antiparkinsonian drugs examined may be related to the mechanism of their therapeutic activity. Considerable evidence suggests that neuronal uptake of norepinephrine terminates its physiological actions at synapses in the periphery and in the brain (*4*). It is possible that, analogously, the dopamine uptake system in the corpus striatum may inactivate synaptically released dopamine. Tricyclic antidepressant drugs are thought to exert their therapeutic effects by inhibiting norepinephrine uptake at central synapses and potentiating its synaptic actions (*10*). We propose that antiparkinsonian drugs have as a mechanism of action the inhibition of dopamine reuptake, with consequent potentiation of the actions of dopamine released at striatal synapses.

This hypothesis helps explain the clinical observation that patients with increasingly severe Parkinson's disease become progressively refractory to drug therapy. In patients with very severe Parkinson's disease, there would be little dopamine available for potentiation by antiparkinsonian drugs. Antiparkinsonian drugs are more effective in the treatment of drug-induced than idiopathic Parkinson's disease. Patients with the drug-induced syndrome presumably have intact dopaminergic neuronal systems, so that adequate amounts of dopamine are available for potentiation. Recent evidence suggests that phenothiazine drugs that induce Parkinson's disease block dopamine receptors, resulting in enhanced dopamine synthesis and turnover (*11*).

Many antiparkinsonian drugs are also effective anticholinergic agents; and cholinomimetic agents accentuate parkinsonian symptoms (*12*). Thus, it has been postulated that antiparkinsonian drugs antagonize a presumed hyperactivity of cholinergic neurons in the striatum of affected patients (*12*). However, in some studies antiparkinsonian activity failed to correlate with anticholinergic potency (*13*); and amphetamine, which is effective in the treatment of the akinesia and rigidity, exhibits no direct anticholinergic action in therapeutically effective doses. Conceivably, there may be a close interrelationship between cholinergic and dopaminergic mechanisms in striatal neurons, as has been suggested for peripheral noradrenergic neurons (*14*).

We propose that some clinically untried potent inhibitors of striatal dopamine uptake may be useful antiparkinsonian drugs. Such agents might include diphenpyraline, an antihistamine which we found to be a very active inhibitor of striatal dopamine uptake (ID_{50}, $4.9 \times 10^{-7}M$). *d*-Amphetamine has been employed in the treatment of Parkinson's disease, but its central stimulant effects limit dosage. Recently we observed that *d*-amphetamine was ten times more potent than *l*-amphetamine as an inhibitor of catecholamine uptake in nonstriatal brain regions (*7*). However, in the striatum, *d*- and *l*-amphetamine were equally potent and highly effective competitive inhibitors of catecholamine uptake (K_i, $1.0 \times 10^{-7}M$). *l*-Amphetamine, which could be administered in higher doses with fewer central stimulant side effects than *d*-amphetamine, may also be an effective therapeutic agent in Parkinson's disease. In preliminary experiments we examined the effects of these drugs on the tremor and rigidity produced in mice by oxotremorine, a compound that produces a syndrome in animals resembling Parkinson's disease (*15*). As predicted by our hypothesis, *d*- and *l*-amphetamine were equally effective in preventing oxotremorine effects; and diphenpyraline was a highly active anti-oxotremorine agent, almost as potent as benztropine.

JOSEPH T. COYLE*
SOLOMON H. SNYDER

Departments of Pharmacology and Experimental Therapeutics and
Psychiatry and the Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

