Response to marijuana as a function of potency and breathhold duration

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Abstract. The present study examined the effects of systematic manipulation of breathhold duration (0 and 20 s) on the physiological and subjective response to active (M; 2.3% delta-9-THC) and placebo (P; 0.0% delta-9-THC) marijuana in a group of ten regular marijuana smokers. During the eight-session experiment, subjects were exposed twice to each of four experimental conditions (P0, P20, M0, M20), scheduled according to a randomized block design. A controlled smoking procedure was used in which the number of puffs and puff volume were held constant. Expired-air carbon monoxide (CO) levels were used to monitor smoke intake. Breathhold duration affected CO absorption; significantly more CO was absorbed from both P and M smoke after 20 s of breathholding (mean CO boost = 6.9 ppm) than after no breathholding (mean = 4.4 ppm). Heart rate was minimally affected by the breathhold manipulation. Effects of marijuana on mood were not consistently affected by breathhold duration. The results confirm previous findings that prolonged breathholding does not substantially enhance the effects of inhaled marijuana smoke.

Key words: Marijuana – Smoking – Smoking topography – Human – Carbon monoxide – Subjective effects

Both anecdotal reports and laboratory studies indicate that marijuana smokers often hold the smoke in their lungs for prolonged periods (10–15 s) (Perez-Reyes et al. 1981, 1982; Wu et al. 1988) apparently in the belief that prolonged breathholding intensifies the effects of the drug. The topography of marijuana smoking may be clinically relevant, since extended breathholding could conceivably increase the health risks associated with marijuana smoking by increasing the pulmonary deposition or absorption of toxic smoke components (Wu et al. 1988). We recently examined the effects of breathhold duration on the physiological, cognitive and subjective response to marijuana, and found little evidence that response to marijuana was related to changes in duration of breathholding (Zacny and Chait 1989). In that study, subjects smoked active marijuana according to a controlled smoking procedure and were exposed to three breathhold duration conditions (0, 10 and 20 s). The increase in expired air carbon monoxide (CO) level (an index of smoke absorption) and heart rate after smoking was similar across breathhold duration conditions, and so too was the magnitude of subjective effects. The lack of a breathhold duration effect on CO absorption was unexpected, however, since CO absorption from tobacco smoke is enhanced by prolonged breathholding (Zacny et al. 1987).

The present study is a systematic replication of the previous one (Zacny and Chait 1989), with modifications designed to examine possible reasons why CO levels did not increase as a function of breathhold duration. One possible reason for the lack of effect was that maximal CO absorption may have occurred in the minimal (0-s) breathhold condition, due to the amount of time that it took to inhale and exhale the smoke in the controlled smoking procedure. In the present study, the smoking procedure was modified to minimize the duration that smoke resided in the lungs in the 0-s breathhold condition. A second possible reason for the observed lack of a breathhold duration effect on CO absorption is that THC (or some other component present in marijuana smoke but not in tobacco smoke) facilitates the absorption of CO, such that long breathhold durations are not required for complete CO absorption. This possibility could not be addressed in the prior study because a placebo control was not included; such a control was included here.

Materials and methods

Subjects. Six male and four female adults participated (mean age = 25 years; range = 18–35). All were experienced marijuana smokers.
Average use of marijuana during the 30 days prior to participation ranged from one to six times per week. No subject had a history of substance use disorder (DSM-III criteria), except for tobacco dependence. Three subjects smoked tobacco cigarettes (range: 10-20 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 and general procedures. The study consisted of eight experimental sessions. In each session, subjects were exposed to one of four experimental conditions in which they smoked either placebo (P) or active (M) marijuana under one of two breathhold duration conditions (0 or 20 s). Each of the four experimental conditions (P0, P20, M0, M20) was enacted twice, and the order of conditions was scheduled according to a randomized block design.

Sessions were held on Monday and Thursday evenings, from 7:00-8:30 p.m. 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 two practice sessions 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 h 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 performed several tasks on a computer, and then rested in a chair for 20 min so that heart rate would stabilize. Immediately prior to smoking, subjects filled out mood questionnaires, had their heart rate monitored, and delivered a breath sample. All measures were redetermined one or two times after smoking.

