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TITLE OF THESIS...DRUG-INDUCED...MODIFICATIONS...OF.....
CONCURRENT...AVOIDANCE...AND...FIXED...RATIO
RESPONDING...IN...THE...SQUIRREL...MONKEY.

UNIVERSITY...OF...ALBERTA...(EDMONTON).....

DEGREE...PH.D.....YEAR GRANTED...1968.....

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DRUG-INDUCED MODIFICATIONS OF CONCURRENT AVOIDANCE AND FIXED-RATIO RESPONDING IN THE SQUIRREL MONKEY, (SAIMIRI SCIUREUS)

by

© SAMUEL D. DALRYMPLE

A DISSERTATION

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE

DEGREE OF

DOCTOR OF PHILOSOPHY

DEPARTMENT OF PSYCHOLOGY

EDMONTON, ALBERTA

AUGUST, 1968

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "Drug-Induced Modifications of Concurrent Avoidance and Fixed-Ratio Responding in the Squirrel Monkey, Saimiri Sciureus" submitted by Samuel D. Dalrymple in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

Three squirrel monkeys (Saimiri Sciureus) were trained to respond according to the parameters of a concurrent free-operant avoidance/FR escape schedule. Following stabilization of performance it was found that the delivery of unavoidable electric shocks during several consecutive experimental sessions was followed by changes in the rate and temporal patterning of responding. These changes persisted throughout the ensuing 100 experimental sessions during which the subjects were exposed to the original, unmodified concurrent schedule.

The effects of each of two drugs, d-amphetamine sulphate and chlorpromazine, were examined in terms of the modifications of performance on the concurrent schedule which followed administration of the drugs in solution. Over the range of dosages studies, the results were consistent with those of previous workers in the field. The detailed effects of each dosage are discussed.

The final experiment represents an attempt to extend to behaviors maintained by aversive control, previous findings concerning d-amphetamine-chlorpromazine antagonism. A dosage of chlorpromazine (0.3 mg/kg i.m.) which suppressed responding was administered jointly with various dosages of d-amphetamine. The rate suppressive effect of chlorpromazine was attenuated by d-amphetamine; this effect was directly related to increasing dosage of the latter. The results are discussed in terms of ongoing rate and patterning of responding as determined by the different components of the complex schedule.

ACKNOWLEDGMENTS

The author wishes to express his gratitude to Dr. R. Stretch for his help and guidance during the planning and execution of this study.

The experimental work was supported in part, by grant No. APA 159 awarded to Dr. R. Stretch by the National Research Council of Canada.

The writer also wishes to express his gratitude to Mrs. F. Kent for her invaluable assistance in the preparation of the manuscript.

Samuel D. Dalrymple

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Introduction

Operant Behavior

The term operant behavior was introduced by B. F. Skinner in 1932, to describe those aspects of the behavior of an organism which are controlled by their consequences. The term emphasizes the fact that the organism operates upon, and thereby changes its environment. These changes in turn, affect the organism and its future behavior.

An important principle, implicit in the above statements, and forming the basic conceptual framework for research in the operent area, is that the characteristics of an organism's behavior are largely determined by what the environmental consequences of that behavior have been in the past. The process of manipulating the behavior of an organism, as a function of its environmental consequences is known as "operant conditioning."

A major characteristic of operant methodology is that the behavior of individual subjects is studied in detail under strictly controlled experimental conditions. A response is selected for measurement and manipulation, and it is one that the organism can perform easily and immediately be in a position to repeat. A common example is the depression of a lever, requiring very little pressure, and permitting rapid repetition. An environmental consequence is selected which increases the probability of the subsequent emission of the response which it follows in time. This is the defining characteristic of an environmental consequence known as a reinforcer.

As Honig (1966) points out, under these conditions, the behavior of the individual subject is predictable from one experimental session to the next, and this frequently provides a stable "baseline" performance against which the effects of the independent variable of interest is evaluated. It should also be emphasized that in a study involving more than one subject the baseline performance usually stabilizes at a different level for each animal.

In operant experiments, the major stimulus events occurring in the experimental space are reinforcing stimuli. The two important functions of a reinforcer are i) that it induces a relatively stable pattern of behavior, and ii) that given adequate control, it will maintain this behavior almost indefinitely. In operant studies, reinforcers are delivered according to carefully specified rules known as schedules of reinforcement. A schedule of reinforcement is defined by Morse (1966) as follows:- "In situations which permit the identification of discrete, unitary responses, a schedule of reinforcement is the prescription for initiating and terminating stimuli, either discriminative or reinforcing, in time and in relation to responses." If a given behavior pattern is invariably followed by a reinforcer, then a continuous reinforcement schedule is operative. However, this is rarely the case in the natural habitat of an organism where it is more likely that a response will be reinforced intermittently.

A wide variety of schedules of intermittent reinforcement have been developed which specify either that a given time interval must elapse or a fixed number of responses be emitted between consecutive presentations of the reinforcer. In practice, these schedules are of fundamental importance in determining the temporal patterning of the subject's responses, and changes in the schedule-parameters can induce marked changes in response rate. At this stage, it should be noted that stimuli which strengthen behavior when they are terminated or avoided are also important controlling factors. These are known as aversive stimuli, and their termination may be regarded as a reinforcing event.

One further type of stimulus is commonly employed in operant work. This is the discriminative stimulus, and it is presented to the subject independently of responses, and may be regarded as setting the occasion for the subject to respond in a specified manner.

The most important data in operant work are those obtained from the rate and pattern of responding of the organism. Since this measure is based on the number of events occurring over a specified time period, then it is meaningful to refer to amounts of responding. If, in a specified time interval, twice as many responses are emitted on one occasion than on a second occasion, then twice as much behavior occurred during the former period.

Psychologists using operant methodology to study behavior tend to emphasize observable causes when describing behavior and to avoid

reference to unobservable processes. Hønig (1966) suggests that the primary reason for this approach is that the observable causes can be manipulated according to the demands of scientific analysis. As a result of this approach, the terms and concepts that have been developed in the operant area are functionally defined in terms of such observable processes.

Over the past three decades, operant techniques have been applied to an ever-increasing variety of problems in behavioral research, with the result that the field is now relatively diverse.

An area of research that is of particular relevance to the present study is concerned with behavior controlled by aversive stimuli. Kelleher (1965) defines this area in the following manner: "In technical terms, an aversive stimulus is a stimulus that an organism will work to escape from or to avoid, for example, a severe electric shock is an aversive stimulus for most organisms. Operant conditioning experiments emphasize the study of the effects of aversive stimuli on the rate or pattern of occurrence of responses that are related in different ways to the presentation of these stimuli."

Hence, with regard to aversive stimuli, several procedural operations are available to the experimenter, and these have been described by Church (1963). Church recognizes four alternative procedures:-

a) The escape procedure. The noxious stimulus is present and the response terminates it.

b) The avoidance procedure. The aversive stimulus is absent, and a response prolongs its absence.

c) The punishment procedure. The noxious stimulus is absent and the response produces it.

d) The preservation procedure. The noxious stimulus is present and the response prolongs its presence.

In terms of the present study, one of the more important of these is classified as an avoidance schedule. A good representative example of the study of avoidance behavior is provided by an experiment reported by Clark (1961). Chimpanzees were trained to avoid shock under the following parameters of the free-operant avoidance schedule. Brief electric shocks were delivered to the feet of the animal which was restrained in an appropriate harness. These shocks were delivered every 3 seconds (the shock-shock interval) unless the animal responded; each response delayed the shock for a 20 second (response-shock) interval. Clark reported that during the initial sessions, brief periods of responding occurred after some shocks, but numerous shocks were delivered. During subsequent sessions, relatively prolonged periods of responding occurred after each shock until the final pattern of performance appeared which was characterized

by relatively stable rates of responding that were high enough to avoid almost all shocks. Other workers using this type of schedule, have found that subjects exposed to such parameters develop a stable baseline rate of responding which shows little variation over prolonged periods of time. This type of schedule formed one component of the complex schedule employed in the present study.

Escape schedules are described by Kelleher as those in which a subject will respond in order to terminate aversive stimuli. Azrin, Holz and Hake (1962) have demonstrated that squirrel monkeys (Saimiri sciureus) will respond at high rates on an escape procedure in which responses intermittently terminate an exteroceptive stimulus in the presence of which unavoidable shocks are presented. In more detail, the initial procedure consisted of the delivery of unavoidable foot shocks at irregular intervals of time, averaging 2 minutes, in the presence of a visual stimulus. In the absence of this stimulus, shocks were not presented, (i.e. a "safe" period); thus the visual stimulus became established as a period during which both stimulus and shocks were present. Finally, the parameters of the schedule were such that a number of responses specified by a fixed ratio schedule[1] were required to produce termination of the aversive stimulus.

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[1] A fixed ratio (FR) schedule, is defined by Ferster and Skinner(1957) as "A schedule of intermittent reinforcement in which a response is reinforced upon completion of a fixed number of responses counted from the preceding reinforcement." (p. 272).

Azrin et al. found that when the number of responses required to produce the safe period was 150 or less, the monkeys responded at a high rate in the presence of the stimulus, but when the response requirement was 250 to 350, a pause after each safe period appeared. This pause was followed by a high response rate that was sustained until the aversive stimulus was terminated. Shock delivery occurred while the subject was responding at the high rate, but was not followed by any reduction in this rate. Kelleher, in his summary of these results, concludes that "the scheduled relation between responses and termination of the stimulus is apparently more important than the unscheduled relation between responses and shocks." In other words, the subjects continued to respond at a high rate, in spite of shock presentation, in order to terminate the aversive stimulus. More recently, Morse and Kelleher (1966) have shown that squirrel monkeys will terminate a schedule complex, consisting of an exteroceptive stimulus (houselight) associated with an aversive stimulus (brief electric shocks) under the parameters of fixed-interval, fixed-ratio and multiple fixed-interval, fixed-ratio schedules. They found that the patterns of behavior under these schedules were similar to those generated when food is acting as the reinforcement, and conclude that the actual schedule of reinforcement is more important in the control of behavior than the nature of the reinforcer.

Termination of an aversive stimulus complex according to the parameters of a fixed ratio schedule, formed the second component of the complex schedule employed in the present study.

Many workers in the operant area have reported successful attempts to maintain performance on complex schedules having more than one component. Many examples of such behavior are reported in Ferster and Skinner (1957). However, of the complex schedules, the concurrent schedule[1] is of particular relevance to the present study. Sidman (1962) reported an experiment in which rhesus monkeys were initially trained to press a lever in order to postpone brief electric shocks (free-operant avoidance) and simultaneously, to pull a chain a fixed number of times in order to obtain a food reinforcement (FR). Subsequently, the author showed that performance was maintained when the reinforcing event following the completion of the FR requirement was a period of time out from the avoidance procedure instead of food. The schedule employed in the present study was very similar to the one used by Sidman.

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[1] A concurrent schedule was originally defined by Ferster and Skinner (1957) as "Two or more schedules independently arranged but operating at the same time, reinforcements being set up by both." (p. 724). This type of schedule may be programmed either for a single manipulandum, involving only one type of response, or with one manipulandum for each component of the schedule, where more than one type of response would be required. Catania, Deegan and Cook (1966) argue in favor of the term conjoint when referring to the former experimental arrangement and reserve the term concurrent for describing the latter form.

Behavioral Pharmacology.

In recent years, pharmacologists and clinicians have discovered many new drugs, for example, the phenothiazines, with hitherto unsuspected kinds of effects on behavior. This has resulted in increased concern with behavioral pharmacology, since it has become important that an understanding of the mode of action of these drugs should be achieved. While interest was directed initially, towards the possible utility of these drugs in the psychiatric field, behavioral pharmacology is now concerned with the more general problems associated with drug-induced behavioral modifications.

Experiments designed to investigate the effects of drugs on behavior have been classified by Dews and Morse (1961) into two major divisions: 1) the effects of drugs on unconditioned behavior 2) the effects of drugs on conditioned behavior. The former type of study is concerned with the gross behavioral changes following drug administration, and is illustrated by an experiment first reported by Gunn and Gurd (1940), the findings of which, were subsequently confirmed by Chance (1946, 1947). In each case, several mice were placed together in a single cage following the administration of amphetamine to each subject. The primary finding was that the lethal effects of amphetamine were enhanced by the aggregation of the animals in a relatively confined space. The statistical measure employed in order to evaluate this effect was the LD_{50} dosage. This is the dosage level which, when administered to a sample of animals selected at random from a population (defined statistically) exerts

a lethal effect on 50 per cent of the subjects. The workers mentioned above, found that when several mice were grouped together in a single cage, the LD_{50} dosage of amphetamine was reduced to approximately one tenth of the dose necessary for mice caged individually. Weiss and Laties (1959) made a further important contribution to this area of research when they demonstrated that the toxicity of the drug was enhanced by the administration of electric shocks to a rat.

This type of experiment gave important information on the gross behavioral changes induced by drugs. However, a different approach was necessary in order to identify drug effects in detail. This has been supplied by the administration of drugs in dosages which are not lethal to the subject, but are sufficient to induce changes in behavior. A further aspect of this approach is that the dosage is administered to an animal conditioned to perform a given response under carefully specified experimental conditions. Thus, following a detailed specification of the subject's performance under these experimental conditions, the behavioral effects of a drug can be evaluated in terms of deviations from this control behavior pattern following the administration of the drug to the animal.

An example of this type of study is given by an experiment performed by Verhave, Owen and Robbins (1959). Using rats as subjects, the authors trained each one to rotate a small wheel in the wall of a specially constructed cage in order to avoid shock that was otherwise delivered to the feet of the animal through the grid floor. A buzzer served as a warning signal, and was sounded for seven seconds prior to shock

delivery. If the subject failed to avoid the shock, then the latter was delivered continuously until terminated by rotation of the wheel. Thus, the paramaters of the schedule also included an escape contingency.

The behavioral effects of two drugs were of interest to the experimenters; chlorpromazine and secobarbital, both of which have been regarded as drugs that depress behavioral output. They found that chlorpromazine in a dosage of 4 milligrams per kilogram (mg/kg) of body weight caused an 80 per cent reduction in avoidance responding and approximately a 5 per cent reduction in escape behavior. A dosage of 25 mg/kg of secobarbital was followed by a reduction of approximately 70 per cent in avoidance behavior and a 40 per cent reduction in escape responding.

The important principles emerging from this type of study may be summarized in the following manner:

1) Drug dosages of the magnitude employed in the above study exert effects which are relatively temporary.

2) The effects of the drug are evaluated in terms of a specific aspect of behavior in an environment which can be controlled and manipulated by the experimenter according to the principles of scientific analysis.

3) The conditioned response provides a baseline control performance and the drug effects are evaluated in terms of a deviation from, and subsequent return to this control level; permanent effects may be identified by the absence of the latter.

4) It is apparent from studies such as the one by Weiss and Laties cited above that drugs cannot be loosely classified as behavioral depressants or excitants, but that their effects must be examined in terms of the ongoing behavior patterns.

It appeared, to many workers, that the practical demands of points 2 and 3 (above) were most adequately fulfilled by the use of operant methods. An example of this type of study is one cited by Sidman (1955) in which he examined the effects of amphetamine on the performance of rats under conditions of positive reinforcement. The subjects were deprived of water which they were able to obtain during experimental sessions by depressing a lever according to the requirements of a DRL schedule.[1] This schedule specifies that a response will be reinforced only when it occurs after a given interval of time has elapsed since the immediately preceding response. Thus, the important dependent variable in Sidman's experiment was the time elapsing between responses (i.e. the distribution of interresponse times)... The author found that there was a significant reduction in the duration of these interresponse times following the administration of amphetamine. This of course, indicates an increase in the relatively low rates of responding which is characteristic of performance maintained by a DRL schedule.

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[1] A DRL schedule is defined by Ferster and Skinner (1957) as a schedule in which reinforcements occur only when the [response] rate is below some specified level.

In examining the results of this study, it is evident that the experimental design gives information on the deviations in performance from the control baseline following drug administration. Furthermore, the question regarding the relatively temporary and/or permanent effects of the drug are revealed by the data obtained from subsequent control sessions during which the drug is not administered.

Several questions are raised by experiments of this nature; for example, is the effect of amphetamine reported in Sidman's study specific to the ongoing behavior pattern, or may it be regarded as a general stimulant which invariably increases behavioral output? One approach to this problem is to evaluate the effects of this drug against a variety of baseline performances maintained by different schedules of reinforcement. Many workers in this area have shown that the effects of amphetamine and other drugs which exert behavioral modifications, are determined by the pattern of ongoing behavior. Of particular relevance is the work of Dews (1956). Using food-deprived pigeons as subjects, two types of behavior were generated according to the requirements of a multiple schedule[1] technique. Each of the schedule components was under appropriate stimulus control, so

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[1] A multiple schedule is defined by Ferster and Skinner (1957) in the following manner:- "Reinforcement is programmed by two or more schedules, alternating, usually at random, each schedule accompanied by an appropriate stimulus as long as the schedule is in force."

that when the response key was transilluminated by a red light, 60 pecks of the key were required in order to produce grain (the reinforcer), and when a blue light was substituted for the red, the first peck was reinforced which occurred 15 minutes after the preceding reinforcement. Thus the two components of the schedule were a fixed ratio (FR) of 60 responses and a fixed interval (FI) of 15 min.

When acting independently, the FR and FI schedules typically generate different rates and temporal patterning of responding. When a FR schedule is operative, the subject typically pauses briefly following the delivery of a reinforcement, and then responds at a relatively high rate until the next reinforcement is obtained.

Under FI conditions, a reinforcement is usually followed by a pause in responding which is followed by a relatively low but accelerating response rate which is relatively high immediately before the delivery of the next reinforcement.

Dews was interested in the effects of pentobarbital sodium on these two patterns of behavior (this drug had previously been classified as a general depressant which decreased behavioral output). He found that the drug reduced responding on the FI component almost to zero. The response output on the FR component was reduced, but the subject maintained a relatively substantial output.

Thus, it was demonstrated that pentobarbital sodium does not exert a general depressive effect on all behavior, but that a major determinant of its action is the ongoing rate and temporal pattern of responding

Similar findings have been reported for other psycho-active drugs, and the work of Dews (1958a, b), Herrnstein and Morse (1956), Sidman (1956), Blough (1957) amongst others, has lent support to the important principle that ongoing behavior is a major determinant of the behavioral effects of drugs.

Since behavioral pharmacology is a relatively new science, interest has been confined largely to those drugs which have been generally classified according to the marked behavioral changes which followed their administration. Primary amongst these are the stimulants such as d-amphetamine, methamphetamine and methylphenidate; the antidepressants, consisting primarily, of the monoamine oxidase inhibitors, and the depressants such as chlorpromazine, trifluoperazine and the barbiturate hypnotics. To a lesser extent, the anticholinergic drugs such as atropine and scopolamine have been studied [notably in the work of Carlton (1963)], and some attention has been given to the hallucinogens such as lysergic acid diethylamide.

Finally, analgesic drugs such as morphine have been examined by workers in the area following initial investigations of which the work of Weiss (1956) serves as an example.

Since two of the drugs mentioned above, d-amphetamine sulphate and chlorpromazine, were employed in the present study, these will be examined in greater detail in terms of their pharmacological and behavioral properties.

d-Amphetamine sulphate i) Pharmacological properties. d-Amphetamine is described as a sympathomimetic noncatechol amine. Dextro-amphetamine is the d-isomer of the compound, and is usually prepared in the form of the d-amphetamine sulphate salt. Goodman and Gilman (1965) describe this drug as one of the most potent of the sympathomimetic amines with respect to the stimulation of the central nervous system. Animals given a sufficient dosage of d-amphetamine characteristically show muscular tremor, increased motor activity, agitation and sleeplessness. Pharmacologists have suggested that these effects are due to cortical stimulation, and possibly, to stimulation of the reticular activating system. The drug also stimulates the respiratory center, increases heart rate, and tends to exert an anorexic effect.

II) Behavioral effects.

One of the earliest demonstrations of the effects of the amphetamines on behavior maintained by operant techniques was reported by Dews (1956). This was described in the report mentioned earlier in this section. He examined the effects of methamphetamine on behavior maintained by an FI schedule. Pigeons were maintained on partial food deprivation, and, after being trained to peck at an illuminated plastic key, were given access to the key for a few hours each day.

The interval requirement was then gradually introduced, until after several sessions, a stable behavior pattern at FI 15 minutes had emerged. Thus, an animal was required to wait 15 minutes, and

then to peck the key once after which a food reinforcement would be presented for 4 seconds. Under these conditions, Dews was able to generate the characteristic FI behavior pattern (described earlier) in all the subjects.

When behavior maintained by the FI 15 min. schedule had stabilized and was showing very little variation over consecutive experimental sessions, a dosage of 3 mg/kg of methamphetamine was injected into the subject. Dews found that the characteristic effect of methamphetamine is to lead to an increase in the number of responses made per interval. However, the maximum rate of responding is not increased, instead, the animal responds steadily at the beginning of the interval at a time when, under control conditions, there is little or no responding.

Since Dews' early work in this field, a considerable body of literature has accumulated on the effects of amphetamines on behavior. Many studies have shown that where animals are required to emit a given response in order to avoid shock, amphetamine tends to increase the rate of avoidance responding.

Verhave (1958), using rats as subjects, showed that methamphetamine in the dosage range 0.5 to 1.0 mg/kg increased the response rate on a free-operant avoidance schedule. At relatively high doses (2 mg/kg) there was a depression of the response rate, and at very high doses (4 mg/kg) there was a temporary elimination of responding. Verhave also demonstrated that behavior returned to the pre-drug level within 3 to 6 experimental sessions following drug administration.

Hearst and Whalen in 1963, analyzed this finding in some detail. They demonstrated that, in a discriminated avoidance situation where a warning signal precedes shock, a dosage of 3 mg/kg of d-amphetamine increased the number of shocks avoided. They also noted that the general topography of the animals' behavior was affected by the drug. For example, it showed less tendency to crouch when the warning signal was presented, and was, therefore, more likely to emit the required response. The authors argued that since many studies have failed to show improved avoidance performance with increased shock intensitites, the augmentative effect of amphetamine upon avoidance responding is probably not a function of the drug increasing the aversiveness of the shock.

The influence of amphetamines has also been studied in punishment and conflict situations. In 1956, Brady reported that the response rate of an animal during a stimulus paired with shock decreased under 2 mg/kg of amphetamine. Teitelbaum and Derks (1958) found that the effect of d-amphetamine varied with dosage. Rats were used as subjects, and were required to lick from a water bottle in order to avoid shock which was paired with a discriminative stimulus. A dose of 0.5 mg/kg tended to suppress response rates in the presence of the shock-paired stimulus, but increased the rates in the absence of that stimulus. With a higher dosage of 1 mg/kg the animal responded continuously at high rates, both in the presence and absence of the stimulus. Geller (1962) and Sidley (1963) have both presented evidence that lower rates of response under amphetamine,

result when the subject is punished. However, studies by Barry, Wagner and Miller (1962; 1963) failed to confirm this finding.

Kelleher and Morse (1964) compared behavior under shock-escape schedules with that induced by food reinforcement schedules. They found that d-amphetamine (0.1 to 1.0 mg/kg) produced essentially similar effects upon response rate regardless of whether food reward or shock escape was programmed. An additional finding was that the direction of the drug-induced behavioral change varied as a function of the reinforcement schedule maintaining the behavior. When fixed ratio contingencies were programmed, high doses of amphetamine decreased the response rate while fixed interval responding was accelerated. This phenomenon was further investigated by C. B. Smith (1964) who used a multiple Fixed Interval (300 sec.) - Fixed Ratio (33 responses) schedule to study the effects of d-amphetamine on interval and ratio behavior. Smith used pigeons as subjects, and each was exposed to a daily 90 minute experimental session. During this period, the subject was placed in an experimental chamber where it had access to an illuminated key, and was permitted to obtain 40 reinforcements. The key was transilluminated by a blue light during the ratio component, and by a red light during the interval component. On a day when a drug was to be administered, d-amphetamine was injected 5 minutes prior to the experimental session for that day. At least 3 days elapsed between any two consecutive injections.

The most important result to emerge from Smith's work was an indisputable confirmation of Kelleher and Morse's finding. d-amphetamine increased rates of responding during the fixed interval component and had the opposite effect on the fixed ratio component. In fact, his results permitted him to make the more general statement that d-amphetamine tends to increase rates of responding during portions of a schedule characterized by low rates of responding (FI), and suppress response rates during the schedule component characterized by high rates of responding (FR).

The important points of the paper are that Smith was able to demonstrate that 1) Amphetamine modifies behavior in different ways depending on the schedule of reinforcement and 2) Both FI and FR schedules are sensitive to the drug. This second point is contrary to many previous reports of workers in this field, who have noted the apparent insensitivity of behavior under FR schedules to modification by drugs. However, it is compatible with the report of Owen (1960) who found that FR performance maintained by positive reinforcement, was considerably affected by amphetamine, which increased post-reinforcement pausing, and consistently decreased response rate under an FR 30 schedule.

When the schedule of reinforcement requires temporal spacing of responding as in the case of the differential reinforcement of low rates (DRL) schedule, amphetamine tends to produce a general increase in response rate. This has been demonstrated by Schuster and Zimmerman (1961) and subsequently confirmed by Mechner and Latranyi (1963). Performance on DRL schedules is often analyzed in terms of

the time elapsing between responses relative to the time required to elapse before a response is reinforced. Thus, if the schedule parameters specify that 20 sec must elapse between a given response and the preceding response in order that the former be effective in producing a reinforcement, then the performance is analyzed in terms of the number of responses occurring in each 2 sec component of the 20 sec period (which is reset by each response). The above authors found that following the administration of amphetamine, a greater number of responses occurred during earlier 2 sec components of the 20 sec period than was the case under control (non-drug) conditions.

It is of interest to note that drugs generally classified with amphetamine as stimulants, exert a similar effect. Stretch and Skinner (1967) demonstrated that the administration of methylphenidate to rats in which performance was maintained by a free-operant avoidance schedule, was followed by an increased response rate. A further important finding of these authors was that when a warning signal was introduced which preceded shock delivery, the administration of methylphenidate was followed by an increase in the occurrence of short response latencies after signal onset. This introduces the topic of drug effects on performance where a discriminative stimulus is programmed to occur. Weiss and Laties (1966) demonstrated that the effects of d-amphetamine on behavior maintained by an FI schedule were markedly offset when a stimulus

referred to as an added clock[1] was introduced into the programme. The authors were attempting to verify the suggestion by Dews (1955, 1958 a + b) and Morse and Herrnstein (1956) that behavior controlled by internal stimuli may be more sensitive to modification by drugs than behavior controlled by exteroceptive stimuli. The experimental parameters were as follows:- The length of the interval was 5 min. and the clock when present, consisted of 5 different visual symbols projected on the response key in an invariant order. Each symbol represented a 1 min. period within the interval. Under non-drug, control conditions, the subjects tended to place their responses in the last minute of the interval when the clock was present, and this tendency persisted following the injection of d-amphetamine sulphate. When the clock was not present, the administration of amphetamine was followed by an overall increase in response rate in the earlier part of the interval, in accordance with Dews' (1956) findings summarized in the preceding part of this section.

