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3 Contributions of the Matching Law to the Analysis of the Behavioral Effects of Drugs

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INTRODUCTION

William James (1890) used the apt phrase "stream of consciousness" to describe mental life. Had he chosen to describe an organism's overt behavior, he could just as aptly have used the phrase "stream of behavior." For behavior, like consciousness, is continuous, plastic, and reflective of the play of many simultaneously acting forces. Even the task of describing a "simple" organism, such as a rat, engaged in a "simple" task, as pressing a lever, requires that we consider a host of variables, including the response requirement, degree of deprivation, the consequences of lever pressing, and the consequences of engaging in competing activities. Moreover, these variables may interact in complex ways, and historical conditions may matter as well. Faced with this complexity, psychologists have developed techniques for fractionating performance into its component elements. For example, with the method of signal detection (Swets, Tanner, & Birdsall, 1961), it is possible to distinguish changes in perception from changes in motivation. In this chapter we describe a method that decomposes changes in behavior into two components: those that depend on reinforcement processes and those that are a function of motor performance. The method we use is based on the matching law equation (Herrnstein, 1970). Our purpose is to summarize the contribution that this method has made to some long-standing problems in behavioral pharmacology.

THE PROBLEM OF MEASURING A SUBJECT'S SUSCEPTIBILITY TO REINFORCERS

Over the last decade, the interpretation of the effects of antipsychotic drugs on reinforced behavior has been the subject of many research and review papers (e.g., Fibiger, 1978; Wise, 1982). The basic observation is that antipsychotic drugs (often referred to as "neuroleptics") attenuate reinforced responding. For example, they decrease operant responding maintained by the presentation of food and water, and the decreases occur at doses that did not affect food and water intake (compare, e.g., Block & Fisher, 1975; Heyman, 1983; Heyman, Kinzie, & Seiden, 1986; Towell, Muscat, & Willner, 1987; Zis & Fibiger, 1975). The phenomenon has generality, occurring in a wide range of species, including humans (e.g., Fischman & Schuster, 1979), and with a variety of reinforcers, including ones that are not consumed, such a brain stimulation (e.g., Gallistel & Karras, 1984). However, the behavioral mechanisms mediating the effects of neuroleptics on reinforced behavior have not been clearly established.

Some evidence suggests that neuroleptics attenuate reinforcement processes. For example, in a threshold prodcedure in which the reinforcer was brain stimulation and the subjects were rats (Zarevics & Setler, 1979), pimozide, a neuroleptic, increased the threshold. That is, the subjects had the capacity to respond, but required a higher level of reinforcement to do so. However, other results appear to contradict the reinforcement interpretation and suggest instead that neuroleptics produce a motor deficit. For example, Ettenberg, Koob, and Bloom (1981) showed that a neuroleptic induced decrease in reinforced responding depended on the response requirement. A 0.1 mg/kg dose of alpha-flupentixol reduced reinforced lever pressing by about 35% but had no effect on reinforced nose-poking. This suggests that alpha-flupentixol affected the capacity to respond and therefore the more effortful response was differentially affected.

These apparently conflicting findings stimulated attempts to experimentally dissociate reinforcement efficacy and motor performance. However, despite numerous studies, the controversy persisted (see, for example, Wise, 1982, and accompanying commentary). The problem has been in part methodological. Most results could be interpreted in at least two ways. For example, consider a study that is frequently cited as showing a neuroleptic-induced reinforcement deficit.Wise, Spindler, deWit and Gerber (1978) compared the effects of pimozide and extinction (removing the reinforcer) on response rate. Rats served as subjects, and in baseline conditions, each response (a lever press) was reinforced. Pimozide and extinction produced similar patterns of response rate decline. At the beginning of the session, response rates were at baseline levels and, then, with time, gradually subsided. Wise et al. (1978) explained the pimozide effect as a drug induced attenuation of reinforcement. They reasoned that pimozide affected reinforcement process and not motor performance, because its effects were similar to those that follow removing the reinforcer. However, the

results are also compatible with the view that pimozide produced a motor deficit. In the Wise et al. study, reinforcement rate was proportional to response rate. Thus if a motor impairment slowed response rate, it would also reduce reinforcement rate. The decrease in reinforcement rate would in turn decrease response rate, and, because of this positive feed-back loop, response and reinforcement rate would gradually decline, just as in extinction. In support of this motor interpretation, pimozide does not produce an extinction-like pattern of response rate decline in procedures which do not maintain a proportionality between response and reinforcement rates (e.g., Fibiger, Carter, & Phillips, 1976).

The extinction procedure for measuring reinforcement efficacy thus seems ambiguous, and in other studies researchers found that neuroleptics changed response rates in ways not observed during extinction (Gramling, Fowler, & Collins, 1984). In contrast, the matching law equation, as we hope to show, leads to measures of reinforcement efficacy and motor performance that are logically independent and have been empirically validated. The results displayed in Fig. 3.1 (Heyman & Monaghan, 1987) introduce the matching law approach.

THE MATCHING LAW EQUATION: BASIC FINDINGS

The top left panel shows the effects of deprivation on response rate. The subjects were 8 water deprived rats, the response requirement was a lever press, and the reinforcer was a small portion of water (0.025 ml). The basic reinforcement contingency was set by a variable-interval schedule, which intermittently reinforced lever press responses according to the passage of time. Each session consisted of a series of five variable-interval reinforcement schedules, and each schedule was available for 9 min with a 5 min time-out period between reinforcement schedules. The mean programmed reinforcement times ranged from 150 sec (25 reinforcers per hour) to 5 sec (720 reinforcers per hour). The two deprivation periods were 6.0 and 47.5 hours.

Response rate was a negatively accelerated function of reinforcement rate, and, relatedly, at the two highest reinforcement rates (approximately 340 and 700 per hour), response rates were similar, especially in the extended deprivation period (47.5 hours). In other words, there was a response rate ceiling, as indeed there must be, so that once responding approached this level, further increases in reinforcement rate had little effect on response rate. The horizontal dashed lines are an estimate of the response rate asymptotes for the two conditions (an explanation of how this limit was estimated is offered in the description of the matching law equation).

Deprivation increased response rates, and the increases were an inverse function of reinforcement rate. Or, in terms of the estimated response rate asymptotes, deprivation increased the rate at which response rates approached their

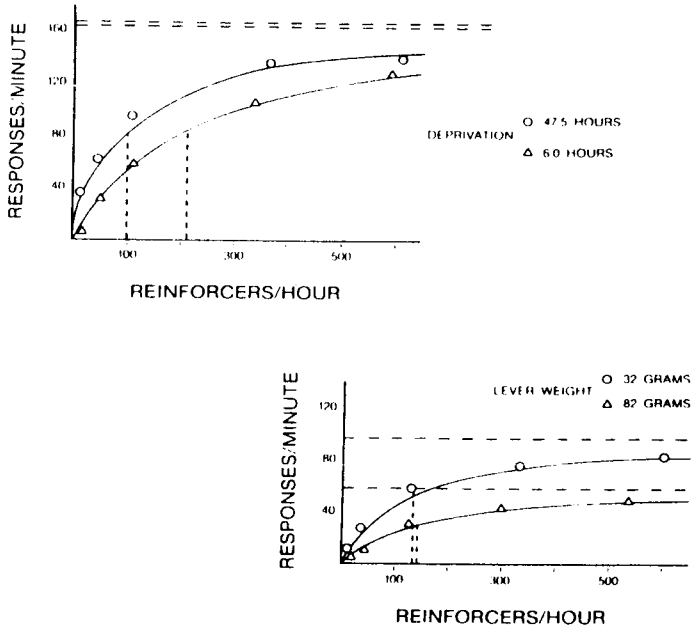


FIG. 3.1. The effect of water deprivation and lever weight on reinforced responding. The open symbols represent group median results (Heyman & Monagahan, 1987). The curves show the predicted relationship between response rate and reinforcement rate, according to the matching law equation. The horizontal dashed lines indicate the response rate asymptotes (k), and the vertical dashed lines represent the rate of reinforcement that maintained a one-half asymptotic response rate (R_e).

asymptote. This effect was conveniently shown by the two vertical dashed lines. They mark the rates of reinforcement that maintained a one-half asymptotic response rate. For example, in the high deprivation condition, 100 reinforcements per hour maintained a one-half asymptotic response rate, but in the low deprivation condition, a rate of about 220 reinforcers an hour was needed to maintain a one-half asymptotic response rate. Thus for the longer deprivation condition, water was a more potent or efficacious reinforcer. This finding suggests that the rate of reinforcement for a one-half asymptotic response rate can be used to measure reinforcement efficacy.

The lower right panel of Fig. 3.1 shows the results from a study in which the weight of the lever was varied. The deprivation period was fixed at 23.5 hours and the response requirement was varied, but otherwise the procedure was identical to that used in the previous study (including the same 8 rats). Changes in the

response requirement produced a different pattern of response rate shifts than did changes in deprivation. As the horizontal dashed lines indicate, there was a shift in the estimated response rate asymptote, whereas the rate of reinforcement for a one-half asymptotic response rate remained about the same (the vertical dashed lines). Other researchers have shown that increases in the weight of the manipulandum increased response duration (see Fowler, Gramling, & Liao, 1986). Consequently, it is likely that the decrease in response rate asymptote was due to an increase in response duration. In any case, the study suggests that the response rate asymptote can be used to measure the effects of treatments that affect motor performance.

The Matching Law Equation

The smooth curves and dashed lines in Fig. 3.1 were obtained by fitting the matching law equation to the data sets. The customary notation is:

$$B = \frac{k\,R}{R + R_e}, \tag{1}$$

where B represents response rate, R represents reinforcement rate, and k and R_e are fitted parameters. Figure 3.2 shows the equation along with the parameter

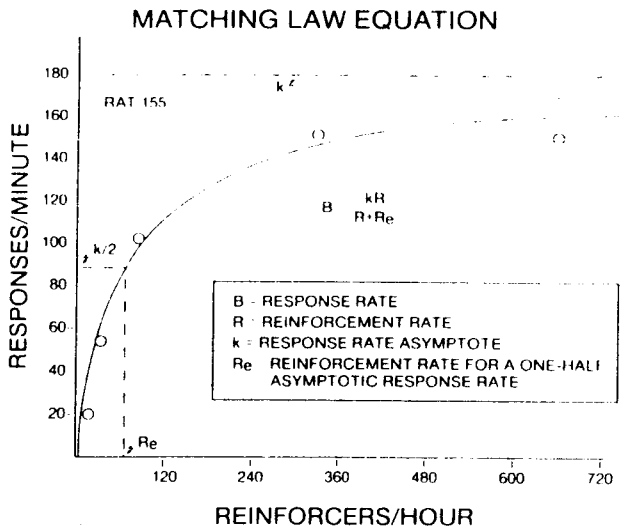


FIG. 3.2. The matching law equation and representative results (Heyman & Monaghan, 1987). The open circles show the average response rates.

definitions and a data set from our laboratory. The magnitude of k is equal to the estimated asymptotic response rate (note that response rate approaches but does not exceed k as reinforcement rate is increased). Thus the horizontal dashed lines in Figs. 3.1 and 3.2 were obtained by fitting the matching law equation to the data sets and finding the values for k. For example, in the deprivation study summarized in Fig. 3.1, the estimated values of k were 170 and 166 responses per min (k is measured in the same units as is the dependent variable, e.g., responses per minute). The parameter R_e is equal to the rate of reinforcement that maintains a one-half asymptotic response rate ($B = k/2$ when $R = R_e$). Thus the vertical dashed lines in Figs. 3.1 and 3.2 were determined by fitting the matching law equation to the data and finding the value of R_e. For example, in the lever weight experiment (Fig. 3.1), the estimated values of R_e were 143 and 147 reinforcers per hour (R_e is measured in the same units as is the independent variable, e.g., reinforcers per hour). Equation 1, then, says that response rate is a function of three variables: reinforcement rate, the determinants of the asymptote (k), and the determinants of the rate of reinforcement that maintains a one-half asymptotic response rate (R_e).

