

# Differential effect of amphetamine on successive post-reinforcement periods in variable-interval schedules<sup>1</sup>

*Efectos diferenciales de la anfetamina en periodos pos-reforzamiento sucesivos en programas de intervalo variable<sup>1</sup>*

Joao Claudio Todorov<sup>2</sup> and Cherry Watanabe Terada

Universidad Nacional Autónoma de México and  
Universidade de Brasilia.

## ABSTRACT

Four pigeons responded under a variable-interval schedule of food presentation. Local response rates were recorded in three successive post-reinforcement periods. The effects of amphetamine (0.5, 1.0, and 2.0 mg/kg) on local response rates were relatively greater on the 10-sec period following reinforcements than on later periods. A rate-dependent effect was observed, but in the opposite direction of that predicted by the rate-dependency hypothesis: lower local response rates were proportionately more depressed by the 2.0 mg/kg dose than higher local response rates.

DESCRIPTORS: amphetamine, variable-interval schedule, local response rates, post-reinforcement rates, key pecking, pigeons.

## RESUMEN

*Cuatro pichones respondieron en un programa de intervalo variable de presentación de alimento. Se registraron las tasas locales de respuesta en tres periodos post-reforzamiento sucesivos. Los efectos de la anfetamina (0.5, 1.0 y 2.0 mg/kg) en las tasas locales de respuesta fueron relativamente mayores en los periodos de 10 seg. inmediatamente después de los reforzamientos que en periodos posteriores. Se observó un efecto dependiente de la tasa, pero en una dirección opuesta a la esperada por la hipótesis de la dependencia de la tasa: las tasas locales de respuesta más bajas fueron proporcionalmente más deprimidas por la dosis de 2.0 mg/kg. que las tasas locales de respuestas más elevadas.*

DESCRIPTORES: anfetamina, programa de intervalo variable, tasas locales de respuesta, tasas pos-reforzamiento, picoteo en la tecla, pichones.

<sup>1</sup> This report is based on a presentation made at the 1978 APA Annual Convention and also at the International Symposium on Behavioral Pharmacology, Mexico City, 23-25 November, 1978, sponsored by the National Autonomous University of Mexico.

<sup>2</sup> On leave of absence from the Universidade de Brasilia.

Typically, rate-dependent effects of drugs (Dews, 1958) are investigated in behavior maintained by fixed-interval schedules (*cf.*, Kelleher and Morse, 1969; but see MacPhail and Gollub, 1975). A fixed interval schedule of reinforcement specifies a minimum interval between some stimulus change and the opportunity for a reinforced response. After extended training, the pattern of responding is characterized by pauses after reinforcements, followed by spaced responses, with response rate increasing rapidly to a maximum as time for the next reinforcement approaches. By recording responses occurring in tenths of the interval, for instance, it is possible to observe different local response rates within interreinforcement intervals, and to study how a drug affects responding in different parts of the interval. Amphetamine has been shown to increase low control response rates early in the interval and to decrease the typically high control rates later in the interreinforcement interval.

In the present investigation, the effects of different doses of amphetamine were observed in local response rates in successive postreinforcement periods in a variable-interval schedule. Contrary to fixed-interval schedules, where reinforcement follows responding only in the last subperiod of the interreinforcement interval, variable-interval schedules program a determined local rate of reinforcement for successive post-reinforcement periods of time. Local reinforcement rates will depend on the relative number of specific interreinforcement intervals comprising the schedule (*cf.*, Catania and Reynolds, 1968).

## METHOD

### *Subjects*

Four male, adult, domestic pigeons, with a varied experience with schedules of positive reinforcement, were used. Subjects were food deprived and maintained at approximately 80% of their normal weight, determined during a period of free access to food. All subjects had received drugs in a previous experiment.

### *Apparatus*

A standard chamber for operant conditioning studies with pigeons (Grason-Stadler, USA), with two response-keys, was used. The right response-key was dark and inoperative throughout the experiment. The left key was transilluminated by a red light at the beginning of the session and turned off at session ending. Houselights were on all the time, except during reinforcements, when both key and houselights were turned off, and the feeder was illuminated. Reinforcement was a 5-sec period of access to grain. The

experimental room was sound-attenuated; standard electromechanical circuitry, in a separate room, automatically controlled the scheduling and recording of events.

