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Refined Cigarette Smoke as a Method For Reducing Nicotine Intake

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ROSE, J. E. AND F. BEHM. *Refined cigarette smoke as a method for reducing nicotine intake.* PHARMACOL BIOCHEM BEHAV **28**(2) 305–310, 1987.—We developed a method of refining tobacco smoke to deliver sensory components of cigarette smoking while minimizing the delivery of nicotine and other toxic smoke constituents. In the first experiment, smokers rated puffs of their own brands of cigarette, a commercial low tar and nicotine cigarette, and refined smoke. The refined smoke was rated significantly stronger and more desirable than the low tar and nicotine cigarette despite a comparably low nicotine delivery; subjects' own brands were rated best, but in standardized smoking tests delivered over ten times more tar, nicotine and carbon monoxide. In the second experiment, subjects smoked five times on each of two mornings; one day they received refined smoke and the other day smoked a low tar and nicotine cigarette. The refined smoke produced significantly more satisfaction, yet delivered far less carbon monoxide and tar (assessed by mouth intake). Nicotine intake was comparable to that of the low tar and nicotine cigarette. Because refined smoke substantially reduced subjects' craving for cigarettes while reducing nicotine intake, it may prove to be a useful short-term adjunct to a smoking cessation program. Additionally, the method may be useful in research analyzing the relative contributions of pharmacologic actions of inhaled smoke and the sensory cues associated with nicotine intake as reinforcers maintaining smoking behavior.

Tobacco Cigarette smoking Nicotine Reinforcement Cancer Cardiovascular disease Ciliatoxicity

THE widespread recognition of health hazards associated with tobacco use has prompted numerous attempts to eliminate dependence on cigarettes. Smoking cessation methods include behavior therapy, group support, and pharmacologic aids [17]. Recently, much attention has focused on nicotine substitutes as potential cessation aids; alternative means of administering nicotine include nicotine chewing gum [14], transdermal nicotine [17], and nicotine nasal solution [20]. Smokers can obtain some relief from tobacco withdrawal symptoms by receiving alternative sources of nicotine [21]; however, to date, neither nicotine substitution nor other methods of smoking cessation has achieved dramatic success rates [4]. One complaint associated with cigarette abstinence that has been notably refractory to treatment is the report of "craving" for cigarettes [13]. Generally, the administration of comparable or even larger doses of nicotine than those usually obtained from smoking has surprising little effect on craving for cigarettes [6,10].

Given that nicotine replacement is only partially successful, an alternative approach to reducing cigarette smoke intake is to supply smokers with a substitute that delivers many of the familiar sensory cues in smoke while greatly reducing the delivery of nicotine and other smoke constituents. One might hope to achieve this goal with low tar and nicotine cigarettes which filter and/or dilute smoke to eliminate many toxic constituents along with nicotine [15]. Unfortunately, smokers tend to maintain tar, nicotine and carbon monoxide intake by taking more puffs, larger puffs or inhaling deeper than usual [2,8]. Moreover, cigarettes with extremely low nicotine deliveries are almost uniformly unsatisfying to smokers. Despite compensatory increases in smoking, the diluted smoke from these cigarettes lacks the customary sensory cues smokers want (flavor, etc.). Therefore, in conducting the present study, we focused on a new strategy for delivering desired sensory characteristics of smoke while dramatically reducing nicotine and other harmful components of smoke.

Our approach involved the development of a method of refining cigarette smoke. This method consists of a two-step process for selectively eliminating toxic components, while maintaining many of the desired flavor components. In the first step, cigarettes are smoked by machine and the particulate fraction of smoke, or condensate, is collected by methods described in detail below. This step eliminates or greatly reduces many harmful gases in smoke, such as carbon monoxide (CO), formaldehyde, nitric oxide, ammonia and hydrogen cyanide [9].