The matching law equation accounted for over 90% of the variance in response rates for the results displayed in Fig. 3.1. Similar results have been obtained with different species, including humans, with different reinforcers, including ones that are not consumed, such as brain stimulation, and with different response requirements, for example, running, lever pressing, and swimming. (For a review of the matching law literature see de Villiers & Herrnstein, 1976.) Thus the matching law equation provides a quantitative and general account of the relationship between response rate and reinforcement rate.

Experimental Manipulations that Affect the Matching Law Parameters

Figure 3.1 suggests that the matching law equation can be used to evaluate the effects of drugs on motor performance and reinforcement efficacy. We reviewed the literature to determine the generality of this conclusion. The review was restricted to studies in which the parameter estimates were based on at least 5 data points and in which the response was maintained by a positive reinforcer.

There were four experiments in which k systematically changed and R_e did not (see Heyman & Monaghan, 1987 for references). In each one, the experimenter varied the response requirement. For example, in a study in which the subjects were pigeons, the manipulandum was varied: a button, which the pigeons pecked, was replaced with a treadle, which they kicked (McSweeney, 1978). The primary result was a 60% decrease in k. In contrast, changes in R_e were small and non-systematic. Changes in the response requirement alter the topography of the response, for example, its duration, and also, perhaps, affect the subject's capacity to respond. In addition to these empirical results, derivations

of the matching law equation (Herrnstein, 1974, 1979; Heyman, 1988) support the conclusion that k measures motor performance. Thus both empirical and logical considerations lead to the conclusion that k is a measure of motor performance.

There are 10 studies in which R_e systematically varied but k did not. The experimental manipulations included changes in reward magnitude, reward quality, and deprivation (see Heyman & Monaghan, 1987, for references). Thus changes in the conditions of reinforcement altered R_e, with increases in reward magnitude and deprivation period producing decreases in R_e. For example, in a study with rats in which the reinforcer was brain stimulation (Hamilton, Stellar, & Hart, 1985), increases in current intensity decreased R_e without affecting k. (The more potent the reinforcer, the less needed to maintain a one-half asymptotic response rate.) In addition to the empirical studies, the previously mentioned derivations of the matching law equation (Herrnstein, 1974, 1979; Heyman, 1988) implied that R_e was a function of the relative reinforcing efficacy of the reinforcer maintaining the response. Thus there is both empirical and logical support for the conclusion that R_e provides a measure of the efficacy of the reinforcer maintaining the measured response.

There are also several studies in which a change in the reinforcement conditions affected both k and R_e (e.g., Bradshaw, Szabadi, & Bevan, 1978; Snyderman, 1983). This result is not necessarily discrepant with a change in just R_e. For example, rats do not lever press in the same way for food and water reinforcers (e.g., Davey & Cleland, 1982; Hull, 1977), so that a change from water to food reinforcement should affect both k and R_e. However, the experiments in which both k and R_e changed were similar to ones in which just R_e had changed. For example, in four studies, differences in deprivation produced systematic differences in R_e but not k. (Bradshaw, Szabadi, Ruddle, & Pears, Conrad & Sidman, 1956; Heyman & Monaghan, 1987; Logan, 1960). In contrast, Snyderman (1983) found that changes in deprivation affected both k and R_e. This apparent discrepancy may be due to factors other than deprivation. For example, in the Snyderman experiment, the richest reinforcement component typically did not maintain the highest response rate. This may have occurred because the subjects had either partially satiated and/or were not given sufficient time to consume the reinforcer (see Heyman & Monaghan, 1987, for details). Moreover, it the data are analyzed without the non-monotonic data point, the results show a systematic relationship between deprivation and R_e and little change in k, just as in the other deprivation studies (Heyman, 1988). Thus the simplest account of the literature is that k measures motor performance, R_e measures reinforcement efficacy, and, in addition, there are a number of experiments in which changes in reinforcement conditions were associated with changes in k because of uncontrolled factors. Importantly, that k and R_e can vary independently does not deny that certain, more complex, manipulations will systematically alter both parameters.

NEUROLEPTICS

Next we describe studies in which the matching law equation was used to analyze the effects of neuroleptics on reinforced responding. A change in the rate of reinforcement that maintained a one-half asymptotic response rate was used to measure reinforcement effects. Throughout this chapter this measure is referred to as "reinforcement efficacy" or "susceptibility to reinforcement." When it changes, a given rate of reinforcement maintains more or less responding relative to the subject's asymptotic response rate. Change in the asymptotic response rate was used to measure motor performance. As noted in the discussion of Figs. 3.1 and 3.2 this measure varies systematically with changes in the response requirement.

The procedure for the neuroleptic studies was similar to the deprivation and lever weight studies summarized in Fig. 3.1. Rats served as subjects (6 to 8 per experiment). They were water deprived for 23.5 hours, and the reinforcer was a small portion of water (0.025 ml). Sessions were divided into five reinforcement periods. Each period provided a different reinforcement rate, with a range of about 20 to 700 reinforcers per hour, and each period was available for 7 to 9 min depending on the study. The five different reinforcement rates were distinguished by combinations of auditory and visual stimuli, and the order was random, without replacement. A time-out period separated reinforcement components; its duration was 5 to 9 min, depending on the study.

The drugs tested were: chlorpromazine, pimozide, fluphenazine decanoate, and cis-flupentixol. Chlorpromazine, pimozide, and cis-flupentixol were administered acutely, either once or twice per week. The acute injections were at a concentration of 1 ml per kilogram and were delivered intraperitoneally. Each dose was given three times, and vehicle injections were interspersed between drug doses.

Drug effects were described in terms of changes in response rate and changes in the matching law parameters. The parameters were obtained from each subject in each condition. These quantities were then subjected to either paired t tests or analysis of variance to determine statistical significance. A weighted least squares technique was used to fit the equation and estimate the parameters (Wilkinson, 1960). The method is based on the fact that the reciprocal transformation of the matching law equation is linear: $1/B = 1/k + R_e/kR_e$. The sample sizes for the fitting procedure were three sessions for acute drug conditions, 6 sessions for chronic drug conditions, and typically 10 or more sessions for baseline and vehicle conditions.

Chlorpromazine and Pimozide

Figures 3.3, 3.4, and 3.5 show the effects of pimozide and chlorpromazine on response rate. The changes were dose dependent, and individual subject response rates (Figs. 3.3 and 3.4) were similar to group median response rates (Fig. 3.5)

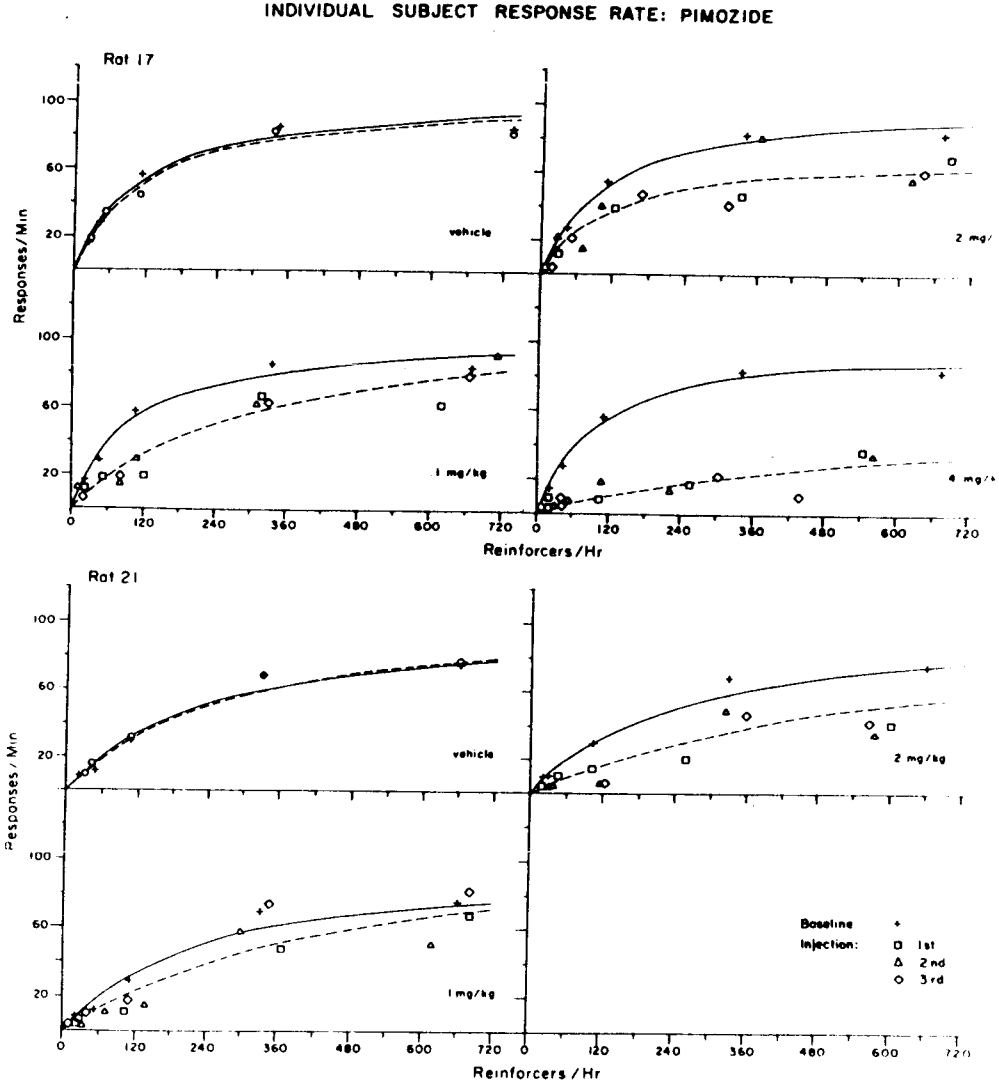


FIG. 3.3. The effect of pimozide on reinforced responding for two representative subjects. The open symbols show the response rates for each of the three sessions that each dose was administered. The crosses show the average response rates in baseline.

