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Fluoxetine Decreases Fat and Protein Intakes But Not Carbohydrate Intake in Male Rats

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HEISLER, L. K., R. B. KANAREK AND A. GERSTEIN. *Fluoxetine decreases fat and protein intakes but not carbohydrate intake in male rats.* PHARMACOL BIOCHEM BEHAV **58**(3) 767–773, 1997.—Administration of fluoxetine, a selective serotonin reuptake inhibitor, results in decreases in food intake and body weight. The present study investigated whether the anorectic actions of fluoxetine were due to a general decrease in caloric intake or macronutrient specific. Male Long–Evans rats were maintained on a dietary self-selection regime with separate sources of protein, fat, and carbohydrate. During the acute phase of the experiment, nutrient intakes were measured 2, 4, 6, and 24 h after injections of 0, 5.0, and 10.0 mg/kg fluoxetine hydrochloride. Fluoxetine significantly decreased protein and fat intakes in a dose-related manner at all measurement times. In comparison, fluoxetine had a less pronounced effect on carbohydrate intake. During the chronic phase, rats were divided into two groups, one receiving daily injections of 10.0 mg/kg fluoxetine, and the other, vehicle injections. Drug injections continued for 28 days, and were followed by a 28-day withdrawal period. Rats given fluoxetine on a chronic basis consumed significantly less calories and gained significantly less weight than rats injected with the vehicle. Both caloric intake and body weight returned to control values during the withdrawal period. Fat and protein intakes also were significantly reduced throughout the drug injection period, and were restored to baseline levels during the withdrawal period. In contrast, carbohydrate intake was not reduced on an absolute basis, and actually was increased as percent of total caloric intake during the drug period. The results of this experiment call into question the idea that increased serotoninergic activity is related to selective reductions in carbohydrate intake. © 1997 Elsevier Science Inc.

Fluoxetine Diet selection Carbohydrate Fat Protein Serotonin Food intake Body weight

OVER the past 20 years substantial evidence has accumulated strongly supporting a relationship between serotonin [5-hydroxytryptamine (5-HT)] and food intake. Evidence for this relationship has come from research demonstrating that pharmacological agents that increase levels of 5-HT in the central nervous system (CNS) suppress food intake (2–5,8, 11,16–25,28–35,38–40), whereas drugs that antagonize the actions of 5-HT increase food intake (1,6,9,26).

Recent experiments have addressed whether the anorectic effects of serotonerigic agonists are due to a general decrease in energy intake, or are specific to a particular macronutrient. It has been proposed that serotonergic neurons are responsive to food-induced changes in neurotransmitter synthesis, and thus may serve as sensors in the brain's mechanisms governing nutrient choice (38–40). This proposal was derived from research examining the effects of nutrient intake on neurotransmitter synthesis (7). Results of this research demonstrated that intake of pure carbohydrate meals increased synthesis of 5-HT in experimental animals while intake of protein meals had no effect on 5-HT synthesis in the CNS (7). The difference in the effects of these two macronutrients on 5-HT synthesis was determined to be a function of the plasma ratio of the amino acid tryptophan, the dietary precursor for 5-HT, to other large neutral amino acids (LNAA). Tryptophan is carried by an active transport mechanism into the brain where it is converted into 5-HT. However, tryptophan must compete with the other LNAA for transport into the brain. Thus, the ratio of tryptophan to the other LNAA is critical in determining the amount of tryptophan that enters the brain to be converted to 5-HT. Carbohydrate meals stimulate the secretion of insulin that leads to the uptake of the LNAA, with the exception of tryptophan, from plasma into muscle. As a result, there is an increased proportion of tryptophan relative to the other LNAA, available for transport from the blood into the brain. The consequent elevation in brain tryptophan facilitates 5-HT synthesis (7). It is hypothesized that this carbohy-

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drate-induced increase in 5-HT synthesis provides feedback about recent nutrient intake, and thus leads to a subsequent decrease in carbohydrate consumption (7).

Intake of high-protein meals also stimulates insulin secretion. However, high-protein meals also add exogenous amino acids to the circulation, and thereby elevate plasma levels of all LNAA. The outcome of eating a high-protein meal is that levels of tryptophan and the other LNAA increase proportionately. Thus, there is no net change in competition for carrier transport across the blood–brain barrier, and neither brain tryptophan nor 5-HT levels are altered (7).