More recently McMillan and Morse (1967) have confirmed that stimulus control of performance is not reliably affected by the administration of d-amphetamine.

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[1] An added clock is defined by Ferster and Skinner (1957) as follows: "A stimulus, some dimension of which varies systematically with time, usually measured from the preceding reinforcement, but possibly from some other point."

The following conclusions may be drawn from the above review of the behavioral effects of the amphetamines:-

1. The effects of amphetamine are determined to a considerable extent by the pattern of ongoing behavior.

2. There is evidence that the administration of amphetamine is followed by an enhancement of relatively low response rates and a decrement in relatively high rates of responding.

3. A greater degree of control of ongoing behavior exerted by the schedule parameters, appears to be associated with a reduction in the behavioral changes that follow the administration of amphetamine.

Chlorpromazine 1) Pharmacological properties.

Chlorpromazine is a derivative of phenothiazine and is widely used in medical practice as a sedative. Goodman and Gilman (1965) describe its gross behavioral effects in terms of the "neurolytic syndrome." This is characterized by a reduction in psychomotor activity and emotional reactivity accompanied by an affective indifference to objects and events in the environment. Spontaneous motor activity is depressed, and following the administration of high doses, a cataleptic effect may appear. The drug appears to cause changes at all levels of the cerebro-spinal axis and its mode of action appears to be due to a blocking of the action of norepinephrine in the brain. It is usually prepared in the form of the chlorpromazine hydrochloride salt.

ii) Behavioral effects.

A great number of behavioral effects of chlorpromazine have been studied in many experiments. The following review is selective in that only those of immediate relevance to the present study have been included.

The study reported by Verhave et al. (1959) mentioned earlier in this section serves as an introduction to this topic. Rats were required to avoid or escape from shock by rotating a conveniently located wheel within 7 sec of the onset of a warning signal. As already mentioned, the administration of chlorpromazine was followed by an overall depression of responding under the parameters of the schedule. It should be recalled, however, that as was the case with the amphetamines, the modifications of behavior which followed the administration of chlorpromazine were dependent on the ongoing rate of responding. The results of Verhave's study showed an 80 per cent reduction in avoidance responding, but only a 5 per cent reduction of escape responding. Weissman (1959) has also reported a clear demonstration of this differential drug effect. He used food deprived rats as subjects, and a multiple schedule of reinforcement consisting of an avoidance component, a continuous reinforcement (CRF) component (with milk as the reinforcer) and an extinction component. Under control conditions, the first component sustained a relatively high response rate, the second a slower but constant rate, and the third, a very low rate. Chlorpromazine in dosages within

the range 1.0 to 3.0 mg/kg reduced the high avoidance rate, but the lower rate maintained by the CRF component was relatively unchanged. The latter was maintained even at the highest dosage when the avoidance response rate was reduced almost to zero.

The above studies by Verhave et al. and Weissman emphasize the fact that it is misleading to classify chlorpromazine as a general depressant drug. It is also confusing to group a variety of different drugs, which exert similar gross effects, in the same class. As already stated, Verhave et al. (1959) demonstrated the different effects of secobarbital and chlorpromazine, which are both classified as depressant drugs. Blough (1958) has reported an experiment in which he demonstrated that pentobarbital and chlorpromazine exerted opposite effects on the ongoing behavior. He trained pigeons to block, with the head, 2 horizontal light beams that crossed the cage at right angles to each other. This involved each subject keeping its head at the point of intersection of the beams, and this produced a food reinforcement. Following each occasion on which food was obtained by this method, the length of time during which the subject was required to block the light beams was increased by 2 sec. Simultaneously, and independently, this time period was reduced by 2 sec in every 4 min. Thus, performance stabilized at approximately one reinforcement every 4 min. The average required response duration was 5 sec under control conditions. This increased to an average value of 10 sec following the administration of 10 mg/kg chlorpromazine, and decreased to about 2 sec following the injection of 10 mg/kg pentobarbital. Morse (1964) has shown that chlorpromazine and

barbiturates differ in their effects on responding maintained by a simultaneous food reinforcement and punishment schedule. Using pigeons as subjects, key-pecking responses maintained by a variable interval schedule of food reinforcement, were punished by brief electric shocks. Under control (non-drug) conditions, responding on the simultaneous food and punishment schedule was suppressed and occurred at a uniform rate that appeared to be inversely related to the punishment intensity. Administration of amobarbital partially restored responding suppressed by punishment, but chlorpromazine showed no tendency to attenuate this suppression of responding.

Chlorpromazine appears to exert similar effects on behavior maintained by both positive reinforcement and aversive control. A study reported by Waller and Waller (1962) illustrates this point. Dogs were used as subjects, and they were trained to perform according to the parameters of a multiple schedule having both appetitive and avoidance components. The authors obtained no evidence that chlorpromazine had a differential depressing effect as a function of the schedule component. The dosage range of chlorpromazine was from 30 to 225 mg. At the low dosage, the response rate on the food reinforced component increases slightly while the avoidance response rate remained relatively unchanged. At the higher dosages, both components showed an approximately equal degree of response rate depression. The authors conclude that the results of the study indicate that there are no reliable differences between the effects of this drug on the behavior maintained by the two components of the

schedule, apart from some indication that the food-maintained behavior is slightly more sensitive to chlorpromazine.

Bindra and Anchel (1963) have reported that under certain experimental conditions the administration of chlorpromazine in relatively low dosages is followed by an increase in response rate. They trained rats to remain immobile in order to avoid the delivery of electric shock. Following the injection of the lowest chlorpromazine dosage of the range (2 mg/kg) a decrement in the immobility response was noted in all subjects.

As was the case with the amphetamines, the introduction of a discriminative stimulus tends to modify further, the behavioral effects of chlorpromazine. Sidley and Schoenfeld (1963) reported an overall depression of avoidance behavior following the administration of chlorpromazine, when no warning signal was present. However, in the Weiss and Laties (1966) report described earlier, the presence of an added clock decreased the effect of chlorpromazine on behavior maintained by a FI schedule. The authors emphasize, however, that the influence of the added clock is much lower following chlorpromazine administration, than was the case with amphetamine.

A further example of the differential effects of chlorpromazine which has a direct bearing on the present study, is that of Thomas (1965). He studied the performance of pigeons on a concurrent schedule, and the effects of chlorpromazine on this behavior. The schedule consisted of a time out (TO) from avoidance component, and a variable ratio (VR) of 140 responses as the second component.

Each avoidance response postponed the occurrence of a TO period for a specified time interval. Under control conditions, the avoidance response rate was very low with respect to the VR response rate. Thomas was able to demonstrate clearly, that chlorpromazine in dosages from 2.5 to 5.0 mg/kg, increased markedly the rate of responding in the avoidance component, but decreased the response rate associated with the concurrent VR component.

Effects following the simultaneous administration of d-amphetamine and chlorpromazine.

The determination of whether or not two drugs influence the action of each other when administered simultaneously, is an important area of research in pharmacology. One of the basic techniques used involves the determination of the dosage of each drug that is effective in producing a certain result. Then the dose of each is reduced in relation to the other in order to determine:- 1) whether the combined use of each drug at half the effective dosage level yields the result that either would give at the full effective dose. Such an effect is known as addition or summation. 2) whether the use of one in the full effective dosage fails to give the usual effect because of the simultaneous use of the other in any dosage. This is the antagonizing of the effects of one drug by the other. 3) whether one in reduced dosage, is brought up to its full effects by some dosage of the other. In this case, one of the drugs synergizes the other (Beckman, 1961).

A different approach to the question of drug interactions is taken by behavioral pharmacologists who examine the problem in terms of modifications in rate and temporal patterning of responding. An early series of experiments by Carlton (1961) and Carlton and Didamo (1961) is illustrative of the approach adopted by workers in this area. Using rats as subjects, the effects of the simultaneous administration of d-amphetamine and an anticholinergic drug on avoidance behavior were examined. The anticholinergic drugs used were atropine, and scopolamine which are closely related chemically, and usually induce drowsiness and sleep when administered singly. Relatively low doses of each anticholinergic drug that were found to be behaviorably inactive when administered alone, were used. When either atropine or scopolamine were administered in combination with d-amphetamine, there was a clear augmentation of the tendency of the latter to increase the response rates of the subjects in the avoidance situation. Reports dealing with the effects of chlorpromazine and d-amphetamine when administered simultaneously, indicate that such a dosage combination results in an antagonistic effect between the two drugs. Brown (1963) reported that chlorpromazine reinstated responding that had been blocked by d-amphetamine. Using food deprived rats as subjects and an FR 10 (milk reinforced) schedule, he found that a dosage of 2.5 mg/kg of d-amphetamine completely suppressed all responding for a period of 60 min. However, when chlorpromazine was administered simultaneously with the above dosage of d-amphetamine, the

the suppression of responding induced by the latter was diminished. In addition, Brown found that 1.5 mg/kg of chlorpromazine was the dosage which resulted in maximal antagonism of the 2.5 mg/kg dosage of d-amphetamine. It should also be noted that this 1.5 mg/kg chlorpromazine dosage was not followed by any observable deviations from the control (non-drug) performance when administered independently.

Davis (1965) has confirmed this finding by demonstrating that food deprived pigeons under a FR 30 (food reinforced schedule) cease to respond following an injection of 6.0 mg/kg of d-amphetamine. Responding was reinstated when a dosage of chlorpromazine between the range 3.0 and 17.0 mg/kg was injected shortly after the blocking of responding by d-amphetamine became apparent.

Both Brown and Davis referred to the antagonism of the effects of d-amphetamine by chlorpromazine. However, it should be emphasized that this is a reciprocal process between the two drugs. This is emphasized by Rech (1964) in his report on the antagonism of Reserpine behavioral depression by d-amphetamine [Reserpine is a rauwolfia alkaloid, and is generally classified, like chlorpromazine, as a depressant drug. The modifications in behavior which follow its administration are similar to those induced by chlorpromazine (Stein, 1962), thus the study reported by Rech is relevant to the present topic].

Rech trained 110 female rats under conditioned avoidance parameters in a shuttle box, using a 600 cycles per sec tone as the conditioned stimulus which preceded shock by 5 sec. The subjects were required to reach a 50 per cent successful avoidance performance before

drug treatments were started. The drugs employed were reserpine and d-amphetamine. A dosage of 2 mg/kg of reserpine was injected, and the subjects were tested at 2.5, 8, 24 and 48 hours afterwards. Immediately after each of these sessions 2 mg/kg of d-amphetamine was administered, and the subjects again tested 30 minutes thereafter. Cumulative effects from the repeated amphetamine dosages were not expected, since the drug is metabolized relatively rapidly and no trace of it is found in the brain approximately 4 hours after intraperitoneal injection. The behavioral effects of reserpine were completely abolished by the amphetamine and performance was enhanced up to 8 hours after reserpine administration. However, when amphetamine was injected at the 24 and 48 hour stages, performance again deteriorated due to the hyperactivity induced by the amphetamine the effects of reserpine being less potent at this stage. With a dosage of 0.5 mg/kg of amphetamine, maximum antagonistic effects against 2 mg/kg reserpine were observed 24 hours following the administration of the latter; l-amphetamine was also tested under similar experimental conditions and found to be less effective than the d-form in counteracting the effects of reserpine. The author suggests that this difference may be related to the lesser potential of l-amphetamine for releasing brain norepinephrine.

The present study was primarily concerned with the modifications in behavior which followed the administration of d-amphetamine sulphate and chlorpromazine, both singly, and in several joint dosage combinations. As was mentioned earlier in this section, the schedule employed in the experiments to be reported in the present study was a concurrent free-operant avoidance/FR escape schedule.

It was pointed out earlier in this section, that Dews (1956) has demonstrated that by use of a complex schedule, it is possible to evaluate in the same animal, the differential effects of drugs on two different rates of responding during the same experimental session. He was also able to show that the drug-induced behavioral modifications of each response rate were the same as those which appeared when either response rate was emitted independently.

The concurrent schedule used in the present experiments also generated two different rates of responding, thus providing two stable baselines for the evaluation of the effects of d-amphetamine and chlorpromazine. Of primary interest were the effects of simultaneous administration of the two drugs in various dosage combinations. Again it has already been mentioned that Brown (1963) and Davis (1965) have examined the antagonistic effects exerted by d-amphetamine and chlorpromazine on each other. However, both authors used an FR schedule in which responding was maintained by a positive reinforcer, and other studies reported in this section have already pointed out that the effects of drugs on behavior maintained by aversive stimuli may be quite different from the effects on behavior maintained by positive reinforcement. In addition, workers in this area have emphasized that both of the above aspects of the effects exerted by a drug must be examined in order to obtain an adequate characterization of the drug in behavioral terms.

The experiments reported in the present study represent the first attempt to examine the simultaneous effects of chlorpromazine and d-amphetamine on behavior characterized by two different response rates and maintained by aversive stimuli. Finally, it should be noted that Herrnstein and Morse (1956) have emphasized the use of drugs as analytical tools in operant research. In a study which closely resembled that of Dews (1956) reported above, they concluded that the effects of the drug employed in their experiment clearly separated the two behaviors maintained by the two components of the complex schedule on which the subjects were trained. Thus, the authors obtained evidence that complex performances could, by use of these techniques, be analyzed into the single components.

Method

Subjects

Three adult male squirrel monkeys (*Saimiri sciureus*) designated D1, D3 and D4 respectively were used as subjects. Each animal was caged individually in a temperature- and humidity-controlled colony room and was permitted unrestricted access to food and water except during each experimental session. The animals had acquired no previous experimental histories prior to the present work.

Apparatus

The experimental chamber was a Lehigh Valley Electronics small animal test cage (Model LVE 1417) situated within a ventilated, sound-attenuating cubicle. The grid floor consisted of 16 stainless steel rods, and was wired for the delivery of electric shocks to the feet of the subject. Two retractable rat levers (Model LVE 1405R) were mounted on one wall of the chamber, each 6 5/8 in. above the grid floor and separated by 5 3/4 in. Lever dimensions were 1 in. by 1 1/8 in. by 3/8 in. Six small stimulus lights were mounted on the wall of the test cage. These consisted of 2 red, 2 green and 2 white lights, one of each color being situated immediately above each lever. In addition, the chamber was fitted with a Chicago Miniature No. 304 28V dc houselight, and a 4 ohm speaker mounted within the cubicle, delivered "white noise" at an intensity of 75 db s.p.l.

as measured by a Dawe Type 1400F sound level meter. A constant current shock generator (Model LVE 1531) and grid scrambler (Model LVE 13115S) were employed to produce shocks of 500 msec. duration at an intensity setting of 12 ma. The experimental conditions were controlled automatically by a system of relays, stepping switches and timers located in an adjoining room. Data were recorded by an Elmeg print-out counter (Grason-Stadler Model E12505A), Sodeco digital counters, and by two Gerbrands cumulative-response recorders.

Procedure

The study consisted of six consecutive phases.

Phase I. Free-operant shock-avoidance training[1]: Lever A

During this period, experimental sessions were of 4 hr. duration with approximately 20 hr. elapsing between consecutive sessions for each subject. In addition, only one lever (designated Lever A) was present in the chamber.

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[1]The following rationale for the use of this term is given by Sidman (1966) "The basic technique has been given several names, e.g. nondiscriminated avoidance, the method of temporal pacing, continuous avoidance . . . . . and Sidman avoidance. The term free-operant avoidance, if not self explanatory, is more accurate descriptively than the first of these, is not as theoretically committed as the second and third, and gives a more appropriate historical credit than the last." (p. 449).

Each monkey was trained to respond by reinforcing successive approximations to the lever press. Reinforcement consisted of interrupting, for 20 seconds, brief inescapable shocks which otherwise occured every 5 seconds. Each subject acquired the response within an hour of training, and was transferred to a free-operant avoidance schedule of the Sidman type (Sidman, 1953) which was programmed for the next 15 consecutive sessions. According to the parameters of the schedule, a 12 ma. shock of 500 msec. duration was presented at regular 5 second intervals (the shock-shock interval), if a response did not occur. If the subject pressed the lever, however, the next shock was delayed for 20 seconds (the response-shock interval). Each response that was made reset the response-shock interval, thus permitting the subject to avoid shock presentation indefinitely. Shock presentation was not averted by prolonged depression of the lever. It is also important to note that no exteroceptive stimulus preceded an impending shock. Each shock that occurred was of 500 msec. duration, and could not be terminated by a response. The subject postponed shock presentation each time it pressed the lever. During the experimental sessions of this phase, a white light above Lever A, and the houselight were illuminated in the test chamber, and white noise was present continuously, throughout each session.

Phase II. Escape training: Lever B.

When all subjects had received 20 sessions of the free-operant shock-avoidance schedule, Lever A was withdrawn, and the second lever (designated Lever B) was extended into the chamber. Eight consecutive experimental sessions, each of 2 hr. duration, followed. During each session, brief (500 msec.) shocks were delivered at regular intervals, in the presence of the houselight, white noise, and a white light above the lever. Morse and Kelleher (1966) refer to this as a schedule complex, and have reported that the termination of a schedule complex comprising a stimulus in the presence of which brief presentations of electric shocks are scheduled, is a reinforcer.

A fixed ratio (FR) schedule[1] specified the number of times the animal was required to press Lever B in order to terminate the schedule complex and produce a time out of 30 seconds' duration. When a time out period was in effect, the houselight noise and white light were switched off, shocks were discontinued, Lever B was withdrawn, and a green light was illuminated above the Lever B station. Following time out,

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[1] A fixed ratio (FR) schedule, as defined by Ferster and Skinner (1957), is "A schedule of intermittent reinforcement in which a response is reinforced upon completion of a fixed number of responses counted from the preceding reinforcement." (p. 727).

the first shock occurred 5 seconds after noise-light onset, and subsequently, at 5 second intervals, until the next TO period was produced by responding on Lever B. Initially, each response on Lever B produced a time out; however, during the first session the required number of responses was gradually increased to FR 5. The FR requirement was increased in subsequent sessions to a maximum of 40 responses (FR 40).

Phase III. Concurrent free operant avoidance - FR escape schedule

Both levers were present in the chamber from the start of this phase, and for the remainder of the experiment. An important point is that session length was of 4 hr. duration at the start of this phase. However, during stabilization of performance, and for the remainder of the study, session length was reduced to 3 hr. or the time taken to initiate 80 TO periods, whichever occurred first.

The parameters of the concurrent schedule[1] specified that

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[1] A concurrent schedule. (See footnote page 9 Introduction section).

responses on Lever A would postpone brief electric shocks for 20 seconds; in the absence of such responses, shocks were programmed to occur every 5 seconds (the free-operant avoidance contingency). Concurrently periods of time out could be produced by pressing Lever B according to the response requirement specified by a FR schedule.

When a white light above each lever station, and the houselight, were illuminated, and white noise was present, the avoidance schedule was operative with respect to Lever A. A fixed number of Lever B responses terminated noise and switched off the lights for a 60 second TO period during which the levers were retracted, shock presentations discontinued, and a green light was present above each lever station. When a 60 second time out ended, the green lights were switched off and both levers were automatically extended into the experimental space. Re-introduction of the levers (requiring approximately 300 msec.) was followed immediately, by the reinstatement of the stimuli associated with the two concurrently programmed contingencies which then came into operation. The first shock was scheduled to occur 5 seconds after a time out had ended.

Sidman (1962) has noted that if an animal were to press Lever B and produce a TO period immediately after an avoidance response (Lever A), the time out might constitute an adventitious reinforcer for responding on Lever A. To prevent this, a 2-second change-over-delay (COD) was incorporated within the concurrent

schedule. Only if the animal refrained from pressing Lever A for 2 seconds could a response on Lever B reduce the FR requirement for time out, or produce, in the case of the terminal (75th) FR response, a time out.

During the first session of the phase, the value of the FR requirement was gradually increased from 2 to 5 responses. Over the next 20 sessions, this requirement was further increased to a final value of FR 75. The phase concluded when data had been obtained from 20 consecutive sessions in which the performance of each subject on the final parameters of the schedule, was stable (see Results section).

Phase IV. The introduction of unavoidable shocks

Over a period of 6, consecutive experimental sessions, additional shocks were programmed to occur independently of the subject's behavior. In each of the 6 sessions, these shocks were introduced following the 10th time out and discontinued at the 20th TO period. The subject was unable to influence the delivery of the shock, which occurred, on average, every 10 seconds. No shocks were delivered during time out. The duration and intensity of these shocks were identical to those that were presented if the subject failed to avoid shocks by pressing Lever A. Any shocks which the subject failed to postpone by Lever A responses, continued to be delivered according to the requirements of the avoidance component of the concurrent schedule.

On completion of the 6 sessions, the presentation of unavoidable shocks was discontinued, and daily performance over the

following approximately 100 experimental sessions was examined for any irreversible or lasting changes that may have been induced by the unavoidable shock presentation procedure.

Phase V. Evaluation of the independent effects of d-Amphetamine sulphate and Chlorpromazine

This period, together with Phase VI, formed the major phases of the experiment and extended over a period of 6 months. During Phase V, the modifications of performance engendered by the concurrent schedule, following the administration of d-amphetamine sulphate[1] and chlorpromazine[2], were determined, independently, for each drug. Subjects D1 and D3 were assigned to the amphetamine, and subject D4 to the chlorpromazine, determinations. Four dosage levels of each drug were evaluated, and are stated below in terms of milligrams of the drug per kilogram of body weight of the subject

d-Amphetamine	Chlorpromazine
0.03 mg/kg	0.03 mg/kg
0.10 mg/kg	0.10 mg/kg
0.30 mg/kg	0.15 mg/kg
1.00 mg/kg	0.30 mg/kg

[1] d-Amphetamine sulphate, dissolved in distilled water at solution concentrations of 20 mg/20 cc. and 20 mg/100 cc.

[2] Chlorpromazine hydrochloride dissolved in distilled water, at concentrations of 20 mg/20 cc. and 20 mg/100 cc.

The effects of each drug upon concurrent responding was evaluated by pooling the data obtained from six determinations of each dosage level. Thus, each of the three subjects received a total of 24 drug administrations during this phase. Two or three control sessions both preceded and followed each drug administration, since only two dose determinations were made each week (on Tuesdays and Saturdays). In addition, on five of the control sessions, selected at random, an injection of isotonic saline solution was given. This control procedure permitted evaluation of any behavioral effects that may have resulted from the actual administration of these solutions, and would thus obscure the drug effect. For example, the insertion of the needle or the volume of solution injected might have induced a behavioral change apart from that attributable to the drug. Volume of all injections was kept as constant as possible, within the limits 0.2 to 0.5 cc. Route of administration was by injection into the muscles of the lower hind limb.

On completion of the amphetamine dosage series, six determinations of the 0.3 mg/kg chlorpromazine dosage were obtained from subjects D1 and D3. Again, each injection was followed by two or three control sessions.

Phase VI. Evaluation of the joint effects of d-Amphetamine and Chlorpromazine

After dose-response effects had been determined in the manner described in Phase V, all three monkeys were subjected to a further series of treatments. These involved simultaneous administration of d-amphetamine and chlorpromazine according to the following dosage combinations:

d-Amphetamine		Chlorpromazine
0.10 mg/kg	and	0.3 mg/kg
0.30 mg/kg	and	0.3 mg/kg
1.00 mg/kg	and	0.3 mg/kg

Each combination of the two drugs was administered on five separate occasions, drug treatments being interspersed, as before, with control (non-drug) sessions.

Behavioral measurements.

It should be emphasized that the basic data for the following measures, were collected only when both levers were extended into the experimental space (i.e. during active time). No responding could occur during time out when the levers were retracted. Throughout the experiment, the measurable properties of performances engendered by the concurrent schedule were recorded in terms of:

1. The average time (in seconds) taken by the animal during the complete session, to initiate each period of time out.

2. The rate of avoidance responding per minute (Lever A) for each session.

3. The average number of avoidance responses for each period of active time throughout each session.

4. The rate of FR responding per minute (Lever B) for each session.

5. The average number of FR responses that were emitted during the COD (initiated by each avoidance response) throughout the session. As specified by the schedule, such responses were ineffective in reducing the FR requirement of 75 responses.

6. This final measure which is concerned with the alternation of responding between the two manipulanda, and which may be referred to as switching behavior, requires more detailed explanation.

Sidman (1962) has pointed out that when an animal is responding on an independently programmed FR schedule, it rarely pauses once it has begun to respond after each reinforcement. Close examination of the fixed ratio records, obtained from the performance of a monkey on the schedule employed in the present experiment, revealed that the animal often paused, briefly, as it progressed in the ratio sequence. During these pauses, the subject typically made one or more avoidance responses. The same behavior patterns were apparent in the present study, and as Sidman found, more detailed analysis revealed additional features of the subject's pattern of alternation between pressing Lever B

and pressing Lever A. Thus, in this measure, records were obtained of the number of FR responses (Lever B) made by the animal before it made one or more avoidance responses (Lever A). Each set of FR responses may be conveniently referred to as a "run," and the number of responses in each of these Lever B runs may be plotted graphically, as a function of the run's serial position in the ratio sequence, relative to the time out period. In graphs of this nature, presented in the Results section, each point on the curve is the average size of that particular run, for the complete session; the final run being indicated on the abscissa by F, the run preceding the final one by 1, and so on as far back as the fifteenth run preceding each time out. A maximum of 15 runs was plotted since this number was rarely exceeded, and within this range, the major changes in control performances, induced by drug treatments, were apparent.

RESULTS

The material in this section is presented in terms of the results obtained from each of the phases of the experiment as described in the Method section. The order of presentation of these phases also adheres to that adopted in the Method section.

Throughout the experiment, individual differences between the subjects were consistently observed. However, in many instances, careful examination of the data showed substantial intra-subject stability, and in these cases, the results are best interpreted in terms of the performances of individual subjects.

Phase I. Free-operant shock avoidance training: Lever A

The performances of each animal throughout this phase are summarized in Figure 1. Figure 1 (upper graph) shows the rate of avoidance responding per minute for all three subjects, for each session. Over the 15 sessions in this phase, a slight elevation of response rate occurred in all animals. By the 14th session, the response rate for all subjects was within the range of 13 to 18 responses per minute.

The average number of shocks received per hour by each subject during each session, is plotted graphically in the lower part of Figure 1. A pronounced reduction in the frequency of the shocks occurred over the first four sessions, and is most evident in subjects D1 and D3. However, it should be noted that of the high number of shocks received by monkey D3 during the first session, the majority of these were delivered during the first hour when the animal was being trained to depress the lever to postpone shock. Over the last four sessions of the phase, the shock rate was low for all subjects and was within the range 0 to 2.5 shocks per hour.