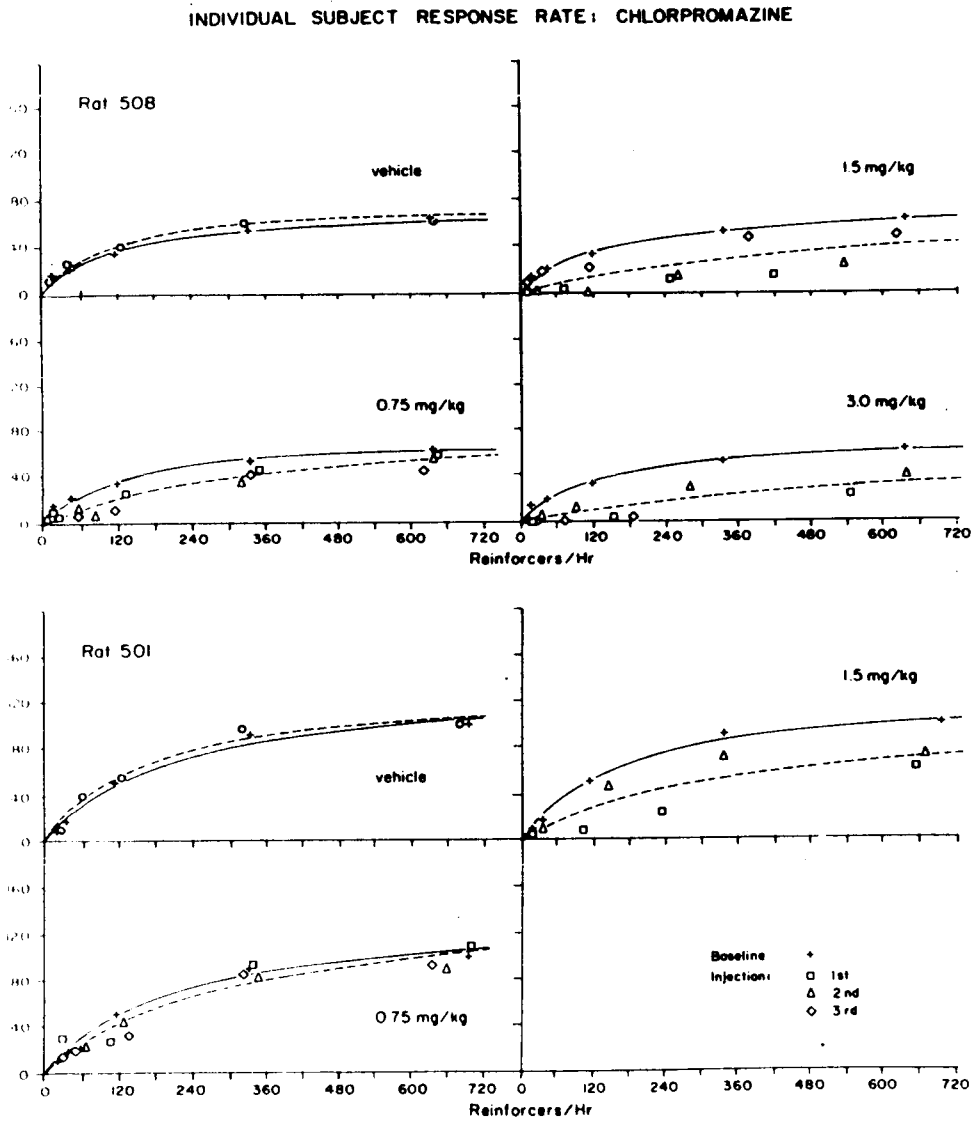


FIG. 3.4. The effect of chlorpromazine on reinforced responding. The format is the same as in Fig. 3.3.

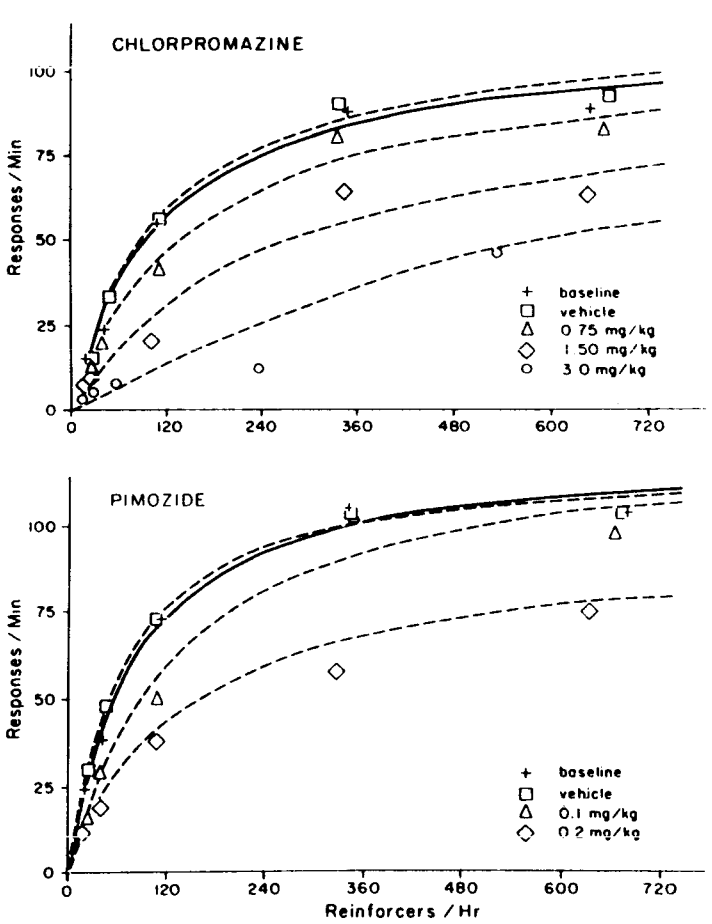


FIG. 3.5. The median response rates in the pimozide and chlorpromazine experiments.

The lowest dose of pimozide (0.1 mg/kg) and chlorpromazine (0.75 mg/kg) decreased response rates maintained by the lower reinforcement rates, but had little or no effect on response rates maintained by the highest reinforcement rate (VI 5 sec schedule). For example, drug session response rates for Rat 17 at the 0.1 mg/kg dose of pimozide (open symbols in Fig. 3.3) were invariably lower than baseline session response rates (crosses) in the four lowest reinforcement rate components. In contrast, drug session response rates overlapped baseline session response rates in the richest reinforcement rate component (VI 5 sec schedule). However, at higher doses, chlorpromazine and pimozide decreased

response rates in all five reinforcement rate components. For example, drug session response rates for Rat 17 at the two higher pimozide doses (0.2 and 0.4 mg/kg) were invariably lower than baseline response rates. (Rat 17 was atypical in that it continued to respond at the 0.4 mg/kg dose.)

The 0.1 mg/kg dose of pimozide and 0.75 mg/kg dose of chlorpromazine produced response rate changes that were similar to those that occurred in studies in which the deprivation period or amount of reinforcement was decreased (see Fig. 3.1; Heyman & Monaghan, 1987). Thus at these doses, pimozide and chlorpromazine decreased reinforcement efficacy independently of changes in motor performance. However, at higher doses the pattern of response rate change was more complex, resembling the combined effects of changes in the response requirement and reinforcement conditions.

Figure 3.6 shows that chlorpromazine and pimozide produced dose dependent increases in R_e. The changes were large, with 7 of 8 subjects showing an increase at the lowest chlorpromazine dose and 7 of 7 showing an increase at the lowest pimozide dose. Changes in k were also dose dependent, but at the lowest dose neither pimozide nor chlorpromazine systematically affected k. Thus, according to the matching law equation criteria, these two neuroleptics decreased reinforced reponding in two different ways: they reduced reinforcement efficacy and reduced motor performance.

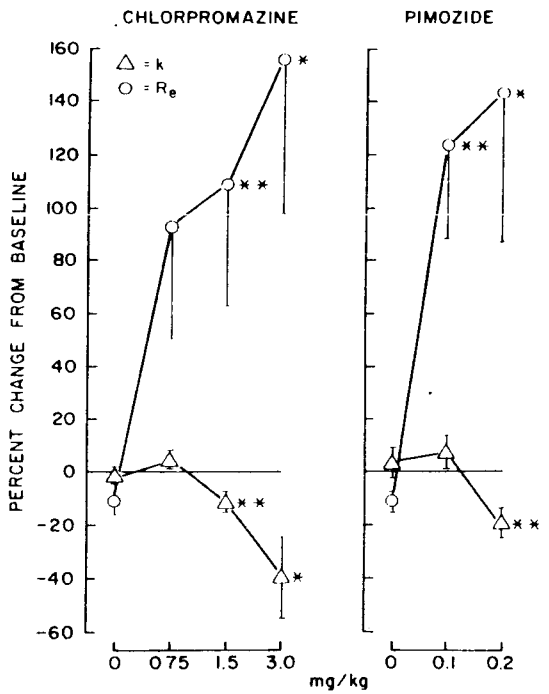


FIG. 3.6. Changes in k and R_e as a function of drug dose. The open symbols depict the average percent change from baseline. A single asterik indicates a significance level of .05 and two asteriks indicate a .01 level, according to a paired t test.

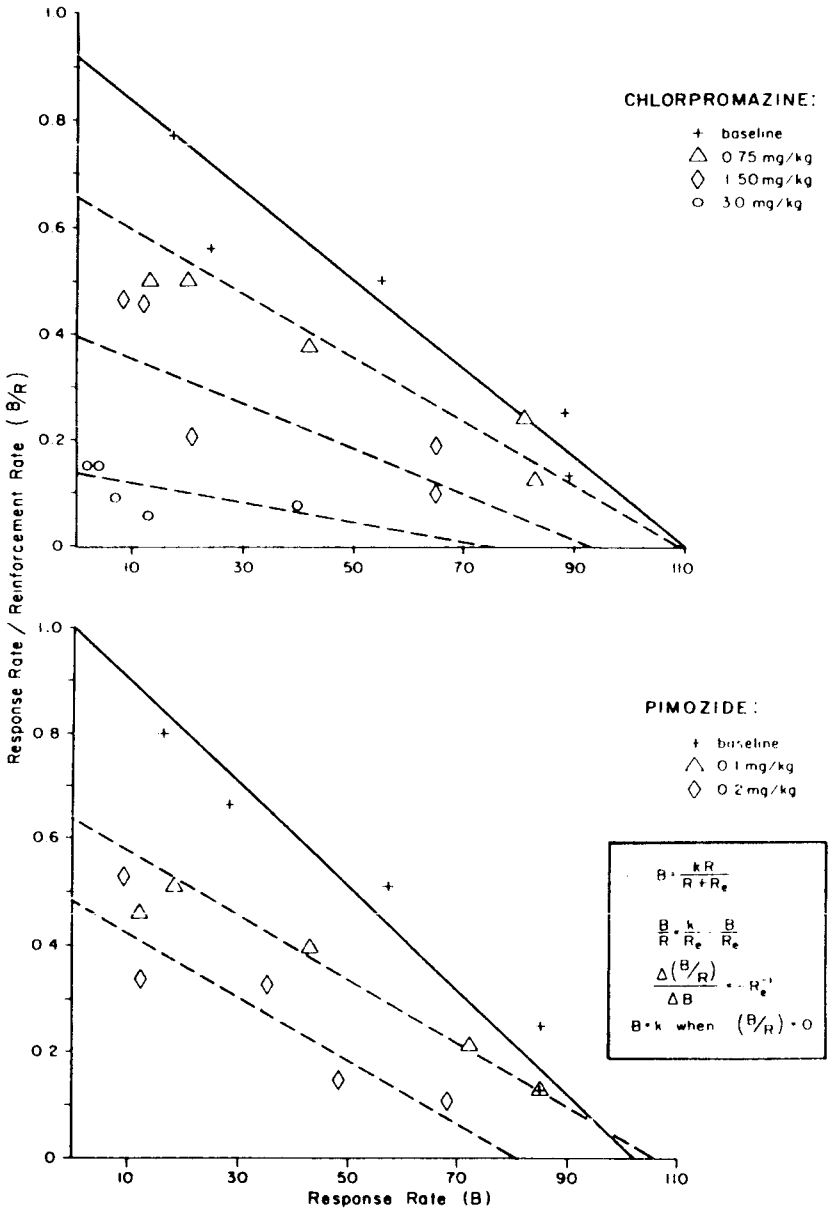


FIG. 3.7. Scatchard plot of the effects of chlorpromazine and pimozide on response rate. This graph is based on analogies between receptor binding and reinforced behavior (Heyman, 1988). A decrease in the slope is equivalent to a decrease in reinforcement efficacy and a leftward shift in the x-axis intercept is equivalent to motor slowing.