Some support for the hypothesis that increases in 5-HT activity within the CNS lead to reductions in carbohydrate intake has come from animal research investigating the effects of serotonin agonists on diet selection. When comparing intakes of a high-carbohydrate/low-protein diet and a low-carbohdyrate/high-protein diet, a number of researchers have observed a selective decrease in intake of the high-carbohydrate/low-protein diet after peripheral and central administration of serotonergic drugs (16,23,25,38–40).

Other researchers, however, have communicated that a number of variables including feeding schedule, diet composition, and hydration of the diets interact with the actions of serotonergic drugs on diet selection (2,18,19,27). For example, Blundell and colleagues found that *d*-fenfluramine did not lead to a selective suppression in carbohydrate intake in a dietary situation in which rats were fed a separate source of either a sweet (sucrose) or bland-tasting (Polycose) carbohydrate solution in addition to a standard laboratory diet. In fact, when the carbohydrate supplements were presented in a hydrated form, rats given *d*-fenfluramine, actually consumed a significantly greater percentage of their calories from the carbohydrate supplements than nondrug-treated animals (18). Under similar conditions, Orthen-Gambill (29) reported that *dl*-fenfluramine significantly decreased chow intake without affecting sucrose consumption. Furthermore, Holder and Huether (12) found that although injections of tryptophan reliabily increased brain serotonin, the injections did not decrease consumption of food pellets high in carbohydrate relative to high-protein pellets.

Studies comparing the effects of serotonergic drugs on nutrient choice using diets varying only in protein and carbohydrate content (38–40) also are limited because the diets contain equivalent amounts of fat. Thus, it is impossible to determine from these studies whether serotonergic agonists have an effect on fat intake, or if the presence of a separate source of fat alters the actions of the drug on nutrient choice (13–15). Experiments using individual sources of the three macronutrients have indicated that fat intake is modified by serotonergic agents (15,30,32,35). For example, we previously reported that acute administration of the serotonergic drug, *dl*-fenfluramine led to substantially greater reductions in fat and protein intakes than in carbohydrate intake in rats given separate sources of the three macronutrients (30). Additionally, using a similar dietary paradigm, peripheral administration of serotonin led to a greater suppression in fat intake than in intake of either protein or carbohydrate (15).

A number of researchers have reported that fluoxetine (Prozac), a drug that augments 5-HT activity by selectively inhibiting reuptake of the neurotransmitter into the presynaptic nerve terminal (36,37), decreases food intake and body weight in both experimental animals and human subjects (4,5,11, 20,25,28,33,39). Fluoxetine and similarly acting serotonergic drugs are being suggested as potential long-term treatments for human obesity (20,36). It is, therefore, important to examine both the short- and long-term actions of these drugs on nutrient choice. The majority of studies examining the effects of fluoxetine on nutrient selection have used composite diets and have only measured nutrient intake over relatively short periods of time. The present studies addressed these issues by using separate sources of the three macronutrients, and by examining macronutrient selection and body weight as a function of acute and chronic administration of fluoxetine. This research has both clinical and theoretical applications. Clinically, it provides information regarding the effect of chronic use of fluoxetine on food intake and body weight and theoretically, it assesses the biological behavioral feedback hypothesis of carbohydrate intake and central serotonin levels.

GENERAL METHOD

Animals and Diets

Sixteen adult male Long–Evans rats (CD outbred, Charles River Breeding Laboratories, Portage, MI), weighing between 236–261 g at the beginning of the experiment were used. Rats were housed individually in standard stainless steel cages in a temperature-controlled room (21 ± 1°C) maintained on a 12:12 h reverse light–dark cycle (lights off between 0800–2000 hr). Animals were allowed to select diets ad lib from separate sources of protein, fat, and carbohydrate. The composition of the diets appears in Table 1. Fresh diets were made approximately once every 2 weeks and were refrigerated to prevent spoilage. Protein and carbohydrate were provided in dry form in food cups (LC-306A Wahmann, Timonium MD) with spill-proof lids, and fat was available in 50 ml glass jars. Protein and carbohydrate cups were alternated daily to ensure that animals were not consuming a particular nutrient as a result of a position preference. All food sources were secured to the cage to reduce spilling. Body weights and nutrient intakes were measured daily at the beginning of the dark portion of the 24-h cycle. Nutrient intakes were measured to the nearest 0.1 g, and food cups were refilled with fresh diets to the same level each day. Food spillage was measured for all rats each day; minor spills (<0.5 g) were not mea-