### *Procedure*

Subjects were exposed to a variable-interval 1-min schedule of reinforcement for 39 daily one-hour sessions before drug administration began. The schedule was comprised of 11 intervals arranged in a random order; interval lengths were 5, 12, 24, 48, 60, 72, 84, 96, 108, and 115 sec. Sessions began with the first response being reinforced. Reinforcement periods were not considered in session time. Counters registered responses occurring before 10 sec elapsed after each reinforcement, in the period between 10 and 20 sec after reinforcements, and a third counter registered all responses occurring after 20 sec since the last reinforcement. Associated counters registered numbers of seconds in a session during which a subject was exposed to each one of these post-reinforcement periods.

*Drug administration.* *d*-Amphetamine sulfate (0.5, 1.0, and 2.0 mg/kg) was injected into the pectoral muscle 15 min before the experimental session, dissolved in saline. Drug sessions were separated for at least four control sessions. The 1.0 mg/kg dose was repeated for all subjects. Doses were administered in an increasing order: 0.5, 1.0, 1.0, and 2.0 mg/kg.

*Data analysis.* For each session, local response rates were computed by dividing the numbers of responses in successive periods after reinforcements by the time a subject was exposed to such periods. The relationship between drug and control rates was examined as suggested by Gonzalez and Byrd (1977). Control rates were considered as the averages of four control sessions before the drug sessions.

## RESULTS

Average local response rates in successive periods after reinforcements, from the four control sessions, are shown in Figure 1. Brackets indicate one standard deviation above and below the mean. A clear tendency for increases in response rate as time since reinforcement increases is seen in the data from subjects 195 and 251. For the other two subjects no clear tendency is observed. Figure 1 also shows a decrease in variability in local response rates as time since reinforcement increases, for subjects 194, 195, and 251.

Figure 2 shows the effects of three doses of amphetamine on local response rates from three successive periods after reinforcement. Brackets indicate one standard deviation above and below mean rates in four control sessions. Data referring to 1.0 mg/kg are the average of two determinations. Clear rate-increasing effects of amphetamine on local response rates can be

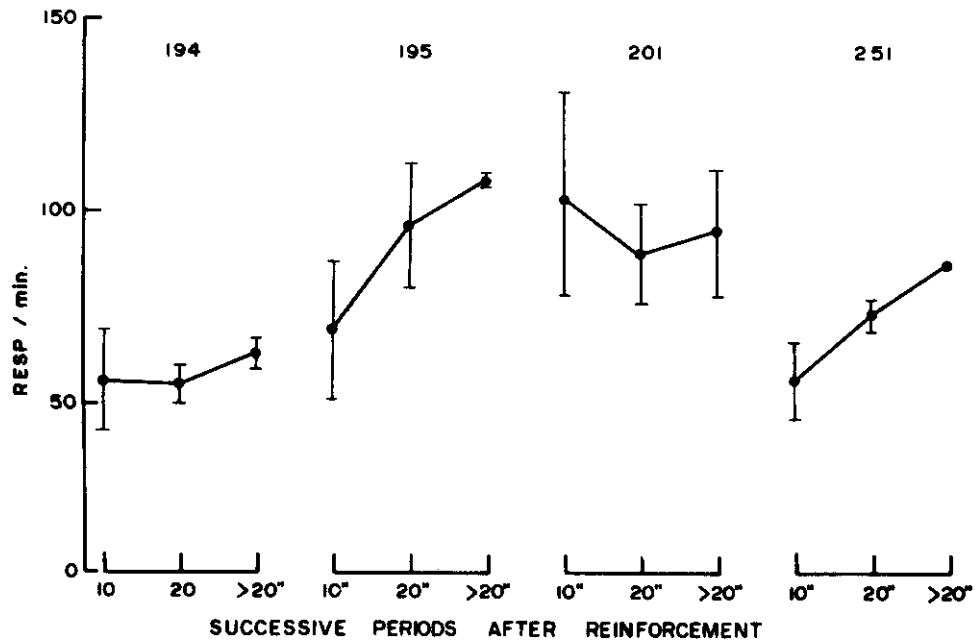


Fig. 1. Control local response rates (resp/min) in successive postreinforcement periods. Data are the average of four control sessions. Brackets represent  $\pm 1$  standard deviation.

