

# BRIEF COMMUNICATION

## Extinction-Induced Mirror Responding as a Baseline for Studying Drug Effects on Aggression<sup>1</sup>

MITCHELL S. MOORE, R. LAWRENCE TYCHSEN AND DONALD M. THOMPSON

*Department of Pharmacology, Georgetown University, Schools of Medicine  
and Dentistry, Washington, DC 20007*

(Received 21 March 1975)

MOORE, M. S., R. L. TYCHSEN AND D. M. THOMPSON. *Extinction-induced mirror responding as a baseline for studying drug effects on aggression*. PHARMAC. BIOCHEM. BEHAV. 4(1) 99–102, 1976. – Pigeons worked individually in a chamber containing a response key and a mirror. Responding on the key was controlled by a multiple schedule in which a brief period of continuous food reinforcement alternated with a 5 min period of extinction. Under baseline conditions, aggressive behavior (responding on the mirror) occurred at the onset of each extinction period. After 10 saline control sessions, 5 mg/kg of chlordiazepoxide was injected IM 30 min pre-session for 60 daily sessions. The drug initially produced a marked decrease in aggressive behavior but had little or no effect on key pecking. The aggressive behavior generally remained suppressed during the chronic drug regimen and returned to control levels when the drug was withdrawn. It was concluded that the technique of extinction-induced mirror responding in pigeons provides a stable, sensitive and recoverable baseline for objectively assessing selective drug effects on aggression.

Extinction-induced aggression    Mirror responding    Chronic chlordiazepoxide administration

PREVIOUS research has shown that extinction following a schedule of positive reinforcement will induce aggressive behavior in rats [4,19], pigeons [1, 13, 15, 17, 18], monkeys [11] and humans [7,12]. Very little is known, however, about the effects of drugs on such extinction-induced aggression. In one of the few experiments in this area, Polifko [15] studied the effects of chronic pentobarbital administration on extinction-induced mirror responding in pigeons. It had previously been determined that responding on a mirror was functionally similar to responding on a live or stuffed target pigeon [3]. More specifically, Polifko used a multiple schedule in which a brief period of continuous reinforcement (each key peck produced food) alternated with a 5 min period of extinction (no food). Under these baseline conditions, there was typically a burst of mirror responding at the onset of each extinction period; such responding decreased in frequency as the extinction period elapsed and never occurred during the reinforcement periods. The initial administration of pentobarbital (10 mg/kg IM) produced a marked decrease in mirror responding but had little or no effect on key pecking. During repeated drug administration (about 25 daily sessions), mirror responding generally remained well below the control values.

The present research used extinction-induced mirror responding in pigeons as a baseline to study the effects of another prototype drug, chlordiazepoxide, under conditions of chronic administration. The method was basically the same as that used by Polifko [15]. A microswitch was attached to the mirror in order to provide accurate and objective measurement of the aggressive behavior. Using a mirror also provides a relatively stable target within and across sessions and eliminates the severe injury that may occur to live targets [3]. Since key pecking is monitored concurrently with mirror responding, a selective effect of the drug would be readily apparent (cf. [2]).

### METHOD

#### *Animals*

Two adult male White Carneaux pigeons were used. Both had been used previously in drug experiments involving extinction-induced mirror responding [15]. The pigeons were maintained within 10 g of 80 percent of their free-feeding weights throughout the research by food presented during the sessions and by post-session supplemental feeding. The 80 percent values were 552 g and 524 g for

<sup>1</sup> This research was supported by Public Health Service Grants FR 5360 and FR 5306. The chlordiazepoxide (Librium) was kindly donated by Hoffmann-LaRoche Inc. We wish to thank Dr. Annette S. Thompson for comments on the manuscript.

No. 4524 and No. 4939, respectively. Water and grit were always available in the home cages.

