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Sensory Blockade of Smoking Satisfaction[1]

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ROSE, J. E., D. P. TASHKIN, A. ERTLE, M. C. ZINSER AND R. LAFER. *Sensory blockade of smoking satisfaction.* PHARMACOL BIOCHEM BEHAV **23**(2) 289–293, 1985.—Cigarette smokers were presented with controlled doses of cigarette smoke to determine whether the resulting reduction in cigarette craving depended upon perceiving the sensory qualities of the smoke. Cigarette craving was assessed before and after inhaling controlled doses of smoke in two conditions: (1) Local anesthesia of the upper and lower respiratory airways, induced by mouth rinsing, gargling and inhalation of a mist containing the topical anesthetic lidocaine; and (2) no-anesthesia control, in which all solutions were saline. A sham smoking procedure was presented in both conditions. Craving and ad lib smoking behavior were also assessed 30 minutes after controlled smoking. The results indicated that smoke, as opposed to sham puffs, significantly reduced reports of cigarette craving, and local anesthesia significantly blocked this immediate reduction in craving produced by smoke inhalation. Puffs were also rated as less desirable in the anesthesia condition. Thirty minutes after smoking, craving was no different in the anesthesia and saline control conditions. However, craving as well as smoking intake in both conditions was less when smoke had been given previously than in the sham smoking control. These results suggest that sensory cues accompanying inhalation of cigarette smoke are important determinants of immediate smoking satisfaction. However, the sustained effects of smoke intake on subsequent smoking behavior (30 min later) may be mediated by processes other than sensory stimulation of the respiratory tract, such as plasma nicotine levels.

Nicotine Cigarette smoking Satiation Anesthesia Conditioned reinforcement Chemosensory cues

AS smoke passes from the burning cigarette into a smoker's mouth and past the pharynx and larynx into the lower respiratory tract it produces a variety of sensations. It has been hypothesized that these chemosensory cues become potent conditioned reinforcing stimuli due to their association with the reinforcing actions of nicotine in the central nervous system [1,2]. In a previous study [14], we showed that local anesthesia of the mouth, pharynx and lower respiratory airways produced a graded reduction in reported cigarette craving. Ratings of puff desirability were also reduced by the sensory blockade.

However, in the latter study the subjective satisfaction obtained from smoking, as measured by the reduction in cigarette craving after smoking, could not be clearly assessed because smoking topography was not controlled. There was a nonsignificant trend for CO level to increase less after smoking when subjects' airways were anesthetized, suggesting there may have been less inhalation of smoke than in the no-anesthesia condition.

In the present study we measured the change in cigarette craving produced by a fixed dose of cigarette smoke both with and without local airway anesthesia. We hoped to determine whether elimination of a major portion of the local sensory feedback would block the reduction in craving usually produced by smoking, which would test the hypothesis that this sensory feedback is reinforcing to smokers.

METHOD

Subjects

Eight subjects (6 males, 2 females) with a mean age of 29.8 years (s.d.=7.5) participated in the study. Subjects smoked at least 15 cigarettes per day (mean=24.8, s.d.=7.8) with a mean nicotine delivery (by FTC method) of 1.0 mg (s.d.=0.19), and a mean total particulate delivery of 15.6 mg (s.d.=3.2). All subjects except one smoked filtered cigarettes, and two subjects smoked cigarettes with ventilated filters.

These subjects had been selected in a preliminary screening session which determined the degree and duration of numbness reported by subjects after local anesthetic administration. The aim was to include only those who showed a comparable time course of anesthesia. In our prior study [14], using methods of administering lidocaine similar to those of the present study, subjective ratings of numbness in the mouth and throat were found to correlate highly with the

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following indices of anesthesia: (1) depression of taste sensation, using different concentrations of sucrose, (2) reduction in the objectively stimulated gag reflex and (3) reduction in cough elicited by serially increasing concentrations of citric acid, a standard irritant.

In the screening session prior to the present study, subjects reported the degree of numbness in the mouth and throat for 30 min after local airway anesthesia. Subjects reported numbness every 5 min, using rating scales in which "0" corresponded to "no numbness" and "10" represented "complete numbness." Criteria for inclusion in the study were that subjects report substantial numbness of the mouth and throat (a rating of at least 5) for at least 5 min after receiving the local anesthetic, and by 30 min the ratings of numbness must have fallen to a low level (a rating less than 2). Approximately 60% of the subjects screened met these criteria. Thus, for all subjects included in the study, the time course of anesthesia was comparable.

