

# Nicotine Preference Increases after Cigarette Deprivation<sup>1</sup>

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ROSE, J. E., M. E. JARVIK AND S. ANANDA. *Nicotine preference increases after cigarette deprivation.* PHARMACOL BIOCHEM BEHAV 20(1) 55-58, 1984.—In order to test the theory that nicotine is a reinforcing constituent in tobacco, smokers' nicotine preference was assessed after two hours' cigarette deprivation and immediately after smoking two cigarettes. Preference was measured by allowing subjects to freely adjust the nicotine concentration of each puff using a smoke mixing device. Nicotine preference was significantly higher after deprivation, showing that nicotine in cigarette smoke is positively reinforcing and smokers' attempts to obtain nicotine vary with prior cigarette consumption.

Nicotine      Cigarette smoking      Tobacco      Puffing      Satiation

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NICOTINE is the main pharmacologically active constituent in tobacco, and is hypothesized to be the principal reinforcing component maintaining cigarette smoking [2, 12, 21]. Although this view is widely accepted, attempts to confirm that smoking is an instance of nicotine-seeking behavior have so far provided no definitive evidence [3, 13]. The main research strategy has been to vary the nicotine delivery of cigarettes in order to observe compensatory changes in smoking behavior. Presumably, if smokers regulate nicotine intake, reducing the nicotine yield of cigarettes should cause them to increase the number of cigarettes smoked and/or the number and size of puffs taken from each cigarette, depth of inhalation, etc. These studies have typically demonstrated only slight compensation for substantial changes in nicotine delivery [9]; however, findings concerning nicotine regulation do not bear directly on the question of whether nicotine is a positive reinforcer for smoking. Even perfect regulation of nicotine intake would be consistent with the hypothesis that nicotine is aversive, with smokers limiting their smoke intake so as not to exceed some level of nicotine [20]. Conversely, the complete absence of regulation would be consistent with the theory that nicotine retains its reinforcing value over a wide range of doses. The results indicating partial regulation do not unambiguously support the belief that nicotine is positively reinforcing. Studies examining the influence of intravenous nicotine on cigarette smoking face similar interpretational problems [16, 17], although there are reports that nicotine injections may be considered pleasant under some conditions [8, 14, 15].

The goal of the present study was to determine directly whether cigarette smoking indeed has a nicotine-seeking

component, using a new methodology for measuring smokers' nicotine preference. This technique allowed subjects to selectively adjust the nicotine concentration in cigarette smoke with each puff by means of the smoke mixing device depicted in Fig. 1. Turning the knob on the mixer blended smoke in graded amounts from a high nicotine (2.45 mg) and a low nicotine (0.48 mg) reference cigarette (University of Kentucky Tobacco Research Institute cigarettes 2R1 and 2A1). Both cigarettes delivered roughly 36 mg tar. The flow of smoke through each barrel of the mixer was continuously monitored with pressure transducers attached to each side. Details of the device and measurement procedure have been described elsewhere [18]. Since the nicotine delivery, rather than overall smoke delivery, was under the subject's control, the rewarding and/or aversive properties of nicotine could be inferred by the nicotine level chosen at a particular time, unconfounded by other constituents in smoke or sensorimotor and social aspects of the habit. Positively reinforcing aspects of nicotine would be unambiguously demonstrated by the choice of a mixture delivering more than 50% smoke from the high nicotine side, and, conversely, an aversion to nicotine would be clearly evidenced by a selection of the lowest nicotine delivery. Selection of a 50-50 mixture would indicate either indifference to nicotine or a positive preference for that intermediate nicotine level. Selection of mixtures delivering between 0 and 50% from the high nicotine side are similarly ambiguous in that they would be consistent either with a mild aversion to nicotine or simply a preference for a positively reinforcing, but lower concentration of that substance. The 50-50 mixture point is a conservative choice for an indifference point in that it corresponds

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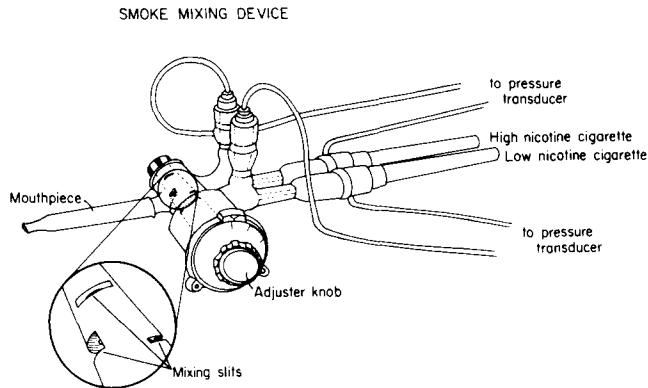


FIG. 1. Smoke-mixing device used to assess smokers' nicotine preference. The knob controls the positions of mixing slits which blend high and low nicotine smoke to achieve intermediate nicotine deliveries. Tar delivery is held constant with the research cigarettes employed. The mixture setting chosen with each puff is measured with pressure transducers that monitor the flow of smoke through each barrel of the mixer.

to a nicotine delivery of roughly 1.5 mg, which is higher than most commercial brands. However, a conservative test seemed appropriate to provide a more stringent test of the nicotine hypothesis than had been conducted previously.

