Neuropsychological effects of marijuana

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Summary: This study assigned 81 non-naive subjects, divided into low- and high-dose groups, to four experimental conditions (marijuana/marijuana, marijuana/placebo, placebo/marijuana and placebo/placebo) for two sessions separated by about one week. The low dose was 4.8 mg. Δ^9-THC followed by 2.4 mg. one hour later. The high dose was 9.1 mg. followed by 4.5 mg. one hour later. A battery of neuropsychological tests was administered.

The low dose produced generalized impairment of all mental processes (concept formation, memory, tactile form discrimination and motor function) and the effect was generalized to all modalities. The high dose resulted in more extensive impairment, again generalized.

The drug effects noted were explained in terms of generalized impairment of central integrative processes. The effects of marijuana on learning as well as memory were explained in terms of impaired output (recall), but the impairment was transient.

Résumé: *Les effets neuropsychologiques de la marijuane*

La présente étude a porté sur 81 sujets de maturité normale. Ils ont été répartis en deux groupes distincts, le groupe des doses faibles et celui des doses fortes. Ils ont été soumis à quatre essais (marijuane/marijuane, marijuane/placébo, placébo/marijuane et placébo/placébo) pendant deux séances, séparées par un intervalle d'environ une semaine. La dose faible était de 4.8 mg de Δ^9-THC, suivie une heure plus tard d'une dose de 2.4 mg. La dose forte était de 9.1 mg, suivie une heure plus tard d'une dose de 4.5 mg. Durant l'expérience, tous les sujets ont subi une série d'épreuves neuropsychologiques.

La dose faible a entrainé une altération généralisée de tous les processus mentaux (idéation, mémoire, forme de discrimination tactile et fonction motrice). Cet effet a été généralisé dans toutes les modalités expérimentales. Avec les doses fortes, l'altération a été plus considérable et, ici encore, généralisée.

Les effets de la marijuane ont été définis comme une altération généralisée des processus d'intégration mentale. Quant à ses effets sur la faculté d'apprendre et sur la mémoire, ils ont été expliqués par une altération de la faculté de se souvenir (rappel). Cette altération a cependant été transitoire.

The earliest culturally-relevant experimental marijuana research is confined to four studies.[1-4] The first published study on marijuana that can withstand critical evaluation is the 1968 report of Weil, Zinberg and Nelsen[5] which concluded that sustained attention was not affected by marijuana usage; general alertness, muscular coordination and attention decreased at both dose levels (4.5 and 18 mg. Δ^9-THC), but only for the naïve subjects.

Subsequent to the study of Weil, Zinberg and Nelsen, seven groups of investigators have reported on the psychological effects of marijuana administered by smoking. Caldwell, Myers and Domino[6] found that marijuana minimally affected sensory acuity. Manno *et al*[7] reported a significant decrement in performance levels in motor and mental tests. Abel[8] reported that marijuana did not affect retrieval of information already present in memory but did interfere with the initial learning, significantly affecting acquisition processes involved in the storage of information. Kiplinger *et al*[9] observed dose-dependent decrements in performance levels in motor and mental tasks as well as in stability of stance. Meyer *et al*[10] concluded that most of their perceptual tests showed a mild degree of impairment. Dornbush, Fink and Freedman[11] reported that short-term memory and reaction time were adversely affected only by high doses of marijuana. Le Dain[12] measured short-term

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serial position memory and general alertness, among other variables, in subjects who smoked average doses of 0.7, 1.5 and 6.2 mg. Δ^9-THC, using a standardized and closely controlled smoking technique. Impairment was found in the former but not the latter measure.

Five studies between 1968 and 1971 have reported on the psychological effects of marijuana, using an oral route of administration. Clark, Hughes and Nakashima[13] reported that learning, time estimation and reaction time were most consistently affected by the drug. Hollister and Gillespie[14] reported that only number facility was significantly affected. Melges *et al*[15] found that immediate memory was adversely affected, and the authors concluded that this impairment may hinder the individual's ability to compare current perceptions with memories. No consistent dose-response relationship was observed in their study. Waskow *et al*[16] reported little, if any, impairment in memory. Rafaelsen *et al*[17] observed decreased scores in memory and attention, but only for the higher-dose condition.