Figure 3.7 shows another way of displaying matching law analyses of changes in reinforced responding. The graph was adapted from a Scatchard (1949) plot of receptor binding. The data can be displayed in this way because the matching law equation has the same form as the basic equation used to describe the relationship between concentration of ligand and concentration of bound receptors (see, e.g., Clark, 1933). The analogous independent variables are reinforcement rate and ligand concentration and the analogous dependent variables are response rate and bound receptor concentration. (The relationship between the matching law equation and receptor binding equation is described in more detail elsewhere; see Heyman, 1988). In order to display the data as in Fig. 3.7, the matching law equation was rearranged so that: $B/R = (k\text{-}B)/R_e$. In this form there is a linear relationship between B/R and B, and the resulting line has a slope of $-1/R_e$ and intersects the x-axis at k. Thus, decrease in slope indicates a decrease in reinforcement efficacy, and a leftward shift in the x-axis intersection indicates a decrease in motor performance.

Fluphenazine Decanoate

Pimozide and chlorpromazine were administered once or twice a week, and their effects could be measured in hours. In contrast, psychiatric patients are dosed daily or are given long lasting depot injections. We attempted to mimic the clinical dosing regime by giving the rats intramuscular injections of a neuroleptic-lipid mixture: fluphenazine decanoate. The lipid slowly breaks down, thereby releasing the fluphenazine. The release rate is very gradual. For example, in a study with humans the drug was detected as long as 6 months after administration (Wistedt, Jorgensen, & Wiles, 1982).

Figures 3.8 and 3.9 show the effect of fluphenazine decanoate on k and R_e as a function of time since injection. The points represent the median subject value, using blocks of six consecutive sessions as the samples (in the acute studies, three sessions were used). In that there were 6 subjects in the 2.50 mg/kg group and 8 in the 5.0 mg/kg group, the data points represent 36 and 48 sessions respectively.

The 2.5 and 5.0 doses increased R_e and decreased k, just as did higher doses of pimozide and chlorpromazine. The magnitude and duration of the changes were dose dependent. The effects of the 2.5 mg/kg dose persisted for about 30 to 40 sessions, and at the 5.0 mg/kg dose, the return to baseline took about 90 sessions for k and about 54 sessions for R_e. Put somewhat differently, the mass of data summarized in Figs. 3.8 and 3.9 underscores the point that widely used neuroleptics decrease both reinforcement efficacy and motor performance. The data in Fig. 3.8 (changes in k) also suggest that chronic fluphenazine decanoate may have produced irreversible motor effects. For 11 of 14 subjects (both groups), k recovered to higher than baseline levels. This overshot could have been due to chronic drug treatment or, of course, age related changes (the rats were approximately five months old when drug treatment began).

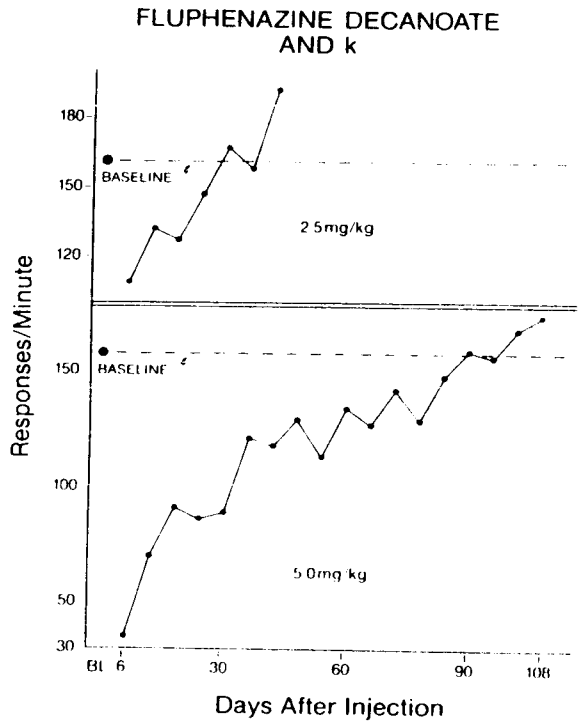


FIG. 3.8. The effect of fluphenazine decanoate on k. The data points show the group medians, as calculated from samples of six consecutive sessions.

Cis-flupentixol

Cis-flupentixol is derived from phenothiazine and, accordingly, is structurally similar to chlorpromozine (see, e.g., Baldesarrini, 1980). It is referred to as a neuroleptic and shares a number of the defining characteristics of this class of drugs. It is an effective antipsychotic (Stauning, Kirk, & Jorgensen, 1979), it attenuates reinforced responding (e.g., Hamilton et al., 1985), and it antagonizes the behavioral effects of dopamine agonists (e.g., Herrera-Marschitz & Ungerstedt, 1984). However, unlike chlorpromazine, pimozide, and fluphenazine decanoate, cis-flupentixol decreased reinforced responding at doses that did not decrease reinforcement efficacy. Two studies showed this result.

Heyman, Monaghan, and Clody (1987) evaluated the effects of cis-flupentixol on k and R_e in a study in which the procedure was identical to that used in the pimozide and chlorpromazine experiments. The subjects were 8 rats, the reinforcer was water, and the response requirement was a lever press. Figures 3.10, 3.11, and 3.12 show the results. Cis-flupentixol produced dose dependent de

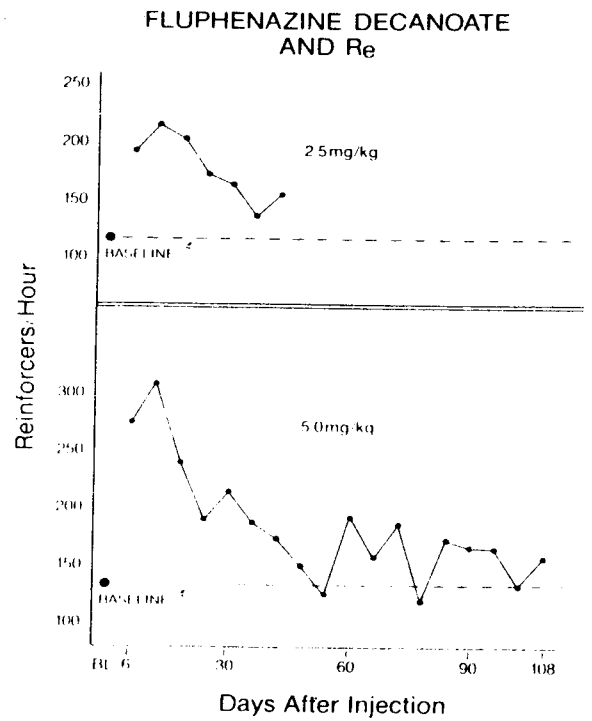


FIG. 3.9. The effect of fluphenazine decanoate on R_o. The format is the same as in Fig. 3.8.

creases in k (Fig. 3.11). In contrast, changes R_e were not systematic (Fig. 3.12), although at the two lowest doses (.005 and .01 mg/kg) there was the suggestion of a decrease in R_e and there was an overall increase in the variability of R_e, which was not dose dependent. Hamilton et al., (1985) obtained similar results. The reinforcer in their study was brain stimulation, but otherwise their procedure was like the ones described in this chapter. They tested three subjects and found dose dependent decreases in k for two (.05 to .20 mg/kg), whereas the changes in R_e were not systematic. Thus cis-flupentixol, unlike the other neuroleptics that we evaluated, reduced motor performance at doses that did not reduce reinforcement efficacy.

The matching law analysis distinguished cis-flupentixol from other neuroleptics. Biochemical and clinical criteria also distinguish cis-flupentixol. Cis-flupentixol is a mixed D1-D2 antagonist. Its affinity for D2 sites is within the range set by pimozide and chlorpromazine (Hyttel & Arnt, 1986). However, its affinity for D1 sites is quite different. Cis-flupentixol's affinity for D1 sites is more than 15 times greater than that of chlorpromazine and about 100 times greater than

that of pimozide (Hyttel & Arnt, 1986). Fluphenazine is similar to pimozide and chlorpromazine in that it has a higher affinity for D2 sites than for D1 sites. Thus cis-flupentixol's effect on motor performance may be related to its capacity to bind about equally well to D1 and D2 sites and/or its relative high affinity for D1 sites. The receptor affinity findings also suggest that chlorpromazine and pimozide's effect on reinforcement efficacy may be related to the difference in their affinities for D1 and D2 sites, namely that they have a higher affinity for D2 receptors.

Cis-flupentixol is used in the treatment of schizophrenia and schizoaffective disorder (Parent & Toussaint, 1983; Singh, 1984). According to clinical impres-

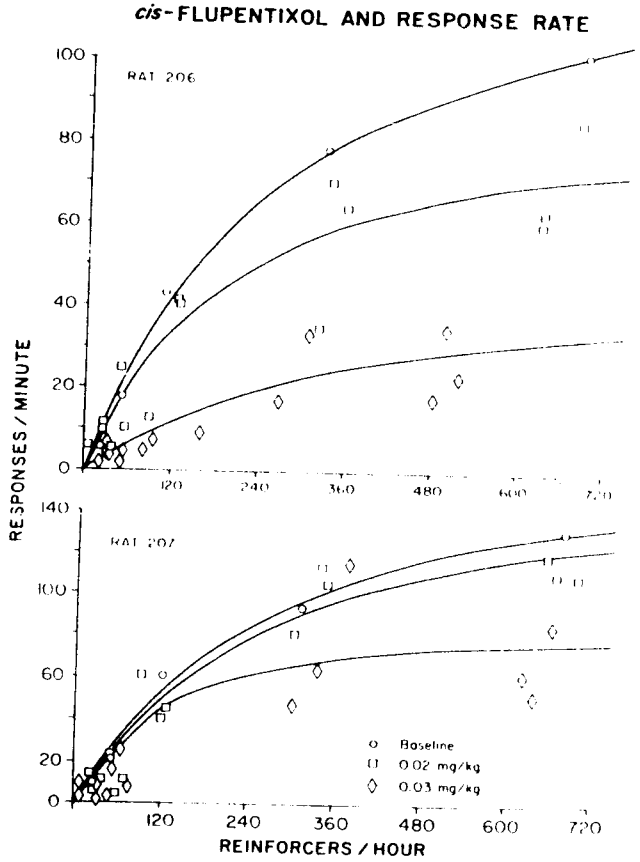


FIG. 3.10. The effect of cis-flupentixol on reinforced responding. The open squares and diamonds show the response rates for the three sessions that each dose was administered. The open circles show the average baseline response rates.

