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Selection for Growth Alters the Feeding Response to Injections of Biogenic Amines

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DENBOW, D. M., H. P. VAN KREY AND P. B. SIEGEL. *Selection for growth alters the feeding response to injections of biogenic amines.* PHARMACOL BIOCHEM BEHAV **24**(1) 39–42, 1986.—Two experiments were conducted to determine if selection for growth altered the response to intracerebroventricular (ICV) injections of methoxamine and 5-hydroxytryptamine (5-HT). Lines of chickens divergently selected over 25 generations for 8-week body weight were used. The ICV injection of methoxamine into fully fed birds significantly increased food intake in the high-weight line but had no effect on food intake in the low-weight line. Conversely, the ICV injection of 5-HT had no effect in fully fed birds but significantly decreased food intake in 24-hr fasted birds in both weight-lines. Food intake was affected by 5-HT for a much longer period in the high-weight line than in the low-weight line. These results suggest that selection for growth alters the brain response to biogenic amines.

Food intake Methoxamine 5-HT Serotonin Chickens Intracerebroventricular

DURING the last two decades, biogenic amines within the central nervous system have been implicated in the regulation of food intake [18]. Intracerebroventricular (ICV) and intrahypothalamic injections of norepinephrine and epinephrine increase food intake in the rat [14, 21, 25] as well as in several other mammalian species [2, 3, 12, 34]. Epinephrine appeared to be more potent than norepinephrine [15, 16, 31]. The primary site of action for adrenergic-induced feeding appeared to be the paraventricular nucleus [17] with the effect being mediated by α-adrenoceptors [16,31].

The indoleamine 5-hydroxytryptamine (5-HT) has also been implicated in the neurochemical control of feeding [23]. Injection of 5-HT into the perifornical hypothalamus [8], the lateral hypothalamus [13] and the medial paraventricular nucleus [19] of the rat decreased food intake. In addition, specific 5-HT agonists, including quipazine [26] and Lilly 110–140 [9], decreased food intake.

We recently reported that ICV injections of epinephrine stimulated food intake in fully-fed broiler chickens [5] but had no effect in Leghorn chickens [7]. Conversely, the ICV injection of 5-HT decreased food intake in fasted Leghorns [7] but not in fasted broilers [6]. These results demonstrated breed differences in the feeding response to ICV injections of neurotransmitters. Since there are large differences between broilers and Leghorns other than in food intake, the present study was designed to further investigate possible differences in the response to neurotransmitters using genetically selected high and low-weight lines of chickens that originated from a common base population.

METHOD

Animals

Chickens were obtained from lines of White Plymouth Rocks that had undergone 25 generations of selection for high and low body weight at 8 weeks of age [29]. The base generation for the selected lines was a segregating pool that originated from crosses of 7 inbred lines. Means and standard deviations of body weights for the males at 8 weeks of age were 1383±104 and 265±63 g for the high and low-weight lines, respectively.

The birds were reared in heated batteries with raised wire bottom floors until 8 weeks of age at which time they were individually caged. They were provided the same diet consisting of 20% protein and 2684 kcal ME/kg as has been used for their genetic selection [28].

Surgical Preparation

Under sodium pentobarbital anesthesia, a 23-gauge, thin-walled guide cannula [20] was implanted stereotaxically into the right lateral ventricle of each chick as previously described [5]. Topazone (Norden Laboratories, Inc.) was applied prophylactically to the incision to control infection, and the birds were allowed a minimum of 3 days to recover.

Experiment

In Experiment 1, methoxamine, an α_1-adrenergic receptor agonist [33], was prepared in concentrations of 0, 50 and 100

TABLE 1

THE EFFECTS OF INTRACEREBROVENTRICULAR INJECTIONS OF METHOXAMINE ON CUMULATIVE FOOD INTAKE [g OF FOOD CONSUMED/(g OF BODY WEIGHT)$^{0.75}\times10^{-3}$] OF CHICKENS SELECTED FOR HIGH AND LOW 8-WEEK BODY WEIGHT

	Time (minutes)						
Treatment	15	30	60	90	120	150	180
High weight							
0 μg	11 ± 2.4*†	18 ± 3.5†	28 ± 4.4	37 ± 6.5	46 ± 7.8	58 ± 7.6	69 ± 8.3
50 μg	21 ± 6.3‡	31 ± 8.6‡	37 ± 9.3	38 ± 9.3	40 ± 9.8	48 ± 9.9	54 ± 9.6
100 μg	22 ± 3.6‡	34 ± 4.6‡	47 ± 5.9	53 ± 6.5	59 ± 7.9	60 ± 8.3	63 ± 8.9
Low weight							
0 μg	22 ± 3.5	31 ± 3.7	41 ± 5.7	50 ± 6.4	62 ± 8.1	70 ± 9.0	80 ± 10.7
50 μg	35 ± 4.5	44 ± 5.7	53 ± 5.4	58 ± 5.2	60 ± 5.5	66 ± 6.6	68 ± 6.3
100 μg	26 ± 6.7	39 ± 8.7	55 ± 9.0	60 ± 10.1	64 ± 9.8	70 ± 10.6	75 ± 9.8

*Mean ± standard error.
†‡Means within a treatment group and time period with different superscripts are significantly different ($p<0.05$).

