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DRUG EFFECTS IN COMPLEX BEHAVIORAL REPERTOIRES IN MONKEYS, BABOONS, AND MAN

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I: INTRODUCTION

In the last decade and a half important advances have been made in behavioral pharmacology by the application of the techniques of experimental analysis of behavior to the measurement of behavioral response to drugs. The contribution of modern behavioral analysis has been twofold: 1) increases in the sensitivity with which the effects of a compound upon behavior can be detected and 2) the demonstration that a particular effect depends not only upon the compound used but upon the conditions for animal performance which obtain during the period of drug action. Alterations in the animal's behavior caused by the drug under conditions of positive reward, aversive stimulation or simple discrimination have been obtained. The ability of human subjects to perform complex functions while under the influence of psychopharmacologic compounds has also been of particular interest. Behavioral techniques now permit us to establish complex performances in higher primates which are quite analagous to human "cognitive" performances, permitting evaluation of these relevant compounds with animals prior to their being administered to humans.

Both the human and the animal experiments include several important procedures in common: the complexity of the stimulus material; differential positive and negative consequences of correct and incorrect performance; the development of performance "chains"; the use of intermittent schedules of reinforcement. These variables will be discussed in their appropriate contexts in greater detail in the main body of the report. Also, both the human and animal experiments make explicit and permit manipulation of variables crucial to the acquisition and the maintenance of complex behavior. Within this framework the same compound may be given to both humans and animals with the possibility of finding similar variables controlling the drug effects.

In the first year of the contract we demonstrated that a complex performance analagous to simple human counting can be established reliably in a baboon and that relatively difficult portions of the performance may be differentially sensitive to debilitating effects of a behaviorally-active compound.

In working with this performance during the first six months of this year, we have continued to discover properties both contributing to and conflicting with the efficiency of counting. The complete counting routine has been extended to two more baboons and a variation of counting which amplifies demands on recent memory has been established with two rhesus monkeys. During this year, a reliable baseline on a cognitive problem-solving procedure has been developed with a human subject in daily sessions which have continued for several months. Changes in performance as a function of the consequences have occurred, similar to those we have been accustomed to observing in animal experiments. A single compound, chlorpromazine, has been extensively investigated using baboons and the human subject.

II: ANIMAL EXPERIMENTS

A: The Experimental Environment

The baboons are maintained under conditions of full environmental control; that is, the animals live continuously in experimental chambers which are designed to serve all maintenance functions as well. The chambers are roomy enough to permit limited exercising and contain a bench upon which the animal may sit or sleep and a removable bedding pan on the floor filled with wood shavings which are periodically replaced. A more detailed description of the environment has been given in the 1962/63 annual progress report.

B: Baboon Counting Routine

The example of complex behavior we have chosen to develop in baboons we call "counting." By counting we do not imply an extensive arithmetic repertoire, but rather the simple behaviors engaged in by a child in school who is learning to count.

The baboon counting routine has been described in detail in the annual progress report for the 1962/63 contract year. In brief, a baboon "counts" by operating two levers which are mounted on one wall of the living chamber. A number of geometric forms are presented visually to the animal in a small window on the same wall of the chamber. There are five different patterns containing from one to five geometric forms respectively. The animal presses one lever, producing a tone at each discrete press. In a correctly performed problem, the baboon presses the lever until he has generated a number of tones equal to the number of geometric forms in the visual pattern on that particular problem. The second lever is pressed to "give an answer" after the baboon "decides" that an appropriate number of tones have occurred. If the answer or register response is correct, a higher pitched tone immediately results. An incorrect answer is followed by a brief "time-out" period (which is literally time out from the opportunity to obtain food); all the lights in the chamber go out and the levers become non-functional. After the baboon has counted correctly on a specified number of problems he is automatically rewarded, or technically, reinforced, by the delivery of a food pellet. The food pellet delivered at the end of the counting sequence ensures that the baboon will continue to produce counting responses. In a similar, but less powerful fashion, the high-pitched tone after each correct response supports the animal's behavior through the sequence of problems prior to the reinforcement.

Numerical data are obtained on electrical impulse counters; continuous, fine-grain records of correct and incorrect counting are collected in graphic form on cumulative response recorders. For the purpose of data analysis, a correct or error response is defined as the registration response following an appropriate or inappropriate number of responses on the counting lever. Accuracy levels are defined by the

number of correct responses divided by the number of correct plus incorrect (total) responses. This value is multiplied by 100 to express accuracy as a percentage score.

C: Behavioral Experiments

The behavioral experiments have been conducted in the last six months in parallel with a continuing effort to study the effects of behaviorally-active compounds upon the counting performance. The behavioral analysis of counting has been principally concerned with five major areas: 1) a stimulus "fading" technique for greatly accelerating the acquisition of the counting performance; 2) a continuing investigation of consequences of counting which have differential effects upon the accuracy of performance; 3) the effects of problem sequence on counting; 4) an analysis of the kinds of persistent errors which are occurring and attempts to determine the conditions producing them; and 5) the development of a different counting routine in two rhesus monkeys -- delayed response counting, which places much heavier demands upon memory for the number of counting tones produced.

1. Acquisition experiment - stimulus "fading" technique

In order to make the stimulus numerosity display more discriminable and to broaden the generality of the counting problems, new geometric forms and patterns have been used for the two new baboons. White disks in various patterns from 1 to 5 are presented; each pattern is associated with a particular background color - 1 with dark blue, 2 with light green, 3 with orange, etc.

The new problem stimuli permitted the use of a new procedure, stimulus fading, which has been used successfully in other laboratories to develop difficult discrimination repertoires (Terrace, 1962; Schaefer, 1963; Goldiamond, 1964). The application of the technique of fading to the present performance involved reducing the intensity of the background color after the correct number of counts were produced as an additional stimulus for making a register response. For example, if the baboon is working on a counting-to-three problem, on the third press of the counting lever the intensity of the orange background color is dimmed almost completely. The baboon is thus given an explicit discriminative stimulus for making the register response.

The ultimate aim of the training procedure was to build a counting performance without any additional "hint" as to when the correct number of counts had been produced. Unlike the earlier training procedures we have used, in which a new problem is introduced only after the previous ones have been mastered, under this method the baboon started with all five problems equally represented in the sequence. A large dim was initially used on all problems: the background essentially became dark gray when the correct number of counts was produced.

The baboons rapidly learned to look for the dimming stimulus and to make the register response immediately after it occurred. As training progressed, the stimulus was progressively weakened and finally was removed altogether. Some behavioral disruption was usually evident after each dimming change; the next change was not made until the baseline level of accuracy had returned. When the dim was removed entirely so that no stimulus change followed the production of the correct number of counts, the animals continued to perform at the general level of accuracy which had been obtained with the dim in effect. A similar procedure had been used by Schaefer (1962) to develop counting in a rhesus monkey.

It is of interest that while the dimming procedure was in use, there were relatively few cases in which a particular problem was consistently performed with more or less accuracy than other problems. This was especially true of the performance of one baboon, Cassius. However, as the dimming stimulus approached recognition threshold, Cassius's differential performance on the various problems dramatically spread so that problems 1 and 2 were consistently the most accurate, and 4 and 5 the least. This change is presented graphically in Figure 1. Seven consecutive sessions representative of data obtained under strong dim are contrasted with the transition to weak dim and then no dim. In other words, once the animal was "on his own" the effect of problem complexity was felt on the performance and a relative decline in accuracy on 4 and 5 occurred.

These data support the interpretation that the lower accuracies obtained from the other baboons on problems 4 and 5 are a result of problem complexity, not serial position of the problems in a fixed 1 through 5 sequence. The problems for the new baboons are presented in random order. Nevertheless, as Cassius's data demonstrate, accuracies generally become distributed in terms of problem complexity.

There were characteristic differences in performance between the two new baboons. Cassius responded on the counting lever at an extremely high rate and consequently made a large number of overcounting errors. For this reason an automatic overcount reset was introduced into the performance for every problem; that is, if the problem were 3 and Cassius pressed 4 times on the counting lever, an incorrect response was automatically produced and the problem was reset and was required to be repeated.

Another difference between the baboons which can probably be attributed to rate of responding on the counting lever is that the stability of their performances was markedly different. The mean accuracy for Cassius ranged between 70 and 90 percent with relatively large shifts from day to day. On the other hand, Fore was extremely stable with a mean ranging normally between 85 and 87 percent and with performance on the individual problems grouped fairly close togetner. As a corollary of a lower counting rate Fore seemed to rely on the dimming

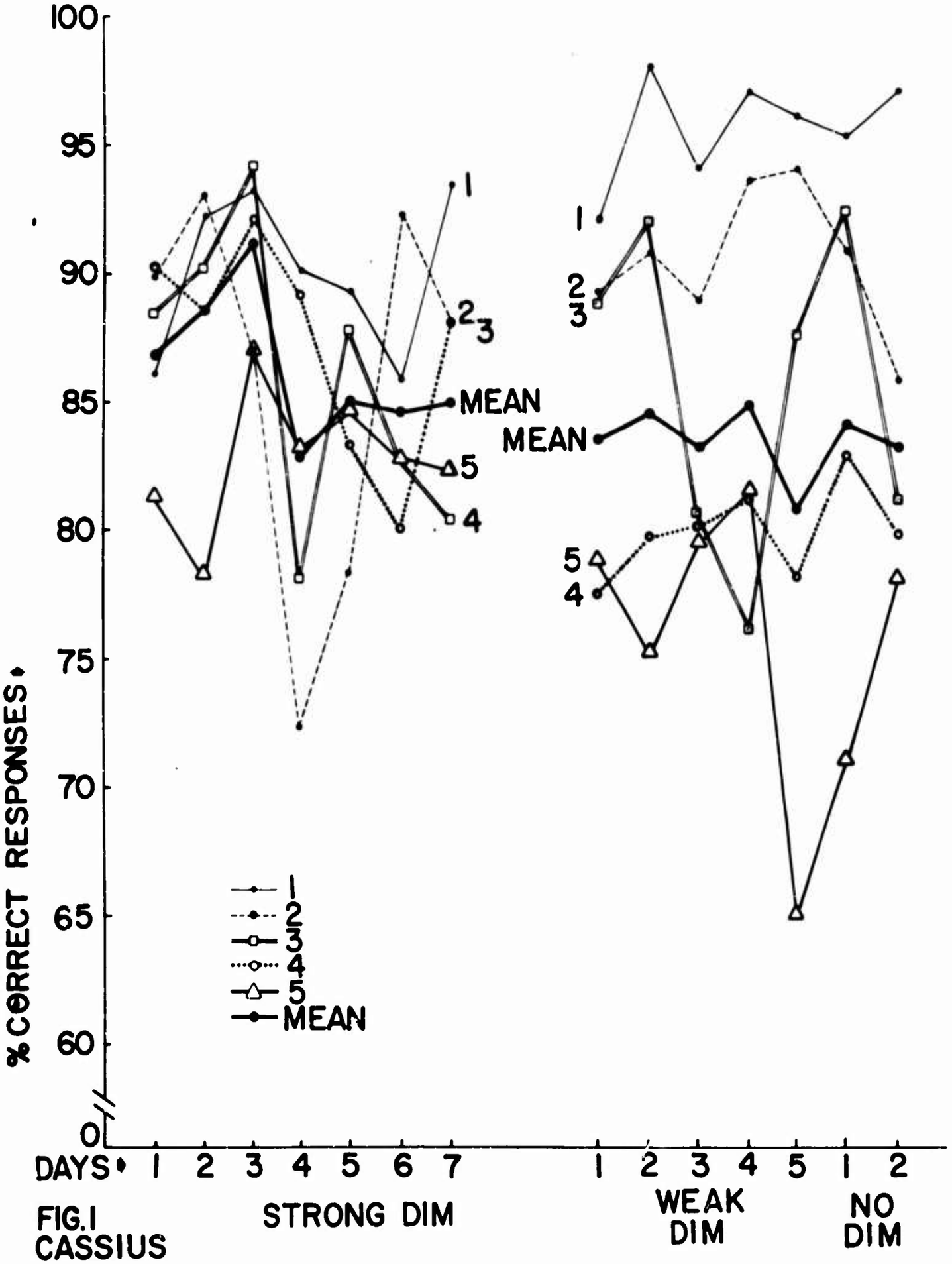

FIG.1
CASSIUS

TRANSITION FROM 'STRONG DIM' TO 'NO DIM' ACCURACY (% CORRECT RESPONSES) FOR PROBLEMS 1, 2, 3, 4, 5, AND MEAN

stimulus more than Cassius, and hence produced a steadier performance.

The new training method differs from the one which had been used with Cowboy and Dolores in that rather than gradually establishing correct counting under the control of differential positive reinforcement alone, an attempt was made to evoke correct counting almost immediately by making the discrimination very simple at the outset of training. In comparison with the time necessary to bring counting under good control with the original procedure using differential positive reinforcement alone, it is concluded that the fading technique is more effective in rapidly developing an adequate counting performance.

2. Scheduling of consequences affecting counting accuracy.

The rate of acquisition of efficient counting and the extent to which counting is maintained at high levels once acquired is strongly dependent upon the differential consequences of correct and error counting responses. The techniques fall into three general categories: 1) increasing the work requirement necessary for reinforcement; 2) increasing the length of a "time-out" period from the opportunity to obtain reinforcement following an error, and 3) the arrangement of differential positive consequences of accurate counting.

a) Increasing Work Requirement. On a typical counting baseline the animal is required to perform on five problems correctly before he is reinforced, or technically, on a fixed ratio five (FR 5) schedule. Reinforcement after every correct problem (continuous reinforcement) is used only in the initial stages of acquisition. The effect of the increased work requirement is to strengthen the accuracy of counting. Fixed ratio schedules have been used selectively to "force" an increase in accuracy when the animal has acquired the basic counting repertoire but is not "paying strict attention" to the performance. On these occasions a dramatic rise in accuracy can often be seen.

A consequence of increasing a ratio requirement is to reduce the amount of reinforcement an animal received for a given number of responses. Theoretically, this decreased proportion of reinforcement to work requirement can approach total absence of reinforcement or extinction. Therefore, the number of pellets delivered with each reinforcement cycle is typically increased by one for every increase in five problems on a fixed ratio schedule. For example, on fixed ratio 10, the animal receives two pellets per reinforcement cycle. The additional amount of reinforcement maintains the behavior at high strength without impairing the properties of this schedule to force an increase in accuracy.

b) Time-out from Positive Reinforcement. A counting error, that is, a register response after the wrong number of counts have been produced, is typically followed by a period in which all the lights (in the chamber) are turned off and the counting levers become non-functional. This procedure effectively increases the time the animal must wait before he can receive the next reinforcement.

