Cognitive Correlates of Long-term Cannabis Use in Costa Rican Men

Cognitive Correlates of Long-term Cannabis Use in Costa Rican Men

Jack M. Fletcher, PhD; J. Bryan Page, PhD; David J. Francis, PhD; Kimberly Copeland, MA; Mary J. Naus, PhD; Chester M. Davis, PhD; Robin Morris, PhD; Dina Krauskopf, MA; Paul Satz, PhD

Background: Cognitive correlates of long-term cannabis use have been elusive. We tested the hypothesis that long-term cannabis use is associated with deficits in short-term memory, working memory, and attention in a literate, westernized culture (Costa Rica) in which the effects of cannabis use can be isolated.

Methods: Two cohorts of long-term cannabis users and nonusers were studied. Within each cohort, users and nonusers were comparable in age and socioeconomic status. Polydrug users and users who tested positive for the use of cannabis at the time of cognitive assessment after a 72-hour abstention period were excluded. The older cohort (whose age was ~45 years) had consumed cannabis for an average of 34 years, and comprised 17 users and 30 nonusers, who had been recruited in San José, Costa Rica, and had been observed since 1973. The younger cohort (whose age was ~28 years) had consumed cannabis for an average of 8 years, and comprised 37 users and 49 nonusers. Short-term memory, working memory, and attentional skills were measured in each subject.

Results: Older long-term users performed worse than older nonusers on 2 short-term memory tests involving learning lists of words. In addition, older long-term users performed worse than older nonusers on selective and divided attention tasks associated with working memory. No notable differences were apparent between younger users and nonusers.

Conclusion: Long-term cannabis use was associated with disruption of short-term memory, working memory, and attentional skills in older long-term cannabis users.

Arch Gen Psychiatry. 1996;53:1051-1057

From the Departments of Pediatrics (Dr Fletcher) and Psychiatry and Behavioral Sciences (Drs Fletcher and Davis), University of Texas–Houston Medical School; Department of Psychiatry, University of Miami (Fla) School of Medicine (Dr Page); Department of Psychology, University of Houston (Drs Francis and Naus and Ms Copeland); Department of Psychology, Georgia State University, Atlanta (Dr Morris); Department of Psychology, University of Costa Rica, San José (Dr Krauskopf); and the Neuropsychiatric Institute, University of California, Los Angeles (Dr Satz).

WITH THE exception of anecdotal reports and clinical observations,[1,2] the adverse effects of long-term cannabis use on cognitive skills have not been clearly demonstrated. Most studies of nonintoxicated North American users have found polydrug use and low levels of chronicity among these users.[3-6] These studies have generated null results, with the exception of 1 study that found deficiencies in memory retrieval processes.[7] The subjects in this study also used drugs other than cannabis and were not assayed for abstinence. Although cross-cultural studies of Egyptian[8] and Indian[9,10] cannabis users have been interpreted as showing adverse cognitive effects, sampling and other methodological problems limit these studies.[11,12] Cross-cultural studies that were designed better yielded mostly null results for cognitive correlates of long-term cannabis use.[13,14]

The most recent cross-cultural study was conducted in San José, Costa Rica, from 1985 to 1986.[15] Anthropological and neuropsychological studies of 27 long-term, frequent cannabis users and 30 nonusers were conducted; these studies were derived from a case-control study of 41 users and 41 nonusers, who were evaluated in San José from 1973 to 1975.[14] These subjects were originally matched for age, occupational status, education, marital status, and consumption of alcohol and tobacco. No consistent differences were found between users and nonusers on sociocultural variables other than those associated with a lifestyle involving cannabis use (eg, occasional imprisonment and solitary living arrangements). The biomedical and neuropsychological tests yielded uniformly null results. However,

See Subjects and Methods on next page

SUBJECTS AND METHODS

SUBJECTS

Data collection took place in San José during a 15-month period beginning in January 1990. The cohort originally studied in 1973 was the product of a street recruitment approach, where field-workers observed potential subjects in the everyday context of their lives in the neighborhoods of San José. Observing and informally interviewing people in their natural habitats led to the identification of networks of social relations among people in the neighborhoods. This allowed identification of cannabis users through other users of cannabis and identification of nonusers from the same neighborhoods.[14]

A sample of younger, shorter-term users and comparable nonusers was recruited in 1990. To remain consistent with the accrual of the older cohort, no new subjects with a history or evidence of psychiatric or neurological disorders or a history of habitual use of drugs other than cannabis and alcohol were recruited. Specifically, no subjects who had ever abused inhalants or who reported use of cocaine or other drugs (eg, lysergic acid diethylamide, heroin, and other opiates) more than twice in their lives were included. Any subject with a history of treatment for alcohol abuse, evidence of alcoholic dementia, or a history of delirium tremens was eliminated.

