Chlorpromazine: Direct Measurement of Differential Behavioral Effect

Abstract. *A retarded child with a high stereotyped rocking rate was conditioned to pull a ball on a reinforcement schedule in which the fixed ratio of rewarded to nonrewarded responses was 100. Results show no rocking movements during ball-pulling; but when ball-pulling was on extinction, rocking returned to its original rate. Chlorpromazine blocked rocking movements during extinction, but had no effect on ball-pulling. Delivery of one free reinforcer was sufficient to reinstate ball-pulling after extinction, but the stimulus properties of the free reinforcer were not affected by the drug.*

In the experimental analysis of drug-behavior relationships, the method of "free-operant" conditioning provides a powerful and sensitive method for the measurement of these relationships (*1*, *2*). This method provides for the control of response contingencies and consequences (schedules of reinforcement) and for direct continuous and automatic recording of one or more behaviors of a single individual. The goal of this study was to apply these methods to the precise measurement of drug-behavior relationships with human subjects.

The subject was an institutionalized, severely retarded adolescent female. She had a chronological age of 15 years and a mental age of approximately 4. Prior to the start of this study, the subject had served in a study on the operant control of stereotyped movements. Although she had a history of stereotyped rocking, the episodes generally did not produce continuous stable rates. With the use of operant-conditioning procedures, her rate of rocking was stabilized at 80 responses per minute on a schedule of reinforcement in which the fixed ratio was 25. The rate of rocking remained stable in the laboratory long after rocking produced no programed consequences (extinction), that is, the behavior did not reverse.

In a previous study of stereotyped rocking movements, I found that fixed-ratio schedules of reinforcement produced accelerated stable rates of rocking. Three of the subjects showed a deceleration of rocking movements on extinction, and three subjects did not decelerate. The subject described in this report was one who did not decelerate.

All testing was conducted in the operant laboratory (*3*). The subject sat on a bench, and a ball-manipulandum was mounted directly in front of her (*4*). A 900-g pull downward on the manipulandum would actuate a microswitch, and this in turn was connected to a pulse former, cumulative recorder, counter, and so forth. The stereotyped rocking movements were also recorded automatically, and this was accomplished through a hinged back on the experimental bench. The bench back was attached to the subject with an automobile seat belt, placed around her upper abdomen. When the subject rocked forward from the vertical 5 deg, a bar attached to the movable bench back would break an infrared light beam of a photosensing device. The breaking of the light beam resulted in an impulse to the automatic programing equipment. On the subject's left was a plastic food well and a plastic liquid dispenser (*5*). Candy and Kool-Aid were employed as reinforcers for ball-pulling and were alternated every other presentation. A buzzer sounded when candy was presented and a bell when Kool-Aid was presented.

The subject was conditioned to make a ball-pulling response. This was accomplished by reinforcing ball-pulling on a fixed-ratio (FR) schedule in which the required number of pulls for a reinforcement (candy or Kool-Aid) was gradually increased from one (FR-1) to 100 (FR-100), that is, the 100th pull produced the reinforcement. The results show that the programed consequences