#### Apparatus

A modified two-key pigeon chamber (BRS-Foringer PH-001) and connecting automatic control equipment were used. The translucent response key on the left side of the intelligence panel could be transilluminated by two Sylvania 24ESB indicator lamps, with red and green plastic end caps. A minimum force of about 20 g was required to close the microswitch on this key. Because previous research [20] had indicated that the aggressive responding of pigeons increased as the available space decreased, the chamber was divided approximately in half by a wooden partition (see Fig. 1). With this modification, the dimensions of the chamber were 36 × 25 × 35 cm. The one-way observation window in the chamber door was also divided by the partition. The part of the window to which the pigeon had access was covered with a piece of cardboard, as was the aperture to the right key on the intelligence panel. This key (BRS-Foringer PPK-001) was removed from the panel and attached to the back of a mirror (19.8 × 13.4 × 0.2 cm). The plastic part of the key was centered at the bottom of the mirror and secured in place with epoxy resin. The mirror-plus-key was then mounted in a black wooden frame on the rear wall of the chamber (see Fig. 1). Thus, the mirror was hinged so that it could be displaced backwards. The minimum force needed to close the microswitch was about 30 g, as measured by a dynamometer at the center of the mirror, approximately 3 cm from the top. A nylon string whose tension could be varied through a hole in the rear of the chamber was attached to the back of the mirror to prevent excessive bounce as the mirror fell forward after a backward displacement by the pigeon. The scheduling of events was accomplished by means of timers, steppers and associated relay circuitry; the recording was by counters, a running time meter and a cumulative recorder. White noise was continuously present in the chamber to mask extraneous sounds.

#### Procedure

**Baseline conditions.** Mirror responding was induced by using a two-component multiple schedule of food reinforcement for key pecking. The components were continuous reinforcement (CRF) and extinction. During the CRF component, the keylight was green ( $S^D$ ), and each of 5 key pecks was reinforced with food (4 sec access to mixed grain). Presentation of the food magazine was accompanied by the offset of both the keylight and the houselight and the onset of the magazine light. The total time that the green keylight was on ( $S^D$  time) indicated the amount of pausing that occurred when food reinforcement was available. During the extinction component, the keylight was red ( $S^A$ ), the houselight remained on, and food reinforcement was unavailable for at least 5 min. Responses made on the red key ( $S^A$  responses) had no effect during the first 4.5 min of extinction. However, an  $S^A$  response (or a mirror response) during the last 30 sec of extinction extended the component for an additional 30 sec. This delay contingency was used to prevent superstitious reinforcement [10] of responses by the onset of the  $S^D$ . It should be noted that except for the delay contingency, mirror responding had no scheduled consequences in either component. Each daily session began with the CRF component, which alternated

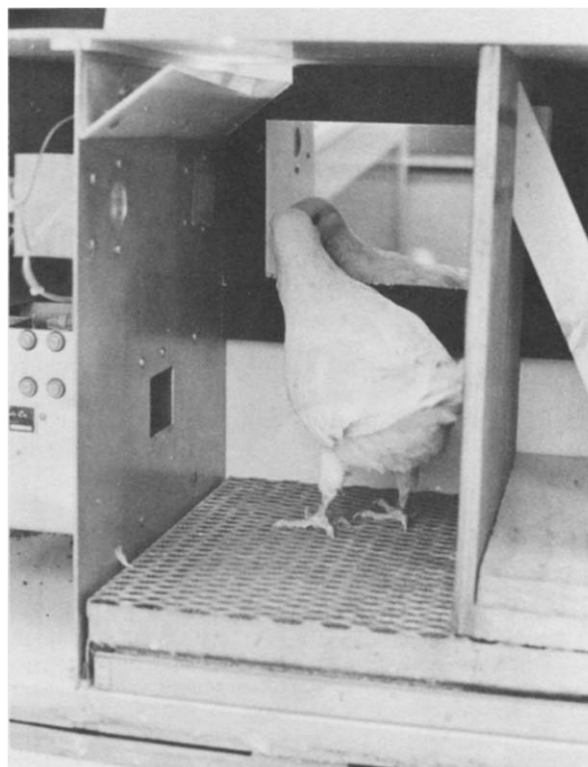


FIG. 1. Photograph of opened experimental chamber showing intelligence panel (with response key and aperture to food magazine), partition, and pigeon pecking at its image in the mirror.

with the extinction component for 10 cycles. A blackout (all lights off) of variable duration preceded and followed each session.