Baseline time-out periods are adjusted to the characteristics of the particular baboon, and currently range from 1.5 to 5 seconds. As example of the effectiveness of this procedure is an occasion on which an increase in time-out duration for Dolores from 1.5 to 5 seconds was arranged. The first day of the increase the accuracy improved more than three percentage points, and the following day achieved another ten percentage point increase.

The effect of the procedure is most strongly felt in the first few days of the increase. Further increases are sometimes necessary to produce additional increments in accuracy. On occasion, in order to correct a persistent error, duration of time-out for Dolores has been doubled. The difficulty readily responds to the increase, and time-out duration may then be reduced with the accuracy remaining stable.

A procedure termed resetting the ratio has properties of both time-out and increased work requirement. When relatively high levels of accuracy are achieved using fixed ratio and time-out procedures, further increases may be obtained by immediately increasing the work requirement to complete the ratio following an error response. For example, Cassius is now running on FR10 reset; this means that following any error response, regardless of the proportion of the ratio requirement completed, the ratio is "reset" to ten and the baboon must complete an additional ten problems errorlessly to be reinforced.

The immediate effect of the reset is to increase the ratio requirement for the next reinforcement; repeated error prior to reinforcement will generate a very long ratio. Because of the drastic nature of the reset requirement, it is typically reached gradually. For example, in the first step, the animal may make errors on the first eight problems of the ratio without a reset, but must produce two more correct problems whenever the error occurs on the 9th or 10th problem. Technically, we call this schedule tandem fixed ratio 8, fixed ratio 2 reset. The reset component is then gradually increased and the first component decreased until FR10 reset is achieved.

The effectiveness of this schedule can be seen on Cassius' baseline. When the reset procedure was initiated, Cassius was running on a straight FR15 at about 85 percent accuracy. When the tandem reset procedure had been completed and FR10 reset achieved, accuracy was above 90 percent and continued to increase to an average of about 93 percent.

The strength of the reset procedure derives from two sources: (1) the functional increase in time-out from positive reinforcement which results - the amount of time before the animal can be reinforced is equal to the time it takes him to "run off" the reset ratio; (2) the properties of ratio schedules in generating increases in accuracy, described above.

c) Differential Positive Consequences. Schedules are used in which the successful completion of a counting chain without an error is reinforced by the delivery of two or more pellets. A stimulus light remains on until the animal makes an error. If an error occurs, the light goes out and the reinforcement cycle produces only one pellet. Therefore, the animal is differentially reinforced for accurate counting. Animals running on this schedule tend to maintain high levels of accuracy for long periods of time.

A restriction on the application of the techniques described above is that in general their effectiveness increases with higher levels of accuracy on the counting baseline. We have confirmed findings of Ferster and Hammer[1] on a complex performance with chimpanzees which show that when a complex repertoire is in the early stages of acquisition or is severely disrupted, increasing the work requirement or lengthening the time-out is likely to be ineffective or even detrimental. Ratio reset and time-out increase will tend to suppress total counting output when performances are at low levels. On the other hand, small increases in work output (ratio increases) are effective except in the very early stages of acquisition.

For serious disruptions in performance other techniques are indicated. Two successful techniques have been 1) increasing the proportional representation of the problem or problems which are weak, giving the animal more experience with them; 2) in the case of persistent overcounting, using an immediate problem reset procedure, which we call overcount reset. Overcount reset is programmed by producing the error consequence immediately after the first overcount has occurred instead of after the register response, as is the usual case. For example, on one drug recovery run, Cowboy began persistently overcounting on problem 1; this behavior was not responsive to the negative consequences which followed the incorrect register. An overcount reset of problem 1 was arranged: the second counting response on this problem produced an immediate time-out and problem reset. The effect on overcounting was felt very rapidly and Cowboy's original level of accuracy on this problem quickly returned. In summary, the effectiveness of specific negative consequences of counting errors and of differential positive reinforcement are greatly increased when the counting baseline is not severely impaired. Special techniques are available to correct particularly persistent errors.

3. Experiments on the effects of problem sequence on counting.

There are two ways in which the animal "knows" how many counts he should produce on a given problem. 1) The principal determining factor is the problem display; that is, the pattern of geometric forms to which a particular number of counting responses has been conditioned.

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[1]Unpublished data.

2) If a fixed sequence of problems is used, the baboon also learns that completing one particular problem is the occasion for the appearance of another. In a sense, he partially "memorizes" the problem sequence.

Experimental probe: Cowboy, the male baboon who had acquired the full counting routine in the fixed sequence 1, 2, 3, 4, 5 at the time of the last annual report has been maintained on that same series for measurement of drug responses. Despite his long history on the fixed sequence, Cowboy still looks at the pattern of geometric form before he begins counting. It was of interest to determine the extent to which over a period of months the baboon had come to "depend" upon the number of the preceeding problem as a stimulus for performance of the problem which followed it.

An experimental "probe" was introduced which consisted of programming a problem out its usual sequence at the beginning of the serial chain. Normally, each chain started with problem 1. Under the probe, the stimulus patterns for problems 2 through 5 were placed randomly at the beginning of the chain.

Results. The probe forced the baboon to count 2, 3, 4 or 5 without the help of having just produced the usual preceeding problem correctly. Only on problem 5 was accuracy disrupted by the procedure. Cowboy tended to count 4 on problem 5; however, he would invariably produce the correct count immediately following his error.

It was concluded that even after months of problems presented in the same fixed sequence, the problem stimulus display alone was still capable of evoking the correct count.

Random Series Experiment. After the determination that an intact counting sequence was not necessary for correct performance, an experiment on the effects of a random series of counting problems was performed. It was addressed to the question of to what extent a long history on a particular sequence of problems would interfere with establishment of counting on a randomized sequence of problems. On a random sequence the baboon might, for example, be required to count 3, 5, 2, 4, 1 with reinforcement following the correct completion of problem 1. A unique 11 problem sequence was programmed.

Results. There was remarkably little disruption produced on the first day on this sequence. Problems 1, 2 and 4 were essentially unaffected. Problem 3 dropped 9 percentage points in accuracy and problem 5, 15 points. On the following session the sequence was re-randomized and disruption shifted from problem 3 to problem 4 with problem 5 continuing to decline in accuracy. The experiment was attenuated at this point by the animal's become sick with a gastrointestinal disturbance resulting in a total cessation of counting behavior.

The differences in the two experiments described above are that in a novel problem sequence not only does the counting performance

lose the benefit of a well-learned sequence, but also, it is susceptible to the interfering effects of the tendency to "expect" the original sequence of problems.

Interference was felt in the relatively greater disruption resulting on the second experiment. Nevertheless, the overall counting performance remained well intact.

Additional evidence regarding the effects of random sequence is available from the experiments with the new baboons and from a temporary training change in Dolores' counting history. The two new baboons have been counting on a random sequence since the inception of their training; random sequences were arranged on an 11 position stepping switch and were changed approximately twice a week. Frequently behavioral disruption followed the presentation of a new random sequence. Although the decrements were relatively small, it seems clear that partial learning of the eleven-problem sequence was contributing to increased accuracy.

At one stage of her training, Dolores, the female baboon, had been placed on a random sequence of problems 1, 2 and 3. Acquisition of relatively good counting under this measure was rapid and comparatively stable.

The new baboons are now being programmed on long random sequences using a five-channel punched-tape system. One animal, Cassius, has achieved very high levels of performance within these long sequences, demonstrating that improved performance can result when the animal does not rely to any extent on learning the sequence, and is thus "forced" to attend more carefully to the problem display.

It is concluded that particular problem sequences are learned along with learning to discriminate among the various problem displays. However, the control exercised by a particular problem stimulus is not greatly reduced by a long history of running on a fixed sequence. Furthermore, when extremely long random sequences are programmed, a baboon will learn to count entirely under the control of the problem stimulus, and may even show an enhancement in performance.

4. Analysis of Persistent Errors.

A functional analysis of counting reveals three classes of errors which occur: 1) In the very early stages of acquisition gross errors are seen; relatively random numbers of counting responses may be emitted in the presence of a problem stimulus. However, errors with respect to a particular problem soon become very restricted. For example, it is unusual for an error other than counting 2 or 4 to occur on problem 3. 2) There is a class of infrequent errors. Even at high levels of performance the animal is likely to produce a few error responses on a problem in a session. Characteristically, (a) these are immediately

corrected and (b) a single error occurrence is not predictive of the repetition of that error. 3) There is a class of persistent errors in which the animal will follow the negative consequences of the incorrect response immediately with the same response. For example, Cowboy's most frequently observed error is counting 4 on problem 5. In sessions in which problem 5 is relatively severely disrupted he will often emit a sequence of episodes of counting 4 and registering before 5 responses are produced. On occasion, the cumulative effects of repeated "punishment" for persistent errors result in the gradual development of more gross errors; e.g., counting 3 on problem 5. In this case, the effects may "spread" to other problems, producing a general decline. Such performances are usually characterized by greatly reduced response output; the relatively infrequent reinforcements earned during a poor performance are not sufficient to sustain the behavior.

The explanation of persistent errors requires the description of another phenomenon. Occasionally, a particular error will "snowball" over a number of sessions so that an initial small decrement is amplified into a totally inept performance. These reactions are most frequent in response to drugs.

It appears that the "snowball" effect can be attributed to two factors. First, the animal in a sense creates a new problem stimulus by producing repetitive errors. A specific problem display is only part of a greater stimulus pattern which controls counting performance. That is, a particular stimulus appears in a specific position on a particular panel in his chamber under certain conditions of illumination, etc. This general stimulus pattern also includes the recent consequences of his behavior. If the negative consequences of incorrect counting on a problem are frequently-repeated time-outs, problem recycle, and postponment of reinforcement, then the animal eventually responds to these events as a change in problem conditions. In this case, it is still less likely that correct counting will occur. Counting errors do not appear to be the result of poor visual discrimination among the problems displayed. Rather, the animal is not effectively discriminating his own performance. In a sense the baboon doesn't "know" that it is producing four counts on problem 5. Repeated error consequences then appear to indicate to it that the "rules of the game" have been changed. In brief, a temporary breakdown in the animal's discrimination of its own counting behavior which might be induced by a drug leads to an increasing difference in the stimulus characteristics accompanying the problem presentation.

Second, to account for repetition of a particular number of counts in persistent error behavior, it is necessary to look at the animal's recent reinforcement history. Almost invariably, the number of counts the baboon is producing in making a persistent error are appropriate to a problem on which at that time counting is very accurate. For example, when Cowboy is persistently counting 4 on problem 5, accuracy on problem 4 is usually extremely high; hence, the animal is being strongly reinforced for a number of counts which differ only slightly from a number which is

appropriate. As the stimulus conditions weaken in the fashion described above, counting 4, which is strongly reinforced, begins progressively to replace counting 5 when problem 5 is displayed. If counting is to be maintained at all, the baboon eventually manages to emit 5 counts, permitting it to move on to another part of the sequence. It then has an opportunity to be reinforced for counting 4 again when problem 4 is displayed.

The foregoing interpretation of persistent errors represents an analysis of behavior occurring "spontaneously" or in response to drugs. It is possible to arrange problem schedules to experimentally induce the snowball effect, and thus determine the validity of the analysis.

In summary, we can distinguish between occasional errors and those which occur frequently and in repetitive bursts. Persistent errors appear to result from an initial weakness in discriminating the number of counts which have been produced. This error leads in turn to a progressive change in overall stimulus conditions and to the substitution of a frequently reinforced and similar number of counts for the correct number. This analysis can be put to an experimental test by the arrangement of systematic conditions for producing it.

5. Delayed Response Counting Experiments - Rhesus Monkeys

The difficulty in the performance of the counting routine results not only from the stimulus and response complexity of the task, but also from its temporal dimensions. Response-produced stimuli, such as the counting tones, must be remembered and integrated by the animal over some period of time, if successful counting is to occur.

A counting routine has been established in two rhesus monkeys which emphasizes demands upon memory rather than discrimination among a large set of problems. The routine involves "counting" in the same sense that it is used in the baboon experiments: in response to a discriminative stimulus the animal presses a response manipulandum to produce tones; when the number of tones produced is equal to the number of the counting problem, a register response will be reinforced. However, the procedure is very different in its temporal dimensions from the baboon routine; lengthy tones and lengthy minimum inter-tone intervals are used. Heavy demands are placed upon the animal both for remembering the number of counting responses that he has previously produced, and for keeping track of the consequences which had resulted from his last counting response. Sufficiently long intervals produce a continually difficult performance which does not lend itself to "over-learning." This procedure should provide for a useful and sensitive baseline upon which to measure drug effects.

Procedures. Two rhesus monkeys are housed in individual 60 x 40 x 40 inch chambers identical to those containing the counting baboons. The intelligence panel is very similar to the panels used by the two new

counting baboons, containing a "house" light, a stimulus display light, a plastic response key over the face of the display unit, and a lever underneath the unit. The food hopper is on one side of the panel; a drinking tube provides continuous access to water.

The opportunity to count is available only during a 30-second period when the house light is turned on. At any time during this interval, the monkey may press the plastic response key to turn on a continuous tone; further responses during the tone have no effect. The tone remains on for the duration of the 30 second "time-in" period. Hence, its duration is determined by how long the animal waits before he makes the response. For example, if he responds at the 29th second, then the tone is 1 second in duration. This period is followed by a 30 second "time-out" period in which both the house light and stimulus panel light are turned off and the response manipulanda are functionally disconnected. Absence of responding in the time-in period is also followed by a 30 second time-out.

The task of the animal is to count to a specified number. At present only a single problem, counting to 3, is being programmed, because of the interest in exploring demands upon memory rather than discriminations among problems. However, Findley and Weissman (1964) have obtained reliable counting behavior on five problems of this type in a baboon.

In counting to three, the monkey must produce a tone in each of three consecutive or non-consecutive time-in periods, and then press a register lever to "give the answer." Registration during the third tone produces a reinforcement magazine cycle during which 10 pellets are delivered into the food hopper while a clicking stimulus of 10 seconds duration is presented. The clicking stimulus, which develops conditioned reinforcing properties from its association with food delivery, is also presented after the first and the second tone if the animal witholds his register response for the tone duration; i.e., he is reinforced for not responding.

Two types of errors are possible. The animal may undercount by registering during either the first or the second tone, or may overcount by allowing the third tone to terminate before he registers. The consequence of either type of error is to start the 30 second black-out period immediately and to reset the problem so that the animal must produce three sequential tones once again.

Schematically, a correct counting-to-three response goes through the following sequence: (1) in the presence of the house light and the stimulus light on the panel (time-in condition) the animal presses the plastic key and produces a tone which lasts for the remainder of the 30 second period; (2) he does not operate the register key and is reinforced at the end of the 30 second period by a 10 second presentation of the clicker stimulus; (3) this sequence is repeated again after a 30 second black-out (time-out condition) period has intervened; (4) after the second time-out period the animal produces the tone and then makes the

registration response during the tone. The response is followed by the delivery of 10 food pellets and the conditioned reinforcer clicker.