Subjects smoked marijuana in a controlled manner so that the volume of smoke inhaled and subsequent breathhold duration were controlled. The controlled smoking procedure was a modification of the procedure used in our previous study (Zacny and Chait 1989). Briefly, the smoking apparatus consisted of a 100-ml glass syringe (Becton-Dickinson) and a 3-way polypropylene stopcock (Nalgene). 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 ml of ambient air into the syringe, then attached it to the cigarette holder via the rubber tubing and drew 50 ml of smoke into the syringe. The syringe was then attached to one end of the stopcock. A plastic mouthpiece was attached to the opposite end of the stopcock. In order to standardize the point in the respiratory cycle at which 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) took a deep and rapid inhalation, 3) held their breath 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-s condition, subjects exhaled the smoke immediately after inhalation. Subjects took four “puffs,” spaced about 60 s apart.

Marijuana cigarettes. Marijuana cigarettes weighing approximately 800-900 mg were supplied by the National Institute on Drug Abuse (NIDA). The cigarettes contained either 0.0% or 2.3% delta-9-TTHC (assayed by NIDA). Cigarettes were stored in air-tight containers in a cold room, and were humidified for at least 24 h at room temperature before use. Cigarettes were cut in half and lit mechanically by the experimenter. Two 50-ml “puffs” were obtained from each of the half-cigarettes.

Dependent variables. Sitting radial heart rate was measured digitally before smoking and 5 and 20 min after smoking.Expired air samples were obtained after a 20-s breathhold and were analyzed for CO (ppm) with a portable CO meter (MiniCO Model 1000, Catalyst Research Corp., Baltimore, MD) before smoking and 5 min after smoking.

Subjective effects were measured with three questionnaires. Two of the questionnaires were administered before smoking and 15 min after smoking—a 53-item version of the Addiction Research Center Inventory (ARCI), and a series of six visual analog 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 (Chait et al. 1985). On the End-of-Session questionnaire (administered 60 min after smoking), subjects were asked to rate 1) the intensity of the marijuana effect at its peak (from 1 = “I felt no effect from it at all,” to 5 = “I felt a very strong effect.”); 2) how high they got from smoking at the time of peak effect (on a visual analog scale of 0-100 with the following descriptors: 0 = not high at all; 50 = my usual level of high from marijuana; 100 = the highest I have ever been from marijuana); and 3) how much they liked the marijuana effects (on a visual analog scale of 0-100 with the following descriptors: 0 = disliked a lot; 50 = neutral; 100 = liked a lot).

Psychomotor/cognitive performance was assessed with four computer tasks (logical reasoning, backward digit span, free recall and simulated driving) before and again 20 min after smoking. Since none of these tasks was significantly affected by marijuana in this study, no results will be presented.

Data analysis. Individual subject means of the two determinations under each condition served as the basic units of analysis. Three-way univariate analysis of variance (ANOVA) with repeated measures (Dixon 1983) was used to assess the effects of Drug (2 levels: P and M), Breathhold (2 levels: 0 and 20 s) and Time (2 or 3 levels: pre- and post-smoking) on heart rate, CO level, and ARCI and VAS scores. Two-way repeated measures ANOVA was used to assess the effects of Drug and Breathhold on scores from the End-of-Session questionnaire. For all variables, effects were considered statistically significant for P < 0.05, with adjustments of within-factors degrees of freedom (Huynh-Feldt) to protect against violations of symmetry (Dixon 1983). When a significant Drug X Breathhold interaction was obtained, a single a priori paired t-test was used to compare the M0 condition to the M20 condition.

Results

The increase in CO level as a result of smoking marijuana (CO boost) was greater after the 20-s breathhold for both P and M [Fig. 1, left panel; Breathhold X Time: F(1,9) = 51.7, P < 0.001]. CO boost and its dependence upon breathhold duration did not vary significantly across the two drug conditions, and considerable differences in response were observed between subjects.

Smoking M increased heart rate [Fig. 1, center panel; Drug X Time: F(2,18) = 73.7, P < 0.001]. A significant Drug X Breathhold X Time interaction was also observed [F(2,18) = 3.8, P < 0.05]. This interaction mainly reflects the fact that the heart rate increase 5 min after smoking M was lower after the 0-s breathhold (19.9 bpm) than after the 20-s breathhold (25.3 bpm). However, the difference between these two means was not statistically significant (paired t-test, T = 2.11, P = 0.06).