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BRIEF COMMUNICATION

The Role of Physical Activity in Nicotine's Effects on Body Weight[1]

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GRUNBERG, N. E. AND D. J. BOWEN. *The role of physical activity in nicotine's effects on body weight.* PHARMACOL BIOCHEM BEHAV **23**(5) 851–854, 1985.—The present study examined the effects of chronic nicotine administration and cessation of nicotine administration on body weight and 24-hour physical activity of rats. There was a significant, inverse, dose-effect relationship between nicotine administration and body weight. Cessation of nicotine was accompanied by increased rates of body weight gain compared to controls. The changes in body weight during nicotine administration could not be explained by changes in physical activity. However, decreases in physical activity after cessation of nicotine appeared to contribute to post-drug body weight increases. These findings have implications for weight control after cessation of cigarette smoking.

Nicotine Physical activity Body weight Caloric expenditure

CIGARETTE smokers weigh less than comparably aged nonsmokers, and smokers who quit smoking gain weight [2,11]. In addition, there is an inverse relationship between nicotine administration and body weight [2]. Recent animal and human studies indicate that these changes in body weight result partially from changes in caloric intake. Specifically, nicotine administration decreases consumption of sweet-tasting high caloric foods and cessation of nicotine results in increased consumption of these foods [2,4]. When animals are provided with only bland food, nicotine administration still causes decreased body weight without affecting bland food consumption (although the body weight effect is attenuated compared with decreases found when sweet-tasting food is available) [3, 6, 8]. Therefore, factors other than changes in caloric intake must be involved in body weight changes associated with nicotine administration.

Besides caloric intake, changes in caloric expenditure may contribute to the nicotine/body weight relationship. Physical activity is a behavioral factor that affects caloric expenditure. Increased physical activity (without decreased caloric intake) could lead to decreases in body weight. If nicotine affects physical activity, then activity-induced changes in caloric expenditure could contribute to nicotine's effects on body weight.

Several animal studies have examined the effects of nicotine administration on physical activity. Some studies report that nicotine increases physical activity [1, 9, 10]. Other studies report that nicotine decreases activity [5,7]. For several reasons it is difficult, if not impossible , to draw conclusions from these studies about physical activity's contribution to body weight changes during and after nicotine administration. First, body weight was not measured in any of these studies. Therefore, the role physical activity plays in nicotine's effects on body weight cannot be directly assessed. Second, all of these studies used bolus injections of nicotine for less than a week rather than chronic administration over a longer period of time. Acute and chronic administration of nicotine have different effects and the body weight changes most relevant to human smokers are associated with chronic administration nicotine over weeks or months. Therefore, the methods of nicotine administration used in these activity studies have limited meaning for the body weight/nicotine relationship in both humans and animals. Third, in all previous studies physical activity was measured for less than 45 minutes a day. Changes in physical activity that could affect body weight might not be apparent from these brief measurements. Fourth, none of these studies measured physical activity after cessation of nicotine administration—a time when humans show weight gains. With these problems in mind, the present study was designed to examine physical activity and body weight in rats during and after nicotine administration.

METHOD

Subjects

The subjects were 24 male 350 g Sprague-Dawley rats (purchased from Charles River, Inc.). Animals were individually housed in standard polypropylene shoebox cages (35.6 $\times$15.2$\times$20.3 cm) fitted with metal grill lids and elevated floors, beneath which were absorbent wood Pine-Dri shavings. All cages were placed on four-shelved double-sided

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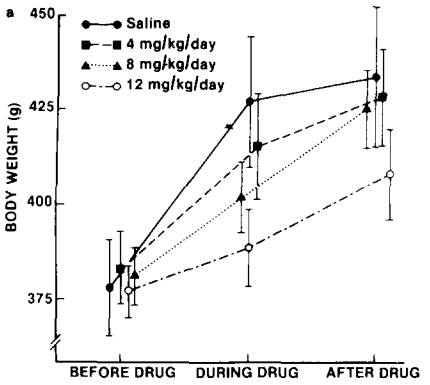

FIG. 1a. Mean body weights for each experimental group during all monitoring days before, during, and after drug administration.

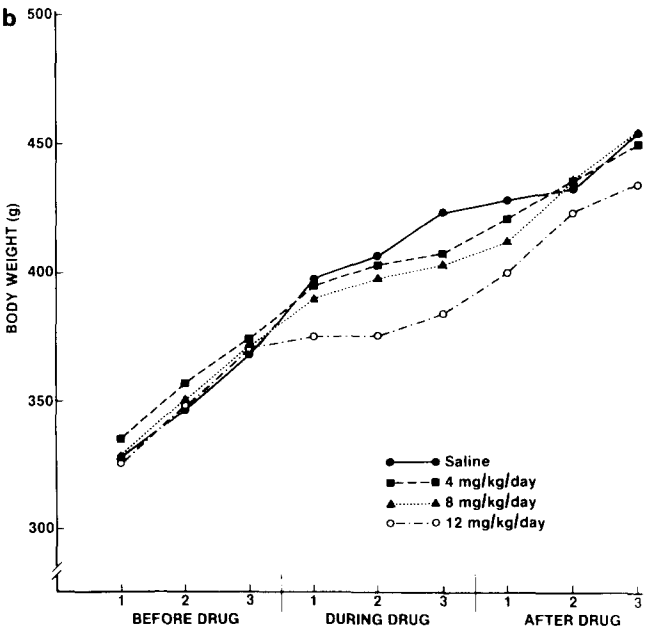

FIG. 1b. Mean body weights for each experimental group for each monitoring day before, during, and after drug administration.

