Pharmacology Biochemistry & Behavior, Vol. 15, pp. 701–704, 1981. Printed in the U.S.A.

Amphetamine and Apomorphine Induced Stereotyped Behavior in Adult Pigeons

IRVING J. GOODMAN

Department of Psychology, West Virginia University, Morgantown, WV 26506

Received 28 July 1980

GOODMAN, I. J. *Amphetamine and apomorphine induced stereotyped behavior in adult pigeons.* PHARMAC. BIOCHEM. BEHAV. 15(5) 701–704, 1981.—Induced pecking by apomorphine has been reported in the past in pigeons. Research has supported the view that its mechanisms are, at least in part, dopaminergic in nature. This study tested the ability of amphetamine to induce stereotyped pecking. Amphetamine was found effective within a narrow dose range, displaying a relatively low potency for stereotyped pecking and high toxicity compared with apomorphine. The latter drug produced appreciable pecking rates that were proportional to dose over a wide range. The description of other stereotyped responses of the head and mouth, including swallowing, mandibulating and head shaking, which are produced by both of these drugs, supports the idea that common neural mechanisms are involved. It was suggested that the qualitative and quantitative measures afforded by pecking and non-pecking stereotyped behavior in the pigeon make this a useful animal model for the study of the mechanisms of stereotyped behavior.

Drug induced stereotyped behavior Apomorphine pecking Amphetamine pecking Avian behavior

STEREOTYPED pecking has been observed in pigeons under a variety of test circumstances. Food deprived animals peck at non-food targets in their home cages in the absence of food throughout the day, but at elevated rates just preceding and especially following predictable and restricted feeding periods [10]. Electrical stimulation of the brain, through chronically implanted electrodes located in the dopamine rich paleostriatum augmentatum, evokes stereotyped floor and body pecking in pigeons [6]. Drug induced stereotyped pecking results from apomorphine administered systemically [3,4] or intracerebrally, within paleostriatum [6].

The case made for the dopaminergic nature of apomorphine pecking by Cheng and Long [2] is supported by the above findings. Yet, Cheng and Long found no facilitative effect of amphetamine pretreatment upon apomorphine induced pecking. The only indication that amphetamine alone is able to induce stereotyped pecking comes from a briefly mentioned personal communication to that effect, noted by Randrup and Munkvad [12]. If in birds, as is generally accepted in mammals, amphetamine enhances dopamine's action by facilitating its release and inhibiting its reuptake [11,12] while apomorphine stimulates dopamine receptors directly [1,5], then it would be reasonable to expect similar stereotyped behavior induced by amphetamine.

The present study attempted to further explore the dopaminergic nature of stereotyped behavior in pigeons by trying to verify and characterize amphetamine's ability to induce stereotyped pecking and associated stereotyped activities, and to compare these effects with the more fully explored apomorphine ones.

METHOD

Animals

Adult White Carneaux and homing pigeons (*Columbia livia*), weighing 450–750 g were obtained from commercial suppliers. They were individually caged under controlled lighting (12 hr on/12 hr off) and temperature (20–24°C) and were allowed unrestricted access to food (mixed grains) and water throughout the experiment. The birds selected had previously demonstrated apomorphine induced pecking (3 mg/kg) in a 60 min screening test (carried out over 2 wks prior to testing).

Apparatus

Birds were tested in a chamber 93×48×51 cm high and made up of a painted white ceiling, floor and walls, except for a clear plexiglas front wall. The chamber was brightly illuminated by a 20 W cool white fluorescent bulb. A Sony video camera, microphone and videocorder (AV-3600) were used to monitor and selectively record behavior. This was displayed on a Sony video receiver in an adjoining room.

Procedure

At the beginning of each test session, birds were observed for 10 min in the test chamber, weighed, injected with the test drug and returned to the test chamber. One-min duration behavioral observations were made 5 min prior to and 1, 5, 10, 15 min and subsequent 5 min intervals, up to 60 min, following drug injection (14 one-min observations in all).

