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2532

Neuropsychological Assessment of Undergraduate Marihuana and LSD Users

Charles M. Culver, MD, PhD, Francis W. King, PhD

An extended battery of neuropsychological tests was administered to three groups of college seniors (lysergic acid diethylamide [LSD]/mescaline users; marihuana/hashish users; and controls) who were matched on predrug usage intellectual and personality dimensions. The study was replicated one year later. In the combined-years' analyses, the three groups showed statistically significant differences only on the Trail Making Test: LSD/mescaline users performed within normal limits but significantly worse than either of the other two groups. Since the three groups also differed significantly in the extent of their alcohol usage, a covariance analysis was carried out that indicated that this variable did not account for the LSD/mescaline group's performance on the Trail Making Test. Inference about possible organic dysfunction cannot be drawn from these findings, but prospective neuropsychological testing might prove useful.

There is a pressing social need to learn more about the possible neuropsychological effects of chronic marihuana and lysergic acid diethylamide (LSD) usage. For example, there have been recent reports, though the studies have critical methodological shortcomings (see Altman and Evenson[1]), of neurological impairment[2] or even cerebral atrophy[3] associated with chronic marihuana use; these reports contrast sharply with the sometimes persuasive claims of heavy marihauna and LSD users that they have incurred no cognitive impairments whatsoever. While several studies have recently appeared (see below), comparing the neuropsychological performance of LSD and/or marihuana users with control subjects, they have often used groups that were not clearly matched on intellectual and other possibly relevant variables before their drug use began. This study attempted to achieve as precise a retrospective matching as possible.

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From the Department of Psychiatry, Dartmouth Medical School, Hanover, NH.

Reprint requests to the Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755 (Dr. Culver).

Subjects and Methods

Subjects were members of the Dartmouth senior classes during either the 1970 through 1971 or 1971 through 1972 academic years. All were between 20 and 25 years of age. Initially, each year a questionnaire (an extension of that described by King[4]) was sent to all (about 800) seniors that asked whether or not and to what extent they had used a great variety of drugs. The questionnaires were plainly coded for identification purposes and students were assured of strict confidentiality. Two follow-up requests were sent to nonrespondents; a return rate between 74% and 75% was obtained each year.

Each year three subject-groups of 14 students each were formed:

1. A *control group* with no history of marihuana or LSD use.
2. A *marihuana group* with the following characteristics: no use of marihuana or hashish before college; no use at all of LSD or mescaline; use of marihuana and/or hashish for at least 12 months, with an overall frequency of at least twice per month.
3. An *LSD group* (all of whom had also used marihuana and/or hashish) with the following characteristics: no use of marihuana, hashish, LSD, or mescaline, before college; use of LSD and/or mescaline for at least 12 months with an overall frequency of at least once per month.

Students were excluded from all groups who had injected "speed"; used psilocybin, DMT, STP, or heroin; used cocaine more than four times; or used either pep pills or barbiturates for any purpose more than a total of 20 times each during their more than 38 months since first coming to college.

It is realized that subjects who reported LSD and mescaline usage usually had in fact no knowledge of the true pharmacologic contents of the substances they had ingested; the availability of true mescaline in northern New England is reputedly especially low. However, the intent of the study was to investigate possible cognitive differences among discriminable subgroups who use certain broad classes of drugs rather than to investigate precise and specific drug-behavior relationships.

From the three groups, triads of subjects were formed, matched according to the following criteria:

1. Verbal Scholastic Aptitude Test (SAT) scores within 70

Table 1.—Subject Characteristics

	Study 1, 1971*			Study 2, 1972*		
	Control	Marihuana	LSD	Control	Marihuana	LSD
Scholastic Aptitude Test						
Verbal	638	643	643	646	654	662
Math	697	709	709	714	714	712
Alcohol, total days used 3+ drinks						
Mean				88.9	321.8	371.3
Median				60	156	264
Range				4-405	4-949	8-1365
Marihuana, days used						
Mean					230.5	334.5
Median					162	337
Range					24-1323	93-647
LSD, days used						
Mean						22.8
Median						17
Range						12-58

* N = 14 for each group.