This procedure has several properties which make accurate counting performance by the animal very difficult. The monkey must remember without the benefit of a verbal mediating system the number of counts that he has produced over relatively long periods of time. The time of onset of the tone and the duration of the tone will vary according to when the animal initiates the response. The monkey must also remember whether, on the last presentation of the tone, he received 1) a reinforcement or 2) a time-out for incorrect registration, either of which resets the problem to the beginning, or 3) the conditioned reinforcer tone which indicates that he should continue counting until he reaches the third tone. The difficulty of the task may be further increased by randomizing the durations of the time-in, time-out, or tone-on periods.

In acquiring this sequence, the monkey was first trained to count to 1; then the count to 2 problem replaced 1, and when this was acquired at reliable levels the problem was changed to counting-to-3. The two rhesus monkeys have satisfactorily acquired the repertoire necessary to count-to-3 using this procedure.

In summary, counting-to-three under a delayed response procedure which includes very difficult memory requirements has been established in two rhesus monkeys. The procedure is expected to provide a useful and sensitive drug baseline.

D: Injection Procedure - Report

The special drug injection procedure described in the 1962/63 annual report has been published as a technical note (Levison, et al, 1964).

E: Drug Experiment - Animals

1. Properties of the Baseline

A counting performance permits two measures of drug effects to be taken: 1) the disposition to respond, which is measured by the total work output of the animal in the experiment on the drug compared to non-drug days, and by the distribution of the responses over the eight hour experimental course, indicating the onset and duration of the acute drug effect; 2) accuracy of performance, the accuracy of counting may be impaired by a drug, even though the total response output remains stable. In this respect counting is more sensitive to drug effects than is a simple response. Furthermore, the problems range in complexity from 1 to 5. The more complex counting problems have been shown to be more easily disrupted. In brief, the amount of drug information which can be obtained from this baseline is considerably greater than from the simple operant with a discrimination requirement, in which case the animal either does or does not make a single response, depending upon reinforcement conditions.

2. Chlorpromazine Experiments

Two baboons, Cowboy and Dolores, have been given a range of doses of chlorpromazine by the oral route. The drug in solution was added to fruit juice. On control days fruit juice and quinine were given to present a comparably bitter solution. The drug was administered only if the counting baseline had an overall mean accuracy higher than 90 percent and none of the individual problems were severely disrupted. There were no measurable effects from the placebo solution.

a) Baseline of Problems 1-5. Most of the chlorpromazine data were obtained from Cowboy counting on problems 1-5 in the fixed serial order 1, 2, 3, 4, 5; the principal drug effects are presented in Figures 2 and 3. The mean accuracy for all five problems, and the accuracy on problem No.5, which is the most sensitive to disruption, are presented for each dose level. In general, chlorpromazine had a disrupting effect on Cowboy's counting performance, both in lowering accuracy and, at higher dose levels, in also depressing total response output. However, the dose-response relationships are not simple ones and specific drug effects were dependent upon a number of variables.

Pre-treatment. Initially 2, 4, 6, 8 and 10 mg /kg doses were administered two hours before the beginning of the counting session. Pre-treatment was used because of the complex nature of counting. It was desirable to eliminate a possible unique effect of a specific and undetermined rate of absorption of the compound upon the counting baseline.

Results. The curves in Figure 2 describe the pre-treatment drug effects. The arrow indicates day of chlorpromazine administration. There were no measurable effects at 2 or 4 mg /kg. Higher doses showed a progressively increasing depression of the total response output over the preceeding control day. Accuracy was less affected than total responses on the drug day, with only the 8 mg /kg dose showing a pronounced decrement. However, the accuracies obtained at 10 mg /kg are based upon a total response output which was less than 10 percent of that produced on the control day.

Immediate start. Chlorpromazine was also administered immediately before the start of a counting session, at doses of 6, 7 and 10 mg /kg. The curves describing the drug effects are shown in Figure 3.

Results. There was a more marked impairment of accuracy than under pre-treatment, but less depression of total response output. The greater effects on accuracy over the pre-treatment drug experiment may well reflect greater sensitivity of accuracy to progressive changes in the organism produced by the drug uptake. On the other hand, gradual changes in the state of the organism would be less likely to produce strong response depression.

The drug data obtained under this procedure at 10 mg /kg represent particularly well the effects of chlorpromazine over an eight-hour drug

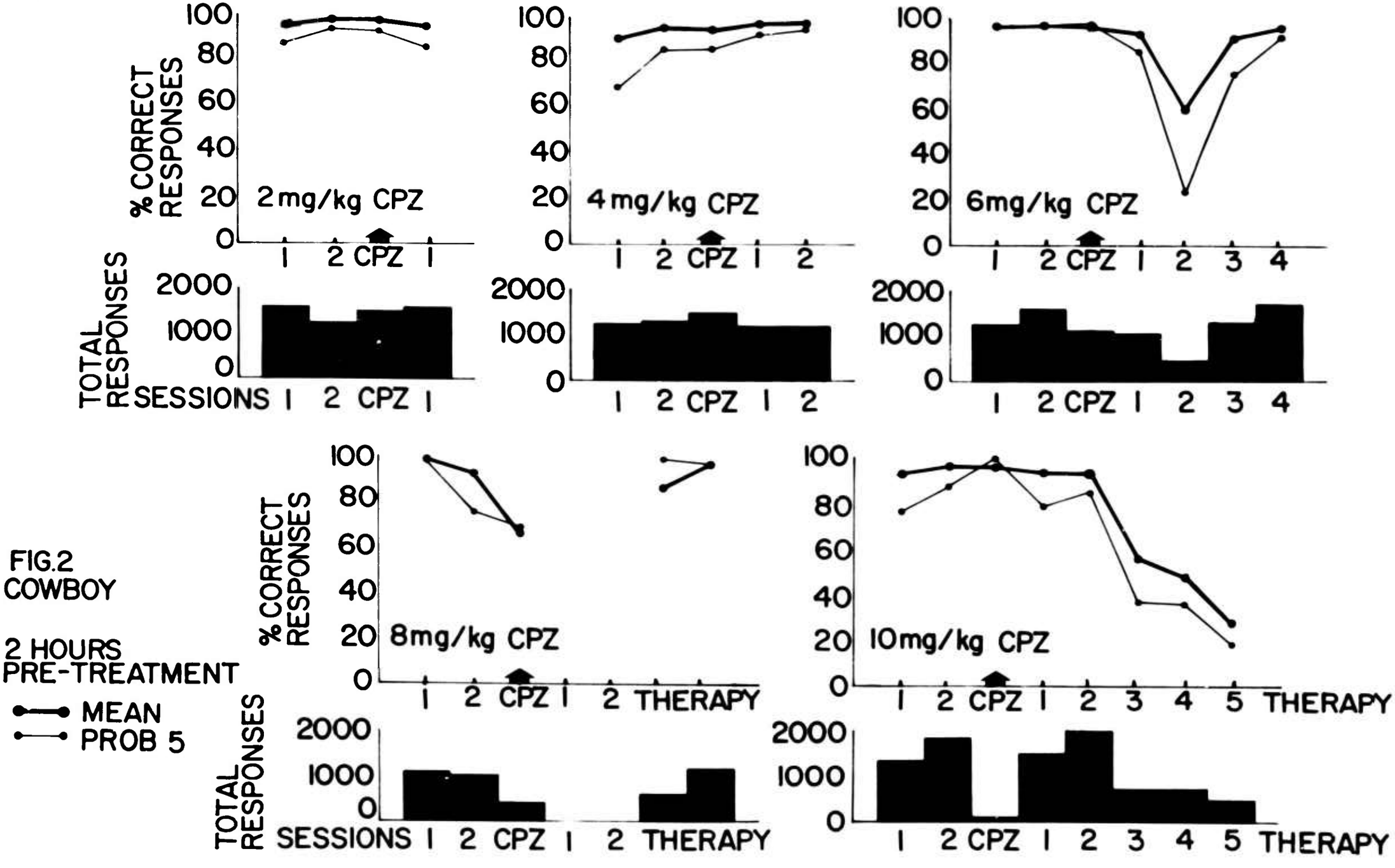


FIG.2
COWBOY

2 HOURS
PRE-TREATMENT

MEAN
PROB 5

BASELINE, CHLORPROMAZINE SESSION, AND RECOVERY TO BASELINE FOR 2, 4, 6, 8, AND 10 mg/kg CPZ. ACCURACY (% CORRECT RESPONSES) FOR MEAN OF ALL PROBLEMS AND PROBLEM 5 AND TOTAL RESPONSES FOR EACH SESSION.

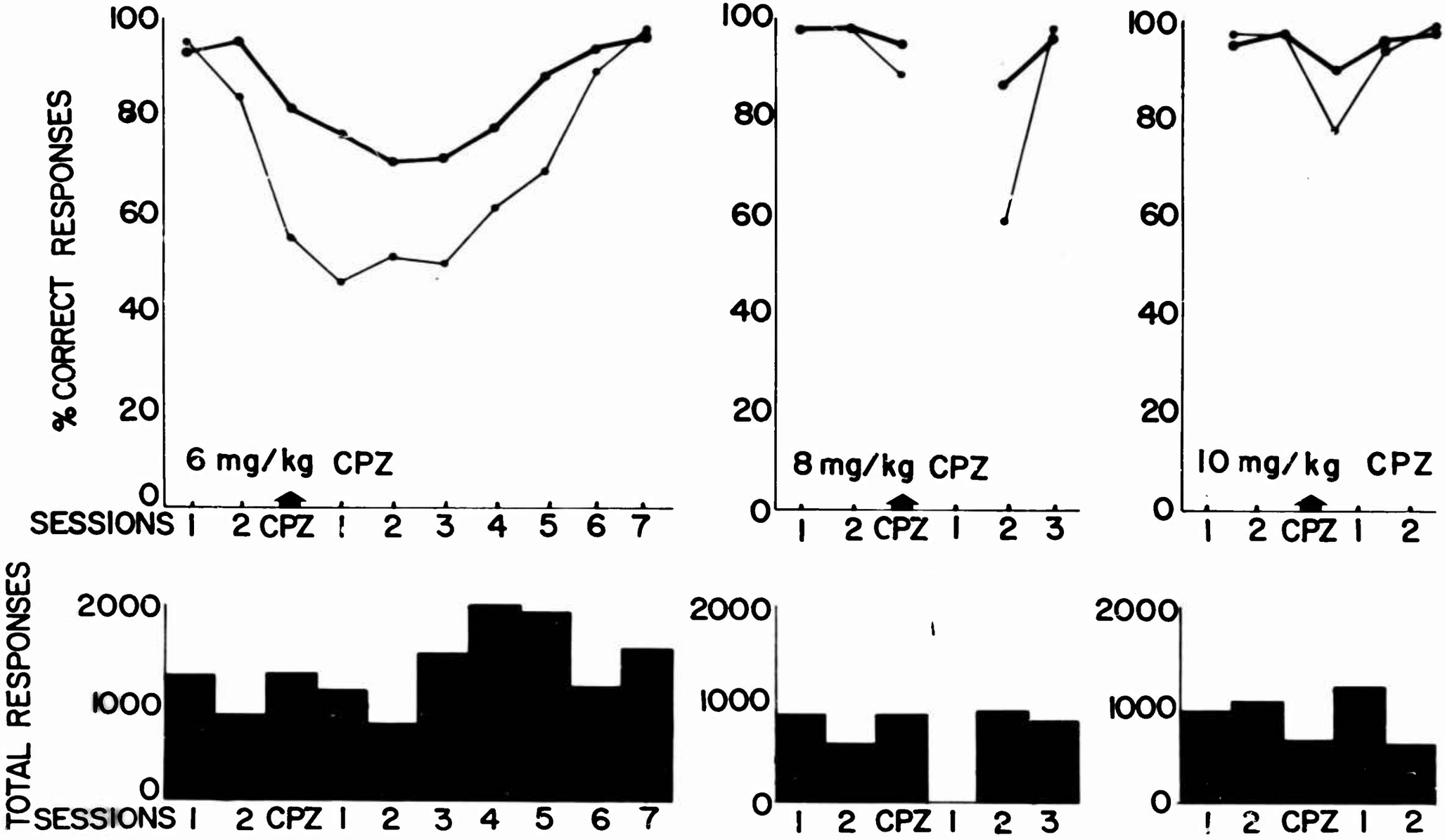


FIG.3 BASELINE, CHLORPROMAZINE SESSION, AND RECOVERY TO BASELINE FOR 6, 8, & 10 mg/kg CPZ. ACCURACY (% CORRECT RESPONSES) FOR MEAN OF ALL PROBLEMS AND PROBLEM 5 AND TOTAL RESPONSES FOR EACH SESSION.