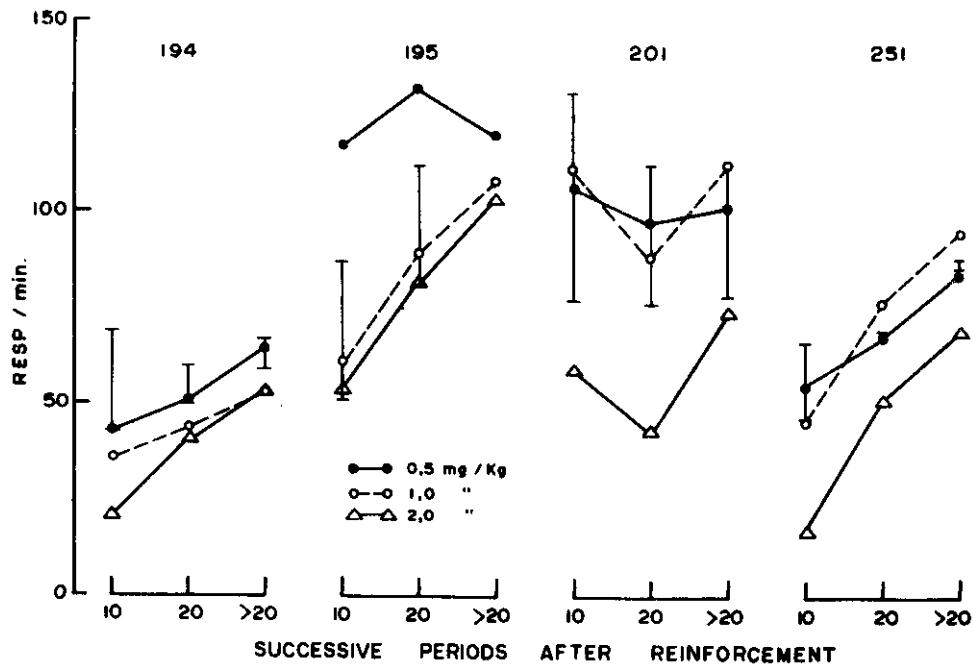


Fig. 2. Local response rates (resp/min) in successive post-reinforcement periods under the three doses of amphetamine. Data referring to the 1.0 mg/kg dose are average of two determinations. Brackets represent average control rates  $\pm 1$  standard deviation.

seen only for the 0.5 mg/kg dose in the data from subject 195. The 2.0 mg/kg dose clearly depressed local response rates in subjects 194, 201, and 251. For all subjects, a differential effect of amphetamine on response rates in successive periods after reinforcement is seen in the tendency for a decrease in range as time since reinforcement increases: the effects of a given dose, either rate-increasing or rate-decreasing, are generally greater in response rates in the 10-sec periods after reinforcement than on later periods.

Figure 3 relates the effects of the three doses of amphetamine to average local response rates in the control sessions. The diagonal lines indicate the

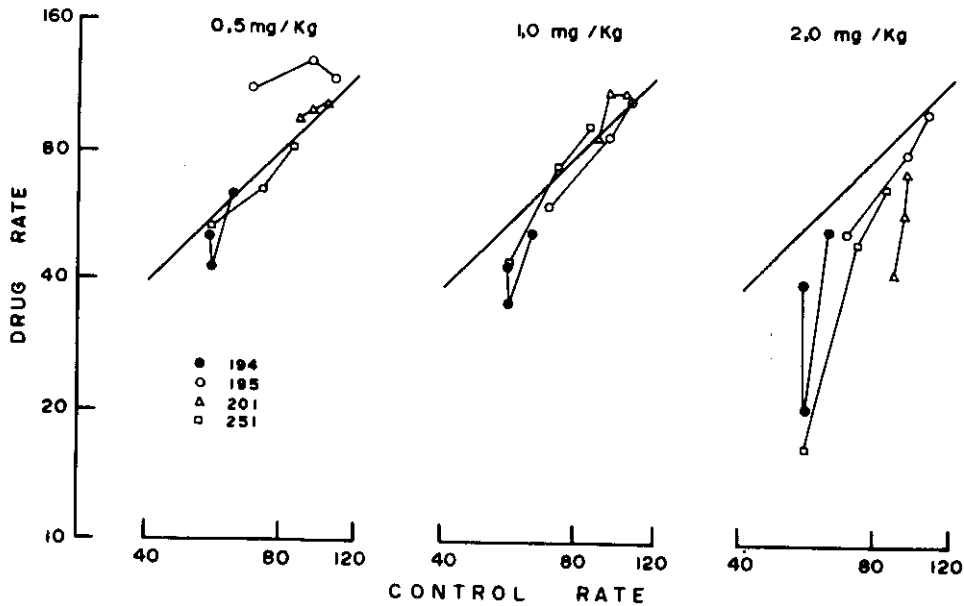


Fig. 3. Drug rates as a function of control rates for the three doses of amphetamine. Coordinates are on logarithmic scales.

