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Profile of Drug Effects on Temporally Spaced Responding in Rats[1]

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ANDO, K. *Profile of drug effects on temporally spaced responding in rats.* PHARMAC. BIOCHEM. BEHAV. 3(5) 833–841, 1975. – A differential reinforcement of low rate schedule was used with rats to test 15 psychotropic drugs. The computer analysis was based on interresponse time (IRT). Mean IRT, IRT standard deviation, median IRT, IRT midrange, modal IRT, frequency of modal IRT, and an efficiency index, in addition to numbers of responses and reinforcements and the IRT histogram were obtained for each rat in each drug test. An increase in number of responses and a peak shift to shorter IRTs in the histograms were observed with amphetamine, methamphetamine, pipradrol and nicotine, as reported by many other investigators. Decrease in IRT midrange and less change in number of responses were observed with diazepam and chlordiazepoxide. Long pauses were found with LSD-25, 2,5-dimethoxy-4-methylamphetamine (DOM) and mescaline. In a factor analysis, the following main factors were obtained. High values in factor loading a_1 were observed with chlorpromazine, chlordiazepoxide, pentobarbital, imipramine, nialamide, LSD-25, DOM and mescaline. With these drugs, mean IRT and IRT standard deviation were also high. Values for a_2 were high with amphetamine, methamphetamine, pipradrol and nicotine. High a_3 values were observed in some rats with chlorpromazine, diazepam, chlordiazepoxide, pentobarbital, pipradrol and caffeine. The changes in a_3 values were correlated with changes in the IRT midrange. These results may be valuable in classifying new compounds in drug screening programs as being of the amphetamine type, nicotine type, diazepam type or LSD-25 type.

Psychotropic drugs Differential reinforcement of low rate schedule Interresponse time
Factor analysis

IN the differential reinforcement of low rate (DRL) schedule a lever pressing response is reinforced only if it occurs at a specified time after the preceding response [22]. The time intervals between successive responses under a DRL schedule are often analyzed by plotting interresponse time (IRT) distributions. With repeated training under the schedule, IRTs around the specified time tend to be most frequent, except for the shorter IRTs called response bursts [21]. Sidman [21] demonstrated drug effects on the IRT histogram, where it was observed, for example, that amphetamine shifted the IRT distribution toward shorter values, whereas alcohol had little effect on the relative IRT distribution but produced prolonged periods of no response. Since then, much attention has focused on amphetamines and other drugs in this context, with the finding that separate characteristics of responding under a DRL schedule can be differentially affected by various drugs [4, 6, 7, 8, 9, 11, 12, 13, 19, 20, 24]. Most previous studies of drug effects on responding maintained by a DRL schedule have tested 2 or 3 drugs and have employed a few measures such as numbers of responses and reinforcements, or visual inspection of the IRT distribution.

Our present purpose was to obtain the profiles of a number of psychotropic drugs on a single DRL baseline for more measures than those previously used. The data recording, measure calculation and factor analysis were done by general purpose computers.

METHOD

Animals

Naive adult male Sprague Dawley rats having free access to food and water and weighing about 400 g were maintained at 80 percent of their previously determined body weights. Thirty-six rats were used for this experiment, with 4 rats being used for each drug. Some rats received more than one drug. The first group of 4 rats received chlorpromazine, diazepam, pentobarbital and amphetamine; the 2nd group, chlordiazepoxide and pipradrol; the 3rd group, caffeine and tetrahydrocanabinol; the 4th group, imipramine and LSD-25; the 5th group, methamphetamine; the 6th group, nicotine; the 7th group, nialamide; the 8th group, DOM; and the 9th group, mescaline.

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Apparatus

Four operant conditioning chambers (22 X 20 X 25cm) in separate cubicles were used. A force of 20 g was required to operate a switch attached to the response lever. DRL contingencies were controlled by a BRS Digibits logic module system. A PDP8/I computer (Digital Equipment Corporation) recorded IRTs with a resolution of 20 msec on high speed punched paper tape, and performed calculation of the measures from these tapes afterwards. Gerbrands cumulative recorders also recorded responses and reinforcements.

Procedure

In the present DRL 20 sec schedule, lever presses spaced at least 20 sec apart were reinforced with a 45 mg food pellet. Following magazine training and lever pressing acquisition, each rat was exposed to a DRL 20 sec schedule in 3 hr sessions until a stable temporal pattern of responding emerged for several sessions [1]. Rats had free access to water during sessions and in their home cages.

Each drug test consisted of several 2 hr sessions. Each session was not started until several consecutive reinforcements and the constant response rates were observed for more than 5 min on the cumulative recorder in the warm-up period which was given before each session.

