

CHANGES IN BLOOD PRESSURE AND HEART RATE DURING FIXED-INTERVAL RESPONDING IN SQUIRREL MONKEYS

JO DEWEESE

HARVARD MEDICAL SCHOOL

Episodic and sustained increases in heart rate and mean arterial blood pressure can occur with recurring patterns of schedule-controlled behavior. Most previous studies were conducted under fixed-ratio schedules, which maintained a consistent high rate of responding that alternated with periods of no responding during times when the schedule was not in operation. The present study examined changes in heart rate and blood pressure under fixed-interval schedules which maintained a range of rates that varied from little or no responding at the beginning of the fixed interval to high rates at the end of the interval. The relations of cardiovascular function to rate of responding were examined. Squirrel monkeys prepared with arterial catheters were trained to respond under fixed-interval schedules of electric-shock presentation. The duration of the interval was varied across sessions and cardiovascular parameters were examined. Local rates of responding were typically near zero during timeout periods, low at the beginning of each fixed-interval cycle, and then increased as the fixed interval progressed. At most schedule durations, arterial blood pressure and heart rate levels were lowest at the beginning of the interval cycles, increased as the rate of responding increased, and then decreased during the timeout periods. At all parameters studied, there was a direct relationship between changes in response rate within fixed-interval cycles and changes in heart rate and blood pressure. The results suggest that a much closer concordance of these cardiovascular parameters and schedule-controlled responding is obtained by examining ongoing behavior as it occurs within the contingencies by which it is maintained.

Key words: operant behavior, blood pressure, heart rate, fixed-interval schedule, squirrel monkey

Episodic increases in mean arterial blood pressure and heart rate in the squirrel monkey, as well as sustained elevations in blood pressure, can occur with recurring patterns of behavior controlled by schedules of reinforcement (Benson, Herd, Morse, & Kelleher, 1969; Herd, Morse, Kelleher, & Jones, 1969; Kelleher, Morse, & Herd, 1972; Kelleher, Morse, Goldberg, & Herd, 1974; Morse, Herd, Kelleher, & Grose, 1971). In most of these previous studies, monkeys were studied under fixed-ratio (FR) schedules, in which a visual stimulus associated with occasional electric shocks terminated (stimulus–shock termination) when a lever had been operated a fixed number of times. Under these FR schedules,

periods of rapid constant responding alternated with periods of no responding. Both blood pressure and heart rate commonly increased during responding, and fell during periods without responding. Further, there was evidence of a relation between the rate of responding, or FR parameter, and overall mean blood pressure (Herd et al., 1969; Morse et al., 1971).

Studies in ambulatory populations of human volunteers have also suggested a role of physical activity in the control of blood pressure. For example, a number of studies have indicated that blood pressure is significantly higher in the work place than at home, and during waking hours compared to hours of sleep (e.g. Pickering, Harshfield, Kleinert, Blank, & Laragh, 1982). Studies using statistical techniques have attempted to further delineate respective roles of activities and time of day (e.g. Clark et al., 1987). Use of “spontaneous” changes in objectively recorded activity have also shown a relationship between activity and blood pressure, as well as pulse (Kario, Schwartz, & Pickering, 1999).

All of the studies of ambulatory volunteers have suggested a relation between activity and blood pressure; however, these studies are

This work was supported by grants MH07658, MH02094, DA00499 and training grants MH07084 and MH14275 from the U.S. Public Health Service.

I thank Professors P.B. Dews, W.H. Morse, and the late R.T. Kelleher for their advice, encouragement, and helpful comments about the manuscript. The technical assistance of Rose Diaz-Cordes and the services of Carolyn J. Mosher, Stanley Rose and Lynda Levy in the preparation of the manuscript are gratefully acknowledged.

