emplacement rather than from ejecta from the mare basin, there is no need to invoke multiple major impacts as part of the process of formation of the Mare Imbrium–Oceanus Procellarum complex. The irregular western boundary of Oceanus Procellarum is evidence that its configuration is the result of topography rather than excavation. Whether the highland radioactivity is the result of emplacement or ejecta, what seems clear from these observations is that the radioactive material was a major component of the excavated basin as well as of the subsequent lava flows which filled the basin and the surrounding regions of lower elevation.

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Cannabis and Temporal Disintegration in Experienced and Naive Subjects

Abstract. *The effects of 3.3 and 6.6 milligrams of Δ^9-tetrahydrocannabinol and of placebo on performance of three cognitive tasks were compared for naive subjects and experienced cannabis smokers. No differences in performance or reported subjective effects were found between these two groups. A significant decrement was found following dosage at both levels, replicating earlier findings of temporal disintegration during cannabis intoxication.*

Behavioral tolerance to the effects of cannabis intoxication has frequently been claimed by experienced users of the drug (*1*, *2*) and has recently received some support from experimental data. Prolonged administration of Δ^9-tetrahydrocannabinol (Δ^9-THC) to pigeons has resulted in evidence of behavioral tolerance (*3*). Weil *et al.* (*4*) found a difference in the performance of experienced and naive subjects after smoking cannabis on two of the three performance tasks employed. They did not, however, control for practice effects for the experienced users, so the lack of performance impairment for these subjects cannot be considered definitive evidence for behavioral tolerance. Two further studies using human subjects have investigated the experience variable (*5*, *6*). Both of these studies compared casual users with heavy users of cannabis and found trends toward less impairment of heavy users' performance, although only one of the eight tasks used in the two studies showed a significant difference between the two groups.

In the present study, performance of naive and experienced subjects was compared on three cognitive tasks, previously shown to be impaired after oral ingestion of cannabis (*7*). While a significant dose-related impairment occurred in two of these tasks, indicative of temporal disintegration, no significant differences in performance between the two groups were found. There was also no difference in reports by experienced and naive subjects of subjective effects experienced during intoxication.

The basic task investigated was the Goal Directed Serial Alternation task (GDSA), a task which required the subject to simultaneously hold in mind and coordinate information as well as perform mental operations relevant to pursuing a goal. The subject was assigned a starting number in the range 106 to 114 and asked to subtract 7 and then add either 1, 2, or 3 and to continue such alternate subtraction and addition until the initially assigned goal number was reached. Two other simpler tasks were employed to measure short- and long-term memory during cannabis intoxication. These were the Serial Subtraction of Seven task (SSS) which required subjects to repeatedly subtract 7 from an assigned starting number, in the range 96 to 104, until zero was reached, and finally, the Digit Span (DS), both backward and forward. There was a significant dose-related decrement in performance after smoking cannabis for both experienced and naive subjects on both the GDSA and the SSS, and no impairment in the performance of either group on the DS both backward and forward.

Eighteen male volunteers were screened by a psychiatric interview and a psychological test before taking part in the study. Nine of these had no experience with cannabis and nine had histories of smoking cannabis socially, ranging from 18 months to 10 years (median, 3 years). Frequency and regularity of use fluctuated considerably and varied within the group from about once a month to three times a week (median, once a week). The two groups of naive and experienced subjects were matched with regard to age and education.

The placebo material was prepared by extracting leaf in a Soxhlet apparatus with hexane for 3 hours. This gave material with smell and taste very similar to those of the active leaf. This placebo material was generally accepted as a low dose of cannabis during the experimental session. Cigarettes containing 500 mg of active leaf material, 250 mg of active leaf material, or placebo material alone were prepared with a hand rolling machine. The active leaf was sandwiched between placebo material so that no active leaf was lost during lighting or left in the unsmoked butt. The total leaf content of all cigarettes was 700 mg. The ciga-

Table 1. Mean performance following the three administrations for experienced (E) and naive (N) subjects. The results were tested by using two-way analyses of variance. The F values are for the drug-level effect. The between-groups effects were nonsignificant for all four measures. N.S., not significant.