Procedure

The procedures for administering the local anesthetic and for delivering fixed doses of smoke were used in every condition and will be described first.

Upper and Lower Airway Anesthesia Procedure

Subjects rinsed their mouths with 2% lidocaine for 90 sec on each of three consecutive occasions. Mouth rinsing was followed immediately by gargling three times with 2% lidocaine. Following this, subjects inhaled 60 breaths (tidal breathing) from a nebulizer that delivered a mist containing 4% lidocaine (pH of 6.3). The lidocaine aerosol was generated by adding 4 cc of 4% lidocaine solution to a flow through nebulizer (DeVilbiss, Model 646) attached to a compressor-driven aerosol generator (Pulmo-Aide DeVilbiss 561 series; Somerset, PA 15501). The inhalations required approximately five minutes, at the end of which subjects rated numbness in their mouth and throat using tenpoint scales.

Controlled Smoke Delivery Method

To control total smoke intake, the number of puffs, puff volume and inhalation volume were controlled. Before each puff was delivered, a water-displacement spirometer was first primed with 500 cc air. Then a 40 cc puff was drawn from the subject's own brand of cigarette using a syringe. The smoke was immediately emptied into a temporary storage bag (in which it remained less than 5 sec before being inhaled). Two electronically operated valves (Skinner electric valve No. V52DA1125) controlled the flow of air and smoke into a short length of tygon tubing which was attached to a face mask. The face mask was modified from an Ambu resuscitator mask, and formed an airtight seal around the subject's nose and mouth. When instructed to inhale a puff, subjects held the mask over their nose and mouth, and placed their lips around the tygon tubing which protruded through the mask approximately 5 cm. At the beginning of an inhalation, one valve opened, permitting smoke to flow into the tygon tubing mouthpiece. Immediately after the smoke (40 cc) was inhaled from the storage bag, a second valve opened, allowing 500 cc air to be inhaled from the spirometer. Subjects exhaled completely as soon as the air had been drawn from the spirometer. This procedure was repeated for each puff.

Each subject was presented with four conditions, and because each condition required approximately 1 3/4 hr, only two conditions were given in the same day, with a 5 minute rest in between the first and second halves of the session. To minimize sequence effects, the order of presentation was counterbalanced across subjects. The four conditions were as follows:

(1) Controlled smoking with local airway anesthesia. Controlled smoking periods were interspersed with presentations of lidocaine, to maintain the anesthesia throughout smoking satiation and also to avoid oversatiating subjects by presenting a long uninterrupted series of puffs. Subjects received three sets of puffs, in which the number of puffs, puff volume and inhalation volume were controlled with the technique described above. Each of the three smoke preloads, presented every 10 min, consisted of 15 puffs, taken from 2 successive cigarettes. The interpuff interval was 30 sec. Immediately prior to each set of puffs, subjects rinsed their mouths, gargled and inhaled lidocaine, according to the airway anesthesia procedure described above, except that the "booster" anesthesia presentations immediately prior to the second and third set of puffs required only 1 rinse, 1 gargle and 40 inhalations of lidocaine.

(2) Controlled smoking without anesthesia. This condition was identical to Condition 1, except that subjects rinsed, gargled and inhaled saline instead of lidocaine.

(3) Sham smoking with airway anesthesia. In this condition, lidocaine anesthesia was administered at the same times and in the same manner as in Condition 1; however, instead of receiving controlled preloads of smoke, each puff (15 puffs per preload) was drawn with a syringe through a plastic cigarette holder (Water Pik "One Step at a Time" Filter No. 4) which diluted the smoke stream with smoke-free air by approximately 95%. (We determined this by weighing the residue trapped in Cambridge filter pads after smoking cigarettes in a standard manner either with or without the cigarette holder.) Puffs were always delivered from behind a partition so that subjects would not observe whether the puff to be delivered was undiluted smoke or diluted smoke ("sham").

(4) Sham smoking without airway anesthesia. In this condition, saline was presented instead of lidocaine, and sham puffs were given instead of smoke.