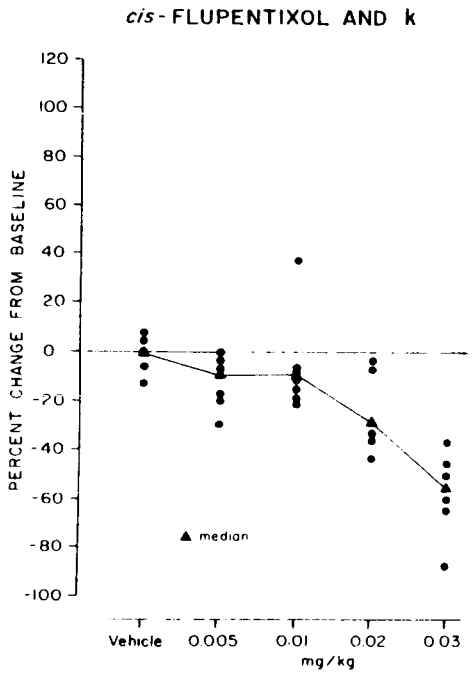


FIG. 3.11. The effect of cis-flupentixol on *k*. Each point shows the percentage change for one of the 8 subjects. (However, there are not always 8 points, because some subjects' scores were too close together to represent with two points.)

sions and data collected using the Brief Psychiatric Rating Scale (BPRS), it is more likely to reduce depression and anxiety than the other neuroleptics with which it has been compared. For example, Singh (1984) observed that cis-flupentixol reduced depression, whereas other neuroleptics produce dysphoria; Parent and Toussaint reported that cis-flupentixol produced a significant decrease on the depression-anxiety subscale of the BPRS, whereas haloperidol did not.

Although we have tested just four neuroleptics, the available results show a correlation between change in R_e and changes in mood: Chlorpromazine, pimozide, and fluphenazine decanoate increased R_e and are reported to produce dysphoria; cis-flupentixol is said not to produce dysphoria and did not increase R_e.

Summary of Neuroleptic Results

Other researchers have used the matching law or similar methods to analyze the behavioral effects of neuroleptics. Although procedures varied from laboratory to laboratory, the results were similar. In a study in which the subjects were food deprived rats and the reinforcer was a small portion of milk (Heyman, 1983), pimozide increased R_e and decreased k, just as in experiments in which the subjects were water deprived. Similar results were obtained in a study with nondeprived rats (Hamilton et al., 1985). The procedure was a five component multiple schedule, as in the studies discussed earlier, but the reinforcer was brain

stimulation. Pimozide increased R_e and decreased k_e just as in experiments in which the subjects were food and water deprived. Thus pimozide produced the same pattern of changes in the matching law parameters independently of the subject's deprivation state and the type of reinforcer. Gallistel and his colleagues (e.g., Gallistel, Shizgal, & Yeomans, 1981) developed a method for distinguishing between changes in motor performance and reinforcement efficacy that is similar to the matching law approach. In their experiments rats were used as subjects and brain stimulation was the reinforcer. In each session a dimension of brain stimulation was varied (e.g., current intensity), and the experimenters estimated the subject's asymptotic response level and the reinforcement setting that maintained a one-half asymptotic response level. Gallistel estimated these parameters by eye, however de Villiers and Herrnstein (1976) showed that the matching law equation described Gallistel's results.

In the brain-stimulation reward studies (Gallistel & Davis, 1983; Gallistel & Karras, 1984) chlorpromazine and pimozide decreased reinforcement efficacy. There were no apparent changes in motor performance, so that changes in reinforcement efficacy had a lower dose threshold, as in the water deprivation studies. Franklin (1978) used Gallistel's approach to evaluate the effects of pimozide on reinforced behavior in a runway apparatus. The rat was placed in a start box and then given a brief pulse of brain stimulation upon reaching the end of the alley. Pimozide increased the current intensity required to maintain a one-

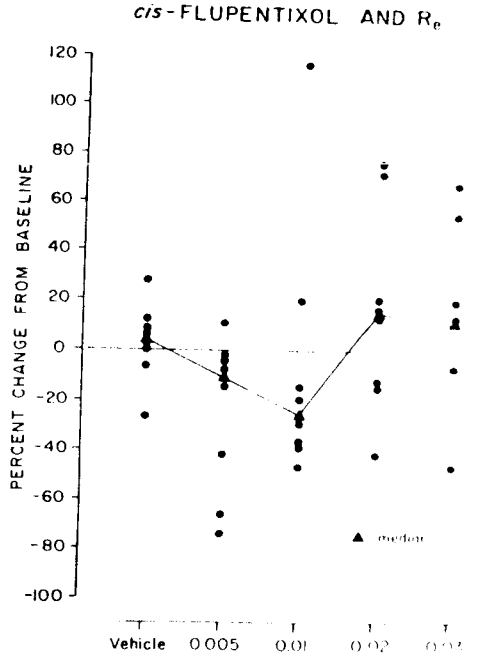


FIG. 3.12. The effect of cis-flupentixol on R_e. The format is the same as in Fig. 3.11.

half asymptotic running speed, and did so at doses that did not reduce the estimated asymptotic running speed. Thus the results from several laboratories indicate that pimozide and chlorpromazine reduced both reinforcement efficacy and motor performance and that the dose threshold for the reinforcement effects was lower. More generally the findings suggest that the pharmacology of reinforcement processes has core elements that are common to a number, perhaps all, reinforcers.

In contrast to the results just reviewed, Morley, Bradshaw, and Szabadi (1984) concluded that pimozide slowed motor performance at doses that did not affect reinforcement efficacy. Their evidence is the pattern of response rate changes in two different variable-interval schedules. One schedule provided a relatively high reinforcement rate (VI 10 sec), the other a relatively low rate (VI 100 sec). Each schedule was run separately, and the VI 10-sec schedule was in effect first. As there were just two reinforcement schedules, it was not possible to estimate k and R_e. However, Morley et al. pointed out that it is possible to infer how these parameters behaved. Proportional shifts in response rate imply that k changed and larger response rate shifts in the low reinforcement rate schedule imply that R_e changed. Pimozide (.125 to .5 mg/kg) reduced response rates, but at some doses the decreases were larger on the VI 10 sec schedule and at other doses the decreases were larger on the VI 100 sec schedule, so that there was no difference as a function of reinforcement rate. Morley et al. concluded that pimozide reduced motor performance. However, inferences about motor performance and reinforcement efficacy that are based on the performance in just two conditions may be ambiguous. One of the problems is the following.

Morley et al. used dose levels that in the 5-condition procedures produce both motor and reinforcement effects. However, Morley et al. did not test whether their procedure would detect changes in reinforcement efficacy if changes in motor performance also occurred, and, more generally, validation studies were not conducted. Possibly, then, Morley et al.'s results are not discrepant, but simply ambiguous because the procedure under certain conditions is not sensitive to changes in reinforcement efficacy. In any case, in experiments in which the researchers employed enough conditions to estimate the matching law parameters, pimozide has affected the reinforcement efficacy parameter. (Franklin, 1978; Gallistel & Karras, 1984; Hamilton et al., 1985; Heyman, 1983; Heyman et al., 1986).

AMPHETAMINE

Several lines of evidence indicate that neuroleptic behavioral effects are mediated in a significant way by the neurotransmitter dopamine. In vitro studies show that neuroleptics block dopamine postsynaptic receptor sites and that their affinity for such sites typically is higher than for other sites (e.g., Creese, 1983). Patients receiving neuroleptics often show parkinsonian symptoms, and postmortem evaluations indicate that parkinson's patients suffered from a depletion of dopamine cells in the neostriatum (e.g., Iversen & Iversen, 1975). Consequently, it is plausible that the neuroleptic-induced changes in k and R_e were mediated by dopamine receptors. This hypothesis was tested by evaluating the effects of amphetamine on the matching law parameters. Amphetamine increases the availability of dopamine at postsynaptic receptor sites (e.g., Cooper, Bloom, & Roth, 1986). Thus if dopamine mediates changes in k and R_e, amphetamine, especially at low doses, should increase k and decrease R_e. A matching law analysis of amphetamine was also of interest because of previous interpretations of its behavioral effects. According to some researchers, amphetamine induced changes in response rate are mediated by changes in reinforcement processes, whereas others attribute the response rate effects to changes in motor performance. For example, Berlyne, Koenig, and Hirota (1966) suggested that low doses of amphetamine increased reinforcement efficacy and high doses decreased it, but Lyon and Robbins assumed that amphetamine's primary behavioral effect is to alter response topography, and, in support of this view, Fowler, Filewich, and Leberer (1977) showed that amphetamine increased response force at doses of 0.8 and 1.6 mg/kg. Thus, as with neuroleptics, the interpretation of the behavioral changes was uncertain.

Changes in Response Rate and Matching Law Parameters

The procedure for the amphetamine experiment was virtually the same as the one for the pimozide, chlorpromazine, and cis-flupentixol studies. The subjects were rats, the reinforcer was water, and five different reinforcement rates were presented in random order, with a range of about 20 to 700 per hour. Figure 3.13 shows that under these conditions, 0.25 to 1.0 mg/kg doses of amphetamine typically increased response rates, with relatively larger increases at the lower reinforcement rates. In contrast, the 2.0 mg/kg dose increased response rate only at the highest reinforcement rate, and the 3.0 mg/kg decreased response rate at all reinforcement rates. Figure 3.14 shows that changes in R_e were bitonic. Low doses decreased R_e and high doses increased it. The average change in k was monotonically increasing (but see individual results below). The 2.0 mg/kg dose produced a significant increase, but the 3.0 mg/kg dose did not because of subject variability (see below). Thus the changes in reinforcement efficacy followed the pattern predicted by Berlyne et al. (1966): Low doses increased reinforcement efficacy and high doses decreased it. However, there were also changes in motor performance as suggested by Lyon and Robbins (1975). There was a dose dependent increase in the average response rate asymptote.

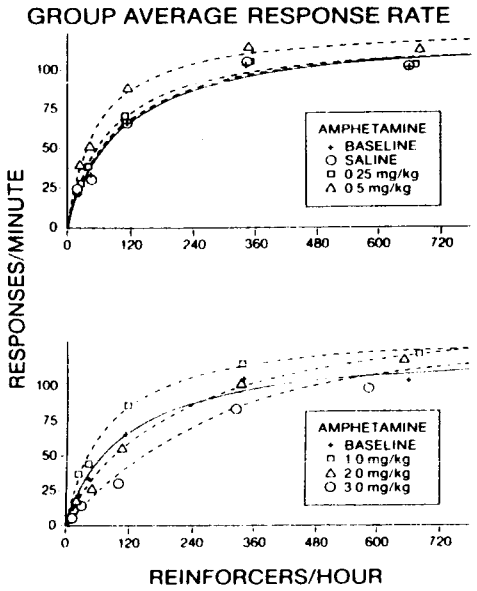


FIG. 3.13. The effect of amphetamine on reinforced responding. The data points show the group average response rates. The curves show the matching law equation predictions of the relationship between response rate and reinforcement rate.