Amphetamine testing involved the use of 59 animals. Individuals were tested at 1–3 different doses of d-amphetamine sulfate, which were administered in a random order within and across animals receiving multiple doses. Of the five amphetamine dosage groups (0.5, 1.0, 5.0, 10.0 and 20.0 mg/kg, IP), each contained 15 animals. Seven or more days (mean=12.5 days) were allowed between test sessions, in order to minimize interaction effects with prior drug administrations.

When amphetamine testing was completed, and following an interval of 60 days, six animals were randomly selected from among those tested at only a single amphetamine dose for further apomorphine testing. They were each tested over six dosages (0.1, 0.3, 1.0, 3.0, 5.0 and 10.0 mg/kg, IP). Likewise, a minimum of 7 days (mean=10.6 days) was allowed between test dosages administered in a random order.

Test sessions for each animal tested more than once were scheduled for the same time of day, in order to minimize effects attributable to circadian variability.

Behavioral Assessment

Stereotyped responses, which were initially defined and catalogued during pilot observations, were assessed in this study, in most instances, by two raters. They were uninformed as to drug dose and previous behavioral test results at the time of testing. Inter-rater reliability checks indicated that reliability was greater than 95%. The following scoring definitions were employed:

(1) Pecking—rapid, bidirectional head thrusts in the same plane (e.g., forward and backward, upward and downward) that were distinguished from head bobs. Pecking was scored in two ways: (a) Total number of pecks over 1-min sampling periods within a session; (b) Characterization of a session as containing or not containing pecking. A conservative estimate of this score was employed; a session was scored as one characterized by pecking if the animal was observed to peck a total of 26 or more times following drug injection, over the 60 min session (an average of two or more pecks per 1 min observation).

(2) Swallowing—pumping movements in the throat region. The criterion used for scoring a session as one containing swallowing was the observation of this behavior at least twice within three or more 1 min observation periods.

(3) Mandibulating—opening and closing of the bill. The frequency criterion used was the same as that used for swallowing.

(4) Head shaking—rapid, bidirectional, horizontal head movements. The frequency criterion used was the same as that used for swallowing.

(5) Crouching— legs bent with body lowered toward the floor (bowing and sitting were excluded). If the animal remained in the crouched posture for 5 min or more, the session was scored as one containing crouching.

Drugs

D-amphetamine sulfate (Smith, Kline & French) and apomorphine hydrochloride (Merck) were used. Drugs were freshly dissolved in normal saline for each day's testing, and injected intraperitoneally in a volume of 1 ml/kg of body weight. Doses of the drug refer to the salts.

RESULTS

The 1 min observation made 5 min prior to drug injection in each session revealed an absence of pre-drug stereotyped behavior (pecking and nonpecking) for all animals, for d-amphetamine and apomorphine, at all tested dosages.

D-Amphetamine Effects

Stereotyped pecking. Amphetamine induced stereotyped pecking was observed in some pigeons. Pecking frequencies varied across 1 min observations within a session, displaying low frequencies early and late in the session and peaking at 25–40 min into the session. The largest 1 min total was 95 pecks, with the largest session total of 315 pecks.

