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16. Abstract

Marihuana, or its principal active ingredient, delta-9-tetrahydrocannabinol (Δ^9-THC), impairs performance on complex behavioral tasks in animals and man. Although there exists some evidence that altitude-induced hypoxia potentiates the physiological effects of marihuana, the interaction between altitude and marihuana on behavioral tasks has not been established. In the absence of evidence that use of marihuana is less frequent among members of the aviation community than among the general population, it was necessary to evaluate the effects on performance of any interaction between hypoxia and marihuana. Two baboons were trained to perform on a delayed matching-to-sample task at ground level and altitudes of 8,000 and 12,000 feet. The animals were orally administered doses of Δ^9-THC, ranging from 0.25 to 2.0 mg/kg, 2 hours prior to experimental sessions at each altitude. No effects on accuracy of matching performance were observed for any of the drug doses or altitudes used. Amount of work output, as measured by number of trials completed and speed of responding, was not affected by Δ^9-THC at ground level but was markedly reduced by the higher drug doses at the 8,000- and 12,000-feet altitudes. This interaction suggests that the behavioral impairment produced by marihuana can be potentiated by hypoxia.

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INTERACTION BETWEEN MARIHUANA AND ALTITUDE ON A COMPLEX BEHAVIORAL TASK IN BABOONS

I. Introduction.

It is now widely established that marihuana, or its principal active ingredient, delta-9-tetrahydrocannabinol* (Δ^9-THC), impairs performance on complex behavioral tasks in animals and man.[7] Although there exists some evidence that altitude-induced hypoxia potentiates the physiological effects of marihuana,[4] the interaction between altitude and marihuana on behavioral tasks has not been established. In the absence of evidence that use of marihuana is less frequent among members of the aviation community than among the general population, it is necessary to evaluate the effects on performance of any interaction between hypoxia and marihuana. To this end, we chose to study this interaction in a complex performance task at ground level and at two commonly experienced altitudes.

II. Method.

A. *Subjects.* Two female adolescent baboons (Eva and Zsa), between 3 and 5 years of age, served as subjects. Normal free-feeding weights were approximately 10.2 kg for Eva and 10.4 kg for Zsa. Experimental sessions were run on weekdays only and at the same time each day. The animals were fed after every experimental session and at equivalent times on weekends when no experimental sessions occurred. The amount fed each animal was adjusted to maintain approximately 95 percent of its free-feeding weight, with the exception that food allotments were not reduced during the weight increase of the turgescent phase of the menstrual cycle. Both animals were experimentally naive and had no previous drug experience.

B. *Apparatus and Drug.* The living cages of the baboons were modified to hold an intelligence panel containing three Plexiglas response keys. The sample response key was positioned in the upper center of the intelligence panel. Two choice response keys were mounted below and to either side of the sample response key. A three-color (red, white, or green) lamp unit was mounted behind each response key. Reinforcement consisted of a 750-mg Noyes banana pellet delivered into a foodwell located near the bottom center of the intelligence panel.

The Δ^9-THC used in the experiment was obtained in a dehydrated alcohol solution from the National Institute of Mental Health (batch SSC 79124). The drug was stored in a darkened refrigerator until just before each use. Drug doses of 0.25, 0.5, 1.0, or 2.0 mg/kg were given orally in a vehicle consisting of Tang, molasses, sesame oil, and butyl acetate. Approximately 0.10 cc of ethyl alcohol was added to the vehicle on all nondrug days.

C. *Procedure.* Both baboons were trained to perform on a delayed matching-to-sample task. Under this task, the sample response key was illuminated at the beginning of each trial with one of the three colored lights. Ten responses to the sample response key were required to turn off the sample key light and initiate a delay period. The delay period was 0.1 second for Eva and 20 seconds for Zsa. Responses made to the unilluminated response keys during the delay period had no effect on the experimental contingencies. At the end of the delay period, the two choice response keys were illuminated

* Synthetic Δ^9-trans-tetrahydrocannabinol was obtained by approval of the FDA-NIMH Psychomimetic Agents Advisory Committee. The animals used for this experiment were lawfully acquired and treated in accordance with the "Principles of Laboratory Animal Care" issued by the Animal Facilities Standards Committee of the Animal Care Panel, United States Department of Health, Education, and Welfare, Public Health Service, March 1963.