That performance on the free-operant shock avoidance schedule was relatively stable is supported by the representative segments of cumulative response records for each subject, shown in Figure 2. The upper record was obtained from subject D1 during the 13th session of this phase. The avoidance response rate per minute

Fig. 1 Graphs showing the performance of each subject during free-operant shock avoidance training, in terms of i) avoidance response rate per minute (upper figure) and ii) the average number of shocks received per hour (lower figure).

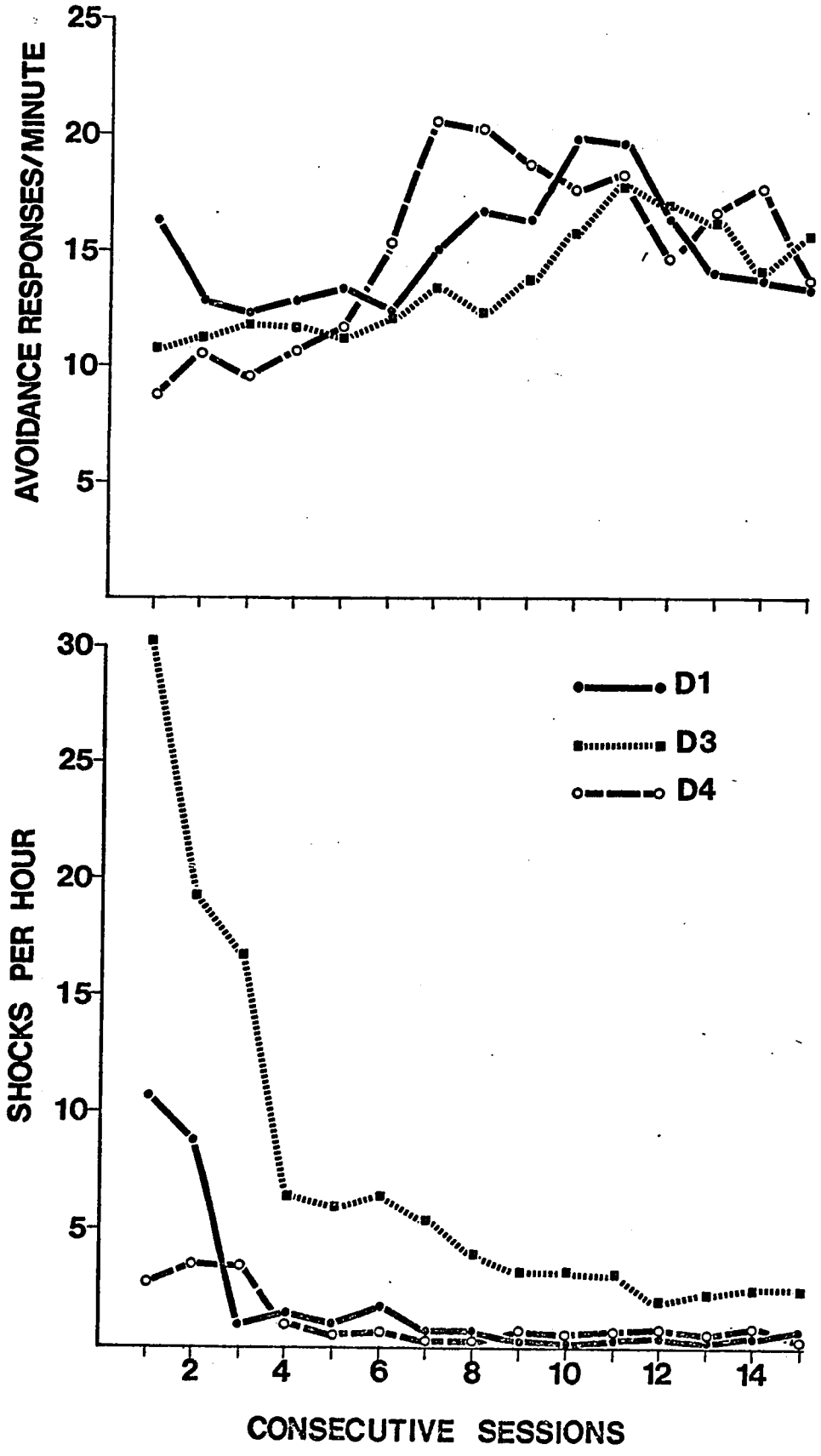
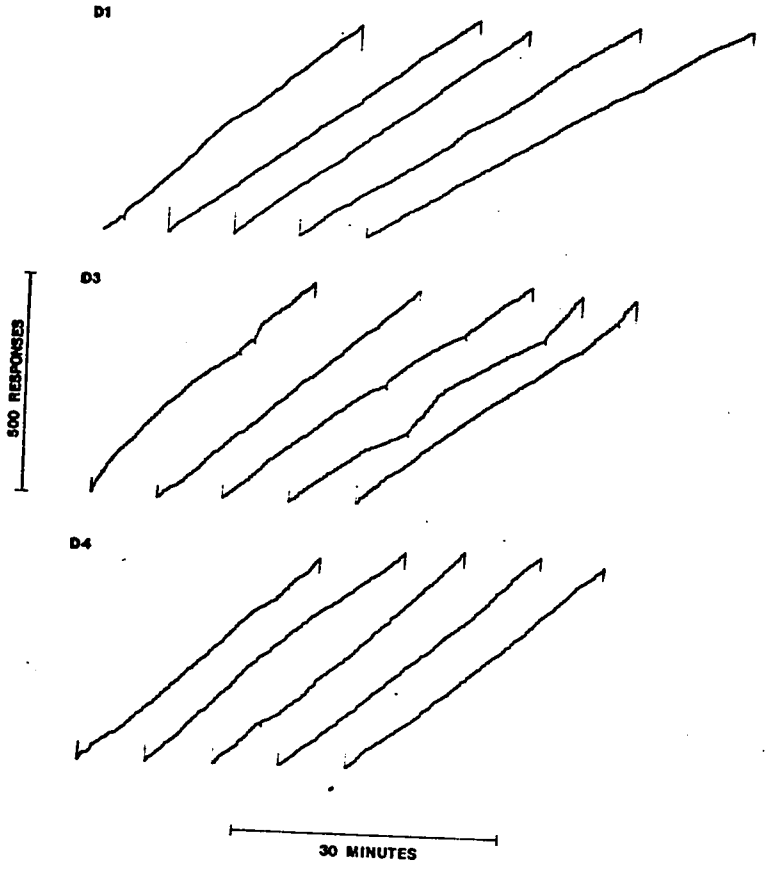

AVOIDANCE RESPONSES/MINUTE
25
20
15
10
5
SHOCKS PER HOUR
30
25
20
15
10
5
D1
D3
D4
2
4
6
8
10
12
14
CONSECUTIVE SESSIONS

Fig. 2. Selected cumulative response records for each subject, showing behavior engendered by the free-operant shock avoidance training. Oblique downward deflections of the pen indicate shock deliveries.


D1
D3
D4
500 RESPONSES
30 MINUTES

for the session was 14.0 and the shock frequency was 0.25 per hour. The center record was obtained from subject D3 during the 12th session of avoidance conditioning. The overall response rate was 16.5 per minute and the shock frequency, 2.25 per hour. On receiving a shock, D3 tended to emit a number of responses in rapid succession, and such bursts of lever-pressing can be seen on the record immediately following a shock, which is represented by an oblique, downward deflection of the pen.

The lowest trace is a record of the performance of monkey D4 during the 12th session of this phase. The avoidance rate was 18.0 responses per minute and the shock frequency was 0.75 per hour.

Phase II. Escape training: Lever B

Before reporting the results of this phase, it should be noted that the number of FR responses (Lever B) that each monkey was required to emit in order to initiate a time out period on any one of the eight sessions, was dependent on the experimenter's evaluation of that subject's ongoing behavior, and its performances during the preceding session. For example, if a subject was maintaining a stable response rate at FR 15 during a given session, then the value of the FR requirement would be increased to 20 either at the start of the next session, or, while the present experimental period was in progress. Conversely, if the performance showed signs of instability, the FR requirement was lowered. This procedure was adopted in order to ensure that a high rate of responding on Lever B was generated prior to the

exposure of the animals to the parameters of the concurrent schedule (see Introduction section). Since the schedule parameters were frequently changed throughout the eight sessions, in the manner described above, it was not possible to employ measures such as FR response rate per minute and shock rate per hour, and the cumulative records formed the best available estimate of performance.

The development of the performance of each animal during the phase can be seen in Table 1 which shows the total number of time out periods and total number of shocks received per session by each subject.

TABLE 1

Total number of time out periods and total number of shocks received per session by each subject.

Session No.	D1		D3		D4	
	TO periods	Total shocks	TO periods	Total shocks	TO periods	Total shocks
1	118	42	110	85	56	31
2	105	66	98	152	51	18
3	132	140	67	132	53	16
4	94	207	97	206	55	3
5	74	191	75	207	53	7
6	52	195	73	161	54	2
7	38	171	74	159	54	1
8	51	162	71	200	51	0

The wide differences in the number of shocks received is attributable in part, to the differences in rate of responding between the subjects. However, reference to the cumulative records of performance presented in Figures 3, 4 and 5 permit a more detailed evaluation of these differences. Figure 3 shows cumulative records obtained from subjects D1, D3 and D4 during the first session of this phase. For subject D1, the FR value at the start of the session was 2, and after three periods of time out, was raised to 5 responses. However, the number of shocks delivered during this subject's first experience of FR 5 was regarded by the experimenter as excessive and likely to lead to a cessation of responding on the part of the animal (the experimenter regarded as excessive, more than 5 shocks occurring between consecutive time out periods). The FR value was, therefore, reduced to 3 and remained at this level for the rest of the session, apart from subsequent, brief, unsuccessful attempts to raise the requirement to FR 5. For monkey D3, the FR requirement was 2 at the start of the first session, but immediately after the first time out period had commenced, this was increased to FR 5. The FR requirement remained at this value throughout the session except for two occasions where an attempt was made to increase it to FR 10. The first session for D4 also started at FR 2, and after the first time out the FR requirement was moved up to FR 5, at which level it remained without alteration throughout the session.

Fig. 3. Cumulative response records showing the performance of each subject during the first session of FR escape training. The values of the FR requirements for each subject were:- D1: FR 3; D3: FR 5; D4: FR 5. Oblique downward deflections of the pen indicate periods of time out initiated by the responses of the subjects; the paper drive was halted during each time-out period.

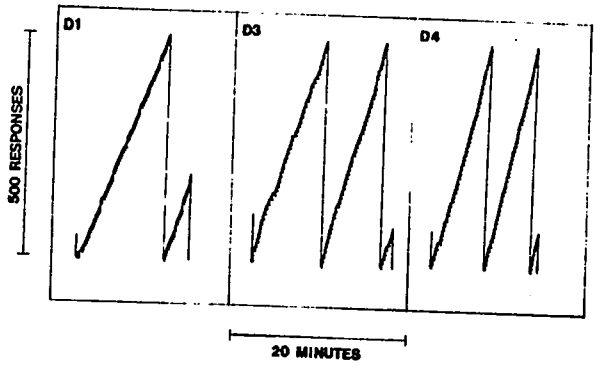

D1
D3
D4
500 RESPONSES
20 MINUTES

Fig. 4. Cumulative response records of the performance of each subject during the third session of FR escape training. The FR requirement was 15 responses in each case.

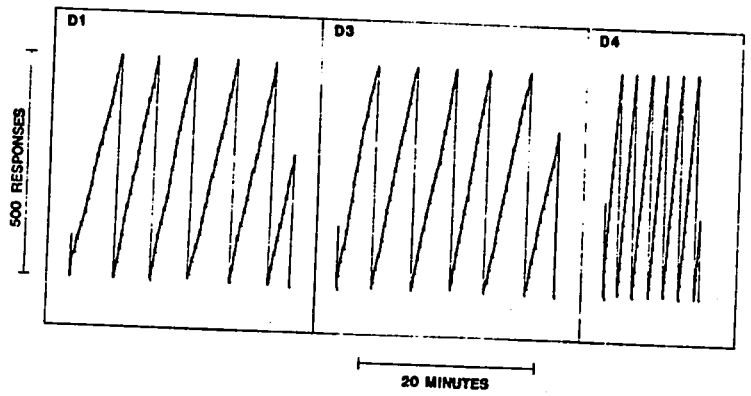
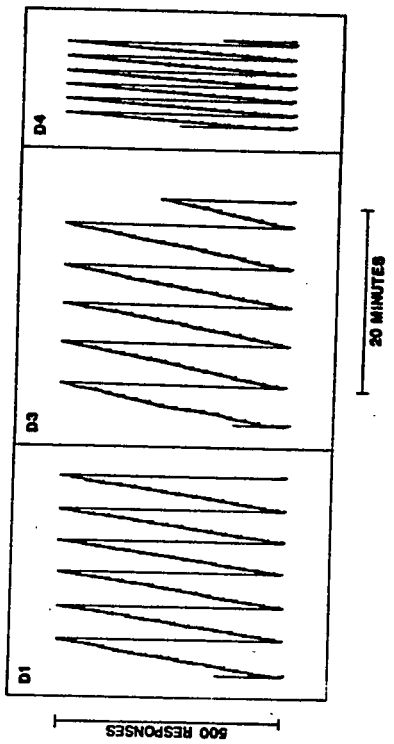

D1
D3
D4
500 RESPONSES
20 MINUTES

Fig. 5. Cumulative response records of the performance of each subject during the final session of FR escape training. The value of the FR requirement was 30 responses in each case. Each oblique deflection of the pen indicates a period of time out during which the paper drive was halted.


D4
D3
D1
20 MINUTES
600 RESPONSES

In Figure 4, cumulative records are reproduced for all three subjects during the third session of this phase. At this stage, all animals were exposed to an FR requirement of 15 responses in order to initiate a period of time out. It is evident from Table 1 which shows the difference between the subjects in terms of total shocks received during the session, that the performance of subject D4 was more effective in terminating the stimulus complex than that of the remaining two subjects. It is possible that the difference may be attributable to the difference in treatment during the first session, since with monkeys D1 and D3, a greater number of shocks were received during the first session than was the case with monkey D4.

During the final session of this phase, shown in Figure 5, monkeys D3 and D4 were giving a stable performance on FR 30. The same was true of monkey D1, but in this case, the FR requirement was raised on several occasions to FR 40. The important point is that all subjects were responding at a stable, relatively high rate on the FR schedule, a condition found to facilitate the development of stable performances under the concurrent schedule (Stretch, Dalrymple & Goforth, 1968).

Phase III. (A) Concurrent free-operant shock avoidance - FR escape schedule

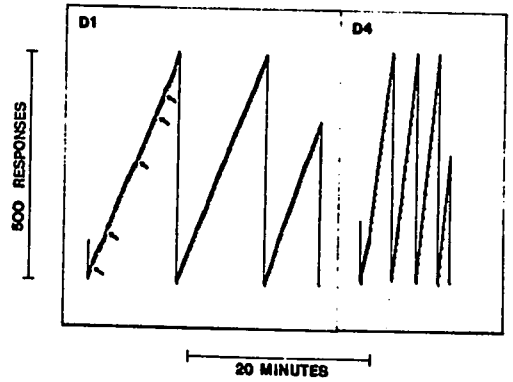
As was the case during the preceding phase, the value of the FR requirement was frequently changed during the first part of the present phase, until the final value of FR 75 was operative for all subjects. As a result of this training procedure, following the

first occasion on which any subject was exposed to the final parameters, it was not necessary to reduce the FR requirement during any subsequent session. Prior to the establishment of the FR 75 value, the increase or decrease in the FR value for any subject was dependent upon the experimenter's evaluation of that subject's ongoing behavior. Thus, exposure to the final parameters occurred on different experimental sessions for each animal; D1 after 32 sessions and D3 and D4 after 36 sessions.

Following stabilization of the subjects on the final parameters, it is possible to evaluate performance in terms of the six measures listed in the Method section (see p.43, 44). However, this was not possible while the FR requirement was changing, and performance during this period is summarized in Figures 6 - 10.

Figure 6 shows cumulative records of the performance of subjects D1 and D4 on the FR escape component of the schedule during the first session of the phase. The record at the left is of the performance of D1; the ratio requirement (Lever B) was FR 2 throughout the session, apart from five occasions (arrows) when unsuccessful attempts were made to increase the requirement to FR 5. The performance of subject D4 during the first session of this phase is shown at the right of Figure 6. The session started, for this subject at an FR value of 2 responses on Lever B, and was raised to FR 5 during the second time out period of the session. It remained at this value until the 16th time out period had started, at which stage it was judged appropriate to increase the FR value to 15

Fig. 6. Cumulative response records of performance on the FR component obtained from subjects D1 and D4 during the first session during which the concurrent free-operant shock avoidance/ FR escape schedule was operative. The value of the FR requirement was 2 responses for D1. The arrows indicate attempts to increase the value to FR 5. For D4, the value was increased from FR 2 to FR 15.


D1
D4
800 RESPONSES
20 MINUTES

responses. No further increase in the FR value took place for the remainder of the session, apart from four tentative attempts to raise the value to FR 20.

Figure 7 shows cumulative records of the performance of subject D3. The value of the FR requirement was 2 responses, and it remained at this value throughout the session since the response rate on Lever B was relatively low compared to that of subjects D1 and D4.

Figure 8 shows the performances of subjects D1, D3 and D4 when the FR value had been elevated to between 30 and 40 responses. This had occurred, for subject D1, by the 10th session of this phase and the resulting cumulative record is the upper one of the three shown in Figure 8. This performance at FR 30 remained stable throughout the session, and no attempt was made to increase it at this stage.

It is important to note that at this stage, brief pauses in responding on the FR lever often appeared immediately following the time out periods (indicated by oblique deflections of the pen) before the subject started to respond on Lever B. The center record on this figure is of the performance of D3 at a similar stage in the training period of this phase. At the start of the session the FR requirement was 20 responses, and during the 13th time out period, this was raised to FR 30, at which level it remained for the rest of the session. Again, there is some evidence of a brief pause in Lever B responding following a time out.

Fig. 7. Cumulative response records obtained from subject D3. The upper record is of performance on Lever A (free-operant avoidance component): the lower record shows performance on the FR escape component (Lever B) during which the value of the FR requirement was 2 responses.

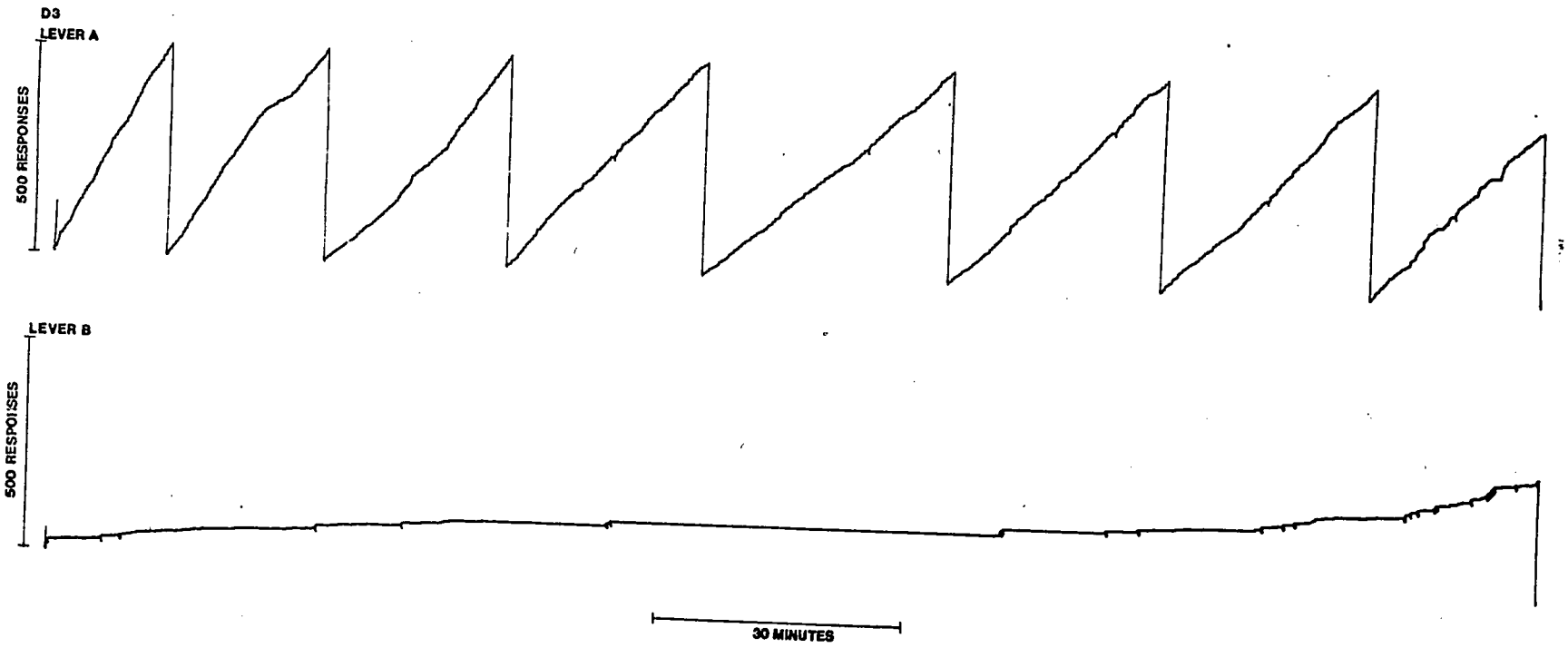
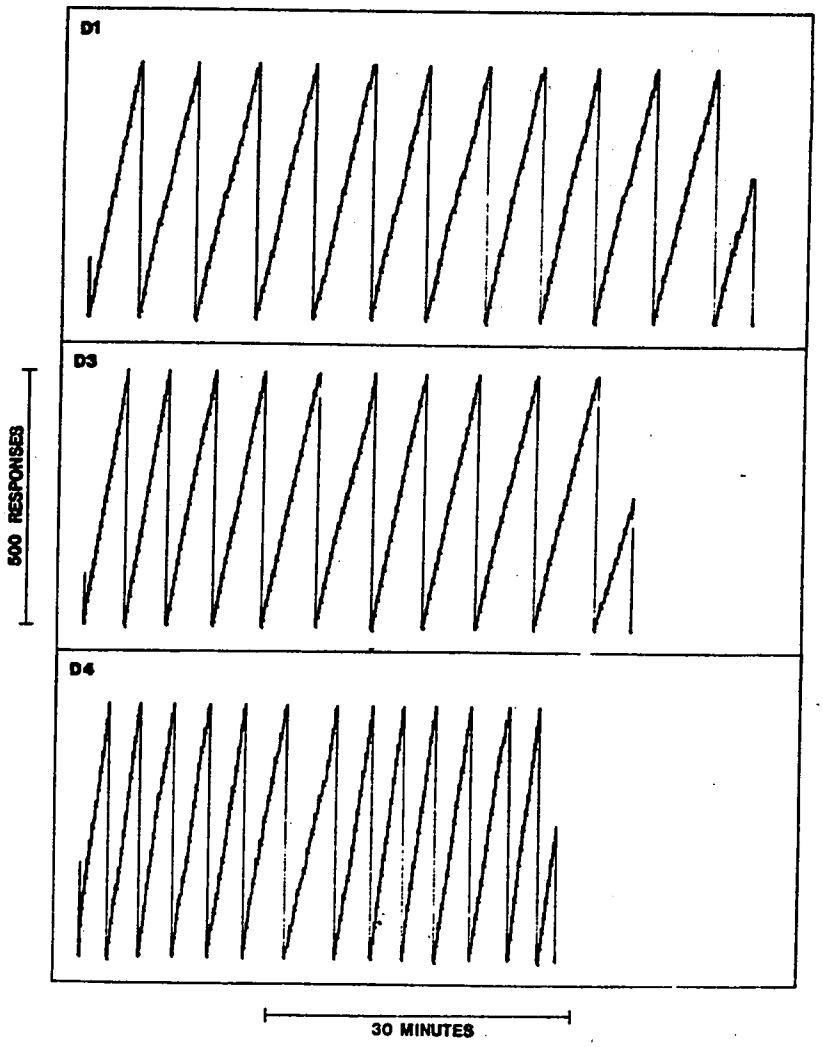

D3
LEVER A
500 RESPONSES
LEVER B
500 RESPOISES
30 MINUTES

Fig. 8. Cumulative response records of the performance of subjects D1, D3 and D4 on the FR escape component of the concurrent schedule (Lever B) when the FR value had been elevated to between 30 and 40 responses.


D1
D3
D4
500 RESPONSES
30 MINUTES

The lower record was obtained from subject D4 when the FR requirement was 30 responses. Several attempts were made to raise the FR value to 40, but stable performance was not sustained by the subject under these conditions, and FR 30 was the dominant value throughout the session. This subject also showed a tendency to pause immediately after a time out period had elapsed.

Figure 9 shows the performance of all three subjects following exposure to the final parameters of the schedule. Wide differences between the subjects in terms of rate of responding on Lever B, are apparent. However, they have many important features in common. Typically, at the end of each TO period, there was a brief pause in responding on the FR lever. This is most clearly marked in subjects D3 and D4. Also with reference to D3 and D4, this brief pause was succeeded by a low but accelerating period of responding on Lever B. Finally, in any period of active time, following the period of acceleration of responding, the subject tended to respond on Lever B at a relatively high rate. This pattern was not apparent at this stage in monkey D1 which tended to pause in its responding on the FR lever through each cycle of active time.