Thus, in each of these four conditions, three puffing periods (smoke or sham) alternated with three anesthesia (or saline) presentations. Subjects reported their cigarette craving using a tenpoint scale before and after each set of puffs. Carbon monoxide concentrations were measured before and after each series of puffs using an electrochemical analyzer (Ecolyzer, Model A). Each sample was collected after 20 sec breath holding and exhalation of the first 500 cc of expirate to eliminate dead space air from the sample.

A thirty-minute period followed, in which no smoking was permitted, during which any numbness induced by previous anesthesia dissipated. Subjects then reported their cigarette craving and were allowed to smoke freely for 15 minutes (ad lib test), using their customary brand of cigarette. The purpose of this test was to assess the sustained effects of prior smoke or sham inhalations on cigarette craving and smoking behavior. Subjects smoked each cigarette through a cigarette holder containing a self-heated thermistor sensor which reacted to changes in smoke flow [5]. Flow signals were integrated to provide an estimate of cumulative puff volume inhaled and also to provide an estimate of the number of puffs. The change in endexpired carbon monoxide concentrations after ad lib smoking was also measured.

RESULTS

Reliability of Puff Delivery System

Controlled smoke doses. Each set of controlled puffs increased endexpired air carbon monoxide concentrations by a uniform amount (approximately 12 ppm), which did not differ between anesthesia and control conditions. (Anesthesia×Puffing Period analysis of variance for the smoking condition only: $F(1,7)=0.00$, $p>0.9$). These results indicate that the puff delivery system prevented compensatory changes in smoking topography that might have otherwise caused variations in the amount of smoke inhaled.

Subjective reports of cigarette craving were significantly reduced after each preload of smoke as opposed to sham smoke (a mean change in craving of −2.8 after smoke vs. 0 after sham (Smoke×Puffing Period analysis of variance for no-anesthesia conditions; $F(1,7)=38.97$, $p<0.001$). Puffs of smoke were also rated as significantly more desirable than sham puffs (4.6 vs. 0.7 in the no-anesthesia conditions (Smoke×Puffing Period analysis of variance: $F(1,7)=18.02$, $p<0.01$). Controled puffs of smoke were only somewhat less desirable than puffs taken freely through a cigarette holder during the ad lib test: the mean rating across the three smoke periods was 4.6 (in the no-anesthesia, real smoke condition) vs. 6.5 during the ad lib test, paired $t(7)=2.3$, $p>0.05$. Hence, we conclude that although smoke was delivered in a highly stereotyped and artificial manner, it was nonetheless subjectively satisfying.

Effectiveness of Anesthesia

The extent and duration of anesthesia were assessed by subjective ratings of numbness in the mouth and throat. Ratings of numbness after saline rinses, gargles and inhalations were always near zero. Immediately after the first administration of lidocaine, ratings of numbness in the mouth and throat were 8.8±1.01, and 8.7±1.29, respectively. Thus, while some ability to perceive the local chemosensory stimulation of smoke no doubt remained, these sensations were substantially blunted.

Effects of Sensory Blockade on Cigarette Craving and Smoking Satisfaction

To analyze the effects of airway anesthesia on the subjective satisfaction produced by the fixed preloads of smoke, craving before and after smoking was compared between anesthesia and saline control conditions. Mean craving in the real smoke conditions, before the first smoke delivery, was lower in the anesthesia condition than in the no anesthesia condition (2.4 vs. 3.8, paired $t(7)=3.25$, $p<0.05$), replicating the finding in our previous study [14]. The mean reduction in craving after each set of controlled puffs of smoke was significantly less in the anesthesia condition than in the saline control condition (a mean reduction of 1.1 vs. 2.7, Anesthesia×Puffing Period analysis of variance: $F(1,7)=18.18$, $p<0.01$), suggesting that smoking satisfaction was partially blocked by lidocaine anesthesia (see Fig. 1). This reduction in the effects of smoke on craving in the anesthesia condition was not simply the result of a lower pre-smoking level of craving in the anesthesia condition. An analysis of covariance on post-smoking craving, partialling out pre-smoking craving showed a significant main effect of anesthesia, $F(1,6)=11.74$, $p<0.02$. Desirability ratings of puffs of smoke were also reduced by the anesthesia,