References and Notes

1. O. Hornykiewicz, *Pharmacol. Rev.* **18**, 925 (1966); N. A. Hillarp, K. Fuxe, A. Dahlström, *ibid.*, p. 727.
2. O. Hornykiewicz, *Wien. Klin. Wochenschr.* **75**, 309 (1963).
3. M. D. Yahr, R. C. Duvoisin, M. M. Hoehn, M. J. Shear, R. E. Barrett, "L-DOPA. Its clinical effects in parkinsonism," paper presented at the American Neurological Association (Washington, D.C.), 17 June 1968; A. Barbeau and L. Gillo-Jeffroy, "8 years of L-DOPA therapy in Parkinson's disease," paper presented at the American Academy of Neurology (Washington, D.C.), 25 April 1969; G. C. Cotzias, P. S. Papavasilou, R. Gellene, *N. Engl. J. Med.* **280**, 337 (1969).
4. J. Axelrod, *Recent Progr. Hormone Res.* **21**, 597 (1965); L. L. Iversen, *The Uptake and Storage of Noradrenaline in Sympathetic Nerves* (Cambridge Univ. Press, New York, 1967).
5. J. J. Dengler, I. A. Michaelson, H. E. Spiegel, E. Titus, *Int. J. Neuropharmacol.* **1**, 23 (1962); J. Glowinski, I. J. Kopin, J. Axelrod, *J. Neurochem.* **12**, 25 (1965); J. M. Davis, F. K. Goodwin, W. E. Bunney, Jr., D. L. Murphy, R. W. Colburn, *Pharmacologist* **9**, 184 (1967); D. F. Bogdanski and A. Tissari, *ibid.* **9**, 250 (1967); S. H. Snyder, A. I. Green, E. D. Hendley, *J. Pharmacol. Exp. Ther.* **164**, 90 (1968); S. H. Snyder and J. T. Coyle, *ibid.* **165**, 78 (1969).
6. K. Fuxe and U. Ungerstedt, *Eur. J. Pharmacol.* **4**, 135 (1968).
7. J. T. Coyle and S. H. Snyder, *J. Pharmacol. Exp. Ther.*, in press.
8. H. Lineweaver and D. Burk, *J. Amer. Chem. Soc.* **56**, 685 (1934).
9. M. Dixon, *Biochem. J.* **55**, 170 (1953).
10. W. E. Bunney, Jr., and J. M. Davis, *Arch. Gen. Psychiat.* **13**, 483 (1965); J. J. Schildkraut and S. S. Kety, *Science* **156**, 21 (1967).
11. B.-E. Roos, *J. Pharm. Pharmacol.* **17**, 820 (1965); M. DaPrada and A. Pletscher, *Experientia* **22**, 465 (1966); H. Nybäck and G. Sedvall, *J. Pharmacol. Exp. Ther.* **162**, 294 (1968).
12. A. Ahmed and P. B. Marshall, *Brit. J. Pharmacol.* **18**, 247 (1962); R. C. Duvoisin, *Arch. Neurol.* **17**, 124 (1967).
13. M. E. Farquharson and R. G. Johnston, *Brit. J. Pharmacol.* **14**, 559 (1959); E. Frommel, *Presse Med.* **66**, 1745 (1968).
14. J. H. Burn and M. J. Rand, *Nature* **194**, 163 (1959).
15. R. George, W. L. Haslett, D. J. Jenden, *Life Sci.* **8**, 361 (1962).
16. Supported by PHS grants 1-R01-NB-07275 and 1-PO-GM-16492, and by NIMH Research Career Development Award K3-MH-33128 to S.H.S. We thank Smith Kline & French for the donation of chlorpromazine, diphenpyraline, and diethazine, Hoffman-LaRoche for phenindamine tartrate, Merck Sharp & Dohme for benztropine mesylate, Riker Laboratory for orphenadrine, Lederle for trihexyphenidyl, and Geigy for desmethylimipramine.

* Henry Strong Denison Research Scholar, 1968–69; senior medical student.

10 July 1969

Maternal Influence in Learning by Observation in Kittens

Abstract. *Kittens who observed their mothers perform a stimulus-controlled response (lever pressing to a visual stimulus for food) acquired and discriminated that response sooner than kittens who observed a strange female cat's performance. Kittens exposed to a trial and error condition never acquired the response. Initial differences in attentiveness to demonstrator performances disappeared by the second day. "Altruism" (food sharing) and other forms of social behavior were exhibited by both mother and stranger demonstrators.*

In several animal species, including man, mothers care for their young for a long time after birth. During this time, the young develop sensory and motor functions and acquire skills which are necessary for survival. The mother's role in teaching her young a specific skill, such as acquisition of food, has often been observed (*1*) but has not been experimentally demonstrated. Several investigators have suggested that infant mammals may learn from their mothers (*2*), and from their elders (*3*), primarily by observation. We have previously shown that learning by observation in adult cats is a more efficient method of learning than conventional shaping procedures (*4*). In this study, we undertook to determine whether the speed and efficiency of observation