One study has used both smoked and oral routes of administration. Jones and Stone[18] found that only time

Table I
Neuropsychological test battery

Test no.	Test name	Stimuli	Variable no.	Score	Function	Mental process	Description of mental process
1	Halstead Category	208 slides	1	No. errors	Visual	Concept formation (reasoning)	Requires postulation of hypotheses that appear reasonable with respect to recurring similarities and differences in the stimulus material
2	Trail Making	25 circled numbers	2 A	Time	Visual	Conceptual relations	Requires immediate recognition of symbolic significance of numbers and letters, ability to scan and identify and sequence
		25 circled numbers and letters	3 B	Time			
			4 Total				
3	Halstead Tactual Performance	10 blocks and form-board	5 Dom. hand	Time	Tactile (performed while blindfolded)	Tactile discrimination speed	Depends upon tactile form discrimination, kinesthesis, manual dexterity, visualization of spatial configuration and retention of spatial interrelationships
			6 N-dom. hand	Time			
			7 Both hands	Time			
			8 Total	Time			
			9 Memory	No. correct		Incidental learning Memory	
			10 Location	No. correct			
4	Seashore Tonal Memory	30 pairs of tonal sequences	11	No. errors	Auditory	Memory — immediate	Requires alertness and sustained attention and retention
5	Benton Sentence Repetition	26 sentences of increasing length	12	No. correct	Auditory	Memory — immediate	Requires longer span of focused attention and recall of meaningful information
6	Picture Recognition	76 common objects projected, 16 repeated	13	No. errors	Visual	Memory — immediate	Involves visual pattern discrimination and recognition of a stimulus within a serially presented series
7	Peterson Visual Memory	6 common noun trigrams projected, followed by counting 3-digit number and recall of trigram	14	No. errors	Visual	Memory — immediate	Involves retroactive interference (negative transfer), and measures the effect of an interpolated (intervening) activity upon the retention and recall of a stimulus
8	Halstead Finger Tapping	Mechanical finger tapper	15 Dom. hand	Mean of five 10-sec. trials for each hand	Motor	Undirected motor speed — upper extremities	Requires motor speed for brief intervals
			16 N-dom. hand				
9	Foot Tapping	Mechanical foot tapper	17 Dom. foot	Mean of two 10-sec. trials for each foot	Motor	Undirected motor speed — lower extremities	Requires motor speed for brief intervals
			18 N-dom. foot				
10	Klove Grooved Steadiness	Vertical groove	19 Dom. hand	Time	Motor	Directed motor steadiness	Requires gross visual-motor coordination in one plane
			20 Dom. hand	No. contacts			
			21 N-dom. hand	Time			
			22 N-dom. hand	No. contacts			
11	Klove Maze Coordination	Maze	23 Dom. hand	Time	Motor	Dynamic motor coordination	Requires gross visual-motor coordination in multiple planes
			24 Dom. hand	No. contacts			
			25 N-dom. hand	Time			
			26 N-dom. hand	No. contacts			
12	Klove Static Steadiness	Plate with 9 holes decreasing in size	27 Dom. hand	Time	Motor	Static fine visual motor coordination	Requires fine motor steadiness
			28 Dom. hand	No. contacts			
			29 N-dom. hand	Time			
			30 N-dom. hand	No. contacts			
13	Grooved Pegboard	25 identical grooved pegs to be fitted into grooved holes	31 Dom. hand	Time	Motor	Manipulative dexterity	Requires speed, accuracy and eye-hand coordination
			32 N-dom. hand	Time			

estimation was adversely affected by the marijuana — smoked as well as oral.

The purposes of the present study were: (1) to determine the effects of low and high doses of marijuana on neuropsychological functioning and (2) to determine the effects of these dosage levels on learning.