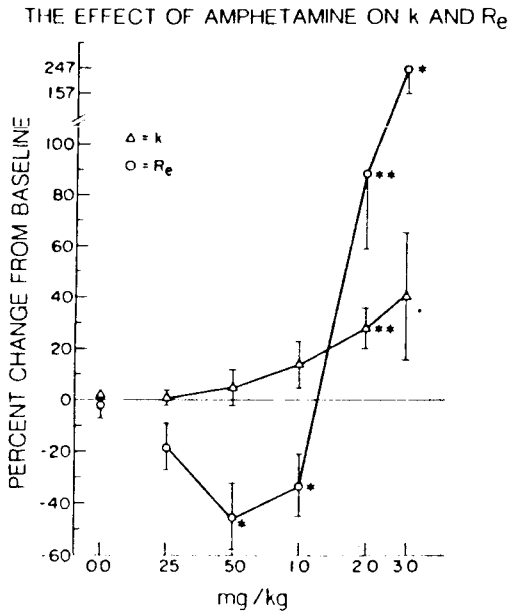


FIG. 3.14. The effect of amphetamine on k and R_e. The open symbols show the average percentage change from baseline. A single asterik indicates a significance level of .05, and two asteriks indicate a .01 level, according to a paired t test.

Individual Differences

Group measures, such as the averages displayed in Fig. 3.14 can reveal general trends. However, averaging can also hide orderly relations if the dependent measure is a nonmonotonic function of the independent variable and individuals differ in terms of their sensitivity to the independent variable. Under these circumstances normalizing the results reveals patterns that would be obscured by averaging. Figure 3.15 provides an example. On the y-axis is change in k and on the x-axis is drug dose as a function of the dose that produced the largest increase (noted as "peak"). For example, for one subject the 3.0 dose produced the largest increase in k, so that the peak-1 dose is 2.0, whereas for another subject, the 1.0 dose produced the largest change so that the peak-1 dose is 0.5 mg/kg. When the results are arranged in this manner, changes in k are bitonic, just as they were for R_e. This pattern is consisted with the findings of other researchers. Bradshaw, Ruddle, and Szabadi (1981) found that amphetamine (0.6 mg/kg) decreased k, and, more generally, high doses of amphetamine typically decrease reinforced responding (e.g., Lyon & Robbins, 1975).

The results from the amphetamine study support the hypothesis that dopamine mediates changes in reinforcement efficacy and/or motor performance. Neu-

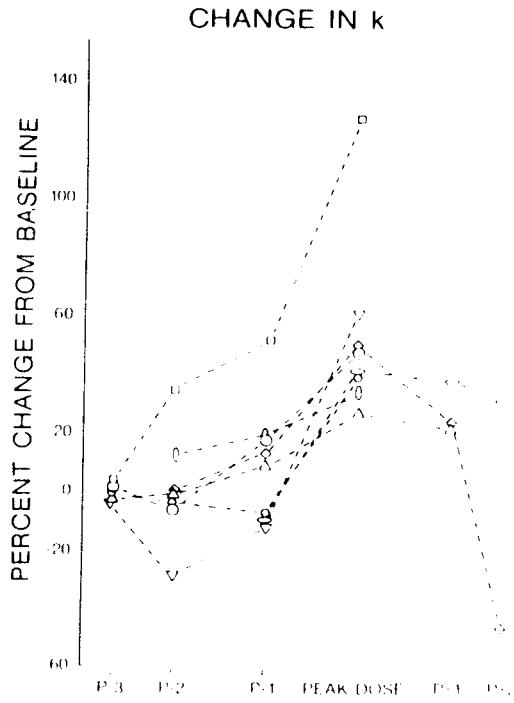


FIG. 3.15. The effects of amphetamine on k, using a normalized x-axis. Each symbol shows the results for one of the 8 subjects, and the x-axis shows dose relative to the one that produced the largest increase in k (see text).

roleptics and amphetamine have opposite effects on the availability of dopamine and they had opposite effects on the matching law parameters. However, the relationships between dopamine and reinforcement efficacy and/or motor performance may be quite complex, since changes in k and R_e were nonmonotonic.

Rate Dependency Principle: A Reinterpretation

We have described the effects of amphetamine on reinforced responding in terms of three variables: reinforcement rate, reinforcement efficacy, and motor performance. An alternative approach is available. In behavioral pharmacology, the effects of amphetamine on reinforced responding are usually described as "rate dependent." This principle, introduced by Dews (e.g., 1958), states that the magnitude of a drug induced change in behavior depends on that behavior's baseline level. For example, if we had presented a rate dependent analysis, the baseline level of responding would have been treated as an independent variable, and it, rather than reinforcement rate, would have been plotted along the x-axes of the graphs. Response based analyses have figured largely in behavioral pharmacology: In scores of studies drug effects have been plotted as a function of baseline response rate (e.g., Dews & Wenger, 1977; Kelleher & Morse, 1968); Robbins (1981) described the principle as one of behavioral pharmacology's two most important contributions to the study of behavior; and Pickens (1977), in his history of behavioral pharmacology, listed rate dependency as one of three major approaches to the study of the behavioral effects of drugs. But according to the matching law equation, response rate is a dependent variable. Consequently, if both the matching law equation and the rate dependency principle can describe the same set of results, it should be possible to establish the logical relationships between the two and, also, determine which provides the more accurate account.

Dews and Wenger (1977) showed that the effects of amphetamine on the rate of reinforced responding was approximated by a two parameter equation. The equation has the form

$$\log (d/bl) = a - b\log(bl), \qquad (2)$$

where d is drug response rate, bl is baseline response rate, and a and b are fitted parameters. In words, Equation 2 says that the logarithm of the drug effect is a linear function with negative slope of the logarithm of the baseline response rate, where drug effect is defined as the ratio of drug and baseline response rates. For drugs that increase response rate, the negative slope implies an inverse relationship between drug effect and baseline response rate: relatively larger increases at lower response rates, or increases at low response rates and no change or even small decreases at high response rates. The parameters of the rate dependency equation (a and b) have not been given interpretations. However, Gonzalez and Byrd (1977) found that the magnitude of the slope parameter (b) was usually between 0.5 and 1.0. This means that the drug effect included a

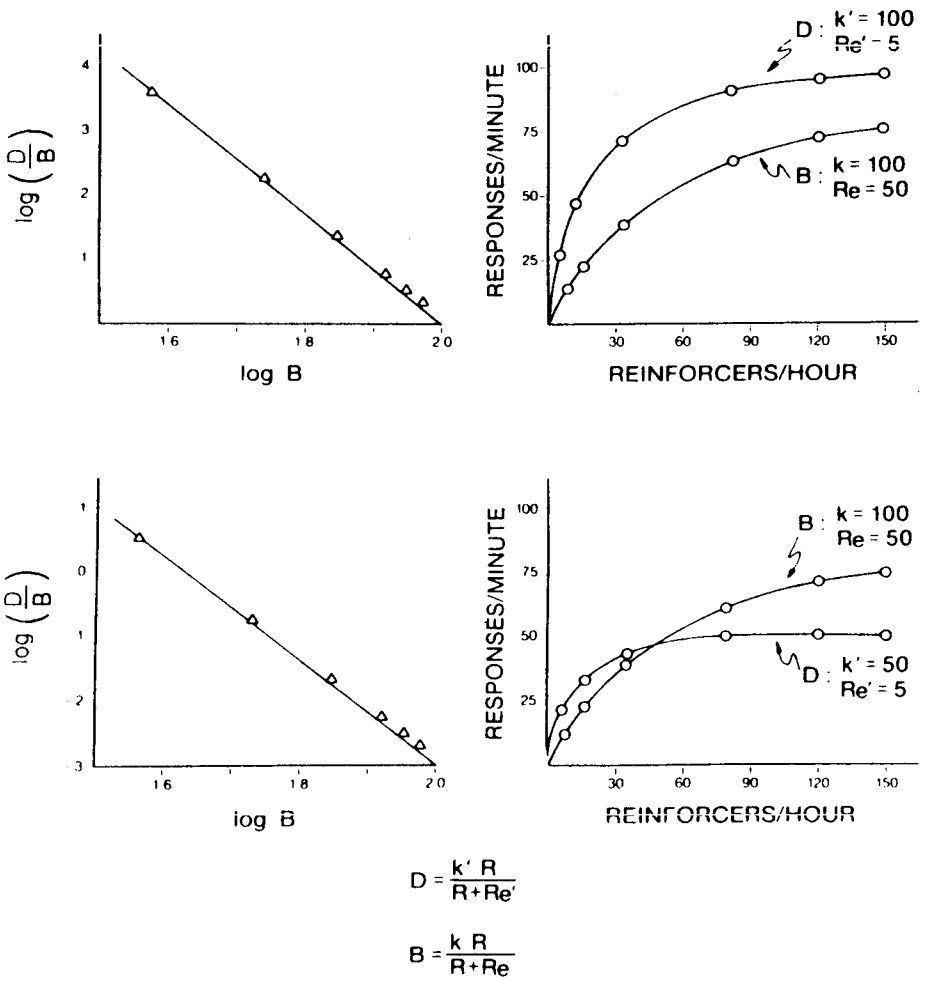
decrease in the range of response rates. For example, as b approaches 1.0 the rate dependency equation implies that the drug condition response rates approached a constant value, equal to the intercept, a, regardless of reinforcement rate.

Results that are consistent with the rate dependency equation are also consistent with the matching law based descriptions. There are several correspondences. First, a decrease in R_e (increase in reinforcement efficacy) means that response rates increased and that the increases were an inverse function of baseline response rate. Second, a decrease in k means that the range of response rates decreased. For example, if k shrinks by one-half then the range of response rates shrinks by one-half. Third, the response rate changes that correspond to a decrease in R_e yield the linear relationship described by the rate dependency equation (Equation 2). This is shown in Fig. 3.16.

On the right side of Fig. 3.16, response rate is plotted as a function of reinforcement rate. For the data in the top panel, hypothetical results, there was a decrease in R_e (from 50 to 5 reinforcers per hour). In the bottom panel there was a decrease in k as well as R_e (k decreased from 100 to 50 responses per minute). On the left side, the same data are graphed in terms of the rate dependency equation. On the x-axis is the logarithm of the baseline response rate: log ($kR/(R + R_e)$), and on the y axis is the logarithm of the ratio of drug to baseline response rates: log $((k'R/(R + R'_e))/(kR/(R + R_e)))$. Consequently, if rate changes that correspond to a decrease in R_e are graphed in terms of the rate dependency equation, there is an approximately linear relationship with negative slope between the logarithm of the drug effect and the logarithm of the baseline response rate. In other words, an increase in reinforcement efficacy in variable-interval schedule experiments produces the results that have been designated "rate dependent." (A rate dependency graph of an increase in R_e was not included in Fig. 3.16. It would plot as an approximately linear function with a positive slope.)

Figure 3.16 shows that the same data set can be described about equally well by the rate dependency equation and the matching law equation (although there are small but systematic deviations from the rate dependent predictions at high response rates). The data, though, were hypothetical so that it would be of interest to determine which account provides the more accurate account of experimental results. The two equations each have two free parameters so that they can easily be compared in terms of how well they fit the data, and, as is noted below, there are situations in which the matching law and rate dependent equation predict qualitatively different outcomes.