The data obtained from the performance of each subject on the free-operant shock avoidance component of the schedule (Lever A), are summarized in Figure 10. Since the parameters of this schedule component did not change throughout the study following the training period in Phase 1, these measures of

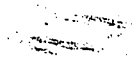
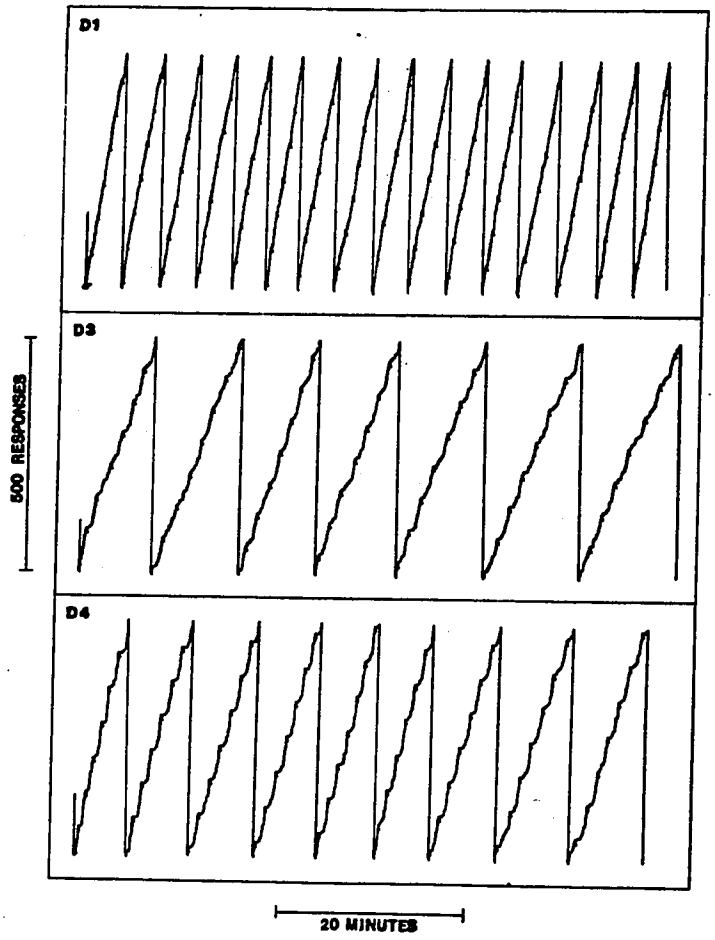


Fig. 9. Cumulative records of the performances of the three subjects on the FR escape component of the concurrent schedule, following exposure to the final parameters of the concurrent schedule.

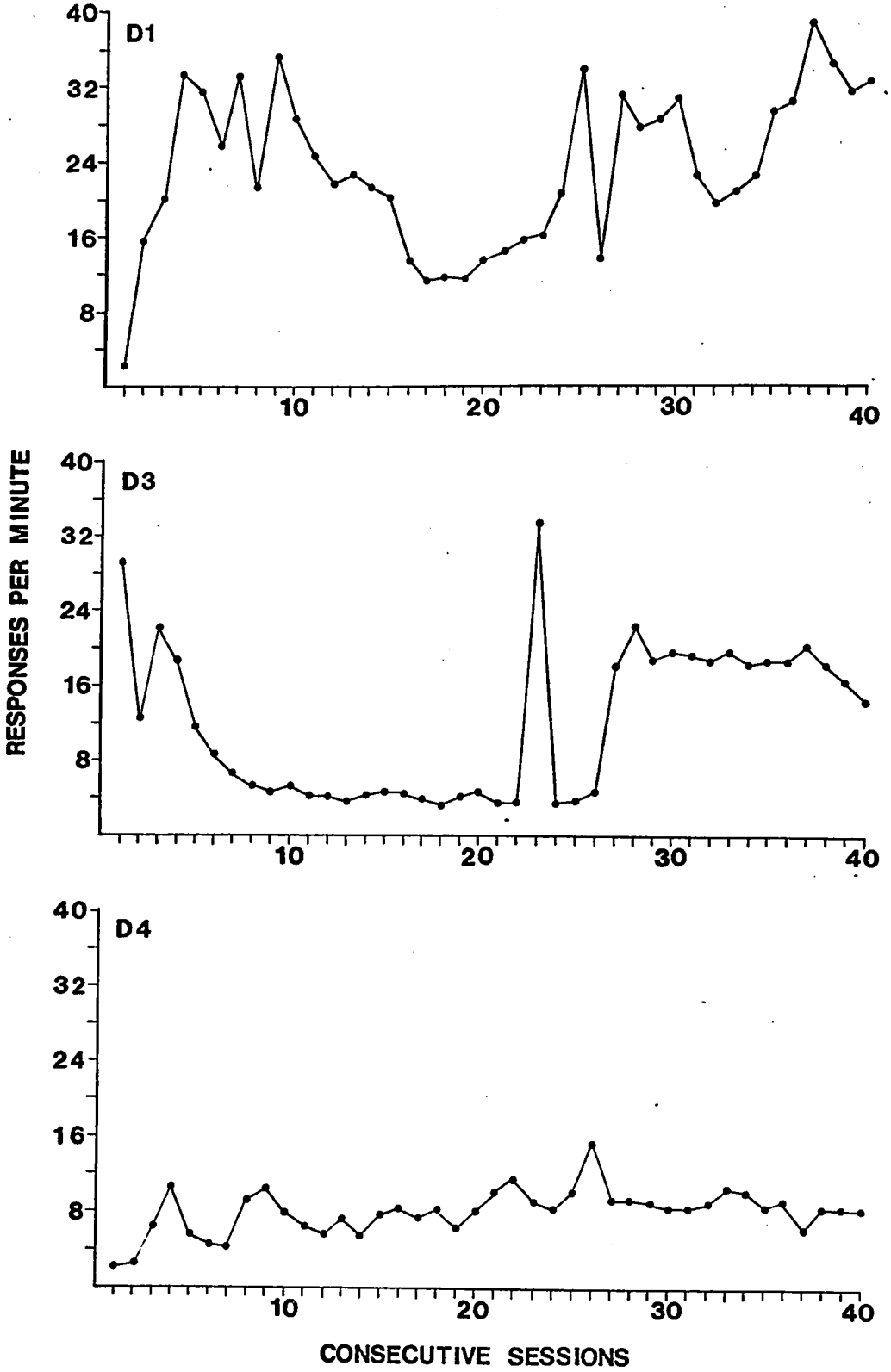

D1
D3
D4
500 RESPONSES
20 MINUTES

both the avoidance response rate per minute and shocks received per hour are relevant in the present phase.

From Figure 10 it can be seen that the avoidance response rate per minute for subject D1 increased over the first 4 sessions of this phase as the FR requirement was elevated from FR 2 to FR 5. Between sessions 4 and 7 there was a considerable amount of fluctuation in the avoidance response rate of D1, and it was during these sessions that the FR requirement was being adjusted between FR 5 and FR 30 according to the experimenters evaluation of ongoing performance. Elevation of the FR requirement was often accompanied by an increase in the rate of avoidance responding followed by a decline in this rate over subsequent sessions. This feature was also identifiable in the performances of D3 and D4, but apart from this, no clearly identifiable trends in performance were common to the three subjects.

There were considerable differences between the three animals in terms of the number of shocks received per hour. However, when the subjects were responding consistently on both levers, and the FR requirement had exceeded 30 responses, the number of shocks received by any subject never exceeded 30 per hour. Thus, unless

Fig. 10. Graphs showing the performance of each subject on the free-operant avoidance component (Lever A) of the schedule. In each case, these measures of the avoidance response rate per minute extend over the period starting with the introduction of the concurrent schedule and continuing through to the establishment of the final FR value of 75 responses.


D1
D3
D4
40
32
24
16
8
10
20
30
40
RESPONSES PER MINUTE
CONSECUTIVE SESSIONS

more than 5 consecutive shocks were delivered to a subject, this measure was not taken into account when evaluating performance.

Stable performance on the final parameters of the concurrent schedule are shown for subjects D1, D3 and D4 in Figures 11, 12 and 13 respectively. These records were obtained on the 45th session following the establishment of the final parameters. The brief pause in responding on Lever B after a time out period had elapsed, followed by a period of acceleration of responding on this lever to a high terminal rate is apparent in the records of all three animals but is most clearly marked in subjects D3 and D4.

Responding on the avoidance lever (Lever A) was relatively constant throughout the session, although the rate was observed to be higher immediately following a TO period. Some evidence of this phenomenon can be observed in the avoidance (upper) record of subject D3 in Figure 12.

Finally, it should be noted that from the time of its introduction at the start of this phase and for the remainder of the experiment, the COD requirement remained constant at 2 seconds.

Phase III. (B) The stabilization of behavior on the concurrent schedule.

As soon as each subject was exposed to the final FR requirement of 75 responses on Lever B, the first 5 of the behavioral measures described in the Method section, were employed in the analysis of the behavior. The data obtained from the 20 control sessions preceding the introduction of unavoidable shocks are summarized in graphical form in Figures 14 to 18 inclusive under Section A of each figure.

Fig. 11. Cumulative records obtained from subject D1, following stabilization of performance on the final parameters of the concurrent schedule (free-operant avoidance/FR 75 escape).

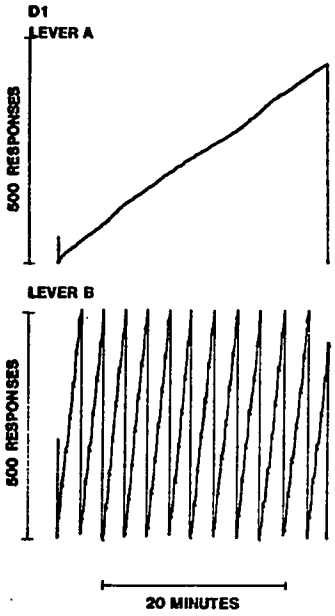

D1
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

Fig. 12. Cumulative records obtained from subject D3, following stabilization of performance on the final parameters of the concurrent schedule.

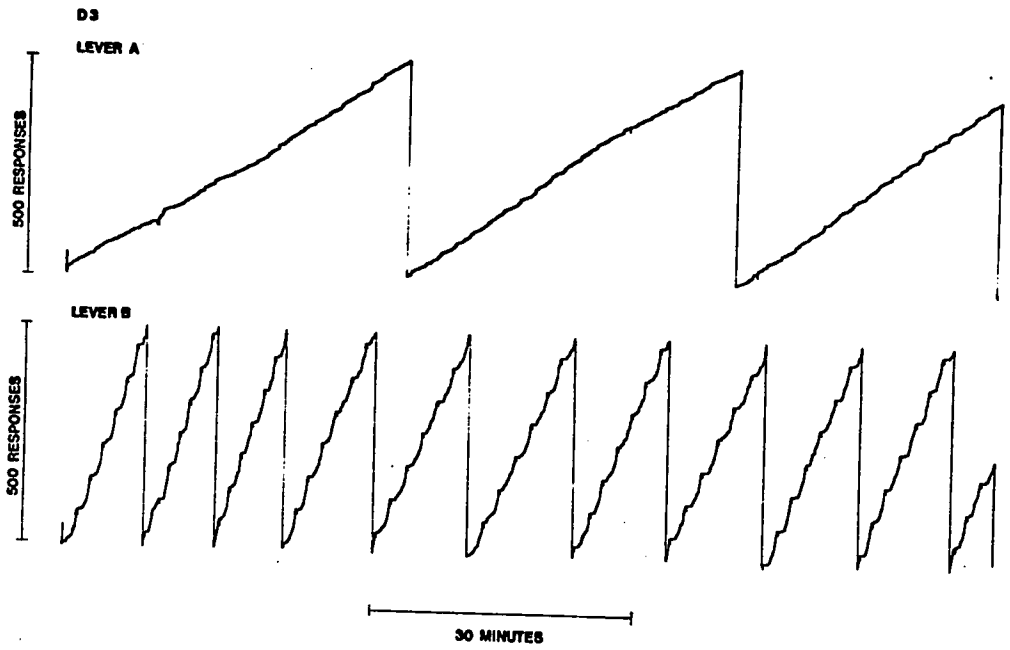
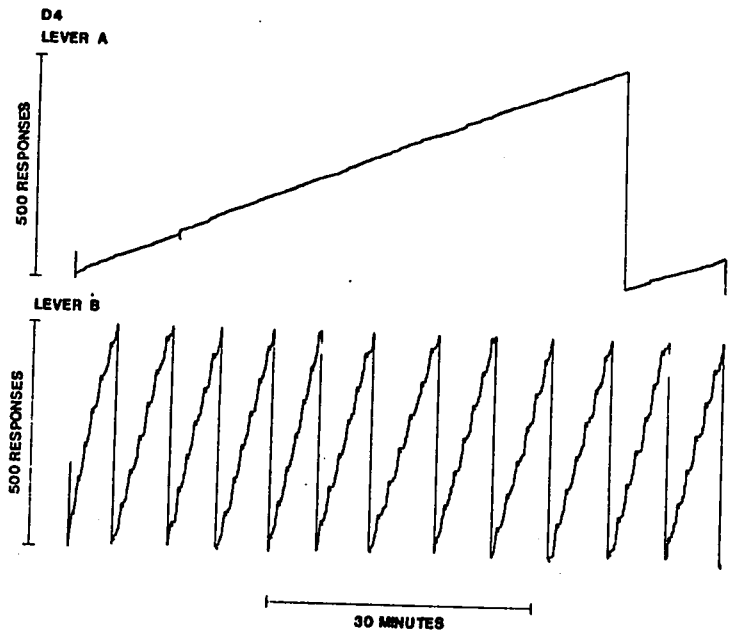

D3
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

Fig. 13. Cumulative records obtained from subject D4 following stabilization of performance on the final parameters of the concurrent schedule.


D4
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

The average time taken by each subject, to initiate a TO period during each of the 20 sessions is plotted in Figure 14. Any point on the graph represents the average time taken to initiate a time out for the complete session. Session number is plotted on the abscissa and time (in seconds) on the ordinate.

The upper graph (D1) indicates that the average time taken to initiate a time out does not vary by more than 22 sec. over the 20 control sessions; the shortest average time being 23 sec. for session 5 and the longest, 45 sec. for session 17. The average time taken by subject D3 (center graph) exceeded that of the other two animals, since the lowest average time was 46 sec. during session 3 and the highest, 63 sec. during session 8. It should be noted, however, that this subject displayed the least fluctuation on this measure, since the difference between the highest and lowest averages was 17 sec.

The performance of subject D4 (lower graph) occupied an intermediate position on this measure with respect to D1 and D3. The shortest average time of 29 sec. was recorded on sessions 3 and 4, and the longest on session 13 when the average time taken to initiate a time out was 52 sec; this gave a range over the 20 control sessions of 23 sec.

The rate of responding of each subject, on the avoidance lever is shown in Figure 15. During the 20 control sessions preceding the delivery of unavoidable shock, the rate of responding per minute on Lever A was relatively stable for all subjects. The

Fig. 14. In these graphs, the average time taken to initiate a time-out period is plotted for each subject over the following blocks of experimental sessions:- (Each point represents an average value for a single experimental session.)

A The 20 sessions preceding the introduction of unavoidable shocks.

B The 6 sessions during which unavoidable shocks were delivered to each subject.

C The 10 sessions immediately following the 6th session of unavoidable shock.

D 10 sessions preceding drug treatment (these were the 58th to the 68th sessions following the 6 sessions of unavoidable shock. No experimental manipulations were introduced during the intervening period).

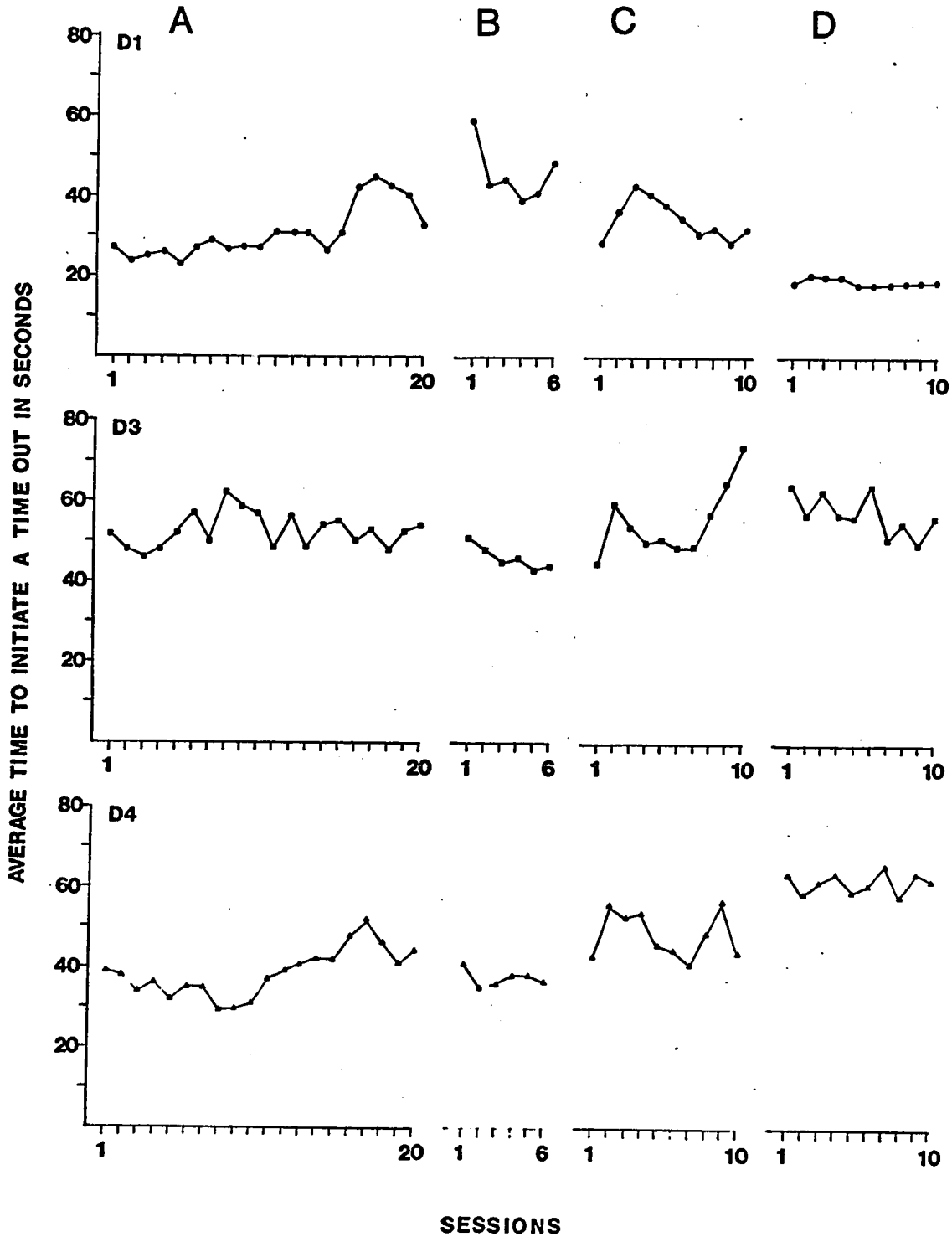

A
B
C
D
D1
D3
D4
80
60
40
20
1
20
6
10
AVERAGE TIME TO INITIATE A TIME OUT IN SECONDS
SESSIONS

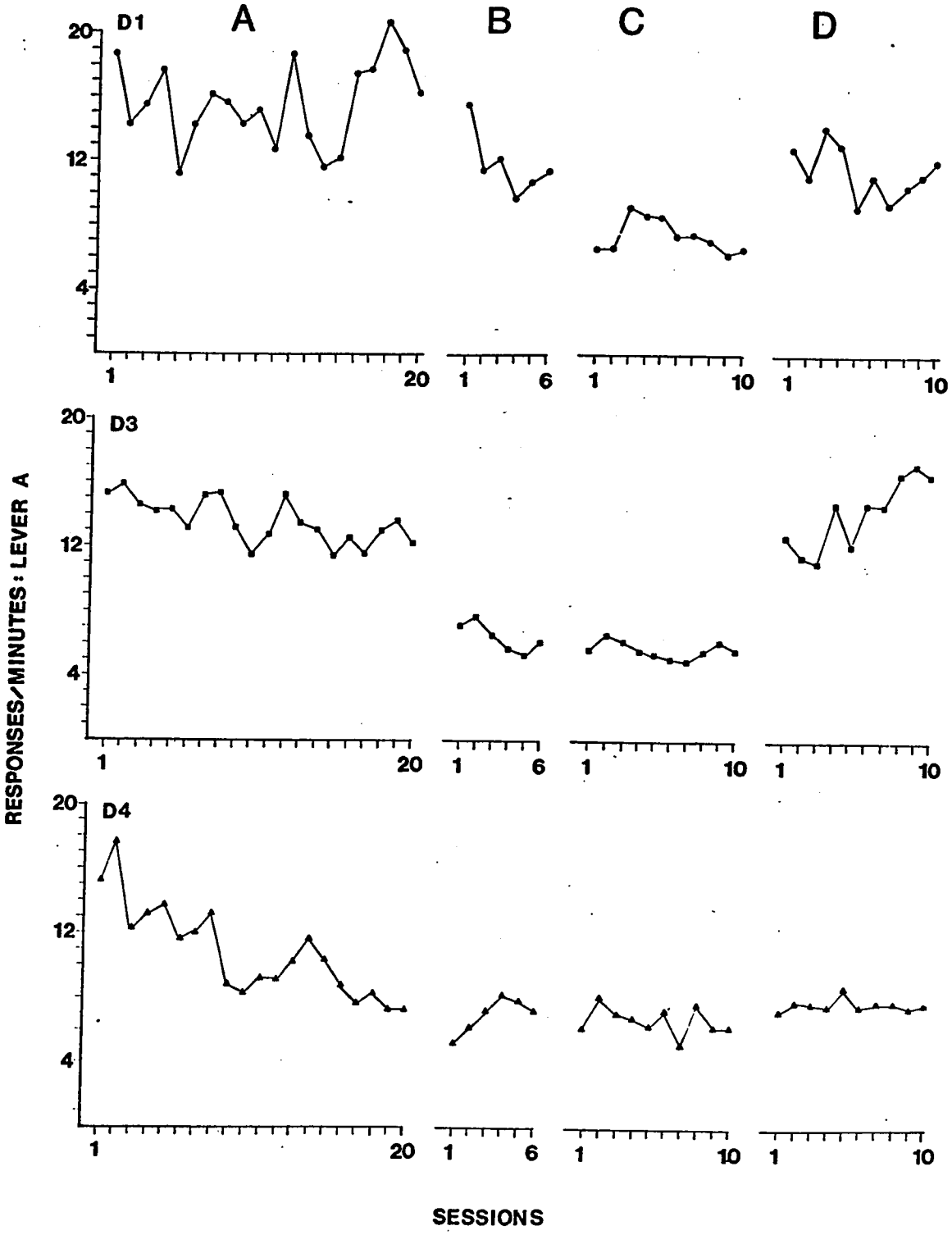
Fig. 15. In the graph shown in this figure, the avoidance response rate per minute (Lever A) is plotted for each subject. Each point represents an average value for a single experimental session.

A The 20 sessions preceding the introduction of unavoidable shocks.

B The 6 sessions during which unavoidable shocks were delivered to each subject.

C The 10 sessions immediately following the 6th session of unavoidable shock.

D 10 sessions preceding drug treatment (these were the 58th to the 68th sessions following the 6 sessions of unavoidable shock. No experimental manipulations were introduced during the intervening period).


D1
A
B
C
D
D3
D4
20
12
4
1
20
6
10
RESPONSES/MINUTES : LEVER A
SESSIONS

greatest variability was shown by subject D1, the lowest rate being 11 responses per minute on session 14 and the highest, 21 responses per minute during session 18. The lowest rate for subject D3 was 11 responses per minute, and the upper value was 16. Subject D4 again occupied an intermediate position with a range of 8 responses, the lower value being 6 responses per minute, and the upper value, 14 responses per minute on sessions 3 and 17 respectively.

Results obtained from the closely related measure of the average number of avoidance responses preceding each TO period throughout a session, are summarized in Figure 16. The performance of all subjects over the 20 control sessions was within the range of 5 to 16 responses, and again, the greatest variation in performance was shown by subject D1.

Turning now, to measures of rate of responding on the FR escape component of the schedule. The rate of emission of FR responses per minute for each subject, over the 20 control sessions is shown in Figure 17.

The differences between the subjects are more marked when performances are examined in the light of this measure. Subject D1 showed the highest overall rate which varied between 242 responses per minute on session 3 and 180 responses per minute on session 15. Rates of responding for subjects D3 and D4 were much lower than that of D1. The performance of subject D3 varied between 100 and

Fig. 16. In these graphs, the average number of free-operant avoidance responses preceding each time-out period is plotted for each subject. Each point is the average value for a single experimental session.

A The 20 sessions preceding the introduction of unavoidable shocks.

B The 6 sessions during which unavoidable shocks were delivered to each subject.

C The 10 sessions immediately following the 6th session of unavoidable shock.

D 10 sessions preceding drug treatment (these were the 58th to the 68th sessions following the 6 sessions of unavoidable shock. No experimental manipulations were introduced during the intervening period).