racks in a 6×3 m room with overhead fluorescent illumination. The room was maintained on a twelve hour light/dark cycle (the light cycle began at 0700 hr) at approximately 21 degrees C and 50% humidity. Rat chow (Charles River RMH 3500 pellets) and tap water were continuously available. Cages, food, and bottles were changed twice a week.

Activity Monitoring

Digiscan Optical Digital Sensor Activity Monitors (Omnitech Electronics) were used to measure physical activity. These monitors use infrared photocells to measure horizontal and vertical activity. When an infrared beam is broken, counters (for vertical and horizontal planes) increment. A data collection printer/timer (Datalogger 8000) interfaced with each activity monitor printed the number of horizontal and vertical beams crossed per hour. During measurement periods subjects were housed in 40.6 cm square clear Plexiglas cages set inside the activity monitors. Food and water were continuously available and wood shavings covered the floor.

Procedure

This experiment was divided into three phases, each of which lasted approximately 18 days: pre-drug, during drug, and post-drug. Six rats, matched for body weight, were assigned to each of four experimental groups (0, 4, 8, and 12 mg nicotine/kg body weight/day). These drug dosages were based on previous research [2,3]. All drug dosages were computed as nicotine base (using nicotine dihydrochloride, J. T. Baker Chemical Co.). Physiological saline was used to make the nicotine solutions and was used as the control solution. Nicotine or saline was administered subcutaneously using Alzet miniosmotic pumps (Model 2002, Alza Corp.). The miniosmotic pumps release their contents at a constant rate of 0.5 μl/hr for 20±2 days.

Physical activity was measured for 24-hour periods in four activity monitors placed on tables in the room in which the rats were housed. (Rats were habituated to these chambers before beginning the study.) Three days of physical activity data were collected for each animal during each of the three phases of the experiment. These nine days were evenly spaced within each phase. Pilot data indicated that this methodological approach was sufficient to reflect physical activity changes throughout all phases of the study. On any given day, one animal from each of the four experimental groups was simultaneously in one of the four activity monitors. The activity monitors were cleaned and prepared with fresh food, water, and bedding every day after animals were returned to their home cages. Body weight was measured daily using Sartorius electronic balances (Model 1264-MPBCD) programmed to provide the mean of 10 separate weighings.

RESULTS

Figure 1a presents mean body weights for each experimental group based on all days that physical activity was monitored before the implantation of miniosmotic pumps, during nicotine (or saline) administration, and after cessation of nicotine (or saline) administration. Before drug administration the body weights of all four groups were virtually identical. During drug administration there was an inverse dose-response relationship between body weight and dosage of nicotine. Rats receiving nicotine gained weight at a slower rate than did saline control animals. Comparing changes in body weight from before to during drug administration, the saline group gained significantly more weight than did both the high nicotine group and the medium nicotine group (interaction $t(10)=4.07$, 2.90, $p<0.01$, 01, respectively) and somewhat more weight than did the low nicotine group (interaction $t(10)=2.04$, $p<0.10$). After cessation of drug administration, animals that had received the medium and high doses of nicotine showed significantly greater increases in

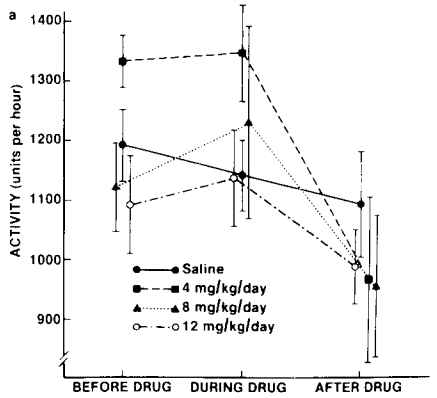

FIG. 2a. Mean physical activity for each experimental group during all monitoring days before, during, and after drug administration.