COWBOY
IMMEDIATE
START
MEAN
PROB 5

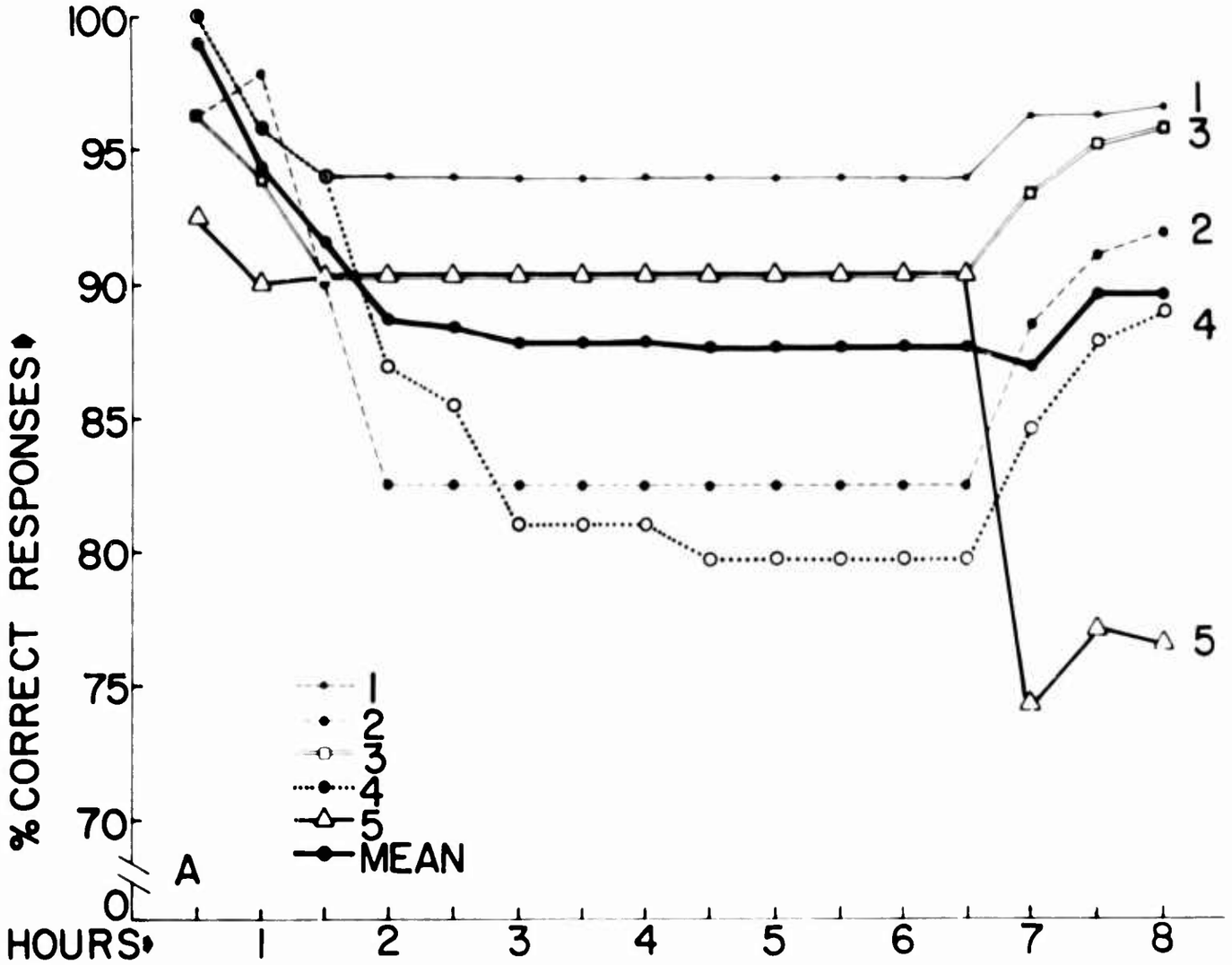
session. Figure 4A describes cumulative accuracies (cumulative percent correct responses for problems 1 through 5 and for the mean of all the problems over the eight hour drug session. The onset of drug effect is seen at about 1 hour, showing a drop on almost all problems; an increase in accuracy on all problems except 5 began at approximately 6.1/2 hours when the drug effect was wearing off. Figure 4B shows cumulative response totals for all problems combined over the same session, clearly indicating onset and recovery effects parallelling the accuracy data. Flat portions of the accuracy curves in Figure 4A can be seen to be accounted for by an almost total absence of responding from the second through the sixth hour, shown in Figure 4B. Particular attention should be drawn to the relative order of the drug effects. It can be seen that overall problems 1, 2 and 3 were less markedly affected than 4 and 5, with 1 showing the least decline. The relatively greater changes in the accuracy curve for problem 4 during the 4 hour period of acute drug effects indicate that the baboon had stopped counting with an error on problem 4 and made a few unsuccessful attempts on 4 during the 4-hour period of response depression. (It may be recalled that a similar succession of sporadic attempts to produce problem 5 correctly were obtained with the CRDL compound described in the last annual report.) A sharp drop in problem 5 obtained at 6.1/2 to 7 hours is an index of the sensitivity of this problem to subtle changes in the performance. It is likely that during the period of the acute drug effects the errors on problem 4 were counting 5 for 4. Consequently, emitting 5 counting responses was intermittently punished, an effect which may have accounted for the depression seen when counting was resumed.

Figure 5, which presents a detailed description of drug response and recovery to 6 mgm/kg chlorpromazine for the immediate start data, provides an excellent example of a drug-induced "snowball effect" and prolonged recovery. The principal drug effect on the day of administration was a sharp drop in accuracy on problem 5 and a smaller decrease on problem 4.

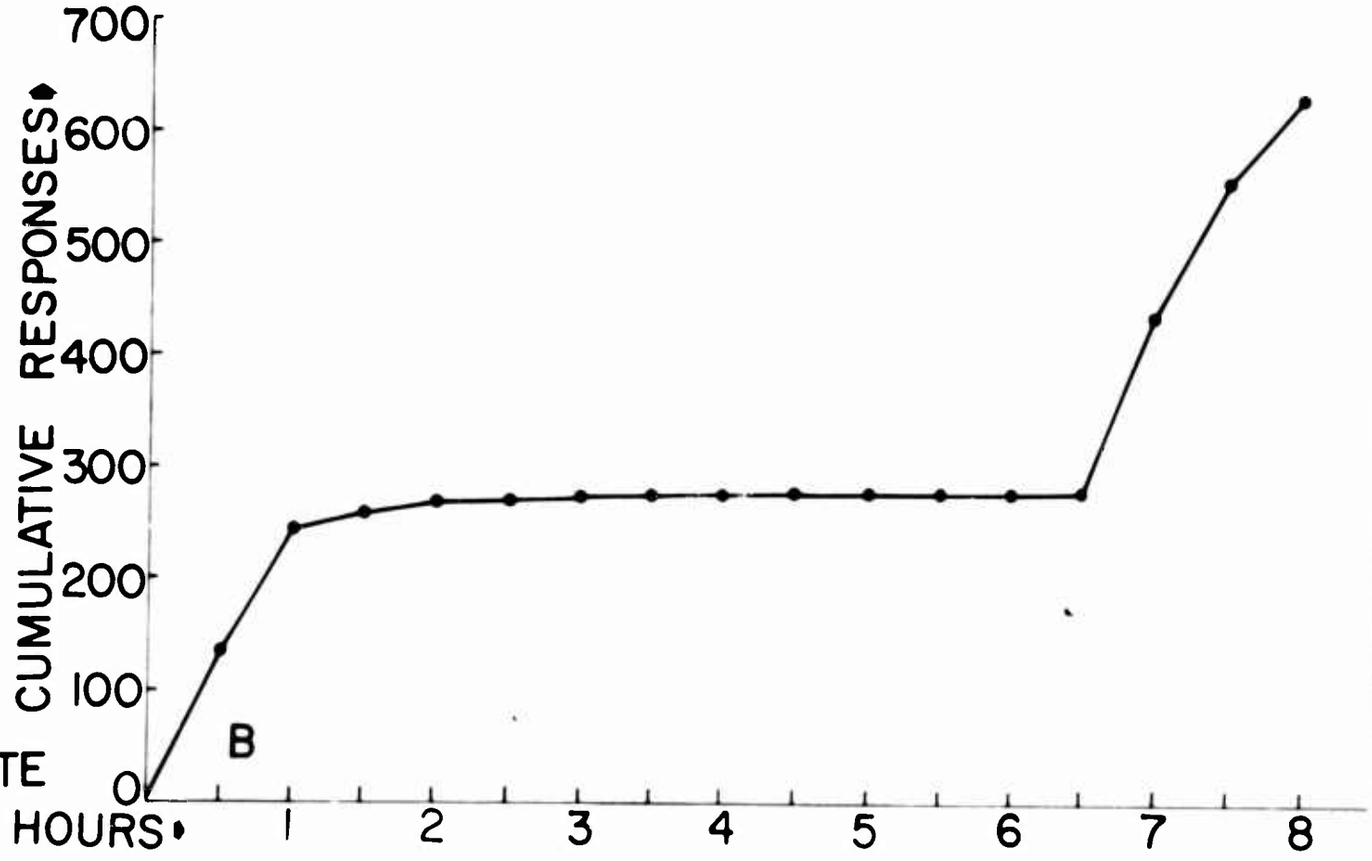
The extent of the effect on problem 5 at a relatively low dose of chlorpromazine can be best understood in terms of a pre-drug weakness in the baseline on that problem. Performance on 5 showed marked instability in the week preceeding chlorpromazine administration.

On the post-drug days, performance on all problems showed a decline as the snowball effect was manifest. By the second post-drug day, accuracy on both 4 and 3 showed marked depression and problem 2 had begun to decline. Initial recoveries were seen in the next few days on problems 2 and 3, with 4 and 5 reaching baseline levels somewhat later.

Detailed chlorpromazine effects on particular problems presented in Figures 4 and 5 support the data obtained on the CRDL compound indicating that the more complex problems are differentially sensitive to drug action. These figures are representative of the order of effects obtained at all drug administrations with respect to the impairment of particular



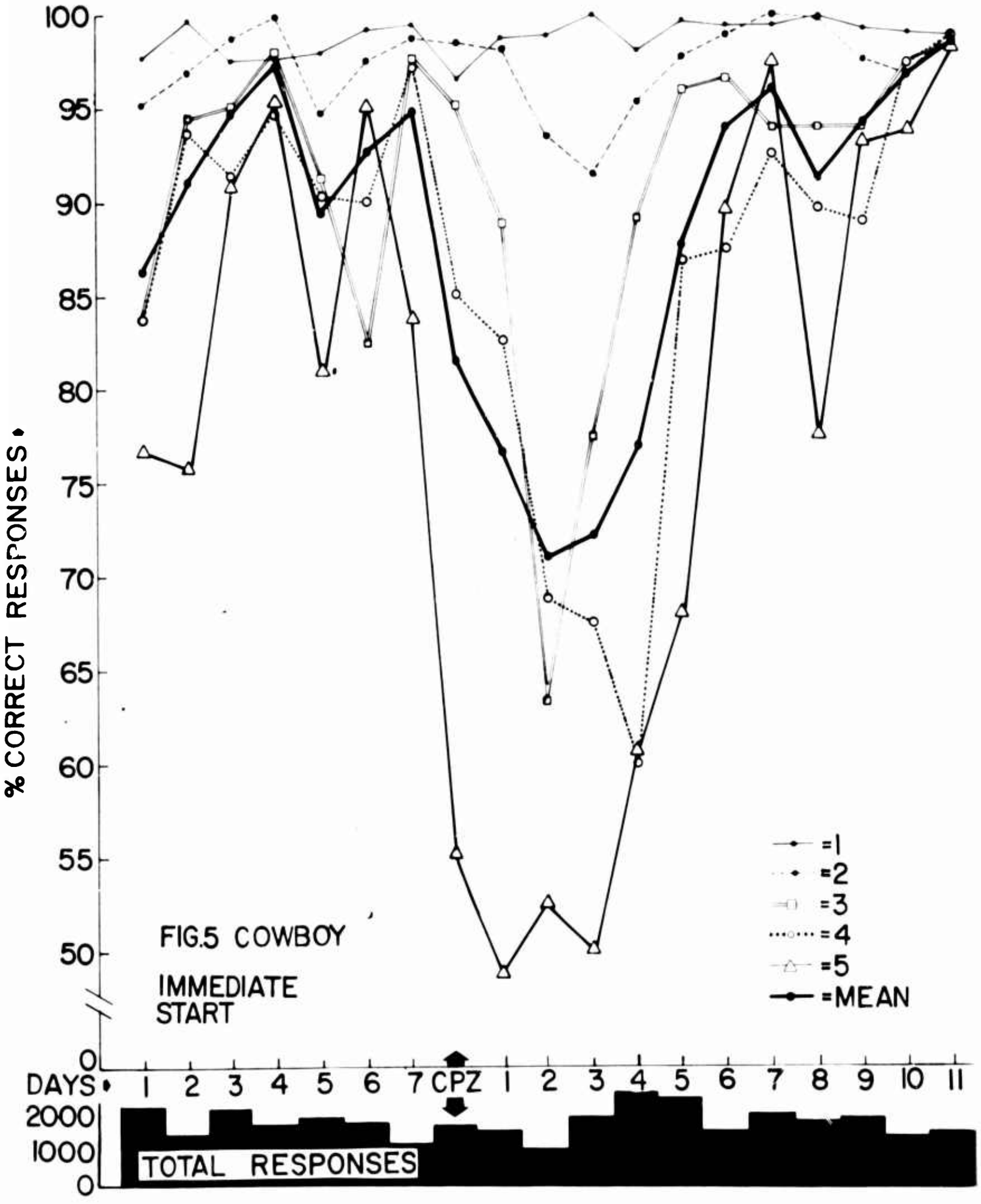
ACCURACY (% CORRECT RESPONSES) OVER AN 8 HOUR, 10mg/kg CHLORPROMAZINE SESSION. PROBLEMS 1, 2, 3, 4, 5, AND MEAN OF ALL PROBLEMS



CUMULATIVE TOTAL RESPONSES OVER AN 8 HOUR 10mg/kg CHLORPROMAZINE SESSION

FIG. 4
A and B

COWBOY
IMMEDIATE
START



BASELINE AND RECOVERY FOR 6mg/kg CHLORPROMAZINE. ACCURACY (% CORRECT RESPONSES) FOR PROBLEMS 1, 2, 3, 4, 5, AND MEAN

problems. Problem 5 almost invariably shows the greatest decrement to drugs and problem 4 is the next most frequently affected.

Recovery Effects. A striking characteristic of the counting performance in response to chlorpromazine as a drug baseline is that the most extreme effects are seen on the recovery days following the drug session. The most marked decrement in performance on post-drug days occur at 6, 8 and 10 mg /kg of the pre-treatment data (Figure 2) and 7 mg /kg of the immediate start data (Figure 3).

At 6 mg /kg pre-treatment the decrement in accuracy on recovery session 2 were so severe that the animal was unable to earn enough reinforcements to sustain his counting and output dropped markedly. On the first two post-drug sessions following 8 mg /kg pre-treatment, Cowboy was unable to count correctly on problem 1 and ceased responding in less than 50 attempts, earning no reinforcements. The effect at 10 mg/kg pre-treatment was more gradual; the progressive disruption on problem 5 accompanied by a spreading of errors to the total performance is an excellent example of the snowball effect described under the section on persistent errors. For both 8 and 10 mg/kg doses, "therapy" procedures were necessary to recover the performance from a total collapse. The overcount reset procedure previously described was used with great effectiveness in recovering the performance.

At 7 mg/kg, under the immediate start procedure, the animal initiated no counting responses on the session following drug administration. The second post-drug day showed strong impairment in problem 5 but recovery was complete within the next 24 hours.

Effect of Baseline. The recovery data show the importance of the status of the counting baseline prior to drug administration. As Figures 2, 3 and 5 show, at 8 and 10 mg/kg of the pre-treatment experiment and at 6 mg/kg of the immediate start procedures, some weakness is seen in counting on problem 5 on one of the two days prior to drug administration. In the first two cases, recovery sessions were marked by a progressive disintegration of the behavior eventually necessitating a "therapy" procedure. At 6 mg/kg, recovery eventually occurred without the use of special procedures, possibly because of the lower drug dose. These data point up the necessity for regarding the control sessions prior to the drug day as part of the drug experiment. In these cases severe post-drug difficulties cannot be clearly understood with reference to the pre-drug baseline.