The study was approved by the University of Texas–Houston Health Science Center Committee for the Protection of Human Subjects and by the Costa Rican government. Separate consents were obtained for the cognitive tests, the drug assays, and the interviews. Subjects were informed that their self-reports would be discussed with family members and friends.

Older Cohort

The 41 users and 41 nonusers in the 1973 cohort were selected from a base sample of 84 long-term users and 156 nonusers. Long-term use was originally defined as the use of cannabis 3 times weekly for at least 10 years. The user and nonuser groups were matched in 1973 for age, sex (all men), occupation, education, marital status, and consumption of alcohol and tobacco.[14] In 1973, the user group had consumed a daily average of 9.6 cannabis cigarettes (the fundamental unit of consumption and sale) for an average of 16.9 years, representing an average exposure to approximately 80 mg of Δ^9-tetrahydrocannabinol daily.[14] For this follow-up, we were able to identify 69 of these subjects, 56 of whom were tested for the study. Thirteen of the original 82 subjects were unavailable for follow-up since 1985.[15] Sixty of the 69 remaining potential subjects were available. Of the 56 subjects who gave consent, 6 users did not abstain for the required 72 hours and 3 users tested positive for cocaine use, leaving 30 nonusers and 17 abstaining users. None of these subjects reported even experimental use of other drugs, which was verified through the social networks. To evaluate possible selective attrition from the original sample in 1973, participants and nonparticipants were compared; they did not differ significantly ($P>.10$) in medical status, consumption of alcohol and tobacco, chronicity of cannabis use, and sociocultural variables.[15]

At this follow-up, the user group had been consuming cannabis for an average of 34 years (a median of 5.2 marijuana cigarettes per day, 2-7 times weekly). Use had decreased from the levels in the 1973 and 1985 studies because of the greater potency and the increased cost of cannabis. Two users had ceased consumption for more than 8 years prior to this study. To avoid biasing the comparisons in favor of rejecting the null hypothesis, these 2 subjects were included in the user group for the cognitive studies but were excluded from the computations of use. For this follow-up, the subjects remained healthy; we observed no evidence of interim major medical problems (eg, head injuries) that might influence the results. The comparability of alcohol abuse was of particular importance. Alcohol abuse was defined by subject acknowledgement of any 1 of the following 3 conditions: (1) drinking 4 to 5 drinks daily, (2) experiencing "blackouts," or (3) drinking in the morning. Approximately two thirds of the older cohort abused alcohol according to these criteria, but the percentages were comparable between groups (**Table**). None of the subjects identified themselves as alcohol abusers nor did any subject or informant report treatment for alcohol abuse.

Younger Cohort

The younger cohort (n=123) was identified and screened by the same methods used to identify the older cohort for this study. To be identified as a user, the subject had to consume cannabis at least twice weekly for 5 years but for no longer than 12 years. Of the 123 cases, a final sample of 49 nonusers and 37 abstaining users was established. Twenty-five users tested positive for use of cannabis at the time of testing, and 12 subjects tested positive for cocaine use; all of these subjects were excluded from the study. The remaining 37 abstaining users had consumed marijuana for an average of approximately 8 years (a median of 3.8 cigarettes per day, 2-7 times weekly).

As the data in the Table indicate, users and nonusers in both cohorts were comparable for age and intellectual level[17] ($P>.10$), but younger users smoked more tobacco ($F[1,183]=15.86$, $P<.001$), were more likely to abuse alcohol ($\chi^2[1,N=85]=17.80$, $P<.001$), and had lower levels of education ($\chi^2[2,N=85]=7.44$, $P<.03$) vs younger nonusers. No comparisons involving the older cohort achieved statistical significance ($P>.10$).

The frequency of polydrug use in the younger cohort, as noted by the number of subjects who tested positive for cocaine use, reflects clear differences between the younger and older cohorts. Initiation to cannabis generally occurred during adolescence for both cohorts but tended to be earlier for the older users ($\approx$15 years) than for the younger users ($\approx$16.5 years). Drug use has greater social consequences (eg, harsher legal penalties and peer rejection) in current Costa Rican society vs the society of 1973, which is reflected by these cohort differences. The lack of comparability between the younger groups leads to the expectation that the younger users will perform worse than the younger nonusers on the cognitive tasks but for reasons other than the use of cannabis. This difference would tend to mitigate against the hypothesized pattern of results, in which differences were predicted only between the older groups.

DRUG ASSAYS

Each subject provided a urine sample to be assayed for use of cannabis and other drugs 72 hours prior to and at the time of the cognitive assessment. Subjects were instructed to abstain from the use of cannabis and other drugs for the interval between the 2 samples. Subjects were informed that reimbursement for participation was contingent on no evidence of drug use on the second urine sample, which encouraged abstention.