Correspondence concerning this article may be addressed to Jo deWeese at 225 Settlers Point, Fountain Run, KY 42133 (e-mail: jodeweese@gmail.com).

doi: 10.1901/jeab.2009.92-379

Table 1

Changes in response rate (RR), blood pressure (BP), and heart rate (HR) as a function of changes in FI duration.*

FI (secs)	S-555			S-556			S-583		
	Resp. Rate	BP	HR	Resp. Rate	BP	HR	Resp. Rate	BP	HR
600	0.38 (0.01)	131 (6.01)	248 (19.6)	0.25 (0.02)	122 (3.74)	278 (2.45)	0.27 (0.03)	122 (3.67)	217 (2.48)
337	0.51 (0.08)	127 (3.67)	261 (11.3)	0.31 (0.09)	120 (4.60)	281 (2.83)	0.44 (0.02)	123 (4.64)	273 (9.65)
							0.57 (0.10)	124 (3.24)	279 (24.3)
180	0.67 (0.12)	132 (3.08)	251 (10.3)	0.82 (0.11)	126 (7.87)	284 (6.79)	0.47 (0.03)	117 (1.78)	274 (29.4)
	0.85 (0.04)	131 (3.19)	261 (6.28)	0.41 (0.09)	126 (1.22)	270 (4.26)	0.37 (0.07)	120 (1.78)	313 (7.12)
60	0.72 (0.18)	131 (7.07)	268 (10.6)	1.54 (0.16)	132 (1.63)	296 (4.97)	0.44 (0.05)	125 (3.94)	301 (13.5)
		134 (4.55)	291 (8.84)	0.67 (0.13)	138 (1.08)	286 (4.60)	0.60 (0.06)	124 (4.30)	291 (17.3)
20	0.42 (0.22)	143 (4.32)	290 (13.0)	1.37 (0.15)	136 (2.86)	282 (8.90)	1.52 (0.10)	125 (4.32)	294 (19.3)
6	NT	NT	NT	NT	NT	NT	1.23 (0.11)	128 (3.27)	310 (7.79)

* Resp. Rate, responses per s; BP, mean arterial blood pressure in millimeters of mercury; HR, heart rate in beats per min

Note. Data are means of the last three sessions (with SEM) obtained. Duplicate values are replications of that particular FI duration.

correlative in nature. The present study directly varied activity using schedule-controlled performances of squirrel monkeys maintained by electric-shock presentation (Kelleher & Morse, 1968), and examined concomitant changes in blood pressure and heart rate under fixed-interval (FI) schedules of reinforcement. While the average rate of responding in each session is quite stable at a given FI parameter, the average rate may change as much as fivefold as FI duration is varied (DeWeese, 1977). These schedules characteristically engender a wider range of rates of responding within individual FI schedule cycles than those shown previously with FR schedules, thus permitting a better elucidation of relations of cardiovascular function to physical activity.

METHOD

Subjects

Three experimentally naive male squirrel monkeys, weighing between 745 and 850 g were handled according to the procedures described by Kelleher, Gill, Riddle, & Cook (1963). The monkeys had free access to food and water in their individual home cages.

Systemic arterial blood pressure and heart rate were measured as described by Herd et al. (1969) and Grose, Herd, Morse, & Kelleher (1971). One end of a polyvinyl chloride catheter was implanted into the abdominal aorta below the renal arteries by way of the left

or right internal iliac artery. The distal end of the catheter was passed through the skin in the middle of the back, sealed with a stainless steel obturator, and protected by a jacket that the monkey wore at all times.

Apparatus

Arterial blood pressure was measured while each monkey sat in a restraining chair within a sound-attenuating isolation chamber (Industrial Acoustic AC3). Teflon tubing was attached to the catheter, led outside the experimental chamber and connected to the fluid-filled chamber of a Statham P23Db strain gauge pressure transducer, which in turn was connected with the same tubing to a Harvard Apparatus Co. constant-infusion syringe pump. A heparin and saline solution (0.08 mg sodium heparin per ml saline) was infused through the gauge and catheter at a rate (0.01 ml/min) that did not alter mean arterial pressure (Herd et al., 1969). The Wheatstone bridge connections of the Statham gauge were electrically connected to a Grass Instrument Co. polygraph (Model 7). Mean arterial blood pressure was obtained by low-pass filtering in the driver amplifier of the polygraph. Heart rate was measured by a Lexington Instruments Corp. cardiometer and was recorded on the polygraph. Patency of the catheters was verified by the flow of blood out of the opened end and was assessed during the session by the amplitude of pressure oscillations synchronous with each heartbeat.