Adaptation Effects. Although the chlorpromazine doses were in general given at widely spaced intervals over several months, there has been a noticeable adaptation to the drug. The immediate start data were obtained more recently than the pre-treatment data, and suggest a greater resistance to drug effects. This suspicion has been supported by two recent chlorpromazine results not presented in the figures. At 8 mg/kg chlorpromazine orally administered both for the pre-treatment and immediate

start procedures, Cowboy was essentially unaffected by the doses either on the drug or recovery days. While we are not in a position to specify the exact nature of this adaptation, it does not appear to be a result of a progressive strengthening of the baseline such as might be attributed to "over-learning." Relatively minor interventions other than drugs are still capable of producing considerable disruption. The adaptation to chlorpromazine appears to be a specific effect to that compound. Experiments with other drugs which are about to proceed are expected to support this position.

Baseline of problems 1-3. A second baboon, Dolores, has now begun counting on the chlorpromazine series. Dolores had been unable to maintain the high levels of accuracy on problems 1 through 5 which are characteristic of Cowboy's baseline. Therefore, in order to make the baselines comparable in terms of levels of performance, she was restricted to the counting problems 1, 2 and 3 presented in serial order. She must count to 3 twice to be reinforced. Thus far in the dose response series, 4, 6 and 10 mgm/kg chlorpromazine have been administered orally. The drug has been given immediately preceeding the start of the session. The pre-treatment procedure will be used after the immediate start dosage series is complete. This reversal in order of procedures is designed to counter-balance for possible confounding effects of adaptation to chlorpromazine.

Results. There were no effects on accuracy at 4 mg /kg. At 6 mg /kg there was a drop of almost 6 percentage points on problem 3, and at 10 mg /kg every problem was affected with the overall accuracy dropping more than 10 percentage points. On none of the drug days was there a drop in response output.

These data are consistent with the results obtained from the lower dose range with Cowboy, which showed a decrease in response output only at the relatively greater dose level. The accuracy and total response data suggest that higher doses of chlorpromazine will be required to produce equivalent effects with a more limited set of problems.

There were no post-drug effects at 4 or 6 mg /kg with Dolores. At 10 mg /kg accuracy on problem 2 did not reach pre-drug levels until the fourth post drug session. Performance on problem 2 has been least stable in Dolores" repertoire in the period in which counting 1-3 has become well established.

Summary. The following conclusions are drawn from the preceeding experiments:

1. At lower doses, the effects of chlorpromazine are felt upon accuracy before there is any significant depression of total response output.
2. At higher doses both accuracy and output are affected.
3. The more complex problems are more sensitive to chlorpromazine, a confirmation of an earlier result with the CRDL compound.

4. The most marked consequences of chlorpromazine administration are seen on the post-drug recovery session.
5. Impairment on the drug day or on the first recovery day may initiate a drug-behavior interaction marked by progressively increasing disturbances in accuracy and total output.
6. The extent of post-drug disturbance is related to the strength of the pre-drug baseline; when decrements in accuracy occur on days immediately preceeding drug administration, the likelihood of severe or prolonged post-drug difficulties is increased.
7. Disruption effects are less at a given dose level with a more limited set of counting problems.
8. There appears to be an adaptation to chlorpromazine after repeated doses which results in an increased dose requirement to produce the same amount of drug effect.

3. Non-drug Disruption Experiment

Severe disruption of both counting accuracy and total response output have occurred on post-drug days, more than 24 hours after chlorpromazine administration. Since the main effects of chlorpromazine occur within a few hours of administration (Dews, 1958) marked disruption on post-drug days probably cannot be attributed to direct action of the drug. The most useful explanatory concept is a drug-behavior interaction. It was of interest to investigate what properties of behavior under a drug might contribute to these delayed effects.

It is postulated that chlorpromazine administration results in two relatively novel conditions on the day of drug administration: 1) the animal is in a unique physiological state; 2) the changes in behavior induced by the drug represent a departure from normal counting in that the animal alters his behavior in an effort to adapt to the drug action. The pertinent question is whether it is necessary for counting to take place on the drug day in order for post-drug effects to be seen.

A control experiment was set up in which the animal was maintained for a day under novel circumstances without the opportunity to perform concurrent counting. Furthermore, an attempt was made in this situation to induce prolonged physiological changes from the animal's normal condition, without administering a drug.

Cowboy was maintained for a day in a holding cage without deprivation of normal food and water intake. The holding cage was chained to the cage of a female baboon in estrous. Cowboy displayed extremely aggressive and excitable behavior and appeared to be highly agitated most of the day. On face value these conditions appear to represent strong differences from the baboon's usual external environment and physiological state. That evening Cowboy was returned to the experimental chamber and the following day was run as usual on the counting routine.

His counting performance was characterized by a high level of accuracy on all problems and a high total output. It is tentatively

concluded that novelty and departure from the normal routine are not in itself sufficient conditions to produce prolonged behavior decrements. The delayed effects appear to result from a drug-behavior interaction produced by the introduction of a novel and distracting condition while counting is occurring.

4. Comparison of Extinction Effects with Drug Effects.

Drug effects upon counting include differentially greater impairment of the more complex problems. A schedule has been in effect which suggests conditions producing a different pattern of impairment.

Experimental extinction is the procedure of witholding the reinforcement which has maintained some specified behavior. The changes in performance which develop are well-known. Bursts of responding and emotional behavior may occur; the most reliable result is a progressive decrease in the response rate over time. Eventually the organism will cease responding altogether. In the counting experiments, whenever there is a mechanical failure of the feeders to deliver food pellets appropriately, changes in counting occur. Decrements in accuracy result as well as the typical drop in output associated with experimental extinction.

Post-Drug Extinction. A feeder breakdown occurred on the third recovery day after a 10 mg /kg dose of chlorpromazine was given to Cowboy. The feeder remained functionally disconnected for four consecutive sessions. Initially, the decrements in rate and accuracy were attributed to a delayed drug effect. Decline in accuracy began on the first two days with problems 3 and 4 and extended to problems 1 and 2 on the last two days of extinction. On days 3 and 4 of the extinction run, accuracy on problems 3 and 4 ranged from 24 to 52 percent. Total response output dropped below 100 for the 8 hour session. However, there was no effect on accuracy on problem 5, which remained at 100 percent throughout the extinction period.

Since problem 5 is normally most sensitive to disruption, this was an apparently paradoxical result. However, it has been frequently observed that when extinction procedures are applied to chained schedules this type of result is obtained (Kelleher and Gollub, 1962).

Technically, the counting routine is a type of chained schedule. That is, when different performances (in the present case, counting 1, counting 2, etc.) are arranged in sequence with their occurrence under the control of different stimuli (the different displays), removal of reinforcement initially affects the earlier members of the sequence, which are temporally the most distant from the reinforcement. Behavior which immediately preceeds reinforcement is the last to be affected by extinction.

In the instance described above, this phenomenon occurred in spite of problem 5 being the most complex component, as well as being

temporally closest to the reinforcement. It is also significant that problems 1 and 2 showed some decrement, although these are normally very resistant to disruption. Thus, effects of another independent variable on counting clearly show that this complex repertoire is specific in its functional relationships; i.e., the more marked effects on the more complex problems previously described are not simply inevitable results of any intervention.

Other data: Dolores' feeder has had a history of intermittent failure. On 4 of 6 occasions when there was at least partial extinction in a session, either problem 1 or 2 or both were relatively disrupted while problem 3, the closest one to reinforcement, remained stable. In one of the two exceptions in this case there was no evident decrement on any of the three problems.

In summary, the effects of extinction on counting are to disrupt the behavior, but in a consistently different pattern from drug effects.

Systematic investigation of this effect is being continued with one of the new baboons. Experiments are planned in which extinction will be combined with drugs to measure the interaction effects of the two variables.

III: HUMAN EXPERIMENTS

A. Matching-to-Sample

A type of cognitive behavior at which the human organism excels is responding differentially to abstract properties of the environment and classifying these abstractions into categories. A method has been developed by workers in the experimental analysis of behavior for continuous measurement of the development of and capacity to respond to abstract stimulus material. This procedure, called technically matching-to-sample, has been successfully used in organisms ranging from the pigeon to man.

Under the basic procedure, the organism is presented with a "sample" stimulus, and a number of "matching" stimuli. The organism must indicate which of the matching stimuli is most similar to the sample.

Usually, the stimuli are presented visually with a center stimulus serving as the sample and one on either side as the matching stimuli. Typically, the subject must make some response on or under the sample display window in order to produce the entire problem. This behavior ensures the "attention" of the subject with respect to the sample. A correct problem solution is obtained by responding to that matching stimulus which has more properties in common with the sample. The organism discovers which stimulus properties are appropriate to "abstract" as the basis of the match by differential positive and negative consequences. That is, a reinforcement or a conditioned reinforcer follows the correct match, and a black-out period or some other punishing stimulus is consequent upon an error. For example: sample is a green triangle, matching stimuli are a red triangle and a green square. Selection of red triangle is reinforced. Geometric form, not color is the appropriate abstraction. In brief, the consequences of behavior determine which abstractions are "correct."

In similar fashion to the baboon experiments, the matching-to-sample procedure permits simultaneous measurement of disposition to respond and of problem solving accuracy. The subject must work to produce the problem stimuli in order to make the matching response.

Both disposition to respond and accuracy are strongly influenced by the strength of the reinforcement and the properties of the schedule under which it is presented. Clearly, cognitive behavior does not occur "in a vacuum." It varies according to the consequences available in the environment. The following experiment involves long-term baseline cognitive performance, functionally similar in terms of repeated measurement, reliable observation, and elimination of extraneous influences to the baboon experiment.

Most cognitive tasks which serve as drug baselines are presented to subjects on a "one shot" basis. Hence the drug effects are confounded with novelty of the situation and the operation of social and transient motivational factors which greatly complicate interpretation of results.

In the experiment to be described below, subjects perform in the same environment under the same general condition for several hours each day for hundreds of experimental sessions. It is our conviction that this kind of experiment represents "real" conditions of behavior to an extent not possible with large groups run on one or two sessions.

1. Apparatus

The experimental chamber is an 8 ft. long by 4 ft. wide by 7 ft. high booth containing a chair, a table and the matching-to-sample console. The chamber is ventilated, illuminated at comfortable intensities, and somewhat sound insulated. The intelligence panel of the matching-to-sample console contains three small windows arranged in a row, with a lever-action switch below each one (Figure 6). The panel also contains a relatively large, white "house light" which is on when the experiment is in progress and which can be turned off to indicate time-out periods. A numerical electrical impulse counter advances once at each reinforcement; the counter dials constitute a visual record for the subject of the cumulative reinforcements obtained in the session. A blue light under the counter flashes briefly after every correct response. The monetary exchange value of a reinforcement is posted under the counter. A small speaker behind the panel produces a tone each time the counter registers a reinforcement. The console is connected remotely by cables to automatic programming and recording equipment located elsewhere in the laboratory.

Five variously colored lights arranged in a column on the left of the panel can be operated to indicate specific conditions. A large button switch on the lower left corner of the panel allows the subject to put herself in "time-out" for obtaining a drink of water, making a 'phone call, etc. A switch on the wall within reach of the seated subject can be operated to ring an alarm bell in the laboratory.

2. General Procedures

Different geometric forms are projected visually onto each of three windows on the intelligence panel. The task of the subject is to produce the problem by pressing the lever under the center window and then to press the lever under that one of the side windows which is most similar to the "sample" projected onto the center window. In the simplest form of this task the dimensions of similarity are geometric; for example, an X is presented in the center window, an X in the left side window and a + in the right side window (Figure 6a). The appropriate response is to press the lever under the left side window, indicating that the X's are most similar. "Correct" responses are followed by presentation of a small light, the conditioned reinforcer, and, intermittently, by reinforcement - the operation of the counter and occurrence of a brief tone (Figure 6f). That is, the counter does not necessarily operate after every correct response, but according to a programmed schedule dependent upon time intervals or work criteria. Each counter tally is

worth a pre-determined unit of money. An incorrect response produces a total black-out of all the stimuli on the panel (Figure 6B) and a period of time in which none of the levers can be operated. Thus the positive and negative consequences of the accuracy of this complex behavior are functionally similar to those in the animal problem-solving experiment.

The procedure may be complicated and the task made more difficult by the use of more abstract dimensions for matching. In the example given above, the stimuli may vary greatly in size, and the match be made on the basis of the relatively abstract property of form alone. In a still more abstract problem, three dots is the correct matching stimulus for a triangle and a square is the incorrect matching stimulus. The correct pair of stimuli have in common the abstract property of three, that is, three sides or three corners of the triangle and three elements of the dot pattern.

3. Simultaneous and Delayed Matching Procedures.

To date, a 20 year-old female subject, R, has been working for almost three months for approximately three and one half hours daily in the matching-to-sample situation. Both behavioral and drug experiments have been performed.

Two variations on the matching procedure are currently in use. (1) For ten minutes in the beginning and ten minutes in the middle of the session, the subject produces all three geometric forms, one in each window, each time she presses the center key to set up a new problem (Figure 6a). The three stimuli are present until the subject makes a matching response. We call this procedure "simultaneous matching." The (red) stimulus light on the top of the left hand column is on during this component. (2) For the remainder of the session a more complex procedure called "delayed matching" is in effect. (Figures 6c, d, e) The set-up response on the center key produces the sample stimulus alone (center window) for a brief period of time (Figure 6c). After the sample goes off there is a delay period during which the subject must remember the characteristics of the sample (Figure 6d). At the end of the delay period the stimuli to be matched are projected onto the two side windows but the center window remains dark (Figure 6c). The subject produces the match by responding under the appropriate stimulus from memory of the sample (Figure 6f). Sample presentation times ranging from approximately .05 to 3 seconds have been used; delay intervals have ranged from 1 to 30 seconds. An amber stimulus light (second from top) is on during delayed matching.

The subject is reinforced on a variable interval intermittent (VI) schedule. At present, she is working on a variable interval 3 minute (VI3) schedule which has the following characteristics: a reinforcement follows the first correct matching response performed after a time interval ranging from 1 second to 6 minutes, with an average duration of three minutes, has elapsed. The time intervals are remotely programmed in

long semi-random series. The subject has no external means of determining when the interval has elapsed. This schedule characteristically produces a relatively slow, steady rate of responding over a session.

The reinforcement is currently worth 15 cents. Ten and 20 cent units have also been used.

Before the first experimental session the subject was given some general orienting instructions toward operation of the matching-to-sample device, and a correct match and its consequences were demonstrated. However, she was not explicitly told which behaviors were "correct." It was strongly emphasized to the subject that there were no specific requirements to be met; her only task was to make money if she wished to do so.

