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Switching to Ultralow Nicotine Cigarettes: Effects of Different Tar Yields and Blocking of Olfactory Cues

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BALDINGER, B., M. HASENFRATZ AND K. BÄTTIG. *Switching to ultralow nicotine cigarettes: Effects of different tar yields and blocking of olfactory cues.* PHARMACOL BIOCHEM BEHAV **50**(2) 233-239, 1995.—Twelve female smokers smoked two of each of three types of cigarettes in three sessions. One cigarette was smoked with and the other one without nose blocking. Total puff volumes increased for ultralow tar/nicotine (tn) cigarettes as compared with habitual regular tar/nicotine (TN) cigarettes and regular tar/ultralow nicotine (Tn) cigarettes, as the result of an increase in the number of puffs. TN and tn, but not Tn cigarettes changed heart rate and beta-power in the electroencephalogram; all three reduced craving, although they differed considerably in subjective acceptance. Blocking of olfactory cues influenced respiration and reduced the average puff volumes, taste, and enjoyment, but it did not differentially affect any parameters among the TN, tn, and Tn cigarettes, which suggests that olfaction plays a minor role in regulating puffing behavior. It was concluded that as compared with regular TN cigarettes, only the tn, but not the Tn cigarettes were oversmoked by about 35%, and that Tn cigarettes might be useful for assessing nonnicotinic factors in cigarette smoking.

Nicotine   Tar   Puffing   Taste   Olfactory sensation   Blocking of olfactory cues

IT IS A WIDELY held notion that smokers adapt their puffing and inhalation behavior to the nicotine yield of their cigarettes. Höfer et al. (7) measured plasma nicotine levels in smokers habituated to "ultralight" cigarettes with nicotine yields between 0.1 and 0.3 mg. These plasma nicotine levels were only about 50% lower than the values obtained in smokers habituated to regular cigarettes with four times higher nicotine yields. On the other hand, requiring subjects to take 2.5 times the accustomed number of puffs per cigarette resulted in increases of plasma nicotine of only about 40%. The assumption that this phenomenon of uptitrating when smoking "ultralight" cigarettes and downtitrating when oversmoking or smoking high yield cigarettes results from the nicotine content of smoke is undermined by the fact that nicotine and tar yields of commercial cigarettes covary rather closely, in a ratio of roughly 1 : 10 (12). Therefore, a more critical approach to the nicotine titration hypothesis would require the independent manipulation of the tar and nicotine yields of smoke.

Nil and Bättig (13) reviewed 12 earlier studies testing varying relations between nicotine, tar, and carbon monoxide (CO) deliveries but found the results to be far from conclusive, suggesting either some or no nicotine or even tar titration. Recently, Robinson et al. (17) compared a 0.06-mg nicotine/7.4-mg tar cigarette with a 0.6-mg nicotine/7.5-mg tar cigarette, and thus a 1 : 123 nicotine/tar ratio with the more conventional 1 : 12.5 ratio. Heart rate and electroencephalogram (EEG) changes were obtained with the conventional tar/nicotine cigarette (TN), whereas the conventional tar/ultralow nicotine cigarette (Tn) produced no EEG changes and only minimal changes in heart rate. The same results with this type of cigarette were also obtained by Domino et al. (5).

As puffing parameters also failed to differ between the Tn and the TN cigarettes in the study by Robinson et al. (17), the notion of nicotine titration might be questioned, but this experiment did not include a comparison with an ultralow nicotine/ultralow tar (tn) cigarette. Such a comparison was made by Hasenfratz et al. (6) in an experiment that assessed subjective parameters, but no puffing parameters, in addition to physiologic effects and nicotine plasma values. The post-smoking increases in plasma nicotine turned out to be in the

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expected order for the TN cigarettes and negligibly low for the Tn cigarettes, whereas the plasma nicotine levels as well as the postsmoking increases in heart rate obtained with the tn cigarettes, amounted to about half of those obtained with the TN cigarettes.

Taste, enjoyment, and postsmoking dizziness were lower for the tn than for the TN cigarettes, and clearly lowest for the Tn cigarettes, whereas subjective strength was similarly lower for the tn and Tn than for the TN cigarettes. Finally, the postsmoking reduction of craving was considerable and similar for all three types of cigarettes, and a quantitative tendency to be smaller with the Tn than with the other two types of cigarettes was supported by only a marginally significant interaction.