The rate dependency equation was fit to the data by the method of least squares. Figure 3.17 shows the results for the subjects that provided the median fit for a given dose level. The rate dependency prediction of a negative slope held for doses between 0.25 and 1.0 mg/kg. But at 2.0 and 3.0 mg/kg, R_e increased. This means that response rates decreased as an inverse function of reinforcement rate. The median fit for the rate dependency equation was $r^2 = 0.58$. This is



$$D = \frac{k' R}{R + Re'}$$

$$B = \frac{k R}{R + Re}$$

FIG. 3.16. Relationship between a change in the matching law parameter R_e and the rate dependency principle. The panels on the right side show response rate as a function of reinforcement rate. In each panel one curve shows baseline responding and the other curve shows the response rates that correspond to a decrease in R_e (top panel) and a decrease in R_e and k (bottom panel). In the left side panels, the same results are graphed according the rate dependency principle. There were small but systematic deviations from the predicted straight line relationship at high baseline response rates.

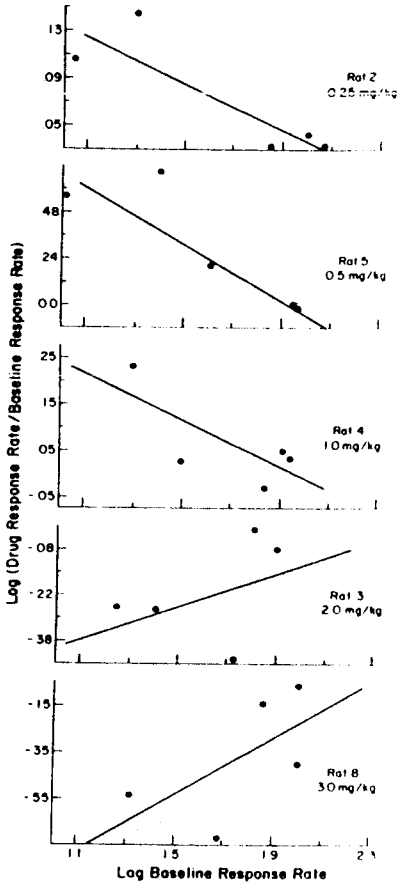


FIG. 3.17. A rate dependency description of the results from the amphetamine experiment. The panels show the subjects that provided the median fit at the indicated dose levels.

similar to what other researchers have obtained. We found four studies in which responding was maintained by variable-interval schedules and the rate dependency equation was used to describe the results (Beecher & Jackson, 1976; Bradshaw et al., 1981; Evans, 1971; Lucki, 1983). The median r^2 was 0.61. In contrast, the median fit for the matching law equation to this data set was r^2 0.96, and in 36 of 38 comparisons (5 drug levels, 8 subjects, and two instances in which subjects did not respond) the matching law equation description was more precise.

There are also situations in which the matching law equation and the rate dependency principle predict qualitatively different outcomes. For example, at high reinforcement rates, response rates typically approach an asymptotic level so that two very different reinforcement rates can be associated with virtually

identical response rates. Under these conditions the rate dependency principle predicts similar changes since the response rates are nearly the same. However, the matching law approach says that identical baseline response rates can differentially change if they are associated with different reinforcement rates and there is a change in R_e. In a previous paper (Heyman & Seiden, 1986) this situation was examined, and it was found that nearly identical response rates differentially shifted when they were associated with different reinforcement rates.

ANTIDEPRESSANTS

In a review of animal models of depression, Willner (1984) concluded that procedures that use intra-cranial self-stimulation as the reinforcer were most promising. His assessment was, in part, based on the assumptions (1) that these procedures measured the reinforcing efficacy of brain stimulation, (2) that depression entails a loss of sensitivity to normally pleasurable activities, and (3) that there is a relationship between pleasure and reinforcement. These assumptions have support. First, the American Psychiatric Association's (1980) description of "major depressive episodes," begins with the sentence: "The essential feature is either a dysphoric mood, usually depression, or loss of interest or pleasure in all or almost all activities and pastimes." Second, there is evidence for a correlation between changes in the matching law measure of reinforcement efficacy and mood. Bradshaw and Szabadi (1978) obtained estimates of k and R_e from a manic depressive patient who participated in a variable-interval schedule experiment (five schedules per session, as we use). These estimates were compared to estimates of mood obtained from an 11-point rating scale. Increases in positive affect were correlated with decreases in R_e and increases in k.

Previous to our work there were two studies that used the matching law or a similar analysis to evaluate the effects of antidepressants on reinforced behavior. Fibiger and Phillips (1981) tested the effects of chronic desipramine treatment on responding maintained by brain stimulation reward. The subjects were rats and the procedure produced measures that are equivalent to k and R_e of the matching law. Chronic desipramine reduced the current level necessary for half-asymptotic responding (that is, it increased reinforcement efficacy). However, Jolly (1983, unpublished undergraduate thesis), using a procedure that was similar to the one used in the amphetamine and acute neuroleptic studies, found that desipramine increased R_e. The different outcomes may have been due to the deprivation conditions. Jolly's rats were water deprived and chronic desipramine appeared to make them sick: they ate less, lost weight, and one died. In contrast, Fibiger and Phillips' subjects were not deprived.

Using a procedure just like the one in the amphetamine and acute neuroleptic studies, we evaluated the effects of two atypical antidepressants: buproprion and nomifensine. Nomifensine was tested at doses from 0.375 to 5.0 mg/kg. Figure

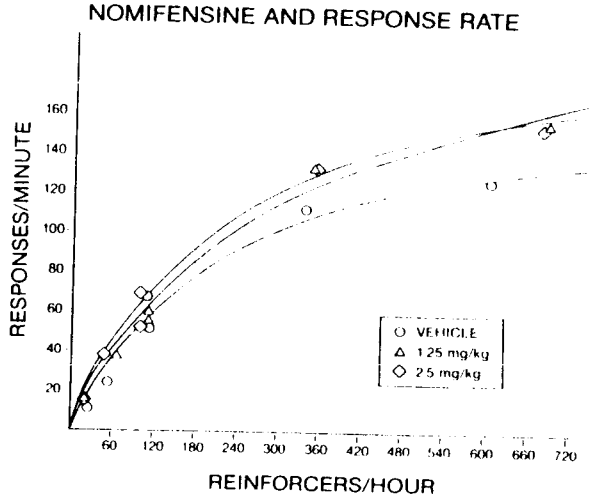


FIG. 3.18. The effects of nomifensine on reinforced responding. The open symbols show the group median response rates.

3.18 shows that the 1.25 and 2.5 mg/kg doses produced modest increases in response rate, and Fig. 3.19 shows that the increases were associated with an increase in motor performance factors. Doses below 1.25 had no discernible effects and doses above 2.5 led to inconsistent, sporadic responding. Buproprion was tested at doses of 5.0 to 40.0 mg/kg. However it produced no detectable change in either k or R_e.

There is evidence that nomifensine, buproprion, and desipramine increased reinforcement efficacy in studies in which the reinforcer was brain stimulation (e.g., Fibiger & Phillips, 1981; Gerhardt & Liebman, 1985; Liebman, Gerhardt, & Prowse, 1982). However in experiments in which behavior was maintained by water and the subjects were deprived, these drugs did not increase sensitivity to reinforcers. In contrast, neuroleptics and amphetamine affected reinforcement efficacy independently of the nature of the reinforcer and deprivation state. The sources for this difference are not known.

NEW DIRECTIONS: AVOIDANCE RESPONDING

De Villiers (1974) showed that the matching law predicted response rates in an avoidance procedure. In his study the subjects were rats, the shocks were presented according to a variable-interval timer, and a lever press eliminated the next programmed shock. Response rates were graphed as a function of the rate of shocks avoided, and the matching law equation approximated the relationship

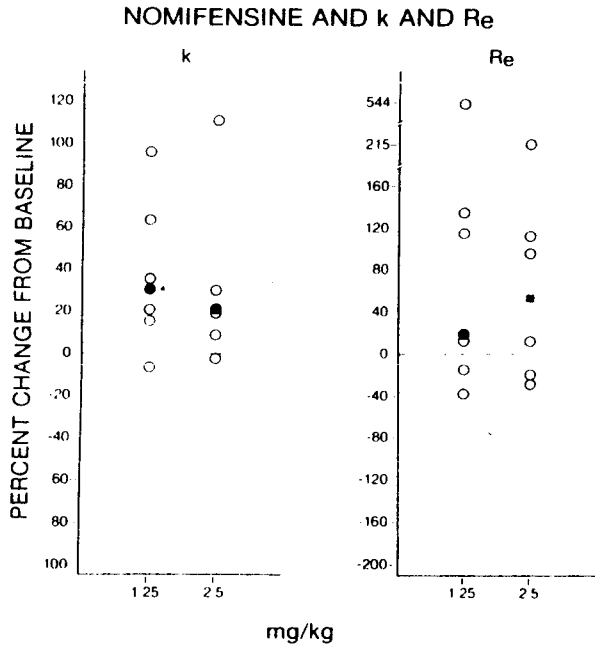


FIG. 3.19. The effect of nomifensine on the asymptotic response rates and rates of reinforcement that maintained a one-half asymptotic response rate (k and R_e). The filled symbols show the group medians. The asterik indicates a .05 significance level, according to the Wilcoxon test.

between these two variables (the mean r^2 was .98). We adapted this procedure in order to test the effects of drugs on avoidance responding.

Squirrel monkeys served as subjects. Each session consisted of five different variable-interval schedules, with each schedule in effect for 9 minutes. When an interval elapsed, a foot shock was delivered. However, if the monkey made a response, a lever press, the next scheduled shock was eliminated. That is, the interval simply elapsed so that responding reduced the frequency of shocks. The intervals varied from 120 sec (30 shocks per hour) to 2.5 sec (1440 shocks per hour). Nine minute time-out periods separated consecutive avoidance schedules. Figures 3.20, 3.21, and 3.22 show some representative results.

As with water and food deprived subjects, low doses of amphetamine increased responding, with response rates in the low reinforcement rate schedules showing relatively larger increases. This pattern of response rate change corresponds to a decrease in R_e. Thus amphetamine increased reinforcement efficacy for responding maintained either by the presentation of a positive reward or the removal of a negative reward.

The 1.5 mg/kg dose of chlorpromazine decreased response rates, with relatively larger decreases in the low reinforcement rate schedules, as in the water reinforcement study. This pattern of change corresponds to an increase in R_e. For example, for this subject the baseline parameter values were k = 136 responses/minute (+/− 8) and R_e = 997 reinforcers/hour (+/− 98), whereas at 1.50 mg/kg chlorpromazine the parameter values were k = 179 responses/minute (+/− 26) and R_e = 1863 reinforcers/hour (+/− 381), little less than a 100% increase.

