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Different Effects of Nucleus Accumbens and Ventrolateral Striatal Dopamine Depletions on Instrumental Response Selection in the Rat

MICHAEL S. COUSINS, JONATHAN D. SOKOLOWSKI AND JOHN D. SALAMONE[1]

Department of Psychology, University of Connecticut, Storrs, CT 06269-1020

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COUSINS, M. S., J. D. SOKOLOWSKI AND J. D. SALAMONE. *Different effects of nucleus accumbens and ventrolateral striatal dopamine depletions on instrumental response selection in the rat.* PHARMACOL BIOCHEM BEHAV 46(4) 943-951, 1993.—This experiment was undertaken to investigate dopaminergic involvement in food-related instrumental behavior. Rats were tested in an operant chamber in which there was a choice between pressing a lever to receive a preferred food (Bioserve pellets) or feeding upon a less preferred food (lab chow). The lever-pressing schedule was a fixed ratio 5 (FR5). Rats usually pressed the lever at high rates to obtain the preferred food, and typically ate little of the lab chow even though it was freely available in the chamber concurrently with the lever-pressing schedule. The neurotoxic agent 6-hydroxydopamine was injected directly into the nucleus accumbens, medial striatum, or ventrolateral striatum to determine the effects of dopamine depletion on the performance of this task. Depletion of dopamine in the nucleus accumbens led to a dramatic shift in behavior in which there was a significant decrease in lever pressing but a significant increase in consumption of lab chow. The shift away from lever pressing and towards chow consumption in rats with accumbens DA depletions was significantly correlated with a decrease in spontaneous locomotor activity. Dopamine depletions in the medial striatum did not significantly affect lever pressing or chow consumption. Ventrolateral striatal dopamine depletions decreased lever pressing but also tended to reduce consumption of lab chow. Rats with ventrolateral striatal dopamine depletions also showed profound deficits in home-cage feeding, and these rats had to receive wet mash or tube feeding to maintain body weight. These data indicate that depletions of dopamine in the nucleus accumbens do not produce a general reduction in food motivation, although accumbens dopamine depletion does decrease instrumental lever pressing for food. In contrast, depletions of dopamine in the ventrolateral striatum produce a profound motor deficit that interferes with both lever pressing for food and food consumption.

Nucleus accumbens Neostriatum Dopamine Motivation Instrumental behavior Motor control

INTERFERENCE with brain dopamine (DA) systems has been shown to impair a wide variety of food-related activities. Systemic administration of DA antagonists or widespread depletion of brain DA impairs food consumption (13,35,40, 47,51,53). Interference with brain DA has been shown to suppress appetitively motivated instrumental responding, which has been interpreted as reflecting dopaminergic involvement in reinforcement (57-59) or aspects of motivation (11,35,38, 39,41,42). In addition to having profound effects on food-related comsummatory and appetitive behavior, interference with DA systems also has been shown to have substantial effects on aspects of motor and sensorimotor function. Although depletion of DA from nucleus accumbens does not lead to a general motor debilitation, accumbens DA depletion does reduce spontaneous, drug-induced and schedule-induced locomotor activity (20,21,26,50,56). Systemic administration of DA antagonists or neostriatal depletions of DA produce cataleptic immobility, akinesia, and sensorimotor impairments (7,13,23,24,48,51,53). Evidence indicates that the deficits in food intake produced by striatal DA depletions are directly related to motor impairments that interfere with food consumption (44,45).

Despite the fact that brain DA is involved in food consumption and in lever pressing to obtain food, interference with DA does not impair all aspects of food-related behavior in a uniform manner. Doses of DA antagonists that suppressed instrumental lever pressing for food did not reduce food consumption (11,35) or simple approach responses for food (38). In most studies of dopaminergic involvement in food intake or lever pressing, these two behaviors are assessed independently. Recently, a novel behavioral paradigm was introduced in which rats had a choice between lever pressing for a more preferred food (Bioserve Pellets) or approaching and consuming a less preferred lab chow that was available con-

[1] To whom requests for reprints should be addressed.