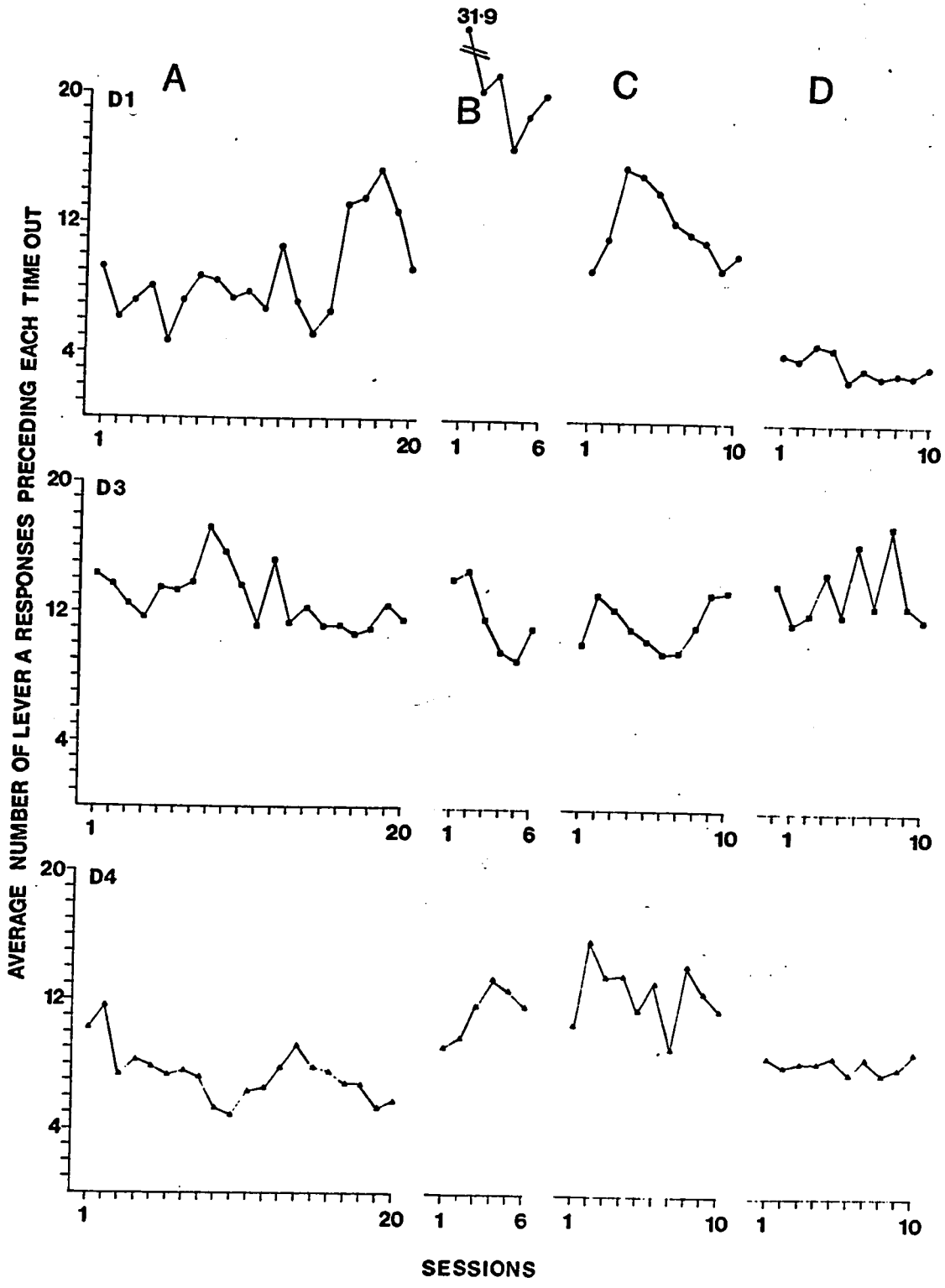

31·9
A
B
C
D
D1
D3
D4
20
12
4
1
20
6
10
AVERAGE NUMBER OF LEVER A RESPONSES PRECEDING EACH TIME OUT
SESSIONS

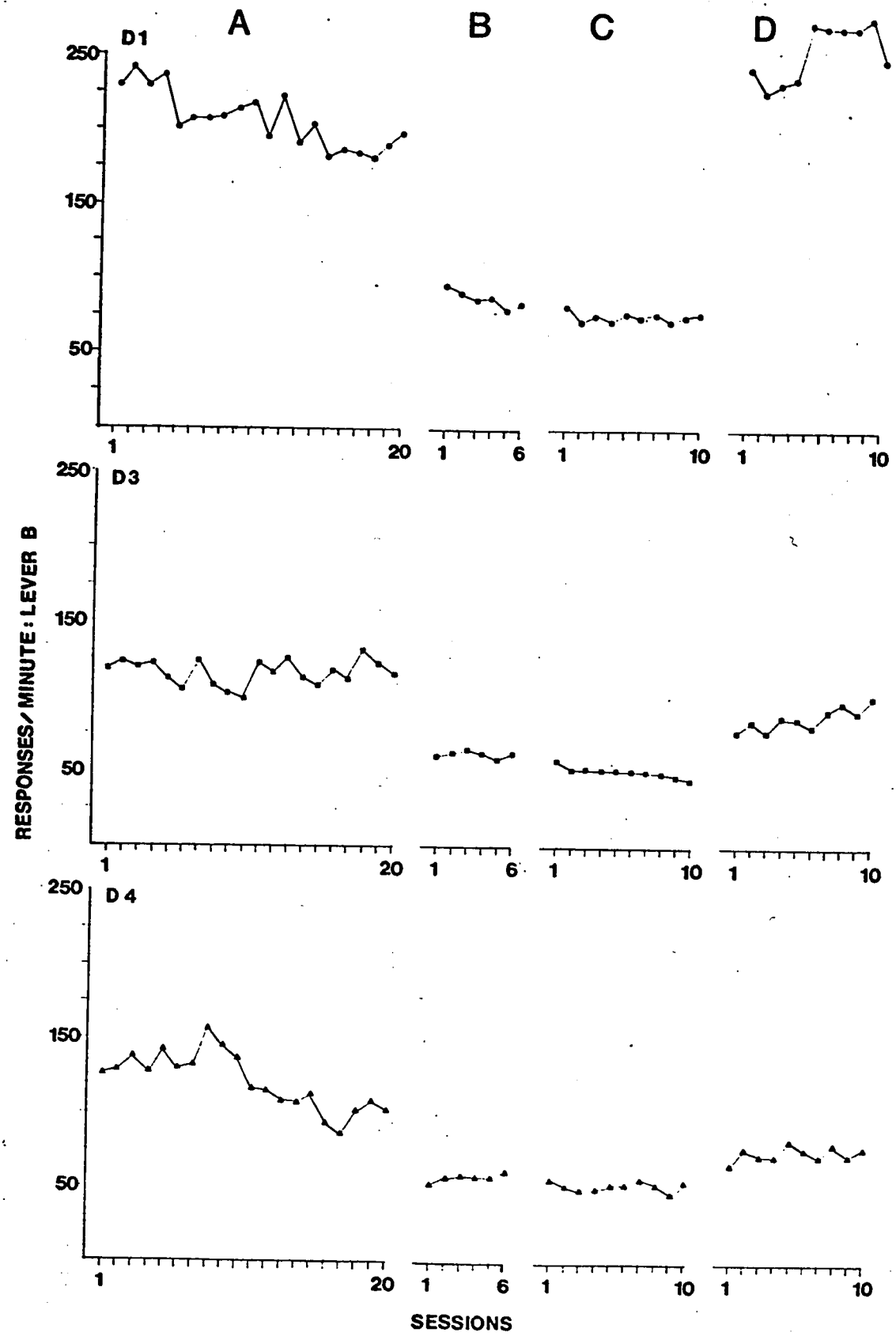
Fig. 17. In these graphs, the response rate per minute on Lever B (FR escape component) is plotted for each subject. Each point is the average value for a single experimental session.

A The 20 sessions preceding the introduction of unavoidable shocks.

B The 6 sessions during which unavoidable shocks were delivered to each subject.

C The 10 sessions immediately following the 6th session of unavoidable shock.

D 10 sessions preceding drug treatment (these were the 58th to the 68th sessions following the 6 sessions of unavoidable shock. No experimental manipulations were introduced during the intervening period).


A
B
C
D
D1
D3
D4
250
150
50
1
20
6
10
RESPONSES/MINUTE: LEVER B
SESSIONS

130 responses per minute and showed less variability than that of D4 which gave a difference between its lowest and highest session rates of 70 responses.

The performance of each subject in terms of the 5th behavioral measure is summarized in Figure 18. In this graph, the average number of responses in excess of the FR requirement that were emitted on Lever B during each period of active time throughout each session, are plotted for the 20 control sessions. The lowest average for subject D1 was 19 of these extra responses on session 15, and the highest was 52 responses on session 19. The record of subject D3 showed slightly less variation, having a lower value of 25 and an upper limit of 50 extra responses.

In terms of this measure, the performance of subject D4 at this stage was the most effective, in that it emitted the fewest responses of the three on Lever B in order to produce a time out. Throughout the 20 sessions, the average number of extra responses never exceeded 12, and the lowest average value was 3 extra responses on session 18.

Phase IV. The introduction of unavoidable shocks.

As described in the Method section unavoidable shocks were introduced over a period of six consecutive experimental sessions. These were delivered, on average, every 10 sec. in each period of active time between the 10th and 20th time out periods of each of these sessions. The location of the period of unavoidable shock delivery within the session, and the resulting general behavioral

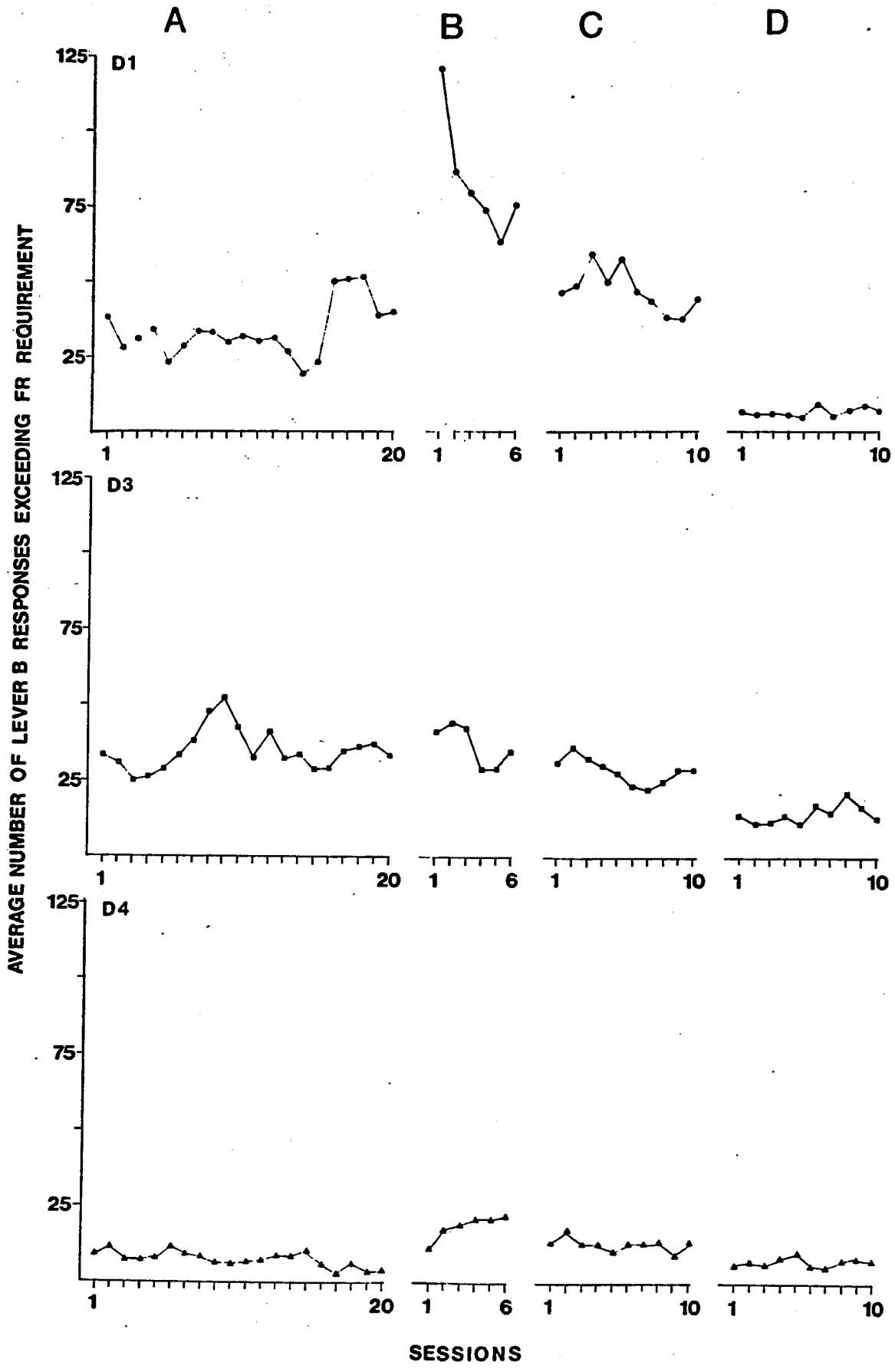
Fig. 18. In the graphs shown in this figure, the average number of responses on Lever B, in excess of the FR requirement, is plotted for each subject. Each point is the average value for a single experimental session.

A The 20 sessions preceding the introduction of unavoidable shocks.

B The 6 sessions during which unavoidable shocks were delivered to each subject.

C The 10 sessions immediately following the 6th session of unavoidable shock.

D 10 sessions preceding drug treatment (these were the 58th to the 68th sessions following the 6 sessions of unavoidable shock. No experimental manipulations were introduced during the intervening period).

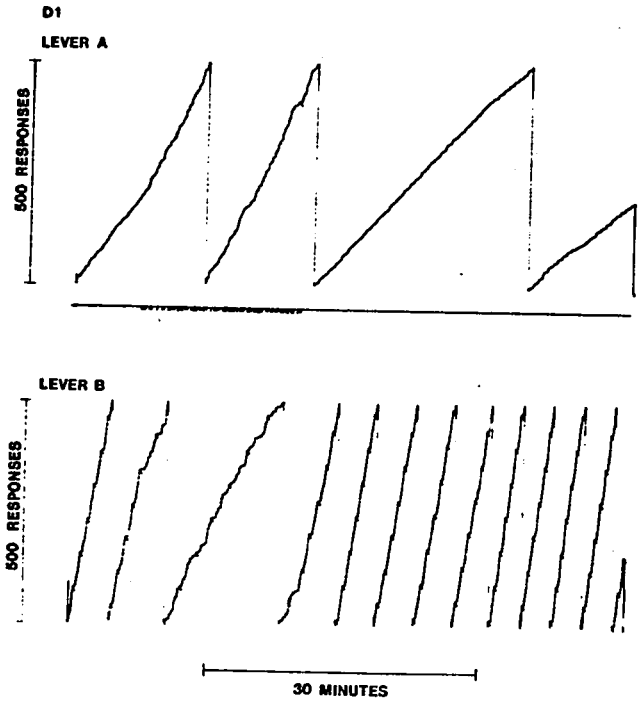

A
B
C
D
D1
D3
D4
125
75
25
1
20
6
10
AVERAGE NUMBER OF LEVER B RESPONSES EXCEEDING FR REQUIREMENT
SESSIONS

changes can be seen in Figures 19, 20 and 21, which are cumulative records of the performance of subjects D1, D3 and D4 respectively on the third session of this phase.

The upper record of Figure 19 is of the performance of subjects D1 on the free-operant avoidance component of the schedule. As in the preceding figures of this nature, shocks delivered in accordance with the parameters of the free-operant avoidance component are indicated by oblique, downward deflections of the pen. Immediately below this record is the trace produced by the event pen of the same cumulative recorder. This pen is not activated by the subjects's responses but is used solely, for the recording of programmed events. During this phase, it was employed to record each unavoidable shock delivered to the subject in the periods of active time between the 10th and 20th time out periods. Each of these shocks was registered by a downward deflection of the event pen from its baseline position.

It is apparent from the upper record of Figure 19, that following the introduction of unavoidable shocks there was a marked increase in the rate of responding of subject D1 on the free-operant avoidance lever. In addition, the pattern of responding became more erratic, and relatively long pauses in responding appeared as this part of the session progressed, until a shock was delivered according to the parameters of the free-operant avoidance component of the schedule shortly before unavoidable shock delivery was discontinued. Following the

Fig. 19. Cumulative records obtained from subject D1 during the third session of unavoidable shock presentation. The upper record is of responding on Lever A: the oblique deflections of the event pen immediately below the free-operant avoidance record indicate unavoidable shocks delivered to the subject and also delimit the duration of unavoidable shock delivery. The lower record shows responding on Lever B. A reduction in the FR escape response rate is apparent during the delivery of unavoidable shocks.

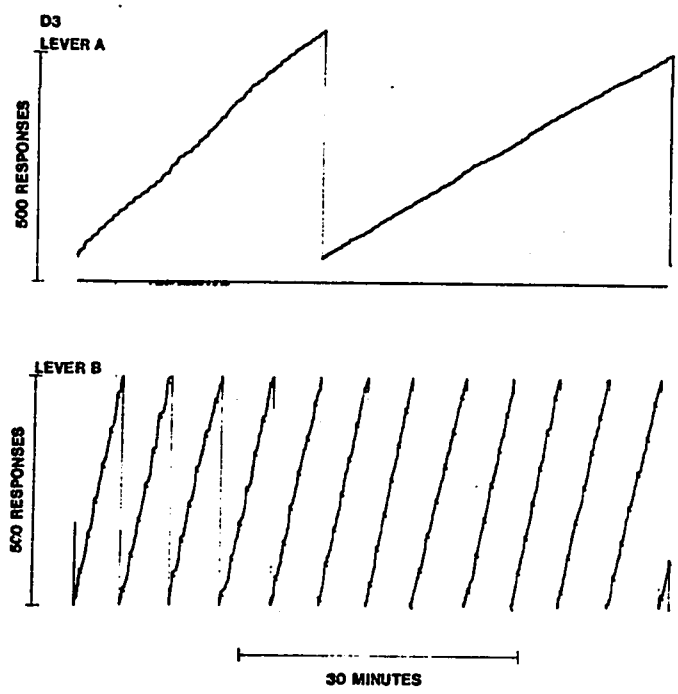

D1
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

cessation of unavoidable shock delivery, the rate of responding on Lever A decreased, and also became less erratic. No further change occurred during the remainder of the session.

The record reproduced in the lower part of Figure 19 shows the performance of subject D1 on the FR escape component (Lever B) of the concurrent schedule during the third session of this phase. Following the introduction of unavoidable shock, an immediate reduction in the rate of responding on Lever B was apparent. The pattern of responding also became relatively erratic, and was characterized by short bursts of responding followed by relatively long pauses, which was quite atypical of the subject's control performance. This erratic, low rate was replaced by a relatively high stable rate with only brief pauses, as soon as the delivery of unavoidable shock was discontinued.

Records of the performance of D3 during the third session of this phase are presented in Figure 20. The upper record of responding on the free-operant avoidance component of the schedule does not show the same degree of change during the period when unavoidable shocks were being delivered, that was noted in the case of subject D1. No change in the rate of responding is apparent from visual inspection of the record; however the pattern of responding appears to be more erratic during the period of unavoidable shock delivery when compared with subsequent performance when the delivery of unavoidable shocks had been discontinued. Inspection of the

Fig. 20. Cumulative records obtained from subject D3 during the third session of unavoidable shock presentation. The upper record is of responding on Lever A, the free-operant avoidance component. The trace immediately below this record is that of the event pen, and oblique deflections indicate the delivery of unavoidable shocks. The lower record is of responding on Lever B, the FR escape component.


D3
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

performance of subjects D3 on the FR escape component (Lever B) of the concurrent schedule during the same session revealed no readily identifiable changes attributable to the delivery of unavoidable shock, in any part of the lower record of Figure 20.

The performance of subjects D4 on both components of the concurrent schedule is reproduced in Figure 21. Some increase in the rate of responding on the avoidance lever following the introduction of unavoidable shocks, is apparent from visual inspection of the upper record.

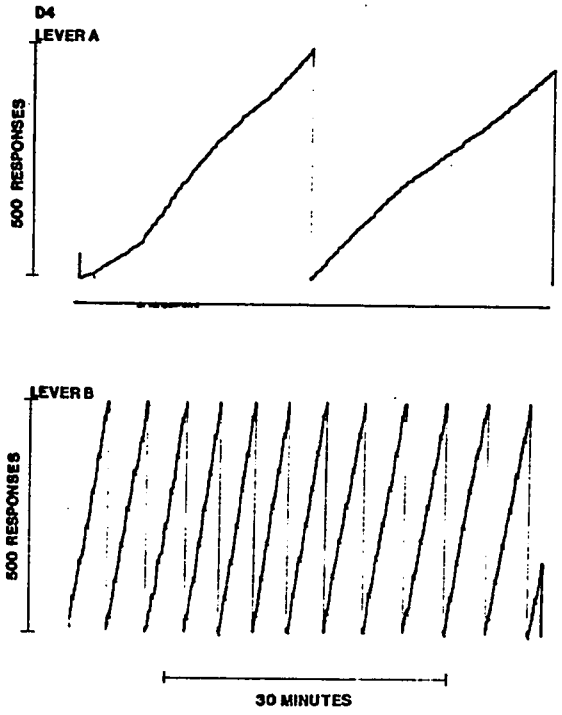
As was the case when considering D3, no changes in the performance of subject D4 on the FR escape component of the schedule can be reliably identified by visual inspection of the lower record of Figure 21.

A more accurate and detailed assessment of the effects of unavoidable shocks, can be obtained from the results of the five behavioral measures described in the Method section. These are presented in graphical form in section B of Figures 14 to 18 inclusive.

The performance of all three subjects on the first of these measures, is shown in Figure 14(B) in which the average time taken by each subjects, to initiate a TO period during each of the 6 sessions of this phase, is plotted graphically.

The curve for subject D1 shows a decrease in the average time taken to initiate a time out, over the 6 sessions. However, it should be noted that during the preceding 20 control sessions, the

Fig. 21. Cumulative records obtained from subject D4 during the third session of unavoidable shock presentation. The upper record is of responding on Lever A, the free-operant avoidance component. The trace immediately below this record is that of the event pen, and oblique deflections indicate the delivery of unavoidable shocks. The lower record is of responding on Lever B, the FR escape component.


D4
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

average time for this subject never exceeded 45 sec., whereas on the first session of the present phase, this value was increased to 59 sec. The tendency for this value to decrease was maintained over the 2nd, 3rd and 4th sessions, but an increase was observed over the remaining two sessions of this phase.

Subjects D3 and D4 gave similar performances, but each differed from D1. During the first session of the phase, both subjects showed a decrease in the average time taken to initiate a time out, to a level below that of the preceding control session. This effect was opposite to that seen in subject D1 where a substantial increase over the preceding control session value was apparent. However, during the early sessions of the phase, a common feature of performance was apparent in all subjects; namely, a decrease in the average time taken to initiate a time out, relative to the first session of the phase. The value of this measure for subjects D3 and D4 did not show any increase over the remaining sessions of the phase. A similar decrease in value was observed in the second measure during the early sessions of the phase. The number of avoidance responses per minute for each monkey during the 6 sessions are presented in Figure 15(B). During the 20 control sessions preceding this phase, the avoidance rate for subject D1 was between 11 and 21 responses per minute. Over the first 4 sessions during which unavoidable shocks were delivered to the animal, this rate decreased to 9.6 responses per minute. A slight increase to 11 responses per minute occurred

during the 5th and 6th sessions of the phase. The same trends were apparent in subjects D3 and D4 but were most marked in D3 when the response rate decreased in the first session of the phase, to 8 responses per minute from a preceding value of between 11 and 16 responses per minute for the 20 preceding control sessions.

Figure 16(B) shows the average number of avoidance responses emitted by each animal during each period of active time for the 6 sessions of this phase. Subjects D1 and D4 show a marked increase in the number of these responses emitted on the first session of the phase. The increase for subject D1 was from averages of between 5 and 16 responses for the preceding 20 control sessions to an average of 32 responses during the first session of unavoidable shock presentation. For subject D4 the average number of responses emitted in each period of active time continued to increase until the 4th session of the phase, but this increase to an average of 13 responses from preceding control averages ranging between 5 and 9 responses was less than that observed in subject D1.

The average number of avoidance responses per period of active time emitted by subject D1 showed a decreaseing trend from the second session through to the end of the phase. A similar decrease was apparent in subject D4 from the 4th to the 6th sessions of the phase.

The performance of subject D3 is also shown in Figure 16(B). The initial increase in the average number of responses noted in D1 and D4 at the start of this phase is absent, but the subsequent

decrease is clearly marked in the record of subject D3 following the 2nd session of unavoidable shock presentation.

The number of FR (Lever B) responses per minute emitted by each subject during each of the 6 sessions of unavoidable shock presentation are plotted in Figure 17(B). A clearly marked reduction in this response rate was apparent in all subjects. Comparison with the corresponding results obtained from the preceding control sessions and presented in Figure 14 shows that during the first session of this phase, the response rate per minute on Lever B for subject D1 was reduced to 95 from control values ranging from 180 to 242. Similarly, the response rate of subject D3 during the same session was reduced to 60 from preceding control values ranging between 100 and 130 responses per minute, and subject D4 to 50 from control values within the range 86 to 156 responses per minute. In each case, the response rate remained at the lower value for the remaining 5 sessions of the phase.

Results obtained from the fifth behavioral measure are presented in Figure 18(B), where the average number of responses on Lever B during each period of active time, that were in excess of the number specified by the FR requirement of the schedule, are plotted for each subject over the six sessions of the phase.

Subjects D1 showed a marked increase in the average number of these responses during the first session of exposure to unavoidable shock, and thereafter, a decline to a value slightly

in excess of the control range. This point is illustrated by comparing Figure 18(B) with the results in terms of this measure of the control performance shown in Figure 18(A). Comparison of the corresponding figures for subjects D3 and D4 reveal a similar marked increase in the average number of Lever B responses in excess of the FR requirement for subject D4 during the first session of the phase. In the case of subject D3, a slight increase relative to the immediately preceding control session was apparent, but was within the limits of fluctuation in this measure that occurred over the 20 preceding control sessions. The increase in the average number of these responses emitted by subject D4 was sustained over the six sessions of the phase.

(B) Re-estabilization of performance under the concurrent schedule

Section C of Figures 14 to 18 show the performance of each subject, in terms of the 5 measures adopted, over the 10 sessions following the cessation of unavoidable shock delivery. These 10 sessions show the immediate effects of the preceding six sessions during which unavoidable shocks were delivered.

In general, the same trends were noted in all subjects over all 5 measures. The average time taken to initiate a TO period [Figure 14(C)], the number of avoidance responses per minute [Figure 15(C)] and the average number of avoidance responses emitted during each period of active time [Figure 16(C)] all returned to a level close to that preceding the phase of unavoidable shock delivery.

The most marked change was in the rate of responding on the FR escape lever per minute. The reduction in this response rate which was apparent in Phase IV remained after the phase had ended, and no tendency for it to increase to the original level was apparent in any of the subjects [Figure 17(C)] as was the case with the first three measures. The 5th measure [Figure 18C)] indicated a return to the values recorded during the 20 sessions preceding the introduction of unavoidable shocks.

The relatively permanent effects of the delivery of unavoidable shocks are shown in Figures 14 to 18 (Section D) which also serve to illustrate the performance of each subject during the 10 control sessions preceding the evaluation of the effects of the drugs employed in the present study.

The lasting effects may be summarized as follows when compared with the respective performances during the 20 control sessions preceding Phase IV:

1) The average time taken to initiate a TO period stabilized at a lower level for subject D1, but at a slightly higher level for subjects D3 and D4.

2) The response rate per minute on the free operant avoidance component stabilized at a lower level in each case.

3) The average number of avoidance responses in each period of active time was, in general, unchanged.

4) The response rate per minute on the FR escape component stabilized for all subjects at the new low level which appeared during the early sessions of Phase IV.

5) The average number of Lever B responses in excess of the FR requirement also stabilized at a new, low level, but its development was relatively slow, since it had not appeared during the 10 control sessions immediately following the period of unavoidable shocks.

Phase V. Evaluation of the independent effects of (A) d-Amphetamine sulphate and (B) Chlorpromazine

The review of previous work in behavioral pharmacology presented in the Introduction showed that drug-induced modifications of ongoing rates of responding are most clearly identified in the individual subject. The pooling of data from two or more subjects may only obscure the effect of the drug, since control rates of responding are rarely the same in any two animals. Thus, the effects of the drugs used in this phase, will be reported in terms of each individual subject, and the rates of responding on each lever form the most important data.

(A) The effects of d-Amphetamine sulphate.

The effects of this drug on the performance of subjects D1 and D3, at each of the four dosage levels in terms of the five behavioral measures employed, are summarized in Table 2. The values presented in this table are averages obtained from the 10 control sessions preceding drug administration, and the five determinations of each drug dosage level.