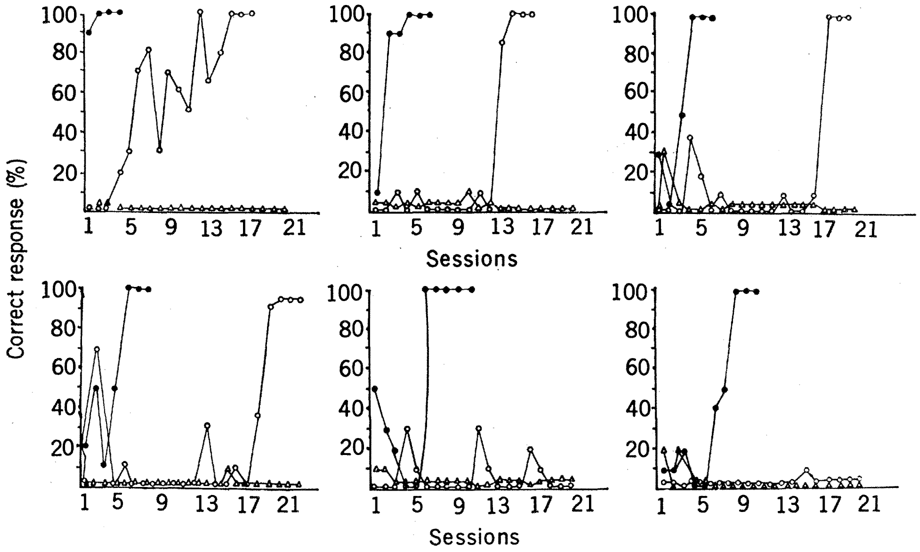

Fig. 1. Acquisition of an approach response (lever press) by observation learning in 18 kittens. Solid circles, kittens who observed their mothers (M kittens); open circles, kittens who observed strangers (S kittens); triangles, trial and error (TE) kittens.

learning is improved by the use of a mother cat as demonstrator.

The subjects were 18 kittens, all between 9 and 10 weeks old when observation began. Each kitten lived with its mother and littermates in a home or homelike laboratory environment, or both, from birth until the end of the experiment. Group I consisted of six kittens who observed their mother's performance (M kittens); group II consisted of six kittens who observed the same strange female's performance (S kittens); group III consisted of six kittens exposed to a trial and error condition (TE kittens). The members of a given litter were randomly distributed to at least two of these three groups, and where possible, to all three groups. All littermates began testing on the same day. Five female demonstrator cats (three mothers and two strangers) were used. Their task performances were equivalent and practically without error throughout the experiment.

The task was a lever press performed within 20 seconds after onset of a flickering light (4 cycle/sec). The lever was made of plexiglass and extended 12.5 cm beyond the front panel of a standard operant conditioning cage. A plexiglass partition divided the cage evenly into a demonstrator and observer compartment. A dipper that delivered a blended mixture of milk and meat was located 3.75 cm away from the lever in the demonstrator compartment.

After being familiarized with the cage, a kitten that had been deprived of food for 24 hours was placed in the demonstrator compartment alone and given one "free" food reward. The demonstrator cat (mother or strange female) was then introduced and performed ten stimulus-controlled lever presses. Although both M and S kittens had physical access to the food during these ten observation trials, they generally did not eat at this time. In fact, the occasional one, or at most two, rewards eaten by an M or S kitten during these ten trials, does not seem to constitute a determinant in their motivation or attentiveness. After these observation trials, the kitten was removed to the adjacent observer compartment for the opportunity to observe 30 more lever presses. The number of times the kitten oriented toward (paid attention to) the demonstrator cat was recorded for the 40 observation trials. The demonstrator cat was then removed, and the kitten was placed back in the demonstrator compartment. Using a blind procedure, an assistant presented ten randomly spaced trials of the visual stimulus. This overall procedure was repeated daily until the kitten had pressed the lever in eight of the ten trials. When this occurred, it was given 20 additional presentations. When the kitten achieved 90 percent criterion for these 30 trials, acquisition was considered to have taken place and it was removed. Thirty trials were then presented daily, without further observation, until stimulus discrimination was achieved. Discrimination was decided to have taken place when the kitten made five or fewer interstimulus presses each day for three consecutive days. No kitten remained just below criterion in acquiring the response. Every kitten stabilized at or above the criterion level. All kittens were tested for 30 days or until they had discriminated the response.

The TE kittens were subjected to the same procedure except that no demonstrator cat was present. A TE kitten received one "free" food reward in the demonstrator compartment and ten presentations of the stimulus, after which it was placed in the observer compartment for 30 trials. During this time in the observer compartment, the stimulus was presented at random intervals and was terminated with the sound of the food dipper, as if a demonstrator cat were performing. The kitten was then placed back in the demonstrator compartment and presented with ten trials.