currently in the test chamber (46). Typically, rats pressed the lever at high rates and ate little of the lab chow. Systemic or intra-accumbens administration of the DA antagonist haloperidol, as well as depletion of DA in the nucleus accumbens, produced a dramatic shift in behavior such that lever pressing was reduced but chow consumption was substantially increased (46). The effects of haloperidol and accumbens DA depletion were demonstrated to be different from the effects of prefeeding (46). In addition, it was demonstrated that haloperidol did not alter food preference between chow and Bioserve pellets in free-feeding preference tests (46). Thus, the effect of interference with DA was to alter the selection of the particular instrumental response (lever pressing for pellets vs. approaching lab chow) rather than changing food choice. In the present experiment, this instrumental response selection procedure was used to compare the behavioral effects of accumbens DA depletions with those of striatal depletions. Intracerebral injections of the neurotoxic agent 6-hydroxydopamine (6-OHDA) were used to deplete DA. The ventrolateral striatum (VLS) was chosen as one locus for 6-OHDA injections because DA depletions at this site have been shown to produce substantial motor impairments (14,45). Another striatal site, the medial striatum, was used to provide a contrast with the effects of VLS DA depletions. Rats were tested on the instrumental response procedure for 3 weeks after surgery, and all rats also were tested for spontaneous locomotor activity.

METHOD

Subjects

A total of 51 male Sprague-Dawley rats (Harlan Sprague-Dawley, Indianapolis, IN) were used for the present study. These rats were individually housed in a colony that was maintained at 23°C, and which had a 12 L : 12 D cycle (lights on 0700).

Behavioral Procedures

Tests of instrumental responding were performed in operant chambers (28 × 23 × 23 cm; Med Associates). The rats were food deprived to 85% of their free-feeding body weight. Rats were initially trained to press the lever for 45 mg food pellets (Bioserve Inc., Frenchtown, NJ) on a continuous reinforcement schedule, then the rats were shifted to a FR5 schedule. Rats continued training on the FR5 schedule for 1 week (30-min sessions, 5 days per week), and then were shifted to the food choice procedure for 2 weeks. Rats were trained for 30-min sessions in which they could lever press (FR5 schedule) for pellets, but 14–20 g of their standard lab chow (Wayne Rodent Blox, Teklad Premier) was also available on the floor of the operant chamber. The total number of lever presses and the amount of lab chow consumed (including spillage) was recorded for each rat. Locomotor activity tests were performed in Plexiglas activity chambers (28 × 28 × 28 cm). Two moveable wire mesh floor panels were mounted on a central rod, and movements of the rats on the panels were detected by microswitches. Each microswitch closure was counted as a single activity count. These boxes have been used in previous experiments to record locomotor activity induced by periodic food presentation (26) and phencyclidine (25,50).

DA Depletion by Injection of 6-OHDA

Depletions of DA were produced by bilateral injection of 6-OHDA (Research Biochemicals Inc.) with the rats under pentobarbital anesthesia. Solutions of 6-OHDA were injected through stainless steel 30 ga injectors into the nucleus accumbens (AP + 2.8 mm, ML ± 1.4 mm, V − 7.8 mm), the medial striatum (AP + 2.1 mm, ML ± 2.0 mm, V − 5.2 mm), or the VLS (AP + 1.4 mm, ML ± 4.0 mm, V − 7.2 mm). Each injection of 6-OHDA consisted of 12.5 μg of the free base of 6-OHDA dissolved a total of 2.5 μl of 0.1% ascorbic acid (2.5 μl of 5.0 μg/μl 6-OHDA solution). A Harvard Apparatus syringe pump delivered the injection at a flow rate of 0.5 μl/min. Control rats received injections of 2.5 μl of the 0.1% ascorbate solution at the same site as 6-OHDA-treated rats. All rats received IP injections of 10.0 mg/kg pargyline 30 min prior to surgery. This dose of pargyline was used because pilot data indicated that larger doses of pargyline, or pargyline in combination with other drugs such as desipramine, could lead to food intake deficits in some rats.

Neurochemical Analyses for Tissue Dopamine

After completion of the experiments, rats were decapitated and their brains were removed and frozen. Coronal sections 0.7 mm thick were cut through the brain, and a 16-ga stainless steel tube was used to dissect cylindrical samples of tissue from nucleus accumbens, medial striatum, and VLS from successive coronal sections. At the time the tissue samples were collected, the investigator noted the approximate location of the injectors to verify the locus of injection site. The tissue samples were placed in 200 μl of 0.1 N perchloric acid, homogenized, and centrifuged. The supernatant obtained from each sample was analyzed using a high performance liquid chromatography (HPLC) system that consisted of a Waters dual-piston pump, a precolumn filter, a reverse phase column, a Coulochem electrochemical detector, and a chart recorder. The mobile phase was a pH 4.5 phosphate buffer that also contained 7.0% methanol, EDTA, and 2.6 ml of 0.4 M sodium octyl sulphate. The oxidation potential used for these analyses was 0.2 V (working vs. reference electrode). Standards of DA (Sigma Chemical Co.) were assayed at the same time as the samples.