Dose of Δ^9-THC (mg)	Measure							
	GDSA		SSS		DS forwards		DS backwards	
	E	N	E	N	E	N	E	N
0.0	117.6	163.9	63.7	57.8	6.8	6.6	5.4	4.6
3.3	178.9	195.7	67.6	74.0	6.3	6.2	5.1	4.4
6.6	229.1	230.4	84.2	69.4	6.4	6.3	4.9	4.6
F values	5.32		3.80		0.92		1.18	
P values	<0.01		<0.05		N.S.		N.S.	

rettes were sealed under nitrogen and frozen at −20°C until required. To assist handling, cigarette-holders were used which enabled the cigarette to be smoked to within 6 mm of the end. The Δ^9-THC content of the plant material was assessed by gas chromatography with a sample of Δ^9-THC supplied by the United Nations Office at Geneva. The Δ^9-THC content was 1.32 percent, giving a THC content of 6.6 mg in the high-dose cigarette and 3.3 mg at the low dose. The dose levels used in this experiment, while low relative to other experimentation, should be interpreted in the light of the finding (*5*) that casual and heavy users, when asked to smoke cannabis cigarettes to achieve their usual social "high," smoked cannabis containing an average dose of 3.6 mg of Δ^9-THC and reported themselves to be "very high." Jones (*6*) has estimated that five smokers may share a cigarette containing only 10 mg of Δ^9-THC in a social setting and obtain satisfactory subjective effects. The dose levels of 3.3 and 6.6 mg used in this experiment are therefore relevant to the social use of the drug.

Using a double blind design the placebo and two dose levels of cannabis were administered in counterbalanced order on three different testing occasions separated by approximately 1 week. Subjects were asked not to use any drugs, including alcohol, on the day of testing. Both subject and experimenter knew cannabis was to be administered but did not know the order of administration. A standard, paced method of smoking was used in which each inhalation was held for 30 seconds. The naive subjects were all tobacco smokers and able to inhale. A highly significant ($P<.001$) dose-related effect of cannabis on pulse rate indicated that a good proportion of the cannabis was absorbed. An increase in pulse rate has consistently been reported to be an effect of cannabis (*5*, *8*, *9*). There was no difference in pulse rate between the naive and experienced group and no significant increase in pulse rate after smoking the placebo. Baseline testing was carried out at the beginning of each session and each subject was tested three times on each task before the drug was administered and three times after smoking the cigarette. The order was always GDSA, SSS, and DS. Administration and scoring of the tests was according to the method of Melges *et al.* (*7*), which gives equal weight to both time taken and errors made, and takes the best performance of each subject during the testing session.

No significant difference in performance was found between the naive and experienced subjects on any of the three cognitive tasks employed. Similar results obtained on a visual vigilence task are being reported elsewhere (*10*). This is a surprising finding in view of frequent claims of experienced users that it is possible to suppress the effects of cannabis (*1*, *2*) and the experimental data which support these claims (*3–6*). In view of the inconsistent results of previous experiments it may be that only certain types of tasks both show impairment in the naive subject and allow for compensation by the experienced user, and the tasks used in this experiment may not cover this area. It is also possible that the present negative finding reflects a lack of motivation on the part of the experienced users to compensate for the drug effects, a procedure which seeems to require conscious effort and which observers have reported will interfere with the pleasurable effects of being high (*11*). The experienced subjects tested were certainly overtly unconcerned with their failures, being amused rather than worried. Grinspoon (*1*) suggests that while an experienced user may feel unmotivated, this may be dispelled by encouragement, and performance will then return to predrug level. Studies of the motivation variable with experienced subjects in laboratory settings are clearly needed.

The results on the GDSA (see Table 1) confirm the previous finding by Melges *et al.* (*7*) of a dose-related impairment during cannabis intoxication. The results on the SSS, unlike those of Melges *et al.* (who used a smaller sample), reached a statistically significant level, indicating impairment either in the long-term memory operations involved in the task, or in the subjects' ability to maintain sustained attention.

The decrements obtained on both the

Table 2. Numbers of subjects in each group reporting variables changed following administration of cigarettes containing placebo material, 3.3 mg of Δ^9-THC, or 6.6 mg of Δ^9-THC.

