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Food Intake and Biogenic Amine Concentrations in Brain Regions of Chicks Following Intracerebroventricular Injection of Six-Hydroxydopamine[1]

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KUENZEL, W. J., N. SNAPIR AND C. E. REXROAD, JR. *Food intake and biogenic amine concentrations in brain regions of chicks following intracerebroventricular injection of six-hydroxydopamine.* PHARMACOL BIOCHEM BEHAV 27(2) 257–263, 1987.—The effect of catecholamine depletion within three brain regions on subsequent food intake and body weight gain were investigated in two week-old chicks. Two levels of pargyline (P; 50 mg/kg and 100 mg/kg intraperitoneally) and three levels of six-hydroxydopamine (6-OHDA; 0, 200 μg (136 free base) and 300 μg (204 free base) intracerebroventricularly) were administered to 36 chicks (n=6 per treatment). The greatest reduction in food intake and body weight gain occurred in the group given 100 mg/kg P, 300 μg 6-OHDA. These chicks displayed an average aphagic response of 4.5 days. Chicks given the higher drug doses were hyperactive when handled and displayed difficulty in orienting their bills when attempting to consume pellets. Biogenic amines were determined in three brain regions (striatum, hypothalamus and brainstem) using high pressure liquid chromatography with electrochemical detection. Dopamine (DA) was reduced ($p<0.05$) in the striatum of all groups treated with 6-OHDA when compared to their respective controls. Significant depletions of norepinephrine (NE) occurred in all three brain regions in all groups treated with 6-OHDA when compared with their respective control groups ($p<0.05$). In contrast, striatal epinephrine levels were elevated in chicks given 100 mg P plus 6-OHDA. It is proposed that depletions of both DA and NE contribute to the aphagic or anorexic response of chicks following administration of the neurotoxin 6-OHDA.

Feeding behavior Six-hydroxydopamine Dopamine Norepinephrine Body weight Chicks

BILATERAL hypothalamic lesions in rats effect aphagia and loss of weight [1]. A neural structure implicated as a cause of the aphagia is the nigrostriatal dopaminergic pathway [15], since this pathway courses through the lateral hypothalamic area and inevitably would be damaged following placement of lateral hypothalamic lesions. In addition, both intracerebroventricular [16,17] and direct application of six-hydroxydopamine (6-OHDA) to the nigrostriatal bundle [15] resulted in aphagia, adipsia and hypoactivity. The effect of 6-OHDA on feeding behavior in birds has not been investigated. It would be of interest to determine if 6-OHDA suppresses feeding in birds since the avian substantia nigra (nucleus tegmenti pedunculopontinus pars compacta) likewise contains efferents that pass through the lateral hypothalamic area prior to terminating within the basal ganglia [5,7]. In addition, the lateral hypothalamic area of birds contains neuronal elements that when bilaterally lesioned effect transient aphagia [8,9].

The purpose of this study was to inject 6-OHDA intracerebroventricularly (ICV) in chicks to determine whether food intake would be significantly depressed. In addition, biogenic amines were quantitated within the striatum, hypothalamus, and brainstem of experimental birds to ascertain whether significant depletions of amines resulted from administration of the neurotoxin.

METHOD

Animals, Feed and Housing

Male broiler chicks (White Rock) were raised in Peter-

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sime batteries with raised wire floors. At twelve days of age, 36 chicks were housed individually in two batteries. All chicks were fed a commercial broiler starter crumble diet containing 24 percent protein, 3234 kcal/kg metabolizable energy and 2.6 percent fiber. Throughout the study chicks were exposed to continuous light.

Experimental Design

A preliminary experiment with 20 chicks was designed to determine a dose of 6-OHDA that would reduce food intake in broilers. Pargyline was first injected IP at 50 mg/kg body weight followed by 6-OHDA injected ICV. The doses of 6-OHDA included: 0, 100, 200, and 400 μg. No effect of 6-OHDA on food intake or body weight gain was detected with 100 μg 6-OHDA. In contrast, two chicks died and two others could not stand up the day following administration of 400 μg 6-OHDA. For these reasons, the dosages of 100 and 400 μg of 6-OHDA were not studied and a more detailed analysis examined doses of 200 and 300 μg given ICV.