TABLE 1
DIETARY COMPONENTS

Protein component (3.76 kcal/g)
960 g casein (ICN Pharmaceuticals, Cleveland, OH)
40 g AIN Mineral Mix (ICN Pharmaceuticals)
20 g Vitamin Diet Fortification Mix (ICN Pharmaceuticals)
Carbohydrate component (3./3 kcal/g)
575 g corn starch (Teklad Test Diets, Madison, WI)
275 g dextrin (Texlad Test Diets)
100 g commercial grade sucrose
10 g Solka-floc (BW-200, James River Corp., Berlin, NH)
40 g AIN Mineral Mix
20 g Vitamin Diet Fortification Mix
Fat component (7.85 kcal/g)
912 g Crisco (Proctor and Gamble, Cincinnati, OH)
48 g Safflower oil (Hollywood Health Foods, Los Angeles, CA)
90 g AIN Mineral Mix
50 g Vitamin Diet Fortification Mix

Vitamin and minerals were added to the components so that the three dietary rations contained equal amounts of these micronutrients on a per kilocalorie basis.

sured, but major spills (>0.5 g) were recorded as a missing value.

Drug

Fluoxetine hydrochloride (Ly 110140) was supplied as a gift by Eli Lilly Co. The drug was dissolved in distilled water and was administered intraperitoneally (IP) in doses of 0.0, 5.0, and 10.0 mg/kg in a volume of 2 ml/kg of body weight. Distilled water was utilized as the control vehicle.

Data Analysis

Nutrient intake data were analyzed using repeated measures analysis of variance followed by comparisons between treatment groups using Tukey's method. Macronutrient intakes were examined both as absolute kilocalories and as percent of kilocalories (kcal intake for specific macronutrient/total kcal). All analyses that reached the $p \leqslant 0.05$ level of significance were reported.

All procedures were approved by the Tufts University Institutional Animal Care and Use Committee.

PART 1: THE EFFECT OF ACUTE FLUOXETINE ADMINISTRATION ON MACRONUTRIENT SELECTION

Procedure

Animals were provided a 4-week acclimation period to ensure stable patterns of nutrient intakes and body weights on the test diets. Rats that consumed less than two standard deviations away from the mean of total kcal of intake or did not gain a minimum of 50 g of weight within the acclimation period were excluded from the data analysis ($n = 2$). Nutrient intakes and body weights were recorded at the beginning of the dark cycle every second day during this period. Animals were given three pretest vehicle injections (distilled water) to familiarize them with the experimental procedure. Data from these injections were not included in data analyses. The experiment was a within-subjects design, such that each rat acted as its own control for each of the drug doses administered (0.0, 5.0, and 10.0 mg/kg).

On each experimental day, food cups were removed at the beginning of the dark cycle, weighed, and refilled to constant levels. After a 2-h food-deprivation period, each rat was injected with fluoxetine (IP) and nutrients were returned to the cage. Macronutrient intakes were measured at 2, 4, 6, and 24 h postinjection. A 7–10 day latency period was implemented between experimental days.

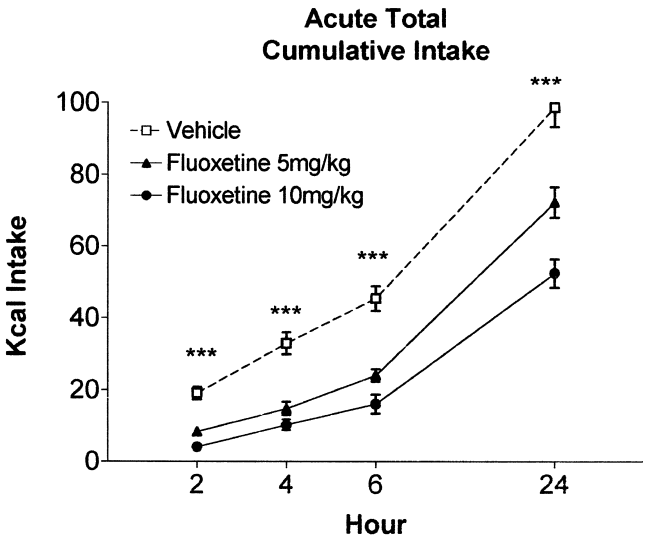

FIG. 1. The effect of acute fluoxetine administration on total cumulative caloric intake (mean ± SEM). Significant dose-related suppressions in total intake were observed at hours 2, 4, 6, and 24 (***$p \leqslant 0.001$). Post hoc comparisons revealed that fluoxetine 5 mg/kg and 10 mg/kg were significantly different than vehicle.