In the first session of each drug test, the vehicle to be used in subsequent drug sessions was administered to rats after the first hour via the same route as in the drug sessions. Five min after this administration, the second hr of the session was begun. In subsequent drug sessions, the same procedure as in the first session was used except that a drug was administered at a certain dose level. The dose level was doubled in each successive session, spaced more than a week apart, until marked changes were observed in the IRT histogram. During the intersession period of the same drug test, the rats were maintained under deprivation conditions in their home cages. For rats that received more than one drug, an interval of at least one month with food and water available and without training under the DRL schedule was allowed for recovery from the preceeding drug effects. A total of 15 drugs were tested in this manner.

Drugs

The following drugs and dose levels were administered subcutaneously (SC) or intraperitoneally (IP). Drugs were dissolved in saline or suspended as noted: Chlorpromazine hydrochloride (0.5, 1, 2 mg/kg, SC); Diazepam (Cercine® injections, Takeda) (0.5, 1, 2 mg/kg, SC); Chlordiazepoxide (4, 8, 16 mg/kg, IP, sodium carboxymethyl cellulose); Pentobarbital sodium (4, 8, 16 mg/kg, SC); dl-Amphetamine sulfate (0.5, 1, 2 mg/kg, SC); Methamphetamine hydrochloride (0.25, 0.5, 1, 2 mg/kg, SC); Pipradrol hydrochloride (4, 8, 16, 32 mg/kg, SC); Caffeine (8, 16, 32, 64 mg/kg, SC); Nicotine (0.1, 0.2, 0.4, 0.8 mg/kg, SC); Imipramine (2, 4, 8, 16 mg/kg, IP, sodium carboxymethyl cellulose); Nialamide (4, 8, 16 mg/kg, IP, 0.1 N hydrochloride); LSD-25 (Lysergic acid diethylamide, 0.002, 0.004, 0.008, 0.016 mg/kg, IP, 0.05 N tartaric acid); DOM (2,5-dimethoxy-4-methylamphetamine, 0.05, 0.1, 0.2 mg/kg, SC); Mescaline sulfate (4, 8, 16 mg/kg, IP); THC (Δ^9-tetrahydrocanabinol, 0.5, 1, 2, 4 mg/kg, IP, tween 80).

DOM has been used extensively in the U.S.A. and Canada and has been informally designated STP [23].

Data Analysis

Analysis of the results was based on the IRT data for each animal. An IRT histogram, numbers of responses and reinforcements, mean IRT, IRT standard deviation, median IRT, IRT midrange, modal IRT, frequency of modal IRT, and an efficiency index were obtained for the first and 2nd hr of each session of each drug test for each animal. IRT midrange was defined as the difference between the 25th and 75th percentiles of IRTs (IRT range which includes 50 percent of total IRTs). In calculating the modal IRT, IRTs less than 4 sec were excluded from the data because a mode was sometimes found in the shorter IRTs which are referred to as response bursts. Efficiency (EF) was defined as $EF = \sum_{t=20}^{39} F(t) \cdot (40-t)$, where F(t) was the response frequency at t seconds of IRT. Factor analysis of the measures was carried out by IBM system 360 Model 195K at the IBM Data Center, Tokyo. The program used for a principal factor method and an orthogonal rotation of the factor matrix was one from the Biomedical Computer Programs [5].

RESULTS

All rats developed stable baseline behavior under the DRL 20 sec schedule. That is, the distribution had a peak frequency around 20 sec and IRTs of no longer than 60 sec in the IRT histogram, and all the measures were consistent within each 2 hr session. Furthermore, vehicle administration did not change the baseline (see, for example, the upper histograms in Fig. 1).

Although animals were not run every day under the DRL schedule during each drug test, only one session per week provided appropriate behavioral baselines. The measures for the first hr were consistent for all of the sessions for each rat. In general, the baselines recovered in the first hr of the next session after a preceeding drug session. In Table 1, each measure for preadministration and post-vehicle administration periods (1 hr each) was averaged for all sessions of all drug tests. Sample numbers (N) for each period were based on (1) the number of all drug tests, where each drug test with 4 rats consisted of several doses, including the vehicle session, and (2) the number of all vehicle sessions of each drug test with 4 rats, respectively. The standard deviations of each measure were relatively low compared to their means in both periods.