The experiment incorporated a 2×3 factorial design to test the effects of two levels of pargyline (P; 50 mg/kg and 100 mg/kg) and three levels of 6-OHDA (0, 200 μg (136 μg free base) and 300 μg (204 μg free base)) on food intake and body weight gain or loss. Chicks were randomly assigned to one of the six treatments.

Surgical Procedures

Pargyline (pargyline hydrochloride, Sigma Chem. Co.) was dissolved in 0.9% saline and injected intraperitoneally between 15 and 30 min prior to the ICV injection of 6-OHDA. Six-hydroxydopamine (6-OHDA hydrobromide, Sigma Chem. Co.) was dissolved in sterilized 0.9% saline to which was added 0.1% ascorbic acid.

Chicks were anesthetized with Chloropent (1.8 ml/kg; Ft. Dodge Lab, Inc.) via the brachial vein. Birds were then positioned in a stereotaxic instrument (David Kopf Instruments) with beak lowered at a 45° angle. A rectangular piece of skull (2×4 mm) on the right side of midline was removed and placed in 70% ethanol. Within the opening, a mark was made 2 mm anterior to bregma and 0.7 mm to the right of mid-line. A 22 gauge needle (38 mm long) was cut, connected via polyethylene tubing (7410 P.E. tubing, Clay Adams) to a 25 μl Hamilton syringe and secured to an electrode carrier of the stereotaxic instrument. Polyethylene tubing was also sleeved over the end of the needle to prevent penetration of the tip more than 3 mm into the brain from the surface of the dura mater. The beveled opening of the needle was directed away from midline and the center of the opening was lowered approximately 2 mm below the surface of the brain using the stereotaxic instrument prior to injection of the neurotoxin. Saline or 6-OHDA in a volume of 20 μl was injected into each brain over a period of 1 min. The needle was left in place for an additional minute prior to withdrawal. The piece of skull was replaced, skin sutured and bird returned to its cage.

Body Weight, Food Intake and Brain Dissections

Body weight and food intake were determined daily for two weeks post-operatively. Birds were then sacrificed and their brains rapidly dissected and placed upside down on glass slides overlying dry ice. Three brain areas were dissected and weighed: hypothalamus, brainstem and striatum. A description of the dissection procedure follows. First both

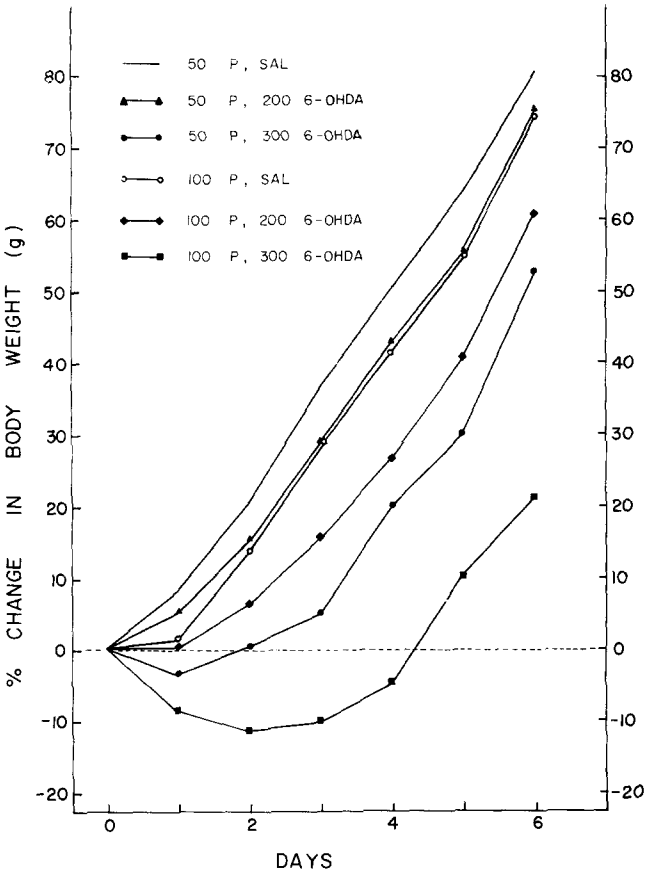

FIG. 1. Percent change in body weight from day of operation. The 100 mg P, 300 μg 6-OHDA had significantly lower changes in body weight when compared to all other experimental groups. P=Pargyline (administered intraperitoneally). 6-OHDA= Six hydroxydopamine (administered intracerebroventricularly).