Experimental Procedure

Rats were trained for 30-min sessions on the food-choice task for 2 weeks prior to surgery. These rats received injections of either ascorbate vehicle (n = 13; nucleus accumbens = 5, medial striatum = 4, and VLS = 4) or 6-OHDA into the nucleus accumbens (n = 13), medial striatum (n = 10), or VLS (n = 15), as described above. After surgery all rats were tested in the food choice procedure for 3 weeks (30-min sessions, 5 days per week, days 3–7, 10–14, and 17–21 after surgery). All rats were tested for locomotor activity on day 8 after surgery in a 20-min test. To maintain body weight, rats received supplemental food in their home cage (lab chow). Rats that could not maintain their weight through lever pressing or consumption of lab chow received wet mash in their home cage. On some occasions, rats were tube fed a liquid diet (concentrated baby formula). Wet mash or tube feeding was done after the behavioral test session on that particular day. When behavioral testing was completed, tissue assays were performed.

Data Analysis

The behavioral and neurochemical data were analyzed using analysis of variance (ANOVA). The lever pressing, feed-

ing, locomotor activity, and tissue assay data were log transformed prior to analyses to reduce variability. The Dunnett test was used for post hoc comparisons to test for overall differences between each of the treatment groups and the control group, whereas the Newman-Keuls test was used to assess differences between all possible pairs of means (19). There were no significant differences between any of the rats with the different control placements, so these rats all were combined into one vehicle control group. The number of lever presses and amount of lab chow consumed were analyzed separately. Percentage of food consumed by lever pressing was obtained by dividing amount of food consumed through lever pressing for Bioserve pellets (lever presses divided by five times 0.045 g) by the total amount of food consumed in the operant chamber (pellets plus lab chow). These three major behavioral parameters (lever pressing, chow consumption, and percentage of total food obtained through lever pressing) were analyzed by calculating the average per day for each of the weeks of testing (i.e., weekly total divided by 5 days). A factorial ANOVA (four groups by 3 weeks) was performed on these behavioral data. Because the percentage of food obtained from lever-pressing measure involved percent data that were restricted to a 100% maximum, these data were arc sin transformed prior to analysis. ANOVA was used to analyze the total locomotor activity data. To analyze the neurochemical data, a separate ANOVA was performed for each of the three brain regions from which samples were taken. The Pearson product-moment correlation coefficient was used to establish relations between neurochemical and behavioral data, with the behavioral data from the first week being used as the behavioral indices. Previous work has shown that substantial depletions of DA are necessary for obtaining behavioral deficits. Thus, any rats that had DA depletions less than 65% (i.e., DA levels >35% of control mean) in their target area were excluded from the DA depletion groups in the ANOVA. However, all rats that received 6-OHDA, regardless of depletion size, were included in the correlational analyses. This was done so that correlational analyses would be used to establish the overall relation between the neurochemical and behavioral variables in the population of rats that received 6-OHDA, whereas the ANOVA was used to assess the differences between rats with substantial DA depletions and control rats [see also (26)].