Table 2.—Neuropsychological Test Results

	Study 1, 1971			Study 2, 1972			1971 & 1972		
Tests	Control	Marihuana	LSD	Control	Marihuana	LSD	Control	Marihuana	LSD
Weschler Adult Intelligence Scale (WAIS)									
Verbal	132.6	131.4	129.3	129.1	131.4	128.1	130.9	131.4	128.7
Performance	126.9*	119.7*	116.8*	119.0	122.0	120.1	122.9	120.9	118.5
Full scale	131.9*	128.6*	125.6*	126.5	128.9	125.8	129.2	128.7	125.7
WAIS									
Information	16.3	16.2	16.4	15.7	16.4	16.5	16.0	16.3	16.4
Comprehension	16.1	15.9	14.9	15.5	15.7	14.9	15.8	15.8	14.9
Arithmetic	14.4	14.9	15.0	14.1	14.4	14.4	14.2	14.6	14.7
Similarities	15.7	14.6	14.4	15.2	15.8	15.3	15.5	15.2	14.9
Digit span	14.1	14.0	12.8	13.9	13.6	13.3	14.0	13.8	12.7
Vocabulary	16.4	16.3	16.6	15.9	16.5	15.9	16.1	16.4	16.2
Picture completion	13.6†	12.0†	11.4†	11.1*	12.4*	12.2*	12.3	12.2	11.8
Block design	15.6	14.7	13.9	14.9	15.1	14.8	15.2	14.9	14.4
Picture arrangement	13.1	11.1	11.8	11.9	11.1	12.4	12.5	11.1	12.1
Object assembly	13.4	14.0	12.7	12.9	14.6	12.6	13.1	14.3	12.7
Trail Making									
A	19.8	19.4	24.1	21.4	19.1	24.9	20.6*	19.3*	24.5*
B	41.1	42.4	53.0	44.0*	39.0*	50.8*	42.6†	40.7†	51.9†
A+B	60.9*	61.9*	77.1*	65.4*	58.1*	75.7*	63.1†	60.0†	76.4†
Category	14.9	13.6	14.1	15.6	15.4	18.0	15.2	14.5	16.0
Tactual Performance									
Total time	479.6	477.7	494.2	519.6	455.9	469.6	499.6	466.8	478.4
Memory	9.0	8.6	8.5	8.5	8.8	8.3	8.8	8.7	8.4
Location	7.3	7.0	5.9	6.7	7.4	7.1	7.0	7.2	6.5
Finger Tapping									
Dominant hand	50.1	49.2	52.1	54.8	54.8	56.6	52.5	52.0	54.4
Seashore Rhythm	28.3	28.5	27.4	27.6	28.6	28.9	27.9	28.6	28.1
Speech Sounds Perception	57.0	57.1	57.1	56.7	56.9	56.9	56.9	57.0	57.0
Hand Dynamometer									
Dominant hand	47.4	51.5	45.9	49.9	50.1	49.9	48.7	50.8	48.0
Tactual Form Board	26.0	28.2	26.6	24.4	23.5	25.3	25.2	25.9	26.0
Laterality Discrimination	50.2	58.1	77.7	73.5*	49.3*	52.8*	61.9	53.7	65.3
Hidden Patterns	93.3	83.3	93.8	89.3	96.9	91.3	91.3	90.1	92.6
Cube Comparisons	29.9†	29.1†	20.7†	26.3	27.1	27.4	28.1	28.1	24.0
Paper Folding	15.7	14.3	11.9	13.0	14.3	12.9	13.7	13.9	12.4
Spatial Orientation	...	...	...	27.1	30.3	34.7	...	...	...
Surface Development	...	...	...	49.7	48.9	46.2	...	...	...
Card Rotation	...	...	...	175.3	170.0	161.1	...	...	...