optic lobes were dissected from the brain. Two sagittal cuts ±7.0 mm from midline were then made which essentially removed parts of the archistriatum and neostriatum. Cross sectional cuts were made anterior to the septomesencephalic tract and just anterior to the third cranial nerves. Between the two cross sectional cuts two sagittal cuts ±2.0 mm from midline were completed thus blocking the entire preoptic-hypothalamic area. A dorsal cut was then made from the anterior commissure to the posterior commissure. Hence the hypothalamic block comprised the entire preoptic area, hypothalamus, optic chiasma and some thalamic tissue.

The brainstem section resulted from the cross sectional cut made through the third cranial nerve and a second cross sectional cut 5 mm caudal to the first. The brainstem section included cranial nerves three through eight and therefore contained the locus coeruleus, substantia nigra, ventral tegmental area and the major portion of the nucleus raphe. The cerebellum was detached and not included with the brainstem section. The striatal section contained the paleostriatum augmentatum, nucleus intrapeduncularis and the paleostriatum primitivum which are comparable structures to those found within the mammalian corpus striatum or basal ganglia [5].

TABLE 1

APHAGIC RESPONSE FOLLOWING INTRACEREBROVENTRICULAR INJECTION OF SIX-HYDROXYDOPAMINE

Experimental Group*	n	Body Weight at Time of Surgery (g)	Number of Days Aphagic
50 mg P–Saline	6	273 ± 3.7[a]†	0 ± 0[a]†
50 mg P–200 (136 free base) μg 6-OHDA	5	266 ± 4.5[a]	0.2 ± 0.50[a]
50 mg P–300 (204 free base) μg 6-OHDA	6	265 ± 3.8[a]	1.8 ± 0.87[ab]
100 mg P–Saline	5	283 ± 6.6[a]	0 ± 0[a]
100 mg P–200 (136 free base) μg 6-OHDA	6	269 ± 6.0[a]	0.5 ± 0.50[a]
100 mg P–300 (204 free base) μg 6-OHDA	6	282 ± 5.1[a]	4.5 ± 2.05[b]

*P=Pargyline, at 50 or 100 mg/kg body weight; 6-OHDA=Six-hydroxydopamine.

†Mean ± S.E.M.: Means with like superscripts within columns are not significantly different ($p>0.05$).

Biogenic Amines

Extraction of biogenic amines was accomplished using 2 ml 0.05 N HCl and a Polytron homogenizer. Each homogenate was centrifuged for 20 min at 20,000 rpm. The supernatant was saved, filtered through an Acro LC13 Gelman (0.2 μm) filter attached to a disposable syringe. One hundred μl was then injected into a reverse-phase high pressure liquid chromatography system with electrochemical detector (HPLC-EC, Bioanalytical Systems, Inc.). Dopamine, norepinephrine, epinephrine, 5-hydroxyindole-3-acetic acid and serotonin were determined in each brain sample. The standards were prepared fresh each day for the HPLC-EC runs and included the following: 5-hydroxytryptamine creatine sulfate complex, 5-hydroxyindole-3-acetic acid, L-arterenol bitartrate, 5-hydroxytyramine HCl, L-epinephrine bitartrate and 3,4-dihydroxy-benzylamine hydrobromide (Sigma Chem. Co.). Each was prepared to contain 4 ng/100 μl when calculated as the free base; 0.1% L-cysteine was added to the stock solution to serve as an antioxidant. The mobile phase consisted of 0.25 g disodium ethylenediamine tetraacetate, 14.2 g monochloroacetic acid, 4.7 g sodium hydroxide and 200 mg octyl sodium sulfate per liter of glass distilled water. After adjusting to a pH of 3.0 and de-gassing for 20 min, 35 ml/l acetonitrile (HPLC grade) and 10 ml/liter tetrahydrofuran (HPLC grade) were added.

Statistical Analysis

A two by three factorial analysis of variance was performed on all body weight data and biogenic amine data for each brain region. When a significant treatment effect was found, Duncan's Multiple Range Test was used to determine which means were significantly different [14].