The initial assay was a toxicological screen (EMIT system, Syva, San José, Calif); Δ^9-tetrahydrocannabinol and other drugs, including cocaine, opiates, amphetamine, and benzodiazepines, were identified by this screen. In addition, a semiquantitative immunoassay of Δ^9-tetrahydrocannabinol and its metabolites was performed based on the enzyme-multiplied immunoassay technique. Finally, Δ^9-tetrahydrocannabinol was measured by a high-performance thin-layer chromatographic procedure that included in situ densitometric scanning for detection. Urine was measured by comparison with a standard curve prepared by adding 50, 100, and 300 ng of Δ^9-tetrahydrocannabinol carbolic acid per milliliter to drug-free urine. Any subject who had a Δ^9-tetrahydrocannabinol concentration greater than 80 ng/mL on the chromatographic test was excluded. The high-performance thin-layer chromatographic assay is sensitive to 25 ng/mL.

As expected, Δ^9-tetrahydrocannabinol concentrations differed between the 2 assays. The average Δ^9-tetrahydrocannabinol concentrations 72 hours before testing were variable but quite high in the user groups (older cohort=238.5±476.3 ng/mL, younger cohort=129.1±272.5 ng/mL). The variability reflects the period and amount of cannabis consumed in the days prior to the test, for which the subjects received no warning. At the time of testing, the concentrations were well below the 50-ng/mL cutoff used to indicate positive results for cannabis use (older users=9.7±16.6 ng/mL, younger users=8.6±22.3 ng/mL).

PROCEDURES

The cognitive studies were conducted in the field office in San José. The evaluation required 4 to 5 hours, depending on whether the intelligence test was administered (only to the younger cohort). Two technicians, who were "blind" to the subjects' identities as users or nonusers, administered the tests in Spanish. Only the field-workers and an office manager knew the group identity of the subjects.

All subjects were systematically interviewed, and self-reports were verified by asking other members of the network about the respondent. The interviews included a sociocultural survey of life history and social, educational, and occupational functioning and questions about psychiatric and medical histories and drug-use patterns. The interviews were conducted in the neighborhoods in an open-ended fashion to encourage the respondent to talk freely and openly with the interviewer, who took notes and then completed a schedule outlining the variables coded for this study.

TASKS

In a series of experiments, separate components of memory and attention were evaluated. Four memory tests were selected, based on a modification of the 3-store model originally proposed by Atkinson and Shiffrin,[18] and used extensively in studies of acute and carryover effects of cannabis.[19,20] A 12-trial Spanish word version of the selective reminding task was used.[21] In addition, a free recall paradigm that instructed the subject to rehearse aloud between trials was employed.[22] Three 3-trial conditions of implicit organization (ie, unrelated/unblocked words, related/unblocked words, and related/blocked words) for 16 words were included in this task. A sorting task was used to evaluate free recall and control processes in short-term memory.[23] Finally, episodic memory was evaluated using a task in which stories were read to the subjects, who were asked to tell everything they could remember about the stories immediately after the reading and 90 minutes later. Probe questions were asked to separate memory for facts and inferences.[24]

The 8 attention tasks evaluated preparedness, selection, and allocation components of attention based on views of attention as a central, limited capacity that can be flexibly shifted or allocated.[25-27] Preparedness was measured with a computer-based, reaction-time procedure.[26] Selection was evaluated using measures of focused and sustained attention. The focused attention tasks included 4 cancellation tasks that required the subject to identify random and organized verbal and nonverbal stimuli under timed conditions[28] and a visual search task that required the subject to search 4 quadrants of 16 letters each for a target letter appearing in only 1 target.[26] For sustained attention, 2 "X-A" versions of the continuous performance test were used.[29] One version had a short interstimulus interval (1 millisecond), and the other version was a vigilance paradigm because of a longer interstimulus interval (1 minute).

To measure allocation, competition paradigms based on dual-task performance were employed.[30] For each task, the subject was asked to depress a manual finger tapper as fast as possible for 15 (task 1) or 60 (task 2) seconds with the right and then the left hand. The subject was then asked to name as many objects as possible in 15 seconds from a specific semantic category (task 1) or complete 1 trial of a free recall memory task not previously employed (task 2). Finally, the subject was asked to tap as fast as possible for the specified period while simultaneously performing the cognitive task. These divided attention tasks permit an evaluation of the allocation of attentional resources by measuring the reduction in performance using dual- vs single-task conditions.[26] The ability to flexibly shift and allocate attentional focus was measured with the Wisconsin Card Sorting Test.[27]

STATISTICAL ANALYSIS

The data were analyzed using a multivariate approach to repeated-measures analysis of variance with 2 between-subject factors, group (2 levels, user and nonuser) and cohort (2 levels, older and younger), and 1 or 2 within-subject factors, which represented subcomponents of a task, the presence of multiple trials, or both. We hypothesized that interactions of group by cohort would emerge, indicating poorer performance by older users vs older nonusers and no significant differences ($P<.05$) between the younger user groups. Significant group by cohort interactions ($P<.05$) were evaluated by testing for group differences within cohorts. To control the level of α, the follow-ups were adjusted using the Bonferroni inequality to control α at a family-wise level of $P=.05$. We considered each task to represent a separate experiment, so the focus was on maintaining Type I errors at $\alpha=.05$ for each task.