TABLE 2

THE EFFECTS OF INTRACEREBROVENTRICULAR INJECTIONS OF 5-HT ON CUMULATIVE FOOD INTAKE [g OF FOOD CONSUMED/(g OF BODY WEIGHT)$^{0.75}\times10^{-3}$] ON AD LIB FED AND 24-HR FASTED CHICKENS SELECTED FOR HIGH AND LOW 8-WEEK BODY WEIGHT

	Time (minutes)							
Treatment	15	30	45	60	90	120	150	180
				Ad lib fed				
High weight								
0 μg	2 ± 1.0*	6 ± 3.1	12 ± 4.4	17 ± 4.4	36 ± 7.1	49 ± 7.6	60 ± 8.3	74 ± 10.7
33 μg	5 ± 2.5	9 ± 3.7	16 ± 5.8	26 ± 6.7	31 ± 8.1	49 ± 9.4	66 ± 8.0	78 ± 7.2
67 μg	1 ± 0.9	4 ± 2.9	12 ± 4.5	15 ± 4.9	23 ± 4.9	34 ± 6.2	46 ± 8.1	62 ± 7.7
100 μg	2 ± 2.0	5 ± 3.1	11 ± 3.9	17 ± 6.0	26 ± 8.9	38 ± 8.6	52 ± 8.8	70 ± 9.2
Low weight								
0 μg	22 ± 5.1	30 ± 5.6	39 ± 4.2	44 ± 4.6	53 ± 6.3	57 ± 6.3	72 ± 8.9	87 ± 10.2
33 μg	16 ± 5.7	17 ± 5.6	26 ± 4.5	39 ± 3.7	57 ± 5.9	65 ± 5.4	85 ± 9.1	99 ± 8.4
67 μg	21 ± 6.0	27 ± 7.3	38 ± 8.9	45 ± 8.8	59 ± 10.1	73 ± 11.2	89 ± 12.6	103 ± 12.5
100 μg	9 ± 5.1	20 ± 7.0	25 ± 8.2	33 ± 8.7	47 ± 7.7	57 ± 7.8	70 ± 9.4	82 ± 9.4
				24-hr fasted				
High weight								
0 μg	23 ± 3.4†	39 ± 4.5†	52 ± 5.0†	62 ± 5.0†	86 ± 5.2†	104 ± 6.3†	120 ± 5.7	134 ± 6.9
33 μg	14 ± 2.3†‡	25 ± 4.0†‡	43 ± 4.9†	56 ± 4.9†	79 ± 4.8†	102 ± 5.6†	114 ± 7.6	127 ± 8.1
67 μg	11 ± 4.2‡	17 ± 5.5‡	35 ± 8.7†‡	44 ± 10.4†‡	62 ± 11.2†‡	81 ± 13.2†‡	104 ± 13.1	117 ± 13.9
100 μg	6 ± 2.4‡	13 ± 5.1‡	20 ± 5.9‡	28 ± 6.9‡	45 ± 8.6‡	67 ± 8.2‡	88 ± 8.2	103 ± 8.9
Low weight								
0 μg	41 ± 5.7†	60 ± 7.2†	76 ± 8.1†	88 ± 7.8	106 ± 7.9	126 ± 7.8	136 ± 7.8	147 ± 8.3
33 μg	17 ± 5.4‡	29 ± 6.9‡	45 ± 8.5‡	59 ± 9.6	84 ± 9.5	109 ± 11.3	131 ± 12.6	142 ± 13.4
67 μg	22 ± 5.8‡	36 ± 8.2‡	50 ± 9.4‡	59 ± 11.4	90 ± 11.1	116 ± 13.2	138 ± 14.0	153 ± 14.1
100 μg	17 ± 6.0‡	28 ± 8.2‡	49 ± 9.9‡	63 ± 10.2	87 ± 10.6	109 ± 10.6	133 ± 9.4	151 ± 10.0

*Mean ± standard error.
†‡Means within a treatment group, genetic line and time period with different superscripts are significantly different ($p<0.05$).