In an attempt to study further the reasons for the absence of compensatory smoking with Tn cigarettes, as opposed to that commonly seen with tn cigarettes, the present experiment was done as an extension of the study by Hasenfratz et al. (6), by including a comparison of the flowmeter puffing parameters among the TN, Tn, and tn cigarettes. The absence of compensatory puffing and inhalation encountered earlier with the Tn cigarettes (17) was seen by Hasenfratz et al. (6) as an argument that smokers may adapt their puffing and inhalation behavior to the tar rather than the nicotine yield of the cigarettes, as was proposed earlier by Stepney (20). Another possibility is that the poor taste qualities of the Tn cigarettes might be responsible for the lack of compensation.

Olfaction and taste have been seen to play a greater role for the acceptability of smoke than nicotine and tar yields (13), but so far the relative roles of the sensory constituents of smoke have received little attention. However, Hummel et al. (8,9) recently reported that distinct boli of nicotine vapors, delivered into the nose, elicited dose-dependent averaged EEG potentials as well as burning, stinging, and odorous sensations. Furthermore, smokers rated the S(−) stereoisomers of nicotine as more pleasant than did nonsmokers, whereas no such difference appeared for the R(+) isomers of nicotine. This raises the possibility that nicotine cues are perceived by the smoker through sensory receptors in the nose. If this were the case, puffing and inhalation should become more similar for TN, tn, and Tn cigarettes with the nose closed than with the nose open. To examine this hypothesis, the present experiment included, in addition to the flowmeter puffing analysis, the manipulation requiring the smokers to smoke both with the nose free and with a nose clamp. The experiment was confined to female subjects, as an earlier study by Höfer et al. (7) revealed no sex differences in compensatory puffing in relation to the smoke yields of cigarettes corresponding to the tn and TN cigarettes used in the present study.

METHOD

Subjects

Twelve female regular smokers, smoking at least 15 cigarettes per day with a nicotine yield between 0.7 and 1.1 mg, were selected for the study. Their mean age was 26.5 ± 6.83 yr (range 21–40), and they reported smoking 24.3 cigarettes ± 6.18 per day (range 15–35). On testing days, they were required to abstain from smoking and drinking caffeinated beverages from the time of rising until the beginning of the session (between 0900 and 1000 h). Subjects were recruited by newspaper advertisement and paid the equivalent of $100.00 for completing three test sessions.

Cigarettes

The three types of cigarettes, as summarized in Table 1, were compared in a crossover design.

The tn cigarettes were of the same brand as the TN ones (subject's accustomed cigarette), or, if not possible, of the same blend of tobacco (Maryland or American). The Tn cigarette was obtained from a test market in Florida, under the brand name "NEXT." This cigarette has a tar/nicotine ratio of 1 : 116.25 as opposed to 1 : 12.6 for the TN and 1 : 8.75 for the tn cigarettes.

The order of the three types of cigarettes was balanced across the three sessions of the experiment.

Nose Clamp

To block the olfactory effects of smoking, the subjects had to smoke one of two cigarettes in each of the three sessions wearing a nose clamp of the type commonly used for spirometric measurements. The within-session order of smoking with or without nose clamp was balanced.

Physiologic and Biochemical Parameters

Blood pressure, electrocardiogram, finger and ear pulse amplitude and arrival time, frontal electromyogram, respiration, body movement, EEG, and electro-oculogram were measured as described elsewhere (5). The CO concentration of the expiratory air was measured using the EC50 Micro Smokerlyzer (Bedfont Instruments, Sittingbourne, England).

Subjective Parameters

Six scalometric questions were presented one after another at the top of a computer screen, and the subjects answered by adjusting a pointer on an 18-cm-long horizontal 0–100 analog scale. The scale was marked with "not at all" at the left and "very much" at the right end, and could be operated by a Logitech (Logitech SA, Romanel-Morges, Switzerland) trackball with the dominant hand. The scale included: craving ("How much would you like to smoke now?"); nervousness ("At the moment I feel nervous"); relaxation ("At the moment I feel relaxed"); enjoyment ("How much did you enjoy the cigarette?"); taste ("How good was the taste of the cigarette?"); and strength ("How strong did you find the cigarette?").