Sociodemographic and Drug-Use Variables by Group (Users and Nonusers) and Cohort (Older and Younger)

	Group			
	Older		Younger	
Variable	Users	Nonusers	Users	Nonusers
Age, y				
Mean	45.31	45.64	29.29	27.28
SD	1.53	1.15	1.04	0.90
Educational level, %*				
Primary or less	47	63	62	33
Secondary	47	33	32	52
High school or university	6	4	5	15
Alcohol abuse, %*				
No	25	33	22	67
Yes	75	67	78	33
Tobacco use (pack-years)*				
Mean	30.43	29.89	14.41	7.80
SD	7.80	1.59	1.38	1.21
Full scale intelligence quotient†				
Mean	110.33	115.50	113.78	115.33
SD	10.54	8.06	11.82	11.59

*$P<.05$ for comparison of younger users and nonusers.
†Spanish version of the Wechsler Adult Intelligence Scale.[17]

when restudied in 1985 and 1986, users performed worse than nonusers on cognitive measures of short-term memory and attention. The users also showed a decline in the level of mental effort at work, the quality of their occupational status, and a continued trend toward more solitary living arrangements.[15]

Problems interpreting these results remained. The cognitive measures that detected poorer performance by the users in the 1985 study were not part of the initial assessment, and comparisons between the studies begun in 1973 and 1985 yielded little evidence for deterioration of cognitive skills in the users during the intervening 12 years. The degree of chronicity required to establish adverse cognitive effects also remained unclear. Most notably, the absence of drug assays made it unclear whether the cognitive deficits observed in the 1985 study were attributable to the long-term use of cannabis, to subacute intoxication, or to carryover effects, which are observed from approximately 24 to 72 hours after consumption and which reflect the amount of time required for cannabis metabolites to fully metabolize out of the body.[16]

This investigation assessed the cognitive functioning of the long-term users and nonusers, who have been observed since 1973. In addition, a second cohort comprising younger, shorter-term users and comparable nonusers was evaluated to determine whether cognitive problems could be observed in these users. We hypothesized that only the older long-term users (vs comparable nonusers) would show poor performance on cognitive tasks related to memory and attention, which could not be attributed to acute or carryover effects of cannabis.

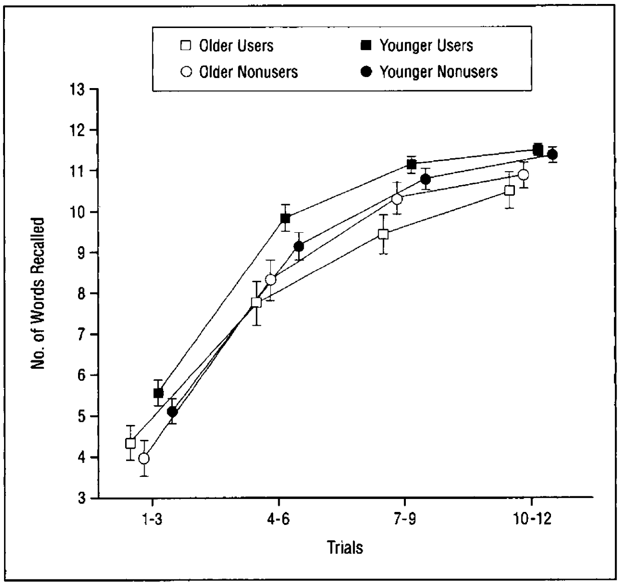

Figure 1. *Long-term storage scores on the verbal selective reminding test by group, cohort, and trials, indicating a poorer performance by the older user group. Bars indicate SE.*

RESULTS

MEMORY TASKS

The 2 more complex tasks involving the learning of a list of words (verbal selective reminding and free recall) yielded significant group by cohort interactions that showed poorer performance by the older user groups. These results differed from the story recall task, which, consistent with our previous studies,[12,14] did not differentiate users group in either the younger or older cohorts.

Analysis of the sorting task showed no group by cohort interaction, but the group by trials interaction was significant ($F[2,113]=4.17$, $P<.05$). Analysis of the group effect at each level of trials did not achieve the critical level of α ($P>.0167$).