Table 2

The effects of each dosage level of d-Amphetamine sulphate on the performance of subjects D1 and D3 on the concurrent schedule

D1

Dose level in mg/kg	Measure 1*	2*	3*	4*	5*
*Control	19.19	3.69	11.52	250.21	5.80
0.3	33.7	11.02	19.35	163.67	15.85
0.1	38.66	16.86	24.18	152.84	33.36
0.3	38.60	16.76	26.02	173.94	35.32
1.0	36.04	11.98	19.72	155.92	16.76

D3

Dose level in mg/kg	Measure 1*	2*	3*	4*	5*
*Control	57.24	13.71	14.12	89.11	14.50
0.03	15.68	3.12	11.95	324.30	6.97
0.1	16.84	4.72	16.00	357.61	17.10
0.3	15.16	5.52	21.42	398.83	24.58
1.0	159.52	48.78	17.04	43.40	33.84

*Control data plotted session by session in Figures 14 - 18 inclusive.

1* The average time (in seconds) taken by the animal during the complete session, to initiate each period of time out.

2* The average number of avoidance responses for each period of active time throughout each session.

3* The rate of avoidance responding per minute (Lever A) for each session.

4* The rate of FR responding per minute (Lever B) for each session.

5* The average number of FR responses that were emitted during the COD (initiated by each avoidance response) throughout the session. As specified by the schedule, such responses were ineffective in reducing the FR requirement of 75 responses.

Considering, first, the major trends emerging from the results of monkey D1. The average time taken by the subject to initiate TO periods was increased relative to the control value, by all dosage levels. Since the degree of increase was much the same following the administration of each dose, the measure did not distinguish between the various concentrations of the drug.

A similar consistency of effect was apparent in the results of the second measure. Each dosage level of the drug increased the average number of avoidance responses emitted by the animal during each period of active time. The greatest increment over the control value was observed at the 0.1 and 0.3 mg/kg dose levels, and was slightly less at both the lowest and highest dosages.

The number of avoidance responses per minute increased as dosage level increased from 0.03 to 0.3 mg/kg.

While the value of the measure at the 1.0 mg/kg dosage was markedly higher than that obtained under control conditions, it was slightly lower than those obtained at both the 0.1 and 0.3 mg/kg levels.

The number of responses per minute on Lever B was considerably decreased by all dosages of d-Amphetamine sulphate; however, no definite trends attributable to increasing dosage level could be identified from these data.

The fifth measure was of the average number of Lever B responses during each time out, that were in excess of the number specified by the FR requirement. Again, these were increased by all

administrations of d-amphetamine sulphate, and the increase was positively related to increasing dosage level from 0.03 to 0.3 mg/kg. Some reversal in this trend was apparent at the 1.0 mg/kg dosage, but the number of these responses was still considerably higher than the corresponding value under control conditions.

The results obtained from monkey D3 over the same five measures differed in some respects from those of D1. The average time taken to initiate a TO period was decreased under the 0.03, 0.1 and 0.3 mg/kg drug dosages. However, this effect was completely reversed following the administration of the highest dosage, and the average time taken to initiate a time out was greatly increased. The same trend was apparent in the second measure, where the average number of avoidance responses emitted during periods of active time were considerably below the control value after administration of the 0.03, 0.1 and 0.3 mg/kg dosages. However, within this range, a slight but consistent increase was noted, from an average value of 3.12 responses at the lowest dosage, to an average of 5.52 responses at the 0.3 mg/kg dose level. At the highest d-amphetamine dosage, there was a marked increase in the value of this measure compared with that obtained under control conditions.

Avoidance responses per minute were increased following administration of all drug levels apart from the lowest dosage, where a small decrease was recorded.

A marked, progressive increase in the responses per minute on Lever B related to increasing dosage level, was recorded at all

drug levels apart from the 1.0 mg/kg dose where a decrease was apparent.

On the fifth measure, responses on Lever B exceeding the FR requirement, a decrease relative to control value was recorded at the 0.03 mg/kg dosage. Thereafter, a progressive increase above the control value was apparent with increasing magnitude of drug dosage.

Using cumulative records of performance and graphical representations of responses rates, it was possible to examine the effects of d-amphetamine on the components of the ongoing behavior in more detail. Figure 22A shows the response rate per minute on Lever B for subjects D1 and D3 as absolute deviations from the respective control baselines. In comparing the two sets of results, it is apparent that there is a consistent depression of response rates in subject D1 where the control rate is relatively high (250 responses per minute). However, when the control rate was relatively low, as in the case of subject D3 (89 responses per minute), d-amphetamine tended to increase the response rate over the dosage range 0.03 to 0.3 mg/kg and only at the highest dosage of 1.0 mg/kg was the response rate depressed. These trends are illustrated in Figures 23 to 28 inclusive in which cumulative response records showing the performance of each subject under each dosage level of d-amphetamine, are reproduced.

Figure 23 shows the performance of monkey D1 following the administration of 0.03 mg/kg of d-amphetamine. When compared with

Fig. 22. The histograms presented in this figure, summarize the effects of each of the 4 dosage levels of d-amphetamine sulphate in terms of the FR escape response rate per minute (A) and the free-operant response rate per minute (B) for D1 and D3 respectively. Each histogram is presented in terms of absolute deviations from the control response rate level. The ranges are indicated by the vertical lines bisecting each histogram bar.

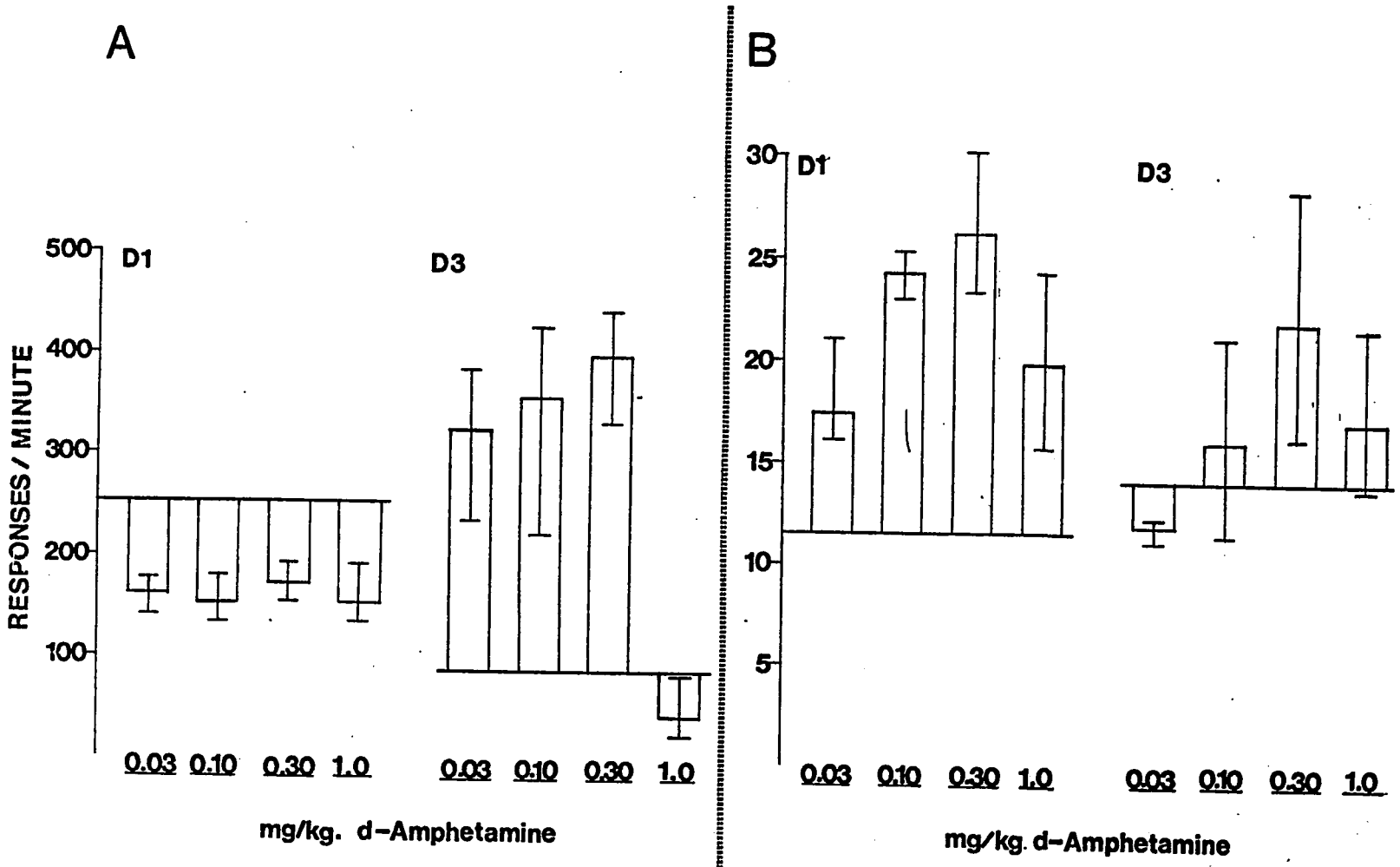
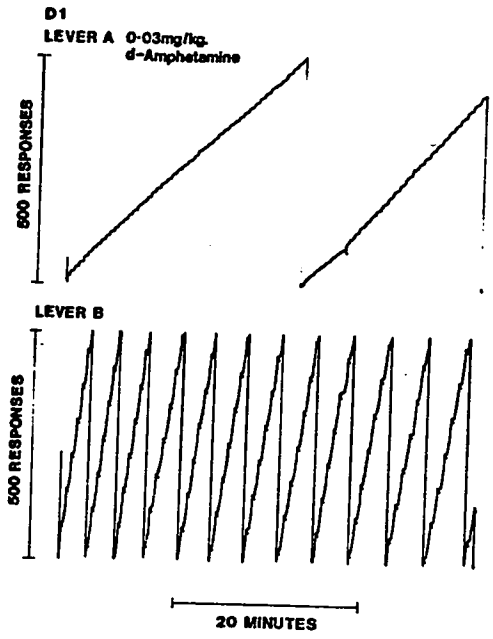

A
B
D1
D3
D1
D3
RESPONSES / MINUTE
500
400
300
200
100
30
25
20
15
10
5
0.03
0.10
0.30
1.0
0.03
0.10
0.30
1.0
0.03
0.10
0.30
1.0
0.03
0.10
0.30
1.0
mg/kg. d-Amphetamine
mg/kg. d-Amphetamine

Fig. 23. Cumulative response records showing the performance of subject D1 following the administration of 0.03 mg/kg d-amphetamine.


D1
LEVER A
0·03mg/kg.
d-Amphetamine
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

the records obtained under control conditions (Figure 11), reduction in the response rate on the FR escape component, is clearly marked. The lower records of Figures 24, 25, 26 show the continuation of this trend under the remaining three dosage levels. The performance of monkey D3 following the administration of 0.03 mg/kg of d-amphetamine is shown in Figure 27. When compared with the control record obtained from this subject (Figure 12), the large increase in the response rate on Lever B is apparent. Again, when compared with the control record, Figure 27 shows a further increase in this response rate following the administration of the 0.1 and 0.3 mg/kg dosage levels of d-amphetamine. Figure 28 shows the marked reduction in response rate on Lever B which followed the administration of the 1.0 mg/kg dosage.

The results plotted in Figure 22B summarize the changes in avoidance response rate per minute in both subjects, at each drug dosage level. The major trends are further illustrated in Figures 23-28. The consistent increase in the avoidance response rate for monkey D1 over all dosages of d-amphetamine is apparent from a comparison of the appropriate records in Figures 23-26 inclusive and the control record (Figure 11).

The upper records of Figures 27-28 are of the avoidance response rate of subject D3 under the four drug conditions. The trends are not as clearly marked as in subject D1, but the increase in the avoidance response rate may be seen when the upper record in Figure 28 is compared with the corresponding control record in Figure 12.

Fig. 24. Cumulative response records obtained from subject D1 following the administration of 0.1 mg/kg of d-amphetamine.

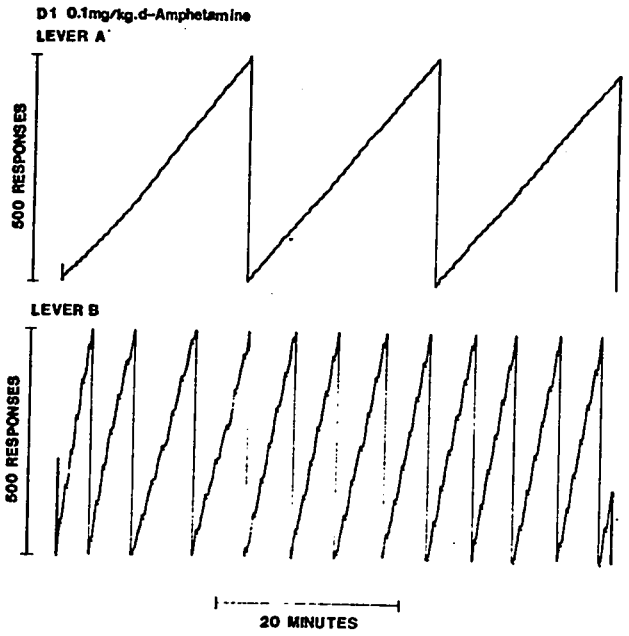

D1 0.1mg/kg.d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

Fig. 25. Cumulative response records obtained from subject D1 following the administration of 0.3 mg/kg d-amphetamine.

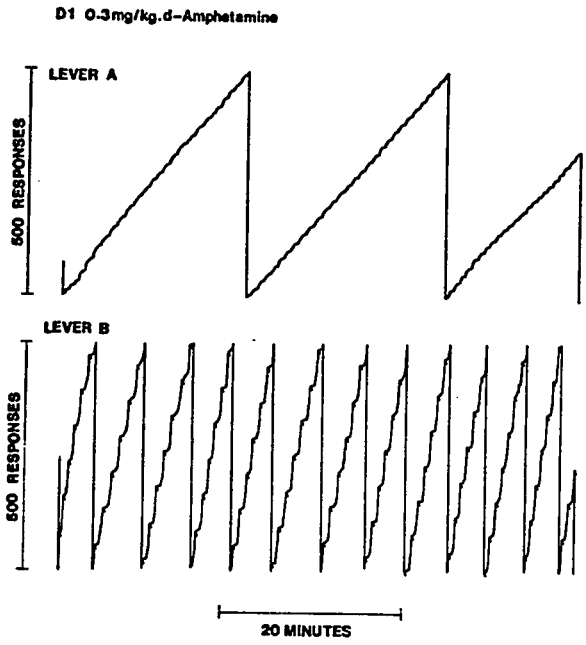

D1 0.3mg/kg.d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

Fig. 26. Cumulative response records showing the performance of subject D1 following the administration of 1.0 mg/kg of d-amphetamine.

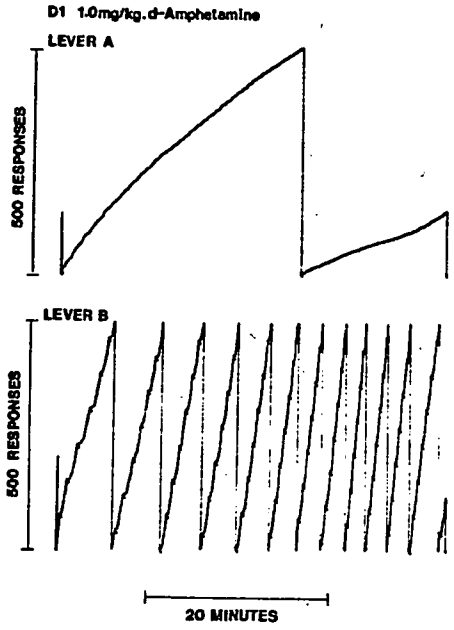
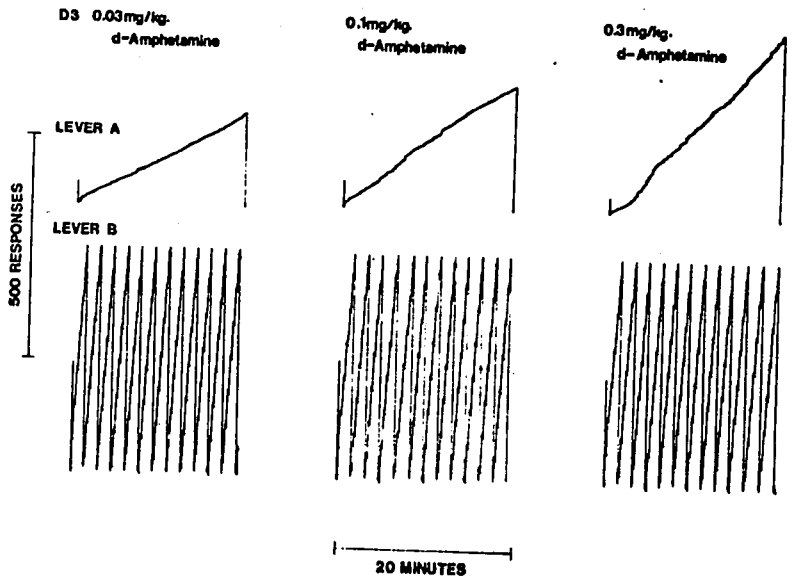
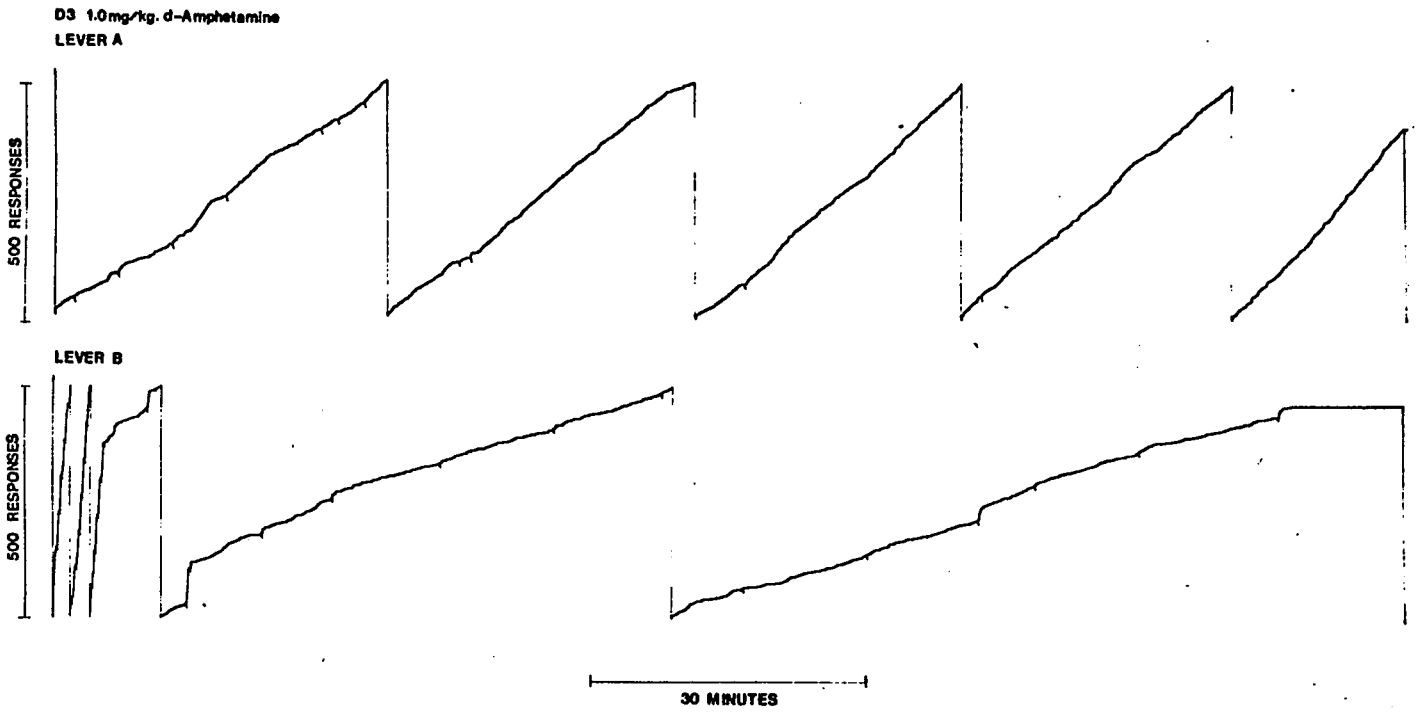

D1 1.0mg/kg.d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

Fig. 27. Cumulative response records obtained from subject D3 summarizing the performance of this subject following the administration of 0.03 mg/kg d-amphetamine (upper and lower traces on the left), 0.1 mg/kg of d-amphetamine (center traces) and 0.3 mg/kg d-amphetamine (right-hand traces).


D3 0.03mg/kg.
d-Amphetamine
0.1mg/kg.
d-Amphetamine
0.3mg/kg.
d-Amphetamine
LEVER A
LEVER B
500 RESPONSES
20 MINUTES

Legends

Fig. 28 .. Cumulative response records obtained from subject D3 following the administration of 1.0 mg/kg of d-amphetamine.


D3 1.0mg/kg. d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

The further point that emerges from Figure 22B is that there was less variability in the performance (as indicated by the response ranges) of monkey D1 compared with that of monkey D3. This was attributable, in part, to the fact that the control performance of both subjects were changing over the period of evaluation of the effects of d-amphetamine. In other words, relatively permanent changes in performance followed drug administration, and these were greater for subject D3 than for D1. Table 3 shows the performance of subjects D1 and D3 on the five behavioral measures over 10 control sessions selected at random from 15 consecutive control sessions introduced prior to the final evaluation of each dosage

Table 3

Control data obtained during drug test series

	Measures				
	1	2	3	4	5
Subject					
1	31.25	11.06	21.37	165.87	10.02
3	15.20	3.00	11.62	307.02	5.09

Comparison with the corresponding control date in Table 2 shows that the major changes in the performance of monkey D3, are an increase in the Lever B (FR) response rate per minute, and a decrease in the avoidance response rate per minute. Similar comparisons show that the changes in the performance of monkey D1 were the reverse of those in subject D3; the FR escape (Lever B) response rate showed a marked decline while the avoidance response rate per minute increased.

(B) The effects of chlorpromazine

These results are presented in the same manner as that adopted in part (A).

The effects of chlorpromazine on the performance of subject D4 are presented in Table 4.

Table 4

The effects of each dosage level of chlorpromazine on the performance of subject D4 on the concurrent schedule.

	Measure				
Dose level in mg/kg	1	2	3	4	5
Control	60.98	8,47	7.81	76.22	7.21
0.03	63.86	9.78	9.20	76.66	7.36
0.1	79.22	10.44	10.00	75.14	10.96
0.15	88.34	13.84	9.54	58.28	9.44
0.03	121.10	11.34	5.72	49.48	15.38

The first important result that should be noted at this stage emerged from observation of the subject rather than from the data. Following the administration of the 0.3 mg/kg dosage, it was invariably necessary to terminate the session, since the animal ceased to respond on both the FR escape (Lever B) and the avoidance lever and thus, was receiving a shock every 5 sec. Since the survival of the subject was threatened, the session was terminated after between 15 and 20 consecutive shocks had been delivered.

It was also noted that the behavioral effects of chlorpromazine appeared between 20 and 30 minutes after injection but that the onset of these effects was relatively rapid (within two consecutive periods of active time). The behavior preceding the appearance of the drug effects was similar to that under control conditions (Figure 13). Thus, the results obtained from the five behavioral measures, following the injection of the 0.3 mg/kg dosage (Table 4, 0.3 mg/kg dosage) are not an accurate representation of the effects of this drug. For example, the time elapsing between the last TO period initiated by the subject, and the termination of the session by the experimenter, was different for each determination of this doage level, and this in turn, affected the values of the avoidance and FR response rates per minute.

The most consistent result emerging from the five measures over the 0.03,0.1 and 0.15 mg/kg drug levels was the increase in the average time taken to initiate a time out, the effect being more pronounced at the higher dosages. The increase in the average

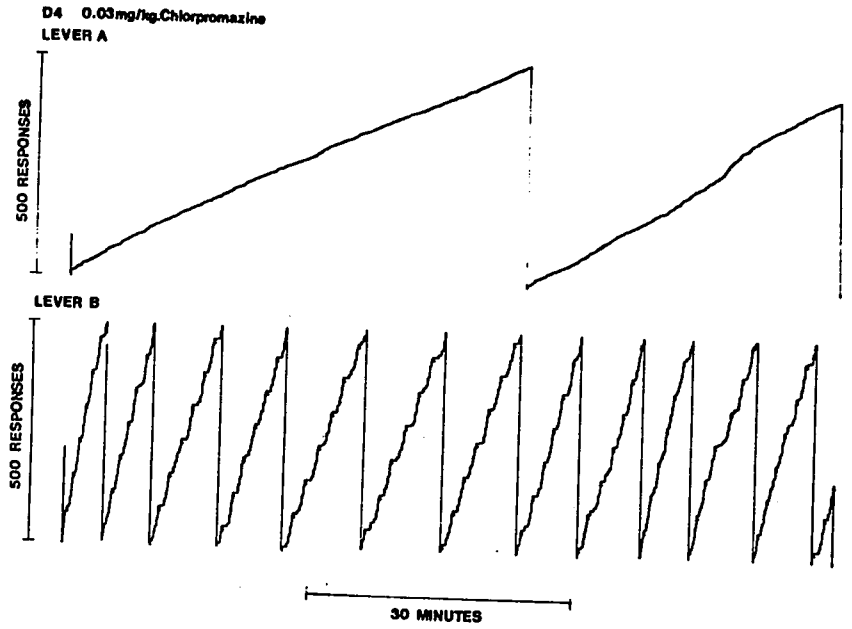
number of avoidance responses in each period of active time was clearly marked over the first three dose levels.

There was a clear increment in the avoidance response rate per minute following each drug administration but this showed no apparent relationship to dosage level. The 0.03 mg/kg dosage was not followed by an apparent change in the response rate per minute on the FR escape (Lever B) lever, but a marked decrease in this response rate was associated with both the 0.1 and 0.15 mg/kg doses.

The number of responses on Lever B in excess of that specified by the FR requirement were increased by the 0.1 and 0.15 mg/kg dosages, but relatively unchanged by the 0.03 mg/kg dose. Figures 29, 30, 31, show representative cumulative records of the performance of subject D4 under each dosage level of chlorpromazine.

The cumulative records of performance following the injection of 0.03 mg/kg of the drug, are reproduced in Figure 29. Comparison with the corresponding control records (Figure 13) shows the increase in the rate of responding on the avoidance lever following drug administration. The response rates per minute on the FR escape lever, under control conditions, and following the injection of 0.03 mg/kg of the drug as listed in Table 4, show an apparent equality in rate. However, comparison of the corresponding cumulative records (Figures 13 and 29) reveals that the pattern of responding is different. The record obtained following the injection

Fig. 29. Cumulative response records, obtained from subject D4, illustrating the effects of 0.03 mg/kg of chlorpromazine on each component of the concurrent schedule.


