Pharmacology Biochemistry & Behavior, Vol. 33, pp. 481–484. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/89 $3.00 + .00

BRIEF COMMUNICATION

Breathhold Duration and Response to Marijuana Smoke

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Received 21 September 1988

ZACNY, J. P. AND L. D. CHAIT. *Breathhold duration and response to marijuana smoke.* PHARMACOL BIOCHEM BEHAV 33(2) 481–484, 1989.—Marijuana smokers are frequently observed to hold the smoke in their lungs for prolonged periods (10–15 sec) apparently in the belief that prolonged breathholding intensifies the effects of the drug. The actual influence of breathhold duration on response to marijuana smoke has not been studied. The present study examined the effects of systematic manipulation of breathhold duration on the physiological, cognitive and subjective response to marijuana smoke in a group of eight regular marijuana smokers. Subjects were exposed to each of three breathhold duration conditions (0, 10 and 20 sec) on three occasions, scheduled according to a randomized block design. A controlled smoking procedure was used in which the number of puffs, puff volume and postpuff inhalation volume were held constant. Expired air carbon monoxide levels were measured before and after smoking to monitor smoke intake. Typical marijuana effects (increased heart rate, increased ratings of "high" and impaired memory performance) were observed under each of the breathhold conditions, but there was little evidence that response to marijuana was a function of breathhold duration.

Breathhold duration Marijuana Smoking Heart rate Smoking topography Carbon monoxide Memory Human Subjective effects

THE topography of marijuana smoking typically includes holding smoke in the lungs. Several studies which have assessed ad lib marijuana smoking have found breathhold durations ranging from 10 to 15 sec (13, 14, 18). In contrast, the topography of smoking tobacco cigarettes does not typically include extended breathholding (1, 8, 16, 18). Many marijuana smokers apparently believe that prolonged breathholding maximizes the subjective response obtained from marijuana smoke, thus providing them with "more bang for the buck" (10,15). Although this may be true, to our knowledge, this theory has not been put to the empirical test. It is possible that prolonged breathholding represents a purely superstitious behavior or social ritual which has no real impact on marijuana effects. Since extended breathholding could conceivably increase the risks associated with marijuana smoking [by increasing the pulmonary deposition or absorption of toxic components of marijuana smoke (9)], the topography of marijuana smoking may be clinically relevant. In the present study, we examined the effects of breathhold duration on the physiological, cognitive and subjective responses to marijuana smoke.

METHOD

Subjects

Seven male and one female adult participated (mean age: 20 years; range: 18–24). All were experienced marijuana smokers. Average use of marijuana during the 30 days prior to participation ranged from one to three times per week. No subject had a history of substance use disorder (DSM-III criteria), except for tobacco dependence. Five subjects smoked tobacco cigarettes but none smoked more than 10 cigarettes per day. Subjects provided a detailed drug and medical history, and received a psychiatric and physical examination (including EKG) before beginning the study. Informed consent was obtained and subjects were paid for their participation at the end of the study.

Experimental Design

The study consisted of nine experimental sessions. Breathhold duration was varied across sessions and was either 0, 10, or 20 sec. These parameters were chosen to encompass the range of values that have been reported in other studies which have assessed ad lib smoking of marijuana cigarettes [e.g., (18)]. Each breathhold condition was enacted for 3 sessions and the order of conditions was scheduled according to a randomized block design.

A placebo control was not incorporated into the study design; that is, all sessions were conducted with active marijuana. A placebo control was not considered necessary since the sole purpose of this study was to examine the effect of breathhold

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duration on response to active marijuana—the 0-sec condition in effect serves as the control condition, and any effect of breathhold duration on drug response would have reduced the need for a placebo condition. Also, the effects of marijuana smoking on most of the dependent variables measured here (heart rate, CO and mood) have already been well-characterized in placebo-controlled studies from this laboratory (4,5).

