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Effects of Varying Marijuana Smoking Profile on Deposition of Tar and Absorption of CO and Delta-9-THC

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TASHKIN, D. P., F. GLIEDERER, J. ROSE, P. CHANG, K. K. HUI, J. L. YU AND T.-C. WU. *Effects of varying marijuana smoking profile on deposition of tar and absorption of CO and delta-9-THC.* PHARMACOL BIOCHEM BEHAV **40**(3) 651–656, 1991.—We investigated the effects of previously observed differences in smoking technique for marijuana (M) versus tobacco (T) on the amount of inhaled tar, the percentage retention of inhaled tar in the lung, the pre- to postcigarette boost in blood carboxyhemoglobin (COHb) and in serum delta-9-tetrahydrocannabinol (THC concentrations), and psychophysiologic responses to THC (increased heart rate and subjective "high"). Ten healthy, habitual smokers of M were studied on 6 separate days. On each day, subjects smoked a single M cigarette (~900 mg, 1.24% delta-9-THC) using one of 6 different smoking profiles typical for marijuana [puff volume (PV) ~70 ml; breathholding time, (BHT) 14–16 s] or tobacco (PV ~45 ml; BHT 4–5 s) or a combination of the two techniques (PV ~70 ml and BHT 4–5 s; or PV ~45 ml and BHT 14–16 s). Inhaled volume (1.5 liters), interpuff interval (30 s) and number of puffs (6) were all fixed, except that for the ~45-ml PV condition, the number of puffs was increased to 10 in 2 additional sessions to standardize the total amount of cigarette consumed to that of the ~70-ml PV condition. The longer BHT significantly increased both percent retention of tar in the lung and the pre- to postsmoking rise in blood COHb, serum THC and heart rate, independent of puff volume and number. In contrast, the larger PV had no significant influence on these variables for the same amount of cigarette consumed. The longer BHT (and not the larger PV) characteristic of M smoking contributes to the greater COHb boost and lung retention of inhaled tar during M compared to T smoking. In addition, the longer BHT appears to enhance THC absorption.

Marijuana Smoking profile Tar Carbon monoxide Delta-9-tetrahydrocannabinol

WE previously observed that, compared to a filter-tipped tobacco cigarette of the smoker's own brand, smoking a marijuana cigarette of similar weight (~900 mg, 1.24% THC) led to a 3-fold greater amount of tar delivered to the smoker's mouth and a one-third increase in retention of the inhaled tar in the lung, as well as a 3–4-fold increase in the pre- to postcigarette boost in blood carboxyhemoglobin (COHb) (19). We also observed that, compared to tobacco, smoking marijuana was associated with considerable differences in smoking topography. The latter included a two-thirds increase in puff volume (78 ml vs. 49 ml), a 4-fold longer breathholding time (14–15 s vs. 3.5 s), and a small (one-third) increase in the depth of inhalation (1.75 liters vs. 1.31 liters) (19). In addition, we found that in vitro smoking of a standard marijuana joint and a filter-tipped tobacco cigarette using a uniform smoking pattern (puff volume 50 ml, interpuff interval 30 s) accounted for only a 2-fold increase in tar delivery from marijuana compared to tobacco and a comparable yield of carbon monoxide (CO) (14). From these observations we hypothesized that factors in addition to varying physicochemical characteristics of tobacco and marijuana, such as variations in smoking topography, contribute to the differences in tar inhalation/retention and in carboxyhemoglobin (COHb) boost observed during natural smoking of these two types of cigarettes.

The purpose of the present study was to manipulate the smoking technique of habitual marijuana smokers so that they would smoke a standard marijuana cigarette using a technique that partially or completely simulated that used by regular tobacco smokers in smoking tobacco in order to determine how these variations in smoking technique influence the amount of inhaled tar, the percent deposition of inhaled tar in the respiratory tract, the carboxyhemoglobin boost, and the amount of delta-9-THC delivered to and absorbed from the lung. The latter was assessed by the pre- to postsmoking changes in serum delta-9-THC concentration, heart rate and self-rated level of intoxication ("high").