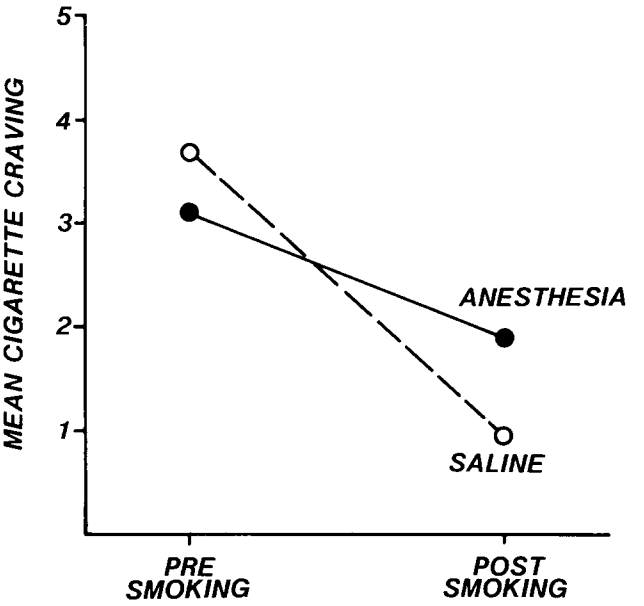

FIG. 1. Mean reported cigarette craving before and after smoking in two conditions: upper and lower airway anesthesia vs. saline control.

$F(1,7)=6.16$, $p<0.05$. Mean desirability was 3.1 in the anesthesia condition and 4.6 in the no anesthesia condition.

Effects of Local Airway Anesthesia on Ratings of Strength and Harshness

There were no significant effects of anesthesia upon puff strength and harshness ratings. This nonintuitive finding was also reported in the Rose *et al.* (1984) study [14]. Smoke was, of course, rated much stronger and harsher than the sham inhalations of diluted smoke (Smoke×Anesthesia×Puffing Period analyses of variance showed a main effect of smoke on strength and harshness: mean strength was 5.6 (smoke) vs. 0.9 (sham), $F(1,7)=29.95$, $p<0.001$; mean harshness was 5.4 (smoke) vs. 0.7 (sham), $F(1,7)=44.61$, $p<0.001$).

Ad Lib Smoking Period

The ad lib test smoking period occurred at least 30 minutes after the last set of controlled puffs, and long enough after previous lidocaine administration for the subjective numbness to have disappeared. After the prior controlled puffs of smoke, craving had been higher in the anesthesia condition than in the saline control condition, yet immediately before the ad lib test smoking period there was no difference in craving (Smoke×Anesthesia analysis of variance: $F(1,7)=0.5$, $p>0.8$). However, the same analysis showed that craving before the ad lib test smoking period was significantly lower in the smoke conditions than in the sham smoke conditions (4.9 after smoke vs. 6.2 after sham; $F(1,7)=24.20$, $p<0.01$). Smoke×Anesthesia analyses of variance for each of the three behavioral measures of smoking during the ad lib smoking period (number of puffs, puff volume, and increase in endexpired CO) showed a reduced voluntary smoke intake after controlled smoke deliveries relative to sham puffing conditions: 14.4 vs. 19.6 for mean number of puffs, $F(1,7)=3.72$, $p<0.1$; 687 cc vs. 926 cc for puff volume, $F(1,7)=3.89$, $p<0.1$, and 7.2 ppm vs. 11.2 ppm

for endexpired CO increase, $F(1,7)=12.53$, $p<0.01$. Thus, two measures of smoking motivation (cigarette craving and CO intake from ad lib smoking) were significantly reduced by prior smoke preloads, and the remaining two indices (number of puffs and cumulative puff volume) showed trends in the same direction.

While prior controlled deliveries of *smoke* influenced smoking during the ad lib test, prior *anesthesia* did not; a Smoke×Anesthesia analysis of variance for each of the smoking measures during the ad lib test showed no difference between anesthesia and saline control conditions, $F(1,7)=0.05$; $F(1,7)=0.99$, $F(1,7)=0.58$, $F(1,7)=1.53$ for craving, CO increase, number of puffs, and puff volume, respectively.