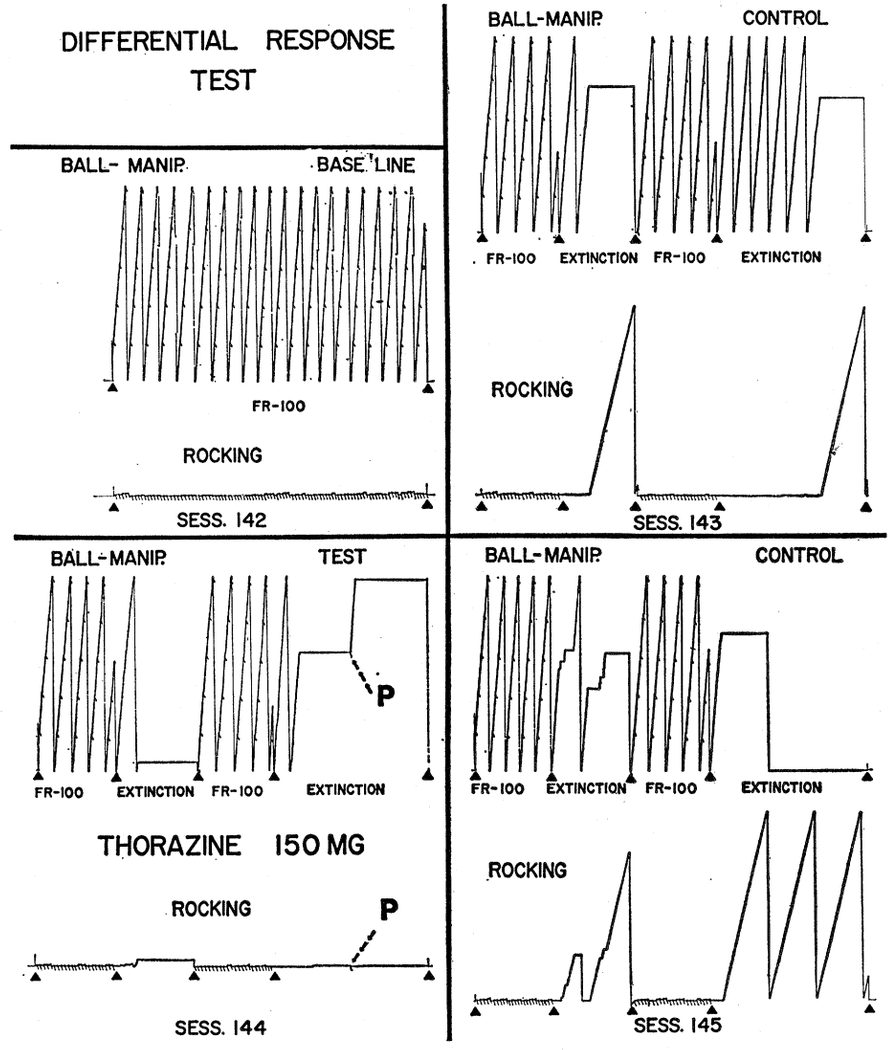

Fig. 1. Cumulative records of simultaneously recorded stereotyped rocking responses and operantly reinforced ball-pulling of a severely retarded 15-year-old female, which show the effects of a single dose of 150 mg of Thorazine (chlorpromazine) on responding-session 144. The drug was administered orally; the subject weighed 41.5 kg. *P* (probe) indicates the delivery of one free reinforcer. With the exception of session 142 (40-minute duration), all subsequent sessions were 50 minutes in duration. Speed of the cumulative recorder paper was 0.5 cm/min, and it reset after 500 responses. Oblique downward pips indicate delivery of reinforcers; this was contingent on ball-pulling responses only.

(FR-100) maintained a high stable rate of ball-pulling at 225 responses per minute and that under this condition no rocking movements were recorded. However, when ball-pulling was placed on extinction (that is, produced no programed consequences) the rocking movements returned to the base-line rate of 80 responses per minute. With the exception of the first session (base line), all experimental sessions were composed of four segments as follows: (i) first 10 minutes, FR-100; (ii) second 10 minutes, extinction; (iii) third 10 minutes, FR-100; and (iv) last 20 minutes, extinction. Rocking movements were recorded continuously during all sessions, but produced no programed consequences. Ball-pulling responses were reinstated after the first extinction segment by delivery of one free reinforcer.

Two drugs were used in this study. Chlorpromazine (Thorazine, 150 mg), the experimental drug, was administered orally in liquid-concentrate form 2 hours before the start of a drug-test session (*6*); secobarbital (Seconal, 100 and 200 mg) was used as a control (*7*, *8*). It was administered orally in capsule form 1 hour before the start of a control session.

Figures 1 and 2 present cumulative records (*9*) for simultaneous measures of ball-manipulandum and rocking movements. The rate of ball-pulling ranged from 225 to 325 responses per minute on the FR-100 schedule of reinforcement. During periods of extinction on ball-pulling, rocking movements occurred at the rate of 80 responses per minute. The data show that after session 143 (Fig. 1) extinction occurred relatively rapidly upon termination of FR-100 reinforcement schedule for ball-pulling.

Two hours before the start of session 144, the subject was given 150 mg of chlorpromazine. This dosage resulted in almost complete blockage of rocking movements during the extinction segments of the test session (Fig. 1). A probe (delivery of one free reinforcement) during the second extinction segment resulted in approximately 200 ball-pulling responses with no rocking or spontaneous motor movements occurring during the subsequent 10-minute period. The effects of chlorpromazine on rocking movements have been systematically replicated with two other subjects. This drug was effective in blocking rocking movements when the ball-pulling response was on extinction. Fitz-Gerald, using chimpanzees as subjects, has demonstrated that chlorpromazine produced a significant decrease in the incidence of stereotyped movements (*6*).

The data show that 100 and 200 mg of secobarbital (Seconal), the control drug, did not significantly affect ball-pulling or rocking movements irrespective of the test conditions. The topography of the cumulative records during these drug sessions (146 and 151) was similar to that of nondrug control sessions (Fig. 2). Although secobarbital (200 mg) did not adversely affect responding, subjective observations indicated that the subject was in a very drowsy state.

