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The Effect of Drugs on Temporal Organization of Behavior

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by

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LIFE

Margaret E. Condon was born in New York, New York, January 26, 1939. She graduated from the Ursuline Academy High School in June 1956, and received a Bachelor of Arts in Psychology from Manhattanville College of the Sacred Heart in June 1960.

From September 1960 until June 1963, the author served as a Research Assistant in the Behavior Laboratory of Loyola University, pursuing her graduate studies on a Fellowship under the National Defense Education Act. The program entered upon was in behavioral science. In September 1963, she was appointed co-investigator of a National Institutes of Mental Health Small Grant, which was awarded to help finance the final analysis of the data contained herein.

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CHAPTER I

INTRODUCTION

The temporal dimension of experience includes two logically independent factors: one rooted in objective or clock time, the other in subjective or experiential time. The latter refers to the internal experience of duration, and a complete discussion of this construct may be found in Haley (1963). In regard to the former, individuals seem to possess a characteristic tempo or speed of performance that remains constant in varying circumstances. This fact is so self-evident that it appears commonly in speech.

That both tempo and subjective time are most probably empirically interrelated has been supported by several studies (Monnier, 1956; Brown, 1959; Block and Bridges, 1962; Fraisse, 1963). The characteristics of this relationship are still to be precisely determined and basic information concerning the parameters of both must be obtained before deductions can be made.

This dissertation is limited to a consideration of tempo. Tempo may be operationally defined as the temporal organization of behavior within the framework of objective time. This definition is in line with more current research. Formerly, some have considered it to be a general, "personality" factor, while others held that it was a specific, "task-induced" variable. More recently, both views have proven untenable and the focus has shifted to the discovery and delineation of its characteristics and limits.

One of the possible areas of study in temporal organization is the effect of drugs upon the constancy of tempo. Since tempo is physiologically tied partially to the nervous system of the organism, the chemical agents that modify the activity of this system may also influence tempo. A study along these lines has been completed using normal human subjects (Cabanski, 1961). The results of this study were equivocal. A possible reason offered for the lack of clearcut results was that only minimal drug dosages could be administered to human subjects. However, this restriction to minimal dosage levels would be removed with the use of animal subjects. It is the purpose of this study to extend the work of Cabanski by using animal subjects and higher dosage levels in order to establish a sharper empirical test of the concepts involved.

The specific hypothesis to be tested is: neither tranquilizing nor stimulating drugs which affect the central nervous system will affect the tempo adopted by an animal performing an operant response. This tempo will be operationally defined in terms of the duration of each response (D), and the inter-response time (IRT).

CHAPTER II

REVIEW OF THE LITERATURE

The term "personal tempo" was introduced in 1900 by Stern in his Psychologie der Individuellen Differenzen (Stern, 1938, pg. 467). He defined it as "an optimal time of rhythmic events and experiences," and considered it to be an all pervasive aspect of behavior, descriptive of a total personality. A thorough review of early work found in Allport and Vernon (1933) shows that the term "tempo" was used throughout the first two decades in a mainly qualitative and semi-philosophical manner. It is with these authors that the first extensive, experimental approach was made to the study of this concept.

The purpose of their investigation was primarily to shed light on deeper intangible aspects of personality through the analysis of measurable activities. Implicit in this is a holistic view of the person. They chose as their measure "expressive movements" which because of intra-individual consistency are "distinctive enough to differentiate one individual from another." Using 32 tests, they obtained an average test-retest reliability coefficient of .75 within a single session. Among the factors found descriptive of these expressive movements, were three tempo factors: verbal, drawing, and rhythmic speed had a corrected internal consistency of .90 and was almost independent of the other two, which had an intercorrelation of .61.

More recent studies of "expressive movements" and their tempos within the

individual have followed divergent paths. On the one side have been investigations that have dwelt on the interpretive value of movement and tempo (e.g. Wolff, 1943). The results of these studies have been incorporated into the field of projective techniques. An excellent review of the development and current use of expressive movements in psychodiagnostics is found in Bell (1948). Other investigators have been concerned with the nature of tempo apart from clinical interpretation. The remainder of this discussion will be devoted to research of this kind.

At the same time that Allport and Vernon were positing a multiple explanation of personal tempo, Frischeisen-Kohler (1933) postulated a general tempo or rate of activity which she held to be a unitary dimension of all behavior. Using tests of finger tapping, foot tapping, and preferred metronome rate, she found high intra-individual consistencies both within and between tasks. She contended that tempo was genetically determined. To test this hypothesis she compared the tempo of monozygotic twins, bizygotic twins, siblings and unrelated individuals. The correlation among the scores decreased as the genetic relationship became more distant. This finding could be related to later research that has posited a physiological basis for tempo in the nervous system (Monnier, 1956; Kastenbaum, 1959), however it must be kept in mind that a limited number of functions were tested here.

Wu (1934) also found a common factor of speed in his study of tempo. He assigned six tasks to nine subjects twice and to twenty-six other subjects once. The tests he used included foot and finger tapping, word writing, number counting, and poetry reading. Both test-retest correlations on the same task and intercorrelations between tasks were high. The average

reliability coefficient was .875 while the intertask correlations reached a maximum of .880. He also tested the relation between natural and maximal speed of subject. Here he found a low, positive correlation of .19.

The hypothesis of a single general tempo or even a broad group of speeds was contraindicated by the results of Lauer (1933) and Foley (1937). Lauer found little relationship between either spontaneous or imposed rates. Foley concluded that rate of activity was determined by environmental, and therefore, specific factors. Here again, however, these investigators employed a limited number of tasks for their investigation.

It is against this background of controversy and scantily supported conclusions that the study of Rimoldi (1951) is to be considered. He proposed to extend the work of Allport and Vernon and to utilize the more recently developed methods of factor analysis for exploratory study of the concept of tempo. He used a battery of 59 tests representing a wide range of psychobiological functions including specified motor movements, reaction times, judgments, expressive movements, and intellectual processes. These were administered to a subject population of 91 male students, 17 of which underwent a second testing in a period of time which varied between 15 and 30 days. The test-retest reliability of the tasks was computed. On those presented over different days, the median coefficient was .79; on those tasks which were repeated within a session, it was .93. These figures support the consistency of an individual on a given task, whether it be performed on the same day or on different days. In the testing of the generality of tempo, the tests themselves were inter-correlated and subjected to a centroid method factorial analysis. Nine primary factors were extracted: large motions of trunk and limbs, small

movements, drawing with feet, drawing with hands, perception, reaction time, cognition, and two factors which were undefined. These primary factors were themselves interrelated and in the second order four factors emerged with clarity: speed of all motor activities, speed of perception, speed of cognition, and reaction time. He concluded that the postulation of a monistic view of personal tempo was not empirically supported but rather there were group factors to which specific activities were related and within these clusters predictability from one task to another was possible. He also states that the heterogeneity and ambiguity of the term "personal tempo" would be greatly reduced, and its experimental value enhanced, if it were limited to describing the consistent temporal pattern adopted by individuals in any given task or related group of tasks.

It is within this structured definition of tempo as individual consistency; i.e., with its use as a dependent response variable, that the remainder of the studies covered in this review are considered. They are concerned with this tempo either casually as an extraneous observation (Buytendijk, 1945; Schaeffer, 1960a) or as the main variable. Mishima (1951) conducted a normative type of study from which he drew conclusions concerning characteristics of tempo on a variety of tasks. He found that tempo was unaffected by a time lapse, distracting conditions, or sex differences. Variance between both tasks and subjects was consistently higher than variance on test-retest within individuals. The same type of "defining" investigation was carried out by Rimoldi and Cabanski (1961). They studied a single task intensively. It consisted of tapping out visually presented patterns of dots. The amount of time spent in tapping each pattern was linearly related to the number of

dots in the pattern, and the time between groups remained a straight line function regardless of the size of the pattern (see Fig. 1).

Various independent variables have been introduced in studying the parameters of tempo in humans. Rimoldi (1946) found it resistant to fatigue

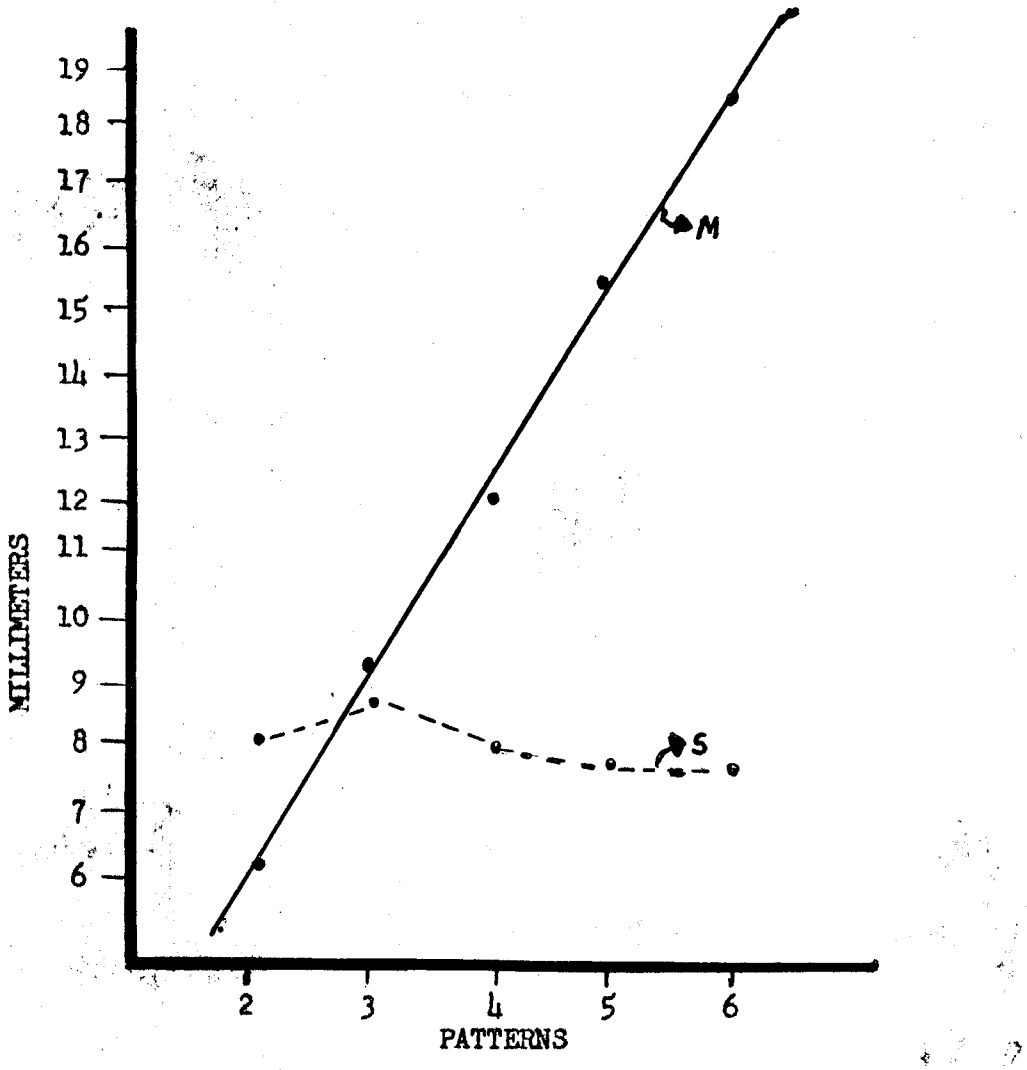

Fig. 1. Reproduction of results of Rimoldi and Cabanski (1961). Graphical representation of the Mean of the Means for the values od patterns M_2 through M6 and intervals S_2 through S6.

in an ergographic task. Fraisse et al (1954) changed the amount of effort required per response by varying the force necessary to close a telegraph key and obtained consistent tempo patterns. Fraisse (1946, 1956) found that imposed rhythms were assimilated more quickly as they approached the spontaneous rhythm of the individual. When an imposed rhythm does not coincide or approximate natural tempo, it has been found to cause fatigue (Sivadon, 1955) and lower work efficiency (Kupke, 1933; Harding, 1932).

As was mentioned briefly before, recent research has linked tempo with the physiology of the organism, and most specifically with the central nervous system. This area of research is reviewed thoroughly in Haley (1963). Suffice it to say that this physiological substrate provides a logical bridge between the work on temporal consistency in the voluntary behavior of animals and the previously cited studies on human motor activities.

Characteristically, the measure utilized in early studies involving operant techniques is rate of response. This is a gross measure, obtained by dividing the number of responses into the total time. Ferster and Skinner (1947) published a compendium of the effects of different schedules of reinforcement and of changes in schedule on this overall rate and found it highly consistent. However, it has been found susceptible to other independent variables. Sines and Keefe (1962) and Owens (1961) obtained reduced response rates under both tranquilizing and stimulant drugs, and Guttmann (1953) found that with the use of different concentrations of a sucrose solution the rate increased to a peak and then dipped down.

It wasn't until 1954 that Hurwitz studied more precise indicators of operant behavior. He investigated the changes in the variance of duration of

bar-press (D) during the phases of learning, stable performance, and extinction, and found that when animals were producing a learned response under conditions of regular reinforcement there was only minimal variance of D. Schaeffer and Steinhorst (1959) found D to vary among animals, but to be definitely characteristic within an individual subject, rarely varying more than one-tenth of a second under regular reinforcement. When the schedule was altered, an initial but temporary change appeared in D, a change which was masked in the measurements taken of rate. Schaeffer has also found D resistant to the effects of mild stress (1959) and to the lessening of the minimal D necessary for reinforcement (1960a), but susceptible to changes in the amount of force required to operate the bar (1960b). This last finding was corroborated by Hingtgen (1963) who placed rats on a force contingency schedule wherein the amount of force required to depress the bar was systematically varied. D decreased as the resistance of the bar increased and when the force required returned to the original amount so also did the D return to its original value.

