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The Chronic Cerebral Effects of Cannabis Use. II. Psychological Findings and Conclusions

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Abstract

This paper examines the research evidence on the question of whether sustained use of marijuana may produce chronic cerebral impairment as measured by neuropsychological measures. Evidence from both American and cross-cultrual studies suggests that marijuana probably does not produce chronic cerebral impairment, although subtle impairment cannot be ruled out. Several suggestions for new lines of research are discussed including prospective studies, effects of cannabis use on later aging processes, and true experimental studies.

Mind-altering substances have been used and abused throughout history, and their abuse continues to be a major social problem. Research to uncover the risks involved in using drugs is needed if we are to establish reasoned policy on how to regulate these substances. In the first paper of this series (Wert and Raulin, 1986), we discussed some of the problems in studying the chronic cerebral effects of a drug such as cannabis and reviewed the neurological studies conducted to date. In this paper we review the psychological and neuropsycho-

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logical findings on the long-term effects of cannabis and suggest some directions for future study.

MODERN PSYCHOLOGICAL AND NEUROPSYCHOLOGICAL APPROACHES

A number of psychological and neuropsychological studies of the long-term effects of marijuana, including several cross-cultural studies, have been reported. Fifteen studies of the chronic cerebral effects of cannabis have used psychological and neuropsychological assessment measures with varying results. Of the nine cross-cultural studies (Agarwal, Sethi, and Gupta, 1975; Bowman and Pihl, 1973; Mendhiratta, Wig, and Verma, 1978; Ray, Prabhu, Mohan, Nath, and Neki, 1978; Rubin and Comitas, 1975; Satz, Fletcher, and Sutker, 1976; Soueif, 1976; Stefanis, Dornbush, and Fink, 1977; Wig and Varma, 1977), five found some evidence for impairment in the cannabis-using group. However, a closer inspection of the studies suggests that the evidence may not be as strong as these numbers might suggest.

Agarwal et al. (1975) claimed to have found evidence of impairment on three psychological tests (Weschler Memory Scale, Bender Visual Motor Gestalt, and Bhatia Battery of Intelligence) in 40 Indian cannabis users. No control group was used. However, on at least two of these tests, the proportions of scores in the "impaired" range as reported by the investigator are almost exactly what would be expected in a random sample from the general population. On the Bender, nearly half of the subjects received low scores, but without a comparison group it is impossible to determine whether this finding was abnormal for their population.

Stefanis et al. (1977) found four statistically significant differences on WAIS subtests between 47 Greek cannabis users and 41 controls. However, only one of these differences was on a subtest thought to be sensitive to cerebral functioning (Digit Symbol) while the others were on verbal subtests less sensitive to cerebral deficit.

Wig and Varma (1977) studied 27 Indian cannabis users and 11 controls on a number of tests including the EEG, Raven Colored Progressive Matrices, Bender Visual Motor Gestalt, and Indian adaptations of the WISC and the Weschler Memory Scale. Users performed significantly more poorly on 4 of the 8 psychological tests. Interestingly, Satz et al. (1976) found no differences between their 41 cannabis users and 41 controls on a very similar battery, and Rubin and Comitas (1975) found only three differences on a very large battery of similar tests.

Soueif (1976) studied nearly 1,700 incarcerated Egyptian cannabis users and controls, using a wide range of psychological tests (Tool Matching, Marking, Trail Making, Reaction Time, Digit Span, Distance and Time Estimation,

and Bender Visual Motor Gestalt). He found that cannabis users performed significantly more poorly on 10 of the 16 measures. However, the differences were very small and significant primarily because of the extreme statistical power associated with such large sample sizes. They did not seem to reflect clinically significant differences. In addition, place of residence (rural vs urban) and degree of literacy were found to affect test scores at least as much as cannabis use. Finally, the test battery was heavily skewed toward tests of attention, concentration, and psychomotor speed; scores on these tests are heavily influenced by variables such as anxiety, psychopathology, lack of motivation, and acute drug effects (although subjects presumably had little access to drugs since they were incarcerated).