RESULTS

Body Weight and Behavioral Results

Body weight response to pargyline (P) and 6-OHDA can be found in Fig. 1. All data are expressed as a percent change

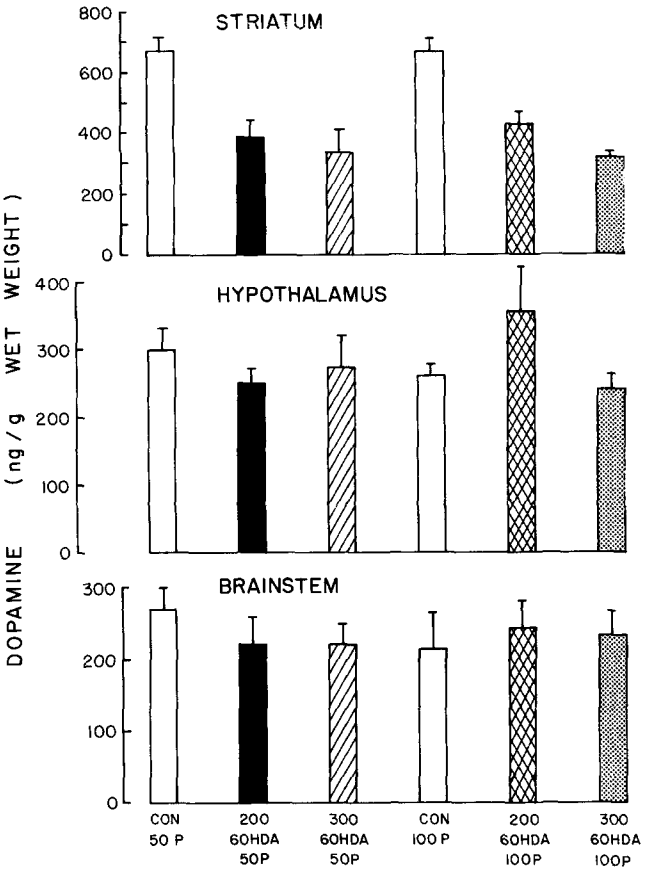

FIG. 2. Concentration of dopamine determined in three brain regions. Vertical lines signify ±1 S.E.M. CON=Controls. 200-6-OHDA=200 (136 free base) μg six-hydroxydopamine (administered intracerebroventricularly). 300-6-OHDA=300 (204 free base) μg six-hydroxydopamine (ICV). 50 P, 100 P=50 mg, 100 mg pargyline (IP). Chicks given 200 or 300 μg 6-OHDA had significantly reduced striatal dopamine.