Millenson and Hurwitz (1961) conducted a normative study on IRT and found the same relationships held for the variance of this variable as Hurwitz had established for D. However, the literature does not contain information regarding the influences of external variables.

Both D and IRT have been considered here because they are the component temporal parts of any operant response. Sidman (1960) in discussing operant conditioning mentioned the need for using more precise measures than rate, but the most complete and heuristic treatment of this problem and a possible solution are found in an article by Gilbert (1958).

Gilbert proposed that all behavior could be analyzed along seven basic quantitative dimensions. These are "fundamental" in that all other operations (e.g. rate of response) can be described with reference to them and they themselves are logically irreducible if measurement is to be meaningful. Three of these are spatial factors: intension, extension and direction. The other four are temporal: Latency, tempo, perseveration and duration. Latency is the time between the opportunity for an operant and its initial occurence. Tempo is the rate of a continuously ongoing operant, or, within a single response as the period of that response. Perseveration is the amount of time after latency spent at the task itself, excluding pauses. Duration is the total time from the initiation of the first to the completion of the last response, including both work and pause times. The effect of any independent variable may be investigated with respect to any or all of these dimensions. Using operant responses as a relatively uncomplicated example, he illustrates the use of the temporal dimensions of this paradigm by an experiment which in design essentially replicates that of Guttmann (1953). He used differential reinforcements of 4, 8, 16, and 32 percent solutions of sucrose. When the total response rate was considered, the results were the same, with output rising to a peak at 16% and then dipping at 32%. When each of the four temporal dimensions were analyzed (the spatial factors being held constant), it was found that each was a different function of the experimental variable. With regard to tempo as measured by the slope of the cumulative response curve, it was invariant throughout the range of sucrose concentration. He also found as had Skinner (1935), Young (1952), and Sidman and Stebbins (1954) that the slope of the cumulative curve was also the same even with the

approach to satiation. Computing Pearson r's, he correlated the tempos both within a day's running and from day to day. The values obtained centered about .98. From all of this evidence, Gilbert concludes that "when the animal works at a task, he works at a tempo that is characteristic of him and thatt is unaffected by the nature of his reinforcers or the extent of his deprivation. . . . There is great variability in tempo between animals and negligible variability within animals from time to time."

No attempt will be made here to review the clinical or experimental literature utilizing the drugs pipradrol and chlordiazepoxide. These drugs were chosen to represent the classes of stimulant and tranquilizing agents in which the primary site of action is the central nervous system and which produce only minimal peripheral and autonomic side effects. Therefore, only the main studies related to these characteristics of the drugs will be cited.

Meretran is the brand name of the drug pipradrol, produced by the William S. Merrell Company. It is a central nervous system stimulant of the analeptic group and differs from drugs of the amphetamine series in that it is not a sympathomimetic and hence does not directly influence the cardiovascular system (Berger, 1960). The primary site of action is in the subcortical regions of the brain. This has been established both from biochemical assays (Blohm, Summers, and Greensmith, 1954), and electroencephalographic tracings (Monroe et al., 1955; Himwixh, 1956; Himwich and Rinaldi, 1957; Sigg and Schneider, 1957). Its behavioral effects include a coordinated hyperactivity, particularly motor, in rats and mice (Brown and Werner, 1954). This eliminates any extrapyramidal involvement since the dysfunction of the latter would affect coordination in motor activity. Reviews of its clinical uses with mild

depression, geriatric patients, and obesity control can be found in Fabing (1955, 1957) and in Allin and Pogge (1956).

Librium is the trade name of chlordiazepoxide (originally methaminodiazepoxide HCl) which is manufactured by Hoffmann-LaRoche Incorporated. It is a psychosedative drug, chemically unrelated to any of the tranquilizer families but qualitatively it is similar in action to meprobamate. It also, like Meretran, affects primarily the subcortical regions of the brain, depressing rather than stimulating the arousal system (Randall, 1960). It decreases spontaneous motor activity in rats, and produces significant calming effects in animals made aggressive by septal lesions (Randall et al., 1960a). In this same extensive study, two other relevant facts are brought out. First, there is some extrapyramidal involvement with Librium since at high doses ataxia is present. Secondly, inter-subject reaction variability to a given dose is high. Clinically, Librium relieves anxiety and tension states and is effective in a wide variety of psychoneurotic and psychosomatic problems. Its muscle relaxant properties have led to its widespread use in internal and orthopedic medicine. It has become one of the most popular tools in present psychopharmacology research, paralleling the use of chlorpromazine (cf. Psychopharmacological Abstracts, 1964).

A final point to be covered here relates to both drugs and more generally to all combinations of pharmocological and behavioral research; it is the question of dosage. The amount of drug to be administered depends not only upon the species of the subject, the route of administration, the body weight, and the safety range, but also on the response variable which is being studied and the conditions under which the behavior involved is elicited. Using

Librium as an example, the dosage required to effect a change in a Sidman avoidance response was four times that needed for "calming" septally lesioned rats (Randall et al., 1960) or for eliminating fixations in an insoluble problem on a Lashley jumping stand (Feldman, 1962). In general, others (Brady and Ross, 1960) have shown that even so minor a detail as the schedule of reinforcement can alter the effectiveness of a specific dose. Thus, it seems necessary for the behavioral scientist who wishes to employ a drug as an independent variable to find a dose which is concomitant with all the major facets of his experimental design. The treatment of this problem was undertaken in a pilot study using the drugs and design pertinent to the present investigation. However, it possessed a rationale independent of the specifics involved. This purpose was to illustrate a possible method for the determination of "optimal dosages", these being ones which would effect a change in, but not preclude, the response under consideration. The procedure and results as they apply to Meretran and Librium for rats in a lever-pressing situation on a positive, continuous reinforcement schedule are included in this report as Appendix 1.

CHAPTER III

PROCEDURE

Subjects

Fifteen male albino rats of the Sprague-Dawley strain served as subjects for this experiment. The animals were maintained on a water deprivation schedule from the age of 100 days until the completion of experimentation. They were handled only during injection or in transfer from home cage to

TABLE I

RESPONSE RATES OF FIFTEEN SUBJECTS UNDER NORMAL CONDITIONS: BASED UPON TEN CONSECUTIVE DAYS OF PRELIMINARY TESTING

Animal Number	Mean	SD
#		
34	24.8	4.79
36	15.5	5.59
37	20.7	2.22
38	21.4	1.75
40	17.3	1.64
41	28.2	2.46
42	20.9	3.06
43	14.98	1.89
44	23.3	2.14
45	28.6	3.95
46	17.5	2.44
47	22.8	2.82
48	23.2	3.14
53	28.5	2.03
54	24.3	4.85

experimental chamber. The water schedule maintained allowed the animals 20

minutes free access to water daily; food was allotted ad lib and consisted of Rockland Rat Pellets. After the shaping of a stabilized bar-press response, the animals were divided into three groups on the basis of response rate. As mentioned earlier, response rate is an individually consistent measure and contains the also stable measures of D and IRT. Therefore, it was used as the distinguishing characteristic. On the basis of thirty, five-minute samples, taken over a period of ten consecutive days, the Mean Response Rate was computed for each animal (see Table 1). Because drugs may differentially affect animals with different individual rates of responding, the groups were matched according to rate of response before assignment to specific treatments. The

TABLE II

RESPONSE RATES AND VALUES OF t FOR THREE EXPERIMENTAL GROUPS

			Values of t		
GROUP	MEAN	SD	L	M	P
L	21.4	3.26		.808	
M	22.2	4.36			.270
P	21.9	4.31	.495		

groups each represent the total range of speed. The groups as established are given in Table 2. In this Table, Group L was assigned to the Librium treatment, Group M to Meretran, and Group P to the Placebo. These designations, L, M, P, will be used hereafter in all references to these groups.

Apparatus

A standard Stoelting Skinner box (#31292) was placed inside an insulated steel chest in order to create a soundproof experimental chamber. The chest was equipped with a device for circulating the air to eliminate any excessive changes in either temperature or atmospheric content during the testing session. The box itself was modified by the addition of a sliding shield (see Fig. 2) which could be manipulated from outside of the chamber by means of a chain and which, when in the down position, made the lever inaccessible to the animal. This was done for the purpose of preventing barpressing during the rest period when no reinforcement was present. This latter condition would simulate an extinction period which is known to affect the stability of response measures (Antonitis, 1951; Margulies, 1961; Millenson and Hurwitz, 1961). Two such chambers were constructed and were equated as closely as possible for all conditions, including the force required to close the microswitch attached to the lever. Based on findings such as those of Notterman (1959), Schaeffer (1960), and Hingtgen (1963), the levers were made as sensitive as possible and the animals were shaped and tested on the same bar at all times.

Three separate recording systems were employed. Electronic counters kept frequency tallies of both bar presses and reinforcements. The correspondence of these two counts provided a running check on the proper functioning of the boxes. A cumulative recorder, set at a speed of eleven feet per hour, presented a molar picture of each response session. The main source of data was an oscillographic recorder. The pen of this machine was connected to the lever so that it was activated by the closing of the microswitch and remained so until

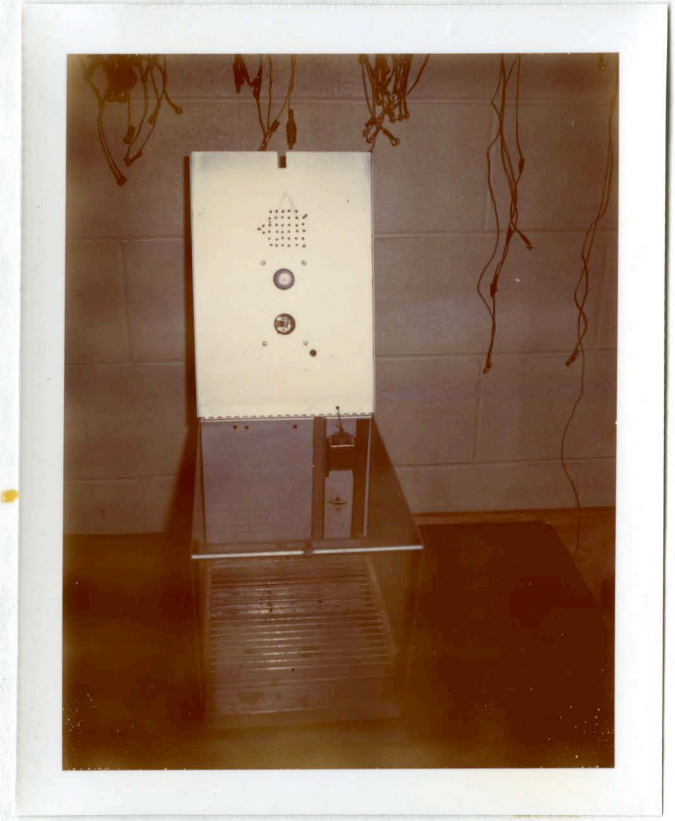

Fig. 2. Photograph of Skinner box showing sliding shield used to cover the lever during rest intervals.

the bar was released. It thus yielded a sequential graphic presentation of each D and IRT. Since the recording paper was marked off in millimeters and was fed through at set speeds, direct translation of the graphs into numerical time measures is possible, accurate to the nearest tenth of a second.

The drugs administered to the groups were Librium, and Meretran. They were chosen because both have their primary site of action in the central nervous system and both have minimal side effects in relation to the behavior involved in this design (see REVIEW OF LITERATURE). The pilot study (see Appendix 1) had established dosage levels of 6mg./Kg. for Meretran and 12 mg./Kg. for Librium. The Placebo employed was a .9% solution of sodium chloride in sterile distilled water (isotonic saline).

Drugs and Placebo were all administered via intraperitoneal injection, and all solutions were so concentrated as to remain within a range of .3 to .6 cubic centimeters in volume. The hypodermics employed were disposable tubercular syringes one cubic centimeter in capacity and graded in hundredths. The needle was 25-gauge and one inch in length.

Since Meretran is stable in solution, one preparation was made at the beginning of the testing and kept under refrigeration in dark bottles. The Librium powder, on the other hand, is unstable in solution and because of this the preparation was made daily at the beginning of each testing session.

Method

All animals were tested for a minimum of nine days. The sequence of these nine days for each group is presented as Table 3. In some cases the drug phase required more than five days of testing in order to obtain five consecutive days of behavior. This was true only in the Librium and is attributed

to the fluctuation of reaction to a given dosage (Randall et al., 1960). Only the five consecutive days are included in the analysis.

TABLE III

TESTING SCHEDULE FOR EXPERIMENTAL GROUPS

GROUP	Testing Day Number 1 2	3 4 5 6 7	8 9
L	No Injection	Librium 12 mg/Kg	No Injection
M	No Injection	Meretran 6 mg/Kg	No Injection
P	No Injection	Placebo .3/.6cc.	No Injection

Each testing session lasted for two hours beginning immediately after injection during the drug phase. During these two hours, eight five-minute periods of bar-pressing behavior were recorded with ten-minute rest intervals between them. During the rest periods, the house light in the chamber and all recording equipment were shut off and the bar was made inaccessible to the animal by lowering the shield. The animals adapted quickly to this schedule during the preliminary runs.

From the data recorded by the oscillograph five 3-minute time samples were extracted for each day. These samples were taken, where possible, from the middle of a session and from the first five sessions of a day. Since the purpose was to study behavior when ongoing and not its presence or absence, this schedule was flexible enough to allow for instances in which either other

minutes or other sessions had to be used. The product of this sampling was a selection of 15 minutes of representatively spaced behavior for each day.

Both the D and the IRT were subjected to the following statistical analyses. The mean and variance for each animal in each phase (pre-drug drug, and post-drug) were calculated and plotted and analyses of covariance (Freund et al., 1960) were performed to investigate between and within group effects.