Mendhiratta et al. (1978) also administered a battery consisting primarily of tests of attention, concentration, and motor speed to 50 Indian cannabis users (25 of whom used less potent cannabis) and 25 controls. Groups were matched on age, sex, occupation, education, and level of psychopathology. They reported that one or both of the user groups scored more poorly than controls on 7 of the 9 measures. The authors concluded that chronic cannabis use may lead to deficits in concentration and attention. However, either acute effects (which were not considered) or motivational differences could have accounted for the obtained results.

It is interesting that Ray et al. (1978), using a test battery similarly skewed toward tests of attention, concentration, and motor speed, found only one significant difference between the groups of 30 Indian cannabis users and 50 controls. Ray et al. included a much smaller proportion of illiterate subjects in their sample than Mendhiratta et al.

Bowman and Pihl (1973) found no differences between 30 Jamaican cannabis users and 24 controls on a battery of tests despite the presence of a greater proportion of illiterate subjects in the user groups. The Bowman and Pihl study is distinguished by the use of several techniques to improve the validity of the findings, including a replication of the findings, an attempt to test subjects blindly, and the use of a monetary payment to increase subject motivation.

None of the studies conducted in the United States (Carlin and Trupin, 1977; Culver and King, 1974; Grant, Rochford, Fleming, and Stunkard, 1973; Mendelson, Rossi, and Meyer, 1974; Rochford, Grant, and La Vigne, 1977; Schaeffer et al., 1981) demonstrated statistically significant differences between cannabis users and controls. Rodin, Domino, and Porzak (1970) reported that cannabis users demonstrated "significantly" poorer Bender Gestalt performance (although still within the normal range) than non-drug users. We did not include this study because no results of statistical tests or even means were given, nor was there a mention that any statistical procedures had been performed. We can only conclude that they used the term "significantly" as a figure of speech rather than in the usual sense of *statistical significance.* Culver and King (1974)

Table 1

A Summary of the Psychological and Neuropsychological Studies of the Effects of Cannabis Use

Author (year) [country]	Sample size and type: users/controls	Findings and comments
Agarwal et al. (1975) [India]	Clients of cannabis shop: 40/0	Half of the subjects had abnormally high Bender Gestalt scores; 20% scored in the impaired range on the Wechsler Memory Scale; 25% had IQs < 90.
Bowman and Pihl (1973) Study 1 [Jamaica]	Volunteers with 10+ yr of cannabis use: 16/10	No significant differences between users and nonusers were found on the Embedded Figures, Paired Associates, Wisconsin Card Sorting, Finger Tapping, Digit Span, and Block Design.
Bowman and Pihl (1973) Study 2 [Jamaica]	Same as above: 14/14	The same tests as above were used, plus Time Estimation and Rhythm Tests. Again, no significant differences were found.
Mendhiratta et al. (1978) [India]	Volunteers with 4+ yr of cannabis use: 50/25	Tests used were Digit Span, Design Recognition, Tapping, Design Cancellation, Time and Size Estimation, Word Association, and Bender Gestalt. Users did more poorly on all tests except Digits Forward and Design Cancellation.
Ray et al. (1978) [India]	Rural males; 25% of each group were illiterate: 30/50	Tests used were Backward Digit Span, Serial Addition and Subtraction, Color Cancellation, Minnesota Perceptodiagnostic Test, and the Wechsler Memory Scale. Users scored significantly higher on 1 of the 10 subtests of the Wechsler Memory Scale.
Rubin and Comitas (1975) [Jamaica]	Paid volunteers with 10+ yr of cannabis use: 30/30	Only three significant differences found on a large number of tests including Ammons Vocabulary, Lowenfeld Mosaic, Maze Steadiness, Graduated Holes, Pegboard, and portions of the WAIS and the Halstead-Reitan Battery.