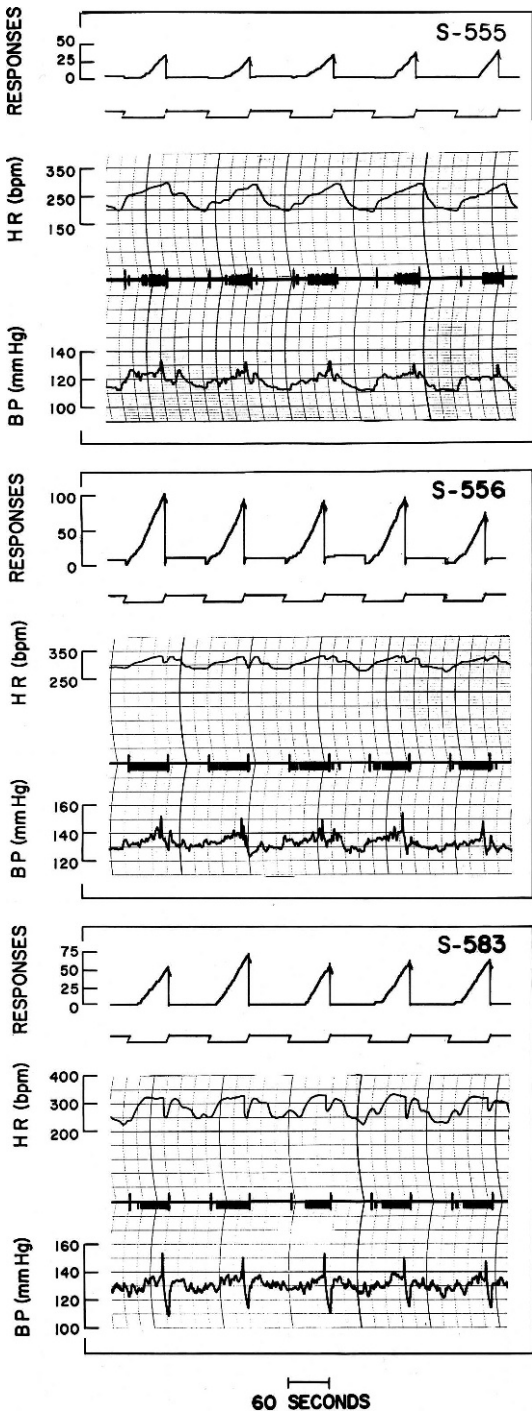


Fig. 1. Representative changes in responding, blood pressure and heart rate of individual monkeys. Five complete FI 60-s cycles are shown. The top record in each frame is a cumulative record of responses. The slope of the cumulative record is directly related to rate of responding. Short diagonal strokes on the response pen show where

Procedure

Experimental sessions were usually conducted 5 days each week. Between sessions the monkeys were housed in individual cages. During experiments each monkey was seated in a Lucite restraining chair (Hake & Azrin, 1963; Kelleher & Morse, 1964), and two brass electrodes rested on the lower portion of the tail. The electric shock was 650 V AC, 60 Hz, delivered through a variable resistor in series with the electrodes to give a 5 mA shock for 200 ms. A response lever (BRS/LVE, 1352) was mounted in front of the monkey on a transparent lucite wall. Pressing the lever with a force of 0.28 N or more was recorded as a response. Two white 6-W lights mounted above the lever were used as visual stimuli.

About 2 weeks after the catheters were implanted, mean blood pressure and heart rate were recorded during two or three 2-hr sessions in which the monkeys sat in the dark chamber. Behavioral training was then begun according to a procedure described by McKearney (1968). When a white light was present, monkeys were trained to respond under a continuous avoidance schedule. Generally, electric shocks were programmed to occur every 10 s in the absence of responding, and each response postponed shock delivery for 30 s. A 60-s timeout period was programmed to occur automatically every 600 s; during timeout, the chamber was dark, shocks were never delivered, and responses had no programmed consequences. When the timeout ended, the white light came on again, and the cycle was repeated 12 times each session. After responding was developed and maintained at a moderate rate, such that no more than one shock per session was delivered for three successive sessions, an FI 600-s schedule of shock presentation was arranged concur-

←
 electric shocks were presented and 60-s timeout periods began. The response pen reset to the bottom of the record at the beginning and end of each FI cycle. The event pen on the cumulative record was up during timeout periods and down during FI cycles. The bottom record in each frame is a polygraph record of mean heart rate in beats per min (upper tracing) and mean arterial blood pressure in millimeters of Hg (lower tracing). On the polygraph event record (middle tracing) a vertical stroke across the line indicates the beginning and end of each FI cycle, a short stroke below the line a response.