D4 0.03mg/kg.Chlorpromazine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

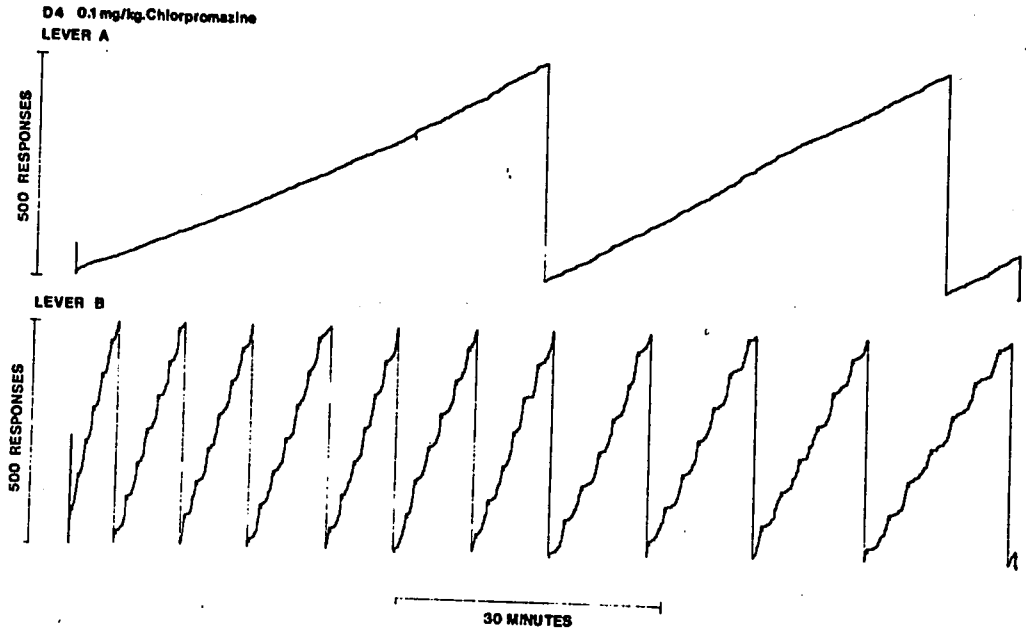
of 0.03 mg/kg chlorpromazine shows that the rate at the start of the session was higher than under control conditions. The effects of the drug appeared after the 12th time out of the session, and thereafter, the periods of active time preceding each time out were lengthened. This took the form of relatively long pauses in responding on Lever B during each period of active time.

The same trends were observed in the cumulative records obtained from subject D4 following the administration of the 0.1 mg/kg dose. The avoidance rate was increased, in both cases, over the control level. Figure 30 showing performance under the 0.1 dosage exemplifies this trend. Similarly, the overall reduction in response rate on the FR escape lever took the form of increasingly frequent pauses in each cycle of active time.

In Figure 31 the cumulative records obtained following the injection of 0.3 mg/kg of chlorpromazine, are reproduced. Comparison with the corresponding control records (Figure 13) shows that the avoidance response rate was lower following drug administration than under control conditions. It is also apparent that this rate decreased to zero, with the result that shocks were being delivered every 5 sec. until the session was terminated. The lower record of Figure 31 shows that the response rate on the FR escape component was similarly reduced to zero at this dosage level.

As was the case with subjects D1 and D3, the data obtained from 10 control sessions, prior to the final determination of each dosage

Fig. 30. Cumulative response records obtained from subject D4 following the administration of 0.1 mg/kg of chlorpromazine.


D4 0.1 mg/kg.Chlorpromazine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
30 MINUTES

value, revealed that changes had occurred in the performance of monkey D4 under non-drug conditions.

The data obtained from the control sessions are presented in Table 5 in terms of the mean values for the 10 sessions, of the five behavioral measures. Comparison with the corresponding results under control conditions presented in Table 4 reveals that the major changes were a reduction in the average time taken to initiate a TO period, and an increase in both the avoidance and FR response rates per minute.

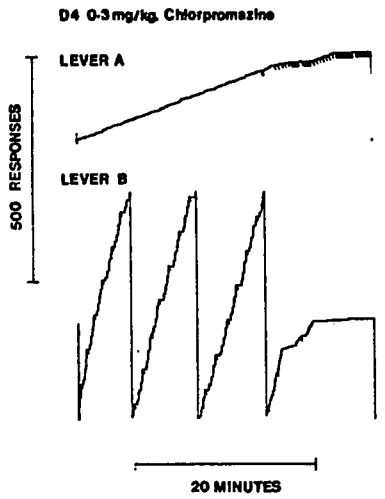
Table 5

Control data obtained during drug test series

	Measures				
	1	2	3	4	5
Subject					
D4	57.7	10.75	11.93	88.86	9.30

The final part of this phase was concerned only with subjects D1 and D3, and was a necessary prerequisite for Phase VI. On completion of the determinations of the effects of d-amphetamine, the behavioral modifications of performance following the administration of the highest (0.3 mg/kg) dosage of chlorpromazine were evaluated. This dosage level of chlorpromazine was administered on five separate occasions with 2 or 3 control sessions intervening between each determination. The behavioral changes following the administration of chlorpromazine at this dosage level were similar in all respects to those already described for subject D4. The resemblence is evident if the cumulative records obtained from subjects D1 and D3, reproduced in Figure 32, are compared with the corresponding records obtained from monkey D4 (Figure 31).

Fig. 31. Cumulative response records obtained from subject D4 following the administration of 0.3 mg/kg chlorpromazine.


D4 0·3 mg/kg. Chlorpromazine
LEVER A
LEVER B
500 RESPONSES
20 MINUTES

As was the case with subject D4 and for the reasons already stated, the five behavioral measures of the effects of injecting 0.3 mg/kg of chlorpromazine in subjects D1 and D3 were not adequate for indicating the more detailed effects of the drug. However, general trends are apparent when the results in terms of these measures, are compared with the corresponding control values, and they are presented in Table 6.

Table 6

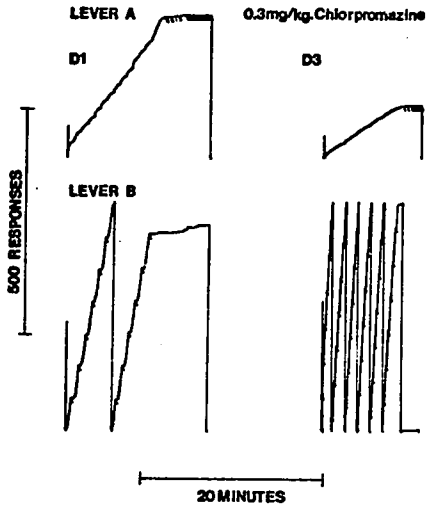
The effects of each dosage level of chlorpromazine on the performance of subject D4 on the concurrent schedule

		Measures				
Dosage Level		1	2	3	4	5
D1	Control	31.25	11.06	21.37	165.87	10.02
	0.3 mg/kg chlor.	66.38	21.34	19.90	126.52	48.62
D3	Control	15.20	3.00	11.62	307.02	5.09
	0.3 mg/kg chlor.	40.74	5.70	8.96	280.72	9.40

Phase VI. Evaluation of the effects of simultaneous administration of d-amphetamine sulphate and chlorpromazine.

In the Method section it was stated that each of the three dosage levels of d-amphetamine of 0.1, 0.3 and 1.0 mg/kg were administered together with 0.3 mg/kg of chlorpromazine. Each of these simulatenous administrations of the two drugs which involved two separate injections, may be referred to as a dosage combination. Injection of the 0.3 mg/kg dosage of chlorpromazine was

Fig. 32. The cumulative response records presented in this figure, summarize the effects of the 0.3 mg/kg dosage of chlorpromazine on the performances of subjects D1 and D3.


LEVER A
0.3mg/kg.Chlorpromazine
D1
D3
LEVER B
500 RESPONSES
20 MINUTES

invariably followed by complete cessation of responding on the levers (Figures 31, 32), and termination of the experimental session. Since the three dosage levels of d-amphetamine, listed above, were consistently followed by a change in performance when administered independently, they were evaluated in terms of their capacity to modify the effects of the 0.3 mg/kg dosage of chlorpromazine.

It has been shown in the results of the previous phase, that the control performances of the subjects underwent relatively permanent modification following independent administration of d-amphetamine and chlorpromazine. Thus, the effects of the dosage combinations were evaluated in terms of each subject's performance over the 10 control sessions, selected at random from the control sessions preceding the final evaluation of the independent effects of each drug dosage.

The results presented in Table 6 were based on five determinations of each dosage combination, and are given in terms of the five behavioral measures employed. THe control values mentioned above, and recorded in Tables 3 and 5 are included in Table 7 in order to facilitate comparisons.

The first point to be made is that the values presented in this table, that were obtained from the 0.3 mg/kg chlorpromazine 0.1 mg/kg d-amphetamine dosage combination do not give sufficient information on the full effects of two drugs acting simultaneously. As was the case when 0.3 mg/kg of chlorpromazine was administered singly, the response rate on both Lever A and Lever B decreased

Table 7

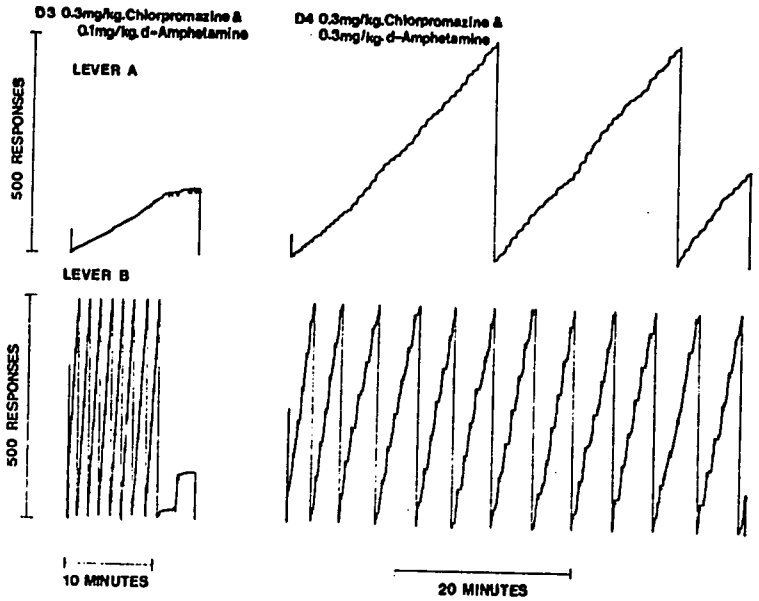
The effects of each dosage combination on the performance of subjects D1, D3 and D4

Subject	Dosage combination	1	2	3	4	5
D1	Control	31.25	11.06	21.37	165.87	10.02
	0.3 Chlor. + 0.1 amph.	29.15	10.75	22.40	191.31	20.95
	0.3 chlor. + 0.3 amph.	46.96	22.92	28.42	170.58	57.62
	0.3 chlor. + 1.0 amph.	33.88	10.50	15.46	178.04	23.58
D3	Control	15.20	3.00	11.62	307.02	5.09
	0.3 chlor. + 0.1 amph.	15.42	2.82	11.12	342.88	10.12
	0.3 chlor. + 0.3 amph.	12.62	2.42	11.42	412.30	11.72
	0.3 chlor. + 0.3 amph.	12.65	2.50	11.87	418.05	13.02
D4	Control	57.7	10.75	11.93	88.86	9.30
	0.3 chlor. + 0.1 amph.	66.70	20.55	18.35	93.82	24.55
	0.3 chlor. + 0.3 amph.	51.58	20.20	22.98	120.56	21.08
	0.3 chlor. + 1.0 amph.	29.30	5.50	11.58	185.86	9.92

to zero following injection of the above dosage combination. Thus, shocks were being delivered every 5 sec., and it was necessary for the experimenter to terminate the session. This was a consistent effect in the results of all the subjects, and a further point of similarity with the effects of the 0.3 mg/kg dosage of chlorpromazine was that, up to the time when the effects of chlorpromazine appeared, performance did not differ in any major respect from patterns emerging under control conditions.

Cumulative records obtained from subject D3 following the administration of the 0.3 mg/kg chlorpromazine 0.1 mg/kg d-amphetamine dosage combination are reproduced in Figure 33. The record is representative of those obtained from all the subjects after injection of this dosage combination. Comparison with the corresponding records obtained from the subject following administration of 0.3 mg/kg chlorpromazine alone, indicates that the effects of chlorpromazine were not obviated by the simultaneous presence of 0.1 mg/kg of d-amphetamine. In spite of the fact that the response rate on the FR escape lever (lower left record, Figure 33) was reduced to zero prior to the termination of the session, the relevant results presented in Table 7 indicate an increase in the response rates relative to the control value, for the duration of the session. The same results were obtained from subjects D1 and D4, and indicates that a rate enhancing effect of d-amphetamine at the 0.1 mg/kg dosage preceded the chlorpromazine effect.

Fig. 33. The cumulative response records presented in this figure illustrate the following effects:- 1) In the upper and lower records on the left is shown the performance of subject D3 following the joint administration of 0.3 mg/kg chlorpromazine, and 0.1 mg/kg d-amphetamine. 2) The upper and lower traces on the right of the figure show the performance of subject D4 following the joint administration of 0.3 mg/kg chlorpromazine and 0.3 mg/kg d-amphetamine.


D3 0.3mg/kg.Chlorpromazine &
0.1mg/kg.d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
10 MINUTES
D4 0.3mg/kg.Chlorpromazine &
0.3mg/kg.d-Amphetamine
20 MINUTES

The administration of the dosage combination of 0.3 mg/kg of chlorpromazine 0.3 mg/kg of d-amphetamine gave results, from each subject, which showed characteristics of performance resembling the effects of each drug when administered independently. The results presented in Table 7 show an increase in the avoidance response rate per minute for subject D1 following the injection of this dosage combination. A similar increase in the avoidance response rate was apparent in this subject following the injection of 0.3 mg/kg of d-amphetamine alone. Subject D4 showed a similar increase on this measure following the administration of this dosage combination, however, the results for monkey D3 showed no apparent change.

The response rate per minute on the FR escape lever was consistently increased for all subjects after injection of 0.3 mg/kg of each drug. Figure 33 shows (at right) cumulative records of the performance of subject D4 following injection of the above dosage combination, and these are representative of the performance of subjects D1 and D3 under the same conditions.

The number of responses on Lever B in excess of the FR requirement were consistently increased from all subjects after injection of 0.3 mg/kg of each drug (Table 7). This resembled the effect of the 0.3 mg/kg dosage of chlorpromazine alone which is shown for subject D4 in Table 4 and for subjects D1 and D3 in Table 6.

Following the simultaneous administration of 0.3 mg/kg of chlorpromazine and 1.0 mg/kg of d-amphetamine, the response rate

per minute on the FR escape lever was again consistently increased relative to the control values, for all subjects (Table 7). The avoidance rate per minute was decreased for monkey D1 but remained relatively unchanged for the remaining two subjects. No other consistent trends were apparent in the results presented in Table 7.

Figure 34 shows cumulative records of the performance of subject D1 following the administration of this dosage combination. The upper trace is the record of performance on the avoidance component. It shows an initial, relatively high rate of responding, which decreased to a level where shocks were delivered to the subject. This indicates that the rate-enhancing effects of d-amphetamine were operative from the start of the session, and that the influence of chlorpromazine was effective at a late stage. The lower record of this figure shows the increase in response rate on Lever B following administration of this dosage combination.

Apart from the temporary reduction in response rate on Lever A, this record is characteristic of the performance of all the subjects under these drug conditions.

The final section of the results is concerned, solely, with the data obtained from the 6th measure listed in the Method section; the analysis of performance in terms of switching behavior. All the graphs presented in this section, were constructed in the manner described in the Method (see "Behavioral measurements: #6)

Fig. 34. Cumulative response records obtained from subject D1 following the joint administration of 0.3 mg/kg chlorpromazine and 1.0 mg/kg d-amphetamine.

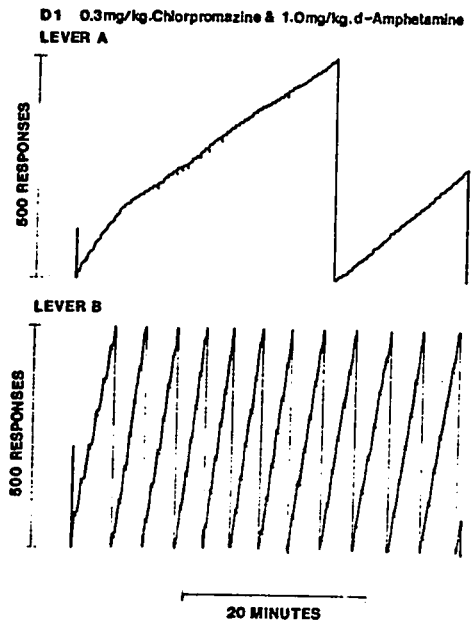

D1 0.3mg/kg.Chlorpromazine & 1.0mg/kg.d-Amphetamine
LEVER A
500 RESPONSES
LEVER B
500 RESPONSES
20 MINUTES

Figure 35 shows the performance of subject D1 in terms of the measure, under control conditions, and following the 0.1, 0.3 and 1.0 mg/kg dosage levels of the drug.

It is apparent that under control conditions, the subject was alternating its responding between the two levers a maximum of seven times during a period of active time, and that during the majority of the periods of active time during this session, the subject alternated between the levers fewer than seven times before initiating a TO period. The average number of responses in each FR run[1] remained very low over the 5th to the 2nd runs preceding time out (i.e. the points on the abscissa marked from 5 to 2.

The average number of responses in the last two runs preceding time out (1 and F on the abscissa) was much greater than the earlier ones, and during the run which initiated the time out, the average number of consecutive responses on Lever B, emitted by monkey D1 was 61.58. The majority of the responses on Lever B emitted by the animal during any period of active time in this control session were concentrated in these two runs.

---

[1]As described in the Method section, the term "run" refers to a set of consecutive FR responses preceding an avoidance response during a period of active time.

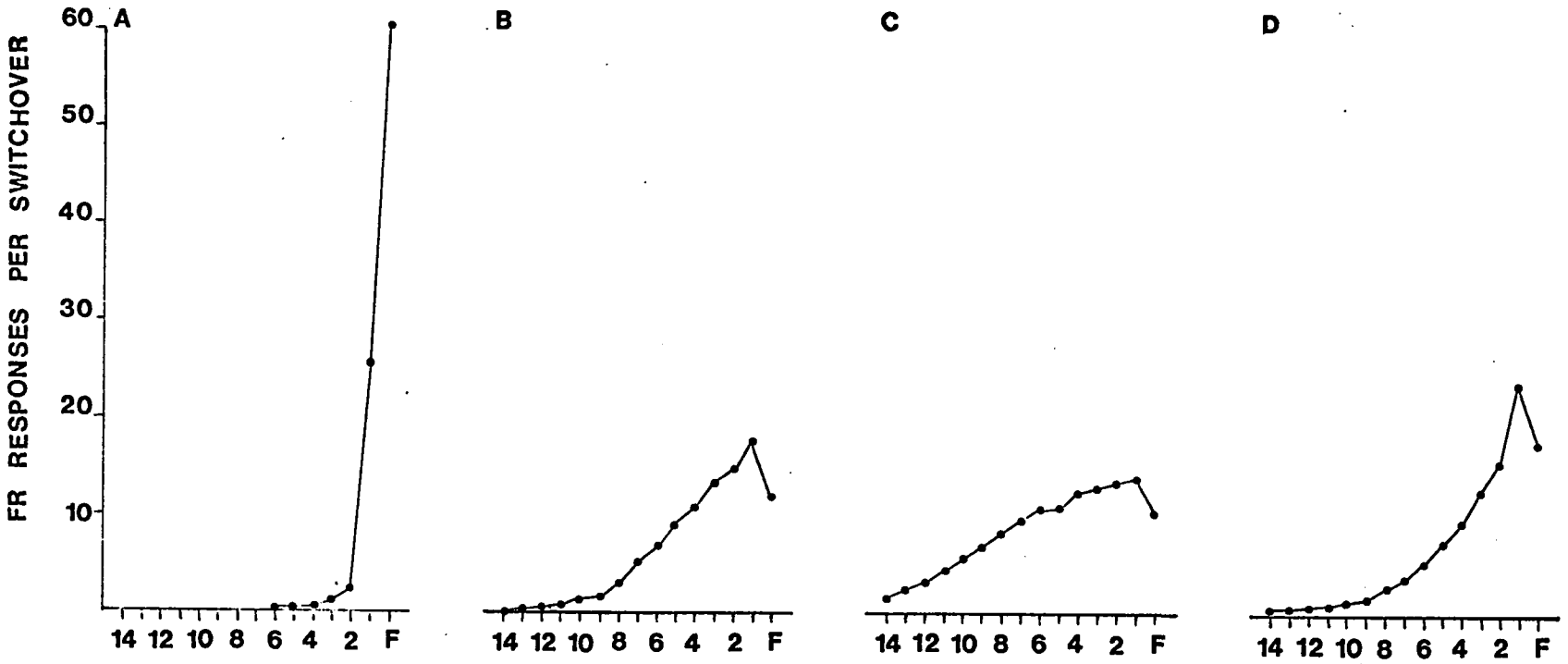
Fig. 35. The graphs presented in this figure summarize the performance of subject DI in terms of the average number of consecutive FR escape responses which precede an avoidance response in each period of active time throughout the session. A maximum of 15 of these runs of consecutive FR responses are plotted (on the ordinate) with the run preceding the time out period marked by "F". The runs preceding the final one (F) are presented in serial order from "2" to "14".

A:- Data obtained from subject DI under control (non-drug) conditions.

B:- Data obtained from subject DI following the administration of 0.1 mg/kg d-amphetamine.

C:- Data showing the performance of subject DI following the administration of 0.3 mg/kg d-amphetamine.

D:- Data obtained from subject DI following the administration of 1.0 mg/kg d-amphetamine.


FR RESPONSES PER SWITCHOVER
60
50
40
30
20
10
A
B
C
D
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
SERIAL POSITION OF RUN RELATIVE TO END OF RATIO

The 0.1 mg/kg dosage of d-amphetamine exerted effects which were subsequently found to be characteristic of the remaining dosage levels of this drug in terms of the performance of monkey D1. First, the frequency of alternation of responding between the two levers was increased, (the number of alternations at the 0.1 mg/kg dosage level increased from a maximum of 7 to a maximum of 15) and consequently, the average number of responses in each FR run was decreased. Secondly, the greatest number of responses now appeared in the penultimate FR run, and the average number of responses in the final run was lower than that of the three preceding runs. However, the runs containing the greatest average number of responses continued to be those closer in serial position to the time out.

The effects of the 0.3 and 1.0 mg/kg dosages on the switching behavior of subject D1 are also shown in Figure 35. The trends described above, were observed under both conditions, and increased in magnitude with increasing dosage level. Following injection of 0.3 mg/kg of d-amphetamine, the number of alternations of responding increased to a maximum in excess of 15, and this was also true of the 1.0 mg/kg condition. In both cases, the greatest number of responses appeared in the penultimate run, and the longest runs were those closer to the TO period. The performance of subject D3 differed in some respects throughout this series of drug effect evaluations. The results obtained under control conditions showed a greater concentration of responses in the final FR run than was the case with subject D1, and this feature persisted at all drug dosage evaluations.

Results obtained from subject D4 under control conditions, and following the administration of the 0.3 , 0.15 and 0.3 mg/kg dosages of chlorpromazine are presented in Figure 36. The results obtained from the control performance show that the longest average FR run was the penultimate one, and this feature persisted at all dosage levels of chlorpromazine. Results obtained under 0.03 mg/kg condition showed an increase in the number of alterations of responding between the two levers, but again the largest runs were those closest in serial position to the time out. These trends were apparent under the 0.15 mg/kg condition and with increasing dosage level, there was further increase in the average values of FR runs more remote from the time out. The modifications of performance in terms of this measure, under the 0.3 mg/kg dosage of chlorpromazine are also shown, for subject D1 in Figure 37. Again with respect to control values, there is an increase in the number of alternations between the two levers, and in the average number of responses in FR runs more remote from the time out.

The effects of the 0.3 mg/kg chlorpromazine 0.1 mg/kg d-amphetamine dosage combination are presented in the same figure and comparison of the two curves illustrates the manner in which the effects of chlorpromazine are modified by the simultaneous action of 0.1 mg/kg of d-amphetamine. The average number of responses were increased in the runs closest to the time out, and decreased in runs that were more remote from the TO period. The

Fig. 36. These graphs summarize the performance of subject D4 in terms of the average number of consecutive FR escape responses which precede an avoidance response in each period of active time throughout the session. A maximum of 15 of these runs of consecutive FR responses are plotted (on the ordinate) with the run preceding the time out period marked by "F". The runs preceding the final one (F) are presented in serial order from "2" to "14".

A;- Data obtained from subject D4 under control (non-drug) conditions.

B:- Data obtained from subject D4 following the administration of 0.03 mg/kg chlorpromazine.

C:- Data showing the performance of subject D4 following the administration of 0.15 mg/kg chlorpromazine.

D:- Data obtained from subject D4 following the administration of 0.3 mg/kg chlorpromazine.