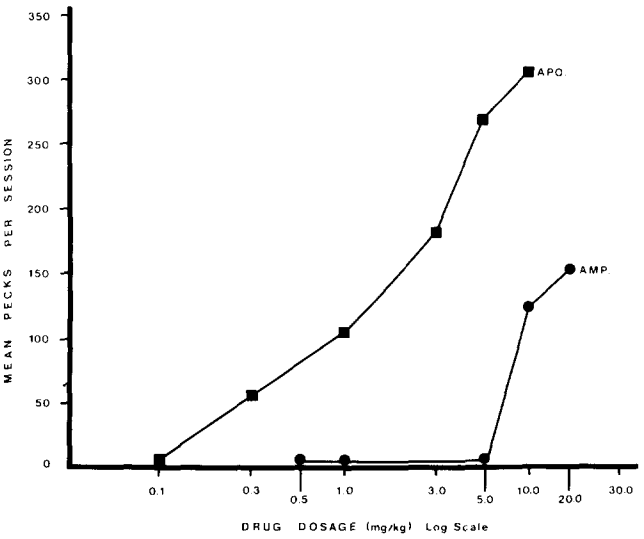

FIG. 1. Dose-response curves for apomorphine hydrochloride (n=6 animals/dose) and d-amphetamine sulfate (n=15 animals/dose) induced stereotyped pecking. Standard error of the mean—Apomorphine: 0.1=0; 0.3=42.4; 1.0=49.5; 3.0=86.0; 5.0=83.0; 10.0=105.3. Amphetamine: 0.5=0; 1.0=0; 5.0=0; 10.0=44.9; 20.0=42.9.

Amphetamine pecking was observed in 12 cases, five of 15 animals tested at 10 mg/kg and seven of 15 animals tested at 20 mg/kg. None of those tested at lower doses (0.5, 1.0 and 5.0 mg/kg) exhibited stereotyped pecking (see Table 1). Among animals pecking at 10 mg/kg the mean session pecking total was 128.4. The mean total for the 20 mg/kg group was 150.7 (see Fig. 1). This mean difference was found not to be statistically significant (t-test, $p>0.05$), however. A similar statistical comparison of mean pecking latencies between these two dose groups also proved not to be statistically different ($p>0.05$); the combined mean pecking onset latency for both doses was 16.9 min.

The topography of pecking showed some variation with respect to target between birds, whereas within birds the pattern was quite consistent across sessions. In each bird exhibiting stereotyped pecking, the bill was usually aimed at one, but occasionally at a second, target, e.g., the air (no contact with a solid object), the pigeon's own body (wings, breast or legs), the wall or the floor. It was not unusual to find that the very early and late pecks of a session were of the less intense "air peck" variety while other pecks made contact with a solid object. In five of 12 cases of amphetamine pecking, pecking bouts were interrupted by body immobilization and staring for several sec or as long as several min, followed by a return to pecking. A number of such oscillations occurred within a session.

Video monitoring and recording allowed raters to differentiate the lateral direction of pecking, to the right or left of the body midline. Most birds displayed a small percentage difference between right and left preference. However, two pigeons showed a greater than 3 to 1 preference for pecking

TABLE 1
PERCENT OF ANIMALS DISPLAYING AMPHETAMINE-INDUCED RESPONSES

Dose (mg/kg)	n	Pecking	Swallowing	Mandibulating	Headshaking	Crouching
0.5	15	0	26.7	6.7	6.7	6.7
1.0	15	0	73.3	13.3	20.0	13.3
5.0	15	0	93.3	46.7	46.7	26.7
10.0	15	33.3	53.3	20.0	53.3	80.0
20.0	15	46.7	33.3	6.7	80.0	100.0

TABLE 2
PERCENT OF ANIMALS DISPLAYING APOMORPHINE-INDUCED RESPONSES

Dose (mg/kg)	n	Pecking	Swallowing	Mandibulating	Headshaking	Crouching
0.1	6	0	16.7	0	16.7	0
0.3	6	83.3	33.3	33.3	83.3	0
1.0	6	83.3	83.3	66.7	100.0	0
3.0	6	100.0	100.0	83.3	100.0	0
5.0	6	100.0	100.0	83.3	100.0	0
10.0	6	100.0	100.0	83.3	100.0	0

toward one side over the other, consistently over two different test sessions.

For five sessions only, grain was scattered on the floor. There was no attempt for floor pecking birds to feed. In two instances, grain appeared to be inadvertently grasped by the bill, but was immediately dropped.