TABLE 1

MAINSTREAM SMOKE YIELDS OF THE THREE CIGARETTE TYPES

	TN	Tn	tn
Nicotine yield (mg)	0.9 ± 0.18 (0.7–1.1)	0.08	0.21 ± 0.03 (0.2–0.3)
Tar yield (mg)	11.4 ± 2.75 (8.0–14.0)	9.3	1.83 ± 0.58 (1.0–3.0)
Tar/nicotine ratio	12.6 ± 1.36 (10.0–15.6)	116.25	8.75 ± 2.26 (5.0–10.0)
CO yield (mg)	9.82 ± 2.0 (7.9–14.9)	9.9	3.3 ± 0.96 (2.0–5.5)
Draw resistance (cm H_2O)	9.28 ± 0.82 (8.2–10.3)	11.3	7.61 ± 0.57 (7.3–9.2)

Data are means ± SD and ranges in parentheses. T = medium; t = ultralow tar yield; *N* = medium; *n* = ultralow nicotine yield.

Puffing Behavior

Puffing behavior was recorded automatically using a flowmeter (CGC Ltd., England, cf. (4)) delivering analog signals for flow and pressure. By off-line analysis, quantitative assessments were obtained for duration, inter-puff interval, volume, mean and peak flow, peak pressure, and latency from the beginning of the puff to the peak pressure of each successive puff. Single puffs were defined by an increase in pressure of more than 1.0 cm H_2O; single puffs with an inter-puff interval below 1.5 s and a volume below 5 ml added up to one puff.

Draw Resistance

The static draw resistance of unlit cigarettes was assessed using a U-type water manometer to which a cigarette holder was connected by rubber tubing. This tubing branched off (T-joint), before connecting to the manometer, to a rotameter, from which it led to a surge flask and then to a vacuum pump. The vacuum pump drew air through the unlit cigarette into the closed system at a fixed flow rate (1 liter/min), thereby developing a negative pressure across the cigarette. The pressure drop reading on the manometer was recorded in centimeters of H_20. The pressure drop of the flowmeter device to be added to the pressure drops of the different cigarettes amounted to 1.9 cm H_20.

Procedure

Each subject took part in three test sessions, in each of which she smoked two cigarettes of one of the three types. To avoid novelty effects, the subjects were given a sufficient supply of the type of cigarette to be smoked in the test session for the day preceding a session.

After arrival at the laboratory, the subjects were fitted with electrodes for recording the multiparametric psychophysiologic signals. Then, after a first measurement of respiratory CO, the multichannel psychophysiologic recording started for a first 4-min rest phase, which was preceded and followed by measurements of blood pressure. During the entire rest phase, the subjects sat quietly with their eyes closed. After a second CO measurement, the subjects completed the first three analog scale ratings and then started to smoke a cigarette as naturally as possible through the cigarette flowmeter holder. After the last puff, CO was measured a third time, all six analog scale ratings were completed, and the second 4-min rest phase was started (5 min after the last puff), again with blood pressure measurements before and after. After this second rest phase and a fourth CO measurement, the subjects were free to read magazines until they wished to smoke another cigarette. When this was the case, the time interval was recorded and the same procedure restarted with a third 4-min rest phase.

Data Processing and Statistics

Physiologic data sets were reduced as described elsewhere (6). The reduced data sets were then submitted to analyses of factors variance (ANOVA; BMDP 2V; BMDP Statistical Software, Inc., Los Angeles, CA). The analyses included the type of cigarette (T: TN, tn, Tn), prepost (P: pre- vs. posttreatment phases), and nose clamp condition (C: cigarette smoked with or without nose clamp). For comparisons among the three types of cigarettes, post hoc contrast analyses (19) were performed. For all significance levels of the ANOVAs, Greenhouse-Geisser probabilities were considered when appropriate.

RESULTS

Table 2 shows the cell means, *F*-values of the ANOVA, and contrast comparisons for those parameters that were significantly affected.

Type of Cigarette

Among the puffing parameters, the tn cigarettes differed from the TN and Tn ones by lower peak pressure, by more puffs, and thereby by greater total but not by greater average puff volumes. Moreover, the average puff volumes did not significantly differ among the types of cigarette when the draw resistances were used as analysis of covariance co-factors. TN differed from tn and Tn by longer puff intervals. The lowest mean flow was obtained with Tn; however, it only differed significantly from tn.

Prepost smoking changes differed for several physiologic parameters among the cigarettes. Respiratory CO increased with TN more than with tn, but not more than with Tn. Heart rate increased with TN more than with tn and with tn more than with Tn, which, according to the cell means shown in Table 2, hardly affected this parameter. Finally, TN and tn, but not Tn produced increases of EEG power in the beta-band. Among the subjective parameters, taste was rated higher with TN than with Tn and tn, and the same was true for the ratings of strength, whereas enjoyment was rated lower for Tn than for both TN and tn.