**Drug testing.** After 25–35 daily baseline sessions to permit stabilization (i.e., no systematic change in mirror responding and  $S^D$  time across sessions), there were 10 daily control sessions in which saline was injected IM 30 min pre-session. The volume of each injection was 0.1 ml/100 g body weight. The chronic drug regimen then began; 5 mg/kg of chlordiazepoxide HCl was dissolved in saline and injected IM 30 min pre-session for 60 daily sessions. This dose was selected because we had found previously (unpublished observations) that when it was administered to pigeons on an acute basis, it blocked extinction-induced aggression against a live target without affecting other observable behavior. After the last drug session, the baseline condition (no injections) was reinstated for 20–25 daily sessions.

#### RESULTS

Representative data obtained before, during and after the chronic drug regimen are illustrated in Fig. 2, which shows cumulative records of the mirror responding of No. 4939. Similar results were obtained with No. 4524, except where noted otherwise. During the saline session, although the amount of mirror responding varied somewhat from cycle to cycle of the multiple schedule, the temporal pattern of mirror responding was consistent in that (1) mirror responding occurred at the onset of each extinction

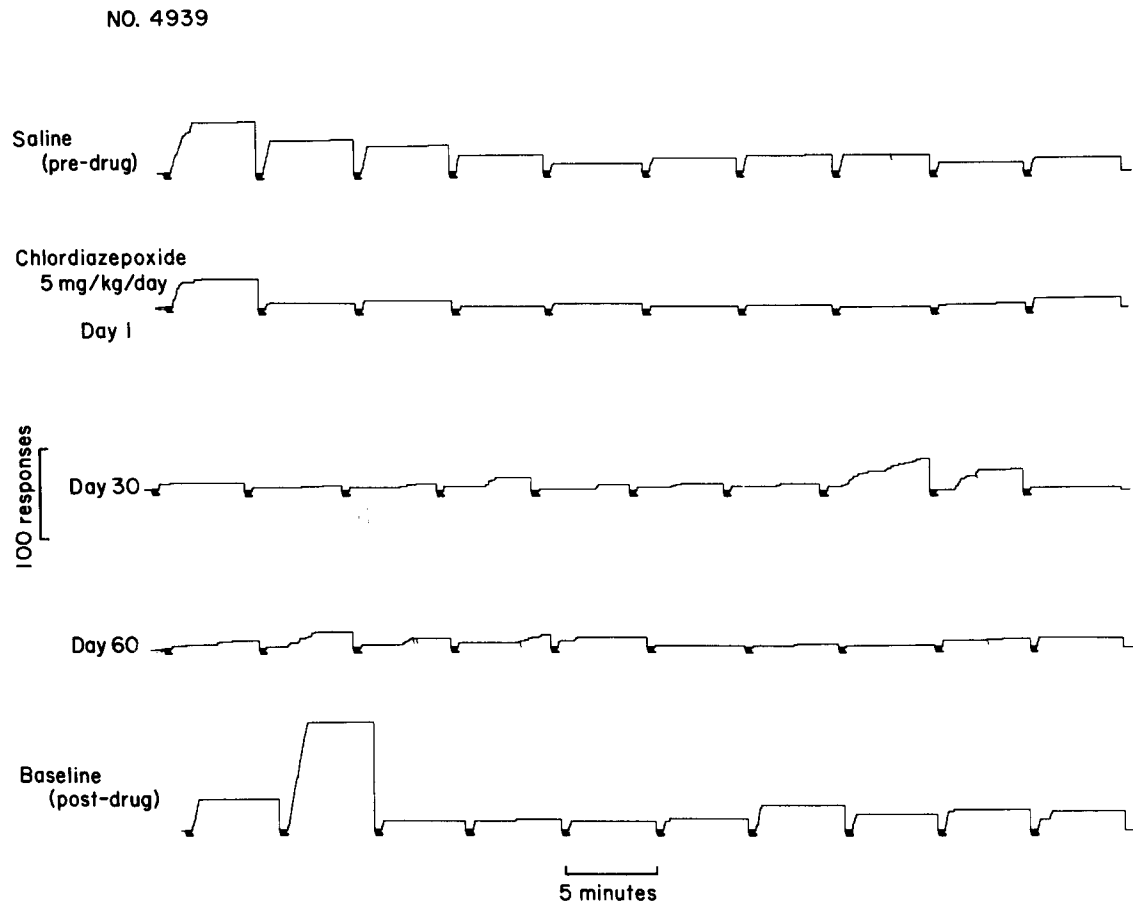


FIG. 2. Cumulative records of the mirror responding of No. 4939 for the last predrug saline session, the first, middle and last drug sessions, and the last postdrug baseline session under a multiple CRF extinction schedule of food reinforcement for key pecking. The response pen stepped upward with each mirror response and reset at the end of each extinction component. A downward deflection of the pen during extinction indicates a key peck ( $S^{\Delta}$  response). During each CRF component, the pen deflected upward with each of the 5 reinforced key pecks, producing the dark segments on the records ( $S^D$  time).

component, (2) almost all mirror responding occurred during the first half of each extinction component, and (3) mirror responding did not occur during any of the CRF components. The initial administration of chlordiazepoxide (Day 1) had a selective action; i.e., the amount of mirror responding decreased markedly, but there was little or no effect on key pecking ( $S^D$  time or  $S^{\Delta}$  responses). Note, however, that when mirror responding did occur, the temporal pattern was generally intact. During repeated drug administration (see Days 30 and 60), the amount of mirror responding remained below the control levels in most of the extinction components; i.e., little tolerance developed to the drug-induced suppression of mirror responding. With No. 4939, the temporal pattern of mirror responding was occasionally disrupted during the chronic drug regimen (e.g., Day 30, Cycle 8; Day 60, Cycle 4) and there was a slight increase in the number of  $S^{\Delta}$  responses (Day 60). Neither of these effects was obtained with the other pigeon, although the  $S^D$  time of No. 4524 occasionally increased slightly during the chronic drug regimen. During the post-drug baseline session, the mirror responding (amount and temporal pattern) and key pecking ( $S^D$  time and  $S^{\Delta}$  responses) were similar to that seen in the predrug saline session.