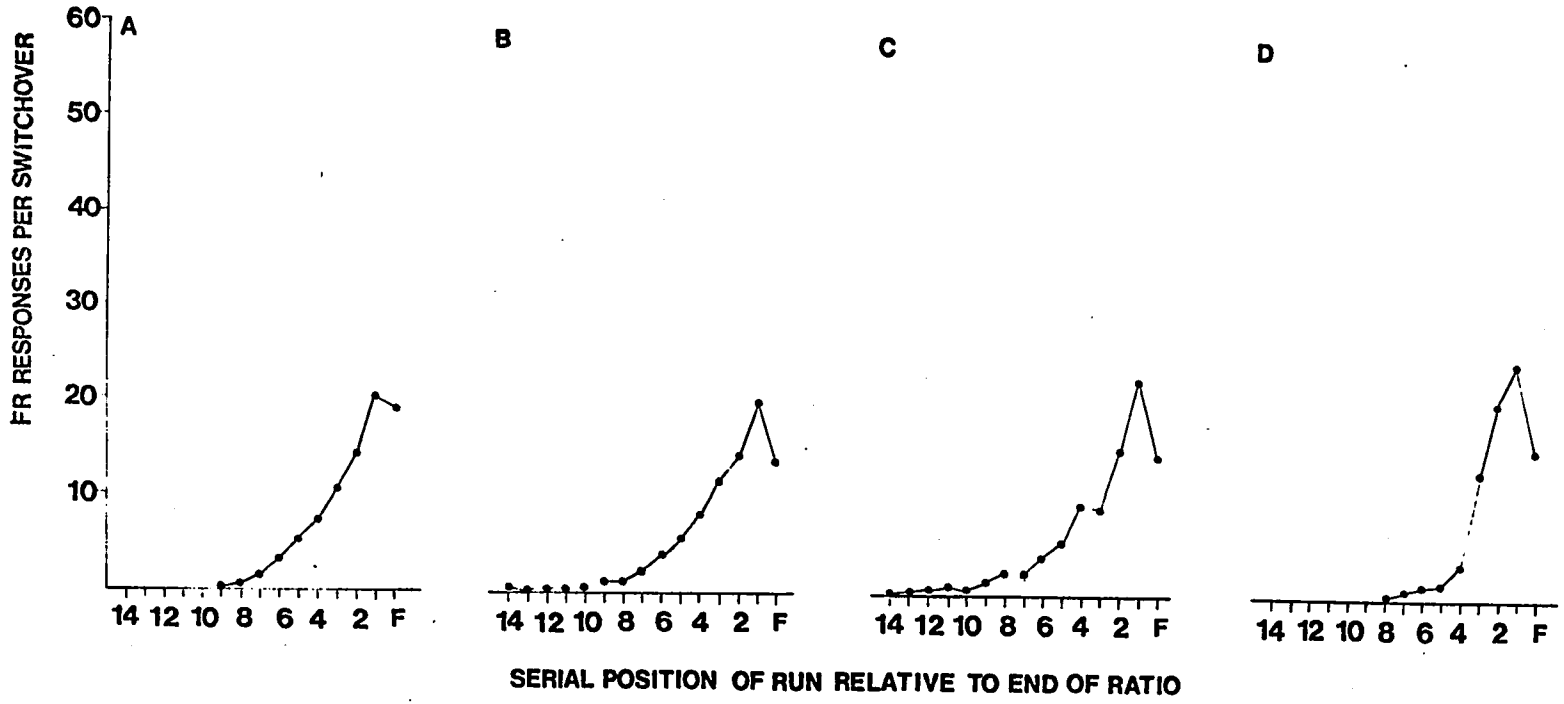

FR RESPONSES PER SWITCHOVER
60
50
40
30
20
10
A
B
C
D
14 12 10 8 6 4 2 F
SERIAL POSITION OF RUN RELATIVE TO END OF RATIO

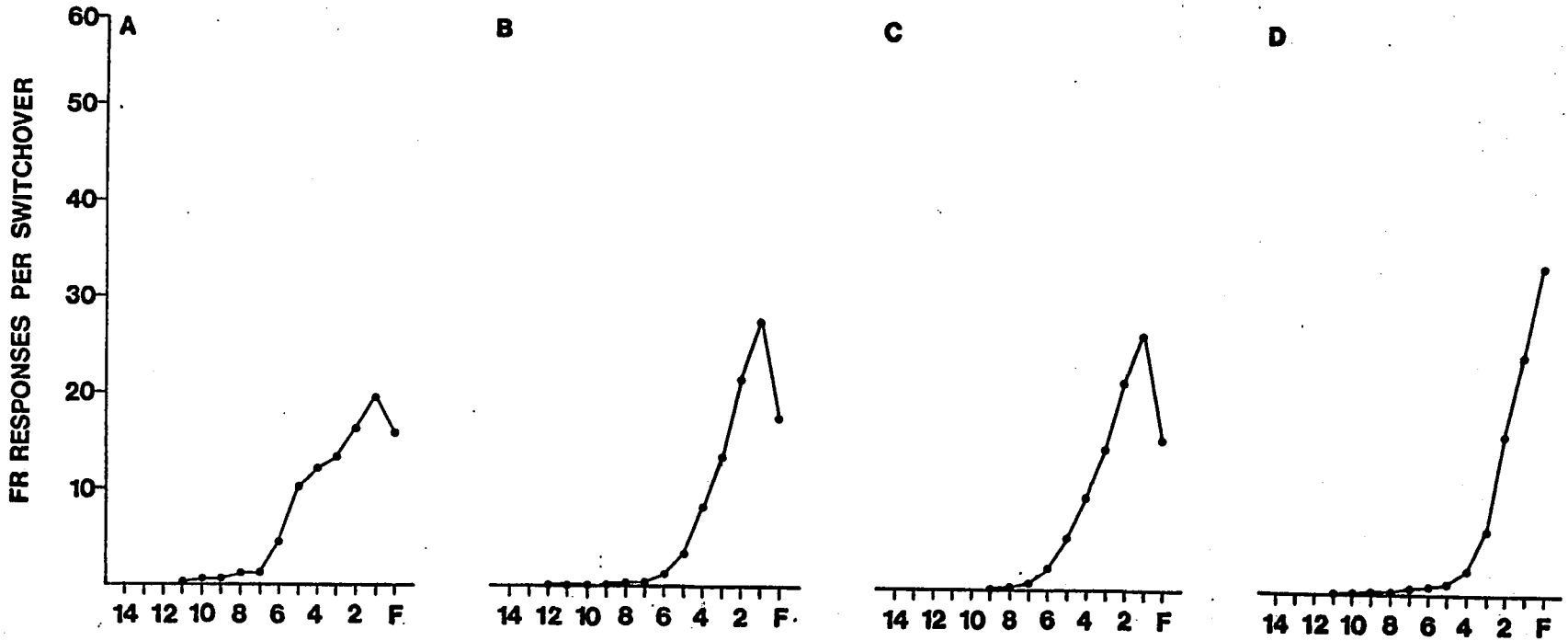
Fig. 37. The graphs summarize the performance of subject D1 in terms of the average number of consecutive FR escape responses which precede an avoidance response in each period of active time throughout the session. A maximum of 15 of these runs of consecutive FR responses are plotted (on the ordinate) with the run preceding the time out period marked by "F". The runs preceding the final one (F) are presented in serial order from "2" to "14".

A:- Data obtained from subject D1 following 0.3 mg/kg chlorpromazine.

B:- Data obtained from subject D1 following the administration of 0.3 mg/kg chlorpromazine + 0.1 mg/kg amphetamine.

C:- Data showing the performance of subject D1 following the administration of 0.3 mg/kg chlorpromazine + 0.3 mg/kg amphetamine.

D:- Data obtained from subject D1 following the administration of 0.3 mg/kg chlorpromazine + 1.0 mg/kg amphetamine.


FR RESPONSES PER SWITCHOVER
60
50
40
30
20
10
A
B
C
D
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
14 12 10 8 6 4 2 F
SERIAL POSITION OF RUN RELATIVE TO END OF RATIO

greatest number of responses appeared in the penultimate run; for subject D1, this was an effect common to each drug acting independently. The same trends were noted in subjects D3 and D4 following this dosage combination.

The same figure shows the performance of subject D1 under the dosage combination of 0.3 mg/kg of each drug. The major effects under these conditions were an extension of those seen under the preceding dosage combinations. Again, the highest average number of responses occurred in the run preceding the final one. The number of alternations in responding between Levers A and B was slightly reduced and there was a tendency for responses to be concentrated in the runs closer to the time out period. These general trends were apparent in the results of subjects D3 and D4 and were intensified following the administration of the 0.3 mg/kg chlorpromazine 1.0 mg/kg d-amphetamine dosage combination. The results obtained from subject D1 under these conditions, are also presented in Figure 37. A marked increase in the average number of responses in the final FR run, a characteristic effect of 1.0 mg/kg of d-amphetamine alone (Figure 35), was apparent in the results of this dosage combination.

The results obtained from subject D1 under these drug conditions did not show any reduction in the number of alternations of responding, but the average number of responses in the runs most remote from the time out were markedly reduced. A reduction in the number of alternations of responding between the two levers was clearly marked in these results obtained from subject D4 and a similar effect was noted in the results of monkey D3.

Discussion

The work presented in this study, was preceded by attempts, using different squirrel monkeys, to establish patterns of responding maintained by a concurrent free-operant avoidance/FR escape schedule.

Verhave (1962) using rats as experimental subjects, reported a successful attempt to establish performance under the parameters of a concurrent schedule similar to that employed in the present study. The subjects were trained to press one lever in order to postpone shock, and by pressing a second lever, initiate a period during which the operation of the avoidance schedule was discontinued (i.e. a time out). Thus, Verhave was able to demonstrate both the maintenance of responding by the parameters of such a concurrent schedule, and the effectiveness of a time out period as a reinforcing event.

The work of Sidman (1962) supported the findings of Verhave, and is of direct relevance to the present study. Using rheus monkeys as subjects, he demonstrated that performance could be maintained by a concurrent schedule with parameters similar to those used in the present study. Specifically, the subject could postpone shock by pressing a lever (free operant avoidance component), and by pulling a chain a fixed number of times (FR component) it could produce a time out. During the TO period, the houselight, which was present whenever the avoidance schedule was in effect, was extinguished, and the avoidance schedule was discontinued for a specified period. On termination of the TO period, the avoidance schedule and its

associated discriminative stimuli were reinstated. Under these conditions, the behavior of the subjects was similar to that of the subjects used in the present experiments as described in Phase III of the Results section. However, prior to the establishment of this performance, there was an important difference in the training of the subjects in the present study and those of Sidman's experiment. Prior to the experiment reported by Sidman, each of his subjects had been exposed to a concurrent schedule in which shocks could be avoided by pressing a lever, and food could be produced by pulling a chain a fixed number of times. Sidman's results suggested that transfer of the FR pattern of responding occurred when a TO period replaced food as the reinforcing event.

The attempts, preceding the present study, to establish performances comparable to those reported by Sidman were not successful. The animals used in these early experiments, were trained on a free-operant avoidance schedule, and following the stabilization of performance, were exposed to the concurrent schedule consisting of the free-operant avoidance component, and an FR escape component. The value of the FR requirement was relatively low, starting at 1 and not exceeding 5 responses. Under these conditions, the subjects continued to respond on the free-operant avoidance component (Lever A) to the almost complete exclusion of responding on the FR escape component (Lever B).

Thus, it seems reasonable to conclude that squirrel monkeys will not readily respond on a second manipulandum to produce periods of time out from an avoidance contingency, when their only previous experimental experience has consisted of free-operant avoidance training. As a result, the subjects used in the present study were trained on both components of the concurrent schedule independently before being exposed to the concurrent schedule (see Method section). As has been shown in the Results section, this procedure greatly increased the liklihood that a subject would respond consistently, on both manipulanda, once the concurrent schedule was made operative. Stretch, Dalrymple and Goforth (1968) have therefore suggested, in view of the efficacy of the Lever B escape training procedure, (i.e. Phase II in the present work), that behavior reinforced by a time-out from an avoidance contingency is best regarded as escape from conditioned aversive stimulation rather than positively reinforced by the stimulus conditions which prevail when a TO is initiated.

The first major experimental manipulation was the introduction of unavoidable shocks. Again, in experiments preceding the present study, it was found that when methylphenidate (a drug exerting behavioral effects similar to those of d-amphetamine) was administered to a subject whose behavior was maintained by concurrent free-operant avoidance/FR escape schedule, relatively permanent changes in the performance of the subject were evident. Immediately following the administration of the drug, it was found that the number of shocks received by the subject were increased. The question arose

as to whether the relatively permanent behavioral changes were a function of the drug, or an indirect result of the increased number of shocks received by the monkeys while the drug was exerting the effect of disrupting performance. The results show unequivocally, that the delivery of unavoidable shocks over 6 consecutive experimental sessions, was followed by a relatively permanent modification in performance. There was an immediate decrease in the response rate per minute on both levers, but the most marked effect was a decrease in the number of FR responses in excess of the number specified by the FR requirement. These results are interrelated since a reduction in the number of responses on Lever A (free-operant avoidance component) was associated with a reduction in the amount of time during which the change over delay was in effect. Thus, a greater proportion of Lever B (FR escape) responses became effective in reducing the FR requirement, and the number of ineffective responses was reduced. Since performance on the FR escape component of the schedule was more effective in initiating time out periods, it is apparent that termination of the aversive stimulus complex was functioning as a reinforcing event. In addition, the TO period was a more powerful reinforcer than the single postponement of shock under the parameters of the free-operant avoidance component, since the absolute behavioral output on Lever B (FR escape) was much greater than that on Lever A.

As has already been stated, all subjects experienced at least 100 consecutive experimental sessions, under control conditions,

during the period intervening between the discontinuation of unavoidable shock and the beginning of the series of drug tests. Evidence presented in the Results section indicate that no further significant changes in performance occurred during this period.

It is appropriate, at this point, to preface the discussion of the effects of d-amphetamine with a reference to a general finding of other workers in this field. It was reported, in the Introduction that several studies have presented convincing evidence in support of the claim, by Dews (1956) that the behavioral effects of the amphetamines are dependent upon the ongoing response rate engendered by the schedule maintaining the performance. More specifically, Dews claims that amphetamines tend to increase a relatively low rate of responding and decrease a relatively high response rate.

Within the dosage range of d-amphetamine used in the present work, the results are in agreement with those of previous investigators insofar as the relatively low (free-operant avoidance) response rate was, in general, increased following the administration of d-amphetamine. This effect was clearly marked in subject D1, but the results obtained from subject D3 do not show the same degree of consistency. A slight reduction in the response rate was evident at the 0.03 mg/kg dosage, but an increase in the response rate was clearly marked at the 0.3 mg/kg dose level.

The performance of subject D1 on the FR escape component following the administration of d-amphetamine, also supports previous findings, since this relatively high response rate was decreased at all dosage

levels of the drug. However, for subject D3, the 0.03, 0.1 and 0.3 mg/kg dosages of the drug were followed by a marked increase in the response rate on Lever B. This effect was the opposite of that observed with subject D1, and was of greater magnitude. Only at the highest dosage of d-amphetamine was a reduction in this response rate observed. These results do not contradict Dews' statement, but they do emphasize the importance of a careful interpretation of his claim. When Dews refers to relatively high or low response rates, it seems reasonable to assume that the response rates are high or low with respect to the performance of a specific subject. Thus a given schedule may generate a relatively high rate of responding in the majority of subjects trained to respond under those parameters when compared with the relatively low response rate emitted by the majority of subjects on a different schedule. However, when referring to the performance of specific animals, there is no sense in which the difference between high and low rates of responding may be equated. This point is illustrated by reference to Figures 11 and 12; the records of subjects D1 and D3 each show relatively low and relatively high rates of responding, but while the free operant avoidance rates are similar, the response rate on Lever B was much higher for subject D1 than for subject D3. As a result, the absolute difference between the high and low response rates are much greater for subject D1 than for subject D3. The same feature is shown in Figure 22 which illustrates the disparity between subjects D1 and D3 in terms of the rate of responding on Lever B (Figure 22A) under control conditions and also under each dosage level of d-amphetamine.

Thus, in terms of Dews' statement the relatively high rate of subject D1 is diminished following the administration of d-amphetamine, but the lower corresponding response rate for subject D3 (see Figure 17 D) even though it is relatively high with respect to its own avoidance response rate, is increased by all but the highest d-amphetamine dosage.

The work of Sidman (1962) which was reviewed in the Introduction, indirectly provides further insight into the mode of action of d-amphetamine. In the relevant part of his report, he compares the performance of a subject on a single fixed-ratio schedule with that of a subject responding on a concurrent schedule similar to that employed in the present study. The important point is that under the simple FR case, animals rarely pause once they have begun to respond after each reinforcement. However, on close examination of the cumulative records of responding on the FR escape component of the concurrent schedule, Sidman found that the animals often paused briefly as they progressed in the ratio sequence. During these interruptions, they usually made one or more avoidance responses. As can be seen in Figures 11 and 12, this pattern of responding was characteristic of subject D3, but there was little evidence of pausing in the performance of subject D1. Figure 28 shows the performance of subject D3 following the administration of 0.03, 0.1 and 0.3 mg/kg of d-amphetamine, and when the FR escape records are compared with the record obtained under control conditions, the most obvious difference is the absence of pausing following drug administration.

One of Dews' most important findings which supports his statement on the behavioral effects of the amphetamines was that these drugs increase low rates of responding and decrease high response rates in behavior maintained by a fixed interval (FI) schedule. The characteristic pattern of responding on an FI schedule consists of a pause immediately following a reinforcement. When the subject starts to respond, it does so at a low but gradually accelerating rate until the next reinforcement is delivered. When d-amphetamine is administered, the pause is obviated, and the relatively high terminal response rate preceding the next reinforcement, is diminished. It would appear that d-amphetamine is exerting a similar effect on the FR escape performance of subject D3 in the present study, insofar as the tendency to pause disappears when the drug is administered. Alternatively, subject D1 maintained a relatively high response rate on Lever B, showing no tendency to pause, under control (non-drug) conditions. Thus, the established high response rate was diminished under drug conditions (for example, see Figures 25 and 26). Further support for this interpretation of the differences found between D1 and D3 is provided by the performance of subject D3 following the administration of 1.0 mg/kg of d-amphetamine (Figure 27). At the start of the session, the drug dosage was not exerting its full effect, and the increase in rate of responding on Lever B, noted at the lower dosages, was apparent. The full effects of the higher dosage appeared approximately 30 minutes after injection, and was expressed as a marked reduction of the relatively high rate of responding which preceded this effect.

The results obtained from subject D4 following the administration of chlorpromazine indicated that there were no marked changes in the rate of responding on either lever at the 0.03 and 0.1 mg/kg dosage levels. However, the time taken to initiate a time out period was clearly increased, and this increment was directly related to increasing dosage level. This increase in time was due to the fact that the pauses in responding on the FR escape component under control conditions (Figure 13) became more pronounced following the administration of chlorpromazine. This is illustrated by a comparison of the control performance with the records obtained under the 0.03 and 0.1 mg/kg dosages, shown in Figures 29 and 30. It should also be noted that when the animal responded on Lever B, it did so at a rate comparable with that emitted under control conditions.

The response rate of subject D4 on Lever B, following the injection of 0.15 mg/kg of chlorpromazine was clearly decreased compared with the control rate. However, the response rate on the free-operant avoidance component remained relatively unchanged. Following the injection of the highest (0.3 mg/kg) dosage of chlorpromazine, the response rate of subject D4 on both levers was reduced to an exceedingly low rate, and the session was stopped. As was pointed out in the Results section, when the subject ceased to respond on Lever A, shocks were delivered every 5 sec and it was thought inadvisable for the animal to receive more than 15-20 consecutive shocks under these circumstances.

The results obtained from subjects D1 and D3 following the injection of 0.3 mg/kg of this drug were similar in all respects to those obtained from subject D4, and sessions were invariably terminated once the rate-suppressive effects of chlorpromazine led to a failure to avoid consecutive shock deliveries.

Joint administration of d-amphetamine and chlorpromazine was followed by patterns of responding which illustrated clearly, the antagonistic effects exerted by each drug on the behavioral modifications induced by the other.

As stated in the Method section, the 0.1, 0.3 and 1.0 mg/kg dosages of d-amphetamine were each administered in conjunction with the 0.3 mg/kg chlorpromazine dosage. The highest dosage of the chlorpromazine range was selected, since its administration was invariably followed by a marked and consistent suppression of responding in all three monkeys.

The performance of monkey D3 following the joint administration of 0.3 mg/kg of chlorpromazine and 0.1 mg/kg of d-amphetamine is representative of the effects of the dosage combination on each of the subjects. Cessation of responding on both levers which was a characteristic effect of the 0.3 mg/kg chlorpromazine dosage acting independently, was evident under these conditions. However, the onset of this effect was delayed by the simultaneous action of the d-amphetamine dosage. This effect is clearly illustrated by comparing the performance records of subject D3 under the two relevant conditions and reproduced in Figures 32 (chlorpromazine) and 33 (chlorpromazine plus amphetamine) respectively.

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The response rate on Lever A showed an overall increase, but the rate decreasing effect of d-amphetamine on the FR component was obviated. Thus, the results obtained following the simultaneous administration of the two drugs are in agreement with the findings of Brown (1963) and Davis (1965), and they demonstrate that the antagonistic effects reported by these authors are sustained when behavior is maintained by aversive rather than positively reinforcing stimuli.

The preceding discussion has examined the behavioral effects of chlorpromazine and d-amphetamine primarily in terms of the resulting modifications in rates of responding on the two levers. However, the data obtained from the alternation of responding between the two levers has also contributed important information on the mode of action of these drugs.

The marked increase in the alternation of responding between the two levers following the administration of d-amphetamine at all of the dosage levels employed, is illustrated in Figure 35 by the data obtained from subject D1. In addition, under control conditions, the largest run of consecutive FR responses is the final one. Following the injection of d-amphetamine, this becomes a consistent feature of the penultimate run, and the length of the final run is reduced at the 0.1 and 0.3 mg/kg dosages, to a level below that of the preceding three FR runs. This result indicates that the administration of this drug, is followed by a change in the performance engendered by the free-operant

avoidance component of the schedule, and that this, in turn, modifies the pattern of responding on the FR escape component. An increase in the response rate on the free operant avoidance component (Lever A) is, by virtue of the schedule parameters, followed by an increase in the amount of time during which Lever B responses are ineffective (COD). Thus, a greater number of Lever B responses will be ineffective in reducing the FR requirement. Under these conditions, the time taken to initiate a time out period should be increased. The results presented in Table 1 confirm this point.

The 0.03 and 0.15 mg/kg dosages of chlorpromazine increased the alternation of responding with respect to the control level. This is clearly illustrated in the records of the performance of subject D4 (Figure 36). However, the degree of alternation was reduced at the 0.3 mg/kg dosage level, and the length of the FR runs were increased. As was the case with d-amphetamine, the length of the final run was reduced following the administration of chlorpromazine. When compared with the control performance, the results obtained following administration of this drug were relatively erratic (see Figure 36 A). The above features of performance lend support to the proposal by Dews and Morse (1961) that chlorpromazine tends to weaken the stimulus control of behavior.

The results obtained following the administration of combinations of the two drugs lend support to the preceding discussion of these effects. The relevent data for subject D1 is presented in Figure 37, and the results obtained from the remaining two subjects were

similar in all major respects. The erratic alternation of responding that followed the injection of 0.3 mg/kg chlorpromazine alone (Figure 37 A) was offset by the joint administration of 0.1 mg/kg of d-amphetamine (Figure 37 B). The same trend was apparent following the administration of 0.3 mg/kg of each drug (Figure 37 C), and in addition, the number of alternations of responding between the two levers was reduced. The administration of 0.3 mg/kg chlorpromazine and 1.0 mg/kg d-amphetamine was followed by an increase in the alternation of responding attributable to the dominant effect of d-amphetamine. Thus, the results obtained from this measure are in accordance with those discussed in the preceding parts of this section.

In the present work, an attempt has been made to clarify the behavioral effects exerted by d-amphetamine and chlorpromazine on behavior maintained by a complex schedule. The findings may be summarized, at this stage, in terms of the conceptual framework within which these experiments were undertaken.

Findley and Ames (1965) have demonstrated that performance can be maintained, in chimpanzees, by a schedule in which fixed interval responding produced time out from a shock avoidance schedule. Apart from the work of Verhave (1959), Sidman (1962) and Findley and Ames (1965), there has been very little work to date, on behavior maintained by consequences only indirectly related to a primary aversive stimulus. In the present work, an attempt has been made to clarify aspects of this problem; in particular, the acquisition of these complex behavior patterns has been studied in detail. The results showed

that certain aspects of the training procedure are critical if performance on the schedule is to be successfully established. Morse (1966) has emphasized the fundamental importance of this point in the following manner:- "The outstanding characteristic of operant behavior is that it can be differentiated in form and in temporal patterning by consequent events. Conditioned operant behavior emerges out of undifferentiated behavior through successive approximations to new and more complex forms by the process of successive differential reinforcement (shaping). Behavior that has become highly differentiated can be understood and accounted for only in terms of the history of reinforcement of that behavior - when, and how, and under what stimulus conditions reinforcers acted to shape the behavior."

Thus, reinforcers must be presented consistently and frequently in order to engender a conditioned pattern of behavior. Once established, however, many behavior patterns can be sustained almost indefinitely, even though the reinforcing consequences of behavior occur relatively infrequently. Responding on the concurrent schedule of the present study was sustained with very infrequent shock presentations; commonly, the performance of the subject was such that no shocks were delivered over 3 or 4 consecutive experimental sessions. Yet, intensive training on each of the schedule components independently, was necessary prior to the introduction of the concurrent schedule in these previously untrained monkeys.

Many different schedules of reinforcement have been studied in the laboratory, and it is quite clear that particular schedules produce extremely stable rates of responding for as long as the schedule is continued (Ferster and Skinner 1957). Even slight changes in the schedule may produce dramatic differences in behavior (Morse 1966; Stretch 1966). These features have led Morse (1966) to claim that schedules of reinforcement are fundamental determinants of behavior. In addition, as has been pointed out in the preceding sections of this study, many workers have shown that the nature of the behavioral effects exerted by a drug are dependent upon the ongoing rate of responding. Thus, schedules are also fundamental determinants of the nature of the behavioral changes induced following drug administration. Operant work has tended to place primary emphasis on the importance of an understanding of the ongoing rate and patterning of responding as a prerequisite for prediction of drug-influenced changes in behavior, and this mode of interpretation was adopted in the present study. The same principle, that schedules are fundamental determinants of the behavioral effects of drugs is also applicable when examining the effects of joint administration of two drugs.

This point is illustrated by the work of Smith (1964) and more recently, by Rutledge and Kelleher (1965). In their experiment, they examined the effects of various combinations of methamphetamine and pentobarbital on performance maintained by a multiple FI FR schedule of food reinforcement in pigeons. The results showed that the combination acted synergistically on the low FI rates of responding

and antagonistically on the higher FR response rates. Similar findings have been reported by Stretch and Dalrymple (1968) who found that within a specified range of dosages, combinations of methylphenidate and pentobarbital exerted a greater rate-enhancing effect on low rates of responding produced by a modified DRL schedule, than either drug administered individually.

Vaillant (1964) studied antagonistic effects exerted by drugs, and has clarified the approach to this type of research adopted by workers in this field:

"The characterization of a drug antagonism usually requires study of the effects of the agonist and antagonist over dosage ranges covering several orders of magnitude. This is ordinarily impossible in behavioral studies. Evidence of specificity must therefore be sought along different lines. It has been shown repeatedly, that different components of a complex pattern of behavioral responding characteristically show greatly different sensitivities to modification by a drug. If a complex pattern of responding that has been profoundly modified by the effect of an agonist can be restored essentially to normal in all its aspects, by a suitable dose of antagonist, then this is evidence for specificity of antagonism. It is analogous to the finding that the agonist is antagonized in a variety of effects on a variety of tissues by the antagonist; such findings have been taken in general pharmacological studies, to be evidence for a pharmacological antagonism."

The experiments cited above, together with those concerned with joint drug effects and reported in the present study, illustrate an important principle, namely, that the nature of the interaction which occurs when two drugs are administered in combination, is determined to a considerable degree by the ongoing rate of responding controlled by different schedules of reinforcement or by different components of a complex schedule.

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