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TABLE 1

EXPERIMENTAL DESIGN

Study Day	Type of Cigarette for Which Smoking Technique Was Typical	Puff Volume (ml)	Breatholding Time (s)	Puff Number (#)	Cumulative Puff Volume (ml)
1	Marijuana	70	14	6	420
2	Marijuana and Tobacco	70	4	6	420
3	Tobacco and Marijuana	45	14	6	270
4	Tobacco	45	4	6	270
5	Tobacco and Marijuana	45	14	10	450
6	Tobacco	45	4	10	450

METHOD

Ten habitual marijuana smokers (history of daily or near daily use of marijuana for 5 or more years) who were free of cardiopulmonary disease were studied on 6 separate days. Subjects refrained from smoking marijuana for ≥12 hours and tobacco for ≥2 hours prior to study. On each study day, subjects smoked a standard NIDA-supplied marijuana cigarette (approximately 900 mg, 1.24% delta-9-THC) using a smoking technique that was characteristic of smoking either marijuana [large puff volume (PV) and long breathholding time (BHT)], tobacco (small PV and short BHT), or a combination of the two (large PV and short BHT; or small PV and long BHT).

The experimental design is summarized in Table 1. On day 1, subject smoked a marijuana cigarette using a method that we have previously ascertained to be typical for marijuana (PV ~70 ml, BHT ~14 s, number of puffs, 6) (19). On day 2, subjects took six large-volume puffs (~70 ml) characteristic of marijuana smoking and held the smoke in their lungs for only a short interval (~4 s) typical of tobacco smoking. On day 3, six puffs of a small volume (~45 ml) were taken (typical for tobacco), but the smoke was retained in the lungs for a relatively long period (~14 s) characteristic for marijuana. Because the smoking profile employed on days 3 and 4 resulted in a considerably smaller cumulative puff volume (~270 ml) than that achieved on days 1 and 2 (~420 ml), subjects were studied on two additional days (5 and 6). Study day 5 resembled day 3, except that 10, instead of 6, small puffs were taken to approximate the cumulative puff volume (an indicator of the amount of cigarette consumed) which was achieved on days 1 and 2. Similarly, day 6 was similar to day 4 with the exception that 10, rather than 6, small puffs were again used. The order of the six study sessions was random except that the condition characteristic of marijuana smoking (day 1) was always first. Inhaled volume was fixed at 1.5 liters, a value typical of marijuana smoking and only one-third higher than that characteristic of tobacco smoking (19). It has previously been shown that variations in inhaled volume that are above 400 ml have little impact on the amount of smoke particulates delivered to and retained in the lung (18), on CO boost or on psychophysiologic effects (21). Interpuff interval was fixed at 30 s.

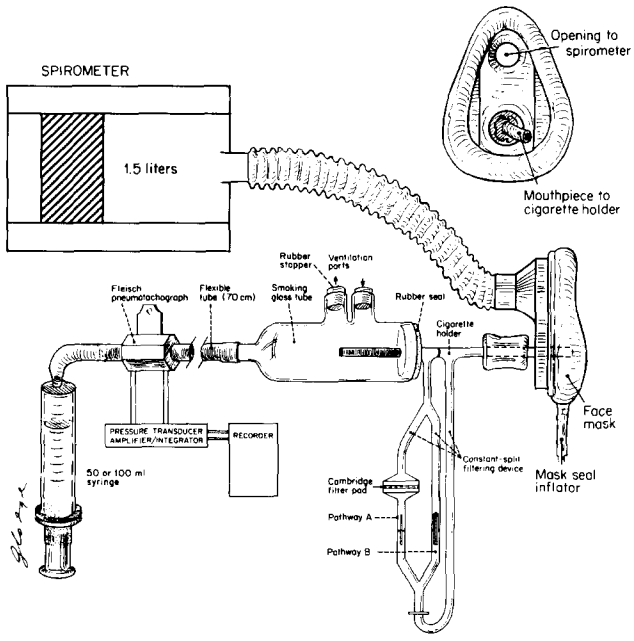

FIG. 1. Smoking apparatus used in marijuana smoking experiments. Proportional split filter device is incorporated in smoking apparatus to estimate amount of insoluble smoke particulates delivered to the smoker's mouth (inhaled tar) from the measured amount of particulates trapped in the Cambridge filter pad. Pathways A and B represent high resistance and low resistance pathways, respectively.