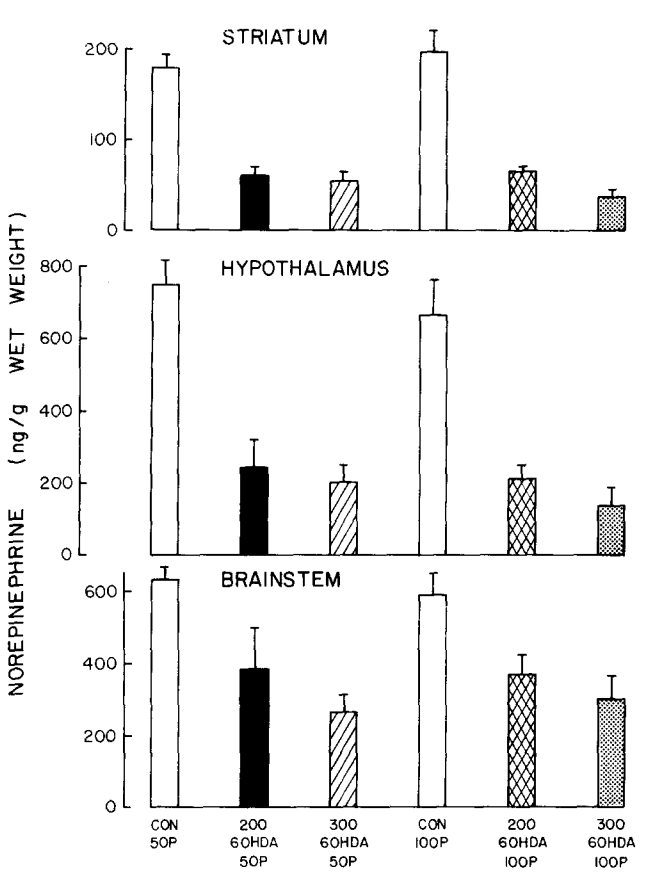

FIG. 3. Concentration of norepinephrine determined in three brain regions. Vertical lines signify ±1 S.E.M. CON=Controls. 200-6-OHDA=200 (136 free base) μg six-hydroxydopamine (ICV). 300-6-OHDA=300 (204 free base) μg six-hydroxydopamine (ICV). 50 P, 100 P=50 mg/kg, 100 mg/kg pargyline (IP). Chicks given 200 or 300 μg 6-OHDA had significantly reduced striatal, hypothalamic and brainstem norepinephrine.

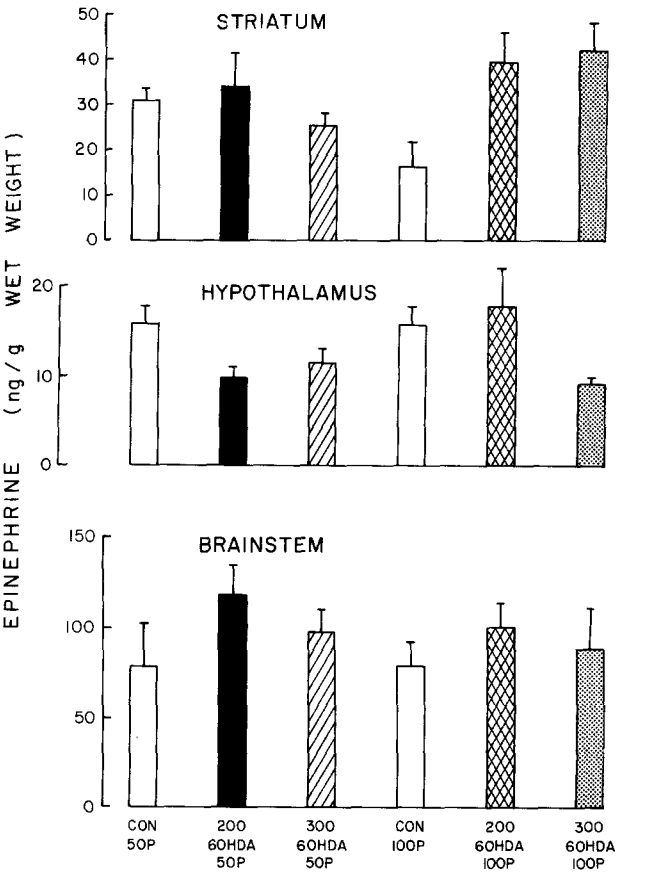

FIG. 4. Concentration of epinephrine determined in three brain regions. Vertical lines signify ±1 S.E.M. CON=Controls. 200-6-OHDA=200 (136 free base) μg six-hydroxydopamine (ICV). 300-6-OHDA=300 (204 free base) μg six-hydroxydopamine (ICV). 50 P, 100 P=50 mg/kg, 100 mg/kg pargyline (IP). A significant interaction was found within striatum between 6-OHDA and P treatments.

in body weight from date of surgery. Mean body weight of each group at time of surgery can be found in Table 1. One chick died in the 100 mg P-Saline group and a second died in the 50 mg P-200 (136 free base) μg 6-OHDA group leaving an n of five in each group. The remaining four treatment groups each had an n of six. The greatest depression in food intake and delay of the normal growth curve in the young chicks occurred with the 100 mg P and 300 (204 free base) μg 6-OHDA group. Analysis of variance followed by Duncan's Multiple Range Test was used to separate means among the six treatment groups at two, four and six days post surgery. The 100 mg P-300 μg 6-OHDA group had significantly lower ($p<0.05$) body weight from its respective control group at two, four and six days after operation. The 50 mg P-300 μg 6-OHDA group had significantly lower body weight from its respective controls at four days post surgery. Neither the 100 mg P-200 (136 free base) μg 6-OHDA nor the 50 mg P-200 μg 6-OHDA chicks had lower body weights from their respective control groups on any of the tested days following surgery.