Nose Clamp Effects

The rating of taste was the only parameter that revealed both a main factor significance for the nose clamp and a significant interaction with the type of cigarette, because the ratings were decreased by half for TN and tn but by roughly 75% for Tn.

Respiratory frequency was significantly higher without the nose clamp with the TN cigarettes than with the Tn and tn cigarettes, and respiratory amplitude was significantly higher without the nose clamp for the TN compared with the Tn cigarettes. Pre- to postsmoking increases in respiratory CO, decreases in the ear pulse amplitude, and changes in the ratings of relaxation were all affected by the nose clamp.

In addition to these interactions, a few parameters were affected only by the nose clamp. The nose clamp reduced the average puff volumes, prolonged the latency of the peak pressure, and reduced the enjoyment ratings.

Nonspecific Effects of Smoking

Effects from pre- to postsmoking without any interaction with the type of cigarette or the clamp condition were observed as a decrease in craving, finger pulse amplitude, and frontal EMG, and an increase in systolic blood pressure.

DISCUSSION

As compared with regular TN cigarettes, the tn but not the Tn cigarettes were oversmoked, with a significant increase in the total puff volumes of about 35%. At first, this might seem a consequence of the differences in draw resistance between the cigarettes. Taking into account the additional resistance of the flowmeter, the draw resistance was 15% smaller for the tn cigarettes than for the conventional TN cigarettes, and 18% greater for the Tn cigarettes. In parallel, among the puffing parameters, peak pressure was 18% lower for tn and 12% higher for Tn, as compared with the TN cigarettes. In contrast, the average puff volumes paralleled these differences

TABLE 2

CELL MEANS AND ANOVA F-VALUES FOR DIFFERENCES AMONG TN, Tn, AND tn CIGARETTES

Variables	Nose Clamp	TN		Tn		tn		ANOVA F-Values						Contrast
		Pre	Post	Pre	Post	Pre	Post	T	C	P	T × C	T × P	C × P	TN : Tn : tn (F-Values)
Puffing behavior								(df) (2,22)	(1,11)	(1,11)	(2,22)	(2,22)	(1,11)	(1,11)
No. puffs	Yes	14.5		13.1		17.4		7.22*	0.68		0.67			tn > TN,Tn (6.47†,13.89*)
	No	15.3		13.9		17.5								
Volume (ml)	Yes	37.9		36.9		41.6		1.78	4.93†		0.01			
	No	40.3		39.4		44.4								
Total puff volume (ml)	Yes	513.6		486.8		719.9		7.56*	2.78		0.73			tn > TN,Tn (8.94*,13.31*)
	No	592.8		537.2		761.3								
Puff interval (s)	Yes	26.3		19.1		18.5		5.75*	0.04		0.78			TN > tn,Tn (8.85*,8.39*)
	No	25.1		19.6		19.7								
Peak pressure [cm H_2O]	Yes	23.3		26.1		20.0		12.26‡	0.28		2.35			tn < TN,Tn (9,14†,24.09‡)
	No	24.3		27.0		18.8								
Mean flow (ml/s)	Yes	22.3		20.3		24.6		5.31†	0.14		0.67			tn > Tn (8.91*)
	No	22.5		21.0		24.1								
Peak latency (s)	Yes	0.62		0.64		0.63		0.28	8.89†		0.06			
	No	0.69		0.71		0.69								
Biochemical parameter														
Respiratory CO (ppm)	Yes	12.8	17.7	11.9	15.9	11.3	15.2	2.36	.69	53.26‡	0.74	5.73*	10.75*	δ-CO: TN > tn (11.42*)
	No	12.0	19.6	11.8	18.3	11.3	15.9							
Physiologic parameters														
Heart rate (bpm)	Yes	75.9	82.7	70.9	71.5	73.8	78.0	10.50‡	0.84	48.07‡	0.02	66.04‡	3.22	δ-bpm: TN > tn > Tn (23.88‡,43.17‡)
	No	74.3	85.6	70.5	72.7	72.6	80.0							
Finger pulse amplitude (units)	Yes	10.0	6.9	8.5	6.2	8.8	5.7	0.22	0.07	56.59‡	1.96	1.69	0.59	
	No	8.5	6.4	8.1	6.8	9.1	5.9							
Ear pulse amplitude (units)	Yes	3.3	2.7	3.6	3.6	3.0	2.7	0.45	0.05	6.67†	0.83	1.14	4.92†	
	No	3.9	2.8	3.9	2.8	2.6	2.5							