μg/10 μl of artificial cerebrospinal fluid (aCSF). The aCSF served as the control and consisted of 155 mM Na^+, 3.7 mM K^+, 2.5 mM Ca^{++}, 2.1 mM Mg^{++}, 140 mM Cl^- and 23 mM HCO_3^- [1] with 0.1 mg/ml of absorbic acid to retard oxidation. The design was a randomized block with twelve birds per replication in each line of birds. The experiment was replicated three times with the birds being randomized for each replication. All the solutions were filtered through a 0.22 μm filter (Millipore Corp.) before injection. Injections were made using a 27-gauge injection cannula connected to a 10 μl Hamilton syringe via a 60-cm length of PE-50 tubing. All injections were made over a 30-sec period, with injection cannula remaining in place an additional 30-sec to insure dispersion of the injectant. Only fully fed birds were used in Experiment 1.

In Experiment 2, both fully fed and 24-hr fasted high and low-weight line birds were injected with 0, 33, 67 or 100 μg/10 μl of aCSF of 5-HT as the salt of creatinine sulfate. Creatinine sulfate, the amount equivalent to that found in the 100 μg 5-HT group, served as the control. The dosages used were based on previous studies using chickens and they did not appear to cause sleep [6,7]. The experimental design was the same as described for Experiment 1.

Cannula Location

Three methods were used to verify the location of each cannula. First, at the time of surgery each guide cannula was examined for the presence of cerebrospinal fluid in the lumen. Second, following recovery each bird was injected ICV and 67 μg of norepinephrine and body temperature monitored, since this neurotransmitter had been previously shown to decrease body temperature [5]. A decrease of greater than 0.5°C was considered evidence that the cannula was in the lateral ventricle. Third, Evans blue dye was injected into each bird at the conclusion of the study and the birds were sacrificed. The brains were removed and frozen, and then examined macroscopically for the presence of dye in the ventricles.

Statistical Analysis

Cumulative food intake (g of food/(g body weight)$^{0.75}$) was analysed using analysis of variance at each time period [32]. Since the body weights of the birds differ markedly between lines, (body weight)$^{0.75}$ was used to standardize the data on a metabolic body size basis [11]. Replication effects were partitioned in the analysis. When treatment effects were significant, the means were separated using Duncan's multiple range test. Significance implies $p<0.05$.

RESULTS AND DISCUSSION

Methoxamine significantly increased food intake at 15 and 30-min post-injection in birds from the high-weight line but had no significant effect on food intake in the low-weight line (Table 1). The initial increase in food intake caused by methoxamine was rapidly compensated for, such that the cumulative food intake was similar between groups at 120 and 180 min post-injection. Methoxamine infusion did not affect water consumption in either line.

The reason for the disparate feeding response of high and low-weight line birds to central methoxamine injections is unclear, but a plausible explanation would involve changes in receptor responsiveness to putative neurotransmitters. Selection for enhanced growth, as in the high weight line, may have increased responsiveness to adrenergic compounds, and, hence, appetite. Selection for decreased growth as in the low weight line may have increased responsiveness to satiety related neurotransmitters. To evaluate this hypothesis, the feeding response of ad lib and 24-hr fasted birds to ICV infusions of 5-HT was investigated.

Infusion of 5-HT was not effective in ad lib fed birds but significantly suppressed food intake in 24-hr fasted high and low-weight birds (Table 2). Food intake was decreased significantly by 67 and 100 μg of 5-HT in fasted birds from the high weight line, whereas 33 μg of 5-HT significantly decreased food intake in the low-weight line. As with methoxamine, the initial changes in food intake caused by 5-HT were compensated for in the subsequent time periods. Food intake was affected by 5-HT for a much longer time in the high-weight than in the low-weight line. These results suggested that not only do the lines differ in sensitivity to biogenic amines but they may also differ in the rate of metabolism of these compounds.

The mechanism(s) by which differing sensitivity to biogenic amines occurs in chickens from lines selected for high and low body weight may involve changes in receptor number and/or affinity. Studies comparing the activity of two inbred strains of rats [24, 27, 30] provide support for such mechanism(s). These strains differed in spontaneous motor activity, cortical and midbrain tyrosine hydroxylase activity, and behavioral responsiveness to norepinephrine and amphetamine. Perry [24] showed that α-adrenergic receptor density was different between the two strains. In addition, Keller [10] observed that the nutritional state of an animal can influence the number of adrenergic receptors in the brain.

It has been shown that the high-weight line is obese relative to the low-weight line [4]. Genetically obese mice have a greater number of α-adrenergic receptors that their lean litter mates [22]. If a similar situation exists between the growth lines used in our study, it would explain the greater responsiveness of the high-weight line to methoxamine than in the low-line chickens.

Our results show that genetic selection for enhanced growth and food intake resulted in increased responsiveness to an α-adrenergic agonist. Many mechanisms are clearly involved in altering growth and food intake, and changes in neurohumoral sensitivity within the central nervous system appear to be involved as well.

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