The effect on feeding following surgery can be found in Table 1. Only the two 300 μg 6-OHDA groups had one or more individuals that showed an aphagic response for at least 24 hr following injection of the neurotoxin. The 100 mg P-300 μg 6-OHDA group displayed the clearest effect of the drug combination with an average aphagic response of 4.5 days which was significantly different from its respective control group ($p<0.05$).

Food intake, however, was not the only variable affected by the neurotoxin. Several abnormal behaviors were recorded during the first week following drug administration. The most consistent effect of 6-OHDA was hyperactivity, based upon a subjective activity score given to chicks during a 5 min period when each was caught and weighed daily. Chicks given 6-OHDA were difficult to weigh on a top-loading balance due to their flightly behavior. The hyperactivity continued for an average of 2.3 and 2.6 days in the two 200 μg 6-OHDA groups and lasted for 3.3 and 3.8 days in the two 300 μg 6-OHDA groups. Other abnormal behaviors were recorded in the two 300 μg 6-OHDA groups. Three of six chicks in the 50 mg P-300 μg 6-OHDA and five of six in the 100 mg P-300 μg 6-OHDA groups showed imbalance. Specifically affected chicks had difficulty perching and when walking had an uneven and unsteady gate. Two of six in the former and four of six in the latter also showed either mild head tremors, a slight tilt of the head or a more pronounced

TABLE 2

CONCENTRATIONS OF SEROTONIN IN THREE BRAIN REGIONS FOLLOWING INJECTION OF SIX-HYDROXYDOPAMINE (ng/g WET WT. BRAIN TISSUE)

Experimental Group*	n	Brain Regions Striatum	Hypothalamus	Brainstem
50 mg P–Saline	6	928 ± 59†	1215 ± 238	986 ± 64
50 mg P–200 (136 free base) μg 6-OHDA	5	823 ± 121	1114 ± 120	1234 ± 129
50 mg P–300 (204 free base) μg 6-OHDA	6	714 ± 125	1146 ± 254	705 ± 160
100 mg P–Saline	5	961 ± 105	954 ± 177	955 ± 145
100 mg P–200 (136 free base) μg 6-OHDA	6	906 ± 61	1200 ± 158	986 ± 213
100 mg P–300 (204 free base) μg 6-OHDA	6	892 ± 129	1015 ± 159	912 ± 179

*P=Pargyline, at 50 or 100 mg/kg body weight; 6-OHDA=Six-hydroxydopamine.
†Mean ± S.E.M.: No significant differences were obtained among any experimental groups within each column using Duncan's Multiple Range Test.

TABLE 3

CONCENTRATIONS OF 5-HYDROXYINDOLE-3-ACETIC ACID IN THREE BRAIN REGIONS FOLLOWING INJECTION OF SIX-HYDROXYDOPAMINE (ng/g WET WT. BRAIN TISSUE)

Experimental Group*	n	Brain Regions Striatum	Hypothalamus	Brainstem
50 mg P–Saline	6	73 ± 7†	208 ± 39	288 ± 46
50 mg P–200 (136 free base) μg 6-OHDA	5	80 ± 8	194 ± 73	385 ± 49
50 mg P–300 (204 free base) μg 6-OHDA	6	66 ± 12	212 ± 28	264 ± 23
100 mg P–Saline	5	77 ± 6	180 ± 33	306 ± 56
100 mg P–200 (136 free base) μg 6-OHDA	6	77 ± 8	197 ± 27	252 ± 48
100 mg P–300 (204 free base) μg 6-OHDA	6	72 ± 8	178 ± 22	242 ± 34

*P=Pargyline, at 50 or 100 mg/kg body weight; 6-OHDA=Six-hydroxydopamine.
†Mean ± S.E.M.: No significant differences were obtained among any experimental groups within each column using Duncan's Multiple Range Test.

arching of the neck compared to controls. Three of six chicks in the 50 mg P-300 μg 6-OHDA and four of six chicks in the 100 mg P-300 μg 6-OHDA groups displayed clear difficulty in orienting their bills when attempting to consume pellets. Chicks were observed pecking at the air and completely missed striking pellets that were scattered on a tray in front of them. The same chicks showed deficits in grasping and mandibulating pellets. The result was that a number of pellets dropped from their mouths back into the food hopper.