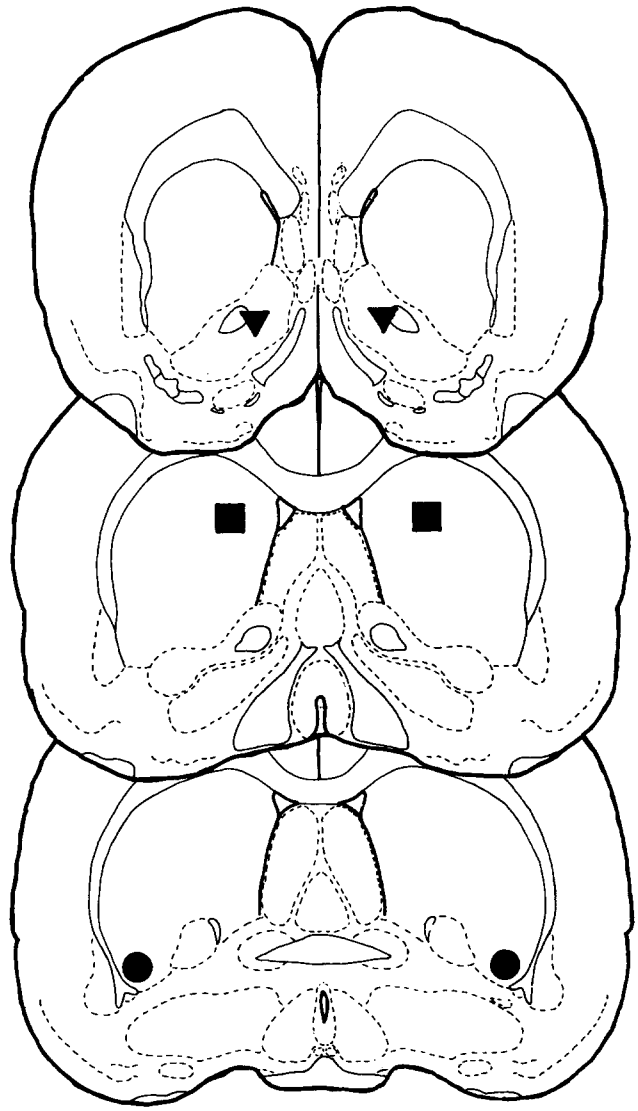

FIG. 1. The three injection sites used in the present experiment (▼ = nucleus accumbens, ■ = medial striatum, ● = ventrolateral striatum).

RESULTS

Neurochemical Results

Figure 1 depicts the target locations for injector placements in the nucleus accumbens, medial striatum, and VLS. Table 1 contains the neurochemical data on the DA levels in each terminal region for the control rats and for those rats that are included in the ANOVA analyses (>65% depletions). There was a significant overall treatment effect on DA levels in the nucleus accumbens, $F(3, 40) = 45.75$, $p < 0.01$. Post hoc analyzes revealed that rats that received 6-OHDA into the accumbens had significantly lower DA levels than all other groups. There was a significant overall treatment effect on DA levels in the medial striatum, $F(3, 40) = 19.05$, $p < 0.01$. Post hoc comparisons showed that injection of 6-OHDA into the nucleus accumbens or the medial striatum decreased medial striatal DA relative to controls, and that the medial striatal group was significantly lower that the accumbens or VLS group. There was a significant overall treatment effect on DA levels in the VLS, $F(3, 40) = 37.78$, $p < 0.01$. Post hoc examinations showed that VLS DA was significantly decreased relative to all other groups in rats that received 6-OHDA injections in the VLS.

Analysis of Lever Pressing and Chow Consumption

The data on total number of lever pressing responses across all 3 weeks of postsurgical testing are shown in Fig. 2. There were no group differences in the baseline period. There was a significant overall treatment effect, $F(3, 40) = 11.6$, $p < 0.01$. Post hoc comparisons revealed that DA depletions in the nucleus accumbens and the VLS resulted in significant decreases in the total number of lever presses. There was a significant effect of test week, $F(2, 80) = 14.1$, $p < 0.01$. There also was a significant group × week interaction, $F(6, 80) = 2.6$, $p < 0.05$. Analysis of simple main effects (19) to identify the source of the interaction indicated that the VLS group showed a significant increase in responding over weeks,

TABLE 1

MEAN (SEM) DA CONTENT (IN ng DA/mg TISSUE) IN BRAIN, AS MEASURED BY HPLC

	Treatment Group			
Brain Region	Control (n = 13)	ACC 6-OHDA (n = 10)	MED 6-OHDA (n = 8)	VLS 6-OHDA (n = 13)
Nucleus Accumbens				
Mean	5.18	0.89*	3.85	4.40
(SEM)	(0.38)	(0.12)	(0.51)	(0.40)
Percent of control	100.0	17.2	74.3	84.9
Medial Striatum				
Mean	9.77	3.90*	1.68*	5.76
(SEM)	(1.15)	(0.72)	(0.22)	(0.60)
Percent of control	100.0	39.9	17.2	59.0
Ventrolateral Striatum				
Mean	7.73	5.99	5.01	1.24*
(SEM)	(0.71)	(0.77)	(0.94)	(0.26)
Percent of control	100.0	77.5	64.8	16.0

*$p < 0.05$, different from control group.

$F(2, 80) = 19.3, p < 0.01$, whereas the other groups did not. Figure 3 depicts the data on lab chow consumption across all 3 weeks of postsurgical testing. There were no group differences in the baseline period. There was a significant overall treatment effect, $F(3, 40) = 17.2, p < 0.01$. Post hoc comparisons with the Dunnett test showed that DA depletions in the nucleus accumbens significantly increased lab chow consumption relative to the control group, and VLS DA depletions significantly decreased chow consumption. There was a significant effect of test week, $F(2, 80) = 8.94, p < 0.05$. However, there was no significant group × week interaction, $F(6, 80) = 0.8$, NS. Figure 4 shows the proportion of total food gained through lever pressing for all 3 weeks of postsurgical testing. There was a signficant overall effect of DA depletion on the percentage of food obtained by lever pressing, $F(3, 40) = 20.5, p < 0.01$. Post hoc comparisons indicated that DA depletions in the nucleus accumbens significantly decreased the proportion of total food obtained through lever pressing. There was no significant effect of test week, $F(2, 80) = 0.63$, NS, and no significant group × week interaction, $F(6, 80) = 0.32$, NS. Lever pressing and chow intake data for two individual rats (one with an accumbens depletion, one with a VLS depletion) are shown in Fig. 5.