The smoking apparatus used in these experiments is shown in Fig. 1. The marijuana cigarette was inserted into a cigarette holder which punctured a rubber stopper that sealed the proximal end of a 120-ml glass cylinder (smoking tube). The distal end of the smoking cylinder was connected by flexible tubing to a 00 Fleisch pneumotachograph for measurement of puff flow, from which puff volume was obtained by electrical integration. The distal end of the pneumotachograph, in turn, was connected to a 50- or 100-ml glass syringe the barrel of which was adjusted to permit the subjects to draw 45 ml or 70 ml through the lit cigarette during puffing maneuvers. Two ventilation ports on the upper surface of the glass smoking tube were occluded by rubber stoppers during puffs (so that the entire puff volume would be drawn through the pneumotachograph), but opened between puffs to prevent accumulation of carbon monoxide or extinction of the lit cigarette. The proximal end of the cigarette holder perforated another stopper which sealed the lower of two orifices in an airtight face mask. Subjects puffed on the mouthpiece extension of the cigarette holder that protruded into the face mask. After the full volume of each puff was taken, subjects opened their mouths and inhaled exactly 1.5 liters of room

TABLE 2

MEAN VALUES OF PUFF VOLUME, CUMULATIVE PUFF VOLUME AND BREATHHOLDING TIME OBSERVED DURING THE SMOKING OF A SINGLE MARIJUANA CIGARETTE DURING EACH STUDY DAY

Study Day	Puff Number (#)	Puff Volume (ml)	Cumulative Puff Volume (ml)	Breathholding Time (s)
1	6	70.5 ± 4.5	423	15.8 ± 1.5
2	6	72.1 ± 3.5	433	4.7 ± 0.6
3	6	47.1 ± 1.9	283	15.3 ± 1.2
4	6	44.7 ± 1.2	268	4.5 ± 0.4
5	10	44.2 ± 2.3	440	15.2 ± 1.1
6	10	44.5 ± 1.0	445	4.4 ± 0.5

air from a rolling-seal volumetric spirometer which was connected by corrugated tubing to the upper orifice in the face mask. That the full 1.5 liters were inhaled was verified by inductive plethysmography (15,16). Upon inhalation of the smoke-air mixture, subjects were carefully instructed to hold their breath for 4 or 14 seconds, as timed by a stop-watch, before exhalation.

A previously described proportional filter device was incorporated into the cigarette holder to permit measurement of the amount of insoluble smoke particulates delivered to the smoker's mouth (10,19) (Fig. 1). This device diverted the mainstream smoke into two parallel pathways. Pathway A had a high resistance and pathway B a low resistance, such that approximately one-fifth of the smoke passed through the former and four-fifths through the latter. The high resistance pathway contained a Cambridge filter pad which trapped virtually all of the smoke particulates, while the smoke traversing the low resistance pathway was delivered to the smoker's mouth. Previous studies have verified that the proportion of the smoke traversing each of these pathways is constant over the usual range of puff volumes (30–60 ml), durations (1–4 s) and flow rates (20–100 ml/s) during the smoking of several cigarettes in tandem (10).

After each cigarette was smoked, the insoluble particulates (tar) trapped in the Cambridge filter pad were eluted with methanol and analyzed using a spectrophotometer (wavelength 400 nm). Because a constant fraction of smoke particulates (approximately 17.2%) was retained in the filter, the actual quantity of tar delivered to the smoker could be calculated by multiplying the amount of particulates trapped in the Cambridge filter by 4.8. At the end of each postpuff breathhold, subjects exhaled the smoke into the large end of a megaphone device, the distal end of which was fitted with another Cambridge filter attached to a vacuum system, as described by Hinds (5). The tar from the latter filter was also extracted with methanol and analyzed spectrophotometrically. Subtraction of the exhaled from the inhaled tar allowed calculation of the percent of inhaled tar retained (deposited) in the respiratory tract.