Satz et al. (1976) [Costa Rica]	Volunteers with 10+ yr of cannabis use: 41/41	No significant differences between users and nonusers were found on the WAIS, Benton Visual Retention, Williams Memory, Facial Recognition, Finger Localization, Finger Tapping, and Tactual Performance tests.
Soueif (1976) [Egypt]	Prison inmates: 850/839	Tests used were Tool Matching, Marking, Trail Making, Reaction Time, Digit Span, Distance and Time Estimation, and Bender Gestalt. Significant differences were found on 10 of the 16 measures with cannabis users scoring more poorly.
Stefanis et al. (1977) [Greece]	Volunteers with 10+ yr of cannabis use: 47/40	Gave WAIS and the Raven Progressive Matrices. Differences were found on Verbal IQ, Comprehension, Similarities, and Digit Symbol subtests.
Wig and Varma (1977) [India]	Volunteers with 5+ yr of cannabis use: 23/11	Cannabis users performed more poorly on WISC, Wechsler Memory, GATB Speed, Time Perception, and Bender Gestalt. No differences were found on Raven Colored Progressive Matrices or Color Cancellation.
Carlin and Trupin (1977) [USA]	Volunteers with 2+ yr of cannabis use: 10/10	Tests used were WAIS and Halstead-Reitan Battery. Controls were taken from Reitan's normative population. The control group did worse on Part B of the Trail Making Test.
Culver and King (1974) Study 1 [USA]	College seniors: 14/14	No significant differences between users and nonusers were found on Laterality Discrimination, the WAIS, Cube Comparison, Hidden Patterns, Paper Folding, and the Halstead-Reitan Battery.
Culver and King (1974) Study 2 [USA]	College seniors: 14/14	Tests were the same as above, plus Card Rotation, Spatial Orientation, and Surface Development. No significant differences were found between users and nonusers. Users were only casual users.
Grant et al. (1973) [USA]	Med students: 29/29	Tests used were Raven Advanced Progressive Matrices, Serial Alteration, and portions of the Halstead-Reitan Battery. Users did more poorly on the Location score of the Tactual Performance Test. Subjects were light cannabis users.

(continued)

Table 1 (continued)

Author (year) [country]	Sample size and type: users/controls	Findings and comments
Mendelson et al. (1974) [USA]	Volunteers with 2+ yr of cannabis use: 20/0	Tests included the WAIS and portions of the Halstead-Reitan Battery. No significant differences between casual and heavy users. Upon clinical examination, 2 heavy and 2 casual users showed impairment.
Rochford et al. (1977) [USA]	Med students: 26/25	No significant differences were found on Tactual Performance, Minnesota Perceptodiagnostic Test, and Bender Gestalt. Subjects were light cannabis users.
Schaeffer et al. (1981) [USA & unspecified Caribbean island]	Religious users of cannabis: 10/0	No evidence of impairment using the tests' published norms were found on the Benton Visual Retention, Trail Making Test, portions of the WAIS, Rey Auditory-Verbal Learning, Raven Progressive Matrices, Symbol-Digit Modalities, and Hooper Visual Organization.

conducted two studies with a total of 28 cannabis users and 28 controls, plus a group of LSD users, all of whom were college students. While there were some significant differences between LSD users and other groups, there were no differences between the cannabis users and controls on any of the measures. However, due to the inappropriate use of analysis of covariance (Lord, 1967) to minimize the effects of group differences in alcohol consumption, the results of their second study should be interpreted cautiously.

Carlin and Trupin (1977) compared 10 cannabis users to 10 members of Reitan's normative sample (Reitan, 1966) who had been tested a number of years earlier on the WAIS and portions of the Halstead-Reitan Battery. Clearly, this is not an adequate control group. Still, there were no statistically significant differences between the groups. Rochford et al. (1977) found no performance differences between 26 cannabis users and 25 controls, all of whom were medical students. Similarly, Grant et al. (1973) found only one difference among a large number of tests using medical students as subjects. Mendelson et al. (1974) found no differences between casual and heavy users of cannabis on a variety of neuropsychological measures.