CHAPTER IV

RESULTS

Due to the large number of observations, an IBM computer was used to calculate the raw score Sums and the Sum of Squares. These were used to group the data into three sections; pre-drug, drug, and post-drug. The Means and Variances of both the duration (D) of the bar-press and the inter-response time (IRT) were then calculated for the time samples of each of the nine testing days. The resulting values are summarized for each animal in Table 4.

The data was further evaluated using an analysis of covariance procedure. Analysis of covariance bombines the methods of analysis of variance and linear regression (Freund, 1960). This particular statistic was chosen because it was not possible to control for the interaction between the original score of the animal and the effect of the treatment. In analysis of covariance, this relationship is taken into consideration and the scores are weighted in terms of the regression of the animals original performance on their subsequent performance. Therefore, the primary emphasis is on the change in a measure rather than its absolute value.

All of the assumptions of analysis of variance must be met for the covariance model; normality of distribution, homogeneity of variance and additivity (linearity) of the cell entries. The first two of these were met by the selection of the sample population. It was found that in the case of the variances, the assumption of linearity and thus additivity was not

TABLE 4

VALUES OF D AND IRT FOR FIFTEEN ANIMALS UNDER THREE CONDITIONS

Animal and Group	IRT Pre M	IRT Pre SD	IRT Drug M	IRT Drug SD	IRT Post M	IRT Post SD	D Pre M	D Pre SD	D Drug M	D Drug SD	D Post M	D Post SD
L-1	1.72	.64	1.69	1.15	2.21	.86	.36	.13	.35	.14	.33	.14
L-2	3.01	1.18	3.67	2.69	3.41-	.78	.23	.11	.35	.29	.19	.04
L-3	2.09	1.02	2.49	1.19	2.56	1.33	.27	.10	.26	.13	.25	.12
L-4	2.52	.75	5.17	3.66	2.92	.41	.24	.63	.32	.18	.23	.16
L-5	1.54	.64	2.29	1.79	2.24	.65	.21	.10	.26	.17	.26	.08
M-1	1.99	.54	2.02	1.12	2.47	.82	.20	.02	.15	.09	.16	.04
M-2	3.08	1.49	3.06	1.02	2.99	1.15	.22	.09	.22	.64	.18	.19
M-3	2.36	2.00	2.38	1.46	2.61	.88	.24	.23	.18	.10	.12	.08
M-4	2.16	.99	2.14	1.27	2.16	1.35	.23	.21	.17	.02	.28	.09
M-5	2.33	1.44	1.98	1.80	1.78	.93	.21	.10	.24	.18	.18	.15
P-1	1.91	.72	1.94	.75	2.05	.18	.23	.19	.23	.18	.15	.10
P-2	2.64	1.31	2.45	1.62	2.36	1.08	.39	.11	.30	.13	.32	.11
P-3	1.98	1.87	1.93	.97	2.16	.58	.40	.19	.31	.22	.17	.03
P-4	2.47	1.27	2.59	1.24	2.22	1.14	.32	.16	.44	.22	.37	.36
P-5	1.77	1.17	2.30-	1.52	2.09	.85	.16	.03	.20	.32	.19	.09

borne out. Therefore a logarithmic transformation was applied which yielded a linear function. In all of the analyses using dispersion as a raw score, the cell entries were the common logarithms of the value raised by multiplying the original score by one thousand in order to eliminate negative characteristics. The logarithmic transformations of these scores are included as Appendix 2.

Although the observation were of unequal numbers, their large size (all over 100) and the lack of any systematic relation between treatment and size permitted the use of unweighted means in covariance computation. The first set of analyses compared the pre-drug condition with the treatment. The pre-drug condition was considered to be the control or normal condition. The results of the analyses for each of the four bar-press measures are presented in Tables 5, 6, 7, and 8. In all conditions the F ratio failed to reach significance ($p.=.05$); that is, there was no difference in the scores under any of the treatments between the normal and experimental conditions.

To determine the relationship between pre-drug and post-drug conditions, analyses of covariance were performed for each behavioral measure. The results of these analyses are found in Tables 9, 10, 11, and 12. Here again no significant differences were found between an animal's performance on days prior to and following the series of drug injections.

Based on the lack of differences between pre-drug and post-drug periods, the data were combined to form a "non-drug" control condition. The resulting means and standard deviations for all fifteen animals are presented in Table 13, days (2 - 5 - 2). The analyses performed for these conditions are presented in Tables 14 through 17. None of the F values obtained reached criterion.

Table 5

Analysis of Covariance of Mean Durations For Three Groups Under Pre-Drug And Drug Conditions

SSx	SSy	SP	SSy'	df	MSy'	F
.0160	.0407	.0212	.0218	2	.0109	3.4062
.0579	.0483	.0273	.0354	11	.0032	
.0739	.0890	.0485	.0572			

Table 6

Analysis of Covariance of Mean Inter-Response Times For Three Groups Under Pre-Drug And Drug Conditions

SSx	SSy	SP	SSy	df	MSy	F
.07	3.01	- .12	3.30	2	1.65	.395
4.37	8.75	4.26	4.60	11	.417	
4.44	11.76	4.14	7.90			

Table 7

Analysis of Covariance of Duration Variance (transformed to common Logarithms) For Three Groups Under Pre-Drug And Drug Conditions

SSx	SSy	SP	SS$\bar{y}$	df	MS$\bar{y}$	F
.551	.171	- .074	.161	2	.080	.314
7.683	2.940	- 1.015	2.806	11	.255	
8.234	3.111	- 1.089	2.967			

Table 8

Analysis of Covariance of Inter-Response Time Variance (transformed to Common Logarithms) For Three Groups Under Pre-Drug And Drug Conditions

SS_x	SS_y	SP	$SS_{\bar{y}}$	df	$MS_{\bar{y}}$	F
.360	.473	- .408	.542	2	.271	2.579
1.37	1.227	- .350	1.156	11	.105	
1.73	1.700	- .058	1.698			

Table 9

Analysis of Covariance of Mean Durations For Three Groups Under Pre-Drug And Post Drug Conditions

SSx	SSy	SP	SSy'	df	MSy'	F
.0160	.0132	.0115	.0057	2	.00285	.607
.0579	.0632	.0260	.0516	11	.00469	
.0739	.0764	.0375	.0573			

Table 10

Analysis of Covariance of Mean Inter-Response Times For Three Groups Under Pre-Drug And Post-Drug Conditions

SSx	SSy	SP	SSy	df	MSy	F
.318	.314	.027	.5084	2	.2542	1.44
5.220	2.227	- 4.667	- 1.9455	11	.1768	
5.540	2.54	- 4.694	- 1.4371			

Table 11

Analysis of Covariance of Duration Variance (transformed to common Logarithms) For Three Groups Under Pre-Drug And Post Drug Conditions

SSx	SSy	SP	SSy	df	MSy	F
24.069	.046	19.862	.167	2	.083	.326
3.773	4.013	- 14.353	2.802	11	.254	
27.842	4.059	5.509	2.969			

Table 12

Analysis of Covariance of Inter-Response Time Variance (transformed to Common Logarithms) For Three Groups Under Pre-Drug And Post Drug Conditions

SSx	SSy	SP	SSy	df	MSy	F
93.888	.411	.040	.930	2	.465	2.447
1.368	2.462	.709	2.095	11	.190	
95.256	2.873	.749	3.025			

The original means and SD's of each of the fifteen animals were plotted for the nine days together with the rate of bar-press and are included as Appendix 3. The non-drug days are plotted first and then the drug days. These figures show that the changes which occur in the measures taken do so on non-drug as well as drug days. It is also interesting to note the variances seem to be a more stable measure than the means and show more of a tendency to differ from non-drug to drug conditions.

The inclusion of rate of response in these graphs is strictly for analysis of changes from day to day. It was impossible to treat these statistically since, by a priori methodology, there was no measure of total time in the bar-pressing box, only the total actual pressing time. Therefore, they are not comparable to the rates found in the literature, nor even to the rates obtained during the preliminary testing. What they do is present a means of relating duration and inter-response time by combining them with reference to a constant time factor.

Table 13

Values of Duration of Response (D) and Inter-Response Time (IRT) for Fifteen Animals under non-Drug and under Drug Conditions

Animal Number	IRT				D			
	NON-DRUG		DRUG		NON-DRUG		DRUG	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
L-1	1.99	.82	1.69	1.15	.34	.17	.35	.14
L-2	3.20	1.76	3.67	2.69	.21	.09	.35	.29
L-3	2.29	1.29	2.49	1.19	.26	.10	.26	.13
L-4	2.77	1.00	5.17	3.66	.23	.13	.32	.18
L-5	1.83	.74	2.29	1.79	.22	.09	.26	.17
M-1	2.35	.77	2.02	1.12	.17	.08	.15	.09
M-2	3.03	1.36	3.06	1.02	.20	.15	.22	.14
M-3	1.81	1.76	2.38	1.46	.13	.19	.18	.10
M-4	2.16	.94	2.14	1.27	.25	.17	.17	.02
M-5	2.06	1.26	1.98	1.80	.19	.13	.24	.18
P-1	1.98	.63	1.94	.75	.19	.16	.23	.18
P-2	2.48	1.21	2.45	1.62	.34	.14	.30	.13
P-3	2.06	.54	1.93	.97	.29	.19	.31	.22
P-4	2.37	1.23	2.59	1.24	.34	.26	.44	.22
P-5	1.94	.79	2.30	1.52	.17	.11	.20	.32

Table 14

Analysis of Covariance of Mean Durations For Three Groups Under Non-Drug And Drug Conditions

SSx	SSy	SP	SS$\bar{y}$	df	MS$\bar{y}$	F
.0173	.0407	.0256	.0117	2	.0058	2.14
.0453	.0483	.0289	.0299	11	.0027	
.0626	.0890	.0545	.0416			

Table 15

Analysis of Covariance of Mean Inter-Response Times
For Three Groups Under Non-Drug And Drug Conditions

SS_x	SS_y	SP	$SS_{\bar{y}}$	df	$MS_{\bar{y}}$	F
.1565	2.0673	.5225	.9062	2	.4531	1.08
2.3690	8.7643	3.1466	4.5849	11	.4168	
2.5255	10.8216	3.6691	5.4911	13		

Table 16

Analysis of Covariance of Duration Variance (transformed to common Logarithms) For Three Groups Under Non-Drug And Drug Conditions

SS_x	SS_y	SP	$SS_{\bar{y}}$	df	$MS_{\bar{y}}$	F
.252	.169	.091	.171	2	.085	.318
.819	2.948	- .051	2.945	11	.267	
1.071	3.117	- .041	3.116			

Table 17

Analysis of Covariance of Inter-Response Time Variance (transformed to common Logarithms) For Three Groups Under Non-Drug And Drug Conditions

SSx	SSy	SP	SS$\hat{y}$	df	MS$\hat{y}$	F
.090	.474	.064	.443	2	.221	2.145
1.700	1.291	.503	1.143	11	.103	
1.790	1.765	.567	1.586			

CHAPTER V

DISCUSSION OF RESULTS

The results of this experiment are clear cut: they present no evidence that any of the conditions employed produced any significant change in the four measures taken of the bar-press. All comparisons of groups produced only changes which could be explained on the basis of chance. It must be remembered, however, that the variable being investigated, tempo, is only part of the total behavior of the animal. The same observational changes which were noted in the pilot study (Appendix 1) were present in these animals. Contrasts such as this are support for the resiliency of these measures which has been reported in the literature (Hurwitz, 1954; Schaeffer and Steinhorst, 1959; Schaeffer, 1959, 1960a; Millenson and Hurwitz, 1961).

This experiment can be considered from three points of view. The first, and most restricted, is that mentioned above; that is a confirmation of earlier findings on operationally defined measures of a particular type of operant. The second is as a corroboration and instance of the type of analysis proposed by Gilbert (1958) which was described in detail earlier (see Review of Literature). The very design of the experiment was such that every conceivable control was employed to insure that the drugs would be the only relevant independent variable. The sampling procedure employed in the analysis of the data partialled all effects of the drug on bar-pressing except those which directly concerned "tempo". If the totality of the information yielded by an animal's performance record were to have been analyzed according to each of the other six dimensions, the results might show that the main effects of these drugs were in one or more of them. For example Sines and Keefe (1961) mention

that amphetamine caused sporadic bursts of pressing. This effect would probably fall along the dimension of perserveration. In some of the animals in the present experiment, their responses did not begin until well into the first minute of a period (latency) or dropped off after three or four minutes (duration). These are but a few of the possible types of information Gilbert's analysis could yield.

The third aspect under which these results might be considered is within the framework of the concept of tempo as it is more generally defined in relation to human activity. It is interesting to note that in Cabanski's study with human subjects and the present study with animals parallel results are obtained, a fact which may be connected to the possibility of a ne neurophysiological substrate. Yet, if this is so, the resistance of tempo to physiological variations and influences is all the more unusual. This same result is being obtained in a current investigation being conducted at Loyola University (personal communication, H. J. A. Rimoldi) wherein a variety of drugs were administered to human subjects over a period of time in a double-blind technique. A battery of tests was administered including some of those used by Allport and Vernon (1933) and later by Rimoldi (1951). A tempo factor has been extracted which thus far has proved resistant to all of the drugs with the exception of atropine. Although these are only preliminary, the similarity of results is noteworthy.

It seems that the concept of tempo is a common element of both human and animal behavior which in both cases is extremely basic and durable. Future research may lead to a more definitive localization of temporal organization or it may conclude that it is a variable only logically distinct from the behavior

involved, a gestalt in which that which is present in the whole is not present in any or all its parts.

It is the opinion of this author, animal research has much to offer in the discovery of the nature and characteristics of tempo, but with a reservation.