Methods

1. *General procedure*

Subjects were 81 non-naïve volunteers (38 men and 43 women) assigned to one experimental condition in a low- (4.8 mg. Δ^9-THC reinforced by 2.4 mg.Δ^9-THC one hour later) or high (9.1 mg. Δ^9-THC reinforced by 4.5 mg. Δ^9-THC one hour later) dose group. The high-dose group included four experimental conditions — marijuana/marijuana, marijuana/placebo, placebo/marijuana and placebo/placebo. The low-dose group included the first three experimental conditions — the placebo/placebo subgroup was used for high- and then low-dose level analyses. The smoking technique was standardized and controlled.

2. *Neuropsychological battery*

The neuropsychological test battery consisted of 13 tests and 32 variables, since multiple measures were obtained from some of the tests (Table I). The test bat-

Table II
Neuropsychological results of F tests for low-dose group-analysis of variance

Test no.	Variable no.	Test name	Between groups	Between trials	Groups x trials	Marijuana effect during initial session†	Marijuana effect during 2nd session (unrelated)‡	Marijuana effect during 2nd session (related)¶
1	1	Category test (err.)	3.27*	47.77****	1.71	11.35****	0.17	1.48
2	2	Trail Making — A (time)	5.46***	7.59***	4.25***	9.28***	5.30*	1.12
	3	Trail Making — B (time)	10.37****	7.83***	4.12***	28.39****	5.25*	0.26
	4	Trail Making — Total (time)	9.96****	9.71***	4.06***	28.52****	6.57**	0.02
3	5	T.P.T. — Dom. (time)	0.45	20.37****	1.05	2.21	2.71	0.30
	6	T.P.T. — Non-dom. (time)	1.00	8.94***	0.42	2.33	5.96**	0.23
	7	T.P.T. — Both (time)	1.19	6.00**	0.55	5.73**	3.41	0.38
	8	T.P.T. — Total (time)	1.05	16.92****	0.80	4.19*	5.72**	0.36
	9	T.P.T. — Memory (corr.)	1.47	5.95**	0.81	3.58	0.00	2.17
	10	T.P.T. — Location (corr.)	0.81	5.72**	0.38	0.31	0.01	0.44
4	11	Seashore Tonal Memory (err.)	2.62*	0.21	0.54	0.93	1.30	2.14
5	12	Sentence Repetition (corr.)	10.69****	0.07	4.04***	7.17***	14.17****	2.89
6	13	Picture Recognition — Total (err.)	0.71	2.95	0.28	2.94	0.01	0.04
7	14	Visual Memory (err.)	9.45****	7.09***	3.25*	20.89****	6.95***	0.08
8	15	Finger Tapping — Dom. (corr.)	1.09	0.10	1.25	3.52	0.13	0.23
	16	Finger Tapping — Non-dom. (corr.)	1.01	0.85	0.08	1.72	0.04	0.32
9	17	Foot Tapping — Dom. (corr.)	1.00	0.31	0.18	0.24	0.65	2.91
	18	Foot Tapping — Non-dom. (corr.)	1.15	0.07	0.06	0.94	0.28	0.03
10	19	Grooved Steadiness — Dom. (time)	2.09	6.52**	1.41	12.50****	0.37	1.08
	20	Grooved Steadiness — Dom. (corr.)	5.22***	4.00*	2.86*	15.06****	0.31	0.20
	21	Grooved Steadiness — Non-dom. (time)	0.31	2.66	0.20	1.39	1.82	1.06
	22	Grooved Steadiness — Non-dom. (corr.)	0.11	2.45	0.05	0.13	0.45	2.45
11	23	Maze Coordination — Dom. (time)	0.64	3.28	0.36	1.98	3.78*	0.01
	24	Maze Coordination — Dom. (corr.)	0.57	2.80	0.37	1.77	3.01	0.02
	25	Maze Coordination — Non-dom. (time)	1.14	4.45*	0.76	1.02	0.05	0.01
	26	Maze Coordination — Non-dom. (corr.)	0.73	8.69***	0.38	0.69	0.24	0.27
12	27	Static Steadiness — Dom. (time)	10.43****	1.30	4.21***	12.97****	14.64****	1.32
	28	Static Steadiness — Dom. (corr.)	5.20***	0.67	1.72	3.57	10.16***	1.25
	29	Static Steadiness — Non-dom. (time)	6.77****	0.15	3.17*	4.47*	8.62***	0.98
	30	Static Steadiness — Non-dom. (corr.)	3.50**	0.02	2.44	1.76	8.98***	1.18
13	31	Grooved Pegboard — Dom. (time)	2.70*	2.07	1.13	1.87	8.11***	0.02
	32	Grooved Pegboard — Non-dom. (time)	2.49	0.41	0.33	0.00	1.27	0.13