Biogenic Amine Concentrations in Brain Regions

A significant treatment effect of 6-OHDA was found among groups in dopamine concentrations within striatum, $F(2,30)=34.42$, $p<0.001$. Further analysis using Duncan's Multiple Range Test [14] showed that dopamine was significantly reduced in all chicks given ICV injections of 6-OHDA (Fig. 2) when compared to their respective controls ($p<0.05$). Even though the 100 mg P-300 μg 6-OHDA group had a significantly lower growth curve compared to all other experimental groups (Fig. 1), striatal dopamine was not significantly reduced in this group from the other 6-OHDA treated chicks ($p>0.05$). No differences were obtained among all treatment groups in levels of dopamine within hypothalamus, $F(2,30)=0.79$, $p>0.05$, and brainstem (Fig. 2), $F(2,30)=0.10$, $p>0.05$.

A significant treatment effect of 6-OHDA was found in levels of NE in striatum, $F(2,30)=80.8$, $p<0.001$, hypothalamus, $F(2,30)=48.48$, $p<0.001$, and brainstem, $F(2,30)=16.72$, $p<0.001$. Duncan's Multiple Range Test indicated that chicks treated with 6-OHDA had significantly lower NE levels in striatum, hypothalamus and brainstem, compared to controls ($p<0.05$). Similar to DA there were no significant differences in concentration of NE among any of the groups treated with 6-OHDA (Fig. 3).

Figure 4 displays the results of epinephrine (E) concen-

TABLE 4

PERCENT DEPLETION OF DOPAMINE AND NOREPINEPHRINE IN SPECIFIC BRAIN REGIONS FOLLOWING INJECTION OF SIX-HYDROXYDOPAMINE

Experimental Group*	n	Striatal Dopamine	Striatal Norepinephrine	Hypothalamic Norepinephrine	Brainstem Norepinephrine
50 mg P-200 (136 free base) μg 6-OHDA	5	−42.3†	−66.7	−68.4	−40.2
50 mg P-300 (204 free base) μg 6-OHDA	6	−49.5	−70.5	−73.3	−58.3
100 mg P-200 (136 free base) μg 6-OHDA	6	−36.2	−67.3	−69.0	−37.7
100 mg P-300 (204 free base) μg 6-OHDA	6	−47.1	−79.6	−79.9	−48.9

*P=Pargyline, at 50 or 100 mg/kg body weight; 6-OHDA=Six-hydroxydopamine.
†Data calculated as a percentage change from each respective control group.

trations. Interestingly there was a significant interaction between 6-OHDA and P treatments, $F(2,30)=4.83$, $p<0.015$, within striatal tissue. Further analysis showed that both 6-OHDA groups pretreated with 100 mg P had significantly elevated striatal E compared to their respective control group ($p<0.05$; Duncan's Multiple Range Test). This result was obtained when data were quantitated by peak height. When the HPLC data were reanalyzed by area the 100 mg P 6-OHDA groups had higher striatal E at the 10% level of significance. Within hypothalamic tissue there was nearly a significant treatment effect of 6-OHDA, $F(2,30)=3.02$, $p<0.064$, while brainstem showed no differences due to 6-OHDA, $F(2,30)=1.97$, $p>0.05$.

No differences in 5-HT (Table 2) nor 5-HIAA (Table 3) were found in any brain regions among any of the treatment groups.

DISCUSSION

Results of ICV injection of 6-OHDA in chicks demonstrated that birds show variable periods of aphagia or anorexia. In this respect the data were comparable to those reported in mammals following intracerebral injection of the neurotoxin to the nigrostriatal bundle [15] or via the lateral ventricles of the brain [16,17]. Chicks in the 300 μg (203 free base) 6-OHDA groups that displayed clear aphagia also showed an abnormal sequence of feeding behavior necessary for efficient consumption of food [10]. Specifically, chicks showed deficits in orienting their bills toward individual food pellets. A few chicks were observed to miss pellets completely during the pecking response. When the chicks oriented accurately, further deficits were noted in their ability to grasp and mandibulate the pellets in preparation for swallowing.