An intravenous catheter was inserted at the beginning of each study session. Blood samples were withdrawn prior to smoking and at 2, 15, 30 and 45 min after completion of smoking for analysis of carboxyhemoglobin (COHb) and serum delta-9-THC. COHb was measured using a CO-oximeter (Instrumentation Laboratory, model 282, Lexington, MA). Serum delta-9-THC concentrations were determined by radioimmunoassay (12) by one of the investigators (J.L.Y.) who was blinded to the study condition. Heart rate was measured before and 5 min after smoking. Subjects rated their level of "high" on a scale of "0" to "10" 20 min after the completion of smoking; "10" represented the greatest level of marijuana intoxication the subject had ever experienced previously.

Data Analysis

Each subject's measurements were averaged for each cigarette smoked. These mean values, as well as the quantity of particulates inhaled, the percentage of inhaled particulates deposited, and the pre- to postcigarette differences in blood carboxyhemoglobin, serum delta-9-THC concentration, heart rate and "high" were averaged for all 10 subjects for each of the six smoking conditions. For those four conditions in which the cumulative puff volume was 420–450 ml (days 1, 2, 5 and 6), data were analyzed by two-way ANOVA (blocking by subjects) in which puff volume and breathholding time were treated as independent variables and possible interaction between these two variables was assessed (2). For the two 45-ml puff volume conditions yielding a cumulative puff volume of only 270 ml (days 3 and 4), the effect of varying breathholding time was determined using Student's t test for paired data. For the four conditions (days 3, 4, 5 and 6) in which puff volume was fixed at ~45 ml, the effect of different cumulative puff volumes (i.e., ~270 vs. ~450 ml) on each of the dependent variables was compared between the conditions with similar breathholding times [i.e., day 3 vs. day 5 (short BHT) and day 4 vs. day 6 (long BHT)] using the paired t-test. p values <0.05 were considered statistically significant.

RESULTS

Mean values for the puff volumes and breathholding times observed during each of the six study conditions are shown in Table 2. The puff volumes and breathholding times actually achieved were close to the targeted values, as were the inhaled volumes as verified by inductive plethysmography.

The effect of varying puff volume and breathholding time during marijuana smoking on the amount of inhaled tar, percent deposition of inhaled tar in the respiratory tract and the pre- to postcigarette boost in blood COHb concentration (2 min) is shown in Figs. 2–4. It should be noted that cumulative puff volume (PV × number of puffs) was larger on days 1, 2, 5 and 6 (420–450 ml) than on days 3 and 4 (270 ml). No effect of PV or BHT on the amount of inhaled tar was noted ($p>0.9$), whereas the quantity of inhaled tar was significantly greater during those smoking conditions associated with a larger cumulative puff volume ($p<0.001$) (Fig. 2). Varying BHT, but not puff

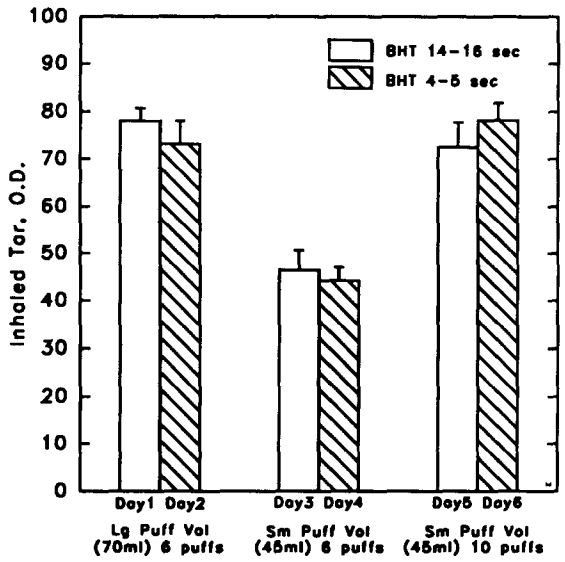

FIG. 2. Effect of differences in puff volume, cumulative puff volume and breathholding time on amount of inhaled tar, expressed in optical density (O.D.) units. Cumulative puff volume = puff volume × number of puffs. Cumulative puff volumes are comparable on days 1, 2, 5 and 6 and are relatively smaller on days 3 and 4 (see text).