In the second step, the condensate is placed in a

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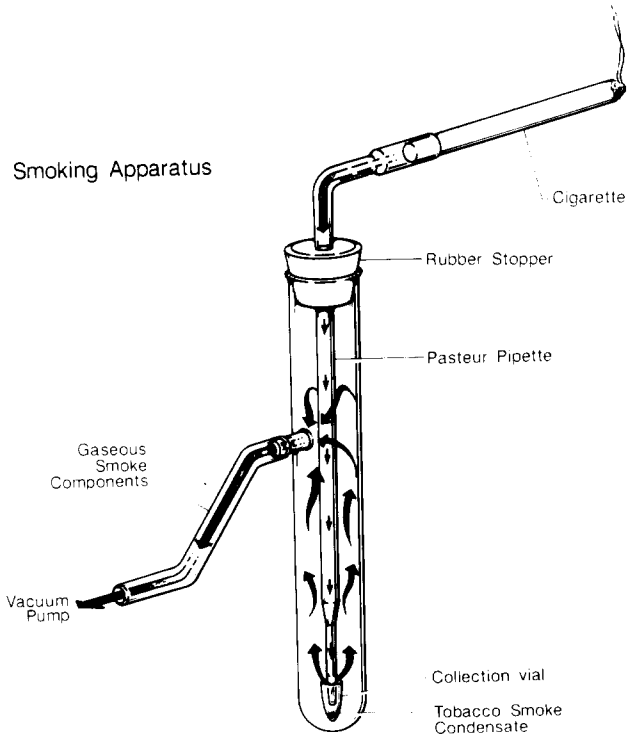

FIG. 1. Cigarette smoke condensate collection system. Smoke particulates are collected by inertial impaction; gases flow through the exit port to the vacuum pump.

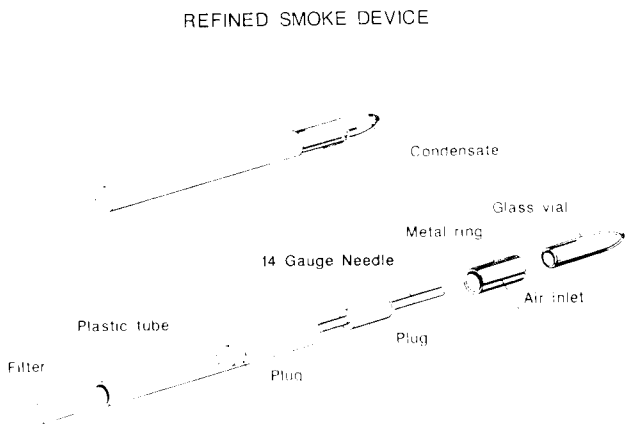

FIG. 2. Refined smoke device, showing assembly from component parts. Before each puff, a flame was applied to the vial containing tobacco smoke condensate.

cigarette-sized tube and heated. As a smoker takes a puff, vapors drawn from the tube condense into an aerosol resembling smoke, both visually and in flavor. The condensate is heated only moderately (300–400 degrees C) so that essentially no carbon monoxide is generated. The moderate temperature is also expected to reduce the delivery of relatively nonvolatile components of condensate, such as benzo[a]pyrene and benz[a]anthracene, which are known carcinogens [9]. Additionally, as will be shown below, the nicotine delivery is also low, relative to the satisfaction reported by smokers who tested the refined smoke device.

EXPERIMENT 1

In this study we compared subjects' ratings of: (1) their own brands, (2) a low tar and nicotine cigarette, and (3) the refined smoke device.

METHOD

Subjects

Nine subjects (6 males, 3 females) between the ages of 20 and 56 (mean age 38) participated in the study. Subjects were recruited by advertisements in local newpapers offering $8 per hour. Subjects reported being in good health and smoking over 1 pack of cigarettes per day.

Apparatus

Smoke condensate trap (see Fig. 1). This apparatus consisted of a cigarette holder attached to a Pasteur pipette inserted vertically (tapered end down) through an airtight seal at the top of a sidearm tube. The sidearm was connected to a vaccum pump so that suction could be applied to a cigarette placed in the holder. The tip of the Pasteur pipette was placed in a 0.5 cc glass collection vial. Upon lighting the cigarette, smoke was drawn down the pipette; as it reached the collection vial the smoke was greatly accelerated (to over 100 m/sec) due to the reduction in cross sectional area of the tip. Most particles were trapped by inertial impaction and accumulated in the vial. Many gases, such as carbon monoxide, flowed through the vacuum port and were expelled. Other gases, that might have dissolved to an appreciable extent in the condensate, were eliminated by boiling the condensate for 30–60 sec until most of the water was removed.

