

Effects of Nicotine on Weight Change and Food Consumption in Rats

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McNAIR, E AND R BRYSON *Effects of nicotine on weight change and food consumption in rats* PHARMACOL BIOCHEM BEHAV 18(3) 341-344, 1983 —The present study was designed to test the effects of nicotine and nicotine withdrawal on weight change and food consumption in rats. Twelve male and 12 female three month old Sprague-Dawley rats were divided into three treatment groups: 0.2, 0.4, and 0.6 mg nicotine/kg body wt. Half were given subcutaneous nicotine treatment for three weeks and then saline for three weeks; treatment sequence was reversed for the other half. Injections were administered three times daily throughout the experimental period. Prior to treatment, baseline measures were established for both food consumption and weight. Mean differences in weight change were calculated on a weekly basis throughout the experiment. Overall tests indicated that nicotine withdrawal produced significant ($p < 0.05$) weight gains and nicotine administration produced inhibition of weight gain. A significant sex \times drug \times time interaction ($p < 0.05$) demonstrated that food consumption increased when nicotine was discontinued and decreased when nicotine was administered. Specific comparison tests showed these effects on food consumption and weight were strongest at the 0.6 level and that larger effects were obtained for males than for females.

Nicotine Food consumption Weight change Cessation

STUDIES on humans in controlled studies have provided evidence that tobacco smokers weigh less than non-smokers [1, 3, 5, 7, 9, 16]. While there has been some indication that the mean weight difference was greatest between moderate smokers and non-smokers [5], Gordon reported this difference to be independent of the number of cigarettes smoked per day [3].

An increase in body weight accompanies the cessation of cigarette smoking in both males and females [5, 9, 14]. Studies on recent ex-smokers indicate that there is a tendency to gain weight in direct proportion to the number of cigarettes smoked per day before cessation as well as a higher average weight gain for females than for males [5, 14]. Furthermore, ex-smokers eventually come to weigh more than their non-smoking counterparts [9].

Only subjective assessment of appetite and food intake have been reported in human studies. Pangborn and Trabue [12] found that as amount of cigarettes smoked increased, reported appetite decreased. Kittel [8] reported that heavy smokers showed impairment in olfactory sensitivity and suggested that this threshold difference plays a role in appetite regulation. When considering changes in appetite upon cessation of smoking, Glauser and his co-workers [2] reported that weight increases in male humans are not necessarily due to an increased caloric intake. They speculated that instead, a metabolic change occurs. These conclusions however were only suggestive since it appears that no human study has been conducted that controls for or directly assesses diet during smoking withdrawal.

Some of the effects of nicotine administration in the rat bear a striking resemblance to effects of cigarette smoking reported for the human. In rats chronically administered

nicotine, either by drug injection or aerosol inhalation, mean body weight was significantly reduced [6, 11, 13, 15]. Schechter and Cook [15] found that following the nicotine administration period, mean body weight returned to pre-administration levels. In similarly treated rats McNair and Bryson [10] showed that when nicotine concentration was reduced, gain in body weight was increased.

The changes in body weight associated with the administration of nicotine may reflect changes in appetite. However, in studies on food consumption in rats, contrasting results have been reported. Mori [11] suggested that lesser food consumption was the probable reason for reduced weight among his male rats. Schechter and Cook [15] on the other hand, have repeatedly demonstrated reduction in weight without a reduction in amount of food consumed when nicotine was administered to female rats. A study conducted in our laboratory [10] showed that an increase in dosage (from 0.0 to 0.2 to 0.4 mg nicotine/kg body wt) corresponded to appetite constancy and a decrease of 0.2 mg/kg per day (using the same dosage levels) corresponded to a mean increase in food intake of 2.5 g per day. These results were obtained from both male and female animals between the ages of 8 and 12 weeks.

The present study was conducted to examine the relationship between weight change and food consumption before, during, and after chronic nicotine administration at three doses in 3-month old male and female rats.