Other stereotyped responses. Stereotyped movements other than pecking were often observed during amphetamine testing. They also involved head and mouth movements; they included swallowing, mandibulating and head shaking. One or more of these responses tended to be present within a session with pecking. However, these responses were also seen in some sessions when pecking was absent; subthreshold doses for amphetamine pecking (below 10 mg/kg) were sometimes able to induce nonpecking stereotypies, whereas at suprathreshold doses nonpecking stereotypies appeared prior to pecking onset. Table 1 summarizes these data, expressed as the percent of animals at each d-amphetamine dosage that displayed these nonpecking responses. The precentages for the occurrance of each of these behaviors did not occur equally or randomly across amphetamine dosages, as revealed by Chi Square analyses (swallowing, $\chi^2(4)=22.4$, $p<0.001$; mandibulating, $\chi^2(4)=16.6$, $p<0.005$; head shaking, $\chi^2(4)=15.6$, $p<0.005$).

Posture. A rather consistent effect of amphetamine was seen in relation to crouching, $\chi^2(4)=43.7$, $p<0.001$; there was an increasing tendency for animals to assume the crouched posture at higher doses of amphetamine. Severe crouching, which occurred at higher doses, was often accompanied by drooping wings and immobilization.

Animal deaths resulting from a high dose of d-amphetamine (20 mg/kg) were seven out of 22 tested (31.8%).

Apomorphine Effects

Stereotyped pecking. Induced pecking rates varied within sessions, with very early rates tending to be lower than those during the middle 15–45 min segment. One min rates were observed to go as high as 250 pecks. The latency to peck, averaged across all doses, was 6.5 min, somewhat shorter than that for amphetamine. A repeated measures design ANOVA which compared the effects of different doses of apomorphine hydrochloride on total session pecking was significant, $F(5,25)=53.9$, $p<0.01$. A Duncan's Multiple Range Test for individual comparisons among groups were all significant ($p<0.05$), except that between 5.0 and 10.0 mg/kg treatments. Session pecking totals were proportional to the dose of apomorphine hydrochloride. The dose-response curve is shown in Fig. 1. Compared to d-amphetamine, the apomorphine dose-response curve is shifted to the left, indicating a greater potency of the latter drug in producing stereotyped pecking. However, caution should be exercised in interpreting this direct comparison because of the methodological differences between the two experiments.

Other stereotyped responses. In addition to pecking, stereotyped responses also included swallowing, mandibulating and head shaking. The number of birds displaying these responses increased with dosage (χ^2 tests, all p values <0.05), along with pecking (see Table 2). A remarkably consistent relationship was observed between head shaking and pecking; one or two head shakes often preceded pecking bouts.

Postural distortion, involving crouching accompanied by immobilization and /or wing drooping, was not observed at any apomorphine dose tested, although sitting or bowing was occasionally noted.

DISCUSSION

This study demonstrated that stereotyped pecking can be induced by d-amphetamine in adult pigeons. Clearly, this behavioral effect is dose dependent; it is observed at high doses (10 and 20 mg/kg) in some individuals, but in none at lower doses (5 mg/kg and below). Apomorphine pecking is likewise dose dependent; however, pecking frequency is proportional to dosage over a larger dose range. Amphetamine's and apomorphine's ability to produce this similar stereotyped response, plus evidence in mammals that both drugs are active at dopamine synapses [1,11] provide support for the view that similar brain structures are being affected by these agents.

Additional support for the involvement of similar brain structures comes from the finding that similar stereotyped responses, other than pecking, are also produced. This represents the first report of swallowing, mandibulating and head shaking induced by sub- and suprathreshold doses (for pecking) of these substances. Given the difference in species, these responses are not unlike stereotyped gnawing, chewing and head movements seen in rats with these drugs [12].

Dopamine rich neural tissue has been identified in paleostriatum augmentatum (PA) [8], a structure designated as the avian homologue of the mammalian caudate/putamen [9]. PA has been found to be involved in the control of stereotyped behavior. Goodman and Stitzel [6] were able to induce stereotyped pecking with the direct application of apomorphine in and electrical stimulation of PA. These results would suggest that PA is that common brain area which is instrumental in supporting apomorphine and amphetamine induced stereotyped behavior. Further testing is needed to support this conclusion.