Locomotor Activity

Figure 6 shows the results of the locomotor activity test conducted on day 8 after surgery. An overall treatment effect

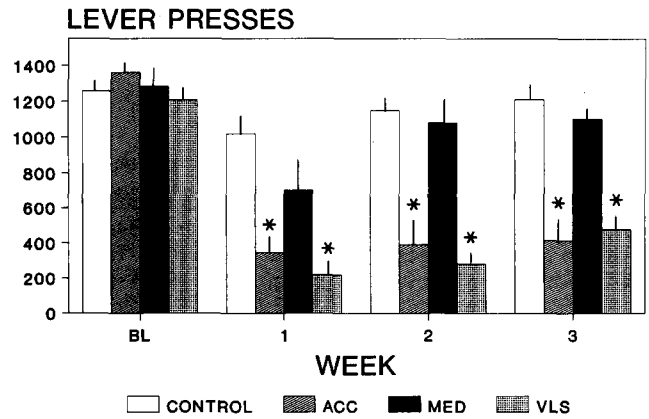

FIG. 2. Mean (±SEM) number of lever presses for rats in the four treatment conditions during the baseline period (BL) and the 3 weeks of postsurgical testing. Data are expressed as the per day average for each of the 3 weeks (*$p < 0.05$, different from control).

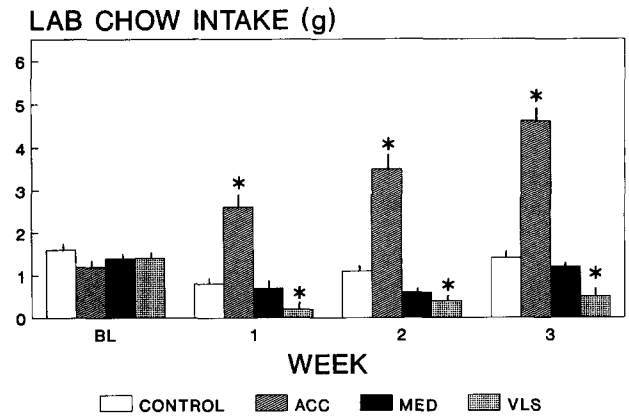

FIG. 3. Mean (±SEM) chow consumption in the four treatment conditions during the baseline period (BL) and the 3 weeks postsurgery. Data are expressed as the per day average for each of the three weeks (*$p < 0.05$, different from control).

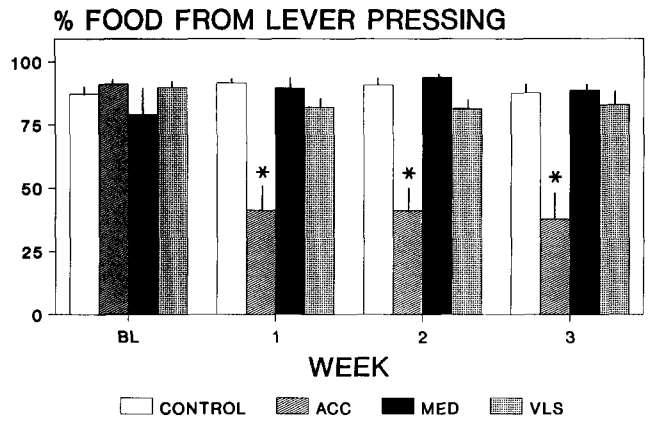

FIG. 4. Mean (±SEM) percent of food obtained through lever pressing for rats in the four treatment conditions during the baseline period (BL) and the 3 weeks post surgery. Data are expressed as the per day average for each of the 3 weeks (*$p < 0.05$, different from control).