This procedure was abbreviated any time a kitten started to press the lever spontaneously during the first ten observation trials when it had access to the lever. The demonstrator cat (if any) was removed, the 30 additional observation trials were bypassed, and the kitten was tested alone. Three M kittens and three S kittens achieved criterion performance in this way.

The M kittens acquired the lever-pressing response faster (median of 4.5 days) than did S kittens (median of 18.0 days) (Fig. 1). One M kitten performed the response at criterion on the first day after observing 29 demonstrator performances. A second M kitten spontaneously performed the response at criterion on the second day, after having observed 16 demonstrator performances on the first day. Two S kittens never acquired the response. No TE kitten ever acquired the response. Once lever pressing was achieved, M kittens brought it under stimulus control within a median of 3.5 days as compared to 14.0 days for S kittens. The M kittens never fell below acquisition criterion once it was reached; two of the four S kittens did so briefly before they discriminated the response.

Kittens acquire and discriminate a lever-pressing response more rapidly and efficiently by observing their mothers than by observing a strange female or by a trial and error procedure. Such rapid learning on the part of M kittens, occurring with relatively little prior reinforcement or practice, suggests that some unique representational process is operative during their observation period. However, it is likely that a representational process also exists in S kittens. Despite the variable rate with which M and S kittens acquired the response, if and when the response appeared, it was accompanied and defined by specific and identical behavior in all kittens: (i) Both M and S kittens made their initial lever presses at criterion with a directness, sureness, and minimum latency indicative of informationally motivated behavior. For example, the average latency of the first lever press made on the first day of response acquisition was 3.5 seconds for both M and S kittens. (ii) Both M and S kittens were similarly attentive—in terms of body orientation and eye movements—to those demonstrator performances that directly preceded their own response acquisition. (iii) With one exception, both M and S kittens had a characteristically sharp response-acquisition curve (Fig. 1). All observing kittens acquiring the response moved from lever pressing at or below 50 percent to lever pressing at 90 percent or criterion as a step function. Thus, whereas the speed, efficiency, and success of response acquisition and discrimination were influenced by whether the kitten observed his mother or a strange female, when the response appeared it was invariably accompanied by the above behavior.

The mother may function as a more effective demonstrator for several reasons. These include her having nursed the kittens, having provided contact proximity, having some kind of maternal "teaching instinct" (*5*), providing a still lactating and therefore stimulating or arousing presence during the observation period (*6*), and providing a familiar and therefore rewarding or relaxing presence during the observation period. All or any combination of the above might constitute a social or affective bond that enhances learning by observation.

Perhaps response acquisition depends on the existence of or, in the case of S kittens, on the eventual formation of an affective or social bond with the demonstrator. In fact, both M and S kittens displayed what are considered friendly relations (*7*) with the demonstrator cat. Both mothers and strangers were generally nonaggressive toward the kittens, licked them, and exhibited "altruistic" behavior by pressing the lever and either sharing or allowing the kitten to eat the entire reward. Also, whereas M kittens observed a mean of 16 demonstrator performances on the first day, as compared with a mean of 7 for the S kittens, this initial difference in attentiveness disappeared by the second day, when M kittens observed a mean of 18 demonstrator performances and S kittens a mean of 16. This suggests that any distraction caused by the strange demonstrator's presence was quickly reduced or eliminated.

In conclusion, these data show that a mother cat may function as an important vehicle for information transmission, via observation. Perhaps the suggested primacy of learning by observation in the adult cat (*8*) and in other mammals (*9*), as opposed to trial and error learning or operant conditioning, stems from the particular social and biological responses developed in the infant by a period of mother-dependence (*10*).

PHYLLIS CHESLER
Brain Research Laboratory, New York Medical College, New York and
Department of Psychology, Richmond College, City University of New York, Staten Island 10301