Results

Fluoxetine (5.0 and 10.0 mg/kg) produced significant dose-related decreases in total energy intake compared to vehicle at all time points [hour 2: $F(2, 26) = 54.97$, $p \leqslant 0.001$; hour 4: $F(2, 26) = 45.24$, $p \leqslant 0.001$; hour 6: $F(2, 26) = 50.82$, $p \leqslant 0.001$; and hour 24: $F(2, 26) = 45.96$, $p \leqslant 0.001$] (Fig. 1).

Fluoxetine (5.0 and 10.0 mg/kg) significantly reduced fat [hour 2: $F(2, 26) = 22.32$, $ps \leqslant 0.001$; hour 4: $F(2, 26) = 18.18$, $ps \leqslant 0.001$; hour 6: $F(2, 26) = 26.57$, $ps \leqslant 0.001$; and hour 24: $F(2, 26)$, $= 32.92$, $ps \leqslant 0.001$], and protein intakes [hour 2: $F(2, 26) = 18.61$, $ps \leqslant 0.001$; hour 4: $F(2, 26) = 35.83$, $ps \leqslant 0.001$; hour 6: $F(2, 26) = 25.99$, $ps \leqslant 0.001$; and hour 24: $F(2, 26) = 20.01$, $ps \leqslant 0.001$] in a dose-related manner (Fig. 2). The results for acute carbohydrate consumption were the least robust. At hour 2, only 5 mg/kg fluoxetine significantly suppressed intake compared to vehicle, $F(2, 26) = 4.10$, $p \leqslant 0.05$, whereas at all other times only 10.0 mg/kg fluoxetine significantly reduced intake [hour 4: $F(2, 26) = 5.39$, $ps \leqslant 0.05$; hour 6: $F(2, 26) = 4.21$, $ps \leqslant 0.05$; and hour 24: $F(2, 26) = 4.25$, $ps \leqslant 0.05$].

The effect of fluoxetine on the percent of calories consumed from each macronutrient was examined at each time point. Across drug doses, the rats consistently consumed a larger percentage of their diets as fat and protein than carbohydrate. At hour 2, when injected with 5.0 mg/kg fluoxetine, rats consumed a significantly larger percentage of their diet as carbohydrate, $F(2, 26) = 6.02$, $p < 0.01$, than when injected with the vehicle or 10.0 mg/kg fluoxetine. At hour 4, rats consumed a significantly greater percentage of their diet as protein, $F(2, 26) = 3.96$, $p \leqslant 0.05$, when injected with 5.0 mg/kg fluoxetine than when injected with the vehicle. No other significant differences in percent kilocalorie of intake were observed as a function of drug administration.

PART II: THE EFFECT OF CHRONIC FLUOXETINE ADMINISTRATION ON MACRONUTRIENT SELECTION

Procedure

The 14 rats (now 395–565 g) that completed the acute phase of this experiment were used in the chronic phase. The rats were divided into two groups: one receiving IP vehicle injections ($n = 5$), and the other injections of 10.0 mg/kg of fluoxetine ($n = 9$). The groups were matched according to typical macronutrient selection and body weights. Drug treatment continued for 28 days and was followed by a 28-day withdrawal period.

At the beginning of the dark cycle each day, body weights and nutrient intakes were measured and food cups refilled to a constant value. Rats then were injected with distilled water or fluoxetine, and nutrients were returned to the cage. The same procedure was used during withdrawal except that rats did not receive injections.

Results

Chronically, fluoxetine (10.0 mg/kg) significantly reduced total daily caloric intake compared to vehicle [main effect of