The dose-effect curves for each drug for the numbers of responses and reinforcements in the individual rats are shown in Figs. 2 and 3. The horizontal axes represent dose in mg/kg including vehicle administration at the leftmost position on the axes, and the vertical axes represent the ratio of the value in postadministration period to that in preadministration period. All the ratios in vehicle-administration were around one except for the low ratios for both measures on Rat 5 in the pipradrol test, and for the unusually high ratios for the number of reinforcements of Rat 3 in the diazepam test and the pentobarbital test. Increases in the number of responses were observed in at least one of the 4 rats with 0.5, 1, and 2 mg/kg of amphetamine, 0.25, 0.5 and 1 mg/kg of methamphetamine, 4, 8, and 16 mg/kg of pipradrol, 8 mg/kg of caffeine and 0.1 mg/kg of nicotine. A decrease in the number of responses was observed at the higher doses with these drugs except for nicotine. Small increases in the number of responses were observed with at least one dose in one or two rats with diazepam, chlor-

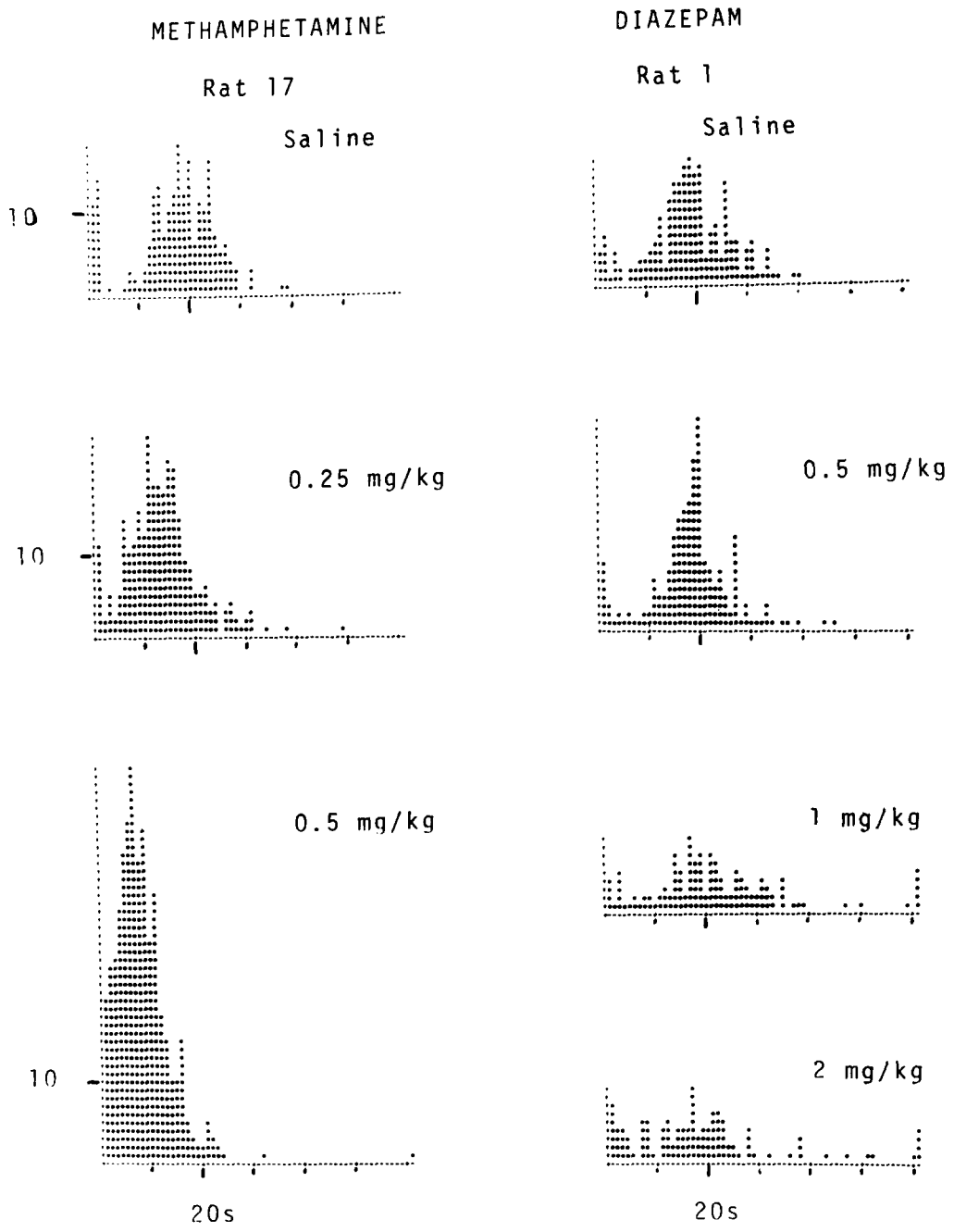

FIG. 1. Computer generated interresponse time histograms for individual rats after saline and drug administrations. Horizontal axes indicate interresponse time in sec. Vertical axes inidcate the number of responses in one hour period.