Refined smoke device (see Fig. 2). The refined smoke device consisted of a glass vial, containing cigarette smoke condensate, attached with a metal ring to a hollow cylindrical plastic tube, approximately the size of a cigarette. A vent in the metal ring holding the glass vial allowed air to be drawn into the device, and also relieved any excess pressure inside the vial. During operation, heat was applied to the vial with an alcohol burner and, upon puffing, smoke was conveyed to the mouthpiece through a 14-gauge stainless steel needle. The needle and surrounding plug forced air taken in the through the vent to pass through the vial before reaching the mouthpiece. A conventional cigarette filter in the mouthpiece removed much of the particulate matter from the smoke. This was indicated by the observation of a discrete circular spot of particulate deposition on the center of the filter surface that faced the smoke stream. The needle may also have filtered large particles of smoke that impacted at its distal end where the entering air stream changed direction.

Procedure

Subjects were asked to rate puffs of the following: (1) their own preferred brands of cigarette; (2) a commercial ultra-low tar cigarette (Carlton 85 mm filter hard pack); and (3) the refined smoke device. The experimenter heated the glass vial containing condensate in the flame of an alcohol burner for 4–5 sec just prior to each puff. The temperature inside the vial, as measured with a thermocouple probe (Omega type K chromel alumel probe with Fluke model 51 K/J thermometer), was 300–400 degrees C. This is substantially lower than the temperature in the burning cone of a cigarette (approximately 800 degrees C).

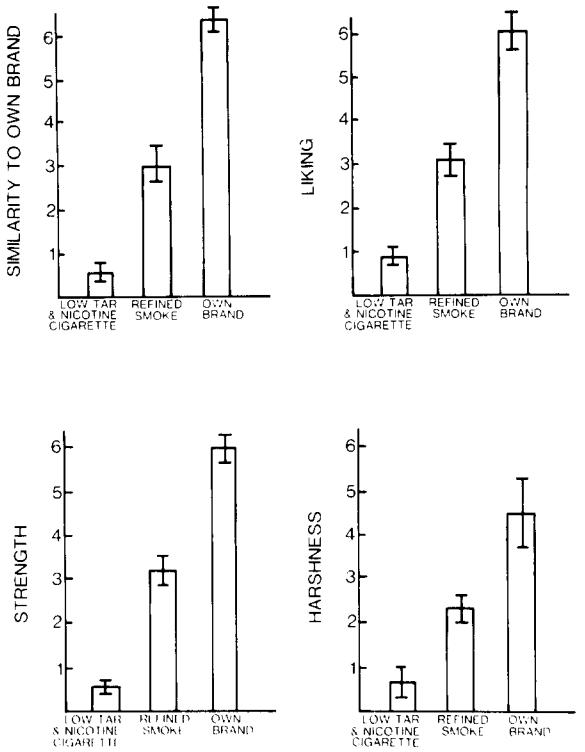

FIG. 3. Subjective ratings of three types of puffs, using scales that ranged from 0–9. Bars denote standard errors of the mean.

In order to minimize subjective bias, all puffs were presented through a mouthpiece that protruded through an opaque screen. Thus, subjects could not identify the cigarettes they were sampling. Puffs were presented in pseudorandom sequences according to Latin square designs. Three sets of puffs, each set presenting one puff of each type, were given in a 10-minute period (a total of 9 puffs). Subjects rated each puff for how much they "liked" it, how "similar" it was to their customary brand, how "strong" it felt, and how "harsh" it was. Ratings of each of these four qualities were made using 10-point scales ranging from 0 ("not at all") to 9 ("very much").