perfect case where the drug would have no effect and response rates on drug sessions would be identical to average rates on control sessions. Drug rates and control rates are presented in logarithmic coordinates, as suggested by Gonzalez and Byrd (1977). Data from different periods after reinforcement are not identified. Figure 3 shows a rate-increasing effect of the 0.5 mg/kg dose for the data from subject 195 only. However, no rate-dependent effect can be ascertained in this case (*cf.*, Gonzalez and Byrd, 1977). No clear rate-dependent effect of the 1.0 mg/kg dose is observed, although the data from subject 251 suggest a slope greater than 1.0 and an intercept lower than 1.0. A rate-dependent effect can be seen on the depressing effects of the 2.0 mg/kg dose, but in the opposite direction of the effect predicted by the rate-dependent hypothesis: low response rates were relatively more depressed than high response rates (slopes greater than 1.0 and intercepts lower than 1.0).

## DISCUSSION

The data show a differential effect of amphetamine on local response rates in successive post-reinforcement periods in a variable-interval schedule. Local rates immediately after a reinforcement were more affected by a given dose than rates on later periods. Figure 2 shows that drug effects, when observed, were always higher in response rates from the 10-sec periods after reinforcements than in rates from later periods, even for subjects which show no clear differences in control local response rates in successive periods after reinforcements (Figure 1). The data from the 2.0 mg/kg dose show an inverted rate-dependent effect: low local response rates were relatively more depressed than high local response rates.

Similar effects of amphetamine were observed on behavior maintained by second-order schedules of reinforcement (Bond, Sanger, and Blackman, 1975). Pigeons' key pecking responses were reinforced with food presentation following the completion of a sequence of three 2-min fixed-interval components. An analysis of the data reported by Bond *et al.*, (1975, Figure 1) showed that amphetamine doses from 0.3 to 3.0 mg/kg affected more response rates in the first component of the sequence, less in the second component, and had practically the same effect on the third (the one followed by food presentation). When drug rates were plotted as a function of control rates in logarithmic coordinates, the data indicated an inverted rate-dependent effect: slopes greater than and intercepts lower than 1.0.

Also with pigeons as subjects, but with concurrent variable-interval, variable-interval schedules, Todorov, Gorayeb, Correa, and Graeff (1972) reported that increasing amphetamine doses decreased relatively more low-rate, changeover key responding (never followed immediately by food presentation) than high-rate, main-key responding (occasionally followed by food presentation), contrariwise to what would be predicted by the rate-dependency hypothesis.

The data reported by Bond *et al.* (1975) and by Todorov *et al.* (1972) indicate that amphetamine may exert greater effect on behavior maintained by weaker reinforcers, assuming that in second-order schedules feeder illumination only is a weaker reinforcer than feeder illumination plus food, and that in concurrent schedules food presentation is a stronger reinforcer than key-color change. It is possible, then, that amphetamines will have greater effects on behavior associated with lower reinforcement rates also, independently of a rate-dependent effect. In the present investigation, the 10-sec post-reinforcement periods were associated with a 33 reinforcement per hour (rfts/hr) local reinforcement rate; periods between 10 and 20-sec after reinforcements, with 36 rfts/hr, and the average reinforcement rate for periods greater than 20 was 72 rfts/hr. The observed differential effect of amphetamine on local response rates may be related to these different local reinforcement rates in successive post-reinforcement periods. On the other hand, the effect may depend also or exclusively on a higher sensitivity of

responding to other variables in short time periods following reinforcements. The higher variability in control response rates from the first 10-sec post-reinforcement periods supports this interpretation.

The present results are not in disagreement with previous data on the effects of amphetamine on schedule-controlled behavior. Analysis of drug effects on local response rates usually are performed on behavior maintained by fixed-interval schedules (*e.g.*, Branch and Gollub, 1974). Such schedules are characterized by pauses after reinforcements, of a length determined by interval duration. In a fixed-interval 5-min schedule, for example, local response rate in the 20-sec period after reinforcements is practically zero. These schedules, then are not adequate for the observation of an effect that is dependent on time since the last reinforcement.