*$P < 0.05$; **$P < 0.02$; ***$P < 0.01$; ****$P < 0.01$

†$(M_1M_2 + M_1P_2) - (P_1M_2 + P_1P_2)$

‡Marijuana effect during second session unrelated to experimental condition in initial session $(M_1M_2 + P_1M_2) - (M_1P_2 + P_1P_2)$

¶Marijuana effect during second session related to experimental condition in initial session $(M_1M_2 - M_1P_2) - (P_1M_2 - P_1P_2)$

tery was designed to measure the following four mental processes, the sensory input being provided by a variety of modalities: (1) concept formation — visual (2 tests and 4 variables); (2) memory — (a) tactile (1 test and 2 variables), (b) auditory (2 tests and 2 variables), (c) visual (2 tests and 2 variables); (3) tactile form discrimination (1 test and 4 variables); and (4) motor (6 tests and 18 variables). The duration of examination and re-examination one week later was approximately 1¾ hours. The order of presentation of the tests during both sessions was randomized from one subject to another in order to reduce bias that might result from examination (or re-examination) during maximal drug effect. Whereas curve of decay from maximal drug effect can be minimized by order of presentation, session-to-session practice effects were not susceptible to control, and hence were included in the statistical analysis of data.

Results

1. *Screening psychological tests*

(a) Wechsler Adult Intelligence Scale: Mean Full-Scale IQ for the population of 81 volunteers was 122.60 (SD = 8.50), within the superior range of mental ability. Intellectual level was high, compared with the population in general, but consistent with the educational and occupational characteristics of the volunteers.

(b) Minnesota Multiphasic Personality Inventory: Mean transformed scores for the validity and clinical scales for these 81 volunteers were as follows: L — 47.93, F — 55.69, K — 57.94, Hs — 50.32, D — 52.38, Hy — 56.94, Pd — 58.36, Mf — 56.52, Pa — 54.43, Pt — 57.22, Sc — 58.96, Ma — 61.09, Si — 50.17, Es — 60.79. The profile for the group is within normal limits, but the group measure would tend to obscure individual scale elevations.

2. *Sex differences*

Separate analyses for men and women were done for marijuana and placebo conditions for the initial and second sessions of the low- and high-dose groups. Of the 136 Student's t-test comparisons for the low-dose group, significantly different scores were obtained by men in five instances and by women in two instances. The same number of t-test comparisons for the high-dose group revealed eight significantly different values for the males and 11 for the females. The very small proportion of significant differences and the even distribution of these differences between the sexes obviates the need for considering sex as a variable in the data analysis.

3. *General effects*

Table II (columns 1-3) presents the results of the analysis of variance for the low-dose group and Table III (columns 1-3) for the high-dose group. There were distinct and numerous significant differences in performance between the subgroups of volunteers assigned to the four experimental conditions, more so for the high dose group (11/13 tests and 20/32 variables) than the low-dose one (8/13 tests and 13/32 variables). Performance improved in the second session in a comparable manner for both dose groups, i.e. learning occurred in 6/13 tests and 15/32 variables for the low-dose group and 5/13 tests and 12/32 variables for the high-dose group. The high-dose group, however, showed a greater incidence of differential change within experimental conditions between sessions, i.e. significant improvement occurred in 8/13 tests and 16/32 variables for the high-dose group compared with 5/13 tests and 8/32 variables for the low-dose group.

4. *Drug effects on performance and learning*

Drug effect (marijuana compared with placebo conditions) on performance during the first session was noted frequently for the low-dose group, i.e. for 7/13 tests and 12/32 variables (Table II, column 4). The adverse effect on performance was, however, much more striking and generalized for the high-dose group, i.e. for 11/13 tests and 28/32 variables (Table III, column 4).