The role of animal studies in the study of human tempo is like that of neurophysiological analyses of the brain in the investigation of human intellect; they are definitely helpful and at times necessary for guiding the paths of research but no generalizations can be made directly from one to the other. The real value of a study such as the one presented here lies, then, in its intrinsic information on one relatively uncomplicated animal activity and in its directional function for future research both on the animal and human level.

CHAPTER VI

SUMMARY

The concept of tempo was operationally defined with respect to four measures of bar-pressing behavior, and was tested for the possible effects of tranquilizing and/or stimulating psychoactive drugs in the following manner.

Fifteen male albino rats were subjected to nine days of testing under conditions of pre-drug (days 1 and 2), drug (days 3 through 7), and post-drug (days 8 and 9). Measurements of the mean and variance were taken for both the duration of the bar-press and the inter-response time. These four values were analyzed in an analysis of covariance technique for comparisons of pre-drug with drug, pre-drug with post-drug, and total non-drug with drug conditions. None of the F ratios obtained was significant at the alpha criterion level of $p = .05$.

The results were discussed with respect not only to their intrinsic informational value at the operational level, but in connection with a model for the analysis of behavior in general. They were also related to the results of human tempo studies noting the similarities and parallels, but also taking into account the necessity for caution in the realm of generalization.

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APPENDIX 1

PILOT STUDY ON DRUG DOSAGE LEVELS : METHOD AND RESULTS

METHOD

A. Subjects: Thirty male albino rats, all one hundred days old at the beginning of the experiment and all experimentally naive, served as subjects. The weight range of the animals was from 250 to 370 grams at the time of injection. The animals used for the measurement of bar-press were previously trained and brought to a level of approximately 20 responses per minute before being injected. In the case of a second injection, the following time schedule was followed. When the second injection of an animal involved a placebo, it was given on the day immediately following the drug injection. When the second injection was another drug injection, a period of at least ten days was allowed to elapse in order to avoid any cumulative effects.

B. Apparatus: Both spontaneous general activity and the learned bar-press response were used as indicators of the effectiveness of the drugs.

The apparatus employed for observation of general activity level was a modified version of a Hebb-Williams open-field maze. In a quiet, dimly illuminated room, an area three feet square was laid out in 4½ inch squares on brown paper and covered with a sheet of hard, clear plastic, yielding a washable surface with standardized markings. This area was enclosed by walls, constructed of pegboard, approximately 15 inches in height.

Measurements of bar-press were taken by means of a standard Stoelting Company "Skinner Box" with control panel (Catalog # 31292). This model delivers a water reinforcement.

The drugs employed were:

Piperidylbenzydrol (Meretran) produced by Merrell Laboratories, Cincinnatti, Ohio

Chlordiazepoxide - formerly methaminodiazepoxide - (Librium), produced by Hoffman-LaRoche Laboratories, Nutley, N. J.

Both drugs come in powder form and were dissolved in a solution of physiologic saline (isotonic saline). The Meretran solution is stable. Therefore, it was prepared at one time in a concentration of 1 mg. of drug per 10cc. of physiologic saline and was stored in dark bottles under refrigeration. Since Librium is unstable in solution, the preparation was freshly made at the time of each injection. For all dosage levels, in the case of Librium, the concentration of drug in saline was adjusted in such a way that the volume of the injections could remain within the range of .3 cc. to .6 cc. notwithstanding the dosage level. This volume has been found optimal for this particular species of animal (personal communication, Dr. C. Proctor, Stritch School of Medicine, Chicago). The injections were made intraperitoneally with a 1 cc. capacity Benton-Dickinson Tubercular Syringe calibrated in gradations of .01 cc. and utilizing a 25 gauge, 1 inch needle.

C. Procedure: Starting with an initial dosage equivalent to one-fourth of the established LD_{50} (as per recommendation of Dr. C. Proctor, Stritch School of Medecine), injections were systematically in accordance with observations of the animals in an open field maze. Based on an evaluation of the maze activity, an abritrary maximum dosage was established for use in studying the bar-press response. Decreasing levels of drug were then employed in the bar-press situation and the presence of the response was recorded for three five-minute periods interspersed with 10 minute rest intervals. This procedure was continued until a tentative operant result was obtained. Then, when a suitable level was considered to have been reached, five additional animals were then tested at the same level with the condition that for the dosage to be accepted as final, all five animals must respond.

Apart from this over-all design, there were some methodological differences in the testing of the two drugs. In the investigation of piperidylbenzydrol, placebo injections were employed in order to differentiate the effects of the drug from effects due to the injection per se. In the study of chlordiazopoxide, this was not considered necessary both because of the previous results obtained and because of the normally high level of activity of these animals.

RESULTS AND DISCUSSION

The following is a summary of the characteristics of behavior which were consistently evidenced by the animals, and the dosage levels finally approved.

A. Piperidylbenzydrol (Meretran)

The general increase of alterness to external stimuli brought on by the drug produced dissimilar reaction patterns. In some, the reaction to stimuli was a decrease in fear responses as opposed to responses under placebo, while in others these fear responses (freezing, crouching) were intensified. In a great number of cases it was found that the animal would establish himself in one corner of the open field and very seldom move from there, but this was not universal, nor was it characteristic of any particular dosage levels.

Cleaning Behavior was notably inhibited or completed absent under the higher levels of drug. This absence was not characteristic of behavior under placebo injections.

With respect to motor responses, there was found to be a spasticity in the hind legs which resulted in a hopping type of walk. The head activity was highly increased, directly relative to the amount of drug injected. This activity was characterized by a bobbing movement and was accompained by intense sniffing behavior.

The peak effects of the drug were evidenced in the period which extended from fifteen to fifty minutes after injection. The intensity of effect did not significantly increase above a level of 12 mg./kg. The effect of higher dosage levels seemed to be a prolongation of the period of effectiveness.

In reference to the retention of ability to produce the bar-press response the maximum dosage was found to be 6 mg./Kg. Above this level, the animals tend to become hyperactive and seem unable to complete the activity cycle of press-approach-consummation.

B. Chlordiazepoxide (Librium)

Gross behavioral effects included general loss of tension in the body, including the tail. This was directly relative to the dosage level of the drug, culminating in the higher levels in the adoption of a prone, immobile position, and a lack of response to any manipulation of position. The particular test of this effect was the placing of the animal on its side or back. Under the higher levels of drug, the animal would remain there, while under lower levels he would slowly right himself. Under normal conditions, it is impossible even to turn these animals to either of the above mentioned positions.

At all levels of the drug, there is a decrease in alertness and in susceptibility to external stimli, and the animals become much more amenable to handling. Chewing behavior is also characteristically noted at all levels of drug injection. The animals attempt to masticate any object which is available, even, in some cases, defecations. In the absence of any object, the chewing responses still continue.

With respect to motor responses, there is a loss of control of the hind legs, causing the animal to fall during walking. This effect on the hind legs is directly proportional to the level of dosage. At the optimal level reached, there is evidence of inhibition in the use of the hind legs, but it is not severe enough to interfere with the desired behavior; i.e., it does not preclude the bar-press response cycle.

The observable reaction to the drug takes place within the first five minutes after injection, and continues for at least one hour. As with the stimulant, it was found that the higher levels seem to prolong the effects rather than to intensify them beyond a particular level.

In reference to the retention of ability to produce the bar-press response, a dosage of 12 mg./Kg. was found to be maximal. Above this level, the animals tended to lie in front of the dipper and fail to respond, even though they would consume any reinforcement which was manually provided by the experimenter.

Comparison of the optimal dosage levels reached in this study with the results available in the literature on these drugs showed that those obtained in the present experiment were considerably lower that the dosages reported as "effective dosage levels." These results would seem to recommend that the levels of any psychotropic agent being used as an independent variable in experimentation involving operant behavior be operationally defined for the species and the type of response required.

SUMMARY

Male albino rats were injected intraperitoneally with various levels of two psychotropic agents, piperidylbenzydrol and chlordiazepoxide, in order to experimentally establish a dosage level suitable for use in a proposed investigation involving operant techniques, specifically the use of the bar-press response.

The optimal dosage levels were found to be 6 mg./Kg. for piperidylbenzydrol and 12 mg./Kg. for chlordiazepoxide. These levels were standardized on additional groups of experimental animals of the same age level as an additional control. The recommendation was made that this type of pilot study is a necessary adjunct to all investigations involving the use of psychotropic agents in connection with operant conditioning techniques.

APPENDIX 2

LOGARITHMIC TRANSFORMATIONS OF VARIANCE SCORES
(Original Score Multiplied by 1,000)

Animal Number	Experimental Condition			
	Pre-Drug	Drug	Post-Drug	Non-Drug
L-1 (IRT)	2.615	3.124	2.872	2.833
(D)	1.230	1.322	1.321	1.447
L-2 (IRT)	3.419	3.858	2.780	3.491
(D)	1.079	1.924	0.301	0.954
L-3 (IRT)	3.020	3.152	3.255	3.220
(D)	1.000	1.230	1.176	1.041
L-4 (IRT)	2.748	4.126	2.233	3.004
(D)	0.602	1.491	1.398	1.230
L-5 (IRT)	2.607	3.507	2.622	2.740
(D)	1.000	1.462	0.778	0.903
M-1 (IRT)	2.462	3.100	2.832	2.771
(D)	0.699	0.903	0.301	0.845
M-2 (IRT)	3.349	3.021	3.121	3.265
(D)	0.954	2.615	1.544	1.324
M-3 (IRT)	3.601	3.329	2.895	3.490
(D)	1.748	1.041	0.845	1.556
M-4 (IRT)	2.991	3.210	3.265	2.949
(D)	1.663	0.699	0.903	1.477
M-5 (IRT)	3.320	3.508	2.939	3.204
(D)	1.176	1.518	1.362	1.255
P-1 (IRT)	2.712	2.747	1.491	2.602
(D)	1.580	1.531	1.045	1.398
P-2 (IRT)	3.235	3.417	3.068	3.164
(D)	1.114	1.230	1.079	1.301
P-3 (IRT)	3.545	2.976	2.521	2.462
(D)	1.556	1.613	0.000	1.556
P-4 (IRT)	3.207	3.187	3.116	3.716
(D)	1.398	1.690	2.124	1.826
P-5 (IRT)	3.138	3.364	2.854	2.792
(D)	0.000	2.009	0.903	1.079

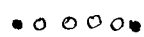
APPENDIX 3

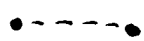
This section contains the graphical representation of the Mean Durations and Inter-Response Times and their respective variances, and the Response Rate (per minute) for fifteen animals on nine days of testing.

The following Legend will be utilized throughout all of the figures.

Response Rate 

Mean Duration 

Mean Inter-Response Time 

Duration Variance 

Inter-Response Time Variance

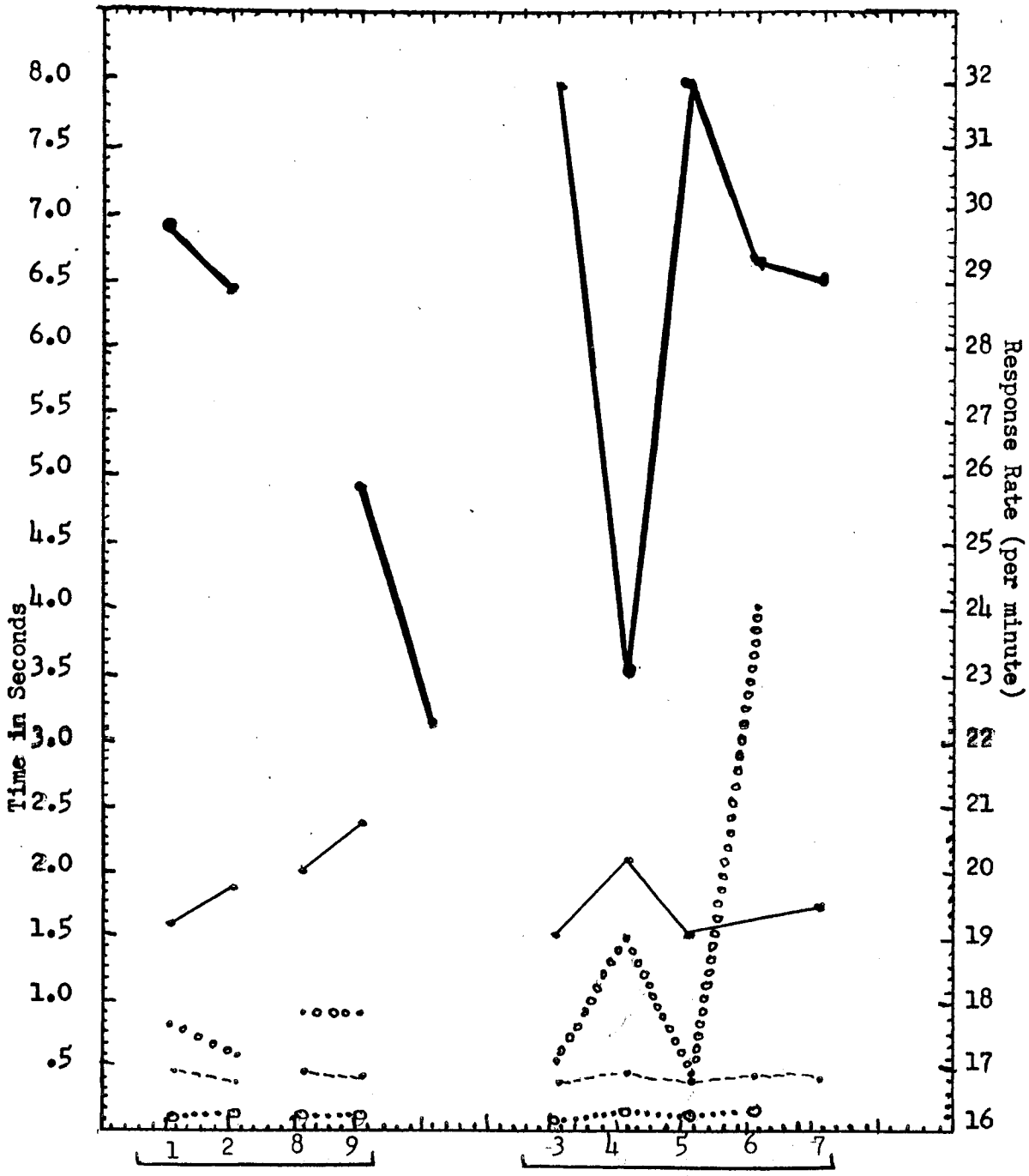


Figure 3. Values for Animal L-1.