The rate-dependent effect of drugs on schedule-controlled behavior has been reported several times (*e.g.*, Smith, 1964; Clark and Steele, 1966) since pointed out by Dews (1958), when interpreting the effects of amphetamine on behavior maintained by different schedules of reinforcement. Generally, it is maintained that drugs affect responding depending upon control response rates, irrespective of which schedule or what stimuli are controlling the observed behavior (*cf.*, Kelleher and Morse, 1969; McMillan, 1969; McKearney, 1968; MacPhail and Gollub, 1975). However, other factors besides control rates have been shown to be important factors in modulating drug effects. Intensity of a light stimulus was shown to be one factor (McKearney, 1970). Thompson and Corr (1974) showed that strong control by discriminative stimuli prevents the rate-increasing effect of *d*-amphetamine. Stitzer and McKearney (1977) report that pause requirements preceding the reinforced response in fixed-interval schedules modified the effects of moderate doses of *d*-amphetamine. Only a slight rate-dependent effect of amphetamine was found by Weiss and Gott (1972) in a microanalysis of fixed-ratio responding. The present investigation offers data on another exception to the rate-dependent effect of amphetamines.

#### REFERENCES

- Bond, N.W., Sanger, D.J., and Blackman, D.E. Effects of *d*-amphetamine on the behavior of pigeons maintained by a second-order schedule of reinforcement. *Journal of Pharmacology and Experimental Therapeutics*, 1975, *194*, 327-331.
- Branch, M.N. and Gollub, L.R. A detailed analysis of the effects of *d*-amphetamine on behavior under fixed-interval schedules. *Journal of the Experimental Analysis of Behavior*, 1974, *21*, 591-539.
- Catania, A.C. and Reynolds, G.S. A quantitative analysis of the responding maintained by interval schedules of reinforcement. *Journal of the Experimental Analysis of Behavior*, 1968, *11*, 327-383.
- Clark, F.C. and Steele, B.J. Effects of *d*-amphetamine on performance under a multiple schedule of reinforcement in the rat. *Psychopharmacologia*, 1966, *9*, 157-169.
- Dews, P.B. Analysis of the effects of pharmacological agents in behavioral terms. *Federation Proceedings*, 1958, *17*, 1024-1030.
- Gonzalez, F.A. and Byrd, L.D. Mathematics underlying the rate-dependency hypothesis. *Science*, 197, *195*, 546-550.
- Kelleher, R.T. and Morse, W.H. Determinants of the behavioral effects of drugs. In D.H. Tedeschi and R.E. Tedeschi (Eds.), *Importance of fundamental principles in drug evaluation*. New York: Raven Press, 1969, Pp. 383-405.

- MacPhail, R.C. and Gollub, L.R. Separating the effects of response rate and reinforcement frequency in the rate-dependent effects of amphetamine and scopolamine on the schedule-controlled performance of rats and pigeons. *Journal of Pharmacology and Experimental Therapeutics*, 1975, *194*, 332-342.
- McKearney, J.W. The relative effects of *d*-amphetamine, imipramine and harmaline on tetrabenazine suppression of schedule-controlled behavior in the rat. *Journal of Pharmacology and Experimental Therapeutics*, 1968, *159*, 429-440.
- McKearney, J.W. Rate-dependent effects of drugs: modification by discriminative stimuli of the effects of amobarbital on schedule-controlled behavior. *Journal of the Experimental Analysis of Behavior*, 1970, *14*, 167-175.
- McMillan, D.E. Effects of *d*-amphetamine on performance under several parameters of multiple fixed-ratio, fixed-interval schedules. *Journal of Pharmacology and Experimental Therapeutics*, 1969, *167*, 26-33.
- Smith, C.B. Effects of *d*-amphetamine upon operant behavior of pigeons: enhancement by reserpine. *Journal of Pharmacology and Experimental Therapeutics*, 1964, *146*, 167-174.
- Stitzer, M. and McKearney, J.W. Drug effects on fixed-interval responding with pause requirements for food presentation. *Journal of the Experimental Analysis of Behavior*, 1977, *27*, 51-59.
- Thompson, D.M. and Corr, P.B. Behavioral parameters of drug action: signalled and response-independent reinforcement. *Journal of the Experimental Analysis of Behavior*, 1974, *21*, 151-158.
- Todorov, J.C., Gorayeb, S.R.P., Correa, D.L., and Graeff, F.G. Effects of amphetamine on choice behavior of pigeons. *Psychopharmacologia*, 1972, *26*, 395-400.
- Weiss, B. and Gott, C.T. A microanalysis of drug effects on fixed-ratio performance in pigeons. *Journal of Pharmacology and Experimental Therapeutics*, 1972, *180*, 189-202.