Inasmuch as smoking abstinence has been shown to be a potent variable influencing subsequent smoking [10,16], our goal was to measure variations in nicotine preference resulting from smoking abstinence and satiation. In analogy to the work of Cabanac [5], who showed that food-deprived subjects preferred more concentrated sugar solutions than satiated subjects, we predicted that if cigarette deprivation produced a nicotine "hunger," subsequent preference for nicotine should likewise increase.

#### METHOD

##### Subjects

Twenty smokers, who regularly consumed at least a pack a day, and whose customary brand of cigarette delivered (by FTC method) over 0.5 mg, were recruited for the study. Subjects included 12 males and 8 females, with an average age of 38 years (s.d.=2.7). Subjects smoked on the average 29 cigarettes (s.d.=11), with a nicotine delivery (FTC) of 1.1 mg (s.d.=0.3).

##### Procedure

We assessed subjects' nicotine preference under two conditions: Deprivation, in which subjects abstained from smoking for approximately two hours, (one hour before entering the laboratory and an additional 50 minutes after arriving); and Satiation, in which subjects smoked two cigarettes of their own brand in the twenty minutes immediately prior to the nicotine preference test.

During the nicotine preference test, subjects were instructed simply to find their preferred nicotine concentration, using the mixing device to blend smoke with each puff from the high and low nicotine research cigarettes. They were free to use any cues for finding their optimal nicotine mixture, including the immediate sensory impact of nicotine [6], or the pharmacologic effects which occur within seconds

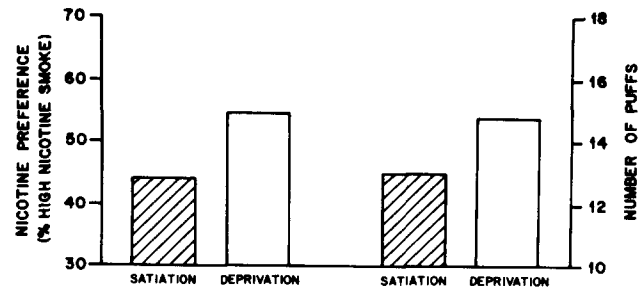


FIG. 2. Mean nicotine preference and number of puffs taken during test smoking period after two hours' cigarette abstinence (Deprivation) and after smoking two cigarettes (Satiation). Significant elevations in both smoking parameters occurred after cigarette deprivation.

of inhalation [21]. To the extent subjects desired the higher nicotine smoke, they could adjust the mixture to as high as 2.45 mg. (Mean nicotine delivery of subjects' habitual brands was 1.06 mg.) For half of the subjects, the high nicotine cigarette was placed in the left barrel of the mixer and for the other half the positions of the high and low nicotine cigarettes were reversed.

Nicotine preference was calculated by averaging the mixture obtained from the high nicotine side for all puffs in each preference test. For each puff:

$$\text{Preference} = \frac{\text{Flow (high nicotine side)}}{\text{Flow (high nicotine side)} + \text{Flow (low nicotine side)}}$$

where the flows were measured using the differential pressure transducer signals recorded on a polygraph.

A replication of each condition was presented (on a different day), and since the results from the days within a condition did not differ, the data were averaged across replications. (Data were missing from four sessions due to apparatus failures.)

Two behavioral measures of smoking were compared between Deprivation and Satiation conditions: (1) average nicotine preference; and (2) number of puffs taken during the test. Additionally, after each puff subjects used two ten-point scales to rate the perceived "strength" and "desirability" of the smoke.

#### RESULTS AND DISCUSSION

Paired *t*-tests (2-tailed) were used to compare puffing, nicotine preference and ratings of strength and desirability between experimental conditions. Figure 2 shows that subjects ( $n=20$ ) preferred significantly higher nicotine concentrations in the Deprivation condition than in Satiation ( $t=2.23$ ,  $p<0.03$ ). Further, subjects who showed consistently higher nicotine preference in Deprivation than Satiation in all sessions ( $n=9$ ), chose a mixture in Deprivation that was not only greater than the low nicotine extreme, but also significantly higher than the 50-50 indifference point ( $t=2.42$ ,  $p<0.05$ ). This constitutes direct evidence confirming nicotine's role as a desired ingredient in cigarette smoke. Ingesting high nicotine smoke was more reinforcing after a period of cigarette deprivation, when nicotine levels were presumably low. A hunger for nicotine thus seems to be evoked by smoking abstinence. For the same nine subjects,

the level of nicotine selected during satiation was marginally lower than the indifference point ( $t=2.22$ ,  $p=0.06$ ), suggesting that nicotine aversion may have influenced preference in Satiation. The assessment of nicotine's aversive qualities depends in part upon whether the criterion for aversion is the choice of a mixture below the indifference point, or selection of the lowest nicotine level possible.