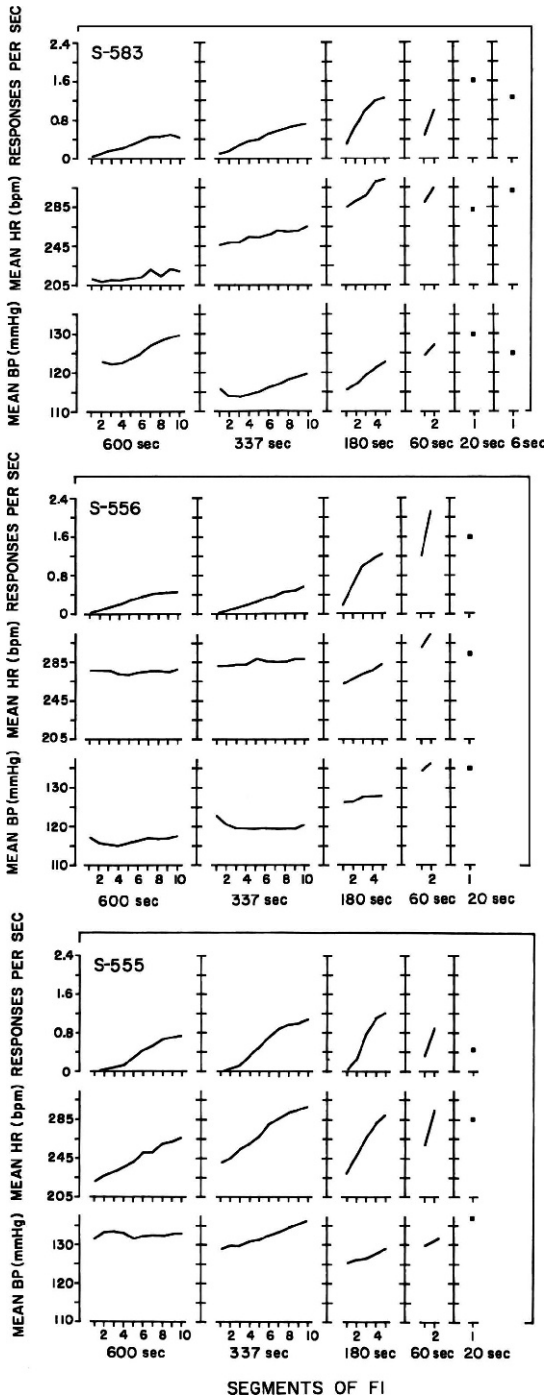


Fig. 2. Changes in response rate, heart rate and blood pressure within FI cycles. A representative session was chosen from the last three sessions at each FI duration. Each FI cycle of 60-s or longer was divided into 30-s segments. Response rates, HR and BP in corresponding segments of each fixed interval were accumulated over the

rently with the avoidance schedule. Under the FI 600-s schedule, the first response to occur after 600 s had elapsed produced a 5 mA shock and the 60-s timeout. When an increasing rate of responding developed within each FI cycle, the avoidance schedule was eliminated and then the FI 600-s schedule of shock presentation was the only schedule in effect. When responding had stabilized under FI 600 s, the duration of the FI was progressively decreased. Each duration was in effect for five successive sessions, which established relatively stable performances assessed by visual inspection of the data. The number of shocks obtained each session was kept constant; therefore, sessions varied in length depending upon the FI value under study. After exposure to the lowest FI value in the series, the duration was increased again to one or more of the values previously studied to ensure reliability of effects. Each experimental session was preceded and followed by a 15-min period when the chamber was dark and responses had no programmed consequences.

Blood pressure, heart rate and responding were recorded continuously on the polygraph and responding was recorded on cumulative response recorders. Average rates of responding (responses per s) during FI cycles, as well as the total number of responses occurring in each tenth of the FI over the entire session, were recorded. Measures of mean blood pressures and heart rates in segments of the FI were derived from horizontal lines of best fit drawn through polygraph records.

