although it is initiated in the spleen and lymph nodes it is reduced and short lived. After a second inoculation the response in the spleen of smoked animals was again reduced (particularly the indirect p.f.c.). The secondary response in the lungs is delayed longer than a normal primary response but resembles a secondary response in magnitude but with a greater participation of direct p.f.c. We found no acceleration of the secondary response in the lymph nodes, and although there is some increase in both direct and indirect p.f.c. the direct p.f.c. predominates.

The degree of reduction of the response seems to be related to the distance of the organ from the primary point of entry of the cigarette smoke. The immunosuppression recorded may well explain the increased susceptibility of smokers to respiratory infections. If immune surveillance[11] has a role in the elimination of cancer cells, then irrespective of any carcinogenic activity of cigarette smoke, damage to lung immunity may allow the escape of the cancer cell from a basic control mechanism.

This work was supported by a grant from the Australian Tobacco Research Foundation. We thank Miss L. Roberts and Mrs M. B. Hart for assistance. W. T. is the recipient of a CSIRO studentship.

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Received January 3, 1973.

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State-dependent Effects of Marihuana on Human Memory

THE abuse potential of marihuana has been widely debated as the use of the drug has increased in Western countries. Overton[1] has suggested that the abuse potential of various drugs may parallel their capacity for producing "state-dependent" effects in animals and man. State-dependent or "dissociated" learning refers to a phenomenon observed in animal and human studies wherein certain behaviour learned in particular drug states transfers more readily when the same drug state is reintroduced than if subsequent testing occurs under the influence of another drug or in a non-drug state[2–8]. This phenomenon has been demonstrated primarily with sedative and hypnotic drugs, such as barbiturates and alcohol, which are relatively susceptible to abuse. In general, drugs with little abuse potential (for example phenothiazines) dissociate weakly or not at all[1].

Barry and Kubena[9] have shown that Δ^9-transtetrahydrocannabinol produces state-dependent effects in rats. In the study reported here we examined the effects of smoking marihuana on various tasks, to see whether the drug produces state-dependency in man. If Overton's hypothesis is correct, detection of state-dependent effects from marihuana would be associated with its possible abuse potential.

Thirty-two men between the ages of 21 and 30 were paid to participate in a training session (day 1) and a test session (day 2) separated by 24 h. All subjects were screened for inclusion in the study using a structured medical and psychiatric interview. No subjects showed evidence of medical or psychiatric illness. All were experienced marihuana smokers; more than half had smoked during 4 or more years at least once a week. None had used marihuana or other drugs for at least 48 h before the experiment. The study was run single blind; that is, the subjects were not told that a placebo would be given. In most cases subjects given placebo were unaware they were receiving it. Because of the objective nature of the tasks, it was not necessary that experimenters be unaware of what subjects received.

Subjects were randomly assigned to one of four groups. One group (MM) received marihuana on both days. A second group (PP) received marihuana placebo on both days. A third group (MP) received marihuana on day 1 and placebo on day 2. A fourth group (PM) received placebo on day 1 and marihuana on day 2. This factorial design permitted analysis of drug, day and change-state effects. The change of state effect (F value) is reported in Table 1.

Table 1 Mean Errors and F Values for Change of State

Task	Day 2 – mean errors				F value
	PP	PM	MP	MM	
Ordered object recall	0.25	3.13	2.88	1.13	12.46*
Avoidance	14.25	13.88	15.38	10.88	0.64
Word association	0.50	2.50	1.25	3.13	0.01
Word strings					
Type *a*	0.69	1.75	1.32	0.94	1.00
Type *b*	2.19	3.07	2.19	2.37	0.15
Type *c*	1.94	2.75	2.62	2.00	0.63
Type *d*	3.06	4.82	6.19	3.94	5.78†
Types *a–d* (combined)	20.50	17.56	20.06	20.00	1.00

Data are based on analysis of four groups of eight subjects each. The first letter refers to the condition on day 1 and the second letter refers to the condition on day 2.
*$P > 0.01$.
†$P > 0.05$.

The marihuana contained 1.5% (−)-Δ^9-transtetrahydrocannabinol (THC) whereas the placebo consisted of marihuana with THC removed. Both drug and placebo were obtained from the National Institute of Mental Health. The marihuana was equivalent in strength to "street" marihuana imported into the United States from Mexico.

The procedure used in combusting and administering the smoke was similar to that used by Renault *et al.*[10]. A 9 l. spirometer (Collins Spirometer) with attached crucible was used. A 1 g sample of placebo or marihuana was burned in the crucible by pulling air through the material as the inner bell of the spirometer was raised, trapping the smoke in the bell. The crucible was then removed and replaced by a rubber mouthpiece. Subjects were instructed in the method of breathing to be used, consisting of inhalation for 5 s, holding the breath for 15 s, and resuming normal breathing for 35 s. This sequence was repeated until three canisters of smoke were inhaled; this required about 15 min. Testing began 15 min after smoking finished.