References and Notes

1. R. G. Burton, *The Book of the Tiger* (Hutchinson, London, 1933); R. F. Ewer, *Nature* **222**, 698 (1969); R. F. Ewer, *Z. Tierpsychol.* **20**, 570 (1963); K. R. C. Hall, *Brit. J. Psychol.* **54 (3)**, 201 (1963); K. Imanishi, *Psychologia* **1**, 47 (1957); P. Leyhausen, *Z. Tierpsychol. Beineft*, 2, (1956); H. L. Rheingold, Ed., *The Maternal Behavior of Mammals* (Wiley, New York, 1963); G. B. Schaller, *The Deer and the Tiger* (Univ. of Chicago Press, 1967); T. C. Schneirla, J. S. Rosenblatt, E. Tobach, in *The Maternal Behavior of Mammals*, H. Rheingold, Ed. (Wiley, New York, 1963); E. F. V. Wells, *Lions, Wild and Friendly* (Viking Press, New York, 1934); C. Wilson and E. Weston, *The Cats of Wildcat Hill* (Duell, Sloan and Pearce, New York, 1947).
2. Z. Y. Kuo, *J. Comp. Psychol.* **11**, 1 (1930); *ibid.* **25**, 1 (1938); see also K. R. C. Hall (*1*) and K. Imanishi (*1*).
3. E. J. Corner, *Proc. Roy. Inst.* **36**, 1 (1955); H. W. Nissen and M. P. Crawford, *J. Comp. Physiol. Psychol.* **22**, 283 (1936).
4. E. R. John, P. Chesler, I. Victor, F. Bartlett, *Science* **159**, 1489 (1968).
5. R. F. Ewer, *Nature* **222**, 698 (1969).
6. One of the mothers responded to nursing attempts by her kittens by walking away or by cuffing them. She continued to press the lever, indifferent to the kitten's meowing.
7. H. Winslow, *J. Comp. Psychol.* **37**, 297 (1944).
8. H. A. Adler, *J. Genetic Psychol.* **86**, 159 (1955); M. J. Herbert and C. M. Harsh, *J. Comp. Psychol.* **37**, 81 (1944); see also E. R. John *et al.* (*4*).
9. A. L. Bandura, in *Nebraska Symposium on Motivation*, M. R. Jones, Ed. (Univ. of Nebraska Press, Lincoln, 1962); ———, in *Advances in Experimental Social Psychology*, S. Berkowitz, Ed. (Academic Press, New York, 1965), vol. 2; J. A. Corson, *Psychon. Sci.* **7**, 197 (1967); M. P. Crawford and K. W. Spence, *J. Comp. Psychol.* **27**, 133 (1939); K. K. Hayes and C. Hayes, *J. Comp. Physiol. Psychol.* **45**, 450 (1952); W. N. Kellogg and L. A. Kellogg, *The Ape and the Child* (Hafner, New York, 1967 reprint of the 1933 edition); D. Mainardi and A. Pasquali, *Soc. Ital. Sci. Natur. Milan.* **107**, 2 (1968); C. J. Warden and T. A. Jackson, *J. Genet. Psychol.* **46**, 103 (1935); C. J. Warden, H. A. Fjeld, A. M. Koch, *ibid.* **56**, 311 (1940).
10. K. R. C. Hall, *Brit. J. Psychol.* **54 (3)**, 201 (1963).
11. I thank E. R. John, A. Rabe, N. Chesler, N. Jody, F. Burgio, and P. Walker for their assistance. Supported by PHS grant MH 08579 and by the New School for Social Research.

30 June 1969; revised 10 September 1969 ■

Object-Carrying by Rats: An Approach to the Behavior Produced by Brain Stimulation

Abstract. *Rats were provided with opportunity to turn reinforcing hypothalamic stimulation on and off by traversing back and forth across a chamber. When provided with edible and inedible objects, all animals that self-stimulated carried them from the stimulation to the nonstimulation side. Neither food deprivation nor a history of stimulus-bound eating produced a preference for the edible objects. Equivalent stimulation provided without regard to the animals' location in the chamber did not elicit object-carrying. Results are interpreted in terms of the natural conditions which normally elicit this species-specific unit of behavior. Implications for understanding other behavior patterns elicited by hypothalamic stimulation are suggested.*

Rodents carry objects in situations related to hoarding, nest building, and retrieving of young. Rodents may also carry items such as stones that do not seem to be related to storing food and maternal behavior and have no obvious utility for the animal at all (*1*). The "pack" or "trade" rat (*Neotoma cinerea occidentalis*), for example, may even leave behind an object it had been carrying in favor of a more desirable shiny object. In a sense, object-carrying by some species may be viewed as a basic, adaptive response that under specific circumstances is incorporated into more complicated behavior patterns which may serve the purposes of specific motivational states.

In the course of studying the behavior that may be elicited by electrical stimulation of hypothalamic structures, we have found circumstances in which