METHOD

Subjects

The subjects were 24 three month old Sprague-Dawley

TABLE 1
THREE WEEK WEIGHT CHANGE UNDER NICOTINE AND
SALINE TREATMENT (g)

Sex	Condition	Treatment	
		First 3 Weeks	Second 3 Weeks
Males (n=12)			
	Saline First, then Nicotine	Saline	Nicotine
	Dose (mg/kg) 0.2	18.58	10.16
	0.4	11.83	9.17
	0.6	26.00	7.33*
	Nicotine First, then Saline	Nicotine	Saline
	0.2	14.75	14.66
	0.4	8.58	17.83
	0.6	-0.02	26.00*
Females (n=12)			
	Saline then Nicotine	Saline	Nicotine
	0.2	10.66	3.84
	0.4	9.00	2.00
	0.6	6.34	2.34
	Nicotine then Saline	Nicotine	Saline
	0.2	5.22	6.50
	0.4	8.50	6.17
	0.6	3.33	8.84*

* $p < 0.05$

derived albino rats bred at San Diego State University. Twelve were male (initial mean weight 289 (SD=47)g) and 12 were female (217 (SD=29)g). All animals were individually housed in wire mesh cages in a temperature-controlled (23°C) environment under normal (unreversed) 12/12 day-night lighting.

Procedures

To establish a baseline, one week prior to experimental treatment, food consumption and weight change were monitored for all animals. Weight was recorded throughout the experiment. Food was weighed before each daily feeding and was provided on an ad lib basis. At the end of each 24 hour period throughout the experiment, the food remaining was also weighed (wet food was first allowed to dry) and the difference was recorded as food consumed.

After one week of monitoring, each animal received three subcutaneous injections daily (at 7 a.m., 1 p.m., and 7 p.m.) of 0.2, 0.4, or 0.6 mg of nicotine dissolved in physiological saline/kg body wt., or 0.9% NaCl in a volume of 0.1 cc/250 g body wt. Lower dosages of nicotine have not previously been useful for eliciting behavioral effects and higher dosages have been associated with convulsive behaviors.

Half of the animals received one concentration of nicotine for a three week period and saline injections for a subsequent three week period. The other half received saline first and then nicotine treatment.

Analysis

Data were analyzed separately for food consumption and weight change. In both cases the design was a 2 (Sex) by 3 (Dosage) by 2 (Time) analysis of variance. When statistically significant differences were observed ($p < 0.05$), Newman-Keuls tests (NKT) were performed to determine which pairs of means differed significantly from one another.

RESULTS

Weight Change

A dosage by time interaction was statistically significant $F(5,12)=8.23, p < 0.05$ (Table 1). The NKT revealed a significant increase in weight gain for both sexes at the 0.6 mg/kg body wt. level when nicotine treatment was terminated.

The sex by dosage by time interaction was also significant, $F(5,12)=3.22, p < 0.05$. The NKT showed a significant increase in weight gain for males upon cessation of nicotine at the 0.6 mg/kg body wt. level as well as a significant decrease in weight gain at the same level after nicotine treatment was begun. Treatment of weight change as a percent of initial body weight resulted in significant inhibition of weight gain for both sexes when nicotine treatment was initiated. Weight change data under saline and three nicotine dosages can be seen in Table 1.

Food Consumption

A dosage by time interaction was observed,

TABLE 2
FOOD CONSUMED UNDER NICOTINE AND SALINE TREATMENTS (g)

Sex	Condition	Treatment	
		First 3 Weeks	Second 3 Weeks
Males (n=12)			
	Saline First, then Nicotine	Saline	Nicotine
	Dose (mg/kg) 0.2	23.72	23.06
	0.4	22.80	22.94
	0.6	26.39	24.28*
	Nicotine First then Saline	Nicotine	Saline
	0.2	22.95	26.67*
	0.4	26.20	29.62*
	0.6	19.26	25.05*
Females (n=12)			
	Saline, then Nicotine	Saline	Nicotine
	0.2	16.96	16.82
	0.4	20.94	20.83
	0.6	20.36	18.83
	Nicotine, then Saline	Nicotine	Saline
	0.2	19.82	20.04
	0.4	18.80	19.08
	0.6	18.52	21.80*

* $p < 0.05$

$F(5,12)=27.42, p < 0.05$ (Table 2). The difference in food consumption was dependent upon whether or not animals started in a nicotine condition and, as with weight change, the nicotine dosage level. NKT showed that when going from the nicotine condition to the saline condition, animals in the 0.2 mg/kg body wt and 0.6 mg/kg body wt treatment groups significantly increased their level of food consumption. When animals changed from saline to nicotine, a decrease in the amount of food consumed was significant for the 0.6 mg/kg body wt level only.