Procedure

Sessions were held on Monday and Thursday evenings, either from 4:30–7:30 or from 7:00–10:00. Each subject was tested separately in a room equipped with an easy chair, reading material, and a radio/cassette player. Before the study began, subjects attended a practice session to become familiar with the experimental setting and procedures.

Subjects were instructed not to smoke marijuana or use any other drugs (except tobacco or caffeine) during the 24 hours before sessions. Tobacco smokers were asked not to smoke within 30 min of scheduled sessions and were not allowed to smoke tobacco during sessions. Subjects were also not allowed to eat during sessions, but drinking water was freely available. After sessions subjects were provided with transportation home.

At the beginning of each session, subjects rested in an easy chair for 20 min prior to smoking so that heart rate would stabilize. Subjects smoked marijuana on two separate bouts, spaced 60 min apart. Only data from the first smoking bout will be presented, since the purpose of the second bout was unrelated to the present study. A smoking bout consisted of six smoke inhalations (see below) spaced approximately 60 sec apart. Baseline measures (heart rate, expired air CO level, subjective effects) were obtained before the smoking bout and 5 and 20 min after the bout. For the first three sessions, subjects performed a computer memory task (see below) approximately 30 min prior to, and 25 min after smoking.

The smoking apparatus consisted of a 100-cc glass syringe (Becton-Dickinson), a 3-way polypropylene stopcock (Nalgene) and a 2-l polyvinyl air collection bag. To begin the smoking procedure, a marijuana cigarette was lit and placed in a hollow plastic cigarette holder. Connected to the proximal end of the holder was a piece of rubber tubing to which the glass syringe could be attached. The experimenter drew 50 cc of ambient air into the syringe, then attached it to the cigarette holder via the rubber tubing and drew 50 cc of smoke into it. The syringe was then attached to one end of the stopcock. To the other two ends of the stopcock were attached a plastic mouthpiece and the air collection bag, filled with approximately 1500 cc of air. This inhalation volume was chosen to correspond to those reported in other studies of marijuana smoking (7,18). In order to standardize the point in the respiration cycle that the smoking maneuver began, subjects first exhaled into a 1-l air collection bag. They then 1) inhaled the contents of the glass syringe, 2) inhaled 1500 cc of air, 3) breathheld for the proper duration, and 4) exhaled. During the smoking maneuver, subjects wore noseclips to prevent nasal breathing. The experimenter timed breathhold duration with a stopwatch and instructed subjects when to exhale. In the 0-sec condition, subjects exhaled the smoke immediately after inhalation. In the other two breathhold conditions, subjects held the smoke in their lungs for either 10 or 20 sec prior to exhaling. Thus, the volume of smoke inhaled, volume of ambient air inhaled, and subsequent breathhold duration were controlled.

Marijuana Cigarettes

Standard, prerolled marijuana cigarettes weighing approximately 800–900 mg were supplied by the National Institute on Drug Abuse (NIDA). The cigarettes contained 1.3% delta-9-THC (assayed by NIDA). Cigarettes were stored in airtight containers in a cold room, and were humidified for at least 48 hr at room temperature before use. Cigarettes were cut in half and lit mechanically by the experimenter. Three 50-cc "puffs" were obtained from each of the half-cigarettes.

Dependent Variables

Sitting radial heart rate was measured digitally. Expired air samples were obtained after a 20-sec breathhold and were analyzed for CO (ppm) with a portable CO meter (MiniCO Model 1000, Catalyst Research Corp., Baltimore, MD). Subjective effects were measured with two questionnaires—a 53-item version of the Addiction Research Center Inventory (ARCI), and a series of six visual analogue scales (VAS). The ARCI items yielded scores for six scales: PCAG, a measure of sedation; BG and A, measures of stimulant effects; LSD, a measure of somatic and dysphoric effects; MBG, a measure of euphoria; and M, a measure of marijuana effects. The six scales of the VAS were "stimulated," "high," "anxious," "sedated," "down," and "hungry." Both questionnaires are described in detail elsewhere (5). Finally, cognitive performance was measured with a computerized version of the Buschke selective reminding test (2,11). This task uses a multiple-trial, free-recall format which allows an analysis of storage, retention and retrieval during verbal learning. A related task (the restricted reminding test) has been shown to be sensitive to marijuana (12).