Schaeffer et al. (1981) found and tested what might be considered an ideal experimental group: 10 members of a religious organization in which regular cannabis use was a part of their religious beliefs. Their subjects reported smoking cannabis virtually every waking moment, which was borne out by the observation of cannabis use during the test administration. In many studies, cannabis users were polydrug users and social deviants, often rebellious, resentful of authority, and unmotivated to perform on the basis of the usual social incentives. However, the cannabis-using subjects of Schaeffer et al. denied the use of alcohol and other drugs, and were described as productive members of society, thus minimizing the confounding effects of these variables. Unfortunately, Schaeffer et al. neglected to include a control group.

The following tests were administered: Benton Visual Retention, Trail Making, portions of the WAIS, Rey Auditory-Verbal Learning, Raven Progressive Matrices, Symbol-Digit Modalities, and Hooper Visual Organization. Despite the likelihood of acute drug effects, subjects' performances were not impaired when compared with the tests' published norms. In fact, mean WAIS scores indicated performance in the superior to very superior range.

Schaeffer et al. (1981) were the only investigators who attempted to estimate precannabis performance of their subjects for comparison with the present performance. They obtained early school achievement test scores for two of their subjects and compared the IQ conversion scores of these early tests with the subjects' present WAIS scores. No significant differences were found. While this use of achievement test scores provides only a rough estimate of the subjects' precannabis level of performance, it is a practical way of collecting information which otherwise would require a prospective study. In addition, Schaef-

fer et al. were the only investigators to use a laboratory test to detect recent marijuana ingestion. The use of this test in studies with positive results (i.e., impairment in cannabis users) would have been helpful in ruling out acute effects as the cause of the impairment.

Studies of the psychological and neuropsychological performance of cannabis users are summarized in Table 1.

Summary. Despite the large number of factors biasing most of these studies toward finding impairment in cannabis users (acute effects, polydrug use, poor nutrition, poor medical care, differences in literacy, etc.), only 1 (Wig and Varma, 1977) of the 15 studies found differences which could not be easily explained by these uncontrolled factors. One would expect a larger number of these studies, especially the cross-cultural studies using very heavy, long-term cannabis users, to have shown positive results if cannabis use indeed did produce cerebral impairment.

DISCUSSION

We have seen that the majority of studies have found no clinically or statistically significant differences between groups of cannabis users and controls on commonly accepted neurological and psychological measures of cerebral functioning. This finding is all the more impressive given the number of other variables (such as polydrug use, low motivation, and acute effects) which bias the results toward finding impairment in cannabis-using subjects.

This general finding of no clinically significant differences between cannabis users and controls may be interpreted in several ways. One possibility is that cannabis does not lead to chronic cerebral impairment. A second possibility is that cerebral deficits do develop but that the individual adapts and overcomes them through a process of relearning. It is well known that a chronic or slow-developing lesion will often be masked by the adaptation of the patient to the deficits produced by the lesion (Golden, 1978). A third possibility is that while the vast majority of cannabis-using subjects are not impaired, there may be a very small number of users who are vulnerable to cannabis-produced impairment. Such a possibility could explain the positive findings of a few studies: Perhaps such studies used a larger proportion of vulnerable subjects. The possibility of differential impairment is an interesting one and is discussed later in this section. Fourth, it is possible that cerebral impairment does exist in the cannabis-using subjects, but that the tests are not sensitive enough to detect it. However, given that these same tests have demonstrated impairment in alcoholics (for reviews, see Bolter and Hannon, 1980; Kleinknecht and Goldstein, 1972; Parsons, 1977; Parsons and Leber, 1981; Ron, 1977; Tarter, 1975; Wilkinson, 1982) and heavy social drinkers (MacVane, Butters, Montgomery, and Farber, 1982; Parker, Birnbaum, Boyd, and Noble, 1980; Parker and Noble, 1977, 1980), this does not seem likely.