diazepoxide, pentobarbital, imipramine, LSD-25, DOM, mescaline and THC. At doses where the number of responses increased, the number of reinforcements generally decreased. Decreases in the number of responses were found in at least one of the 4 rats with 2 mg/kg of chlorpromazine, 16 mg/kg of chlordiazepoxide, 16 mg/kg of pentobarbital, 8 mg/kg of imipramine, 4 and 16 mg/kg of nialamide, 0.008 mg/kg of LSD-25, 0.1 mg/kg of DOM, 16 mg/kg of mescaline and 2 mg/kg of THC. In general, the decrease in the number of reinforcements was similar to that in the number of responses, with some exceptions (for example, Rat 9 in THC test). Little change in number of responses was observed in at least 2 rats with diazepam (0.5–2 mg/kg), chlordiazepoxide (4–16 mg/kg), nicotine (0.1–0.8 mg/kg) and THC (0.5–2 mg/kg), whereas a marked decrease in number of reinforcements was observed

TABLE 1

AVERAGE OF EACH MEASURE FOR PERFORMANCE UNDER DRL 20 SEC SCHEDULE FOR RATS IN PREADMINISTRATION AND POSTVEHICLE ADMINISTRATION PERIODS (ONE HR EACH)

	Preadministration Period (N = 260)		Postvehicle Administration Period (N = 60)	
Measure	Mean	S.D.	Mean	S.D.
Number of response	203.2	38.1	196.3	52.6
Number of reinforcement	82.2	20.1	83.1	21.3
Mean IRT	18.2	3.3	18.7	4.6
IRT standard deviation	8.5	6.9	9.3	9.1
Median IRT	19.5	2.1	19.6	2.5
IRT midrange	8.0	4.1	8.2	3.8
Modal IRT	20.0	2.1	20.2	1.8
Frequency of modal IRT	22.2	5.5	20.3	5.4
Efficiency	1283.4	313.5	1263.4	306.2

for Rat 2 in the diazepam test and for Rat 24 in the nicotine test.

Several patterns of drug effects as they appeared in the IRT histograms were found. The first pattern of effect was a peak shift or modal IRT change to shorter IRTs with a slight change in number of responses (see for example, the IRT histogram for 0.25 mg/kg of methamphetamine in Fig. 1). The second pattern was a peak shift to shorter IRTs with a marked increase in number of responses and an increase in the frequency of the modal IRT (see for example, the IRT histogram for 0.5 mg/kg of methamphetamine in Fig. 1). The third was an increased dispersion of the IRT distribution or increased IRT midrange with a slight change in number of responses (see for example, the IRT histogram for 2 mg/kg of diazepam in Fig. 1). The other effects observed on the IRT histograms were related to a decrease in number of responses.

Although it is difficult to describe completely the effects of the 15 drugs given to 4 rats, with several measures of responding under every condition, Tables 2 and 3 summarize the drug effects on each rat. The trends of the dose-effect function were classified for each rat as decrease (↓), no change (=), increase (↑), and increase and decrease (↕), based on a minimum of a 30 percent decrease or increase relative to the vehicle value in each measure. As the change in the postdrug administration period was compared with the value in the postvehicle administration period in Tables 2 and 3, the trend for numbers of responses and reinforcements was not always the same as the change for the dose-effect curves for numbers of responses and reinforcements in Figs. 2 and 3, where the curves were plotted on the basis of the ratio of the value in the postadministration period to that of preadministration period. However, the change in Figs. 2 and 3 and the trend in Tables 2 and 3 were almost identical for both measures. Mean IRT and IRT standard deviation were easily influenced by just a few long pauses in responding, while median IRT and IRT midrange were relatively independent of them. With LSD-25, DOM and mescaline, an increase in mean IRT and a slight change in median IRT were found for most rats. With diazepam and chlordiazepoxide, an increase in IRT midrange and less change in number of responses were observed for 2 or 3 rats. Modal IRT decreased with amphetamine, methamphetamine, pipradrol and nicotine for at least 2 rats each with an increase in number of responses. An increase in frequency of modal IRT was observed for some of the rats which showed an increase in number of responses. Efficiency decreased in all cases except for 2 rats with THC.

The results of a factor analysis for each rat with each drug as a variable and for each measure as a sample [5], are also presented in Tables 2 and 3. The analysis was based on the slope of each dose-effect function with X as dose on a log scale and with Y as the ratio of each measure in the post-administration period to that in the preadministration period on a log scale. As the logarithm of 0 is not defined, X = 0 or vehicle administration was arbitrarily assigned to be half of the minimum dose tested. This does not significantly affect the regression line. A slope of the dose-effect curve was calculated by the method of least squares for all doses except for some doses in some rats with amphetamine, methamphetamine, pipradrol, caffeine and nicotine. The doses with these drugs which produced a decrease after an increase in number of responses were excluded for each measure in these tests. In decreasing order, eigen values obtained from the correlation matrix were 42.03, 8.68, 6.56, 1.73, 0.72, etc. As the difference between the third