Standardized estimates of "tar," nicotine and CO deliveries were based on smoking procedures established by the Federal Trade Commission (FTC), even though these are not necessarily indicative of what individual smokers obtain (see Experiment 2). According to the FTC procedure [5], a 35 cc puff (2 sec duration) is taken every minute until a certain butt length is reached (approximately ten puffs). The smoke particulate matter is collected with high efficiency Cambridge filters and subsequently analyzed for nicotine content and "tar," defined as total particulate matter minus nicotine and water. To determine the standardized tar and nicotine delivery from the refined smoke device, we used Cambridge filter pads to trap the smoke delivered in ten 35 cc puffs, taken with a syringe. The Cambridge pads were assigned code numbers and sent to the Clinical Psychopharmacology Laboratory at the Veterans Administration Medical Center, Sepulveda, CA, for nicotine assay, using high pressure liquid chromatography. The same method of collection and analysis applied to commercial cigarettes yielded values for nicotine delivery in close agreement with published values [11].

The tar content of Cambridge filters was measured by extracting the smoke particulate matter with methanol and determining the absorption of ultraviolet light (UV) at a wavelength of 400 nm, using a spectrophotometer (Sequoia-Turner Model 340). This method has been shown to correlate highly with the tar determined from weighing dessicated samples, but has the advantages of greater precision (with low tar deliveries) and is also not influenced by water content of the material [12].

To measure the CO content of smoke delivered from the refined smoke device, 35 cc puffs of smoke were drawn through a Cambridge pad (to filter out the particulate matter), and each sample was diluted in 1 liter of air. Samples were then analyzed in an Ecolyzer CO analyzer (model 211). This method was used with subjects' own brands of cigarette (using 3 successive dilutions) and yielded similar values to those published by the FTC.

RESULTS

For every subject, the ratings of the 3 puffs of each type were first averaged to obtain mean ratings of liking, similarity to own brand, strength, and harshness. Planned comparisons were then conducted, using paired t-tests to compare mean ratings of refined smoke with those of subjects' own brands and the low tar and nicotine cigarette.

For each scale, ratings of refined smoke were significantly greater than those of the low tar and nicotine cigarette, $t(8)=5.26$, $p<0.001$ for similarity; $t(8)=4.56$, $p<0.01$ for liking; $t(8)=6.63$, $p<0.001$ for strength; $t(8)=4.84$, $p<0.01$ for harshness. However, subjects rated their own brands significantly higher than refined smoke, $t(8)=8.27$, $p<0.001$ for similarity; $t(8)=5.33$, $p<0.001$ for liking; $t(8)=5.62$, $p<0.001$ for strength; $t(8)=3.64$, $p<0.01$ for harshness. As shown in Fig. 3, the ratings of refined smoke were generally intermediate to those of the two types of commercial cigarette brands.

The FTC tar and nicotine deliveries of subjects' preferred brands of cigarette were available from published information (FTC report, January, 1985): the means were 0.96 mg nicotine (s.d.=0.30), 14.7 mg tar (s.d.=5.1) and 13.4 mg CO (s.d.=1.8). The tar and nicotine delivery of the low tar and nicotine cigarette was below the sensitivity of the FTC method: 0.05 mg nicotine, 0.5 mg tar and 0.5 mg CO; the manufacturer's estimate of the delivery was 0.002 mg nicotine and less than 0.01 mg tar. The reliability of our method of assessing standardized deliveries was comparable to that of the FTC. In ten puffs, the refined smoke device delivered less than 0.05 mg nicotine, 0.5 mg tar and 0.5 mg CO.

EXPERIMENT 2

The previous study showed that many of the sensory characteristics of cigarette smoke could be reproduced while eliminating most of the nicotine, tar and carbon monoxide. An important issue that was not addressed is whether subjects would be satisfied with a relatively low nicotine delivery if they used the refined smoke device repeatedly. Based on previous research implicating sensory factors in smoking satisfaction [18], we predicted that subjects would be satisfied if the refined smoke was perceived as strong. To test this hypothesis, we allowed overnight-deprived smokers to use the refined smoke device five times over the course of a

morning. Actual smoke intake, measured with appartus developed previously [19], and subjective satisfaction were compared with that of a low tar and nicotine cigarette presented on a different morning. The low tar and nicotine cigarette was significantly different from that used in the previous study; instead of using Carlton hard pack cigarettes, with an estimated nicotine delivery as low as 0.002 mg, we used Carlton soft pack cigarettes, with a 0.1 mg FTC nicotine delivery. This pitted the refined smoke against a stronger, more popular brand of low nicotine cigarette. Although not as popular as subjects' own brands, these low nicotine cigarettes represent a product currently available to smokers desiring to reduce their nicotine and tar intake, and these cigarettes have a nicotine delivery comparable to that of the refined smoke device under evaluation.