For the verbal selective reminding test, **Figure 1** displays the significant group by cohort by trials interaction for the long-term storage variable ($F[3,127]=3.83$, $P<.01$). Follow-ups of the group by trials interaction within each cohort at the critical level of α ($P<.025$) were significant only for the older cohort ($F[3,43]=3.74$, $P<.018$). As Figure 1 shows, older users encoded words at a slower rate than older nonusers; no differences between groups were observed in the younger cohort. No significant differences ($P>.05$) were found between the older users and nonusers on consistent, long-term retrieval, although a trend of poorer performance by the older users was apparent.

The most difficult task, free recall, also showed a group by cohort by trials interaction ($F[2,124]=4.44$, $P<.01$) and a group by list interaction ($F[2,124]=3.63$). For the first interaction, analysis of the group by trials interaction within cohorts was performed at $P<.025$. This test was significant only for the older cohort ($F[2,40]=5.94$, $P<.006$). **Figure 2** shows that the older users recalled words at a slower rate than the older non-

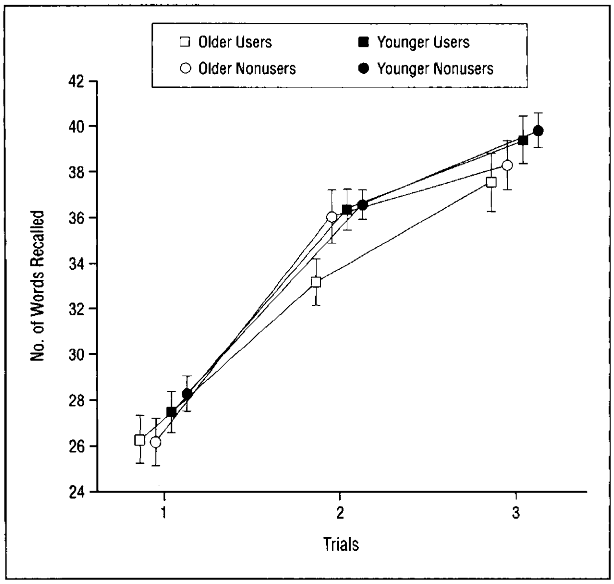

Figure 2. *Percentage of words recalled on the free recall task by group, cohort, and trials, indicating a poorer performance by the older user group. Bars indicate SE.*

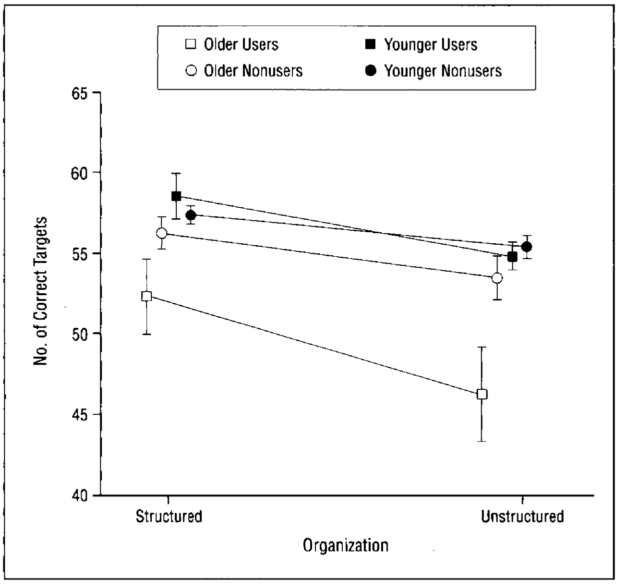

Figure 3. *Number of correctly identified targets on the cancellation tests by group, cohort, and organization, indicating a poorer performance by the older user group. The magnitude of the group difference is larger for unstructured material. Bars indicate SE.*

users, and no significant differences ($P>.05$) between the younger groups are shown. Follow-up of the group by list interaction (ie, no interaction with cohort) did not meet the critical level of α.

ATTENTION TASKS

Analysis of the attention tasks showed significant group by cohort interactions ($P<.05$) on measures of selective and divided attention; performance was always poorer in the older user group. No effects involving group were significant ($P>.05$) for the reaction time measure, visual search, continuous performance tests, or the Wisconsin Card Sorting Test. These results suggest that differences in the cognitive functioning of long-term cannabis users and nonusers are most apparent on more difficult attention tasks, which place time pressure on subjects to respond quickly. Hence, tasks that do not manipulate symbolic material (reaction time), that are self-paced (eg, continuous performance tests and the Wisconsin Card Sorting Test), or that proceed for longer durations of time (eg, the continuous performance test, the visual search, the vigilance test, and the finger tapping–free recall test) are not associated with cannabis use.