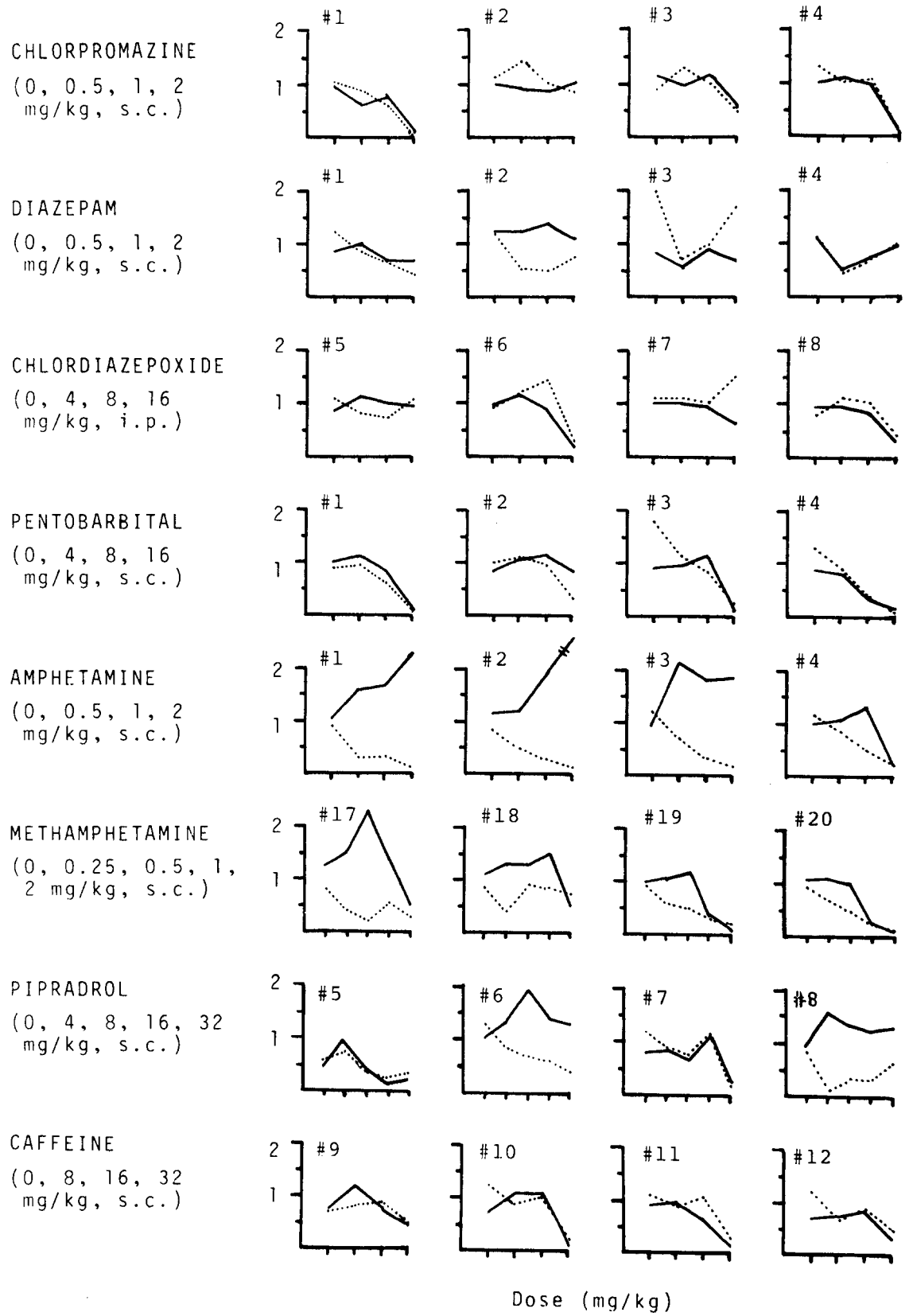

FIG. 2. Dose-effect curves for each drug of numbers of responses (solid line) and reinforcements (dotted line) in individual rats. Horizontal axes represent dose in mg/kg including vehicle administration at the leftmost position. Vertical axes represent the ratio of the value in the postadministration one hour period to that in the preadministration one hour period.