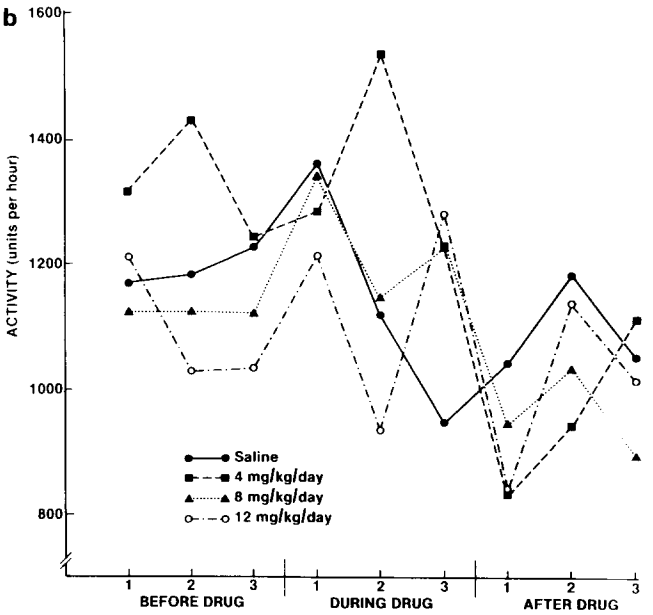

FIG. 2b. Mean physical activity for each experimental group for each monitoring day before, during, and after drug administration.

body weight compared to control animals (interaction $t(10)=3.46$, 3.57, $p<0.01$, respectively). Animals that had received the lowest dosage of nicotine gained weight at a similar rate as did controls (interaction $t(10)=1.29$, n.s.).

Figure 1b presents body weight for each group of animals on the days that physical activity was monitored. Body weights for all experimental groups were similar for the entire period before drug administration. The inverse dose-response relationship between nicotine and body weight is already apparent on the first day that physical activity was monitored during the drug administration period (two days after drug infusion began). The post-nicotine body weight gains began immediately after cessation of drug infusion (the first day after drug in Figure 1b corresponds to the day after pumps were removed).

Figure 2a presents the mean physical activity (horizontal plus vertical) for each group of animals collapsed across all three days before, during, and after drug administration. The individual physical activity values before drug administration overlapped extensively among all groups. Only the mean of the 4 mg group differed from the other three groups but that difference was not significant at the 0.05 level. Therefore, the small differences in baselines do not, we believe, confound the data analyses.

While physical activity of the saline group decreased from before to during drug administration, activity of all animals receiving nicotine increased. This change in physical activity was significantly different for the high nicotine group compared to control (interaction $t(10)=2.91$, $p<0.02$); no other comparisons were significantly different. After cessation of drug administration, the physical activity of the high, medium, and low nicotine groups all decreased significantly more than did the control group (interaction $t(10)=3.16$, 2.28, 5.55, $p<0.01$, 0.05, 0.001, respectively).

Physical activity for each of the monitoring days is presented in Figure 2b. The differences in physical activity between the nicotine and control groups during drug administration do not occur until the second (eight days after drug infusion began) or third (fourteen days after drug infusion began) monitoring day of this phase. Figure 2b also indicates that the post-nicotine hypoactivity is most apparent immediately after cessation of drug (i.e., on the first day after cessation of drug infusion).

Multiple regression/correlation analyses were performed to examine the relative contribution of nicotine dosage and physical activity to the variance on body weight during and after drug. Body weight scores were regressed on nicotine dosage and physical activity in hierarchical models with nicotine dosage entered first. During drug administration nicotine contributed 15% of the body weight variance, while the contribution of physical activity was minimal (less than 1%). After cessation of drug infusion, nicotine dosage contributed roughly 6% of the variance and physical activity contributed an additional 9% of the variance.

DISCUSSION

Similar to previous studies [2,3] there was an inverse dose-response relationship between nicotine and body weight during drug administration. Rats receiving nicotine gained less weight than did control rats. During nicotine administration physical activity of animals receiving the highest dosage of nicotine increased significantly compared to controls. However, these increases in physical activity occurred after the body weight decreases (see Figs. 1b and 2b). Also, the portion of variance accounted for by physical activity during drug administration was small compared to the variance accounted for by nicotine dosage. Therefore, physical activity does not appear to contribute to the body weight decreases during nicotine administration.

After cessation of nicotine administration, rats that had previously received the two highest dosages of nicotine gained weight at a significantly greater rate than did controls. In addition, all animals that had received nicotine showed a

decrease in physical activity after cessation of nicotine administration. This decrease in physical activity occurred immediately after cessation, coinciding with increases in body weight. The multiple regression analysis revealed that after cessation of drug infusion, physical activity accounted for an additional 9% of the variance in body weight beyond the variance contributed by nicotine dosage. Therefore, changes in physical activity after cessation of nicotine administration appear to contribute to the body weight increases after nicotine cessation.

The present study examined a behavioral variable (physical activity) that can affect caloric expenditure. Nonbehavioral factors that alter caloric expenditures (e.g., levels of thyroid hormones, metabolic rate) also deserve research attention in the context of the nicotine/body weight relationship. If the present results with nicotine hold for cigarette smoking by humans, then it seems that the body weight gains after cessation of smoking may be attenuated by maintaining or increasing levels of physical activity. Considering the results of the present study in conjunction with previous animal and human studies of nicotine, cigarette smoking, and body weight [2, 3, 4,], it appears that behavioral factors (i.e., physical activity and specific food consumption) can be used to help control weight gains after cessation of smoking.

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