DISCUSSION

The main finding of this study was that smoking satisfaction, as measured by the immediate reduction in cigarette craving after inhalation of controlled amounts of smoke, was substantially blocked by local anesthesia of the respiratory airways. These results add to our previous findings [14] implicating the chemosensory feedback from smoke inhalation as reinforcing stimuli. Whether these cues are conditioned or unconditioned determinants of cigarette craving can be answered only by further research.

The counterintuitive finding that anesthesia did not affect ratings of strength and harshness of cigarette smoke has been addressed previously [14]. One explanation considered was that subjects altered puffing topography to compensate for the effects of local anesthesia; this possibility is ruled out by the present study, in which smoking topography was controlled. It is likely that incomplete anesthesia of the lower respiratory tract, where harshness and strength may have been perceived, accounts for the absence of a significant influence of anesthesia on strength and harshness ratings. The greater surface area present in the lower respiratory passages may require more anesthetic and/or smaller aerosol droplets than the upper airways to be fully numbed. Also, more effective anesthesia might be necessary to block the irritant properties of smoke than to block other sensory modalities. These irritant effects result from nicotine and gas phase constituents in smoke [4,11]. Those areas or constituents not blocked by the dose of lidocaine used in our study may be adequate for discrimination of strength and harshness, but they are not sufficient to mediate subjective satisfaction.

The results also showed that craving and smoking behavior during the ad lib smoking test period, after the local anesthetic had largely worn off, were no different between anesthesia and control conditions. Nonetheless, craving and smoking behavior were lower in both conditions if smoke had been given 30 min prior to ad lib smoking (versus sham control). This suggests that there may be an important distinction between the immediate satiating effects of cigarette smoke, which were partially blocked by airway anesthesia, and the sustained effects, which were unaffected by prior anesthesia at the time smoke had been given. Conceivably, the immediate satiation following smoking may be mediated to a significant extent by sensory feedback from the respiratory tract, while sustained effects might be due to other effects, such as elevated plasma nicotine levels. If this speculation is borne out, cigarette smoking could be viewed as being analogous to other consummatory behaviors. For example, drinking is initiated by water deprivation which is sensed in the central nervous system and gives rise to a craving for liquids (thirst). Ingestion of liquids stimulates afferent sensory fibers causing immediate satiation well before the physiological deficit which generated the craving has been reversed [3]. Stimulation of respiratory sensations by cigarette smoke may be analogous to peripheral feedback following drinking, and the central nervous system effects of smoking or nicotine may be analogous to the reversal of water depletion following drinking (except that nicotine's central nervous sytem effects occur much sooner after inhalation compared to those of water after drinking).

Our interpretation of the present results predicts that methods of administering nicotine without the specific sensory qualities of smoke would not be perceived as completely satisfying, even though they may partially reduce craving for a cigarette. For example, nicotine chewing gum has been shown to reduce cigarette craving [7,12] but it has undesirable sensory qualities (e.g., bad taste) that do not resemble cigarette smoke. This may account for its low addiction liability [12]. We predict that transdermal nicotine administration [13] would similarly depress cigarette craving without being perceived as an enjoyable substitute for smoking, due to its lack of sensory effects. Nor are intravenous injections of nicotine a complete substitute for cigarettes [6, 8, 10]. Russell and Feyerabend [15] have argued that the rapidity of nicotine absorption from the pulmonary route is important in producing the reinforcing effects of cigarette smoke. However, even large doses of nicotine administered over extremely short periods of time (e.g., 3 mg in 10 sec) do not fully duplicate these reinforcing effects [6]. The view that inhalation of nicotine "boli" is responsible for the uniquely desirable qualities of cigarettes to a smoker has been widely accepted despite the absence of direct experimental support [9]. The results of our present study support an alternative account for the enjoyment and satisfaction reported by cigarette smokers, i.e., the conditioned reinforcing effects of the sensory feedback accompanying inhalation. When these cues were partially blocked (with local anesthesia) the satisfaction of smoking was blunted, despite the fact that equivalent boli of nicotine had been inhaled. It is conceivable that the conditioning of smoking-related cues might be facilitated by the temporal contiguity afforded by the short lung-to-brain transit time for inhaled nicotine. Whether a rapid nicotine absorption is required to effectively condition sensory cues is an issue that should be addressed in future research.

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