#### DISCUSSION

That the present results are relevant to the literature on drugs and aggression is based on the assumption that extinction-induced mirror responding in pigeons constitutes aggressive behavior. This seems to be a reasonable assumption in view of the fact that the temporal pattern of extinction-induced mirror responding (see saline session in Fig. 2) is virtually identical to the temporal pattern of extinction-induced aggression against a live target pigeon [1]. The assumption is also supported by the work of Cohen and Looney [3], who showed that schedule-induced mirror responding was functionally similar to schedule-induced aggression in pigeons; i.e., both measures were affected in the same way when variables in the situation (e.g., the interfood interval) were manipulated.

The present finding that the initial administration of chlordiazepoxide selectively depressed aggressive behavior (mirror responding) is consistent with the results obtained by Heise and Boff [9]. These investigators reported that 5 mg/kg of chlordiazepoxide (PO) reduced aggressive behavior in vicious monkeys without affecting other behavior. It should be noted, however, that such selective antiaggressive effects of chlordiazepoxide have not always been obtained

under other conditions (see reviews: [5,8]). In this regard, Miczek [14] has commented that "probably the main source for the conflicting results can be linked to the way each investigator defines and measures the aggressive behavior under study and how the situation that generates this behavior is specified" (p. 277).

The present finding that little tolerance developed to the antiaggressive effect of chlordiazepoxide when the drug was chronically administered is consistent with the results obtained by Quenzer *et al.* [16]. These investigators found that shock-induced aggression in rats initially decreased and remained below control values throughout the chronic drug regimen (15 mg/kg of chlordiazepoxide, IP, 30 min pre-session for 10 days). Under other conditions, however,

chronic chlordiazepoxide administration has produced an increase in aggressive behavior [6]. In this case, mice were fed a diet containing the drug (0.3 mg per gram of food, ad lib) for 6 days before they were tested in a situation in which spontaneous aggression occurred. The divergent results could be due to a number of methodological differences between the studies, e.g., the type of aggression, the dose and route of administration, and the regimen for chronically administering the drug.