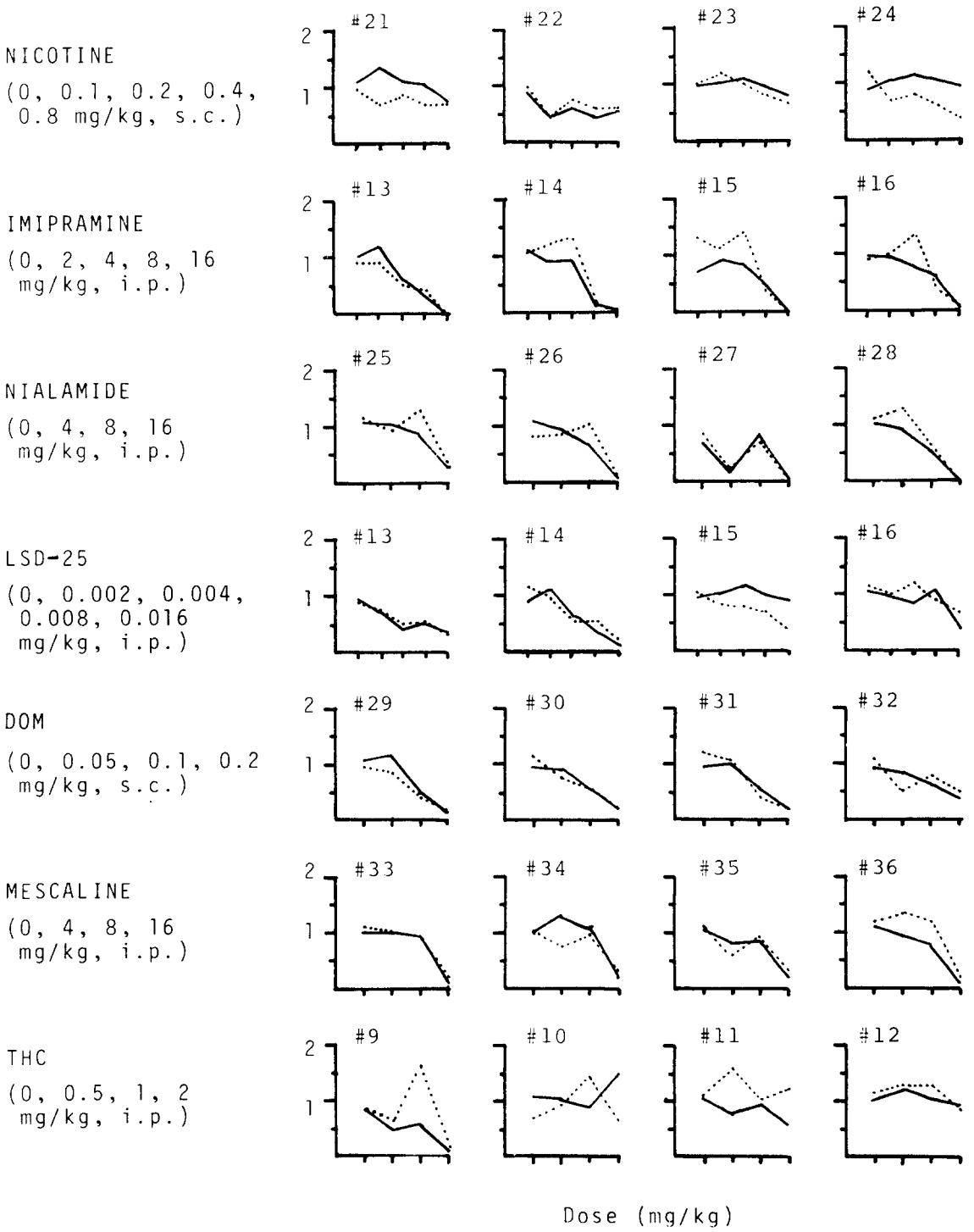

FIG. 3. Dose-effect curves for each drug of numbers of responses (solid line) and reinforcements (dotted line) in individual rats. Horizontal axes represent dose in mg/kg including vehicle administration at the leftmost position. Vertical axes represent the ratio of the value in the postadministration one hour period to that in the preadministration one hour period.