* $P < .05$.
† $P < .01$.

points of one another.

2. Mathematical SAT scores within 70 points of one another.

3. Minnesota Multiphasic Personality Inventory (MMPI) profiles according to the highest one or two clinical scales within them and according to the elevation of their masculinity-femininity scales. Actually, within all but two or three of the 28 triads, the matching was much closer than the above specified limits.

After subjects were matched into triads, they were approached personally and their cooperation elicited. They were fully apprised of the purpose of the study. Of the 84 subjects initially approached, only one refused to participate; he was a control group subject for whom an alternate was found with nearly identical SAT and MMPI scores. Subjects in the two drug groups were asked to abstain from all relevant drugs for seven days prior to their testing session; the impression gathered during their post-testing interviews (see below) was that they had very faithfully done so. Subjects were paid $35.00 for their cooperation.

Testing Measures.—During the first year's testing, the following measures were employed:

1. The Halstead battery of neuropsychological tests: Category Test; Tactual Performance Test; Finger Tapping Test; Speech Sounds Perception Test; and Seashore Rhythm Test. Also, the Hand Dynamometer and the Form Recognition Tests were used (see Reitan[5]).

2. The Wechsler Adult Intelligence Scale (WAIS).

3. The Trail Making Test (Reitan[6]).

4. Laterality Discrimination Test (Culver[7]).

5. Three tests of spatial-perceptual abilities from the Educational Testing Service's *Manual for Kit of Reference Tests for Cognitive Factors*[8]: (*a*) Cf-2, Hidden Patterns Test (flexibility of closure factor); (*b*) S-2, Cube Comparisons Test (spatial orientation factor); and (*c*) Vz-2, Paper Folding Test (visualization factor).

6. The MMPI. (Changes in the MMPI from freshman to senior years as a function of group membership will be the subject of a future publication.)

Because of the outcome of the first year of the study, three additional tests from the *Manual for Kit of Reference Tests for Cognitive Factors*[8] were added to the second year's testing: (*a*) S-1, Card Rotation Test (spatial orientation factor); (*b*) S-3, Spatial Orientation Test (spatial orientation factor); and (*c*) Vz-3, Surface Development Test (visualization factor).

The tests were given in the same sequence both years; the three added during the second year were administered at the conclusion of the first year's battery sequence. Total testing time was about five hours and was usually divided into two sessions but was occasionally done in one or three. Each subject was tested by one of four female technicians employed by the Dartmouth Neuropsychology Laboratory, all of whom had had extensive experience in administering essentially all of the tests to a varied clinical and normal population. The technicians did not generally know to which group a given subject belonged, although sometimes this was volunteered during the testing session.

Interviews.—At a separate session after completion of the testing, each subject was interviewed by one of us. The purpose of the interviews was to obtain personal and qualitative information about subjects' use or nonuse of drugs and to afford the subjects an opportunity to inquire in detail about the rationale and procedure of the study. During the first year's interviews, questions about amount of drug usage were generally limited to making certain that subjects satisfied the criteria of the group to which they were assigned. The second year's interviews went into much greater detail about past drug intake: subjects were asked to estimate how many times per week they had used each pertinent drug during seven separate time periods, ie, their four academic years and the three intervening summers. They were also asked to estimate for each of the seven periods on how many days of the week they had had three or more drinks of an alcoholic beverage. The characteristics of the subjects in each year's groups and their extent of drug usage are summarized in Table 1.

Results

Since all of the tests yield numerical results, it was possible to conduct a single-factor analysis of variance across the groups for each variable. The results are shown in Table 2 for each year separately and for the two years combined.

For the 1971 subjects, certain WAIS scores (performance IQ, full scale IQ, and especially the picture completion subtest) showed significant differences among the groups—and in a consistent, descending order from controls to marihuana-users to LSD-users. Among the 1972 groups, however, only the picture completion subtest yielded significant ($P<.05$) differences—and, *here* the descending order was from marihuana subjects to LSD subjects to controls. There were no significant IQ differences in 1972 and, with the changed ordering of the picture completion subtest, there were no significant WAIS differences for the combined-years' analysis.