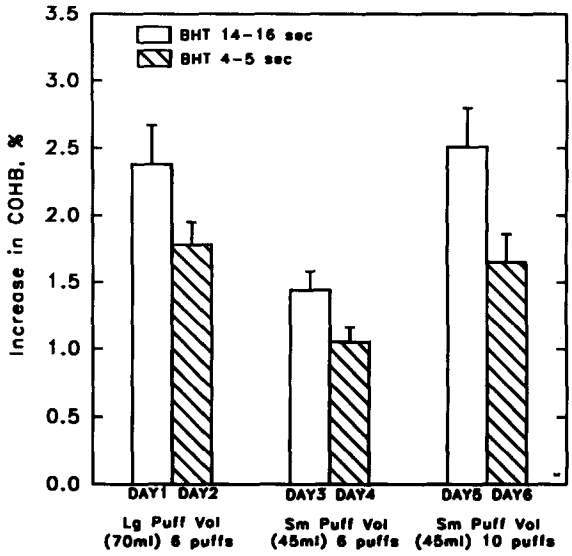

FIG. 4. Effect of marijuana smoking technique on pre- to postcigarette boost in carboxyhemoglobin (COHb) concentration. COHb concentrations were determined immediately prior to smoking and 2 min after completion of smoking.

volume or cumulative puff volume, had a significant effect on the percent deposition of inhaled tar ($p<0.001$) (Fig. 3). The longer BHT was associated with a 30–40% greater retention of the inhaled tar in the lung, independent of puff volume or number of puffs. Similarly, for a cumulative puff volume of 420–450 ml, variation in BHT but not in PV had a significant influence on the pre- to postcigarette rise in COHb concentration ($p<0.001$); the longer BHT led to a 34–52% greater boost in COHb (Fig. 4). A larger cumulative puff volume was also associated with a significantly greater COHb boost ($p<0.001$). No interaction was noted between the effects of PV and BHT on the amount of inhaled tar, percent deposition of inhaled tar or COHb boost.

The influence of variations in marijuana smoking technique on the pre- to postsmoking increases in serum delta-9-THC (2 min), heart rate (5 min) and "high" (20 min) is shown in Figs. 5–7. For the same amount of cigarette consumed, the longer BHT, but not the larger puff volume, was associated with a 33–

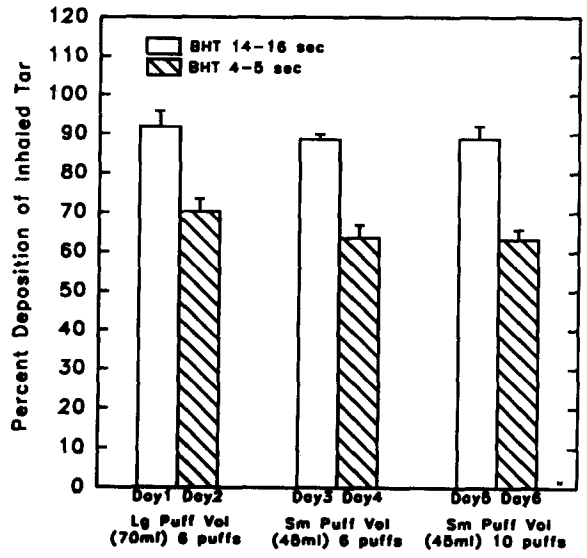

FIG. 3. Effect of differences in marijuana smoking technique on percent deposition of inhaled tar.

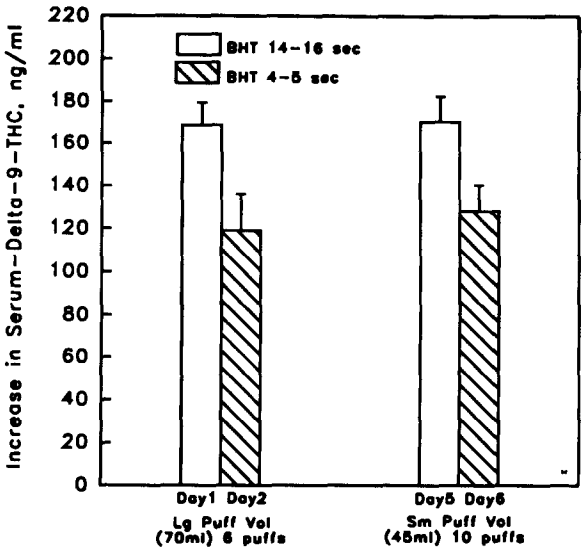

FIG. 5. Effect of marijuana smoking technique on pre- to postcigarette boost in serum delta-9-THC concentration (ng/ml). Serum THC concentrations were determined immediately before smoking and 2 min after completion of smoking.