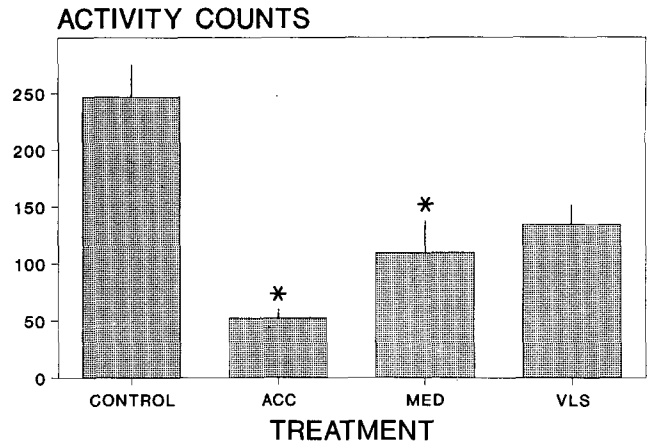

FIG. 6. Mean (±SEM) total number of activity counts over the 20-min locomotor activity test on day 8 after surgery (*$p < 0.05$, different from control).

was observed between groups, $F(3, 40) = 13.49$, $p < 0.01$, for the 20-min session. Post hoc analysis shows that DA depletions in the nucleus accumbens and medial striatum significantly decreased activity relative to rats in the control group. In addition, locomotor activity in the nucleus accumbens group was significantly lower than activity in the other two lesion groups.

Correlational Analyses

Table 2 shows correlations between neurochemical and behavioral data for rats that received 6-OHDA at each of the three placements. Separate correlations were performed on each of the three 6-OHDA injection groups, and the DA levels in each group represent the DA present in the target structure (i.e., accumbens for the accumbens group, medial for the medial group, and VLS for the VLS group). In the group of rats that received intraaccumbens 6-OHDA, accumbens DA levels were positively correlated with lever pressing, positively correlated with the percentage of food obtained through lever pressing, and negatively correlated with chow consumption. Lever pressing and chow consumption were inversely correlated with each other within the accumbens group, demonstrating that the less a rat lever pressed, the more it consumed lab chow. Locomotor activity was positively correlated with accumbens DA levels, and negatively correlated with the percentage of food obtained through lever pressing. The pattern of correlations was different for rats that received injections of 6-OHDA into the VLS. DA levels were positively correlated with both lever pressing and lab chow consumption. Lever pressing and chow consumption were positively correlated with each other in the VLS group, indicating that the impairments in lever pressing and chow consumption were closely related to each other in the rats that received 6-OHDA into the VLS. In addition, locomotor activity scores were unrelated

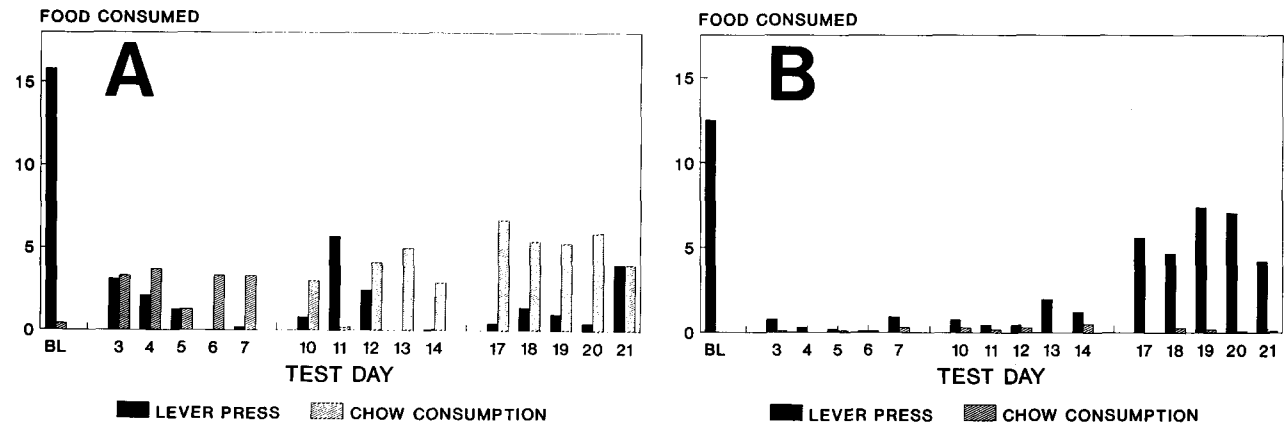

FIG. 5. Lever-pressing data (expressed in terms of quantity of pellets consumed) and lab chow consumption for two individual rats with DA depletions. Data are from the last baseline day and each day of postsurgical testing. (A) Individual rat (#795) with accumbens DA depletion. On most days, the rat obtained more food through chow consumption than feeding. Note that day 11 is the highest day for lever pressing and the lowest day for chow consumption. This illustrates the inverse relation between lever pressing and chow consumption in rats with accumbens DA depletions. (B) Individual rat (#808) with VLS DA depletion. Despite the substantial decrease in lever pressing, chow intake does not increase. This animal showed a substantial recovery of lever pressing, but there were no dramatic increases in chow consumption at any point in recovery.