Diazepam produced a different pattern of response rate changes than did either chlorpromazine or amphetamine. Response rates decreased proportionately. This is the pattern of response rate changes produced by increasing the weight of the lever, and it corresponds to a decrease in k. Thus, unlike amphet-

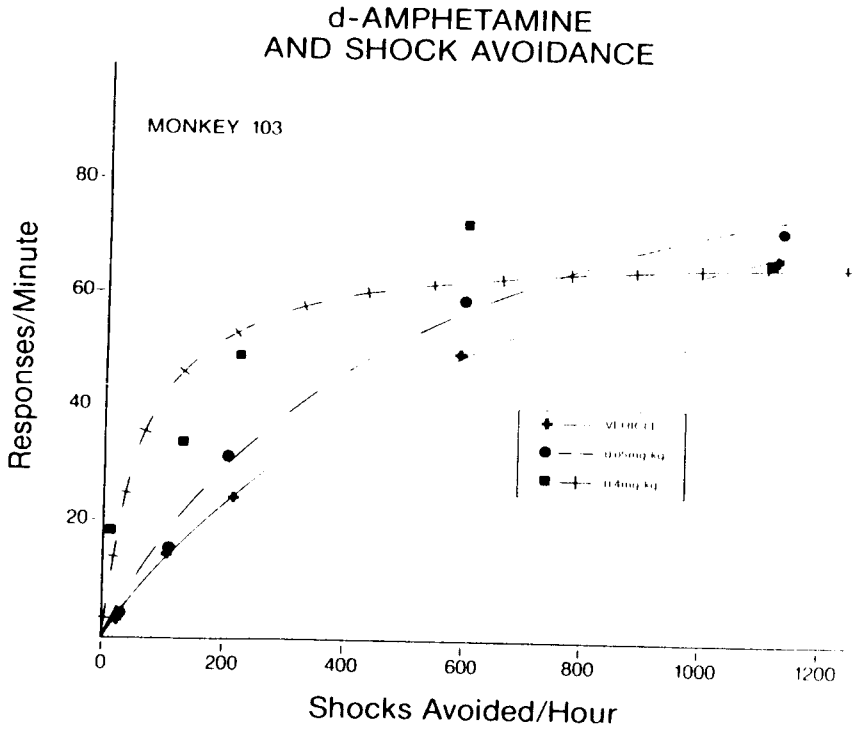


FIG. 3.20. The effect of amphetamine on responding maintained by the avoidance of foot shock. The subject was a squirrel monkey and responses eliminated (avoided) a shock to the foot. The curves show the relationship between response rate and reinforcement rate (shocks avoided) predicted by the matching law equation.

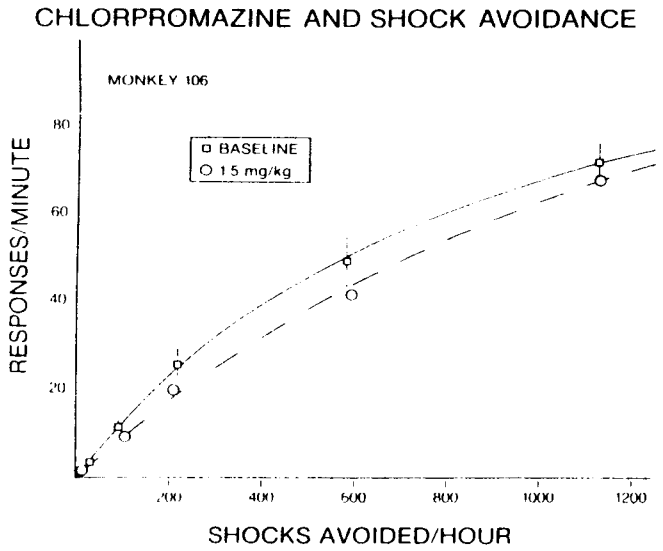


FIG. 3.21. The effect of chlorpromazine on responding maintained by the avoidance of foot shock. The format is the same as in Fig. 3.20.

amine and chlorpromazine, diazepam reduced motor performance. This result may correspond to diazepam's clinical use as a muscle relaxant.

CAVEATS AND SUMMARY

Although methods based on the matching law equation have contributed to our understanding of the pharmacology of reinforced behavior, the approach has drawbacks. First, the experiments take a long time. In our laboratory, subjects have required about 40 to 60 sessions to obtain stable values of k and R_e. Moreover, k and R_e did not always remain strictly stable. In some subjects the parameters gradually drifted, and in others there were abrupt shifts to a new apparently stable level (Heyman & Monaghan, 1987; McSweeney, 1982). In 6 session samples, the average standard error for k was typically between 6 and 12% of its mean and for R_e the percentages were typically 16 to 22% (Heyman et al., 1986 and unpublished data). Second, matching law studies have invariably relied on an individual subject design. That is, each subject is exposed to each treatment level. This has advantages, but between-subject variability in sensitivity to the treatment can obscure an orderly dose-response curve. This may be corrected by normalizing the results, as in Fig. 3.15 or by using a group subject design. Group design studies have not been tried, but could prove helpful. Third,

it may not be possible to obtain reasonable estimates of the matching law parameters if response rates at the two highest reinforcement rates do not approach an asymptote. Without an asymptote, the fitted curve may be more like a straight line than a hyperbola, and, as a result, the parameter estimates will be far outside the range of the observed response and reinforcement rates. Relatedly, it may not be possible to obtain reliable parameter estimates if there is a narrow range of response rates or if the relationship between response rate and reinforcement rate is non-monotonic. The general solution to the curve-fitting problems is is to use as small a serving of the reinforcer as possible and vary the rates of reinforcement over a wide range. This decreases the likelihood of large within session changes in satiation while increasing the likelihood of reinforcement rates that produce asymptotic response rates.

Although there are methodological problems, the matching law approach has been helpful. It was shown in this chapter that the matching law equation described the relationship between response rate and reinforcement rate independently of species, reinforcer, and deprivation state. For example, the equation

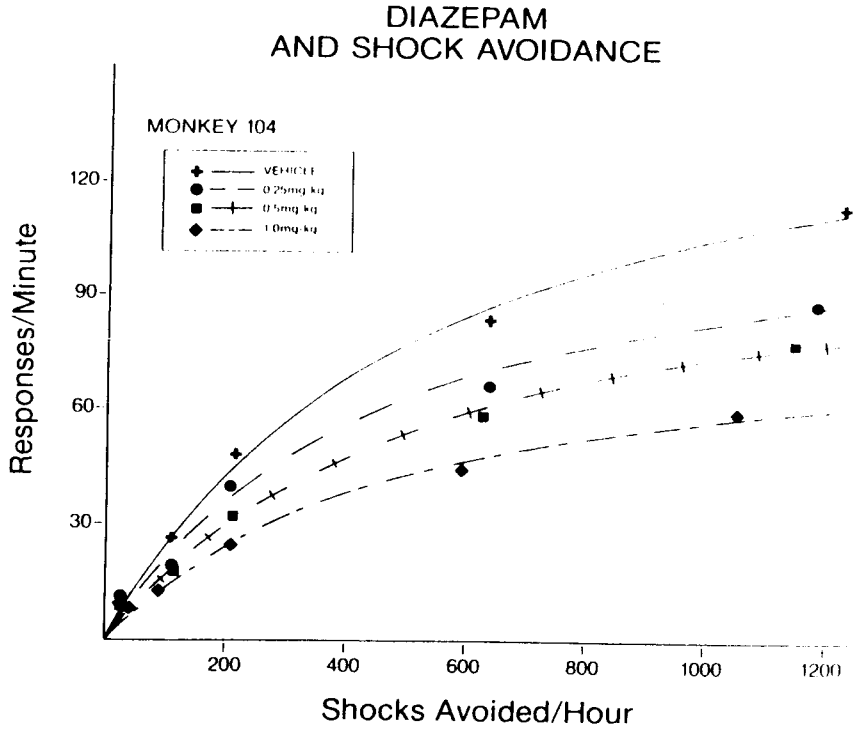


FIG. 3.22. The effect of diazepam on responding maintained by the avoidance of foot shock. The format is the same as in Fig. 3.20.

described the results from appetitive and avoidance procedures equally well, even though in one case a reinforcer is presented and in the other an aversive stimulus is removed. The behavioral pharmacology results were also quite general. Pimozide and chlorpromazine, which were the most widely tested neuroleptics, decreased reinforcement efficacy and slowed motor performance in studies that used different reinforcers, different deprivation conditions, and different response requirements. Amphetamine showed an equally broad generality, increasing reinforcement efficacy for food, water, brain stimulation, and shock avoidance. These findings make it sufficiently clear that certain neuroleptics and amphetamine alter an organism's capacity to be reinforced. This finding sets the stage, we believe, for several lines of research. The following projects seem to us most promising.

First, it would be informative to conduct studies in which the matching law method was combined with more precise biological manipulations. The results from these studies would provide biochemical and anatomical detail not available with systemic injections. Second, changes in reinforcement efficacy are open to further analysis. One path is suggested by the way many researchers have described operant behavior experiments. It is often assumed that an operant procedure is essentially a setting in which the subject chooses between the task the experimenter has arranged and other competing "background" activities, such as resting, exploring, preening, etc. (see, e.g., Baum & Rachlin, 1969; Herrnstein, 1970; McDowell, 1982). From this perspective, R_e is an index of the efficacy of the measured reinforcer relative to the background reinforcement (which is usually not directly measured). Evidence supports this formulation, for example, providing "extra" or free reinforcement increases R_e (Rachlin & Baum, 1972). Thus a drug induced change in R_e may entail a change in the efficacy of the measured reinforcer relative to the efficacy of competing reinforcers. For example, when amphetamine increased the efficacy of water reinforcement it may have done so by decreasing the reinforcing value of activities that competed with lever pressing, such as resting. This hypothesis has not been tested, nor its theoretical implications elaborated. Third, changes in the matching law parameters may have clinical significance. Bradshaw and Szabadi (1978) found that shifts in k and R_e were correlated with mood swings in a manic-depressive patient, and it is possible that the clinical effects of neuroleptics and stimulants are mediated by changes in reinforcement efficacy and/or motor performance. For example, attention is likely to depend, in part, on the reinforcing value of the impinging stimuli. Thus drugs that affect reinforcement processes may affect attentional processes, and, thereby, bring clinical relief.

In the introduction it was pointed out that experimental psychologists have developed techniques for identifying the behavioral mechanisms that mediate changes in reinforced behavior. In this chapter, we reviewed studies based on one of these analytical methods, the matching law equation. The results helped resolve one of the long-standing questions in behavioral pharmacology: whether

or not neuroleptics attenuated reinforcement processes. It was shown that according to the matching law criteria, chlorpromazine pimozide, and fluphenazine decanoate attenuated both reinforcement efficacy and motor performance, but that low doses of cis-flupentixol acted on motor performance without reducing reinforcement efficacy. The matching law equation also led to a reinterpretation of one of the fundamental empirical findings in behavioral pharmacology. It was shown that a decrease in the matching law parameter R_e predicted the rate dependency relationship. That is, according to the matching law criteria, rate dependency reflects an increase in reinforcement efficacy. The results from these matching law studies have, in turn, opened the door to a host of new queries. For example, what biochemical mechanisms account for cis-flupentixol's unique behavioral profile, and would higher doses or a chronic dosing regime lead to changes in reinforcement efficacy? Thus, this chapter, we believe, has demonstrated that the matching law equation offers behavioral pharmacology a a useful analytical tool for interpreting the effects that drugs have on reinforced behavior.

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