Subjects ( $n=20$ ) also took significantly more puffs after a period of cigarette deprivation than when satiated (mean difference = 1.15; s.d. = 1.94;  $t=2.73$ ,  $p<0.02$ ). Subjects thus increased nicotine intake after smoking abstinence in two ways: taking more puffs as well as increasing the nicotine mixture of each puff. The increase in puffing was, of course, not a specific measure of nicotine-seeking (unlike the mixture adjustment), and may have reflected deprivation for non-nicotine factors in the smoking habit, such as oral or manipulative reinforcement.

In the Satiation condition suppression of smoking was not complete. This may have been due to the fact that the two cigarettes presented in Satiation were insufficient to reverse the effects of almost two hours' deprivation, during which many subjects would have smoked as many as three or four cigarettes. Alternatively, there may be an extremely rapid recovery from the satiating effects of cigarette smoking, stemming from the very short distributional half life of nicotine [4]. Plasma nicotine measurements may be useful in future studies to evaluate this possibility, as well as in verifying that behavioral measures of nicotine preference correlate with plasma nicotine increments.

The nicotine preference of some subjects was more affected by cigarette deprivation than others (the standard deviation of the Deprivation-Satiation difference in percent high nicotine smoke chosen by the 20 subjects in the study was 21%). In order to identify characteristics of smokers who were more responsive to the deprivation manipulation, additional statistical analyses were conducted. The two dependent measures of smoking (difference in nicotine preference between Satiation and Deprivation; and difference in puffing between Satiation and Deprivation) were correlated with a number of individual subject variables, including physical characteristics (age, gender, weight), smoking history (number of cigarettes per day, nicotine delivery of customary brand), mean pre-session expired air carbon monoxide levels, and questionnaire scales derived from smoking motivation questionnaires [11]. The single predictor with a significance at the 0.01 probability level was identified for each dependent measure. The magnitude of increase in nicotine preference with deprivation was found to be positively correlated ( $r=.61$ ,  $p<0.01$ ) with the subject's age. In contrast, subjects whose puffing behavior was most affected by the experimental manipulation tended to report smoking most in social situations ( $r=.63$ ,  $p<0.01$ ). The fact that puffing and nicotine preference were correlated with different subject characteristics suggests that these two factors may represent different types of reinforcement gained from smoking.

The subjective judgments of strength and desirability

TABLE 1  
STRENGTH AND DESIRABILITY OF PUFFS IN DEPRIVATION AND SATIATION CONDITIONS

	Deprivation	Satiation	Deprivation-Satiation
Strength	4.85	5.45	-0.60*
Desirability	5.59	4.85	0.74*

\* $p<0.03$ .

were also affected by experimental conditions (see Table 1). Puffs were rated as significantly less strong ( $t=2.26$ ,  $p<0.04$ ), and more desirable ( $t=2.38$ ,  $p<0.03$ ) following deprivation. Desirability ratings did not correlate with nicotine delivery (a one sample  $t$ -test was used to determine whether the mean of subjects' individual correlation coefficients was significantly greater than zero;  $t=0$  and 0.05 for Deprivation and Satiation, respectively,  $p>0.5$ ). This suggests that factors other than nicotine affected the subjective enjoyment of smoking, or alternatively, that each subject's ratings varied nonlinearly with nicotine delivery. Goldfarb *et al.* [7], and Rose [19], also reported the absence of a correlation between satisfaction ratings and nicotine delivery, whereas strength ratings were positively correlated with nicotine. In the present study, subjects generally displayed a positive correlation between nicotine content of each puff and perceived strength ( $t=4.36$  and 6.29 for tests on the mean of subjects' correlation coefficients in Deprivation and Satiation, respectively,  $p<0.001$ , 2-tailed). The fact that subjects rated puffs as weaker in Deprivation, even though the nicotine levels chosen were higher than in Satiation, suggests that smoking deprivation induces a substantial downward shift in the sensitivity to nicotine. The slopes of regression lines relating perceived strength and nicotine content did not differ across conditions ( $t=0.98$ ,  $p>0.3$ , paired test, 2-tailed), so the shift in strength ratings represents a uniform bias rather than a change in discriminability per se. Perhaps this shift reflects a comparison between the perceived qualities of the smoke and the desired level of nicotine as determined by internal cues. Also involved may be the responsiveness of receptors mediating the common chemical sense, located in the pharynx and sublingual regions [6], or the sensitivity of CNS receptors for nicotine [1]. The relative importance of central versus peripheral stimulation in discriminating nicotine's reinforcing effects has not as yet been firmly established.

Further studies which identify the factors affecting nicotine preference and satiation should significantly clarify the psychopharmacologic basis of cigarette smoking. This knowledge can be applied to designing more effective smoking reduction or cessation programs. Fruitful strategies may employ nicotine substitution or alternative ways to make smoking less hazardous while preserving its desired effects.

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