The present investigation was concerned with the experimental analysis and measurement of the effects of psychopharmacologic agents on behavior. The strategy was to adapt free-operant conditioning methods to the laboratory measurement of the psychopharmacologic response (*8*). The study has demonstrated the feasibility of using direct, continuous, automatic, and simultaneous measures in the evaluation of psychopharmacologic agents with humans. This technique has provided precision measures of the differential behavioral effects of chlorpromazine under specified laboratory conditions. The data show that abnormal stereotyped motor movement (that is, rocking) can be controlled by two methods. First, when the alternative activity (ball-pulling) produced programed consequences (FR-100), there was a clear-cut "functional separation" between stereotyped rocking movements and the alternative activity. I have replicated this finding with five additional subjects and ob-

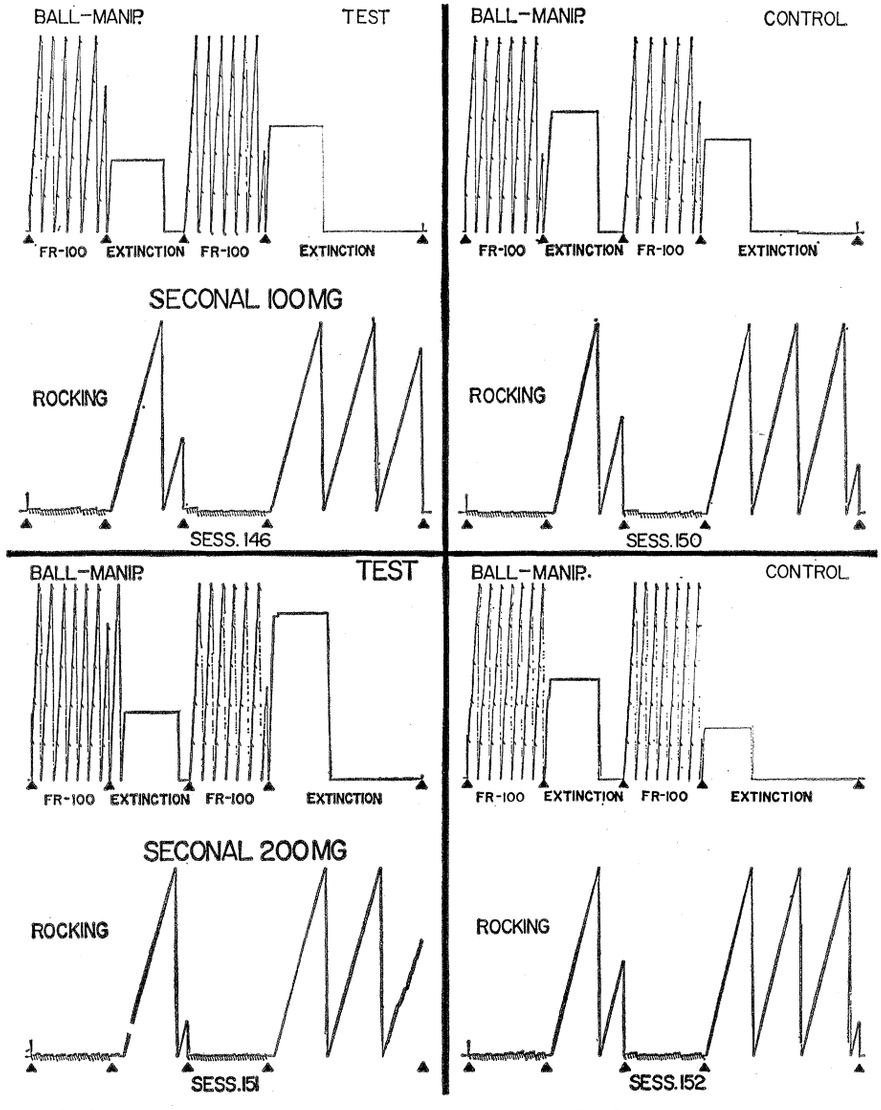

Fig. 2. Seconal (secobarbital) placebo sessions 146 and 151 included as a control. The subject and all conditions of the study were the same as in Fig. 1.

tained similar results. That is, when ball-pulling produced programed consequences, rocking movements did not occur. Second, chlorpromazine blocked the stereotyped rocking movements during the periods when the alternative activity produced no programed consequences.

Finally, the data clearly show that reinforcement had stimulus properties. That is, when a free reinforcer was delivered during extinction of the ball-pulling response, immediate resumption of ball-pulling occurred (*10*). This effect was not changed as a function of the drugs used.