with different colors. One of the choice response keys matched the color of the previously illuminated sample response key, and the other was one of the two remaining colors. The positions of matching and nonmatching choices and the colors of the sample and nonmatching choice were randomly determined for each trial. A correct response to the matching choice key was reinforced. Any choice response, correct or incorrect, immediately extinguished the choice stimuli and terminated the trial. In addition, if a choice response had not occurred within 45 seconds of the onset of the trial, the trial was terminated even if sample responding had been completed. Trials occurred at a rate of one per minute and had a minimum intertrial interval of 15 seconds. Responses during the intertrial interval had no experimental effect. A total of 90 trials was presented each session.

The baboons were orally administered either the drug or the vehicle alone 2 hours before the start of each matching-to-sample session. Although each drug session was preceded by at least two nondrug (vehicle alone) sessions, only the session immediately preceding the drug session was used for analysis of the nondrug condition. One hour before the start of the session the animals were placed in an altitude chamber and adapted to the altitude assigned for the session. The altitudes used were ground level or 1,275 feet, 8,000 feet, and 12,000 feet above sea level. A tone was sounded immediately before the first trial of each session to alert the baboons before the presentation of the first sample color.

III. Results.

Each experimental session under the delayed matching-to-sample procedure consisted of 90 trials, with each trial having a maximum duration of 45 seconds. Accordingly, two measures of efficacy of matching performance were the number of trials completed and the percentage correct on the completed trials. Both baboons completed all of the programed trials at an average of 90 percent correct or better under nondrug, ground-level conditions. Since no differences in performance were observed between the two baboons, their data were combined for subsequent analysis.

Accuracy of matching performance, as measured by the percentage correct on completed trials, was not impaired across the range of drug doses and altitudes used. The percentage correct matching across the four drug doses was 93 percent, 95 percent, and 93 percent respectively for ground level, 8,000 feet, and 12,000 feet. However, marihuana did interact with altitude to produce a dose-related decrease in the percentage of trials completed. As shown in Figure 1, both baboons completed at least 95 percent of the matching-to-sample trials under all drug doses at ground level. At 8,000- and 12,000-feet altitudes, increasing doses of Δ^9–THC produced decreases in the percentage of complete trials.

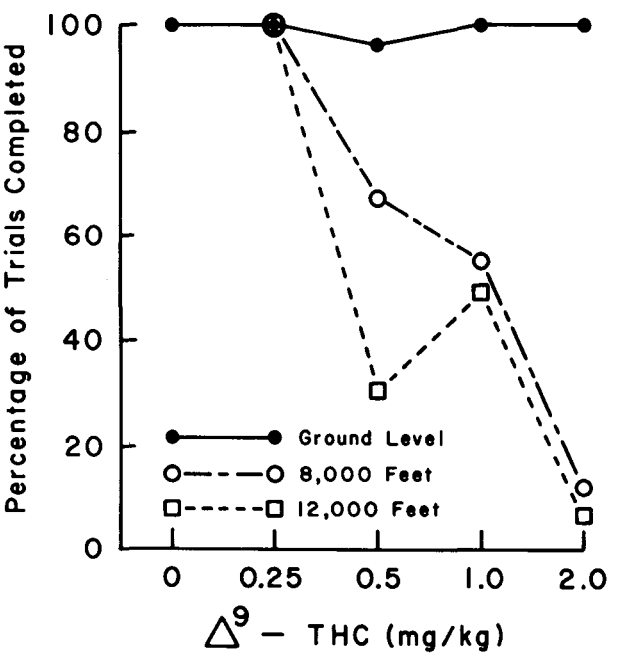

FIGURE 1.—Mean percentages of trials completed at ground level and altitudes of 8,000 and 12,000 feet as a function of Δ^9–THC dose.

Since Δ^9–THC and altitude interacted to affect total work output rather than accuracy of performance, an analysis of the speed of performance was made. Figure 2 displays the mean speed of responding to the sample stimulus (on trials in which a sample response did occur) at 8,000- and 12,000-feet altitudes as a percentage of the response speed at ground level. Under nondrug conditions, response speed was reduced to 73 percent of the ground-level speed at both the 8,000- and 12,000-feet altitudes.