Taken together, the present results and those of Polifko [15] lead to the conclusion that the technique of extinction-induced mirror responding in pigeons provides a stable, sensitive and recoverable baseline for objectively assessing selective drug effects on aggression.

### REFERENCES

1. Azrin, N. H., R. R. Hutchinson and D. F. Hake. Extinction-induced aggression. *J. exp. Analysis Behav.* 9: 191-204, 1966.
2. Cherek, D. R. and T. Thompson. Effects of  $\Delta^1$ -tetrahydrocannabinol on schedule-induced aggression in pigeons. *Pharmac. Biochem. Behav.* 1: 493-500, 1973.
3. Cohen, P. S. and T. A. Looney. Schedule-induced mirror responding in the pigeon. *J. exp. Analysis Behav.* 19: 395-408, 1973.
4. Davis, H. and I. Donenfeld. Extinction induced social interaction in rats. *Psychon. Sci.* 7: 85-86, 1967.
5. DiMascio, A. The effects of benzodiazepines on aggression: reduced or increased? *Psychopharmacologia* 30: 95-102, 1973.
6. Fox, K. A., J. R. Tuckosh and A. H. Wilcox. Increased aggression among grouped male mice fed chlordiazepoxide. *Eur. J. Pharmac.* 11: 119-121, 1970.
7. Frederiksen, L. W. and G. L. Peterson. Schedule-induced aggression in nursery school children. *Psychol. Rec.* 24: 343-351, 1974.
8. Greenblatt, D. J. and R. I. Shader. *Benzodiazepines in Clinical Practice*. New York: Raven Press, 1974, p. 47.
9. Heise, G. A. and E. Boff. Taming action of chlordiazepoxide. *Fedn Proc.* 20: 393, 1961.
10. Herrnstein, R. J. Superstition: a corollary of the principles of operant conditioning. In: *Operant Behavior: Areas of Research and Application*, edited by W. K. Honig. New York: Appleton-Century-Crofts, 1966, pp. 33-51.
11. Hutchinson, R. R., N. H. Azrin and G. M. Hunt. Attack produced by intermittent reinforcement of a concurrent operant response. *J. exp. Analysis Behav.* 11: 489-495, 1968.
12. Kelly, J. F. and D. F. Hake. An extinction-induced increase in an aggressive response with humans. *J. exp. Analysis Behav.* 14: 153-164, 1970.
13. Knutson, J. F. Aggression during the fixed-ratio and extinction components of a multiple schedule of reinforcement. *J. exp. Analysis Behav.* 13: 221-231, 1970.
14. Miczek, K. A. Intraspecies aggression in rats: effects of *d*-amphetamine and chlordiazepoxide. *Psychopharmacologia* 39: 275-301, 1974.
15. Polifko, M. L. Effects of psychotropic drugs on extinction-induced aggression. Doctoral Dissertation. Georgetown University, 1974.
16. Quenzer, L. F., R. S. Feldman and J. W. Moore. Toward a mechanism of the anti-aggression effects of chlordiazepoxide in rats. *Psychopharmacologia* 34: 81-94, 1974.
17. Rilling, M. and H. J. Caplan. Extinction-induced aggression during errorless discrimination learning. *J. exp. Analysis Behav.* 20: 85-92, 1973.
18. Rilling, M. and H. J. Caplan. Frequency of reinforcement as a determinant of extinction-induced aggression during errorless discrimination learning. *J. exp. Analysis Behav.* 23: 121-129, 1975.
19. Thompson, T. and W. Bloom. Aggressive behavior and extinction-induced response-rate increase. *Psychon. Sci.* 5: 335-336, 1966.
20. Willis, F. N. Fighting in pigeons relative to available space. *Psychon. Sci.* 4: 315-316, 1966.