For the low-dose group, the drug state (marijuana compared with placebo conditions) did affect learning during the second session, but the extent of impairment of performance remained unchanged from that noted during the initial session, i.e. marijuana resulted in significantly different scores in 7/13 tests and 13/32 variables during the second session. For the high-dose group, there was also a drug effect on learning during the second session; although the extent of impairment of performance was less striking than in the first session, the impairment was still generalized and still significantly higher when compared with the low-dose group, i.e. marijuana affected 9/13 tests and 20/32 variables (column 5 of Tables II and III).

But the effect of drug state on learning during the second session was consistently unrelated to prior experience during the initial session, for both the low- and high-dose groups. Specifically, we were unable to demonstrate that the administration of marijuana compared to placebo during the first session resulted in a differential decrement in performance levels during the second session (column 6 of Tables II and III).

5. *Dose-effect relationships*

Of the tests and variables adversely affected by the drug in the first session, a dose-related decrement in performance levels was demonstrated for 4/13 of these tests and 16/32 of these variables. Of the tests and variables adversely affected by the drug in the second session, a dose-related decrease in performance was shown for 5/13 of these tests and 13/32 of these variables.

6. *Acute effects and cerebral dysfunction*

The presence of significant differences between marijuana and placebo conditions for various mental processes leads to one set of inferences and conclusions. But when these significant differences derive from scores which are usually associated with cerebral dysfunction, the inferences and conclusions may be more clinical in nature. The results of two tests of the Halstead Battery — Category (a measure of concept formation, visually mediated) and Tactual Performance Total

(a measure of form discrimination and spacial configuration, kinesthetically mediated) — illustrate this phenomenon (Table IV). Neither of these tests was found to be dose-related during the initial session, and only the Category test was dose-related during the second session. In comparing the findings of these two tests during the initial session with ascertained cut-off points (Table IV), it is evident that the result of the Category test is beyond normal limits for both marijuana dose groups while the score from the Tactual Performance test is outside normal limits for only the high-dose group.

Discussion

If one is to generalize from findings of a particular study, the dose level should be relevant to the sociocultural scene as well as to other laboratory studies that have employed marijuana in a standardized manner. The data regarding social usage of marijuana are very sparse. Le Dain,[12] after reviewing the literature, reported that in North America most users smoke less than 10 mg. Δ^9-THC to get "stoned". In Commission laboratory experiments, doses of about 6 mg. Δ^9-THC were smoked to produce "high effects". Our low dose of 4.8 mg. followed by an additional 2.4 mg. one hour

Table III
Neuropsychological results of F tests for high-dose group-analysis of variance