Differences between apomorphine and d-amphetamine induced stereotypies are also conspicuous. First, apomorphine is a more potent agent for eliciting pecking. Second, there appears to be a greater tendency toward postural and movement disturbance (dyskinesia) with amphetamine; over 80% of those tested at amphetamine pecking doses exhibited crouching accompanied by immobilization and/or drooping wings, which was never seen in apomorphine pecking animals. In the latter subjects, the only comparable changes were sitting and bowing while floor pecking. Another critical difference was the high toxicity of the effective pecking dose of d-amphetamine sulfate.

An interesting observation, and one that requires more systematic study in the future, is the noted bias to peck toward one side in two pigeons. This preliminary finding is compatible with the notion of an imbalance in dopamine function in the two halves of the brain in the intact animal, noted in mammals [7], and the report that unilaterally lesioned PA pigeons display drug induced pecking toward the lesioned side [6].

Cheng and Long's [2] failure to find facilitation of apomorphine pecking with amphetamine pretreatment (below 5 mg/kg used) does not contradict the present findings. However, it is still not clear why subthreshold effects of amphetamine would not add to those of apomorphine and thereby increase pecking rates.

The study of drug induced stereotyped behavior in pigeons appears to provide a variety of distinctively labeled, quantifiable behaviors which may prove useful in exploring the neurochemical mechanisms of motor activity under normal and pathological conditions.

ACKNOWLEDGEMENT

The author wishes to thank Smith, Kline & French for their kind contribution of d-amphetamine sulfate for use in this study.

REFERENCES

1. Anden, N. E., A. Rubenson, and T. Hokfelt. Evidence for dopamine receptor stimulation by apomorphine. *J. Pharm. Pharmac.* **19:** 627–629, 1967.
2. Cheng, H. C. and J. P. Long. Dopaminergic nature of apomorphine-induced pecking in pigeons. *Eur. J Pharmac.* **26:** 313–320, 1974.
3. Deshpande, V. R., M. L. Sharma, P. R. Kherdikar and R. S. Grewal. Some observations on pecking in pigeons. *Br. J. Pharmac.* **17:** 7, 1961.
4. Dhawan, B. N. and P. N. Saxena. Apomorphine-induced pecking in pigeons. *Br. J. Pharmac.* **15:** 316, 1960.
5. Ernst, A. M. Mode of action of apomorphine and dexamphetamine on gnawing compulsion in rats. *Psychopharmacologia* **10:** 316–323, 1967.
6. Goodman, I. J. and R. E. Stitzel. Corpus striatal (paleostriatal complex) interventions and stereotyped behaviors in pigeons. *Soc. Neurosci. Abstr.* **3:** 37, 1977.
7. Jerussi, T. P. and S. D. Glick. Drug-induced rotation in rats withoug lesions: Behavioral and neurochemical indices of a normal asymmetry in nigrostriatal function. *Psychopharmacology* **47:** 249–260, 1976.
8. Juorio, A. V. and A. Vogt. Monoamines and their metabolites in avian brain. *J. Physiol.* **189:** 489–518, 1967.
9. Kappers, C. V. A., G. C. Huber and E. L. Crosby. *The Comparative Anatomy of the Nervous System in Vertebrates including Man,* 3 vols. New York: Hafner, 1960.
10. Palya, W. L. and J. P. Zacny. Stereotyped adjunctive pecking by caged pigeons. *Anim. Learn. Behav.* **8:** 293–303, 1980.
11. Randrup, A. and I. Munkvad. Role of catecholamines in the amphetamine excitatory response. *Nature, Lond.* **211:** 540, 1966.
12. Randrup, A. and I. Munkvad. Stereotyped activities produced by amphetamine in several animal species and man. *Psychopharmacologia* **11:** 300–310, 1967.
13. Smith, C. B. Effects of d-amphetamine upon brain amine content and locomotor activity in mice. *J. Pharmac. exp. Ther.* **147:** 96–102, 1965.