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BRIEF COMMUNICATION

Effect of Phenylpropanolamine on Diet Selection in Rats[1]

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SCHWARTZ, D. H. AND B. G. HOEBEL. *Effect of phenylpropanolamine on diet selection in rats.* PHARMACOL BIOCHEM BEHAV 31(3) 721–723, 1988.—Four doses of phenylpropanolamine (PPA; i.e., dl-norephedrine: 2.5, 5, 10, and 20 mg/kg) and saline were injected intraperitoneally in female rats maintained on a dietary self-selection paradigm. Intake of all three macronutrients (carbohydrate, fat, and protein) was equally affected by high doses of PPA. Lower doses decreased fat and protein more than carbohydrate.

Dietary self selection Phenylpropanolamine Macronutrients

PHENYLPROPANOLAMINE (PPA, i.e., propadrine, i.e., dl-norephedrine HCl) is sold commercially as an appetite suppressant. Short-term dose dependent anorectic properties of the drug have been demonstrated in the rat (3, 4, 8, 9, 14, 16, 17). It has also been tested with monkeys and humans (1, 5–7). These earlier studies in animals tested PPA's effects on a single, nutritionally complete diet, but did not examine the drug's effect on nutrient selection.

The dietary self-selection paradigm has been used to study the effects of other anorectic drugs such as fenfluramine and amphetamine (15,18). This procedure allows the animal to self-select its preferred balance of fat, carbohydrate and protein (10). The present study determined the effect of PPA on these macronutrients in addition to its influence on total caloric intake. Given the importance of diet balancing in omnivores, specific neuropharmaceutical influences on macronutrient selection are particularly interesting.

METHOD

Twelve female Sprague-Dawley rats weighing 135–250 grams were housed on a 12 hour light/12 hour dark cycle. They were maintained on a dietary self-selection paradigm for ten days with 24-hour access to three diets, carbohydrate, fat, and protein, each in a separate dish. Water was also freely available. The carbohydrate portion consisted of 580 g corn starch (BioServe), 280 g dextrin (BioServe), 100 g commerical-grade sucrose, 40 g mineral mix (ICN Pharmaceuticals), 20 g vitamin mix (BioServe). The fat portion was composed of 912 g Crisco shortening (commercial), 48 g safflower oil (ICN Pharmaceuticals), 90 g mineral mix, and 50 g vitamin mix. The protein portion consisted of 960 g Casein (ICN Pharmaceuticals), 40 g mineral mix, and 20 g vitamin mix. Each of these diets was available in a separate, 75 cc dish (5×5 cm diameter) attached to a holder at the end of the cage 10 cm off the floor. Spillage in the dish holder was collected and measured; spillage outside the holder was trivial.

At the end of the ten-day adaptation period, three animals not maintaining body weight were eliminated from the experiment. The remaining nine animals grew at a normal rate. They were adapted to a feeding schedule on which they received the diets for five hours per day in the middle of the light cycle. Animals were exposed to this schedule for 10 additional days before being injected with PPA.

Injections of either PPA or saline (control) were administered to the animals in a counter-balanced order at doses of 2.5, 5, 10, and 20 mg/kg body weight. These injections were adminstered 30 minutes before the animals were given access to the diets. Intake of each diet to the nearest 0.1 gram was recorded after 2 and 5 hours. Injections were separated by at least 3 days. Data were analyzed using an Analysis of Variance. Multiple comparisons were made with Dunnett's test, which compared each PPA dose with saline control.

RESULTS

As shown in Fig. 1, PPA caused a dose-dependent decrease in total caloric intake over the 5-hour period. This decrease was significant at the 5 mg/kg dose which resulted in intakes that were 74% of saline control. Figure 2 shows that intake of all three macronutrients decreased in the first two hours as a result of PPA injection. Specifically, carbohydrate intake was significantly reduced by the 10 mg/kg

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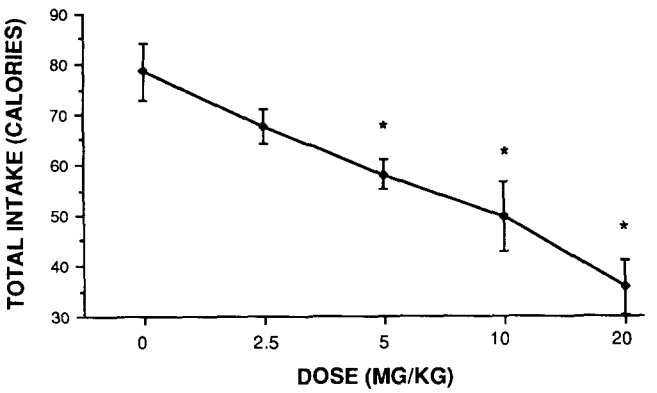

FIG. 1. PPA caused a dose-related decrease in 5-hour total caloric intake (mean±SEM; *$p<0.05$).