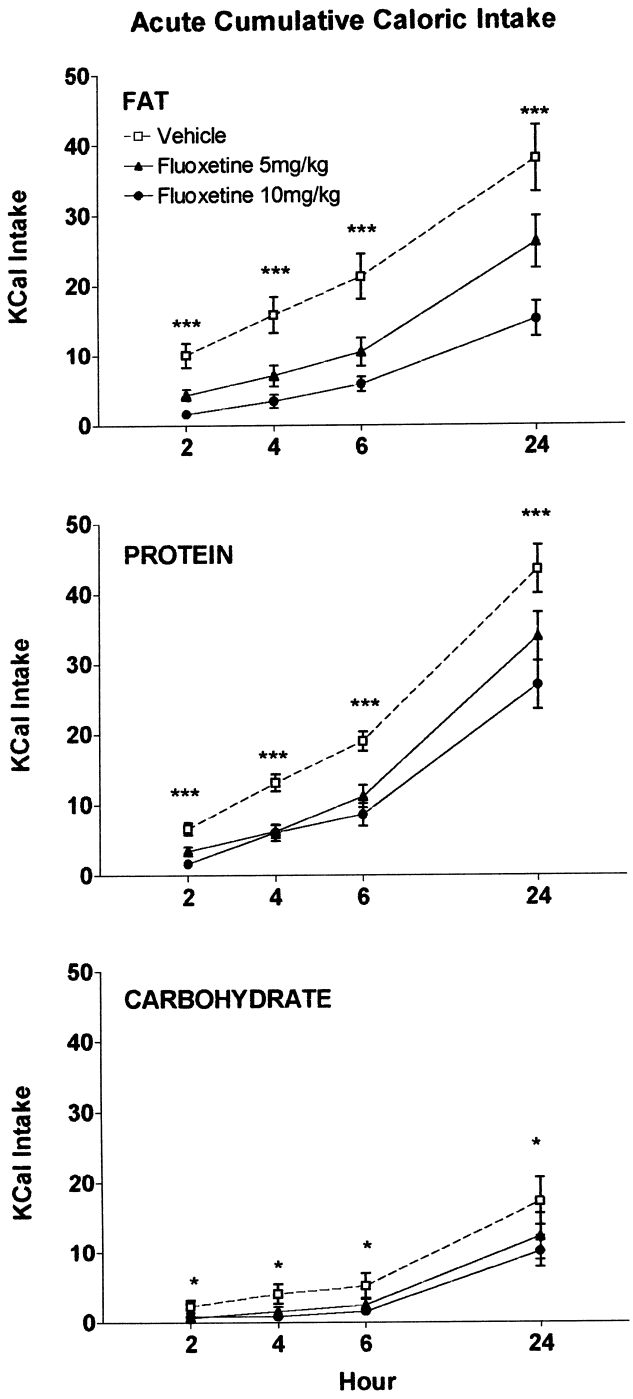

FIG. 2. The effect of acute fluoxetine administration on cumulative caloric intake of each macronutrient (mean ± SEM). Significant dose-related suppressions in fat (top; ***$p \leq 0.001$) and protein intakes (middle; ***$p \leq 0.001$, *$p \leq 0.01$) were observed at hour 2, 4, 6, and 24. Post hoc comparisons revealed that fluoxetine 5 mg/kg and 10 mg/kg were significantly different than vehicle. Carbohydrate intake (bottom) was also significantly reduced (*$p \leq 0.05$). Post hoc analyses demonstrated that fluoxetine 10 mg/kg significantly differed from 5 mg/kg at hour 2, and at all other times (hour 4, 6, 24) fluoxetine 10 mg/kg significantly differed from vehicle.

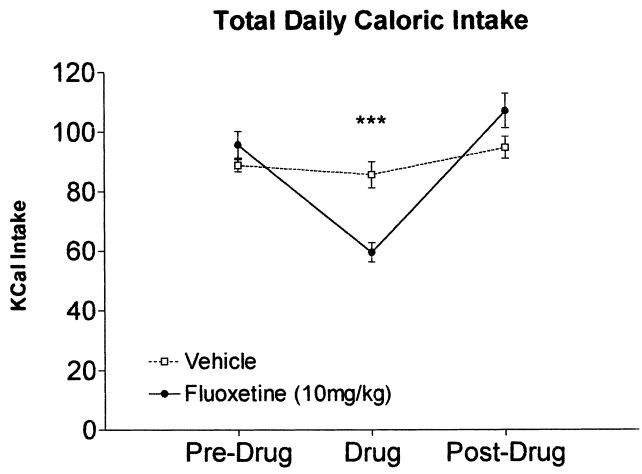

FIG. 3. The effect of chronic fluoxetine on total daily caloric intake. Because there were no differences in caloric intake as a function of time within each treatment period, data were averaged for each treatment period. Fluoxetine-treated animals consumed significantly (***$p < 0.001$) less calories compared to vehicle-treated animals. Total daily caloric intake of fluoxetine-treated animals was also significantly suppressed during the drug phase as compared to the pre- and postdrug phases ($ps \leq 0.001$).

time: $F(2, 24) = 57.27$, $p \leq 0.001$; and time × drug interaction: $F(2, 24) = 30.67$, $p \leq 0.001$] (Fig. 3). Total daily caloric intake of drug-treated animals decreased on day 1 of fluoxetine treatment and remained at a similar level throughout the 28-day injection period. During the withdrawal period, daily caloric intake of animals previously injected with fluoxetine returned to predrug levels, and did not differ from that of rats previously injected with the vehicle.