Again for the 1971 subjects, there were substantial differences among the groups on the S-2, Cube Comparison Test—and in the same descending order of performance as the 1971 subjects above. However, as Table 2 indicates, there is a tight clustering of 1972 means on the S-2 and with no important differences. Again, an analysis of the combined data for the two years yielded no substantial findings.

Although there were no significant differences among the 1971 groups on the Laterality Discrimination Test, there were significant ($P<.05$) findings on this instrument with the 1972 subjects. During this latter year, the best performance was made by the control group. When the data for the two years are combined, there are no significant differences among the groups.

It may be seen from Table 2 that only in the instance of the Trail Making Test were there statistically significant differences for each of the years—both separately and combined. Individual comparisons among the three group means for the Trail Making Tests A, B, and A+B were carried out for the combined 1971 and 1972 data using the Tukey test. For the Trail Making Tests B and A+B measures, the LSD group scored significantly ($P<.05$) higher (ie, less adequately) than either the control or marihuana groups; the latter two groups did not differ from one another. On Trail Making Test A, the LSD group was significantly different (ie, higher; $P<.05$) only from the marihuana group.

It then seemed useful to investigate whether or not there was a relationship within the LSD group between the amount of LSD/mescaline usage and performance on the Trail Making Test. Only the 1972 data contained interview information that was sufficiently detailed for this purpose. Within the 1972 data, Spearman rank-order correlation coefficients were computed between the total estimated number of times of LSD and/or mescaline ingestion and performance on Trail Making Tests A, B, and A+B. These coefficients were, respectively, −.06, −.15, and −.21; none of these are significant.

Alcohol Consumption.—Subjects in the three 1972 groups differed noticeably in their reported degree of usage of alcoholic beverages. The average total number of estimated days, since beginning college, on which three or more drinks were consumed was 88.9 for the control group, 321.8 for the marihuana group, and 371.3 for the LSD group. The actual distribution of values on this variable showed considerable positive skewness, so group differences were assessed with the nonparametric Kruskal-Wallis one-way analysis of variance (Siegel[9]). This test indicated that the group means were significantly ($P<.05$) different from one another.

The relationship between degree of alcohol consumption and neuropsychological test scores was then examined for all of the 1972 subjects as a group. Spearman rank-order correlation coefficients were calculated between alcohol usage and all of the test variables listed in Table 2. The only significant relationship found was for the Trail Making Test A ($r_s=.32$; $P<.05$), although Trail Making Test A+B approached significance ($r_s=.29$; $P=.08$). Trail Making Test B ($r_s=.13$) was not significant.

Thus, there was a suggestion that individuals with higher alcohol consumption performed more poorly on the Trail Making Test A (and possibly A+B) measure. Was it possible that a critical portion of the significantly different performance of the drug groups on the various parts of the Trail Making Test was actually related to alcohol consumption rather than to other drug usage? A rough consideration of the data suggested that drug and alcohol usage were not inextricably intertwined; both the marihuana and LSD groups drank heavily and yet differed significantly ($P<.01$) on the Trail Making Test's B and A+B measures.

Another approach to the same problem was made by carrying out a covariance analysis among the three 1972 groups in which Trail Making Test A+B scores were treated as the criterion variable and alcohol consumption as the covariate. It was first necessary to transform the alcohol consumption scores; because of their positive skewness, a logarithmic transformation was carried out that did nearly equalize the ranges in the three groups (see Winer[10(pp218-222)]). It was found in carrying out the analysis that the F ratio was reduced from 4.14 in the simple analysis of variance to 3.70 in the analysis of covariance; however, both were significant ($P<.05$). Thus, there was still a significant difference among the Trail Making Test A+B means for the three groups after a statistical adjustment had been made for the effect of alcohol consumption. Covariance analyses were not made for the test A separately, because the three 1972 groups did not differ significantly on this measure, nor for the test B, since this measure bore so little correlation to alcohol consumption.