TABLE 2

DRUG EFFECTS ON TEMPORALLY SPACED RESPONDING IN RATS

Drug	Rat	Number of Response	Number of Reinforcement	Mean IRT	IRT Standard Deviation	Median IRT	IRT Midrange	Modal IRT	Frequency of Modal IRT	Efficiency	Factor Loading a_1	a_2	a_3
Chlorpromazine	1	↓	↓	↑	↑	↑	↑	=	↓	↓	0.94	0.15	0.28
0, 0.5, 1, 2mg/kg, SC	2	=	=	=	=	=	↑	=	↓	↓	0.61	0.00	0.71
	3	↓	↓	↑	↑	=	↑	↓	↓	↓	0.81	0.10	0.56
	4	↓	↓	↑	↑	↓	↑	=	↓	↓	0.93	0.08	0.23
Diazepam	1	↓	↓	↑	↑	=	↑	=	↓	↓	0.82	0.10	0.38
0, 0.5, 1, 2mg/kg, SC	2	=	↓	=	↓	=	=	=	=	↓	−0.19	0.55	0.03
	3	=	↓	=	↑	=	↑	↓	↓	↓	0.72	0.21	0.54
	4	=	↓	=	↑	=	↑	=	↓	↓	−0.36	0.05	0.07
Chlordiazepoxide	5	=	↓	=	↑	=	↑	=	↓	↓	0.66	0.27	0.70
0, 4, 8, 16mg/kg, SC	6	↓	↓	↑	↑	=	↑	=	↓	↓	0.92	0.04	0.32
	7	=	=	=	↑	=	↑	=	↓	↓	0.53	−0.27	0.65
	8	↓	↓	↑	↑	=	↑	=	↓	↓	0.90	−0.07	0.36
Pentobarbital	1	↓	↓	↑	↑	↑	↑	=	↓	↓	0.96	0.02	0.12
0, 4, 8, 16mg/kg, SC	2	=	↓	=	↑	↓	↑	↓	↓	↓	0.73	0.25	0.50
	3	↓	↓	↑	↑	=	↑	=	↓	↓	0.93	0.01	0.27
	4	↓	↓	↑	↑	=	=	↓	↓	↓	0.87	0.43	−0.11
Amphetamine	1	↑	↓	↓	↓	↓	=	↓	↑	↓	0.27	0.94	−0.09
0, 0.5, 1, 2mg/kg, SC	2	↑	↓	↓	↓	↓	↑	↓	↑	↓	−0.11	0.99	−0.03
	3	↑	↓	↓	=	↓	↑	↓	↑	↓	0.20	0.91	0.24
	4	↕	↓	=	=	=	↑	↓	=	↓	0.47	0.77	0.35
Methamphetamine	17	↕	↓	↓	=	↓	=	↓	↕	↓	−0.01	0.98	−0.18
0, 0.25, 0.5, 1, 2mg/kg, SC	18	↕	↓	↓	↑	↓	↑	↓	↕	↓	0.25	0.87	0.38
	19	↕	↓	↑	↑	=	↑	=	↕	↓	0.43	0.82	−0.14
	20	↕	↓	↑	↑	↓	↑	=	↕	↓	−0.18	0.91	−0.25
Pipradrol	5	↕	↓	↑	↑	=	↓	↓	↕	↓	−0.91	0.34	−0.22
0, 4, 8, 16, 32mg/kg, SC	6	↑	↓	↓	↑	↓	↑	↓	=	↓	0.02	0.63	0.61
	7	↕	↓	↑	↑	=	↑	=	↓	↓	0.16	0.67	0.54
	8	↑	↓	↓	↓	↓	=	↓	↕	↓	−0.23	0.90	−0.25
Caffeine	9	↕	↓	↑	↑	=	↑	=	↓	↓	−0.23	0.59	0.69
0, 8, 16, 32mg/kg, SC	10	↕	↓	↑	↑	↑	↑	=	↕	↓	−0.55	0.68	0.24
	11	↓	↓	↑	↑	↑	↑	↑	↓	↓	0.58	0.40	0.21
	12	↓	↓	↑	↑	=	↑	=	↓	↓	0.81	0.41	0.06

Trend of dose-effect function: decrease (↓), no change (=), increase (↑), increase and decrease (↕). Three main factor loadings are also presented for each rat.