Fluoxetine also significantly suppressed fat [main effect of time: $F(2, 24) = 13.14$, $p \leq 0.001$; and time × drug interaction: $F(2, 24) = 7.65$, $p \leq 0.01$] and protein [main effect of time: $F(2, 24) = 18.90$, $p \leq 0.001$; and time × drug interaction: $F(2, 24) = 10.23$, $p \leq 0.001$] consumption (Fig. 4). Intakes of both nutrients were consistently suppressed throughout the 28-day drug treatment period. When drug injections were terminated, intakes of both nutrients returned to predrug levels. In contrast to fat and protein intakes, carbohydrate intake was not significantly reduced during fluoxetine treatment and increased slightly during the withdrawal period (Fig. 4).

In addition to determining the amount of each macronutrient consumed, percent nutrient intakes also were assessed. As shown in Fig. 5, the animals consumed the majority of their calories from protein and fat. The vehicle-treated rats did not alter percent nutrient intakes across time. However, fluoxetine produced a significant suppression in the percent of total calories consumed as fat [main effect of time: $F(2, 24) = 7.81$, $p \leq 0.01$; and time × drug interaction: $F(2, 24) = 9.43$, $p \leq 0.01$] and a significant increase in the percent of total calories consumed as carbohydrate [main effect of time: $F(2, 24) = 6.31$, $p \leq 0.01$; and time × drug interaction: $F(2, 24) = 6.21$, $p \leq 0.01$] relative to predrug measures. For both nutrients, percent caloric intake returned to predrug levels during the withdrawal period. Percent protein intake was not modified as a function of drug administration.

The effect of chronic fluoxetine treatment on body weight was also examined. Rats treated with fluoxetine gained significantly less weight during drug treatment than vehicle-injected