Variable	Naive ($N=9$)			Experienced ($N=9$)		
	0 mg	3.3 mg	6.6 mg	0 mg	3.3 mg	6.6 mg
Perception	2	4	7	2	7	5
Memory	3	6	6	4	6	7
Color	1	2	3	2	2	3
Attention	3	7	8	4	9	9
Visual imagery	1	9	9	4	6	8
Sound	1	4	7	3	7	7
Time	5	5	6	4	7	8
Auditory imagery	0	3	4	3	7	8
Touch	1	5	8	1	4	5
Thought processes	3	9	7	6	8	9
Physical relaxation	3	8	8	5	7	7
Emotions	1	2	6	3	4	7
Autonomy (self-control)	0	2	6	0	2	5
Sense of self-identity	1	3	4	0	4	5

GDSA and the SSS, when compared with the findings of Melges *et al.*, confirm the far greater potency of Δ^9-THC when smoked than when orally ingested. This comparison gives a 5 or 6 : 1 potency ratio of smoked to orally ingested material as compared to the 2 or 3 : 1 ratio found by Isbell *et al.* (*12*) using subjective reports and pulse rate. The exact procedure used in the smoking method of administration is not given by Isbell, and it is possible that a larger butt remained unsmoked by his subjects than in the present experiment. Foltz *et al.* (*13*) have reported that up to 21 percent of Δ^9-THC is trapped in the butt during smoking. Isbell's subjects may therefore have absorbed proportionately less of the given dose than the subjects in the present study and this could account for the apparent difference in the relative potency of the smoked and ingested material. It is also important to note that Isbell's criteria of potency differed from ours (decrement on GDSA and SSS).

The results on the DS do not confirm Melges *et al.*'s finding of impairment (*14*). Previous investigations have also found no evidence of decrement on simple digit span (*8, 11*). Waskow *et al.* (*8*) used an oral dose of 20 mg of Δ^9-THC (equal to the lowest dose of Melges *et al.*) and showed no impairment on DS but found a significant decrement on a serial addition task which corroborates the impairment on the SSS obtained in this experiment. The results obtained support conclusions previously drawn (*4, 8, 11, 15*) that doses of cannabis up to 10 mg smoked and 20 mg ingested do not significantly impair simple tasks of short duration such as the DS, whereas more complex tasks involving both short-term memory and serial manipulation of information are impaired.

Reports of subjective effects were obtained at the end of each experimental session by ratings of the strength of the cigarette smoked, the extent of its effect, and which, if any, of 14 variables (see Table 2) had been affected. There was a significant effect of dose level upon ratings both of the strength of the cigarette ($P < .001$) and of subjective effect ($P < .001$), with the 6.6 mg dose being judged the strongest and as having the greatest effect. The placebo was rated as weakest and having least effect but only two subjects (one experienced and one naive) rated themselves as "in no way changed." The number of variables rated as affected, indicating alterations in the subject's state of consciousness, was also significantly related to dose level ($P < .001$). There was no significant difference on any of the rating scales between the naive and the experienced subjects, although there was a slight tendency, in all three conditions, for the experienced subjects to rate more variables as affected than naive subjects. After smoking the placebo material the experienced subjects reported a greater effect on the variables of visual imagery, auditory imagery, and thought processes, than the naive subjects, presumably reflecting the importance of past learning experiences on the induction of cannabis effects. Generally there was little difference between the particular variables rated as affected most frequently by the two groups of subjects.

This finding of approximately equal subjective effects reported by the two groups seems at variance with previous reports that the majority of first-time cannabis users do not become "high" (*1, 4, 5*). However, these results do not rule out the possibility of differing experiences of the naive and experienced subjects. Becker (*16*) suggested that once a person has recognized alterations in his state of consciousness, he has still to learn to interpret such changes as pleasurable. Four subjects in each group were given a card-sorting task which included the adjective "euphoric." All four of the experienced subjects reported themselves as euphoric at both dose levels (after sitting alone in a dark room with no stimulation whatsoever while the electroencephalogram was recorded). Two of the naive subjects reported themselves as euphoric after the 3.3 mg dose and only one after the 6.6 mg dose.

A second possible explanation for this novel finding of equal subjective effects is the type of rating scale employed in this study. The variables used were chosen from those quoted by Tart (*17*) as most consistently reported by experienced cannabis users as changed in some way during cannabis intoxication. This may have formed a more "natural" rating scale than the clinical rating scales often employed by previous investigators, which may fit the experimenters' assumptions better than the users' experience. By using this "natural" rating scale we may have directed the attention of our naive subjects toward the cannabis effects and thus partially trained them in a way which previous studies are unlikely to have done.

Temporal disintegration, that is, the inability to keep track of goal-relevant information over time, as measured by the GDSA has been demonstrated in this study to be a consequence of cannabis intoxication within the range expected to occur following social use of the drug. Melges *et al.* (*18*) have shown temporal disintegration to be correlated with some of the subjective alterations in the state of consciousness induced by cannabis. In the present study equal subjective and behavioral effects were measured in both naive subjects and experienced users of the drug.

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