After the study was completed, a different kind of analysis of the subjects' cognitive performance was made by calculating the grade point averages (GPA) at the end of the junior year for each of the groups. For the control, marihuana, and LSD groups, respectively, the mean GPAs were as follows: 1971 study: 2.51, 2.61, and 2.53; 1972 study: 3.05, 2.68, and 2.64; and 1971 and 1972 studies combined: 2.78, 2.64, and 2.58. Separate analyses of variance were performed, and for neither year alone nor for the two combined years were the mean GPA differences statistically significant.

Comment

The battery of tests administered to the subjects was a comprehensive one in the number of measures used and in the variety of cognitive functions assessed. The sensitivity of the Halstead-Reitan battery in detecting even subtle cortical dysfunction has been fairly adequately demonstrated (Reitan[5]).

The 30 to 33 measures obtained on each year's subjects are not statistically independent; even if they were, it would be expected that each year no more than one or two of the measures would by chance alone attain the $P<.05$ significance level and that probably none would attain the $P<.01$ level.

Perhaps the first conclusion to be drawn from the results is that for the great majority of the measures there was no suggestion of significantly different cognitive functioning among the three subgroups. While the Picture Completion, Cube Comparisons (S-2), and Laterality Discrimination Test measures did significantly differentiate the groups for one or both years, none of the three attained statistical significance in the combined-years' analyses.

Only the Trail Making Test attained some measure of statistical significance for each year separately and for the two years combined. The meaning of this finding, which was due to the LSD groups' performing relatively more poorly than either the control or marihuana group, is less than obvious. So far as we are aware, there is no known specific type of cortical dysfunction that would be reflected in a poor performance of Trail Making Tests A and B that would not affect at least some of the other very abstract tests in the battery (eg, the Category Test or the location score on the Tactual Performance Test). It is also the case that the LSD group's performance on the Trail Making Test, while significantly different from the other two groups, was still well within the normal range according to clinical normative values (for example, see Russell et al[11]). The possibility exists of course that the Trail Making Test is uniquely sensitive to a very mild type of cortical dysfunction that might characterize our LSD group, although it should be noted that there was no correlation within the LSD group between extent of drug usage and Trail Making Test performance.

The particular pattern of statistically significant and insignificant findings in this study is consistent with some earlier studies and inconsistent with others. Cohen and Edwards[12] also found that LSD users did less well than a control group on Trail Making Test A but McGlothlin et al[13] and Wright and Hogan[14] found no substantial differences on either part of the Trail Making Test between these two groups.

This study found no significant differences between the marihuana and control groups on any of the measures. Grant and others[15] compared marihuana and control groups on eight neuropsychological tests; their only significant finding was that subjects in the marihuana group did less well on the localization score of the Tactual Performance Test, a finding not replicated in this study.

The several studies referred to present inconsistent findings, even though similar neuropsychological measures have been used. Some of the inconsistency may be due to the variety of subject populations (psychiatric outpatients; undergraduate students; and medical students) and some due to the overall degree of drug usage by the subject groups. The subjects in this study were certainly biased toward the intact, well-functioning end of the continuum, and the drug usage of the experimental groups was generally in the moderate range.

Although the three groups of subjects in this study were matched on predrug usage intellectual and personality measures with perhaps more precision than any of the above-mentioned studies, there are inherent weaknesses in any retrospective investigation in this area as McGlothlin et al[13] have nicely summarized. Perhaps most troublesome is the impossibility of finally knowing, even with the most careful ex post facto matching, whether group differences on a few tests (eg, Trail Making) might not have for a variety of reasons been present before drug usage began. Since only a prospective study using each subject as his own control can avoid this methodological uncertainty, we have recently completed an initial cognitive testing (using a selected portion of the above battery) and drug usage inventory of approximately 25% of the Dartmouth freshman class whom we will retest in their senior year.

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