Data Analysis

Individual subject means (across the three determinations under each breathhold condition) served as the basic units of analysis. Univariate and multivariate analysis of variance for repeated measures were used to analyze each dependent variable (17). Except for the memory task variables, all ANOVAs were two-way, the two factors being Breathhold Duration (0, 10 and 20 sec) and Time (presmoking, 5 and 20 min postsmoking). Variables from the memory task were analyzed with three-way analysis of variance [Breathhold Condition × Trial (1–10) × Time (before versus after smoking)]. Memory data from one subject had to be discarded when it was discovered that he had not correctly followed the task instructions. For all variables, effects were considered statistically significant for $p \leq 0.05$.

RESULTS

Figure 1 summarizes the results for the primary dependent variables (heart rate, ratings of "high" and CO level). It is immediately clear that there was little evidence that response to marijuana was sensitive to changes in duration of breathholding. All three measures showed significant changes as a function of time after smoking [main effect of Time: $F(2,14) = 18.7$, $p<0.001$, for heart rate; $F(2,14)=177.3$, $p<0.001$, for CO; $F(2,14)=36.5$, $p<0.001$, for "high"]. There were no main effects of Breathhold Duration or interactions between Breathhold Duration and Time.

No significant effects of breathholding were obtained on any of the other subjective effects scales. Significant main effects of Time were observed for LSD, $F(2,14)=11.1$, $p<0.005$, and M, $F(2,14)=24.9$, $p<0.001$. Ratings on these scales increased after smoking and, like the "high" ratings (Fig. 1), were virtually identical at 5 and 20 min postsmoking.

The only indication of an effect of breathhold duration was obtained from the selective reminding test. Significant interactions between Breathhold Duration and Time were obtained for total number of words recalled, $F(2,12)=7.1$, $p<0.01$, number of words in long-term storage, $F(2,12)=4.8$, $p<0.05$, number of

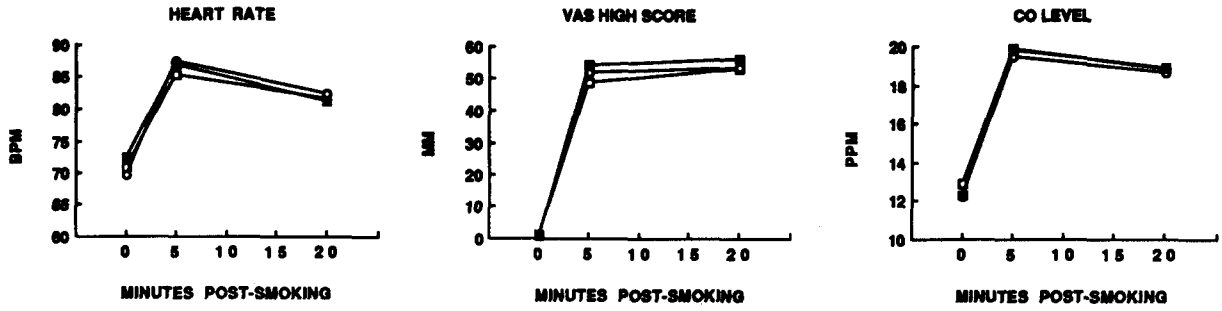

FIG. 1. Heart rate, VAS "high" score and CO level, averaged across subjects (N = 8), plotted as a function of minutes postsmoking for each of the three breathhold duration conditions (□: 0 sec; ○: 10 sec; ■: 20 sec). Minute 0 denotes measures obtained immediately prior to the smoking bout. SEM for heart rate ranged from 3.1–4.8 bpm; for "high," 0.4–9.5 mm; and for CO, 2.9–3.5 ppm.