Test no.	Variable no.	Test name	Between groups	Between trials	Groups x trials	Marijuana effect during initial session†	Marijuana effect during 2nd session (unrelated)‡	Marijuana effect during 2nd session (related)¶
1	1	Category Test (err.)	5.61****	60.06****	2.17	26.40****	4.30*	0.01
2	2	Trail Making — A (time)	2.22	0.01	1.77	5.79**	8.42***	0.09
	3	Trail Making — B (time)	7.99****	4.16*	6.21****	18.95****	17.03****	0.04
	4	Trail Making — Total (time)	7.63****	2.86	5.65****	18.48****	18.23****	0.09
3	5	T.P.T. — Dom. (time)	0.75	44.32****	7.16****	16.77****	7.70***	0.14
	6	T.P.T. — Non-dom. (time)	1.23	14.35****	3.91***	11.57****	4.19*	1.43
	7	T.P.T. — Both (time)	1.76	15.47****	1.85	5.09*	3.08	0.49
	8	T.P.T. — Total (time)	3.71**	34.72****	6.27****	16.28****	7.28***	0.78
	9	T.P.T. — Memory (corr.)	2.50	6.25**	1.19	3.83*	0.80	0.13
	10	T.P.T. — Location (corr.)	1.27	12.73****	0.75	0.48	0.37	0.95
4	11	Seashore Tonal Memory (err.)	2.03	1.25	0.42	0.09	0.98	0.01
5	12	Sentence Repetition (corr.)	17.38****	3.63	5.58****	21.97****	3.25	1.43
6	13	Picture Recognition — Total (err.)	5.73****	2.26	3.10*	6.13**	7.58***	0.48
7	14	Visual Memory (err.)	9.33****	2.98	3.87***	15.19****	15.47****	0.15
8	15	Finger Tapping — Dom. (corr.)	5.59****	0.63	0.82	4.78*	6.58**	0.54
	16	Finger Tapping — Non-dom. (corr.)	3.02*	0.51	1.32	6.79***	5.85**	0.62
9	17	Foot Tapping — Dom. (corr.)	0.90	2.15	0.36	0.94	0.00	0.32
	18	Foot Tapping — Non-dom. (corr.)	0.99	0.98	0.40	2.12	1.64	0.07
10	19	Grooved Steadiness — Dom. (time)	2.94*	1.50	2.14	7.93***	5.45**	2.55
	20	Grooved Steadiness — Dom. (corr.)	2.68*	1.63	1.83	8.30***	5.00*	1.49
	21	Grooved Steadiness — Non-dom. (time)	1.58	1.08	0.66	8.34***	4.62*	0.30
	22	Grooved Steadiness — Non-dom. (corr.)	1.78	0.55	0.71	5.64**	9.21***	1.02
11	23	Maze Coordination — Dom. (time)	3.29**	1.39	2.30	10.87***	2.39	0.90
	24	Maze Coordination — Dom. (corr.)	4.14***	6.83***	2.72*	12.88****	2.06	1.60
	25	Maze Coordination — Non-dom. (time)	2.92*	5.83**	2.11	4.46*	2.66	0.09
	26	Maze Coordination — Non-dom. (corr.)	4.71***	4.58*	2.94*	4.67*	4.27*	0.11
12	27	Static Steadiness — Dom. (time)	2.85*	0.31	3.78**	19.57****	8.78***	1.56
	28	Static Steadiness — Dom. (corr.)	4.53***	0.10	4.31***	15.09****	11.78****	1.41
	29	Static Steadiness — Non-dom. (time)	1.61	0.29	6.20****	13.20****	18.49****	0.00
	30	Static Steadiness — Non-dom. (corr.)	4.70***	0.00	3.98***	10.16***	12.68****	0.06
13	31	Grooved Pegboard — Dom. (time)	25.39****	7.53***	7.64****	25.24****	2.50	0.29
	32	Grooved Pegboard — Non-dom. (time)	16.28****	2.12	3.64**	18.47****	2.69	0.06

*P < 0.05; **P < 0.02; ***P < 0.01; ****P < 0.001
†$(M_1M_2 + M_1P_2) - (P_1M_2 + P_1P_2)$
‡Marijuana effect during second session unrelated to experimental condition in initial session $(M_1M_2 + P_1M_2) - (M_1P_2 + P_1P_2)$
¶Marijuana effect during second session related to experimental condition in initial session $(M_1M_2 - M_1P_2) - (P_1M_2 - P_1P_2)$

later is therefore comparable with Le Dain's definition of socially relevant dose. Data are, however, available regarding the use of higher dose levels in studies. Some of the more credible investigators in the field, such as Weil, Zinberg and Nelsen[5] and Dornbush, Fink and Freedman,[11] used 18 and 22.5 mg. Δ^9-THC, respectively (delivered by smoking). Our high dose of 9.1 mg. followed by an additional 4.5 mg. one hour later falls far short of doses defined as high by some laboratory investigators. Furthermore, questionnaire data currently being analyzed regarding amount of marijuana used socially indicate that our high dose is relevant to the social scene.

Another crucial factor that must be considered within the context of generalization is the nature of the sample studied and the relationship of this sample to the population about which one wishes to generalize. The mean age of our research sample was 22.51 years (SD 2.81, range 19 to 31), which is consistent with the ages of individuals in our society who are the primary users of soft drugs. Male and female subjects were selected on an approximately 1:1 basis (38 men and 43 women), as women are purportedly becoming involved in almost as much experimentation with soft drugs as men (De Fleur and Garrett[19] — male:female, 1:1; Goode[20] — male:female, 3:2). Our study sample was heavily skewed towards subjects with university education and higher occupational status, which again is consistent with the subjects included in current reports on marijuana.