RESULTS

Table 1 presents the mean response rates, blood pressures, and heart rates for each monkey from the last three sessions at each FI duration. The FI schedules maintained the characteristic temporal patterns of increasing rates of responding throughout the FI cycle, as reported in all species studied (e.g., Skinner, 1956). Response rates and patterns were similar to those for squirrel monkeys previously studied under FI schedules of food or

←

12 FI cycles which comprised the session, and average rate of responding, heart rate and blood pressure determined in each segment.

Table 2
Dependence of BP or HR on rate of responding in successive segments of FI cycles

FI (secs)	Measure	S-555		S-556		S-583	
		Overall Mean	Slope	Overall Mean	Slope	Overall Mean	Slope
600	BP	133	0.08	117	2.25	126	13.95*
	HR	245	54.48*	275	25.24*	214	25.99*
337	BP	132	5.89*	120	-2.89	116	8.02*
	HR	273	50.75*	285	13.16*	256	27.46*
180	BP	127	2.58*	127	1.70*	119	7.34*
	HR	264	47.86*	273	17.64*	300	30.55*

Note. To facilitate direct comparisons, the slopes of the regression lines for BP and HR were divided by the mean BP and HR respectively and multiplied by 100 to give percent.

* Slope significant ($p < .05$)

electric shock presentation (DeWeese, 1977; Kelleher & Morse, 1964, 1968; McKearney, 1968). Figure 1 shows representative changes in responding, blood pressure and heart rate for each of the monkeys at FI 60 s. Rates of responding were usually near zero during the timeout periods, low at the beginning of each FI cycle, and then increased as the FI schedule progressed. Both arterial blood pressure and heart rate levels were lowest at the beginning of the FI cycles, increased as the rate of responding increased during the FI, and then decreased during the timeout periods.

The FI cycles at each of the durations of 60 s or longer were divided into segments and the changes in rate of responding, blood pressure, and heart rate within the FI cycles were compared. Heart rate increased as rate of responding increased for each of the monkeys at all parameters studied (Figure 2). Blood pressure also increased with increasing rates of responding within individual FI cycles at all parameters for S-583, at all except FI 600 and 337 s for S-556, and at all except FI 600 s for S-555. Slopes of these linear regression functions and results of significance tests are shown in Table 2.

There were individual features of the patterns of responding and changes in blood pressure and heart rate that were characteristic of each monkey. For instance, S-555 generally paused for a longer time than the others before initiating responding in each FI cycle, and S-556 made a short burst of responses immediately after each shock delivery. The acute change in blood pressure associated with electric shock delivery varied from monkey to monkey. The amplitude of episodic changes in heart rate was least for S-556 and, while heart rate increased gradually throughout each FI

cycle for S-555 and S-556, it quickly increased for S-583 and then remained the same or decreased slightly as each FI progressed.

Figure 3 shows changes in response rate, blood pressure and heart rate as a function of changes in FI duration. Rate of responding typically decreased for each of the monkeys with increases in FI duration. With S-555, however, response rates increased from the shortest FI duration studied in that monkey (20 s) to the 180-s FI. Over the same domain of FI durations, heart rates also decreased with FI duration for S-583 and S-555. Blood pressure decreased with increases in FI value, most prominently with S-556, with S-583 showing little relation between the variables.

In none of the monkeys was there a consistent change in blood pressure and heart rate levels during the 15-min periods preceding and following each session over the course of these experiments as a function of the exposure to the various schedules of electric shock presentation. The mean blood pressures ± 1 S.D. recorded during these control periods were 125 ± 10 , 122 ± 8 , and 119 ± 6 for S-555, S-556 and S-583, respectively, and the mean heart rates ± 1 S.D. recorded during these periods were 228 ± 36 , 269 ± 21 and 245 ± 26 , respectively.

DISCUSSION

At many schedule durations, blood pressure and heart rate usually increased as rate of responding increased within the FI cycle. As overall rates of responding were increased by decreasing the FI duration from 600 to 60 s, heart rates increased in all of the monkeys and blood pressure increased in 2 of the 3. At all