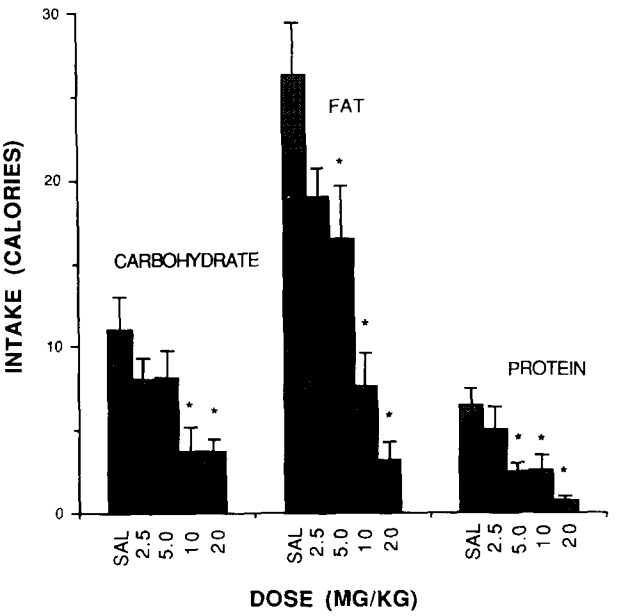

FIG. 2. PPA caused a dose-related decrease in 2-hour macronutrient intake (mean±SEM; *$p<0.05$). Lower doses decreased fat and protein more than carbohydrate.

dose ($p<0.05$), while protein and fat were significantly reduced by the 5 mg/kg dose ($p<0.05$).

After the full 5 hours of access to the diets, carbohydrate intake was significantly reduced below saline controls by the 20 mg/kg dose of PPA, fat was significantly reduced by the 10 mg/kg dose of PPA ($p<0.05$), and protein was reduced by the 5 mg/kg dose ($p<0.05$; see Fig. 3). Using this longer time frame, protein intake seems to be most sensitive to PPA, although fat stilled showed the largest percentage decrease at the highest dose.

DISCUSSION

All three macronutrients were affected by PPA at high doses (10 and 20 mg/kg). At the 5 mg/kg dose, both fat and protein were affected significantly by PPA 2 hours after injection, but carbohydrate intake was not reduced significantly by this low dose of PPA. PPA (5 mg/kg) continued to suppress protein 5 hours after injection.

Many factors can influence macronutrient intake, including age of the animal and the form of the diet (2,13). McArthur and Blundell demonstrated that a drug can affect macronutrient intake differentially, depending on the external sensory qualities of the diets (12). This mutable nature of the dietary self selection paradigm notwithstanding, consistent patterns in nutrient selectivity among related drugs allows reasonable conclusions to be drawn.

Amphetamine and PPA are considered to be primarily catecholaminergic while fenfluramine is serotoninergic. Wurtman and Wurtman reported that amphetamine decreased protein intake more than carbohydrate; whereas fenfluramine "spared" protein intake (18). Other investigators have also reported that amphetamine decreased fat and protein intake, while leaving carbohydrate intake relatively unaffected (11,15). These reports are consistent with the effects of PPA on dietary self-selection reported here. It may be therefore, that amphetamine and PPA share some common mechanism for suppressing fat or protein intake, while having relatively little effect on carbohydrate except at higher doses.

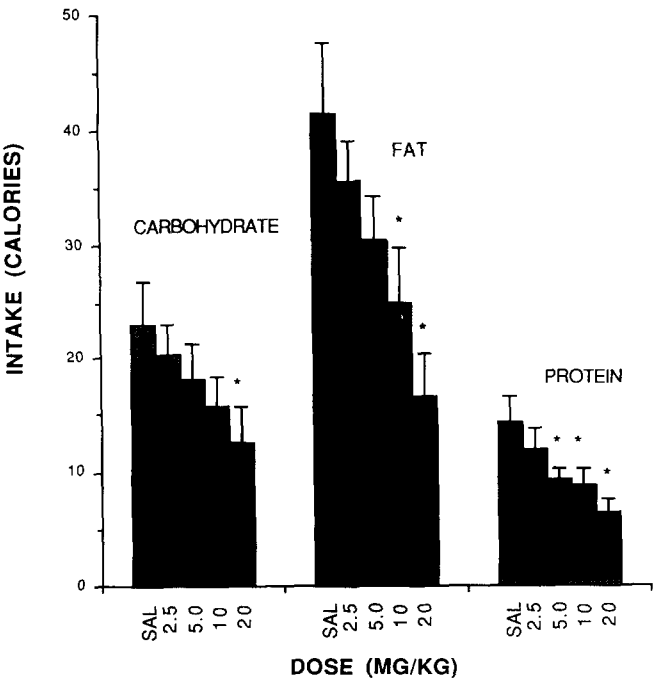

FIG. 3. PPA caused a dose-related decrease in 5-hour macronutrient intake (mean±SEM; *$p<0.05$). Lower doses decreased protein more than fat and carbohydrate.

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