The even distribution of the very limited number of significant differences of men compared with women on the neuropsychological tests, for the low- and high-dose groups, leads us to conclude that there are no discernible sex differences with respect to the effect of marijuana on mental processes. The Mayor's Committee on Marijuana[3] found test results for their female subjects that were not entirely similar to those obtained for the men, but only five women were included in the study and their performance showed great variability. Of more recent investigators, only Abel[8] included female subjects, and Hollister and Gillespie[14] included one female subject. There was no mention of sex differences in these articles.

The dose of marijuana defined as high (9.1 mg. Δ^9-THC reinforced by an additional 4.5 mg. one hour later) administered during the initial session resulted in significant impairment in all four mental processes and, furthermore, the effect was generalized to all modalities (visual, tactile and auditory). It is noteworthy that the dose of marijuana defined as low (4.8 mg. Δ^9-THC reinforced by 2.4 mg. one hour later) also resulted in significant impairment in these four mental processes and all modalities. There were, however, some selective differences in the pattern of impairment between the low- and high-dose groups. Concept formation (Category, Trail Making) was as adversely affected by the low dose of marijuana as by the high dose. Memory, on the other hand, was selectively affected only by the low dose; specifically, tactile short-term memory (Tactual Performance) and auditory immediate memory of notes (Seashore Tonal Memory) were not affected, but auditory immediate memory of meaningful information (Sentence Repetition) was significantly impaired. Whereas visual immediate memory (Picture Recognition) was unaffected, the more complex form of visual immediate recall — measure of retroactive interference on retention and recall (Visual Memory) — was significantly impaired. Tactile form discrimination (Tactual Performance) was also selectively impaired. But the most striking reduction in effect in the low- compared with the high-dose group was evident in the motor sphere. Specifically, of the five tests and 16 variables impaired in the high-dose group, only the two steadiness tests and four variables (Grooved Steadiness, requiring gross visual-motor coordination, and Static Steadiness, requiring fine visual-motor coordination) were impaired in the low-dose group.

The same trend was noted for the second compared with the first session, the second session having been purposefully included to measure learning or practice effect. For the high-dose group, concept formation remained significantly impaired. There was, however, sufficient learning with respect to auditory memory of meaningful information (Sentence Repetition) so that this variable did not discriminate between marijuana and placebo conditions. Both tests of visual memory remained impaired. Tactile form discrimination was somewhat less affected by learning (three instead of four variables were significant). The improvement due to learning was proportional in the motor tasks (11 instead of 16 variables were significant). For the low-dose group there was a differential learning effect on concept formation, in that Trail Making but not Category remained significantly impaired. It should be noted that the Category test is the more pointed and powerful test of reasoning. With respect to memory, auditory immediate memory of meaningful information remained significantly impaired (Sentence Repetition) as did visual recall involving retroactive interference (Visual

Table IV
Mean scores of Category and Tactual Performance tests for low- and high-dose marijuana groups

Test	Session	Placebo	Marijuana low-dose	Percent of change	Marijuana high-dose	Percent of change	Cut-off point
	First	−35.91	−53.28****	48	−56.71****	58	51 or more
Category							
	Second	−17.59	−18.65	6	−25.41*	25	—
Tactual	First	−11.32	−13.82*	22	−16.70****	47	15.7 mins.
Performance							or more
Total	Second	− 6.65	− 9.95**	49	−10.26***	54	—

*P < 0.05; **P < 0.02; ***P < 0.01; ****P < 0.001

Memory). Tactile discrimination also remained apparently unchanged in terms of impairment. The extent of impairment in the motor sphere increased during the second session (from four to six variables). This could possibly be explained on the basis of order effect, in that these particular tests may have been readministered at a time of maximal drug effect. Another possible explanation is variability within data for these two tests.