JOHN H. HOLLIS
Parsons Research Center,
Parsons, Kansas 67357

References and Notes

1. B. F. Skinner, *Amer. Psychologist* **8**, 69 (1953).
2. C. B. Ferster, *Psychol. Bull.* **5**, 263 (1953).
3. J. H. Hollis, *Working Paper No. 168* (Parsons Research Center, Parsons, Kansas, 1967).
4. ———, *Percept. Mot. Skills* **24**, 465 (1967).
5. ———, *ibid.*, p. 156.
6. F. L. Fitz-Gerald, unpublished thesis, McGill University (1964).
7. J. J. Boren, in *Operant Behavior*, W. K. Honig, Ed. (Appleton-Century-Crofts, New York, 1966).
8. O. R. Lindsley, in *Psychosomatic Medicine: First Hahnemann Symposium*, J. H. Nodine and J. H. Moyer, Eds. (Lea & Febiger, New York, 1962).
9. C. B. Ferster and B. F. Skinner, *Schedules of Reinforcement* (Appleton-Century-Crofts, New York, 1957).
10. J. E. Spradlin, F. L. Girardeau, G. L. Hom, *J. Exp. Child Psychol.* **4**, 369 (1966).
11. Supported by grant No. 00870-04 from the National Institute of Child Health and Human Development.

5 February 1968

Observation Learning in Cats

Abstract. *In two experiments cats acquired a stimulus-controlled approach or avoidance response by observational or conventional shaping procedures. Observer cats acquired the avoidance response (hurdle jumping in response to a buzzer stimulus) significantly faster and made fewer errors than cats that were conventionally trained. Observer cats acquired the approach response (lever pressing for food in response to a light stimulus) with significantly fewer errors than cats that were conventionally trained. In some cases, observer cats committed one or no errors while reaching criterion.*

Electrophysiological studies in our laboratories have made it necessary to train many cats to perform conditioned approach and avoidance responses. Experimental schedules have sometimes been disrupted because of the slow acquisition of such responses or by the failure of some cats to reach criterion after extensive training. In the course of seeking more effective methods of rapidly and reliably training our animals to make discriminative responses, we designed two experiments to investigate the acquisition of stimulus-controlled approach and avoidance responses via an observational procedure. Each experiment required the observing animal to acquire and perform a response not previously in his repertoire, without overtly performing it during the observation period.

In the first experiment, 14 young adult cats were used. Six naive "observer" cats composed group 1, six naive "student" cats composed group 2, and two fully trained cats served as "teachers." The apparatus consisted of a standard operant conditioning cage. A lucite hurdle, 6 inches (15 cm) high, bisected the 24- by 24-inch shock-grid floor of the cage.

Each naive observer cat from group 1 was first placed in the training cage alone. A buzzer was presented for 15 seconds, and one foot shock was administered unless a hurdle jump had been performed. After one such "empathy" trial, the observer cat was placed in a small cage with a mesh front, directly behind the training cage. Although no attempt was made to coerce observation, the observer cat was in a position to watch a matched naive student cat from group 2 receive 20 conventional *training* trials of the conditioned avoidance response daily, followed by *performance* of the same number of trials by one of the fully trained teacher cats. This procedure was repeated daily until the student cat reached a criterion of 90 percent performance for 3 days in a row. The observer cat was then subjected to 20 training trials daily until he reached the same criterion. In three cases, observer cats began avoidance training before their matched controls reached criterion, because they had performed an avoidance response on their daily empathy trial.

Figure 1 compares the acquisition of the conditioned avoidance response by animals in these two groups. In five of the six pairs, the observer cat (solid circles) learned the conditioned avoidance response much more rapidly than the student cat (operant, open circles). One observer cat did not acquire the response faster than his group 2 control, although his initial performance was better. This cat became ill after 3 days of training and his schedule was interrupted for several days. It is particularly striking that two cats in group 1 immediately performed at high levels, requiring a total of only one and two shocks each to reach criterion. A two-tailed t-test comparing the total number of failures to perform on the part of the student and observer cats throughout the 6-day period was significant ($P < 0.001$).

In our second experiment, 22 young adult cats were used. Group 1 consisted of six naive observer cats. Two trained cats served as "lever press teachers." In order to establish social compatibility in the training cage, each naive cat shared a home cage with its teacher throughout the training period. An observer cat, together with its teacher, both deprived of food for 24 hours, were placed in a standard, operant conditioning cage. No barrier separated the two cats, and neither was restrained. During three observation sessions, the teacher cat performed approximately 30 approach responses daily, pressing a lever within 15 seconds after onset of a 5-cycle/sec flickering light. The lever was mounted in one wall of the cage, 7 inches above the floor and 3 inches to the left of a dipper, which delivered food. The exact number of trials presented to the teacher cat was limited by the observer cat's attentiveness or apparent readiness to perform. The number of teacher responses apparently observed was recorded, and an attempt was made to achieve daily observation of 30 trials. After the observation session, the teacher was removed from the training cage and approximately 30 test trials were presented to each naive observer cat. The number of test trials presented to observer cats during the first 3 days varied considerably, but they all received 30 test trials for the last 3 post-observation days.

To insure that a stimulus-controlled bar press is not somehow facilitated by the presence of two cats in the training cage or by any effects of exploration or familiarization per se, a second group of six cats (group 2) similarly observed a cage-mate receive food by