METHOD

Subjects

Twelve subjects (5 males, 7 females) between the ages of 20 and 63 (mean age 38) participated in the study. Subjects were recruited by advertisements in local newpapers offering $10 per hour. Subjects reported being in good health and smoking over 1 pack of cigarettes per day (mean=27 cigarettes per day, s.d.=8.1), delivering an average of 1.06 mg nicotine (s.d.=0.20).

Apparatus

Refined smoke device. The device used was similar to that in the previous study (see Fig. 2). However, a smaller air intake vent was used; this reduced the dilution with air and hence increased the strength somewhat. Another refinement was the use of a mixture of condensate and unburned tobacco (approximately 75 mg condensate and 50 mg tobacco) in each vial. This reduced the clogging that occasionally occurred when using only liquid condensate, and may have improved the flavor as well. The standardized nicotine delivery in 10 puffs taken from the device with a 35 cc syringe was approximately 0.1 mg, comparable to that of the Carlton soft pack.

Smoke intake monitor. For six of the subjects, we used a specially designed apparatus to measure their cumulative intake of tar and nicotine [19]. This apparatus split the mainstream smoke from each puff into eight paths and trapped one eighth of the smoke particulate matter in a Cambridge filter for subsequent biochemical analysis.

Procedure

On two mornings, subjects came to the laboratory after overnight abstinence from cigarette smoking. Five smoking periods were presented at 30 min intervals each day. Each smoking period consisted of ten puffs; subjects requested each puff as desired, so that interpuff intervals simulated natural smoking. On one day, subjects smoked a Carlton soft pack cigarette in every smoking period, and on the other day they used the refined smoke device (order counterbalanced). The condensate vial was changed after each set of puffs. As in Experiment 1, visual cues during smoking were minimized by an opaque barrier, and tactile cues were equated by smoking both cigarettes through a plastic mouthpiece.

Subjects rated each set of puffs for satisfaction, strength of flavor/aroma, strength of throat impact, harshness (scratchiness or irritation), and estimated nicotine content.

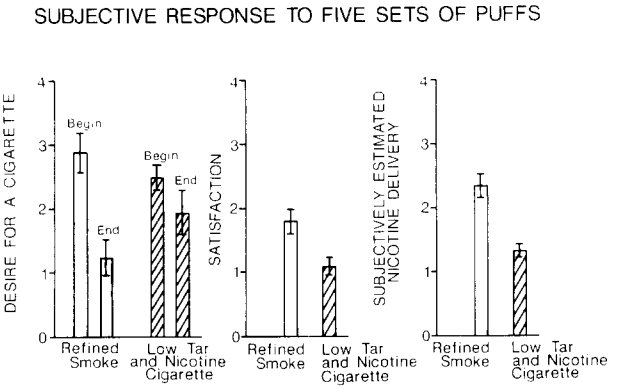

FIG. 4. Subjective response to five sets of puffs from either Carlton soft pack cigarettes or refined smoke device. Scales ranged from 0–4, and bars denote standard errors of the mean.

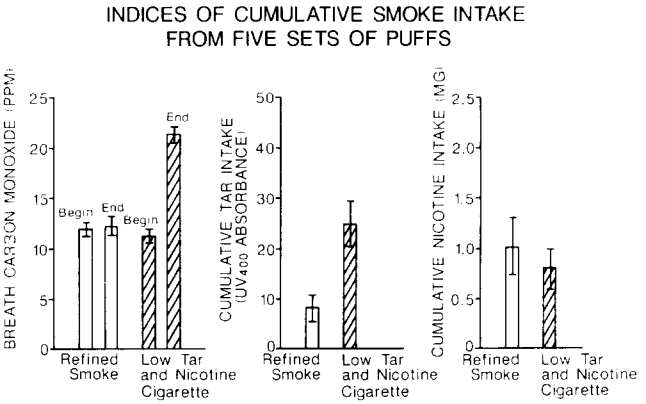

FIG. 5. Cumulative intake of carbon monoxide, tar and nicotine after five sets of puffs from either Carlton soft pack cigarettes or refined smoke device. Tar intake was reflected by UV absorbance of material extracted from Cambridge filters that trapped a portion of inhaled smoke. Bars denote standard errors of the mean.