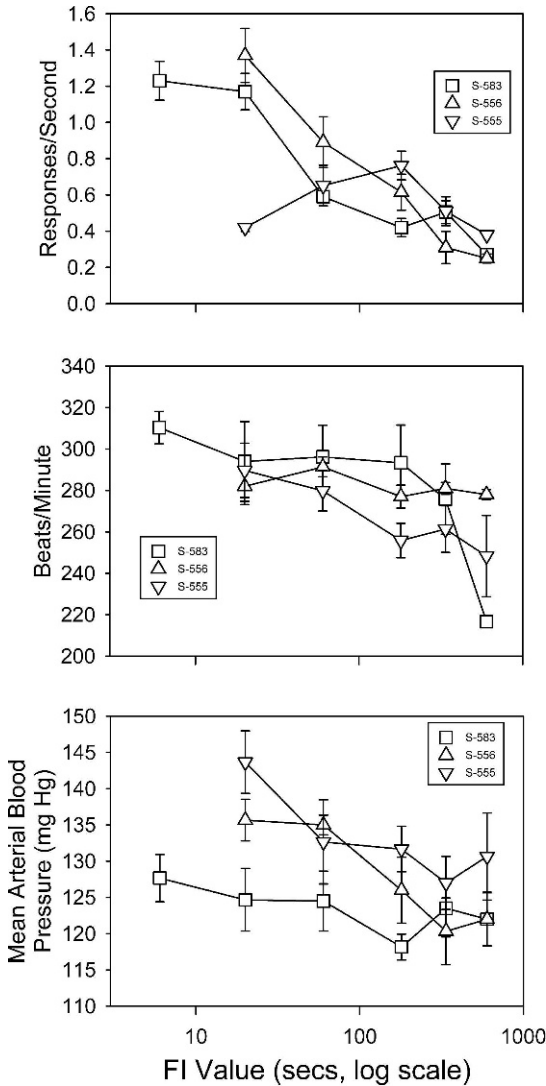


Fig. 3. Changes in response rate, heart rate and blood pressure as a function of FI cycle length. Data are means of the last three sessions (with SEM) obtained. Duplicate values obtained with replications of particular FI durations were averaged for this graph.

parameters studied, there was a direct relationship between changes in response rate and changes in heart rate within FI cycles. At the short FI durations a direct relationship between response rate and mean blood pressure within FI cycles was also clear.

The direct relationship between increases in response rate and increases in blood pressure and heart rate within FI cycles observed in the present experiments are consistent with the

episodic changes in blood pressure and heart rate previously observed under FR schedules of stimulus-shock termination and FR schedules of food presentation (Herd et al., 1969; Kelleher et al., 1972, 1974; Morse et al., 1971). The episodic changes in blood pressure and heart rate during FI cycles are different, however, from those observed under FI schedules of stimulus-shock termination (Herd et al., 1969; Morse et al., 1971). Under FI 120-s or FI 240-s schedules of stimulus-shock termination, blood pressure was highest in the absence of responding and then fell slightly as the rate of responding increased in individual FI cycles. Differences in schedule duration do not appear to account for these differing episodic patterns in blood pressure under FI schedules, as a wide range of FI durations was studied in the present experiment. The event maintaining FI responding in these experiments (electric shock presentation) is different from that in the previously published studies with FI (stimulus-shock termination). However, FR performances maintained by different events have been shown to be associated with similar episodic changes in blood pressure and heart rate (Kelleher, Morse, & Herd, 1976). Thus, whether the maintaining event has an influence on the observed episodic patterns in blood pressure may depend on the schedule of reinforcement. It remains possible that periodic electric shock deliveries produced a temporally regular stimulus that served as a basis for Pavlovian temporal conditioning. In addition, unpublished studies have focused on the role of adjunctive behavior as a factor influencing these different episodic patterns of elevated blood pressure and heart rate observed under FI schedules.

The average resting blood pressure and heart rate levels in these monkeys at the completion of these experiments were within the normal range previously determined for squirrel monkeys (Grose et al., 1971; Herd et al., 1969; Kelleher et al., 1972). Although long-term exposure to appropriate parameters of operant schedules has produced chronic elevations in arterial blood pressure in squirrel monkeys (Benson et al., 1969; Herd et al., 1969), the exposure to an experimental regime of schedules of reinforcement, even when behavior is strongly controlled, does not necessarily cause hypertension in these monkeys. However, average rates of responding

and episodic increases in blood pressure associated with responding were generally lower under FI schedules than those previously observed under FR schedules.