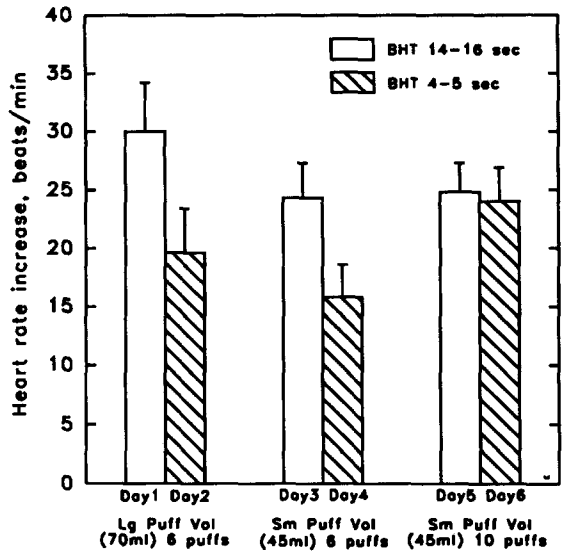

FIG. 6. Effect of marijuana smoking technique on pre- to postcigarette increase in heart rate. Heart rate was measured immediately before smoking and 5 min following completion of smoking.

42% greater boost in serum delta-9-THC than that produced by the shorter BHT ($p=0.01$) (Fig. 5). While PV had no effect on the smoking-induced increase in heart rate, BHT had a borderline significant effect ($p<0.06$) when the cumulative puff volume was large (420–450 ml) and a significant effect ($p<0.03$) when the cumulative puff volume was smaller (270 ml) (Fig. 6). Considering only days 1–4, the longer BHT was associated with a >50% greater rise in heart rate than the shorter BHT, irrespective of puff volume. For the same amount of cigarette consumed, neither PV nor BHT had a significant influence on the smoking-induced "high" (Fig. 7), although the effect of BHT was of borderline statistical significance ($p<0.07$) and cumulative puff volume had a significant effect ($p<0.001$). No interactive effects of PV and BHT on pre- to postsmoking changes in delta-9-THC, heart rate or "high" were observed.

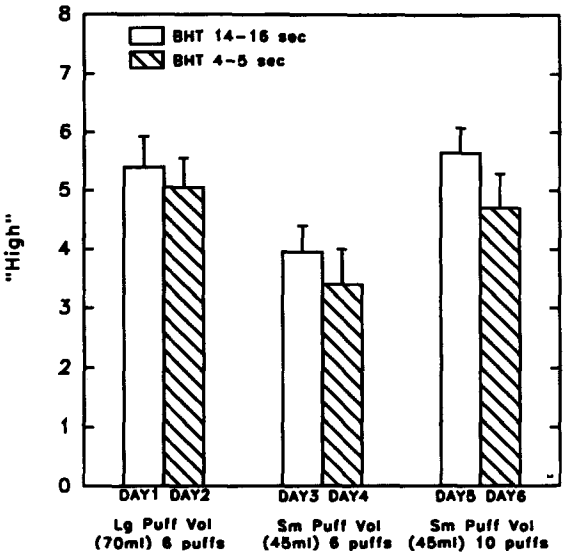

FIG. 7. Effect of marijuana smoking technique on postsmoking level of intoxication ("high"). "High" was subjectively assessed on a scale of "0" to "10" twenty min after completion of smoking. "10" represented the greatest level of marijuana intoxication the subject had ever experienced in the past.

DISCUSSION

The results of the present study indicate that, compared to the relatively short breathhold duration characteristic of tobacco smoking, the longer breathholding time typical of marijuana use (8, 9, 19) significantly increased the percent retention of inhaled tar in the lungs and the pre- to postsmoking rise in blood carboxyhemoglobin concentration, serum THC and heart rate. These effects were independent of puff volume and number. In contrast, the larger puff volume, which is also characteristic of marijuana compared to tobacco smoking, had no significant influence on the amount or percent deposition of inhaled tar or on the pre- to postsmoking rise in blood carboxyhemoglobin, serum THC or those psychophysiological effects of THC which were evaluated ("high," heart rate increase), when the number of puffs of the smaller puff volume was adjusted to equalize the amount of cigarette consumed. On the other hand, larger cumulative puff volumes, which reflect a greater consumption of the marijuana in the cigarette, were associated with significantly greater quantities of inhaled tar and pre- to postcigarette increases in blood COHb and in self-reported "high."