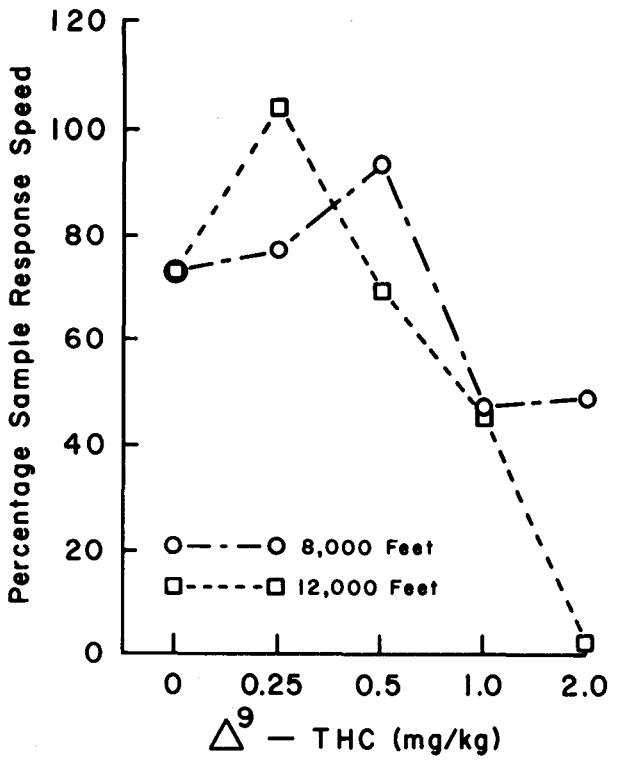

FIGURE 2.—Mean sample response speeds for altitudes of 8,000 and 12,000 feet plotted as a percentage of ground-level sample response speeds across Δ^9–THC doses.

Relative to the nondrug condition, low doses of Δ^9–THC increased response speed while higher doses produced a marked decrease in response speed at each of the higher altitudes.

IV. Discussion.

Several workers have shown that hypoxia can potentiate the behavioral effects of alcohol.[5,6] The present research demonstrates that hypoxia can also potentiate the effects of Δ^9–THC. Whereas Δ^9–THC did not reduce work output or alter response speed at ground level, work output was reduced at altitudes of 8,000 and 12,000 feet as the dose of Δ^9–THC was increased. Previous research using chimpanzees[2] has shown that work output under a delayed matching-to-sample task can be reduced at ground level by administering higher doses of Δ^9–THC than those used in this study. It should be noted that some drug doses used in the present work were within the range of oral doses commonly ingested by the marihuana user.

The Δ^9–THC had a biphasic effect on response speed at both of the higher altitudes as compared to nondrug control sessions. The Δ^9–THC increased and then decreased response speed as the dose of the drug was increased. Similar biphasic dose-response effects have been reported for marihuana under a wide variety of learned and unlearned tasks.[1]

Accuracy of performance was not affected across the range of drug doses and altitudes used in the current study. This finding is at variance with other reports that marihuana impairs the accuracy of performance under complex behavioral tasks, particularly those tasks involving a short-term memory component.[8,9] The delayed matching-to-sample procedure used herein can be conceptualized as a short-term memory task, since the sample stimulus was not available to the baboons at the time the choice response was required. Ferraro, Gluck, Fetterolf, and Marriott[3] have shown that the effects of marihuana are greater on complex tasks than on simple tasks. The complexity of the delayed matching-to-sample procedure can be increased by increasing the number of alternative choices or the length of the delay interval. The present lack of an observed impairment in accuracy under Δ^9–THC may be related to the limited number of choice stimuli or to the lengths of the delay intervals used.

The implications of the present research to the aviation community seem obvious. Clearly, a failure to execute a required behavior or a reduction in the speed of performing complex judgmental or memory tasks can lead to aviation accidents. Our finding that the effects of marihuana can be potentiated by hypoxia suggests that activities performed at common aircraft altitudes are more likely to be affected by marihuana than are ground-based activities.

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