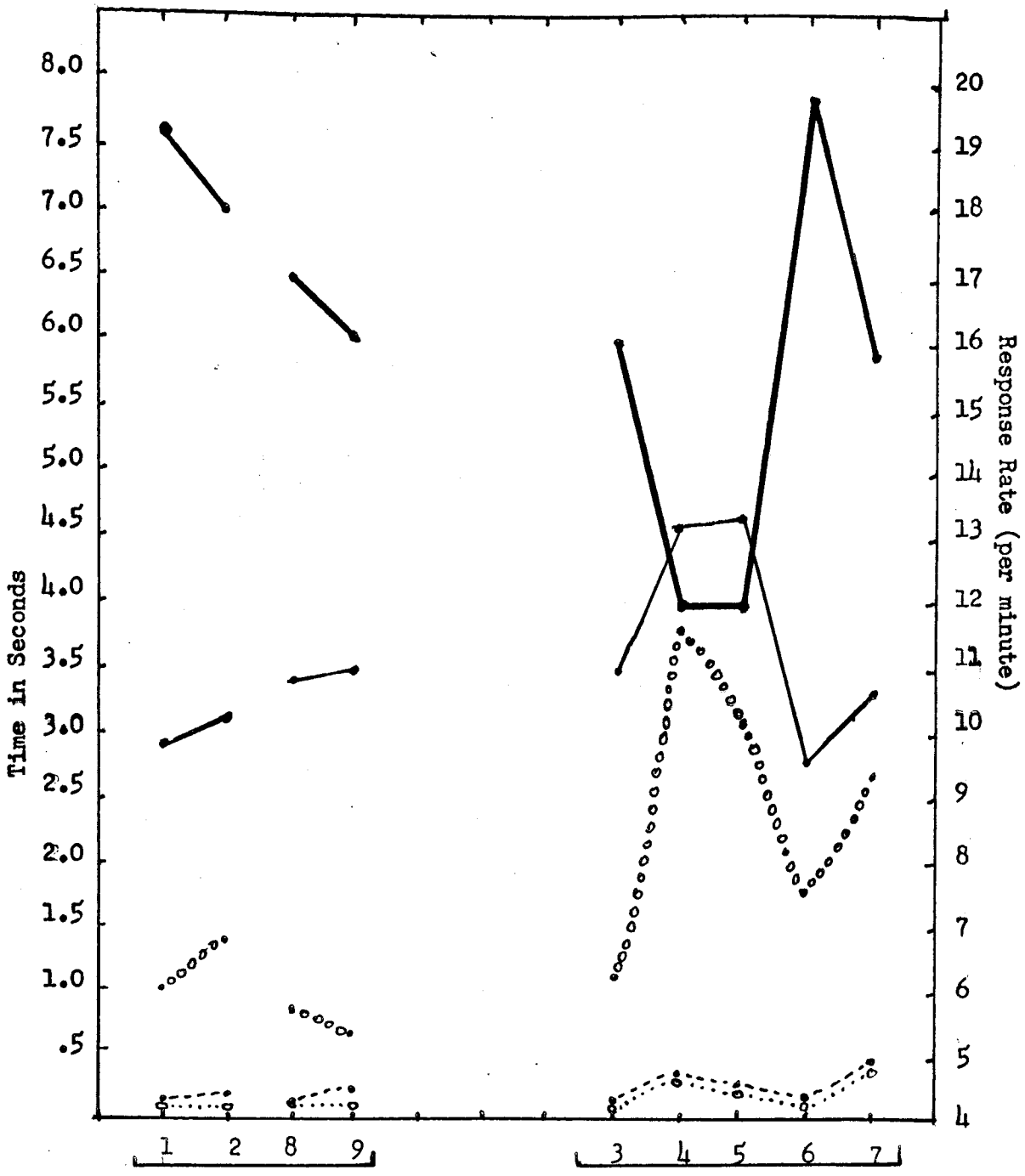


Figure 4. Values of Animal L-2

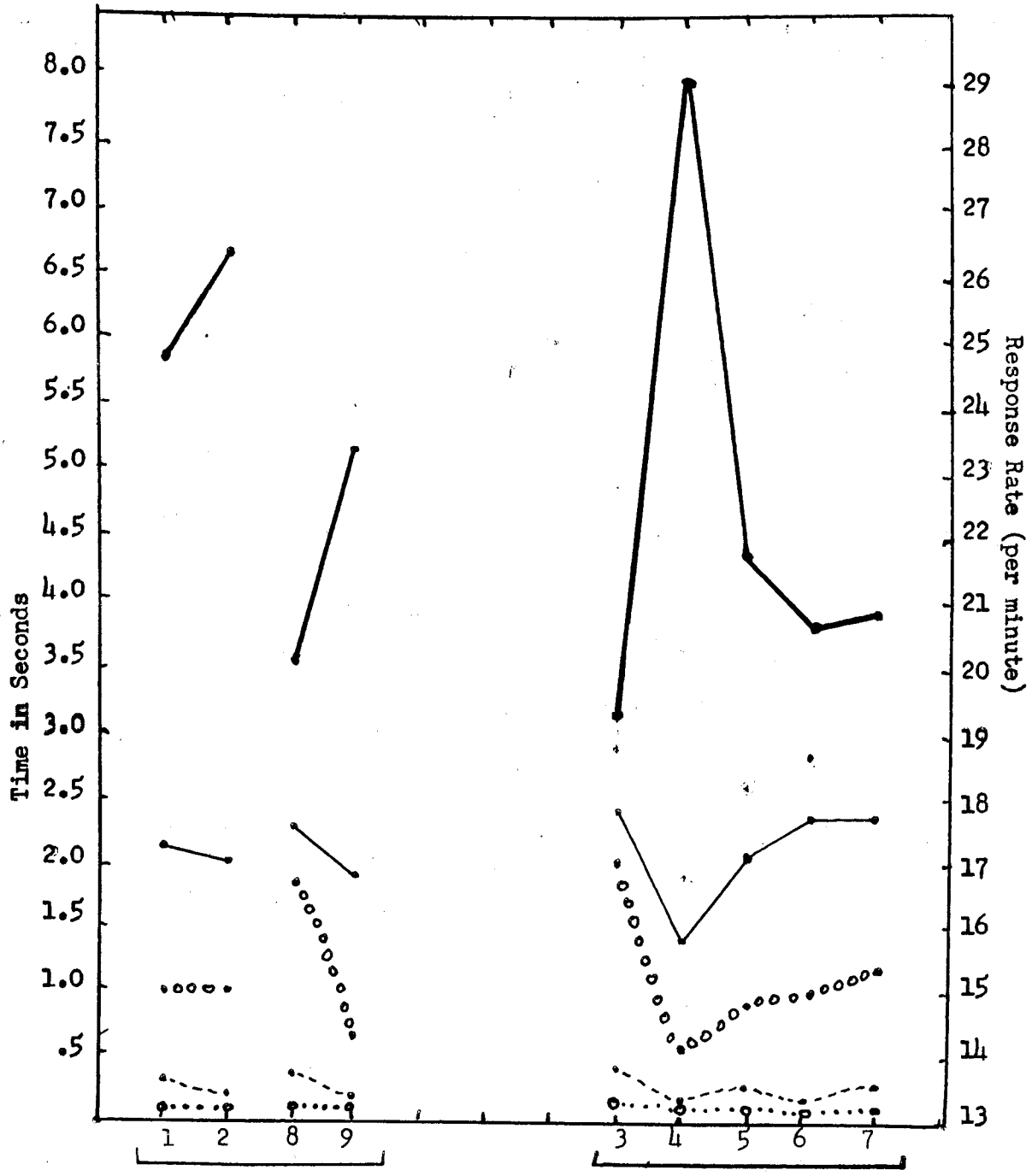


Figure 5. Values for Animal L-3.

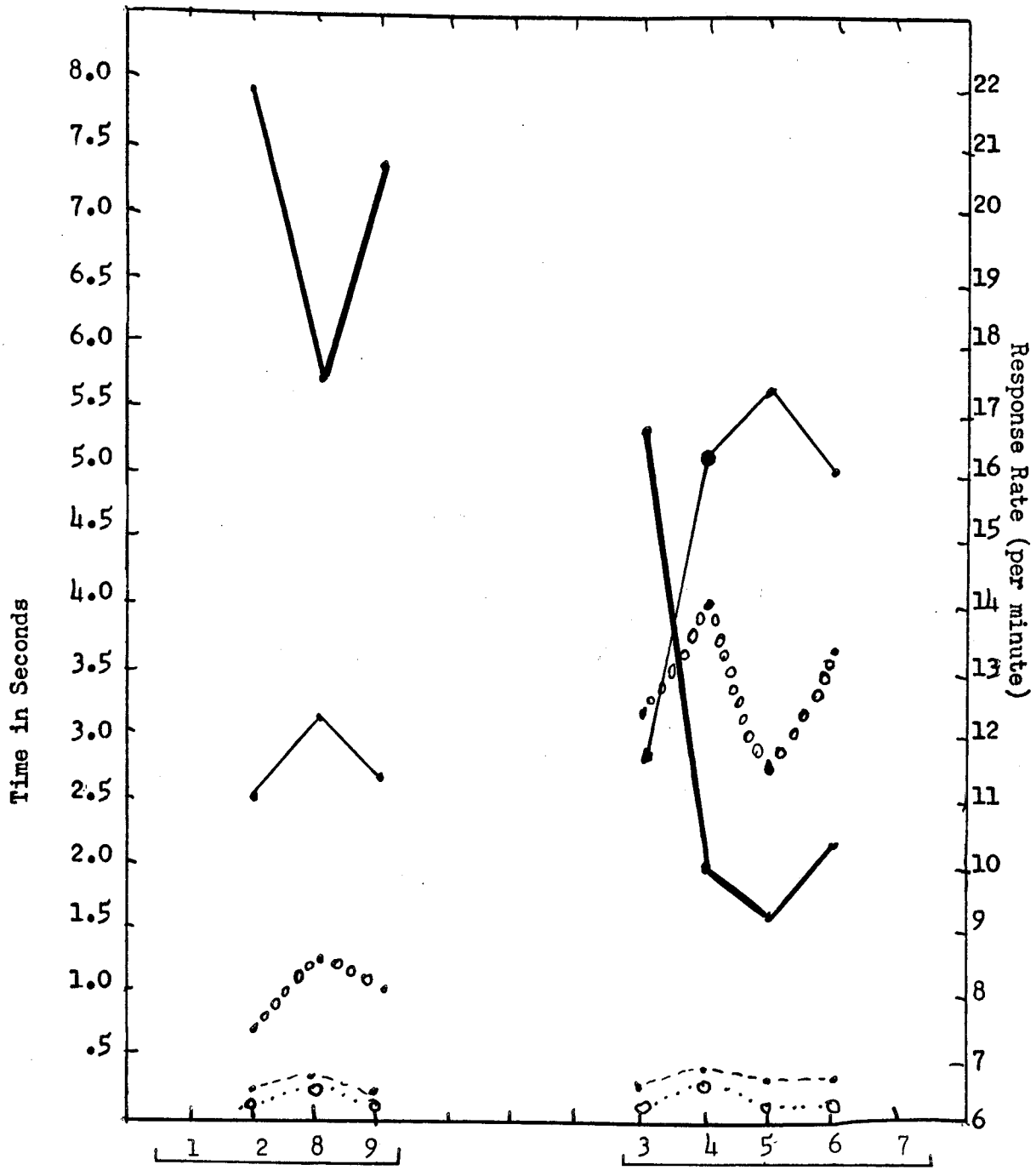


Figure 6. Vaules for Animal L-4.