TABLE 2

CORRELATIONS BETWEEN NEUROCHEMICAL AND BEHAVIORAL VARIABLES IN EACH OF THE 6-OHDA INJECTION GROUPS

	Group		
Variables	ACC	MED	VLS
DA and lever pressing	0.70*	−0.24	0.51
DA and chow consumption	−0.67*	−0.36	0.71*
DA and percent food lever pressing	0.73*	0.25	0.15
DA and motor activity	0.80*	−0.26	0.13
Lever pressing and chow consumption	−0.64*	0.57	0.60*
Motor activity and percent food lever pressing	0.60*	0.42	0.07

*$p < 0.05$.

to ventrolateral striatal DA levels or to the percentage of food obtained through lever pressing. There were no significant correlations in the group of rats that received 6-OHDA injections into the medial striatum.

General Observations

Rats with DA depletions in nucleus accumbens and medial striatum had no difficulty maintaining their body weight through consumption of supplemental lab chow placed in their home cage. DA depletions in the VLS led to substantial impairments in home cage feeding in addition to the impairments they showed in the instrumental response selection procedure. Therefore, rats with VLS DA depletions were given wet mash after the completion of their behavioral testing each day. Eight of the rats with VLS DA depletions had to be tube fed initially after surgery, and three of them had to be tube fed throughout the 3 weeks of postsurgical testing. When they attempted to eat lab chow, rats with VLS DA depletions showed food handling deficits similar to those reported elsewhere (45,47).

DISCUSSION

DA depletions in the nucleus accumbens decreased lever pressing for food but increased consumption of lab chow. This finding is consistent with the previous report that depletions of accumbens DA or intra-accumbens injections of haloperidol decreased lever pressing for food but increased chow intake in the food-choice procedure (46). Previous work has shown that accumbens DA depletion did not impair global indices of food intake (20,45). Together with the present study, these results indicate that rats with accumbens DA depletions remain directed towards the acquisition and consumption of food. The reduction in lever pressing produced by accumbens DA depletion does not appear to result from a general or severe loss of food motivation. Thus, it is too simplistic to state that depletion of DA in nucleus accumbens generally impairs motivation or reward, because aspects of motivation are clearly intact in rats with accumbens DA depletions [see (41,42) for additional discussion]. In addition, the fact that rats with accumbens DA depletions were able to consume large quantities of food also indicates that these rats did not have a severe motor impairment that disrupted the use of the forepaw or oral region. This finding is consistent with the observation that rats with accumbens DA depletions did not have impairments in food handling during food consumption tests (45). Although rats with nucleus accumbens DA depletions also had minor depletions of medial striatal DA, injections of 6-OHDA directly into the medial striatum, which resulted in very substantial medial striatal DA depletions, failed to produced the same behavioral effects as accumbens DA depletions.

The effects of VLS DA depletions were markedly different from those of accumbens DA depletions. Depletion of DA in the VLS produced a severe impairment in both lever pressing and food intake. Depletion of DA in nucleus accumbens decreased the relative amount of food obtained by lever pressing, but VLS DA depletion did not alter this behavioral measure despite the substantial reductions in lever pressing that were observed. In addition, the correlational analyses indicate that several of the behavioral and neurochemical measures were related to each other in different ways in rats that received 6-OHDA injections in these two terminal regions. In rats that received 6-OHDA into the nucleus accumbens, DA levels in the accumbens were positively correlated with lever pressing but negatively correlated with chow consumption. In rats with VLS injection sites, VLS DA levels were positively correlated with chow consumption. Rats receiving intraaccumbens injections of 6-OHDA showed an inverse correlation between lever pressing and chow consumption, which is the hallmark of the shift in food-related behavior that is produced by DA depletions at this site. Yet rats that received injections of 6-OHDA into the VLS showed the opposite pattern in that there was a positive correlation between lever pressing and chow consumption. These results clearly demonstrate that the instrumental response selection procedure is useful for dissociating the behavioral effects of DA depletions in the nucleus accumbens and the VLS.