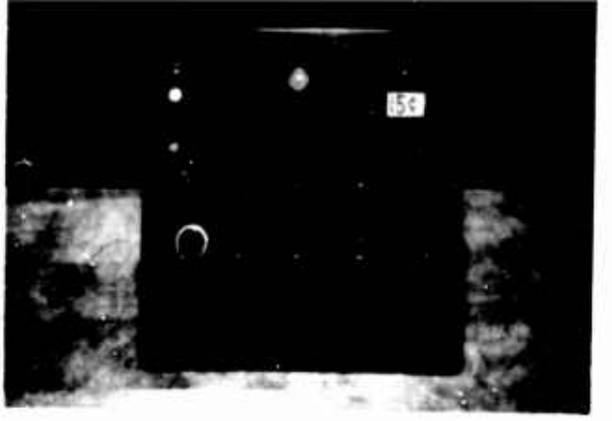
4. Results

Initial acquisition of correct performance on the 25 matching-to-sample problems was accomplished within the first session. Figure 7 demonstrates that initially the accuracy on both simultaneous and delayed matching was very high (above 90 percent) and remained at this level for about 14 sessions (three weeks). The simultaneous matching behavior has continually remained well above 90 percent in accuracy. However, accuracy on the delayed matching component of the performance steadily declined until it levelled off at approximately 75 percent accuracy. On the experimental sessions which followed those presented in Figure 7, accuracy on delayed matching has remained extremely stable at values between 75 and 80 percent for a total session. Accuracy for simultaneous matching has remained well above 90 percent.

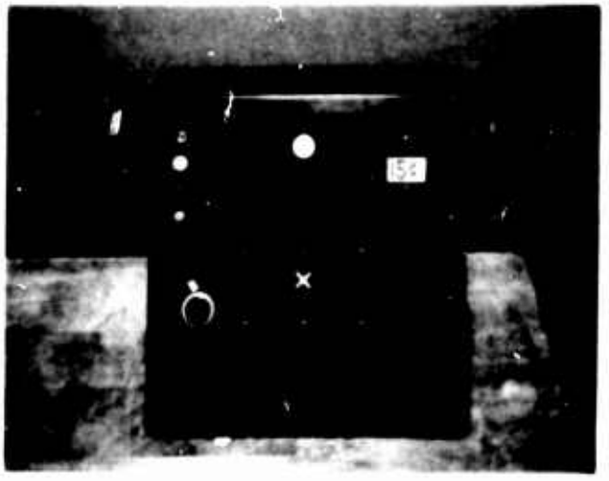
The gradual decline in accuracy on delayed matching presented in Figure 7 shows frequent sharp reversals when duration of memory delay is changed, indicating that changes in delay duration have not been without temporary effects. However, over time these temporary effects have been cancelled out by factors contributing to the weakening of accuracy. For example, at session 15, the first time that the delay interval was changed from 10 to 20 seconds, there was a sharp drop of approximately 5 percentage points in accuracy. However, at session 28, the second time that the 20 second delay session followed a 10 second session, there was no noticeable change in accuracy level.

When accuracy is plotted according to progressive sessions at a particular delay interval, but without regard for consecutive running sessions, the same general decline in accuracy is seen within each delay interval (Figure 8A). For example, the first session at a delay value of 30 seconds resulted in accuracy above 93 percent but on the 5th delay session at 30 seconds accuracy was below 80 percent. In general, a change to a shorter delay interval produced temporary increases in accuracy, and a change to a longer interval temporary decreases in accuracy, relative to the baseline; however, the long term trend in matching was a performance declining to a limit.

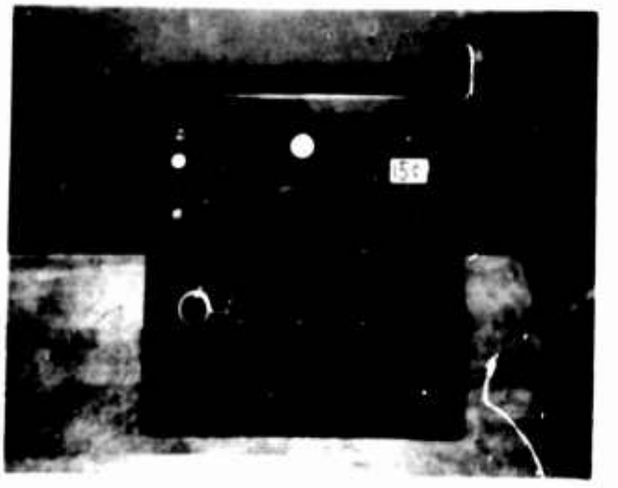
a SIMULTANEOUS MATCHING



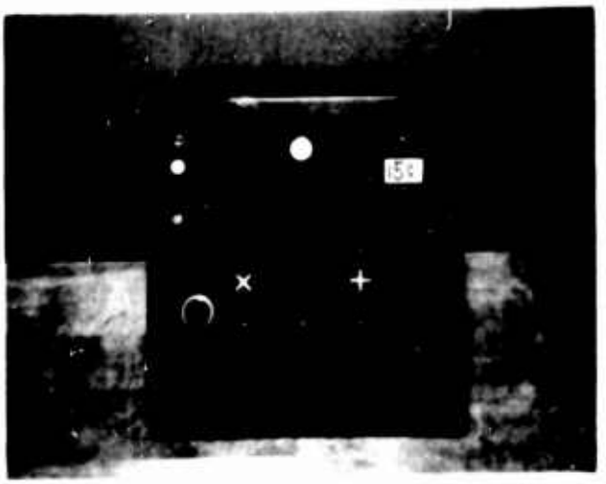
b TIME OUT



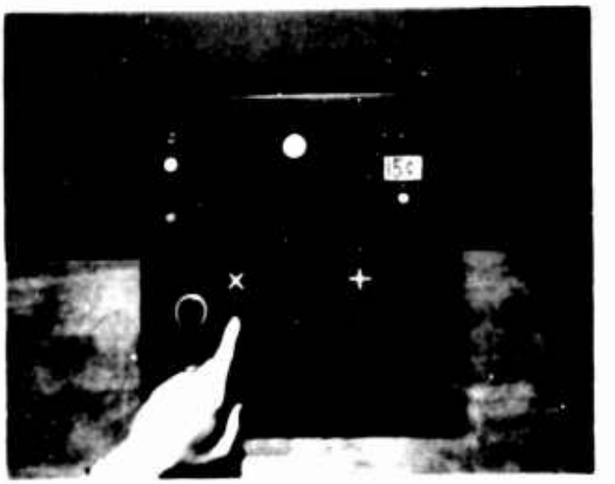
c SAMPLE PRESENTATION



d MEMORY DELAY



e MATCHING STIMULI



f CORRECT RESPONSE AND REINFORCEMENT

FIG. 6 MATCHING TO SAMPLE CONSOLE AND TYPICAL PROBLEM

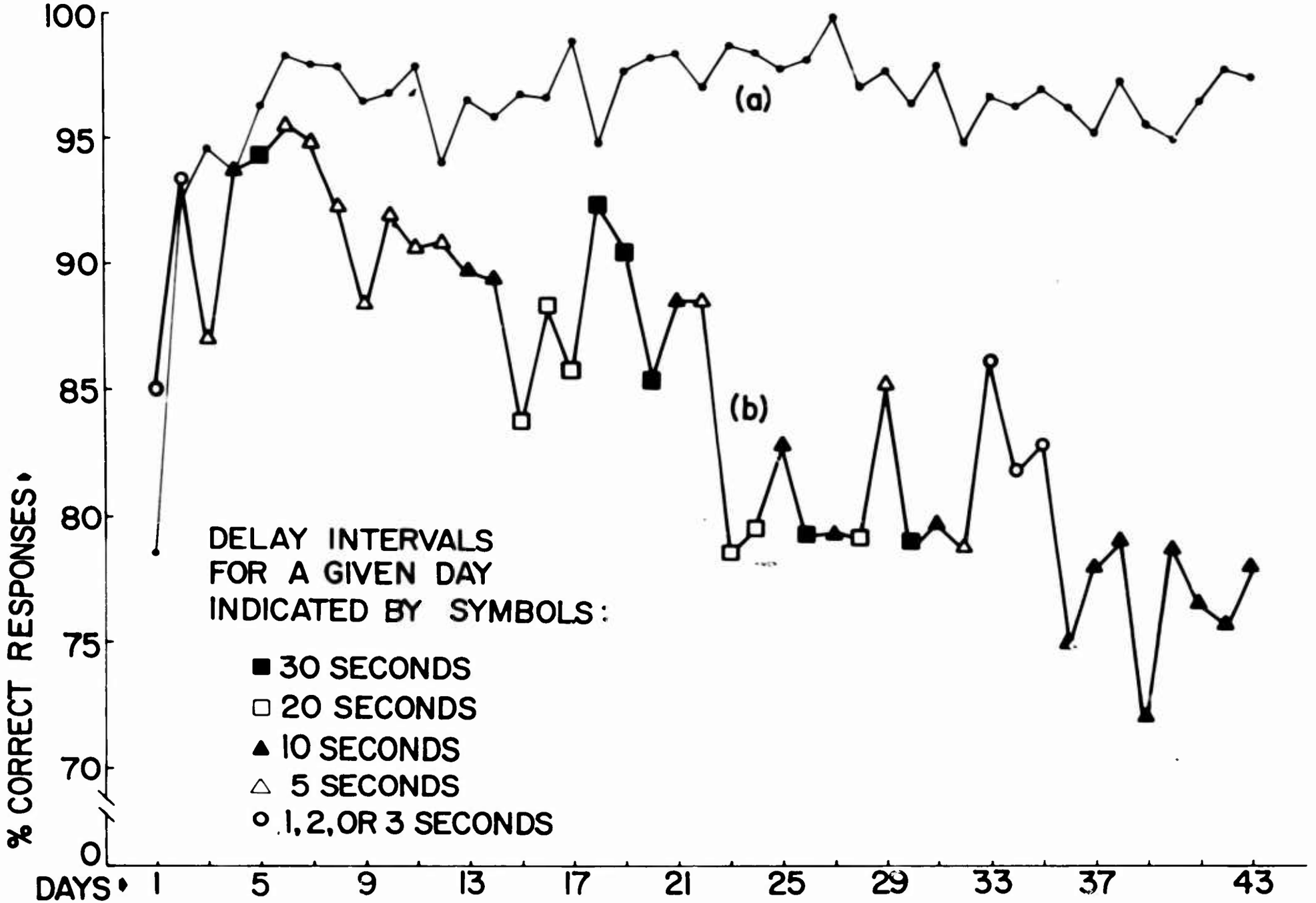
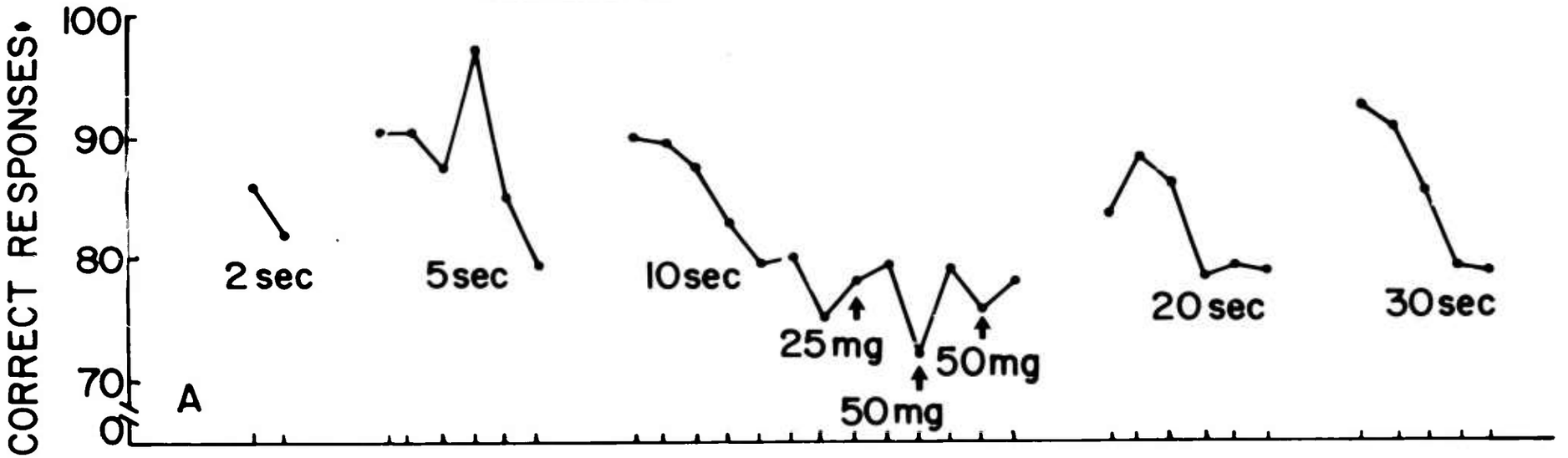


FIG.7 ACCURACY (% CORRECT RESPONSES) OF (a) SIMULTANEOUS MATCHING AND (b) DELAYED MATCHING ON SUCCESSIVE EXPERIMENTAL DAYS
SUBJ R



ACCURACY (% CORRECT RESPONSES) FOR DELAYED MATCHING WITH SESSIONS GROUPED BY DELAY INTERVAL DURATION. ARROWS INDICATE CHLORPROMAZINE SESSIONS AND DOSAGES

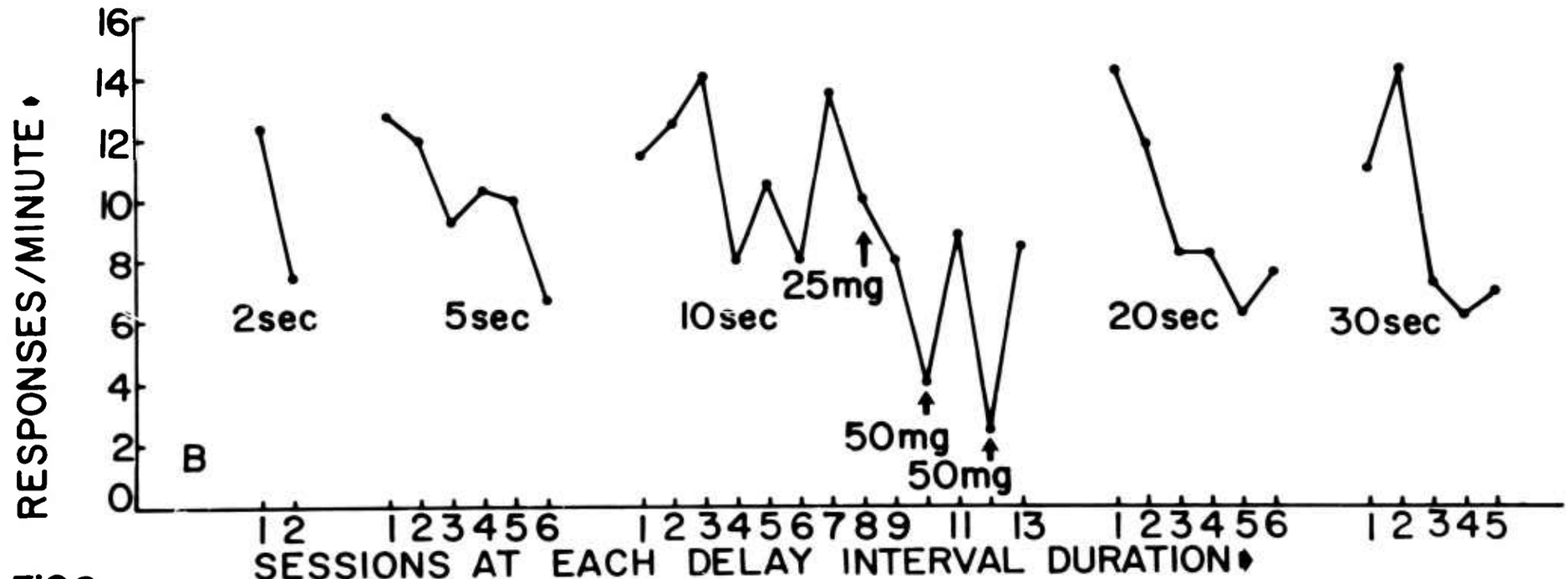


FIG.8 A and B SUBJ R

RESPONSES/MINUTE FOR DELAYED MATCHING WITH SESSIONS GROUPED BY DELAY INTERVAL DURATION. ARROWS INDICATE CHLORPROMAZINE SESSIONS AND DOSAGES

The decline in performance is seen not only in efficiency of matching but also in disposition to respond. Figure 8b shows that the number of responses per minute dropped sharply over sessions in a similar fashion to the accuracy. Under simultaneous matching, response rates have not been as stable as accuracies but there has been no gradual decline in rate of the type seen with the delayed matching procedure. Simultaneous matching response rates usually range between 20 and 25 responses per minute.