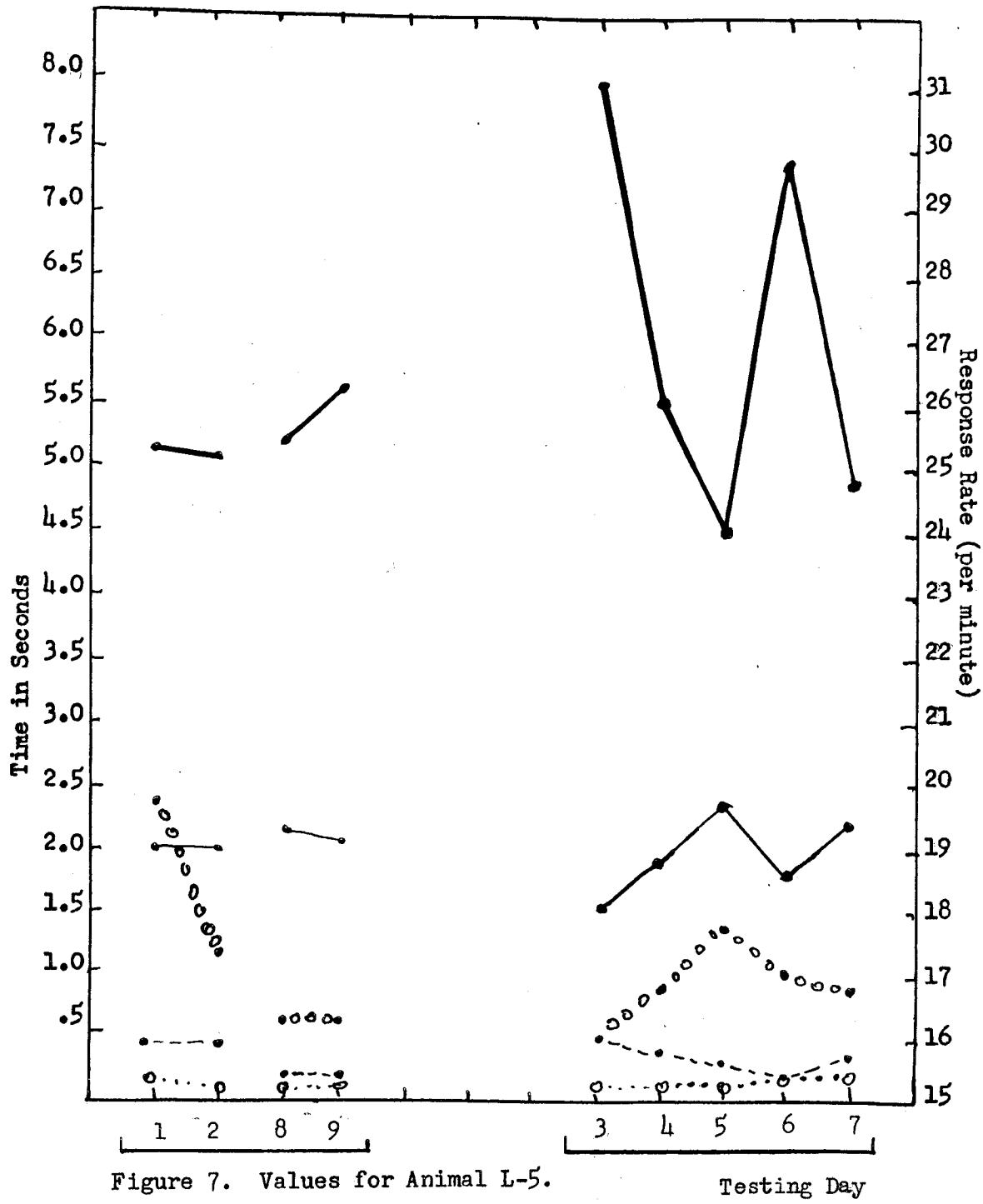


Figure 7. Values for Animal L-5.

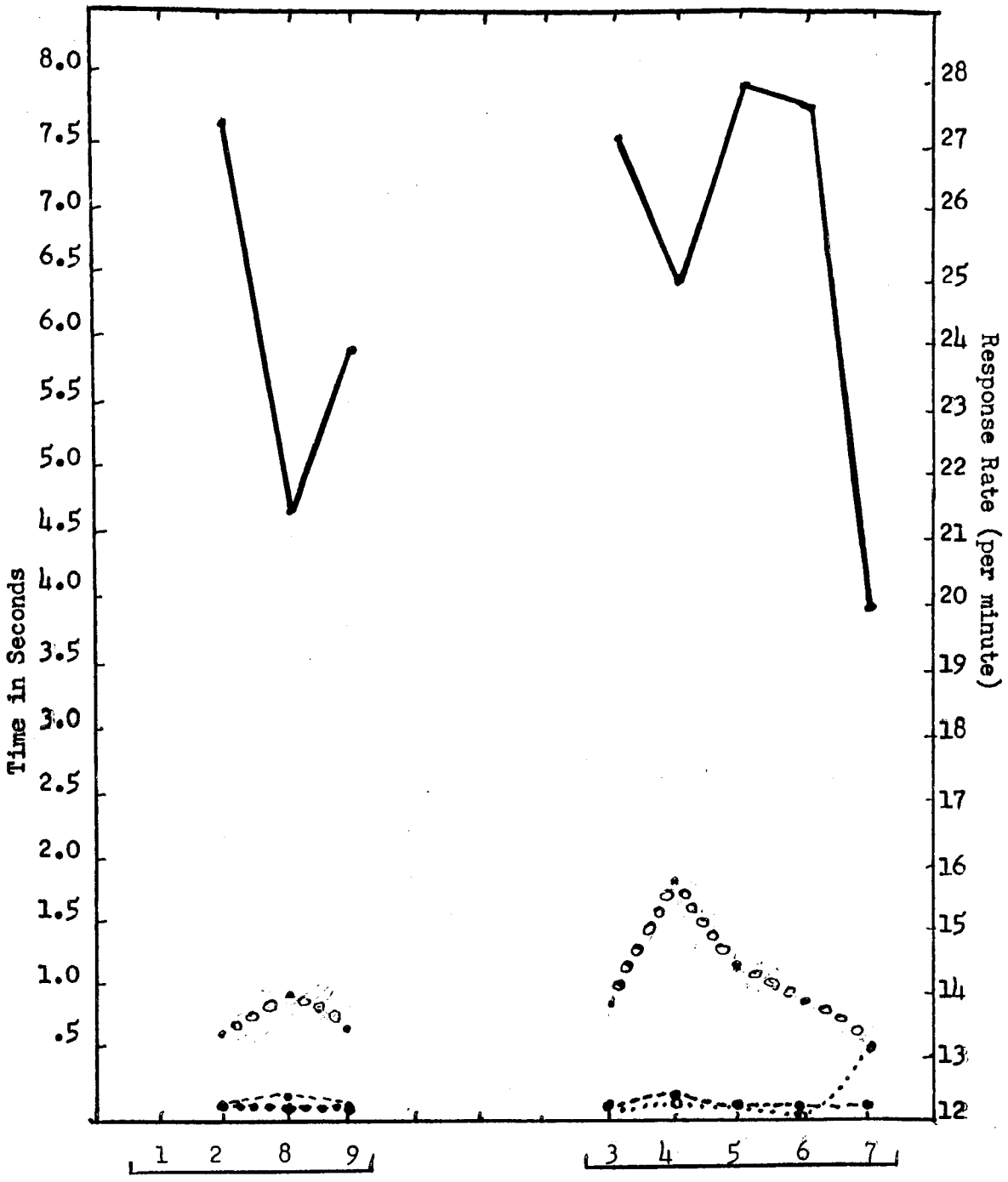


Figure 8. Values for Animal M-1.

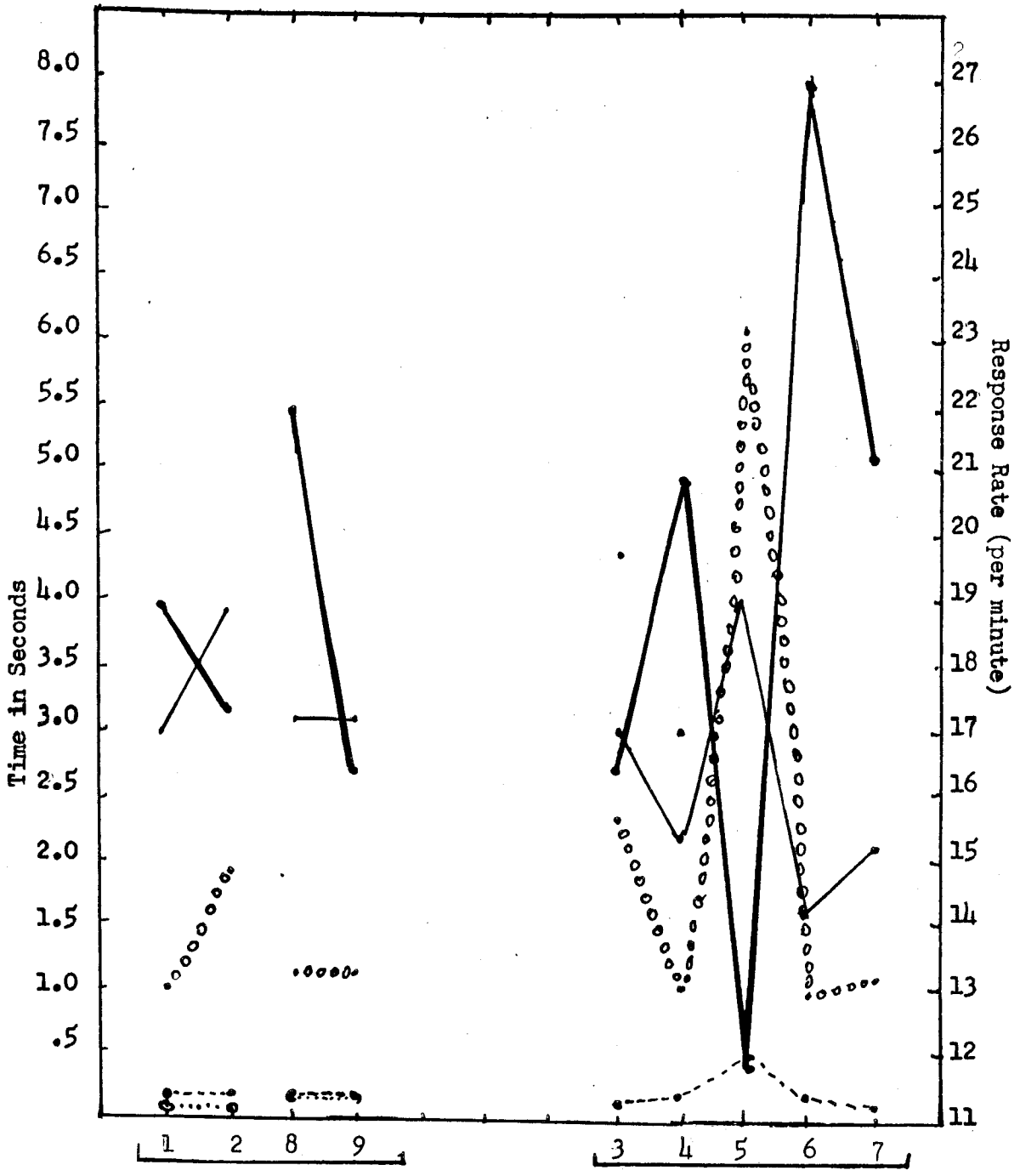


Figure 9. Values for Animal M-2.