Electromyogram (units)	Yes	8.6	7.5	10.4	9.5	8.7	8.1	0.41	1.48	5.18†	0.26	1.00	2.01	
	No	7.9	7.4	8.8	9.4	7.6	7.2							
Respiratory frequency (No./min)	Yes	17.6	18.1	18.4	19.4	18.0	19.5	0.01	2.41	10.68*	5.94*	0.01	0.12	δ-N/min: TN > Tn,tn (10.48*,6.97†)
	No	19.0	20.7	18.4	19.4	18.7	19.6							
Respiratory amplitude (units)	Yes	16.8	20.0	16.7	16.1	14.4	15.4	0.65	0.75	0.37	3.61†	1.80	0.65	δ-units: TN > Tn (6.91†)
	No	14.2	16.1	17.9	17.0	14.6	14.6							
Systolic blood pressure (mmHg)	Yes	98.8	102.1	93.6	97.5	98.2	101.2	2.32	0.11	10.36*	0.23	1.04	0.00	
	No	97.0	104.0	96.1	97.5	98.3	100.2							
Beta power (%)	Yes	32.0	32.9	30.4	29.9	31.0	31.9	7.40*	0.73	12.37*	2.53	5.97*	4.23	δ-%: Tn < tn,TN (7.01†,10.33*)
	No	31.4	34.3	30.9	30.8	30.1	32.3							
Subjective ratings (1–100)														
Craving (%)	Yes	70.1	28.1	65.0	29.2	57.3	30.5	0.62	1.02	19.97‡	0.50	3.49	0.03	
	No	76.6	29.5	64.5	28.2	61.8	37.7							
Relaxation (%)	Yes	75.7	78.2	81.5	71.1	74.0	66.8	0.05	0.00	3.09	1.55	1.97	7.52†	
	No	71.8	77.7	71.0	72.0	81.5	73.7							
Taste (%)	Yes		31.1		7.7		24.9	11.04*	16.58*		4.17†			TN > tn,Tn (6.51†,5.99†)
	No		72.9		29.0		45.4							
Strength (%)	Yes		68.3		26.8		24.4	12.23‡	2.95		0.91			TN > tn,Tn (18.89‡,17.76‡)
	No		54.9		22.8		22.8							
Enjoyment (%)	Yes		26.0		7.9		24.4	7.23*	14.10*		3.13			Tn < tn,TN (5.03†,14.31*)
	No		67.2		31.3		46.7							

Data are cell means, F-values and significance levels. T: Type of cigarette (TN/Tn/tn); C: with or without nose clamp; P: pre- versus post-treatment phase. Significance levels: †$p < 0.05$; *$p < 0.01$; ‡$p < 0.001$. The F-values of the triple interaction T × C × P were omitted, as they did not reach significance.

only for the tn cigarettes, with values increased by about 13% in comparison with the regular TN cigarettes, whereas the average volumes obtained with the Tn cigarettes were nearly identical to those obtained with the TN cigarettes. As a result of these small differences and the considerable interindividual differences, the average puff volumes failed to differ significantly among the three types of cigarettes. Therefore, this physical difference between the cigarettes was apparently too small to explain the differences in the total puff volumes. This finding is consistent with Woodson and Griffiths' observation (21) that draw resistance has to be manipulated beyond the range encountered with commercially available cigarettes to affect the single puff volumes reliably. In contrast to the average puff volumes, the number of puffs was more closely related to the increases in the total puff volumes, as this parameter increased significantly for the tn in comparison with both the TN and Tn cigarettes. This observation is in line with several other reports (1-3,14,17) of correlations between nicotine yields and total rather than average puff volumes.

However, to what extent this picture might represent an artifact of smoking with a flowmeter device remains unanswered. In a study by Höfer et al. (7), which compared flowmeter holder smoking with natural lip contact in male and female smokers habituated to different yield classes, the number of puffs increased gradually across the classes of descending smoke yields when smoking through the flowmeter but not with natural lip puffing, whereas the postsmoking boosts of plasma nicotine remained unaffected by this manipulation across all yield classes. This is in line with our earlier study (6) with the same types of cigarettes as in the present one, in which, with lip smoking, the number of puffs remained unchanged by switching the cigarettes; this suggests that puff volume and depth of inhalation control smoke absorption.