TABLE 3

DRUG EFFECTS ON TEMPORALLY SPACED RESPONDING IN RATS

Drug	Rat	Number of Response	Number of Reinforcement	Mean IRT	IRT Standard Deviation	Median IRT	IRT Midrange	Modal IRT	Frequency of Modal IRT	Efficiency	Factor Loading a_1	a_2	a_3
Nicotine	21	=	=	↑	↑	=	=	=	↓	↓	0.80	0.00	0.42
0, 0.1, 0.2, 0.4, 0.8mg/kg,	22	=	↓	↑	↑	=	↑	=	=	↓	0.78	0.41	0.22
SC	23	↑	↓	=	↑	↓	↑	↓	↓	↓	0.04	0.96	0.22
	24	↑	↓	=	↑	↓	↑	↓	=	↓	0.45	0.69	0.52
Imipramine	13	↓	↓	↑	↑	=	↑	=	↓	↓	0.96	0.20	–0.07
0, 2, 4, 8, 16mg/kg, IP	14	↓	↓	↑	↑	↑	↑	=	↓	↓	0.99	0.08	–0.06
	15	↓	↓	↑	↑	=	↑	=	↑	↓	0.93	0.28	–0.08
	16	↓	↓	↑	↑	↑	↑	=	↑	↓	0.93	–0.07	0.35
Nialamide	25	↓	↓	↑	↑	↑	↑	=	↓	↓	0.90	–0.16	0.27
0, 4, 8, 16mg/kg, IP	26	↓	↓	↑	↑	↑	↑	=	↓	↓	0.93	–0.18	0.18
	27	↓	↓	↑	↑	=	↑	=	↓	↓	0.93	0.17	–0.02
	28	↓	↓	↑	↑	=	=	=	↓	↓	0.97	0.19	–0.07
LSD-25	13	↓	↓	↑	↑	=	↑	=	↓	↓	0.94	0.01	0.25
0, 0.002, 0.004, 0.008,	14	↓	↓	↑	↑	=	↑	↓	↓	↓	0.95	0.10	0.21
0.016mg/kg, IP	15	↓	↓	=	↑	=	=	=	=	↓	0.77	0.26	0.18
	16	↓	↓	↑	↑	=	↑	=	↓	↓	0.89	0.09	0.31
DOM	29	↓	↓	↑	↑	=	↑	=	↓	↓	0.96	0.08	0.27
0, 0.005, 0.1, 0.2mg/kg,	30	↓	↓	↑	↑	=	=	=	↓	↓	0.93	0.01	0.18
SC	31	↓	↓	↑	↑	=	↑	=	↓	↓	0.94	0.04	0.30
	32	↓	↓	↑	↑	=	=	=	↓	↓	0.94	–0.06	0.20
Mescaline	33	↓	↓	↑	↑	=	=	=	↓	↓	0.96	–0.04	0.17
0, 4, 8, 16mg/kg, IP	34	↓	↓	↑	↑	=	↑	↓	↓	↓	0.94	0.03	0.23
	35	↓	↓	↑	↑	=	↓	=	↓	↓	0.93	–0.02	–0.03
	36	↓	↓	=	↑	=	=	=	↓	↓	0.94	0.09	–0.11
THC	9	↓	↓	↑	↑	↑	↑	↑	↓	↓	0.97	–0.01	0.00
0, 0.5, 1, 2mg/kg, IP	10	=	=	↑	↑	↑	↑	=	↑	=	–0.81	–0.08	–0.30
	11	↓	=	↑	↑	=	↑	=	↓	↓	0.90	–0.03	0.27
	12	=	=	↑	↑	↑	=	=	=	=	–0.44	0.19	–0.85

Trend of dose-effect function: decrease (↓), no change (=), increase (↑). Three main factor loadings are also presented for each rat.

and the fourth eigen values was large, only three factor loadings orthogonally rotated by a computer were presented in Tables 2 and 3. The first factor loadings (a_1 values) were higher in all rats with chlorpromazine, chlordiazepoxide, pentobarbital, imipramine, nialamide, LSD-25, DOM and mescaline, and some rats with diazepam, caffeine, nicotine, and THC. In comparison with the change in values of 9 measures, the high values in factor loading a_1 seem to be correlated with the increase in mean IRT and in IRT standard deviation. The second factor loadings (a_2 values) were higher with amphetamine, methamphetamine, pipradrol, and in some rats with nicotine, where an increase in number of responses was found with all these drugs. Higher values in the third factor loadings (a_3) were observed in some rats with drugs which showed an increase in IRT midrange.

DISCUSSION

The increase in number of responses and the peak shift to shorter IRTs found with amphetamines and nicotine were consistent with a number of other studies [6, 14, 16, 19, 20, 21]. The difference between amphetamines and nicotine, in terms of the above effects, was that the amphetamines increased number of responses to a much greater degree than did nicotine. Pipradrol was also found to have the same effects as the amphetamines. Although similar effects were reported by other investigators with chlordiazepoxide [12,17, 18], barbiturates [9], imipramine [10], LSD-25 [3] and THC [15], the effects in the present study with these drugs were not so marked and consistent as with amphetamines. Instead, the disruption of the temporal pattern, defined as increased dispersion of the IRT distribution (or IRT midrange increment) with a slight change in number of responses, was found with diazepam (1 and 2 mg/kg) and chlordiazepoxide (16 mg/kg). The characteristic effects of LSD-25, DOM and mescaline were an increase in mean IRT and little change in median IRT, which indicate the frequent occurences of no-responding or pauses [2]. These results may be valuable in classifying new compounds in drug screening programs as being of the amphetamine type, nicotine type, diazepam type or LSD-25 type.

The results of the factor analysis indicated that there were three main factors. The first factor loading a_1 was correlated with the increase in IRT mean and the IRT standard deviation. The second and the third factor loadings (a_2 and a_3) were correlated with the increase in number of responses and the increase in IRT midrange, respectively. The higher values in a_1 observed in 4 rats each with chlorpromazine, pentobarbital, imipramine, nialamide, LSD-25, DOM and mescaline may reflect the greater response-decreasing effect with these drugs. The higher value in a_2 may distinguish psycho-stimulants like amphetamine from others. The question of whether the higher values in a_3 are a general trend with tranquilizers or not lies beyond the scope of this study.

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