Group differences reflecting long-term cannabis use were most striking for the cancellation (selective attention) and competition (allocation) tasks. For correct responses on the cancellation tasks, the group by organization ($F[1,118]=8.08$, $P<.01$) and the cohort by organization ($F[1,118]=3.78$, $P<.05$) interactions were significant. The 3-way interaction of group, cohort, and organization was not significant ($F[1,118]=1.25$, $P<.27$). However, given the hypotheses and the significance of both 2-way interactions, the group by organization interaction within each cohort ($P<.025$) was examined in the follow-up. **Figure 3** shows that the older user group identified relatively fewer targets on the unstructured task ($F[1,35]=6.03$, $P<.023$) than the structured task ($F[1,35]<1$).

For the competition tasks, a significant 3-way interaction of group, cohort, and condition (**Figure 4**) was found ($F[1,129]=11.68$, $P<.01$). Analysis of the group by condition interaction within each cohort was significant only for the older cohort ($F[1,45]=12.21$, $P<.002$). The older users showed a greater decrement in finger tapping using the dual-task conditions vs the single-task condition. When subjects show a decrement in performance on 1 task, performance on the other task is maintained. We found this to be true in this study, as analysis of the verbal retrieval data showed no effects of group or cohort ($F<1$). The second competition task, which involved a longer period of finger tapping and a free recall task, did not yield effects involving group.

COMMENT

Costa Rica was originally selected as a setting for the evaluation of the effects of long-term cannabis use because long-term, frequent users who did not use drugs other than cannabis, alcohol, and tobacco could be identified. The setting also provided access to nonusers who were from similar sociodemographic backgrounds and who consumed alcohol and tobacco at levels comparable with the users. The older groups were originally matched on multiple sociodemographic and drug-use variables.[14] In this follow-up, the older users and nonusers did not engage in polydrug use and remained comparable in their consumption of alcohol and tobacco.

The results demonstrated that only the older long-term users of cannabis performed worse on measures of selective attention, divided attention, and short-term memory vs comparable nonusers. The most robust effects occurred on the cancellation and competition tasks. On the cancellation tasks, the older users consistently

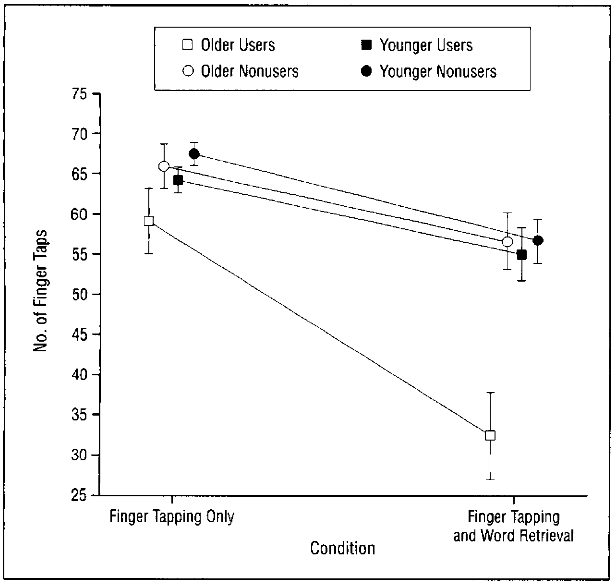

Figure 4. *Speed of finger tapping on the competition task using single- and dual-task conditions. The older user group had poorer performance and larger differences between the single- and dual-task conditions. Bars indicate SE.*

demonstrated an inability to rapidly select relevant information, particularly on the most complex tasks, which involved unstructured, nonverbal material. Poorer performance by long-term users on cancellation tasks was also reported in the studies conducted in Egypt[8] and India[9,10] and in our 1985 follow-up.[15] When divided attention was assessed with shorter trials of finger tapping and verbal retrieval, the ability of the older long-term user group to perform 2 tasks simultaneously was diminished vs the older nonuser group.

On the 2 more complex short-term memory tasks, the older user group showed more difficulty learning and retaining information across trials. These effects were not apparent for material that was contextually related (story recall) or on less complex serial recall tasks (sorting). The only North American study to use selective reminding procedures also found poorer performance in a sample of long-term users.[7]

The short-term memory deficiencies are consistent with studies that show disruption of learning and memory (ie, delayed-match-to-sample tasks) in rats due to acute administration of Δ^9-tetrahydrocannabinol.[31] These acute effects are similar to those observed in rats with damage to the hippocampus.[31,32] In humans, impairment on tasks such as the selective reminding tests has been observed in subjects who have undergone hippocampectomy for epilepsy.[32] In the rat, the hippocampus is rich in cannabinoid receptors.[33] Hence, the poorer performance of the older users may reflect impairment in brain systems associated with short-term memory.