words retrieved from long-term storage, $F(2,12) = 7.0$, $p<0.01$, and number of words consistently retrieved from long-term storage, a measure of list learning, $F(2,12) = 8.6$, $p<0.005$. Graphical inspection of these interactions revealed that memory function deteriorated after smoking, and that the intermediate (10-sec) breathhold duration produced the greatest effect; for example, the mean number of words consistently retrieved (averaged across the ten trials) decreased by 7.7 after the 10-sec breathhold condition, compared with only 2.8 after the 0-sec condition and 1.8 after the 20-sec condition.

DISCUSSION

The effects produced by marijuana smoking in the present study (e.g., on heart rate, CO level, "high" ratings and ARCI M scores) agree well with those obtained in previous studies from this laboratory (3–5), when differences in marijuana potency and number of puffs administered are taken into account. Despite clear drug effects indicative of THC absorption, however, there was little evidence to support the hypothesis that effects of marijuana are potentiated by increasing breathhold duration. The only indication of a breathhold effect was obtained from the memory task. Although the effects of breathhold duration on this task were statistically significant and of substantial magnitude, this finding should be regarded with some skepticism for several reasons. First, subjects were tested only once on the memory task under each breathhold condition and results from one subject had to be excluded. Second, the largest memory deficit was observed at the intermediate (10-sec) breathhold condition, a finding which would be difficult to explain from a physiological standpoint. Third, heart rate and mood did not show a similar pattern of change as a function of breathhold duration as did performance on the memory task; if manipulation of breathhold duration affected the magnitude of response to marijuana, then all measures sensitive to marijuana should have been similarly affected.

Whether THC absorption is affected by breathhold duration cannot be determined conclusively from the present study, since blood levels of THC were not measured. However, several studies have demonstrated that the subjective and cardiovascular effects of marijuana smoking are dose-dependent (3) and related to plasma THC concentration (13,14). Therefore, we feel it is unlikely that manipulation of breathhold duration in the present study could have substantially altered THC absorption while not affecting cardiovascular and subjective responses to marijuana. The present findings are also consistent with a recent report that breathhold duration does not influence the absorption of nicotine from tobacco smoke (19).

CO boosts in the present study did not increase as a function of breathhold duration. This stands in contrast to the results obtained in a recent study (19) in which CO absorption from tobacco smoke was affected by manipulation of breathhold duration (from 0 to 16 sec). In that study, CO boosts increased linearly as a function of breathhold duration, from a mean of 4 ppm under the 0-sec condition to 9 ppm under the 16-sec condition. There are at least two possible reasons for the discrepancy between the two studies. First, in the Zacny *et al.* study, the total amount of time that smoke was in the lungs in the 0-sec condition was about 5 sec; in the present study, smoke was probably in the lungs for several seconds longer, due to the different manner in which the marijuana smoke was puffed and inhaled. Because rate of CO absorption is exponential (6), it is possible that the amount of time that smoke was in the lungs in the 0-sec condition in the present study was sufficient for maximal CO absorption to occur. Second, it may be that THC or some other component of marijuana smoke facilitates the absorption of CO across the alveolar membrane, such that long breathhold durations are not required for complete CO absorption.

Further research will be needed to more fully characterize the relationship between marijuana smoking topography and behavioral and toxicological effects produced by the drug. Based upon the present findings, however, marijuana effects do not appear to be enhanced by prolonged breathholding. Marijuana users might be well-advised to drop prolonged breathholding from their repertoire of smoking behaviors, since they may be needlessly increasing their exposure to potentially toxic smoke components.

ACKNOWLEDGEMENTS

This research was supported by grant DA-03517 from the National Institute on Drug Abuse. The authors wish to thank Drs. S. McCracken and K. G. Chua for subject screening.

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