Recently, Zacny and Chait (20) also examined the effects of breathholding time on the carbon monoxide boost and psychophysiological changes in response to marijuana smoke in habitual marijuana smokers. They studied three breathhold durations (0, 10 and 20 s) while maintaining number of puffs, puff volume and inhaled volume constant. In contrast to our findings, these authors (20) failed to demonstrate a significant effect of breathhold duration on the pre- to postcigarette boost in end-expired CO (a marker of blood COHb), heart rate or "high." The discrepancy between the latter results and our own findings could be due to methodological differences between the two studies. First, since Zacny and Chait (20) measured pre- to postcigarette differences in end-expired CO, rather than blood COHb concentrations, their results may be questioned. Alveolar carbon monoxide, although predictably correlated with COHb levels in subjects who have not smoked for at least 30 min, has been shown to be an unreliable index of carboxyhemoglobin changes during smoking in man, presumably due to transient changes in pulmonary gas exchange induced by smoking (4). Interestingly, in a previous study involving tobacco smokers, Zacny et al. (21) did observe an increase in CO absorption from tobacco smoke when breathhold duration was increased over the range of 0 to 16 s. In addition, Zacny and Chait (20) state that during the 0-s breathhold condition which they employed in their marijuana smoking experiments, "smoke was probably in the lungs for several seconds longer" than 5 s, possibly resulting in a total duration of alveolar retention of smoke that may have maximized absorption of CO and delta-9-THC from the lung. Furthermore, these authors did not measure blood levels of THC, which provide the most objective and reliable indication of delivery and absorption of THC.

We conclude that, of the topographical variables examined, the longer breathholding time (and not the larger puff volume) is mainly responsible for the greater lung retention of inhaled tar and the greater carboxyhemoglobin boost previously observed during marijuana compared with tobacco smoking. It is possible, therefore, that the longer breathhold duration characteristic of marijuana smoking may contribute to the cardiorespiratory hazards of marijuana (19). The greater respiratory tar burden as-

sociated with this pattern of smoking may increase the carcinogenic risk of exposure to certain polycyclic aromatic hydrocarbons and other cancer-promoting compounds in the tar phase of the smoke (6,7), as well as the risk of acute and chronic airways disease due to enhanced exposure to noxious irritants within the smoke. The greater boost in COHb may also increase the cardiac risk of smoking due to reduced myocardial tissue oxygenation (3,11), especially in individuals with underlying coronary artery disease, at the same time that the work of the heart (and hence its oxygen requirements) is increased by the associated THC-induced cardioacceleration (1,17).

Our findings also suggest that the prolonged breathholding characteristic of marijuana smoking (8,9) enhances THC absorption and possibly the associated rise in heart rate and level of intoxication. These findings lend support to the concept that a longer breathhold duration potentiates the subjective response to marijuana. Indeed, this concept may be responsible for the adoption by many marijuana smokers of a distinctly different smoking topography from that employed by tobacco smokers. Unlike the apparent influence of breathhold duration on THC absorption during marijuana smoking, breathholding time has not been shown to influence absorption of nicotine from tobacco smoke (21), perhaps due to a difference in the speed of absorption of nicotine versus delta-9-THC from the lung. This difference might explain why tobacco smokers generally hold the smoke in their lungs for only a few seconds, as opposed to the several-fold longer breathhold duration distinctive of marijuana smokers. Interestingly, smokers of both marijuana and tobacco typically employ a short breathholding time when smoking tobacco, similar to the technique of tobacco only smokers, while they use a much longer breathhold duration in smoking marijuana, similar to that used by marijuana only smokers (13). If the longer smoke retention time characteristic of marijuana smoking determines the degree of intoxication from THC, then it may be difficult to modify this topographic variable in an attempt to reduce the cardiorespiratory hazards of marijuana smoking.

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