The neurotoxin affected other behaviors in chicks. The most consistent effect was hyperactivity (based upon a subjective scoring, see the Results section). Other behaviors recorded in the 300 μg 6-OHDA groups included imbalance and head tremors. Abnormal behaviors have been reported in rats injected with 6-OHDA including walking with a slightly hunched back, hypoactivity or akinesia [15], failure to groom, piloerection, irritability when held and disturbed sensorimotor integration [17]. The disrupted sequence of feeding behavior in chicks (orientation, grasping and mandibulation) appears comparable to the disturbed sensorimotor integration observed in rats following the combination of P and 6-OHDA administration. An apparent discrepancy in the behavioral data was the reported hypoactivity in rats and our data showing hyperactivity in chicks following injection of 6-OHDA. Note, however, that the hyperactivity noted in chicks occurred after handling and weighing them daily and the behavior usually waned by three days post surgery. Hyperactivity in this context could be similar to the reported increased irritability of rats when held following drug treatment [17]. We did not record motor activity throughout the day and therefore cannot state whether overall activity declined postoperatively.

Food intake has been shown to increase in mammals following hypothalamic or intracerebroventricular (ICV) administration of NE or E [2, 4, 13] while DA appeared ineffective in augmenting intake [13]. Data obtained in rapidly growing chicks (broilers) using ICV administration of catecholamines (CA) essentially agree with the mammalian data [3]. One might therefore expect to find depletions of hypothalamic NE and E in chicks which received 6-OHDA and displayed aphagia or hypophagia. As summarized below, the data do show that significant depletions of CA occurred in different brain regions following ICV injection of 6-OHDA. It is not clear, however, which CA and which brain region are most important in altering food intake. Striatal dopamine (DA), striatal norepinephrine (NE), hypothalamic NE and brainstem NE were significantly reduced in chicks given 6-OHDA (Figs. 2 and 3, Table 4). The average DA depletion from striatum was 44% while NE depletions from striatum, hypothalamus and brainstem averaged 71, 73 and 46%, respectively when all 6-OHDA treatment groups were compared to controls (Table 4). The data reported herein, however, cannot distinguish between the importance of DA and/or NE in effecting aphagia or anorexia in growing chicks. Comparable results and conclusions were reported for the rat subjected to IP injection of P followed by ICV injection of 6-OHDA. The drug combination significantly reduced striatal DA and telencephalic NE as well as effected aphagia in the animals [16]. More recently a similar question has emerged in studies attempting to ascertain the cause of hyperactivity in rats subjected to 6-OHDA neonatally. It has been disputed whether DA depletion or a combination of both DA and NE depletion were required for the later devel-

opment of hyperactivity [11,12]. Desmethylimipramine and 6-OHDA were compared to the drug combination of P and 6-OHDA since the former reportedly results in a preferential depletion of brain DA. A conclusion made was that both DA and NE were important for the expression of hyperactivity in older rats since the treatment of P and 6-OHDA resulted in much greater and more permanent hyperactivity than in rats with reduced DA levels alone [12].

Although desmethylimipramine was not used in the present study, it is suggested that a comparable conclusion would apply to the production of aphagia or anorexia in chicks. Depletions of both catecholamines apparently need to occur in chicks to effect aphagia. Indirect evidence supporting that statement include data from our laboratory showing that the greatest demonstration of aphagia in growing chicks occurred after placement of bilateral lesions disrupting the ansa lenticularis (AL), the posterior nucleus of the AL (ALp) and the quinto-frontal tract (QF) within the lateral and far-lateral hypothalamic areas [8]. It should be noted that other brain structures partially destroyed by the large lesions included the lateral forebrain bundle (LFB) and occipital mesencephalic (OM) tract (Table 2 in [8]). Since it has been reported that the major efferents from the locus coeruleus and subcoeruleus to the telencephalon in the pigeon (noradrenergic pathways) ascend via the medial forebrain bundle, LFB, AL, QF and OM tracts [6] and the major efferents from the nigral complex (nucleus tegmenti pedunculopontinus pars compacta and area ventralis of Tsai, dopaminergic pathways) ascend to the telencephalon via the same fiber tracts [7] and hence would be comparable to the nigrostriatal dopaminergic pathway of mammals, it is clear that both dopaminergic and noradrenergic pathways would have been destroyed bilaterally in the published lesion experiments that delineated the lateral hypothalamic area in birds [8,9]. At this time it can only be surmised that in birds both dopaminergic and noradrenergic systems play an important role in the neural regulation of food intake.

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