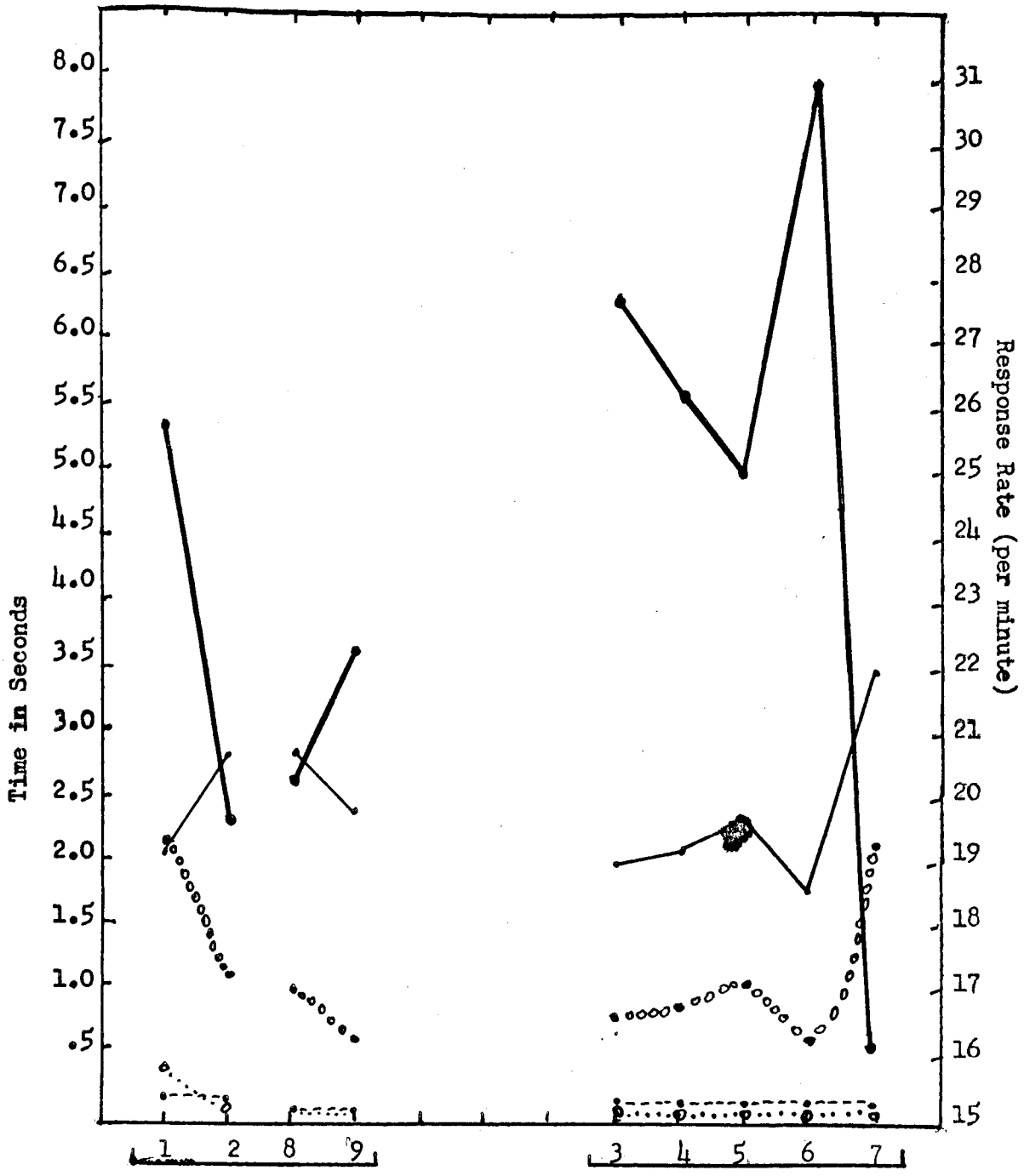


Figure 10. Values for Animal M-3

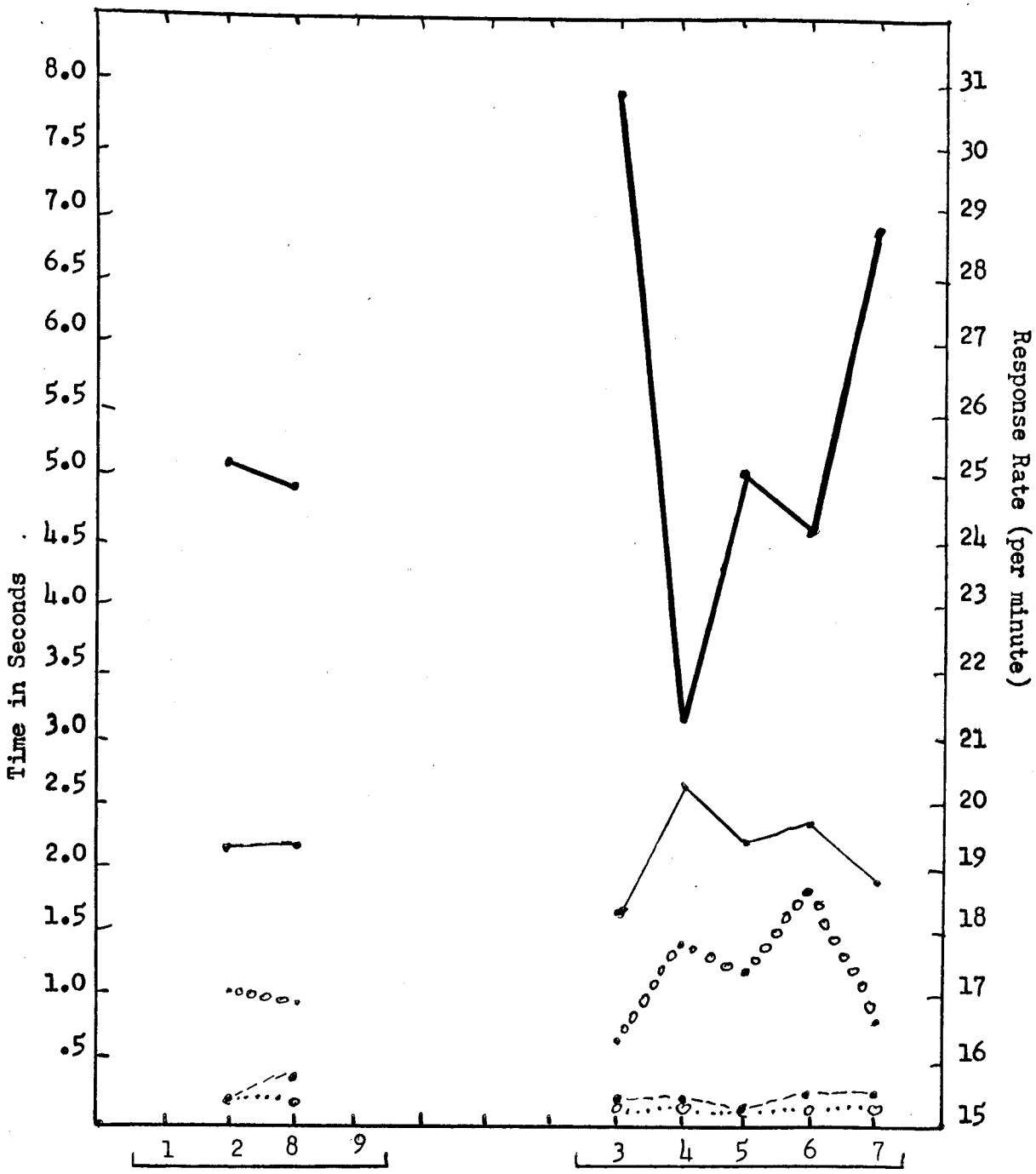


Figure 11. Values for Animal M-4.

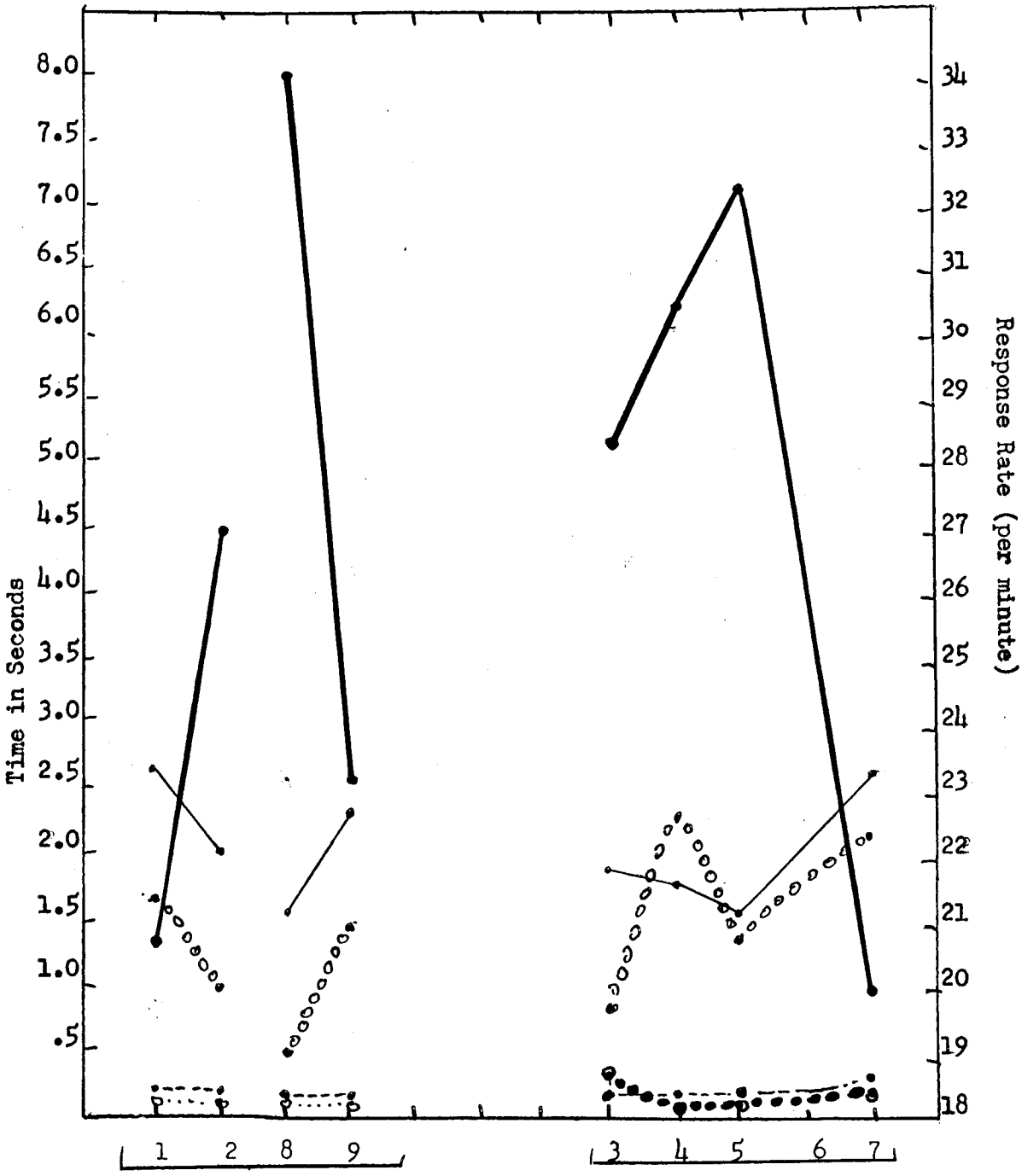


Figure 12. Values for Animal M-5.

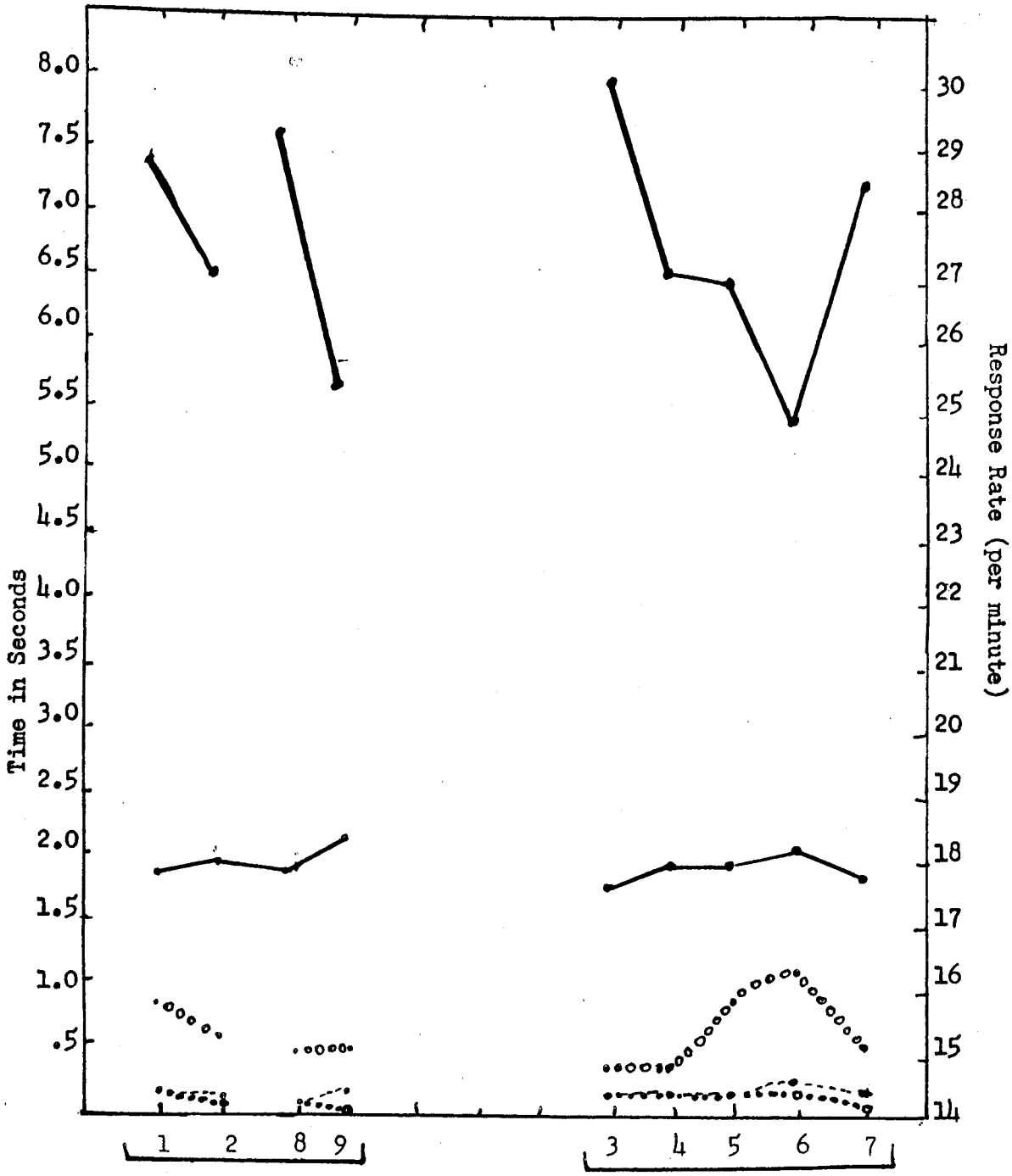


Figure 13. Values for Animal P-1.

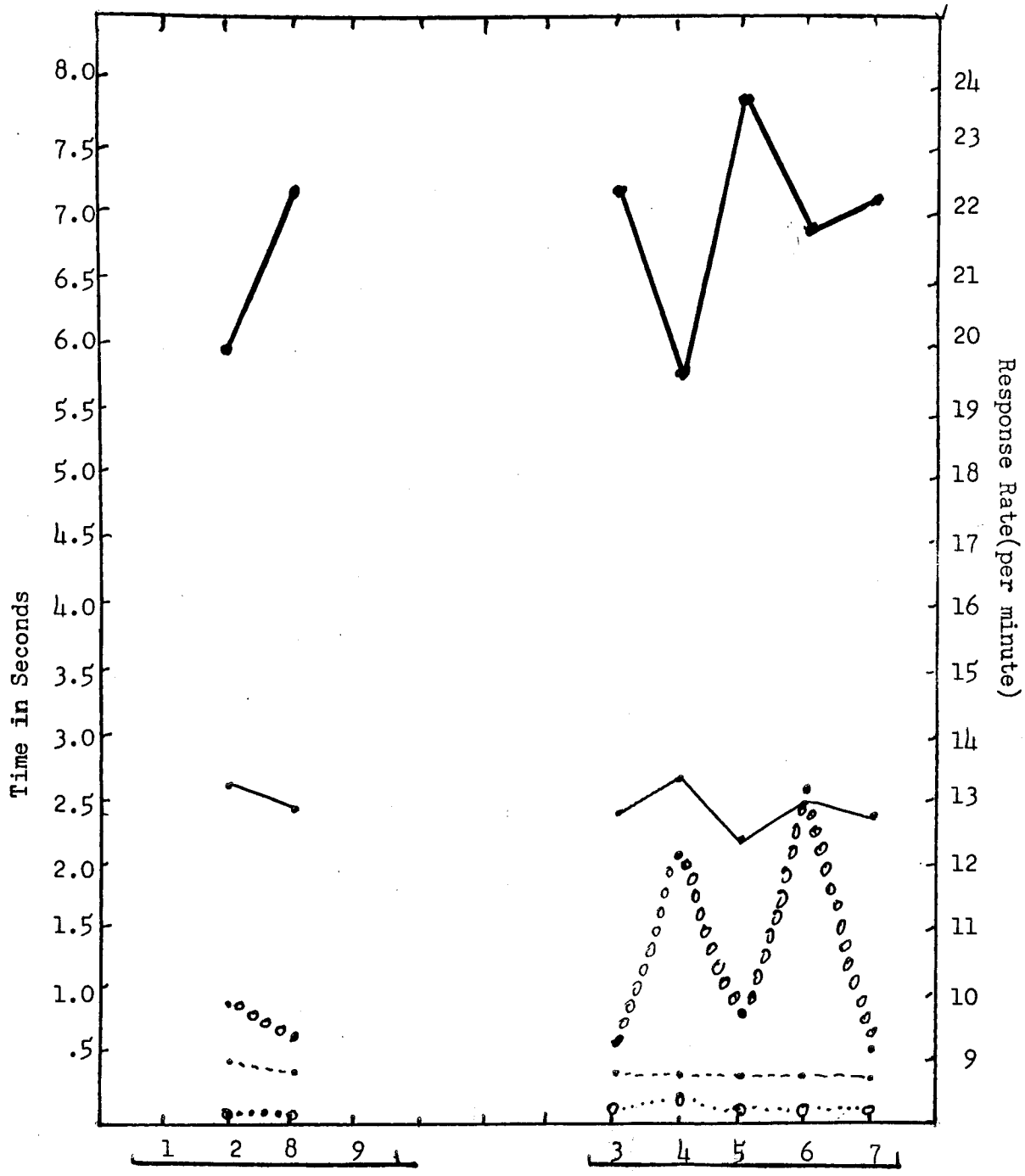


Figure 14. Values for Animal P-2.