Directions for Future Research

Virtually all of the studies reviewed in this paper fit into a single research mold. They are all retrospective studies of preestablished groups (cannabis users and non-cannabis users). Although some of the studies made a commendable attempt to obtain suitable control subjects, this is still a very weak and vulnerable research design. In the remainder of the paper, we propose some alternative research designs and discuss their potential usefulness.

Prospective Studies

The greatest weakness of a retrospective study of preexisting groups is that one is never sure if observed differences between the groups are the result of the defining characteristic (in this case, cannabis use) or whether the differences existed prior to any cannabis use. While the experimenter may try to match users and controls on relevant variables, many times the relevant variables are not known or cannot be controlled for or matched. The prospective study, which uses the subject as his or her own control, is a sound method of dealing with many of the issues that cloud retrospective studies. For example, the possibility that cannabis users would have demonstrated poorer performance even before their use of cannabis is eliminated with this design. The notion that impairment might predate drug use has been expressed by some authors with respect to alcoholism (see Parsons and Leber, 1981, and Tarter, 1975, for reviews), although there has been little research to support or refute this hypothesis as yet.

Prospective studies have been recommended by a number of authors (Culver and King, 1974; Rochford et al., 1977; Wig and Varma, 1977; Institute of Medicine, 1982), although these authors have generally failed to address the complexities of such studies. Prospective studies are extremely expensive since a large number of people must be tested (to assure a large enough group of later cannabis users) and followed for a long period of time. The likelihood of maintaining a continuous funding source over such a long period of time is slim. Furthermore, a prospective study does not automatically deal with many of the experimental problems described earlier in this paper. The investigator would still need to control for variables such as polydrug and alcohol abuse, motivational differences, and acute and withdrawal effects. A prospective study, although it does assess precannabis performance, cannot in itself avoid the methodological issues inherent in research in this area.

There is one area where prospective studies could contribute a great deal to our understanding of possible chronic cerebral effects of cannabis. Prospective studies would be one of the few ways to adequately test the hypothesis of differential vulnerability in cannabis users. Such a hypothesis has been raised by a few authors (Carlin and Trupin, 1977; Jones, 1980). It might well be that some

individuals are predisposed to cerebral impairment as the result of cannabis use, either because of structural or biochemical characteristics which accentuate the possible damaging effects of the drug, or because they have little of the "cerebral reserve" that most of us call on when we experience mild cerebral damage. That functional reserve can mask very real cerebral damage (Weiss, 1975). By having pre- and postcannabis performance scores for subjects, we can identify those subjects (if they exist) who show real impairment in functioning. By comparing those subjects who show impairment with those subjects who do not show impairment, we may be able to identify possible risk factors.

In our opinion, the results of the studies we have reviewed do not provide sufficient evidence of impairment to warrant the investment of time and money required for prospective studies. For those interested in ruling out previous impairment, we recommend the use of information that has already been gathered for other purposes such as school achievement or intelligence test scores or preinduction achievement testing for the Armed Forces. We agree with Schaeffer et al. (1981) that such information provides only a rough estimate of precannabis performance, but it would not appear to be cost-effective to gather more precise information through a prospective study. Indeed, a more worthwhile study might be to compare performance on such achievement tests with performance on neurological and psychological tests of cerebral functioning to determine just how "rough" such an estimate really is.

Studying the Effects of Cannabis on the Aging Process

Almost all of the studies reported in this paper used relatively young subjects. Of the 28 studies reviewed, 17 did not include a single subject over the age of 58. In the remaining 11 studies, either the age range was not given or the vast majority of the subjects were under the age of 60. While in most studies the lack of older subjects seemed to be a result of the population the investigators chose to study (students, volunteers recruited through street people, etc.), in at least one study (Agarwal et al., 1975) elderly people were excluded purposely to eliminate the possibility that any impairment seen in subjects was a consequence of aging.