How can one account for such disorganization, transient in nature, in terms of a brain-behaviour model? Melges *et al*[15] referred to the effects of marijuana on cognitive operations as temporal disintegration, relating the disintegration of sequential thought to impaired immediate memory. The present study found the disintegrative effects to be more generalized. Whereas most problems in concept formation involve the effective use of stored information, one could not account for the rather profound impairment in concept formation noted in this study for both the low- and high-dose groups during the initial session solely on the basis of memory impairment. The decrement in performance levels of motor tasks is unrelated to memory impairment. One would accordingly have to posit a drug-related effect on the individual's central integrative processes, the disturbance in brain function being transient in nature. A finding that merits further investigation is the extent of disorganization in concept formation, as reflected by the Category test, and the low threshold for disorganization in terms of dose of marijuana. Whereas the scores on the Category test were beyond the cut-off point and within the cerebral dysfunction range, further generalizations would be unwarranted at this point.

The effects of marijuana on learning as well as on memory might be explained by the same model. Learning refers to a change in behaviour which is brought about through practice, and the second session in this study was designed to measure learning. Memory involves three stages — input (registration), storage (retention) and output (recall). One must then distinguish those drug effects on learning that are due to effects on memory storage from other effects due to attentional, perceptual and motivational influences. Regarding memory, output (recall) can fail because the subject cannot adopt the set that will enable him to make the appropriate response available to him. Inappropriate set can occur at time of input (registration) or on occasion of output (recall), and independent of registration. In the present study, marijuana effects on mental processes were noted on re-examination (during the second session), but we were not able to demonstrate by statistical analysis that these drug effects were related to prior experimental conditions (marijuana or placebo administration during the initial session). Whereas the drug has a demonstrable effect on learning, the influence on learning is unrelated to prior experience. Furthermore, the impairment noted during the initial session could not have been due to faulty acquisition or a faulty set at time of input, as these would have precluded other stages of memory and subsequent learning. The impairment must therefore be in the storage or output processes, more probably the latter in view of lack of interference with learning regardless of prior experimental conditions.

How does one now reconcile generalized disintegrative effects during the initial session with transfer of sufficient information to ensure learning during the second session? One possible explanation is that the information was coded into storage during the initial session but the output was faulty, due to interference with central integrative processes. The interference was, however, transitory and by the time the subject appeared for the second session the previously learned information was available to the same extent as for the group who received placebo during the initial session. The readministration of the drug still resulted in a generalized impairment of mental processes, but to a lesser extent for the particular mental processes due to prior experience (with marijuana or placebo) and learning. The model of learning proposed in this paper is different from the one suggested by Abel[8] who, in his studies of the effects of marijuana on memory, concluded that marijuana affects concentration and input of information and, as a result, storage and adequate recall are precluded. Corroborative evidence regarding identification of output (recall) as the process most directly affected by marijuana will be presented in the following paper, entitled "The neurophysiological basis of the marijuana experience".

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Retrospect

Dangerous drugs

From one who has made a close study of this subject we are told that in Canada and the United States the illicit use of opium, morphine, cocaine and heroin is becoming an international calamity. Rarely a day passes but one reads in our press of an increasing number of addicts and pedlars who come before our magistrates for offences against the Opium and Drugs Act. For the 12 months ending March 31st, 1922, the Federal Government alone prosecuted 23 doctors, 11 druggists, four veterinary surgeons, 165 illicit dealers and 634 Chinamen, making a total of 835 convictions. These figures do not include provincial and municipal convictions. The municipal convictions for Vancouver in 1921 were 858, and in Montreal for the 11 months of 1922, 646. The estimated number of drug addicts in Canada and the United States is 2,000,000 . . . .

Provision must be made whereby those convicted as addicts may be treated not so much as prisoners, but as people diseased, in the almost forlorn hope that some may be permanently cured, and with the knowledge that in confining the addict they are to some extent preventing the making of others, and certainly suppressing crime, for 85% of narcotic prisoners have criminal records . . . .

The experience of the clinic recently established and now discontinued in New York City, has conclusively proven that the so-called ambulatory or slow reduction method of cure was practically useless . . . .

It has on the other hand been demonstrated that the sudden withdrawal method will cure these unfortunates. — A. K. Haywood: Editorial. Can Med Assoc J *13: 54, 1923.*