The present studies establish a relationship between activity and elevations in blood pressure and heart rate. This relation was particularly evident for changes in response rate and changes in heart rate within FI cycles. That the relationship was less apparent across the different parameters of the FI schedule is consistent with the complexity of the environmental control over cardiovascular function as noted in the clinical literature (for a review see James & Pickering, 1993). Nonetheless, the present studies point to the environmental control of behavior as a critical factor in modulating cardiovascular function.

REFERENCES

- Benson, J., Herd, J. A., Morse, W. H., & Kelleher, R. T. (1969). The behavioral induction of arterial hypertension and its reversal. *American Journal of Physiology*, *217*, 30–34.
- Clark, L. A., Denby, L., Pregibon, D., Harshfield, G. A., Pickering, T. G., Blank, S., et al. (1987). A quantitative analysis of the effects of activity and time of day on the diurnal variations of blood pressure. *Journal of Chronic Disease*, *40*, 671–681.
- DeWeese, J. (1977). Schedule-induced biting under fixed-interval schedules of food or electric-shock presentation. *Journal of the Experimental Analysis of Behavior*, *27*, 419–431.
- Grose, S. A., Herd, J. A., Morse, W. H., & Kelleher, R. T. (1971). Behavioral hypertension in the squirrel monkey. *Federation Proceedings*, *30*, 549.
- Hake, D. F., & Azrin, N. H. (1963). An apparatus for delivering pain shock to monkeys. *Journal of the Experimental Analysis of Behavior*, *6*, 297–298.
- Herd, J. A., Morse, W. H., Kelleher, R. T., & Jones, L. G. (1969). Arterial hypertension in the squirrel monkey during behavioral experiments. *American Journal of Physiology*, *217*, 24–29.
- James, G. D., & Pickering, T. G. (1993). The influence of behavioral factors on the daily variation of blood pressure. *American Journal of Hypertension*, *6*, 170S–173S.
- Kario, K., Schwartz, J. E., & Pickering, T. G. (1999). Ambulatory physical activity as a determinant of diurnal blood pressure variation. *Hypertension*, *34*, 685–691.
- Kelleher, R. T., Gill, C. A., Riddle, W. C., & Cook, L. (1963). On the use of the squirrel monkey in behavioral and pharmacological experiments. *Journal of the Experimental Analysis of Behavior*, *6*, 249–252.
- Kelleher, R. T., & Morse, W. H. (1964). Escape behavior and punished behavior. *Federation Proceedings*, *23*, 808–817.
- Kelleher, R. T., & Morse, W. H. (1968). Schedules using noxious stimuli. III. Responding maintained with response-produced electric shocks. *Journal of the Experimental Analysis of Behavior*, *11*, 819–838.
- Kelleher, R. T., Morse, W. H., Goldberg, S. R., & Herd, J. A. (1974). Behavioral modulation of the cardiovascular effects of 1-norepinephrine in the squirrel monkey. *Journal of Pharmacology and Experimental Therapeutics*, *191*, 269–283.
- Kelleher, R. T., Morse, W. H., & Herd, J. A. (1972). Effects of propranolol, phentolamine and methyl atropine on cardiovascular function in the squirrel monkey during behavioral experiments. *Journal of Pharmacology and Experimental Therapeutics*, *182*, 204–217.
- Kelleher, R. T., Morse, W. H., & Herd, J. A. (1976). A pharmacological analysis of behaviorally-induced changes in cardiovascular function in the squirrel monkey. In: D. I. Mostofsky (Ed.), *Behavior control and modification of physiological activity* (pp. 314–338). Englewood Cliffs, NJ: Prentice-Hall Inc.
- McKearney, J. W. (1968). Maintenance of responding under a fixed-interval schedule of electric shock presentation. *Science*, *160*, 1249–1251.
- Morse, W. H., Herd, J. A., Kelleher, R. T., & Grose, S. A. (1971). Schedule-controlled modulation of arterial blood pressure in the squirrel monkey. In: H. D. Kimmel (Ed.), *Experimental psychopathology: recent research and theory* (pp. 147–164). New York: Academic Press.
- Pickering, T. G., Harshfield, G. A., Kleinert, H. D., Blank, S., & Laragh, J. H. (1982). Blood pressure during normal daily activities, sleep and exercise. *Journal of the American Medical Association*, *247*, 992–996.
- Skinner, B. F. (1956). A case history in scientific method. *American Psychologist*, *11*, 221–233.

Received: August 26, 2003
Final Acceptance: July 20, 2009