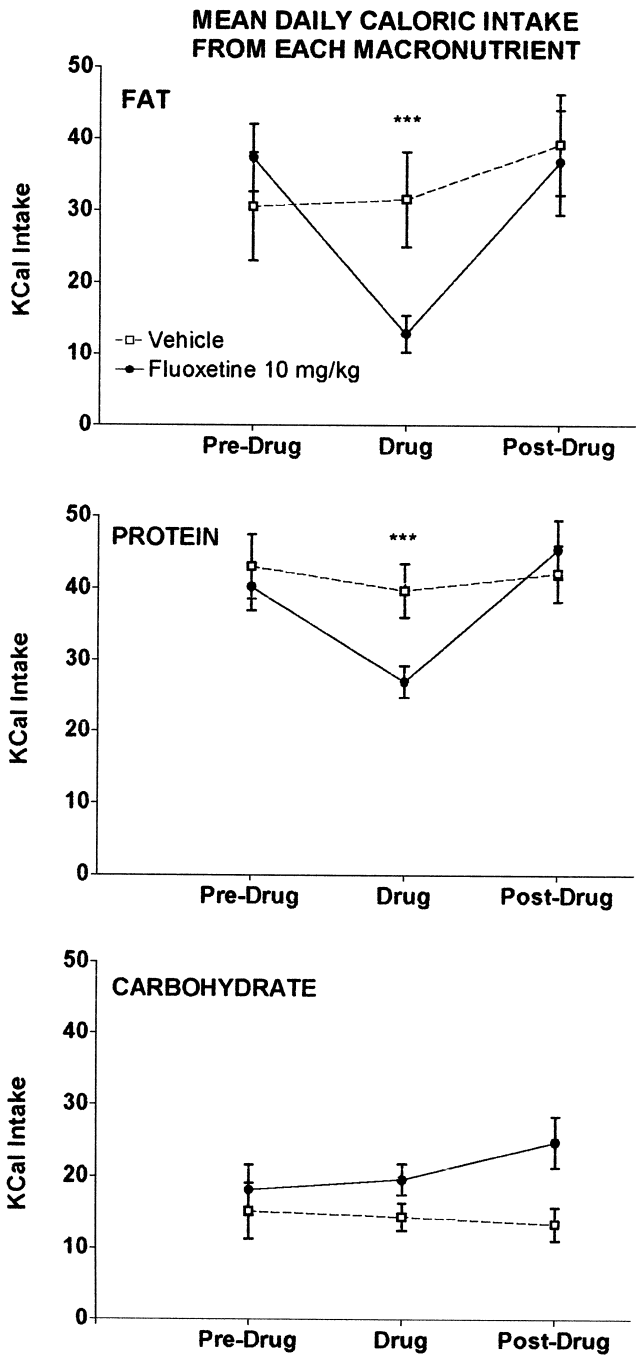

FIG. 4. The effect of chronic fluoxetine on daily intake of fat (top), protein (middle) and carbohydrate (bottom) averaged for each treatment period (mean ± SEM). Fluoxetine-treated animals consumed significantly less fat (*** = $p \leq 0.001$) and protein (*** $p \leq 0.001$) compared to vehicle-treated animals during the drug phase. In addition, fat and protein intakes of fluoxetine-treated animals were significantly ($ps \leq 0.001$) (lower during the drug phase as compared to pre- and post-drug periods. Daily carbohydrate intake did not differ between fluoxetine and vehicle-treated animals, or across the treatment periods.

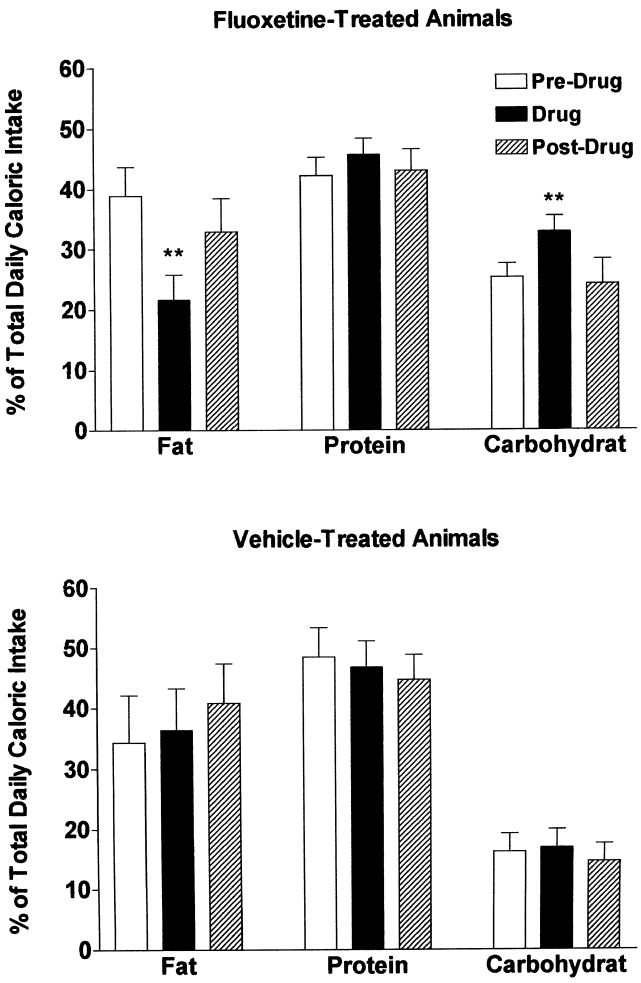

FIG. 5. The effect of chronic fluoxetine administration on percent of calories consumed from each of the macronutrient averaged for each treatment period (mean ± SEM). *Top*: For fluoxetine-treated animals percent of calories consumed as fat was significantly (**$p \leq 0.01$) lower, and percent of calories consumed as carbohydrate was significantly (**$p \leq 0.01$) greater during the drug phase as compared to the pre- and post-drug phases. *Bottom*: For vehicle-treated animals, there were no differences among treatment periods for fat, carbohydrate, or protein intakes.

controls [fluoxetine weight gain = 80 g vs. vehicle weight gain = 158 g; $F(1, 12) = 53.77$, $p \leq 0.001$] and gained significantly more weight during the postdrug period relative to controls [fluoxetine weight gain = 207 g vs. vehicle weight gain = 167 g; $F(1, 12) = 12.64$, $p \leq 0.01$]. Although at the end of the experiment the mean body weight of vehicle-treated rats was greater (588 g) than that of fluoxetine-treated animals (568 g), this difference was not significant.