Inspection of the cumulative response records do reveal some slight changes in disposition to respond under simultaneous matching as the function of number of sessions run. Response rate on simultaneous matching varied somewhat from session to session during the first 22 sessions, but within a given session rates remained very stable. However, after the 22nd session, pauses during simultaneous matching began appearing in the record. It should be noted that this is the same point at which the delayed matching performance began to level off at approximately 75 to 80 percent accuracy. The pauses have generally been compensated for by increased "local" response rates, representing the subject's increased familiarity with the problem set.

In summary, the rate of responding on the delayed matching component declined accompanying the drop in accuracy. Response rates on simultaneous matching generally remained at overall high levels , although pauses began appearing occasionally in the records after the 22nd session.

5. Discussion

Gradual decline in both efficiency and response rate on delayed matching is the most important finding obtained under this baseline. The most reasonable account of gradual decline is in terms of the effects of the VI3 schedule on the baseline. That is, it is not necessary for the subject to maintain a high level of accuracy in order to obtain a maximum number of reinforcements. Initially, social factors in the subject's "trying to please the experimenter" or "trying to demonstrate her problem solving skill" probably operated to maintain high levels of accuracy. However, there were no differential consequences to continue accuracy at this high level. Because of the frequent repetition of the matching problems the subject had no difficulty in performing with few errors on simultaneous matching. Delayed matching places far greater demands on the subject in terms of paying attention to the relatively brief sample presentation and in "storing" the problem sample over the memory delay period. When the subject learned that she would obtain nearly as many reinforcements for the poorer performance and would receive no extraneous punishment from the experimenter, the relative difficulties of delayed matching had a pronounced effect.

The reductions in accuracy which accompanied increase of delay interval probably accelerated the overall decline; that is, on days with 20 or 30 second delay intervals, when accuracy dropped, there were no aversive

consequences. Hence, the behavior tended to stabilize at the low points. This low point remained a reference around which the baseline was temporarily established. The obtained decline in response rate further supports the interpretation that the subject came progressively under the "control" of a variable interval reinforcement schedule and that extraneous social and motivational factors were making progressively less contribution to the performance. Presumably, accuracies levelled off at 75-80 percent because lower levels result in an increase in lost reinforcements which is increasingly aversive to the subject.

It is concluded that these data are of particular importance because of the demonstration that when temporary social factors are eliminated, human behavior will show some of the same motivational properties seen commonly in animal experimentation.

B. Drug Experiments - Human

1. Medical Supervision of Human Subjects

Compounds are administered to human subjects orally in pill form. Dose levels are expressed in total weight of the subject. On control days a placebo pill is swallowed. In general, an effort is being made to keep the human and animal psychopharmacology experiments roughly parallel by use of the same compound and some of the same behavioral variables.

Each human subject is given a thorough medical examination and complete laboratory work-up before any compounds are administered. This phase of medical supervision is being carried out by a physical with a board certification in internal medicine. Psychiatric examination of the subject and liason with the internist is accomplished under the supervision of a research psychiatrist. Daily records of the subject's general health, including report of any specific symptoms both before and after the experimental session are being kept both by the experimenter and the physician. Dosages and scheduling of drug sessions are arranged by the experimenter within the limits determined by the medical consultants. Every foreseeable medical contingency has been taken into account and is covered by a specific plan of action.

2. Chlorpromazine Experiments

a) Regular Baseline. One subject has been administered 25 and 50 mg doses of chlorpromazine immediately before the start of the matching-to-sample session. Subject swallowed the pill with her eyes closed on both drug and placebo days. Double blind procedures have now been arranged so that the person administering the compound has no knowledge of whether it is a placebo or the active form. Matched placebo pills have been obtained from a drug house to prevent discrimination on the basis of oral

sensations.[1]

Results. Effects of 25 and 50 mg of chlorpromazine on the matching performance can be seen in Figure 8A and B and in Figure 9. All drug sessions were run at 10 seconds delay interval for the delayed matching component. At 25 mg there was a very slight increase in accuracy but a drop in response rate of about 3 responses per minute. A recent administration of 25 mg not shown in the figure indicates that this is a reliable result. The first 50 mg dose resulted in a decrement in accuracy of 7 percentage points and of approximately 4 responses per minute in matching rate. The second dose at that level produced a small decrease in accuracy but a relatively large drop in response rate from approximately 13 to 3 responses per minute. There were no observable placebo effects.

In the post-experiment, written, self-report the subject has indicated that she felt sleepy at 25 mg and experienced even greater difficulty with drowsiness at the higher dose. Occasional periods of somnolence have been observed. When the subject ceases responding on the drug day for several minutes, an experimenter looks into the booth to determine that no severe symptoms have developed. On the first 25 mg day the subject pressed the button to put herself into time-out for 6 minutes in order to wash her face and refresh herself. At 50 mg she reported slight dizziness as well as drowsiness and on the second day at that dose took an 8 minute time out. No drowsiness has been reported on placebo days.

Figure 9 shows the progressive effect of chlorpromazine and of the placebo over a 3.1/2 hour session. The first 25 mg and 50 mg doses of the drug are presented along with data from a typical placebo day. Figure 9A presents the accuracy data. The set of curves labelled (a) indicates that accuracy on simultaneous matching remains constant over the session. Curves labelled (b) show an initial increase in accuracy over the first half hour on all drug administrations and then a relatively greater decline for the 50 mg dose. A curve for 25 mg and for the placebo are essentially identical. Cumulative response data (Figure 9B) from the same drug administration parallel the accuracy data except that there is no initial spurt in rate. Effects of the drug on rate are seen at the first half hour; the 50 mg dose produced a lower rate throughout the session; placebo and 25 mg are again essentially the same.

Summary: The most pronounced effect of oral chlorpromazine at 25 and 50 mg is a reduction in rate of responding under delayed matching, with levels of accuracy affected very slightly at the higher dose level. No effects on simultaneous matching were obtained. Drowsiness and some dizziness were some side effects reported. There were no observable placebo effects with this subject.

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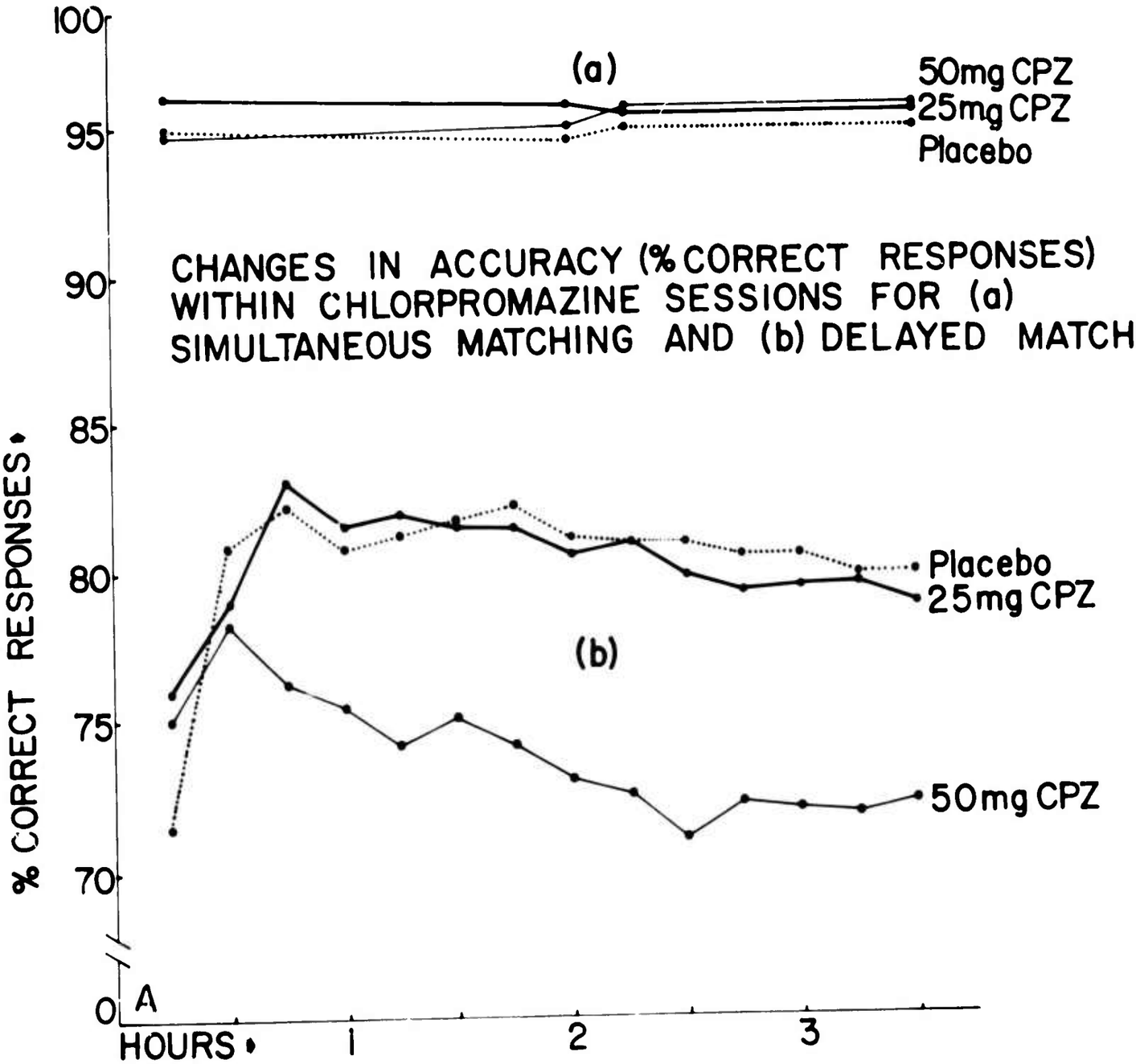
[1]The authors express their appreciation to Smith, Kline and French Laboratories, Inc. for their cooperation in supplying Thorazine and Dexedrine, both for human and animal experimentation.



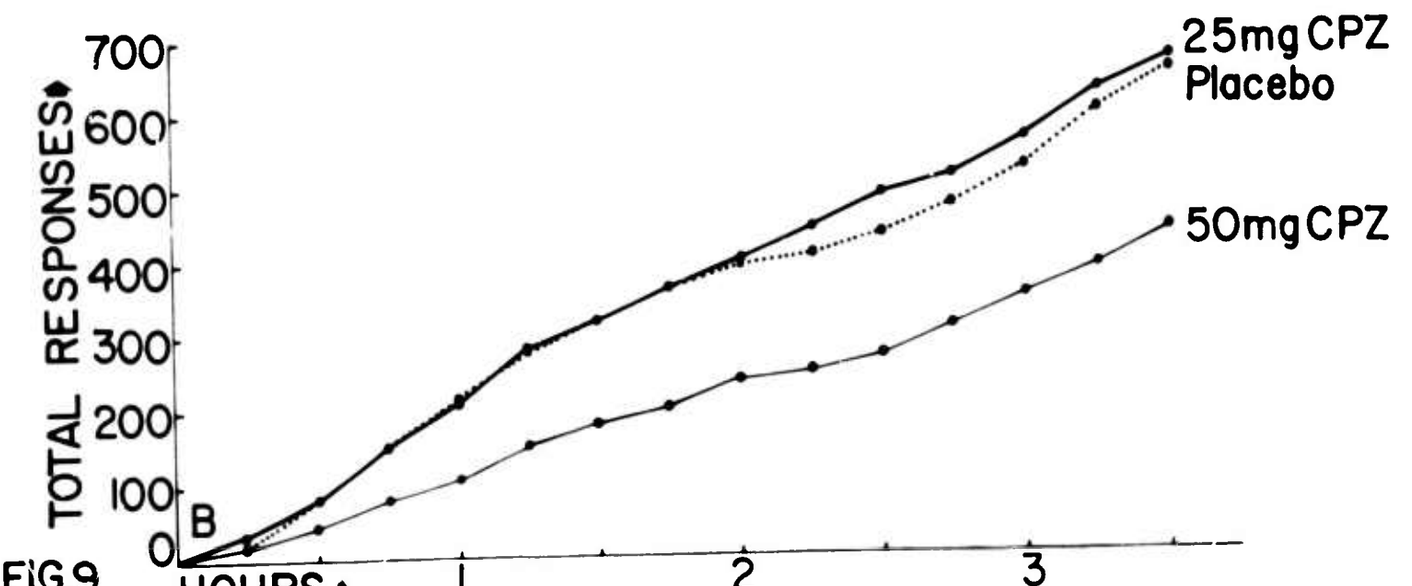


FIG.9 A and B SUBJ R CUMULATIVE RESPONSES WITHIN CHLORPROMAZINE SESSION FOR DELAYED MATCHING

b) The Effects of Chlorpromazine on an Extinction Baseline.

On three baseline days an extinction procedure was arranged as follows: 65 reinforcements, the maximum number usually obtained by the subject in a session were accumulated on the reinforcement counter. Before the subject entered the booth, she was told that these reinforcements were "free" and that regardless of what else happened in the rest of the session she would be able to keep the money which they represented. The counter was then disconnected from the circuit and no further reinforcements were given for the entire session. These conditions obtained for three consecutive sessions. The delay interval was 10 seconds on each day.