The deficiencies on the selective and divided attention tasks may be related to deficiencies in the working memory, a component of the memory system providing a central source of control and allocation of memory and attentional resources.[34] Working memory is mediated by anterior regions of the brain, specifically, the prefrontal cortex.[35] The forebrain is also rich in cannabinoid receptors.[33] The divided attention task is a prototypic working memory task because of the requirement to allocate attentional resources. Although the cancellation tasks could be interpreted to represent the operation of an attention system in posterior brain regions,[27,28] the fact that decrements occurred only on unstructured material is commonly interpreted as an inability to allocate resources from the working memory system.[26,28] Although these parallels between animal and human studies are speculative, the results show impairments in 2 components of the memory system responsible for short-term memory that are consistent with animal studies of the brain metabolism of Δ^9-tetrahydrocannabinol.

This study also has several limitations. A field study of this sort cannot have a statistical design that permits causal inferences. The results are correlational and show an association between long-term cannabis use and performance. Despite the careful approach to sampling, it is always possible that unmeasured factors led to the differences between the older groups. Although no evidence of selective attrition was noted, it is possible that results would be different if all members of the original cohort could be studied. Until recently, North Americans typically did not use cannabis to the degree apparent in these cohorts of Costa Rican users, so the results may not generalize to other cultures. Nevertheless, the consumption patterns are surprisingly similar to those reported in the North American study by Block and Ghoneim.[7] The tasks that yielded group differences did not exist when the 1973 study was completed. This study would have been strengthened with prospective evaluation of these cognitive skills. It is also possible that the associations of cognitive performance and cannabis reflect the use of cannabis and alcohol, tobacco, or both; this pattern of joint use is invariably associated with cannabis use. Finally, the absence of differences between the younger groups may reflect a variety of factors, including higher educational levels, later average initial exposure to cannabis, and less chronicity.

It is also apparent that the deficiencies observed in this study and in the study by Block and Ghoneim[7] are subtle. The older long-term users are largely functional and employable, and they do not demonstrate the types of dementia and amnesic syndromes associated with alcohol use of comparable magnitude. The health of the subjects continues to be adequate over time,[15] and no evidence exists for the severity of health risks associated with use of other drugs, such as alcohol. Nevertheless, the risks of long-term use of even smaller amounts of cannabis are likely magnified in a more technological society, particularly given the possibility of carryover effects. Certain occupations may carry particular risk because of safety issues and effects on productivity and learning. The development of reliable methods for quick and efficient detection of cannabis use is needed. Furthermore, the findings suggest a need to focus efforts on the prevention of cannabis use through balanced educational programs for children and their parents. It is clear that the younger cohort and, to a lesser extent, the older cohort began to move toward polydrug use, a pattern consistent with studies of North American subjects.[36] This pattern under-scores the need for preventive efforts to reduce the risk of consumption of drugs by young people.

Accepted for publication March 26, 1996.

This study was supported by grant 1 R01 DA06555 from the National Institute on Drug Abuse, Baltimore, Md.

We thank Pilar Zúniga Alfaro and Esmeralda Arce Arias for evaluating the subjects; Manuel Monestel Ramirez, Rigoberto Astorga Morales, and Silvia León Cubero for completing the fieldwork; and officials in the Ministry of Health of the Costa Rican government for their continued facilitation of this research.

Reprints: Jack M. Fletcher, PhD, Department of Pediatrics, University of Texas–Houston Medical School, MSB7.142, 6431 Fannin, Houston, TX 77030.