DISCUSSION

Consistent with previous research (4,5,11,22,25,28,35), acute administration of fluoxetine led to a significant suppression in total energy intake. Moreover, chronic administration of fluoxetine was associated with significant reductions in both caloric intake and body weight. There was no indication that tolerance developed to the anorectic effect of fluoxetine, as drug-treated animals consumed significantly less food than

vehicle-treated animals across the entire 28-day drug-injection period. The decrease observed in body weight gain across the drug treatment period is also consistent with past research investigating the effects of chronic fluoxetine administration on body weight in rats fed single diets (4,23,28,33). In previous studies, drug-treated rats fed chow gained significantly less weight than controls over 5 (4), 6 (23), 8 (33), and 21 (28) days of fluoxetine treatment. In the present study, fluoxetine-treated rats gained only half as much weight as control animals during the drug phase. However, in the postdrug period, animals previously treated with fluoxetine gained significantly more weight than controls. By the end of the withdrawal period there were no differences in body weight as a function of prior drug treatment. This result is similar to that observed by others (28). For example, McGurik and colleagues (28) reported that by day 4 of withdrawal from fluoxetine, rats had regained 80% of their lost weight. As mentioned by these researchers (26), the rebound in weight gain after fluoxetine treatment should be considered in the use of the drug as a pharmacological weight reduction method in humans.

In contrast with past research (23,35,39), the reductions in caloric intakes observed during the acute and chronic phases of this study were not associated with a selective decrease in carbohydrate. During the acute phase of this study, fluoxetine led to reductions in intakes of all three macronutrients. However, the suppression in carbohydrate intake was less robust than the reductions observed in fat and protein intakes. Similarly, chronic administration of fluoxetine led to significant reductions in protein and fat intakes, but had no effect on carbohydrate intake. These alterations in nutrient intake resulted in a decrease in the percent of diet consumed as fat, and an increase in the percent of the diet consumed as carbohydrate during the drug phase. One explanation for the differences between the results of previous work and those of the present study may be related to methodological factors. The majority of studies reporting a selective suppression in carbohydrate intake following administration of serotonergic agonists provided a choice between two diets: a high-carbohydrate/low-protein diet and a low-carbohydrate/high-protein diet (22,23,25,37–40). In this situation, serotonergic drugs typically lead to a greater decrease in the intake of the high-carbohydrate/low-protein diet than of the low-carbohydrate/high-protein diet. This obviously results in a reduction in the percent of total calories consumed as carbohydrate. However, because the diets used in previous studies contained equivalent amounts of fat, it is impossible to determine if fluoxetine would have an effect on fat intake, or if the presence of a separate source of fat would alter the actions of the drug on nutrient choice (14).

It should be noted that there are two previous studies that used pure macronutrient diets to examine the short-term effects of fluoxetine on nutrient selection. These studies reported a selective reduction in carbohydrate intake 1 and 2 h, and significant suppressions in protein and fat intakes 11 and 12 h after fluoxetine injections (32,35). The discrepancy between these studies and the present experiment is at hour 2. One possible reason for this difference relates to baseline nutrient intakes. Previous work has shown that baseline preferences for the test diets influence the effects of drugs on nutrient choice (10). In the previous studies, carbohydrate was the preferred nutrient at hour 2, while in the present study, fat was preferred.

It is possible that serotoninergic drugs do not selectively reduce carbohydrate intake, but rather decrease intake of the most preferred nutrient. In previous studies in this laboratory, we found that *dl*-fenfluramine and serotonin reduced intake of fat, which was the most preferred nutrient, to a greater degree than intake of either protein or carbohydrate (15,30). Moreover, in studies reporting that serotonergic drugs lead to a selective decrease in intake of a high-carbohydrate/low-protein diet relative to intake of a low-carbohydrate/high-protein diet, rats preferred the high-carbohydrate/low-protein diet under baseline conditions (22–25). Although a selective reduction in intake of preferred foods may account for a portion of the effects of serotonergic agents on nutrient choice, this is clearly not the complete story. For example, when an isocaloric fat ration was substituted for a high-caloric fat ration, rats ate more carbohydrate than fat, but administration of *dl*-fenfluramine still was associated with a greater suppression in fat intake than carbohydrate intake (30).

Although the notion that an increase in serotoninergic activity is associated with a reduction in carbohydrate intake has received a great deal of attention in the popular press, this relationship is not adequately supported by well-controlled research studies. There are now a large number of studies in both animals and humans demonstrating that administration of serotonin agonists, such as fluoxetine, do not consistently lead to reductions in carbohydrate consumption [e.g., (2,12,15,16–20,29,30)]. It must be realized that a number of factors including diet palatability, hydration of the diet, the dietary choice situation, and the duration of time between drug administration and nutrient intake contribute to the actions of serotoningeric agents on nutrient choice. This realization is particularly important given that clinicians are prescribing certain selective serotonin reuptake blockers as ways of reducing carbohydrate intake in patients with obesity, and the eating disorder, bulimia.

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