Under this special procedure, both the rate of responding and the accuracy remained essentially the same. It is inferred that the subject's personal history with respect to meeting obligations was sufficiently strong to maintain the behavior in the absence of explicit reinforcement. That is, payment before a task is completed in the "real world" does not imply that the task may be abandoned. In fact, failure to meet a prepaid obligation is usually heavily punished.

On the subsequent session the subject was administered 25 mg of chlorpromazine and run on the extinction schedule. Administration of the drug on this baseline produced no change in accuracy but a sharp drop in response rate under delayed matching, and a smaller decrease under simultaneous matching compared to the previous extinction sessions occurred. The extent of the decrease in response output was attenuated, however, by the intervention of the experimenter. The subject fell asleep in the booth and after approximately 10 minutes of the absence of any responding the experimenter opened the door to determine if any severe symptoms had developed. The subject awakened upon questioning and resumed responding, maintaining a relatively high rate for the rest of the session. Hence the actual total rate obtained for the session was spuriously high.

This is the first drug session at any dose level in which the subject has been continuously asleep for any length of time. On the following day, under placebo on the extinction schedule, the rate of responding remained low, although the subject reported no sleepiness during this session.

Results of this preliminary experiment suggest that the extinction procedure will provide an even more sensitive baseline than the VI3 schedule. It is suggested that immediate reinforcement is a stronger condition for maintaining behavior than a personal history with respect to work obligations, and that the subject will be unable to maintain a high level of behavior following the administration of a tranquilizing compound when "meeting obligations" is not reinforced. Chlorpromazine has effectively indicated the relative weakness of this extraneous source of motivation.

3. Future Human Experiments

Experiments are planned to measure the effects of both d-amphetamine and pentobarbital on intermittent reinforcement schedules and on extinction.

Fixed ratio, a different class of intermittent reinforcement schedules, will be included. That is, the subject will be required to produce a specified number of responses prior to reinforcement regardless of the time it takes to emit them. With the baboons, this kind of schedule has been shown to have a marked effect on increasing accuracy. It is of interest to determine whether similar effects will be obtained with human subjects.

A second human subject met the requirements of a thorough physical and psychiatric examination and has begun working on the matching-to-sample baseline.

C: Development of More Complex Cognitive Tasks.

The present matching-to-sample task has provided important information on the maintenance of this kind of behavior under conditions of intermittent reinforcement and has pointed up sharp differences between two only slightly dissimilar types of matching procedures. The independent variation in accuracy versus response rate have provided two independent measures of drug effect. Some procedures, extinction for example, seem particularly promising for measuring drug effects. Nevertheless, the task as it is presently programmed has some definite limitations. The problem sample is too small to remain a challenging cognitive task for any extended period. Therefore, a new system for presenting and recording this behavior is being developed.

Problems will be presented by means of very long 16 mm film strip loops. A device (the "Perceptoscope") is available in the laboratory which has all the capabilities necessary for 16 mm frame-by-frame presentation, reversibility and automatic control. The problems will be projected from the rear onto a translucent screen and the subject will operate switches located under the screen. The correct response on any problem will be programmed by a Western Union teletype tape which will operate in parallel with the film loop. This five-channel tape will be pre-punched to indicate which of the two matching stimuli for a given problem is correct. The tape sequence will exactly match the order of problems as presented on the film strip. The system of utilizing Western Union tape readers is already in use for randomizing problem presentation in the human experiment and in two of the baboon experiments.

It is anticipated that the new system will permit a very rich and diverse population of cognitive problems to be used. Very different dimensions of abstraction may become the basis for a correct match, with the subject given an opportunity to abstract this dimension in the first n trials of any particular sequence.

D: Cognitive Performance in a Short-Term Sustaining Environment

An experiment is under development in which a cognitive performance similar to that required of the rhesus monkey counting procedure and

a matching-to-sample task identical with that programmed for the other two human subjects will be carried out in an environment arranged to maintain the individual completely over an 8 hour period. The experimental room will contain the counting and matching-to-sample intelligence panels, a cot, a reading lamp and reading materials, a machine for dispensing food or cigarettes and a chemical toilet. The subject's access to the cognitive task and to the various components of the supporting environment is programmed by the experimenters. For example, when the period of cognitive activity has been terminated by the program, the subject has several response options. For example, he may select the cot, in which case the amount of time he spends lying there is automatically recorded through a switch closure. On the other hand, lying down during the performance period is punished by automatic reset of the reinforcement counter. The subject's disposition to engage in other activities is measured by the amount and duration of responding on a simple response mechanism to keep the reading lamp on, to obtain food, water or cigarettes. A clock, which is located behind a one-way vision screen, is available. A completion of a specified work requirement will produce a light, briefly illuminating the clock and permitting the subject to determine how much time he has spent in the booth and how much time remains.

The counting routine is functionally very similar to that in effect for the rhesus monkeys. The subject sits in a chair in front of the display, producing the counting tone with one foot pedal and making the register response when appropriate with the other one. Long delay intervals between conditions permitting the occurrence of a tone should make it very difficult for the subject to use his own verbal counting repertoire in remembering how many tones have been produced. The subject is prevented from making any marks with his finger to count the tones by requiring him to maintain a switch in a closed position with each hand. It is expected that a repertoire will be developed which will be functionally similar in many ways to that of the rhesus monkeys.

The administration of drugs will permit comparisons between the human and animal performances on this very similar counting task. Additional relevant information on drug effects will be obtained by measuring the subject's disposition to engage in the supporting activities available in the environment. For example, under a chlorpromazine effect, the subject may maintain his baseline level of accuracy but count less and spend more time on the cot. The administration of d-amphetamine may increase the amount of cigarette smoking and decrease food intake and lying down. Including the matching-to-sample task as an activity in this experiment will permit comparison with the other human experimental situation and will provide a more interesting environment for the subject.

Construction of the apparatus for this experiment is already well under way. It is hoped to maintain a human subject over an eight hour period during the working day. Total environmental control of a human subject has already been achieved over a five month period by one of the principal investigators (Findley, Migler, and Brady, 1964).

SUMMARY AND CONCLUSIONS

In the first six months of the present contract year the analysis of complex behavior and the effects of psychopharmacologic compounds upon complicated repertoires have been further extended. Three different complex performances have been newly established in three different organisms: counting on problems 1 through 5 in two baboons, delayed response counting in a counting-to-three problem with two rhesus monkeys, and a visual matching-to-sample cognitive task with two human subjects. The effects of a tranquilizing compound, chlorpromazine, upon an established counting baseline in two more bab oons and upon matching-to-sample in a human subject have been intensively investigated.

Animal Experiments

Behavior Experiments. Experimental analysis has been extended to several variables crucial to the development and maintenance of the baboon counting routine. A stimulus fading technique for training the counting performance has proved to be highly effective, with a great saving in acquisition time compared to earlier training techniques which utilized the principal of differential positive and negative consequences alone.

It has been conclusively demonstrated in the establishment of counting in the new baboons, and in an experiment with Cowboy, that high levels of accuracy in counting may be maintained on randomly programmed problem sequences. The experiments show that if fixed sequences of problems are repeatedly presented, the animals will to some extent learn and depend upon the sequence. However, a baboon which had been running for months on a fixed counting 1 through 5 serial sequence, was shifted to a random series and continued to perform without serious disruption.

Increased fixed ratio requirements, lengthened time out duration, resetting the response ratio and differential increase in the quantity of food per reinforcement for errorless performance have been used effectively to promote more reliable and accurate counting. Use of these differential consequences is recommended only when the baseline is fairly stable and well established. They are counter-indicated during early stages of acquisition and as corrective procedures for severe disruptions in performance.

Specific counting errors, such as counting four times on problem 5, have been analyzed and distributed into three major categories: gross errors, infrequently occurring errors, and persistent errors. The analysis of persistent errors is linked to a phenomenon designated the snowball effect in which initially small disturbances are magnified progressively until accuracy on the particular problem is severely depressed and the error behavior "spreads" to other problems. It is believed that a few recurring errors on a particular problem constitute a small change in total stimulus properties controlling the number of counting responses produced on a particular problem. The change in stimulus control permits

substitution of an incorrect but strongly reinforced count which is appropriate for an adjacent problem. These conditions result in a remarkable amount of perseveration in making the same error response in spite of accumulating negative consequences. Increasing the representation of the affected problem and immediate overcount reset procedures have been found to be effective therapeutic devices.

A somewhat different counting performance has been established in two rhesus monkeys. The animals work on a single counting-to-3 performance with long counting tones and long inter-response intervals, a procedure which places heavy demands upon memory for the number of response tones which have already been produced on the problem

Drug Experiments. Chlorpromazine has been administered by the oral route to a male baboon, Cowboy, counting on a baseline of problems 1 through 5 in serial order and to a female baboon, Dolores, counting on a baseline of problems 1 through 3 in serial order. Two general procedures for drug administration have been used; (1) pre-treatment, with the compound being given two hours prior to the beginning of the counting session and (2) an immediate start procedure, with counting beginning immediately after the drug is injected.

Baseline of Problems 1 to 5. Two, 4, 6, 8 and 10 mg/kg doses of chlorpromazine have been administered with the pre-treatment procedure and 6, 7, 8 and 10 mg/kg under the immediate start method. Data are presented which show effects of the compound upon accuracy of counting on the component problems and upon the mean accuracy and upon total response output in the drug session. Pre-drug baseline and recovery data have also been presented.

Baseline of Counting 1 to 3. Four, 6 and 10 mg/kg chlorpromazine have been orally administered to Dolores counting serially 1 to 3.

Results. Both pre-drug baseline and recovery data must be taken into consideration in making a dose-response analysis of the data. The principal results are as follows: (1) With a more limited set of problems, counting is less sensitive to disruption at a given dose level. (2) At lower doses the effects of chlorpromazine are principally upon accuracy. (3) At higher doses, both accuracy and total response output are affected. (4) The more complex problems particularly problem 5, are more sensitive to chlorpromazine. (5) The major unique interaction between the drug and the baseline is seen in the recovery sessions. Impairment on the drug day or on a recovery day may initiate a drug-behavior interaction marked by progressively increasing disturbances in accuracy and total output, with the extent of the disturbance related to the strength of the pre-drug baseline as well as to the dose level. (6) There is an apparent adaptation to chlorpromazine after repeated doses which seems to be specific to the biochemical action of the drug.

Non-drug Disruption Experiment. An attempt was made to determine if conditions of altered physiological state and novel environmental stimuli are sufficient to induce the kinds of post-drug disturbances observed after chlorpromazine administration. Cowboy was chained for a day in a holding cage to the cage of a female baboon in estrous with food and water intake maintained at normal levels. There was no disruption on the following day and it was concluded that it is necessary for the counting performance to be occurring in order for post-drug interactions to be produced.

Comparison of Extinction Effects with Drug Effects. Data were presented which show that relatively greater disruption on the more complex counting problems is not the only kind of response obtained under a change in experimental conditions. Data obtained under experimental extinction indicate that the earlier members of the counting chain are weakened more than those closer to reinforcement. In this case, counting serially 1 to 5, 4 and 5 are the problems nearest the reinforcement in the temporal sequence, as well as being the more complex problems. Nevertheless, problem 5 remained at 100 percent through 4 consecutive extinction sessions, a markedly different result from typical consequences of intervention. These data are compatible with results obtained under chaining procedures on different performances in other laboratories. Experiments are planned in which extinction will be combined with drugs to measure the interaction effects of the two variables.

Human Experiments

Matching to Sample. A type of continuous cognitive problem solving task functionally analagous in many respects to the animal experiments was described. A human subject matches a sample stimulus by selecting the appropriate one of two matching stimuli according to dimensions of similarity. Similarity is experimentally defined by the consequences of the matching response: correct matches are reinforced by a counter tally which represents a unit of money; negative consequences follow incorrect matching.

A single human subject has been working on 25 matching-to-sample problems in this situation for several months. A variable interval reinforcement schedule of 3 minutes at a rate of 15¢ per reinforcement have been the principal schedule conditions. The advantages of this procedure over traditional problem solving situations is discussed. There are two components to the baseline, simultaneous and delayed matching. Under the former, all three stimuli appear at once; under the latter, the sample stimulus flashes on briefly and the subject must remember it during a delay interval in which no stimuli are present; the matching stimuli then appear.

Results. The data indicate that the requirements for attention and memory make the delayed matching procedure a considerably more difficult

task. Although the subject was able to attain initial high levels of accuracy, the delayed matching performance dropped regularly to stabilize at 75 to 80 percent accuracy, while simultaneous matching remained well above 90 percent.

The principal importance of these data is to demonstrate that complex human behavior can come appropriately under the control of a schedule of reinforcement, similar to the kinds of control typically seen in animal experiments. In the present case, it is not necessary for the subject to work at high levels of accuracy in order to receive the maximum possible number of reinforcements. Therefore, on the more difficult delayed matching procedure, a lower stable baseline has resulted. It is concluded that extraneous social factors which were maintaining the performance at high levels earlier systematically dropped out.

Drug Experiments. One compound, chlorpromazine has been administered orally in 25 and 50 mg doses. All medical aspects of the experiment are under the strict surveillance of the experimenters and supervision of consulting physicians. Under delayed matching 25 mg of chlorpromazine produce very slight effects on accuracy and response rate; 50 mg result in larger decrements in accuracy but the major effect is large decreases in rate of responding. There were no placebo effects. Side effects of drowsiness and occasional dizziness at the higher dose have been reported. The simultaneous matching accuracy and rate were not affected at these dose levels.

The Effects of Chlorpromazine on an Extinction Baseline. An extinction procedure was run in which the subject received all her reinforcements "free" prior to the beginning of the session. Prior to drug administration the subject maintained normal levels of both accuracy and response rate. However, under 25 mg of chlorpromazine response rate was greatly reduced. The effect was attenuated by the experimenter's awakening the subject from a continuous sleep of over 10 minutes. This is the first drug session at any dose in which the subject has been asleep for a considerable length of time.

It was concluded that "obligation to earn her free reinforcements" based upon her pre-experimental history initially maintained the behavior without decrement. However, without additional reinforcement, this source of control was weakened by the drug, permitting the subject to fall asleep. The more powerful effects of immediate reinforcement are inferred; even at 50 mg on VI3 no prolonged sleeping had occurred.

New Experiments in Progress

Development of More Complex Cognitive Tasks. A method for projecting problems by means of 16 mm film strips is under construction. The new procedure will permit much greater flexibility and difficulty and will permit direct and continuous measurement of cognitive problem solving "in process."

A Short-Term Sustaining Environment. An experiment is under development which parallels the counting procedure in effect with the two rhesus monkeys. In addition, concurrent measures of disposition to nap, read, eat, smoke and use a chemical toilet will be taken. The subject will be maintained over an eight-hour period. The matching-to-sample task will also be included in the situation. This special environment will permit simultaneous assessment of several dimensions of drug effects and comparisons of simpler behaviors with the cognitive performances. Comparisons between the human and monkey counting routines will also be possible.

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