A sex by dosage by time interaction was also evident, $F(5,12)=4.79, p < 0.05$. For males, cessation of nicotine was associated with a statistically significant increase in amount of food consumed for all levels of the nicotine. However, when nicotine was introduced following the saline condition, food consumption was significantly decreased for the 0.6 mg/kg body wt group only ($p < 0.05$).

For females neither initiation nor cessation of nicotine treatment produced significant changes in appetite, though a marginal increase ($p = 0.05$) was observed during withdrawal from the 0.6 mg/kg body wt dosage level. Food consumption data for saline and the three nicotine dosages can be seen in Table 2.

DISCUSSION

These data demonstrate differential effects of nicotine and nicotine withdrawal on both food consumption and weight change in male and female rats. The largest effects

were observed during nicotine withdrawal. Animals gained the most weight and consumed the most food after withdrawing from 0.6 mg/kg body wt nicotine treatment. The strong effects of the 0.6 mg/kg body wt of nicotine on weight gain are consistent with Hjermann and his co-workers' results obtained from human subjects [5] and results found in our laboratory from immature rats. Although there was little change in weight for the animals withdrawing from the 0.2 mg/kg body wt level, the lowest level, the amount of food consumed increased significantly. The 0.4 mg/kg body wt level showed no significant effects on either weight change or food consumption.

Previous studies by Mori using male animals as subjects [11] and Schechter and Cook using female animals as subjects [15] have demonstrated a weight loss for rats exposed to nicotine dosages ranging from 0.4 to 0.8 mg/kg body wt. When the present data were inspected separately for males and females the effect of nicotine and nicotine withdrawal on weight change were significant only for males at the 0.6 mg/kg body wt level. When change was treated as a percent of initial body weight, significant weight inhibiting effects of nicotine were observed for females as well. These results conflict with those obtained by Bjelke [1] in humans in which female subjects showed greater weight changes than males.

Inspection of the data when animals went from the saline condition to a nicotine condition revealed a significant decrease in food consumption only at the 0.6 mg/kg body wt level. This is consistent with subjective reports on appetite found [12] where, as number of cigarettes smoked increased,

the reported perceived appetite level decreased. Although Kittel suggested that the higher olfactory threshold induced by smoking may play a role in appetite regulation [8], the present study suggests that some additional factors must bring about appetite change. Since nicotine was introduced by injection, it seems unlikely that the olfactory threshold was affected.

Separate analyses for males and females showed the decrease in food consumption associated with nicotine treatment was significant for males only. Inhibition of weight gain was therefore associated with appetite depression in the male rats, however, the trend toward weight inhibition observed in the females was not associated with reduced food intake. Similarly, upon cessation of nicotine treatment changes in weight were closely associated with changes in amount of food consumed for the male animals. The females, however, did not show a tendency to gain weight. These results help reconcile the conflicting observations made by

Schechter and Cook [15] and Mori [11]. It is likely that some sex associated variable determines whether or not nicotine induced weight change is accompanied by appetite change.

These observed sex differences warrant further study. While it appears that nicotine effects on weight inhibition are stronger for males than females when absolute body wt change is the dependent measure, the effects also appear for females when change is measured as a percentage of initial body weight. The question of whether males or females are more strongly affected has not been answered unambiguously. However, it does appear that nicotine induced weight change is associated with changes in amount of food consumed for males, but not for females. This may be due to an interaction of nicotine with sex steroids as has been suggested by Hatchell [4]. We are currently conducting research on sexually altered, testosterone or estradiol treated animals in order to better understand sex differences in effects of nicotine.

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