Additionally, subjects rated their lightheadedness (a pharmacologic effect of nicotine). All ratings were made using 5-point scales ranging from "not at all" (0) to "extremely" (4).

Subjective ratings of desire for cigarettes were of special interest, and were assessed in two ways. First, subjects reported their "craving" for cigarettes immediately before and after each set of puffs using a ten-point scale (0–9) employed in previous studies; second, at the beginning and end of the session, subjects filled out mood questionnaires containing 21 items (five-point ratings), in which were embedded "Would you like a cigarette?" and "Do you miss a cigarette?".

At the beginning of the session, and after every smoking period, heart rate and blood pressure were recorded with a portable automated monitor (North American Philips Model HC-3001). Heart rate is a sensitive index of nicotine intake in overnight-deprived smokers [1].

Breath CO concentrations were measured at the beginning of the session (to verify overnight abstinence) and after each smoking period. Subjects held their breath for 15 sec

prior to inflating sample balloons. To minimize variability in breath CO content caused by dilution with dead space air, the sample volume was regulated to 1 liter by a rigid plastic ring (39 cm circumference) surrounding the balloon.

For the six subjects who smoked through the smoke intake monitor, Cambridge filters trapping a portion of the smoke particulates were collected, reflecting cumulative smoke intake during the entire session. These filters were analyzed for tar and nicotine by the same methods as in Experiment 1.

RESULTS

For every subject, the ratings of puffs from the 5 sets were averaged to obtain mean ratings of satisfaction, strength, harshness, nicotine content and lightheadedness. Planned comparisons were then conducted, using paired t-tests to compare mean ratings of the refined smoke with those of the low tar and nicotine cigarette. Refined smoke was rated significantly more satisfying than the low tar and nicotine cigarette, $t(11)=3.78$, $p<0.01$ (see Fig. 4). Moreover, it was rated stronger, $t(11)=3.05$, $p<0.05$ for strength of aroma/flavor; $t(11)=4.81$, $p<0.001$ for strength of throat impact. It was also rated harsher than the low tar and nicotine cigarette, $t(11)=3.79$, $p<0.01$. Interestingly, when asked to estimate nicotine delivery, subjects rated the refined smoke higher (see Fig. 4), $t(11)=3.95$, $p<0.01$. Reports of lightheadedness were low and did not differ significantly between the two smoking conditions, $t(11)=1.34$, $p>0.2$.

Cumulative CO delivery was measured by the pre-post session difference in breath carbon monoxide. The change after smoking the low tar and nicotine cigarette (see Fig. 5) was significantly greater than after using the refined smoke device, $t(11)=9.21$, $p<0.001$; breath CO showed virtually no change after five smoking periods with the refined smoke device, and sustained an approximately 9 ppm increase after five low tar and nicotine cigarettes.

The direct measure of mouth nicotine intake for the first 6 subjects yielded comparable values for the Carlton and refined smoke device, $t(5)=0.62$, $p>0.4$, corresponding to an average of roughly 0.25 mg per set of 10 puffs. However, estimated tar intake was significantly greater in the Carlton condition, $t(5)=3.09$, $p<0.05$ (see Fig. 5).

The pre-post session change in heart rate was not significant in either condition. Mean heart rate at the beginning of the session was 81.5 bpm (s.d.=12.7) in the Carlton condition and 83.2 bpm (s.d.=10.2) in the refined smoke condition. End of session heart rate (immediately after puff set No. 5) was 80.6 bpm (s.d.=7.8) in the Carlton condition and 80 bpm (s.d.=10.5) in the refined smoke condition.