REFERENCES

1. Adamec C, Pihl RO, Leiter L. An analysis of the subjective marijuana experience. *Int J Addict.* 1976;11:295-307.
2. McGlothlin L, West LJ. The marijuana problem: an overview. *Am J Psychiatry.* 1968;125:126-134.
3. Hollister LE. Marijuana in man: three years later. *Science.* 1971;172:21-29.
4. Schaeffer J, Andrysiak T, Ungerleider JT. Cognition and long-term use of cannabis (ganga). *Science.* 1981;213:465-466.
5. Wert RC, Raulin ML. The chronic cerebral effects of cannabis use, II: psychological findings and conclusions. *Int J Addict.* 1985;605:629-642.
6. Grant I, Rochford J, Fleming T, Stunkard H. A neuropsychological assessment of the effects of moderate marijuana use. *J Nerv Ment Dis.* 1973;156:278-280.
7. Block RL, Ghoneim RL. Effects of chronic marijuana use of human cognition. *Psychopharmacology.* 1993;110:219-228.
8. Souief MI. Chronic cannabis users: further analysis of objective test results. *Bull Narc.* 1975;27:1-26.
9. Wig NN, Varma VK. Patterns of long-term heavy cannabis use in North India and its effects of cognitive functions: a preliminary report. *Drug Alcohol Depend.* 1977;2:211-219.
10. Varma UK, Malhotra AK, Dang R, Das K, Nehra R. Cannabis and cognitive functions: a prospective study. *Drug Alcohol Depend.* 1988;21:147-152.
11. Fletcher JM, Satz P. A methodological commentary on the Egyptian study of chronic hashish use. *Bull Narc.* 1977;29:29-34.
12. Peterson RC, ed. *Marijuana and Health.* Washington, DC: National Institute on Drug Abuse; 1977.
13. Fletcher JM, Satz P, Carter WE. Chronic cannabis use: recent cross-cultural evidence from Costa Rica and other cultures. *Contemp Drug Probl.* 1978;7:3-30.
14. Carter WE, Coggins W, Doughty P, eds. *Cannabis in Costa Rica.* Philadelphia, Pa: Institute for the Study of Human Issues; 1980.
15. Page JB, Fletcher JM, True WR. Psychosociocultural perspectives on chronic cannabis use: the Costa Rican follow-up. *J Psychoactive Drugs.* 1988;23:57-65.
16. Yesavage J, Leirer VU, Denari M, and Hollister LE. Carry-over effects of marihuana intoxication on aircraft pilot performance: a preliminary report. *Am J Psychiatry.* 1985;1423:1325-1329.
17. Wechsler D. *Escala Intelligencia de Wechsler Adultos.* New York, NY: Psychological Corp; 1967.
18. Atkinson RC, Shiffrin RM. Human memory: a proposed system and its control processes. In: Spence KW, Spence JT, eds. *The Psychology of Learning and Motivation.* New York, NY: Academic Press; 1968;2:89-195.
19. Miller L, Cornett T, McFarland D. Marijuana: an analysis of storage and retrieval deficits in memory with the technique of restricted reminding. *Pharmacol Biochem Behav.* 1977;8:327-332.
20. Tinklenberg JR, Darley C. A model of marijuana's cognitive effects. In: Braude MC, Szara S, eds. *The Pharmacology of Marijuana.* New York, NY: Raven Press; 1976:45-65.
21. Buschke H. Spontaneous remembering after recall failure. *Science.* 1974;184:579-581.
22. Best DL, Ornstein PA. Children's generation and communication of memoric organizatorial strategies. *Dev Psychol.* 1986;22:845-853.
23. Ornstein P, Naus MJ. Rehearsal processes in children's memory. In: Ornstein PA, ed. *Memory Development in Children.* Hillsdale, NJ: Lawrence Erlbaum Associates; 1978:69-99.
24. Paris SG, Lindauer BK. The role of inference in children's comprehension and memory for sentences. *Cogn Psychol.* 1976;8:217-227.
25. Posner M, Boies SJ. Components of attention. *Psychol Rev.* 1971;78:391-408.
26. Cooley EL, Morris RD. Attention in children: a neuropsychologically based model for assessment. *Dev Neuropsychol.* 1990;6:239-274.
27. Mirsky AF, Anthony BJ, Duncan CC, Ahearn MB, Kellam SG. Analysis of the elements of attention: a neuropsychological approach. *Neuropsychol Rev.* 1991;2:109-145.
28. Mesulam MM. Attention, confusional states, and neglect. In: Mesulam MM, ed. *Principles of Behavioral Neurology.* Philadelphia, Pa: FA Davis Co Publishers; 1985:1075-1168.
29. Rosvold HE, Mirsky AF, Sarason J, Bronsome ED, Beck LH. A continuous performance test of brain damage. *J Consult Psychol.* 1956;20:343-350.
30. Hiscock M. Verbal manual time sharing in children as a function of task priority. *Brain Cogn.* 1982;1:119-131.
31. Heyser CJ, Hampson RE, Deadwyler SA. Effects of delta-9-tetrahydrocannabinol on delayed match to sample performance in rats: alterations in short-term memory associated with changes in task specific timing of hippocampal cells. *J Pharmacol Exp Ther.* 1993;271:294-307.
32. Squire LR. *Memory and Brain.* New York, NY: Oxford University Press Inc; 1987:202-240.
33. Herkenham M, Lynn AB, Johnson MR, Melvin LS, de Costa BR, Rice KC. Characterization and localization of cannabinoid receptors in rat brain: a quantitative in vitro autoradiographic study. *J Neurosci.* 1991;11:563-583.
34. Baddely AD. Working memory. *Science.* 1992;255:556-559.
35. Goldman-Rakic PS, Friedman HR. The circuitry of working memory revealed by anatomy and metabolic imaging. In: Levin HS, Eisenberg HM, Benton AL, eds. *Frontal Lobe Function and Dysfunction.* New York, NY: Oxford University Press Inc; 1991:72-91.
36. Wesson DW, Carlin AS, Adams KM, Beschner G. *Polydrug Abuse: The Results of a National Collaborative Study.* New York, NY: Academic Press; 1978.