Tests included a visual avoidance task; a word association recall task; a verbal learning task measuring memory for "word strings" of varying degrees of meaningfulness, and a test measuring recall of ordered objects. Tests were given in a counter-balanced order during a period of 1 h. All tests except the visual avoidance task were designed to measure positive

transfer of learning from day 1 to day 2. The avoidance task measured interference or negative transfer. Where positive transfer is measured, dissociative learning is suggested when mean error scores in the same-state groups are lower than in the change-state groups. In the avoidance task, designed to measure negative transfer, dissociation would be reflected by fewer errors in the change-state groups than in the same-state groups.

In the avoidance task, four patterns of lights were randomly presented. Each pattern could be extinguished by a specific switch controlled by right and left hands and feet. An incorrect response or failure to respond within 3 s resulted in presentation of a noxious tone. The criterion was twenty correct responses, with number of errors to reach criterion taken as the measure of performance. The task was identical on both days, except that on day 2 the pattern-switch relation was altered. Thus, performance on day 2 was assumed to reflect interference; that is, the greater the number of errors on day 2, the greater the degree of interference.

The rote learning task involved memorizing four five-word "word strings" of varying meaningfulness (normal sentence, anomalous sentence, anagram and word list)[11]. On day 2 subjects were asked to recall the word strings memorized on day 1 after which a relearning session was conducted. The following word strings were used. (*a*) The normal sentence was: "Soapy detergents dissolve greasy stains"; (*b*) the anomalous sentence was: "Pink accidents cause gallant storms"; (*c*) the anagram was: "Neighbours sleeping noisy wake parties"; (*d*) the nonsense word list was: "give odours snows fatal violent". Performance was measured in terms of errors of sequence and omission.

For the word association test, twenty words of low association value[12] were presented. Subjects were instructed to respond to the stimulus words with the first word that came to mind. On day 2 the stimulus words were repeated and subjects were asked to recall their responses on day 1. Performance was measured in terms of errors made in day 2 recall.

In the object recall test subjects were shown seven plastic objects from the Kahn test of symbol arrangement[13]. They were asked to name each so that subsequent deficits in recall presumably would reflect memory loss rather than inattention. The subjects were then asked to order the objects from left to right. On day 2 subjects were asked to recall the seven objects and then arrange them in the same order as on day 1.

All measures of performance were subjected to 2 by 2 factorial analyses of variance. Table 1 presents the interaction F values for the four tasks and the mean errors for each group. The interaction effect tests the marihuana state change effect. Thus, any significant interaction may be taken as evidence of dissociation.

As Table 1 shows, the recall of ordered objects showed a significant interaction effect ($P<0.01$). The dissociative effect arose from the MP and the PM groups making more errors than either the PP or MM groups. Analysis of simple principal effects indicated that both the PM and MP groups differed significantly from the PP group ($F=9.63$, $P<0.01$; and $F=8.03$, $P<0.01$, respectively). Also, the PM group differed significantly from the MM group ($F=4.66$, $P<0.05$).

Neither the avoidance task nor the word association task revealed a significant interaction effect. In the word string task, with errors analysed by type of string, there was evidence of dissociation for the type *d* string (Table 1) in which both syntax and meaningfulness are missing. The other three types of word strings provided these cues. The normal sentence provided both syntax and meaningfulness, while the anomalous sentence provided syntax, and the anagram provided meaningfulness

Although an interaction effect was not found in the word association task, a significant drug effect was evident ($F=8.73$, $P<0.01$). Thus, marihuana disrupts memory for self-generated word associations, though this effect is no more pronounced in the change-state groups than in the same-state groups.

The significant results found in the ordered object recall and the type *d* word string (Table 1) suggest that tasks involving sequential memory may be most sensitive to dissociation. The lack of dissociation found for the *a*, *b*, and *c* type word strings may be explained by the fact that recall of the sequence is aided by long term memory for sentence structure or meaningfulness of words. In contrast, the type *d* string must be recalled sequentially without the aid of either. This task seems to have much in common with sequential recall of the plastic Kahn objects, where meaningfulness also plays an insignificant role.

The results of the present study suggest that marihuana produces "state-dependent" learning when tasks sensitive to dissociation are used. In other studies of state-dependent learning, using other drugs, similar differential effects were found, depending on the task and the drug administered. Other investigators have reported disruptive effects of marihuana on tasks involving sequential adjustments in reaching a goal[14].

If the abuse potential of drugs parallels their capacity to produce state-dependent or dissociated learning, as Overton[1] has suggested, then one must conclude that marihuana has an abuse potential. However, the degree of dissociation obviously varies as a function of task variables in addition to any correlation it may show with abuse potential.

This work was supported in part by grants from the US Public Health Service, and a research scientist development award from the National Institute of Mental Health to D. W. G.

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Received December 18, 1972; revised March 5, 1973.

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Survival of Common Bacteria in Liquid Culture under Carbon Dioxide at High Temperatures

WE report results which are at variance with the general belief that high temperatures are necessarily lethal to microorganisms[1]. *Escherichia coil* B, *Aerobacter aerogenes*, *Bacillus subtilis*, and *Serratia marcescens* were found to survive for 24 h in a CO_2 atmosphere at a temperature of up to 160° C. These organisms were routinely cultured in sterile trypticase soy broth (TSB) medium, and plated on TSB plates containing 1.5% of agar.