Reported desire for a cigarette, as measured by the sum of the ratings on the two items "Would you like a cigarette?" and "Do you miss a cigarette?", decreased significantly more in the refined smoke condition than in the Carlton condition (see Fig. 4), $t(11)=2.31$, $p<0.05$ for the change in reported desire. Mean reported craving for cigarettes, based on 9 measurement points at which the ten-point "craving" scale was administered, was also lower in the refined smoke condition: 3.6 (s.d.=2.27) vs. 5.0 (s.d.=2.42), $t=3.45$, $p<0.01$.

DISCUSSION

The subjective and biochemical results from Experiments 1 and 2, taken together, suggest that refined smoke may duplicate many of the enjoyable sensory aspects of smoking, while greatly diminishing the delivery of many smoke constituents. Most notably, carbon monoxide, a suspected contributor to cardiovascular disease and sudden cardiac death [23], was almost completely eliminated. It is likely that volatile ciliatoxic components such as formaldehyde and hydrogen cyanide were also eliminated. The tar delivery was reduced more than 10-fold relative to the FTC deliveries of subjects' own brands, and was even less than the low tar and nicotine cigarette in Experiment 2. Nicotine delivery—as assessed by mouth intake, heart rate, and reports of lightheadedness—was comparable to that of a low tar and nicotine cigarette. However, subjects in Experiment 2 rated the refined smoke as significantly more satisfying and their craving for cigarettes was reduced substantially. Subjects also believed that the nicotine delivery of the refined smoke was significantly higher. Previous research suggests that subjects may estimate nicotine delivery based on perceived throat impact [3], and the refined smoke has two features which maximize its sensory impact. First, the ratio of nicotine to tar delivery is higher than that of a commerical cigarette (see Fig. 5). Smoke with a relatively high nicotine/tar ratio produces stronger throat sensations than smoke with the same nicotine delivery but higher tar delivery [11]. Second, the relative particle size of the refined smoke was greater than that in conventional cigarette smoke (Rose and Hinds, unpublished data). Therefore, a much higher fraction of the smoke particles (but comparable absolute amount) may deposit in the upper airways [16], producing intense flavor and throat impact.

Based on our results, three broad applications could be proposed for a refined cigarette smoke delivery system, assuming it could be suitably packaged in a convenient form. First, it could be useful in controlling for the sensory components of cigarette smoking in studies of the pharmacologic effects of nicotine. The lack of a convincing low nicotine placebo has confounded laboratory studies seeking to isolate the reinforcing effects of inhaled nicotine.

Second, it merits investigation as an aid to smoking cessation. A cigarette substitute employing the refined smoke method might be used in conjunction with a nicotine replacement technique such as a transdermal nicotine patch [17]. For some smokers, the refined smoke could be discontinued while maintaining the delivery of nicotine with a patch; subsequently, the nicotine dose could be gradually reduced and eliminated. On the other hand, some smokers might prefer to relinquish the nicotine first, while retaining familiar smoking-related cues. The continued use of the cigarette substitute after reduction or withdrawal of nicotine might lead to a gradual extinction of the reinforcing value of the sensory cues. This would presumably facilitate smoking cessation.

Third, the enjoyment of the cigarette substitute may continue indefinitely despite the reduced pharmacologic effects of nicotine (just as people can permanently switch from caffeinated to decaffeinated coffee). It so, and if the health consequences of refined smoke were acceptably low, one could envision the use of refined smoke as a long-term replacement for cigarettes. Before endorsing this application, any long-term adverse health effects would first have to be carefully assessed with chemical and biological assay methods. Conceivably, by reducing overall tar delivery and manipulating particle size to reduce the deposition of smoke particles in the small airways, it is possible that cancer of the lung, the most lethal of cancers caused by smoking, could be eliminated. In contrast, cancers of the larynx and oral cavity ac-

count for less than 3% of cigarette-related deaths [22]. Moreover, chromatographic profiles of the refined smoke suggest that many specific components normally present in tobacco smoke condensate have been eliminated (Rose and Tachiki, unpublished data) and ongoing work seeks to identify these components. Such knowledge could be useful in minimizing the delivery of all harmful smoke constituents; this would be a desirable goal regardless of the particular application of the refined smoke method.

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