Superficially, it may appear as though VLS DA depletions impaired food motivation. Nevertheless, several lines of evidence suggest that it is unlikely that a motivational explanation adequately describes the behavioral effects of VLS DA depletions. It has been reported that rats with DA depletions in the VLS spent normal amounts of time feeding, but instead show substantial deficits in food handling and feeding rate (45). VLS DA depletions produce different effects on feeding rate and feeding time than those effects produced by prefeeding to reduce food motivation (45,47). In the present study, most of the rats with VLS DA depletions eventually maintained their body weight by consumption of wet mash. These rats were directed towards food, and often were seen to consume the wet mash presented in their home cage in a very vigorous and persistent manner. Nevertheless, these rats had considerable difficulty consuming dry chow and pressing the lever. In considering the reasons why VLS DA depletions produce substantial impairments in lever pressing, it is important to emphasize that DA depletions in the VLS region have been shown to produce severe motor deficits. As stated above, rats with VLS DA depletions have substantial deficits in feeding rate and paw usage during feeding (45). Rats with DA depletions in the VLS region have shown severe impairments in tasks that involve forelimb reaching (8,37,55). Thus, considerable evidence would suggest that the fundamental difficulty produced by VLS DA depletion is motor and not motivational. Rats with VLS DA depletions showed some degree of

recovery of function over the 3-week test period, which is consistent with previous studies showing a recovery of motor function after striatal DA depletions (23,47,51).

In the present study, depletions of DA in the medial striatum did not impair lever pressing or food intake. This result is consistent with a number of studies showing that medial striatal DA depletions in the rat produce less severe motor or sensorimotor deficits than lateral striatal depletions (6,7, 10,14,44,45). Studies employing intrinsic cell body lesions of the neostriatum also have shown a similar regional differentiation (33,34). The different behavioral effects of DA depletions in nucleus accumbens, medial striatum, and ventrolateral striatum could be related to the different anatomical connections of each region. Anatomical evidence indicates that the nucleus accumbens of the rat receives cortical inputs largely from mesocortical and allocortical areas (29). The medial striatum receives inputs from a variety of neocortical, mesocortical, and allocortical regions (29). In contrast, the lateral striatum is the target of a profuse innervation from sensorimotor neocortex (5,29,54,60). Evidence indicates that the putamen of primates is organized in a somatotopic manner (1), and it has been suggested that the lateral striatum of the rat may also have some degree of somatotopic organization (14,33,34). The general region of the VLS may specifically be involved in head, orofacial, and forepaw motor control (2,8,14,17,18,29,33, 37,43,45). Thus, it is reasonable to suggest that depletion of DA in the VLS produced deficits in lever pressing and feeding because the VLS is involved in motor or sensorimotor functions of the head and forepaws, which are necessary for performing both these behaviors.

Although depletions of VLS DA severely impaired lever pressing, rats with VLS DA depletions are not akinetic. The locomotor test conducted on day 8 after surgery indicated that there was only a mild suppression of locomotion in some rats with VLS DA depletions, but there was no significant correlation between VLS DA levels and locomotor activity. In addition, there was no correlation between locomotor activity and lever pressing or food consumption in rats that received 6-OHDA injections in the VLS. Previously, it was demonstrated that VLS DA depletions that impaired feeding did not impair locomotion or rearing behavior (14). The present results demonstrate that the impairment in lever pressing produced by VLS DA depletion is dissociable from locomotor dysfunction. Significant reductions in locomotion were observed after depletions of DA in the medial striatum and the nucleus accumbens. These data are consistent with previous reports indicating that the nucleus accumbens is involved in locomotion (20,21,25,26,50,56). It is interesting to note that locomotion was significantly correlated with accumbens DA levels and with the shift away from lever pressing behavior in rats that received intraaccumbens 6-OHDA. Possibly, depletion of DA in nucleus accumbens affects a behavioral regulation mechanism that is common both to locomotor activity and to lever pressing.

The precise nature of the behavioral impairment produced by accumbens DA depletion remains uncertain. Evidence indicates that nucleus accumbens DA is involved in preparatory behavior (3,32) and conditioned incentive motivation (4,9,52). Depletion of DA in nucleus accumbens reduces aversively motivated lever pressing as well as affecting appetitively motivated lever pressing (27). It has been suggested that the nucleus accumbens represents a point of functional interaction between the limbic system and the motor system (30), and that DA in nucleus accumbens is involved in the behavioral activation produced by motivational stimuli (26,39–42). It is possible that accumbens DA is involved in the exertion of effort to obtain access to significant stimuli (16,31,36,39–42,46). Investigators studying foraging in wild animals or employing operant laboratory techniques have emphasized that response variables such as response costs, constraints, or effort affect instrumental behavior (12,15,22,28,49). One of the major functions of nucleus accumbens DA may be to enable organisms to overcome the barriers that separate them from from significant stimuli such as food (39–42).

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