5) the limited education and frequent illiteracy of subjects in many studies outside the United States and Canada—and the special populations involved in some studies, i.e., prisoners (Soueif 1971, 1975, 1976) —raise questions about generalizability of the results to typical, educated individuals in industrial societies and appropriateness of the standardized psychological tests used, many of which were developed for such individuals.

Suggestions for further research

More work is needed to evaluate alternative interpretations of the cognitive impairments associated with heavy marijuana use: does such use produce impairments in CNS function that outlast marijuana's acute effects? Or is the association more indirect, e.g., do heavy users learn less in school, or forget more of what they learn, so that measures reflecting an individual's cumulative learning history over years are particularly sensitive? The latter explanation accords well with the overall impairments in mathematics and verbal expression that we observed, but less so with the selective impairments in memory retrieval processes. Conceivably, the retrieval impairments could be associated with changes in CNS function that outlast marijuana's acute effects and could contribute to the impairments in mathematics and verbal expression.

Future research should attempt to correlate changes in cognitive function associated with heavy marijuana use with possible changes in brain function. Since most of our subjects were young adults, more work is also needed to determine whether heavy use is associated with lower educational attainment and occupational performance later in life. Another high priority should be contrasting cognitive impairments associated with heavy use of marijuana and other drugs, individually and in combination, by studying subjects who differ in the drugs that they use most frequently. In all these endeavors, selecting groups of subjects who are matched on intellectual functioning before the onset of drug use will allow more confidence in the conclusions.

Acknowledgements. Thanks are due to K. Braverman, S. Farnham, S. Siegel, W. Walters, and R. Farinpour for assisting with the conduct of the research; D. A. Frisbie for providing fourth grade scores on the Iowa Tests and advice about these tests; G. Woodworth for statistical advice; and J. V. Hinrichs, R. Noyes, Jr., R. A. Forsyth, A. N. Hieronymus, J. J. Boren, and J. W. Spencer for advice concerning the research. This research was supported in part by grant 5 R01 DA03988 from the National Institute on Drug Abuse to R. I. Block and grant RR59 from the General Clinical Research Centers Program, Division of Research Resources, National Institutes of Health to the Clinical Research Center, University of Iowa.

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