We would like to suggest that the elderly may be the ideal population to investigate the chronic cerebral effects of cannabis use (Smith & Sethi, 1975). This approach has been used successfully in the study of cerebral effects of alcohol use (Blusewicz, Dustman, Schenkenburg, and Beck, 1977; Blusewicz, Schenkenburg, Dustman, and Beck, 1977). The data reviewed in this paper suggest that there are few if any detectable, long-term cerebral effects of cannabis use in young and reasonably healthy individuals. It is reasonable to conclude that any chronic effects that might result from the use of the drug are easily masked by the normal "cerebral reserve." However, the normal aging process

slowly erodes both our functional reserve and, in time, even our primary functional abilities. Chronic cerebral dysfunction is likely to become more noticeable in individuals experiencing additional cerebral deterioration. Thus, a premature intellectual deterioration (senility) might well be expected in long-term cannabis users if cannabis produces even subtle cerebral deterioration. So far, no one has investigated this possibility. Such a study would not be easy since a 60- to 70-year lifetime allows ample opportunity for numerous confounding variables to also affect cerebral functioning. Large sample sizes and some matching of samples on variables known to have chronic cerebral effects would be necessary. However, if any population is likely to show the results of a subtle cerebral impairment, it is likely to be a population of older citizens. Another reason for studying the possible effects of cannabis use on aging is that modern medicine is extending the life expectancy of people. As more people live longer, any variable which increases the level of dysfunction of the elderly will further strain our health care system.

Is It Time to Consider an Experiment?

All of the studies reviewed in this paper used a pseudoexperimental design in which preexisting groups (cannabis users and nonusers) were compared on measures of their cerebral functioning. Any research methods text will describe the weaknesses of such a design. Getting pretest measures (as in a prospective study) strengthens the design somewhat, but there are still numerous confounding variables which could affect the results. The alternative of conducting a true experiment where subjects are randomly assigned to the groups (cannabis users and nonusers) has not been an ethically responsible choice available to investigators. However, it may be time to reconsider the alternative of a true experiment.

We recognize that suggesting an experimental test of the chronic effects of cannabis is controversial, and we want to make it clear that we do not feel that such a test is warranted yet. But if further research were to show little or no effects in vulnerable populations such as the elderly and if the risks to other body systems are shown to be minimal, a carefully designed and executed experiment might add a great deal to our understanding of the long-term effects of cannabis use.

Summary

In this paper we have tried to review the available research on the chronic cerebral effects of cannabis use with a particular focus on methodological issues. Our general conclusion is that the current research does not support the contention that cannabis use results in chronic cerebral impairment. The possibility still

remains that such impairment exists, but it is likely to be either quite subtle or apparent in only a select group of vulnerable subjects. Those studies which did find cerebral effects were either fatally flawed [as in the Campbell et al. (1971) study] or biased in the direction of finding performance differences. For each study where significant impairment was found, several other studies with apparently equal methodological rigor found no impairment.

Any conclusion drawn from the studies reviewed here must be considered tentative because of the limitations inherent in the retrospective design. Although it may be possible to improve on many of the currently available studies in terms of methodology, it would probably make little difference in the conclusions we would draw. Therefore, we have chosen to focus our discussion on new directions for research using alternative designs and/or populations. We do not believe that more retrospective studies, even if they use the finest methodology available, are warranted given the data already available.

The issue of cannabis use is a highly emotional topic with serious political overtones. However, the fact remains that in spite of the illegal status of the drug, its use is widespread. To the extent that potential health risks exist, we have a continuing responsibility to identify them and communicate that information to those affected. Even though the current research does not suggest a risk for cerebral impairment, there are still some areas that have not been adequately investigated. Furthermore, there are areas of risk (e.g., cerebral effects of cannabis use by young children) which have received virtually no study. Now may be the best time to refocus our research efforts and explore these questions.

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