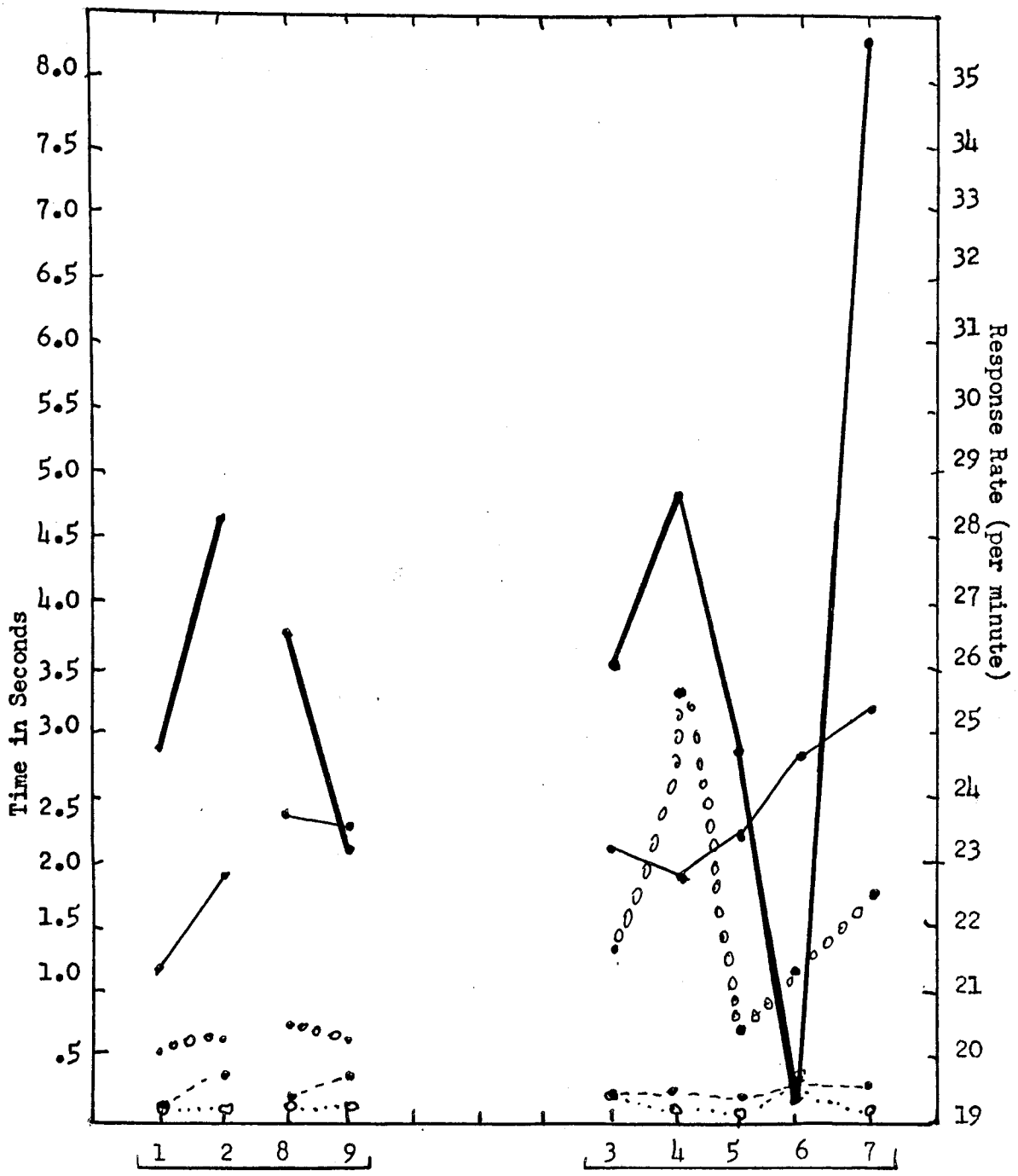


Figure 15. Values for Animal P-3.

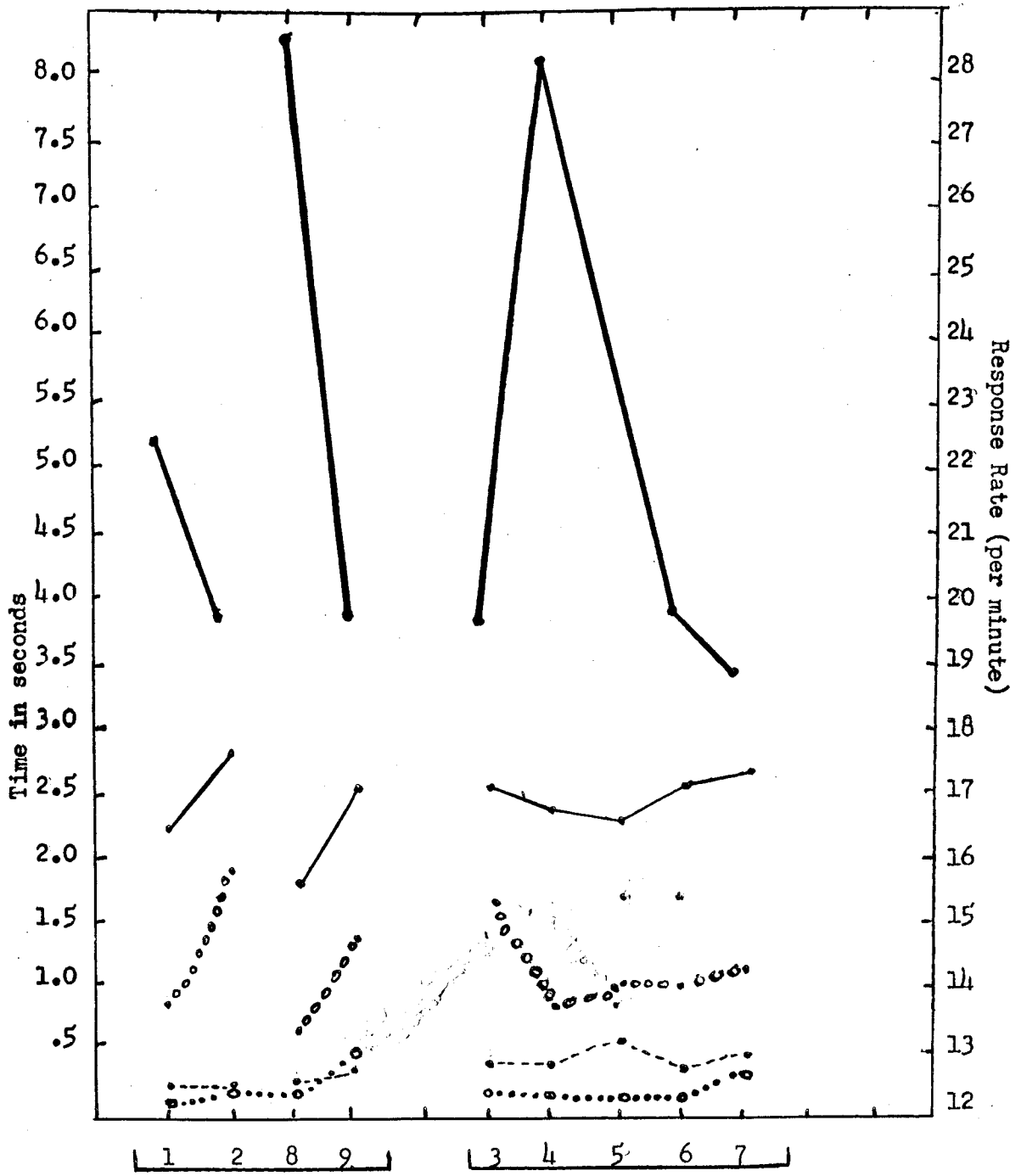


Figure 16. Values for Animal P-4.

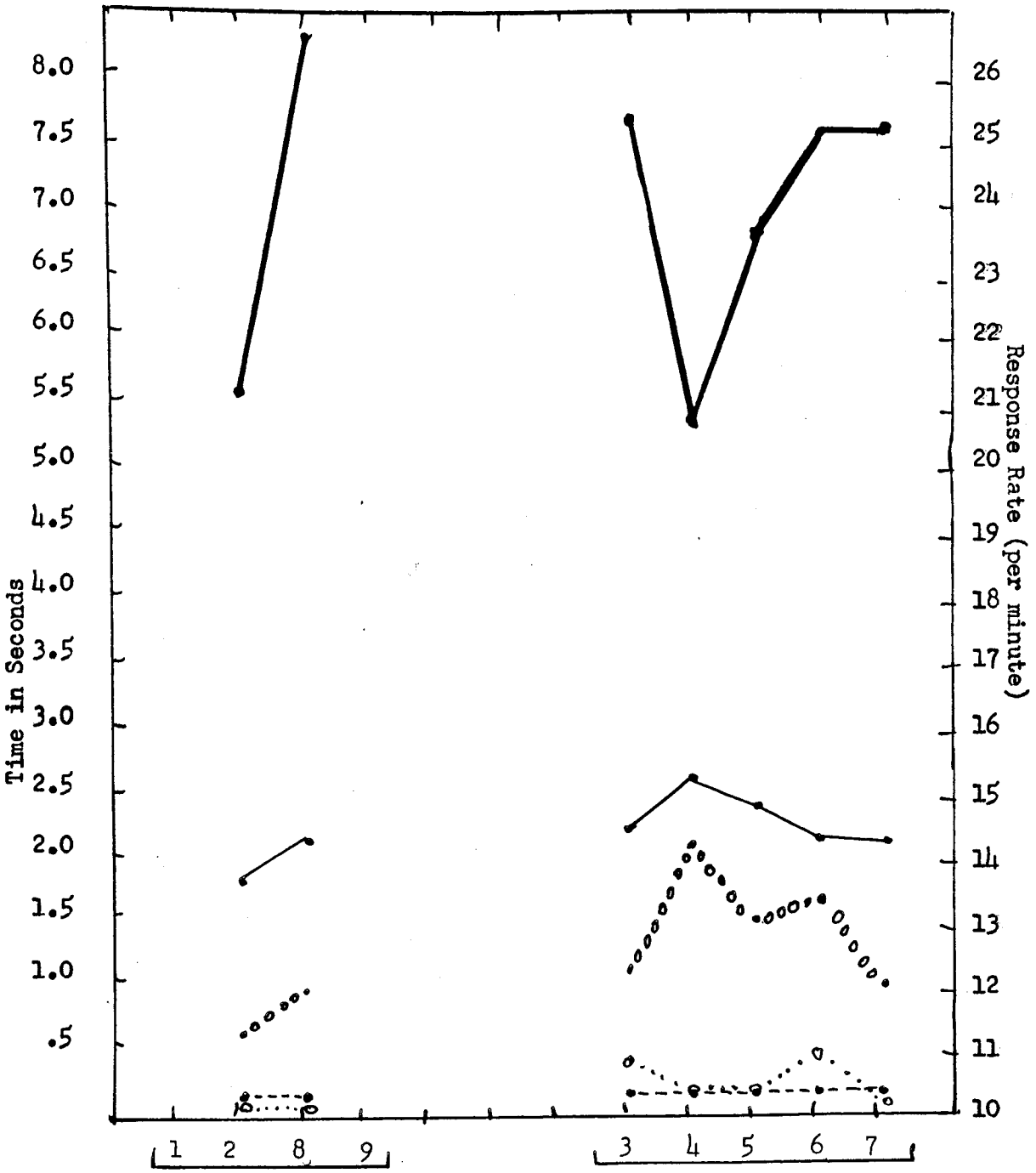


Figure 17. Values for Animal P-5.

APPROVAL SHEET

The dissertation submitted by Margaret E. Condon has been read and approved by five members of the Department of Psychology.

The final copies have been examined by the director of the dissertation and the signature which appears below verifies the fact that any necessary changes have been incorporated, and that the dissertation is now given final approval with reference to content, form, and mechanical accuracy.

The dissertation is therefore accepted in partial fulfillment of the requirements for the Degree of Doctor of Philosophy.

May 26/65
Date

Signature of Adviser