Another physical factor, the burning speed of the Tn cigarettes, might be suspected to be greater than that of the other products. In fact, switching to the tn cigarettes increased the number of puffs and shortened the puff intervals, whereas switching to the Tn cigarettes only shortened the puff intervals, resulting in total smoking times of 336 s with the tn and 264 s with the Tn cigarettes. Draw resistance was highest with the Tn cigarettes, and mean puff flow was significantly lower than for the tn cigarettes, but total passive burning time in the ashtray did not differ between the cigarettes. In combination with the low taste ratings, it therefore appears understandable that the Tn cigarettes were extinguished earlier than the two other types of cigarettes; this is supported by Robinson et al. (17), who also found shorter burning times with the test cigarettes compared with control cigarettes.

Irrespective of the limitations of the flowmeter method and putative differences in physical characteristics, we conclude that tn, but not Tn cigarettes were oversmoked relative to TN cigarettes and that the obtained puffing data closely resemble those obtained earlier by Höfer et al. (7) for female smokers habituated to the yield class 0.1-0.3 mg nicotine (for tn) and 0.7-0.9 mg (for Tn and TN).

In view of these results, the role of the sensory qualities of the smoke merits more attention. Although the nose clamp reduced taste satisfaction and single puff volumes, it did not affect the differences in puffing among the three types of cigarettes. Therefore, the perception of nicotine by olfactory receptors, as evidenced by Hummel et al. (8,9), appears not to be critical, and its elimination is apparently compensated by pharyngeal perception, for which an important role has been documented by Rose et al. (18). The reason for the failure of the Tn cigarettes to induce compensatory puffing in response to the ultralow nicotine content therefore remains open to speculation. One explanation might be that the poor taste of these cigarettes prevented the subjects from oversmoking. This argument is weakened by the fact that both the tn and the Tn cigarettes showed significantly lower taste ratings than the TN cigarettes. Because compensation was obtained with tn cigarettes, another explanation might be that the perception of nicotine might depend on an appropriate tar/nicotine ratio similar to that of the TN cigarettes. In fact, the absence of the stinging and burning taste quality from Tn smoke, which is caused by nicotine, would further explain the unacceptability of these cigarettes. However, the facts that this cigarette is smoked similarly as a conventional cigarette with a similar tar yield, and that, at least in the acute experiment, it reduces craving, may justify its use as an instrument to differentiate better between nicotinic and nonnicotinic effects of cigarette smoking. This suggestion is supported by Perkins et al. (16), who found that in the absence of nicotine intake a placebo nasal spray showed no changes in any subjective ratings, whereas sham smoking increased the desire to smoke, decreased head rush, and even increased heart rate, which suggests that puffing behavior alone may mimic in part the effects of smoking and or the desire to smoke.

The physiologic measurements carried out in the present study suggest that a considerable share of the overall effects may be due to smoke, rather than specifically to nicotine. Effects dependent on nicotine dose, as evidenced mainly by comparing the tn and TN cigarettes, were generally limited to heart rate and some EEG parameters, whereas other effects, particularly those on respiration, frontal electromyogram, and finger and ear pulse amplitudes, were apparently not dependent on nicotine availability. This is not surprising, as smoking not only involves the motor acts of handling and puffing the cigarettes, but also activates taste and olfactory receptors through a multitude of aromatic and irritant substances.

The act of nicotine intake through smoking represents a highly complex pattern of motor and sensory events, which may be rewarding per se, as extensively outlined by O'Connor (15). A recent study demonstrated that shifts in physical activity and heart rate not only accompany, but also precede the lighting of a cigarette (10) as an anticipatory activation. Such changes were found to be recurrent across entire days, although the heart rate increases during smoking faded away over the day. Similar pre- and postadministration changes were also observed for blood pressure and activity with heroin self-administration in rats (11), which suggests a probably general anticipatory phenomenon connected with reinforced behaviors.

In the present experiment, as well as in the previous one by Hasenfratz et al. (6), Tn cigarettes and the other cigarettes reduced craving to a similar extent, suggesting that the reward value of smoking remains high even in the near absence of nicotine availability and low taste acceptability. Together with the small changes in the smoking topography, this points to the possibility that a fixed habit of smoking at individually determined intervals constitutes an important factor beyond nicotine and taste for the maintenance of smoking behavior. However, a systematic analysis of the intraday development both of the smoking intervals and of craving under field conditions with the Tn cigarettes would be needed for further clarification of this issue.

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