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13 ABSTRACT

Three rhesus monkeys were implanted with ECG telemeters and performed a calisthenic exercise requiring complete arm extension above their heads and below their knees. The animals were unrestrained and confined to a large box. The exercise was programmed to produce food pellets on various reinforcement schedules. Heart rate samples were obtained both during sleep and high rates of activity. Two animals provided exercise data and one animal provided data without the exercise task. Highest heart rates were seen in the two exercise animals. No differences in maximum heart rates were related to the different reinforcement schedules. In most instances heart rates were twice those of resting heart rates for 5 minutes or longer. Occasionally, heart rates were three times the resting rates for at least 2 minutes. The resting heart rates from all three animals were generally lower than those reported in previous literature as normal rates in the rhesus. During the fixed-interval reinforcement schedule there was a correlated increase in heart rate along with the increase in response rate.

14 KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Heart rate						
Animal behavior						
Exercise						
Telemetry						
Reinforcement schedules						

RHESUS MONKEY HEART RATE DURING EXERCISE

John de Lorge and John S. Thach, Jr.

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SUMMARY PAGE

THE PROBLEM

During orbital spaceflight unrestrained animals will be in a weightless state, which should lead to a decrease in their muscle tone. Exercising animals while in a weightless state may compensate for the debilitating effect of a lack of gravitational forces on muscle tone and ameliorate the effect. Determining an adequate amount of exercise, however, is an unaccomplished task. Assuming that a 100 per cent increase in the resting heart rate of an animal through exercise is an appropriate amount, the problem is to develop the technique to achieve such an increased heart rate. The present experiment describes various schedules of reinforcement and their relation to heart rates of rhesus monkeys during exercise.

FINDINGS

All the reinforcement schedules produced 100 per cent or higher increments in the heart rates of the monkeys during exercise. Resting heart rates were generally much lower than those previously reported, which was attributed to the lack of physical restraint of the monkeys during recording.

ACKNOWLEDGMENTS

INTRODUCTION

Recent NASA experiments involving nonhuman primates in spaceflight have demonstrated varied effects of weightlessness (1). Some of these effects might be attributed to either the gross restraint of the animals or to the restriction of physical activity. To circumvent such possibilities, some future spaceflights may contain unrestrained animals; i.e., free-floating in the space environment. Even in free-floating animals, however, the antigravity muscles are not used as much as they are in Earth-bound animals. The lack of continued exertion may be responsible for some of the debilitating effects of weightlessness. One remedy for this problem might be to require an animal to perform calisthenics occasionally during the day. The exercise should: 1) be designed to exert the antigravity muscles as much as possible, 2) be transferable to a weightless condition, and 3) help to maintain the animal's physical health. One such exercise procedure for rhesus monkeys has been explored (5), and variations of that procedure are examined in the present study.

Generally, the best indicator of physical health in humans is excellent cardiovascular health, as measured by oxygen consumption during exercise and immediately thereafter (3). A correlate of oxygen consumption is heartbeat of an animal during exercise and rate of recovery to lower heartbeats thereafter. The earlier study of an exercising monkey (5) failed to explore the relationship between the exercise task and the animal's heartbeat. The present study was designed to measure the rate of heartbeat in monkeys while they performed an exercise and to compare it with the rate of heartbeat while the animals were not exercising. The objective was to verify that the exercise would cause the animals to consistently double their heart rate for various periods. If the rhesus heart rate is similar to that of humans, a doubling of heart rate and fast recovery to resting heart rate should be an indication of good cardiovascular health (3).

PROCEDURE

SUBJECTS

Two male and one female rhesus monkey (<u>Macaca mulatta</u>) were the experimental subjects. The animals were between 5 and 6 years of age at the start of the experiment. The female, 2334, and one male, 4Z8, were experimentally naive. The other male, 0Z0, had participated in a previous "exercise" experiment.

APPARATUS AND METHOD

The experimental box was made of Plexiglas and measured 38 inches high by 33 inches deep by 19 inches wide. The floor was of plastic grids with a waste tray beneath it. Access to the box was gained through a guillotine door on the front wall. The rear wall contained the response manipulanda, reinforcement receptacles, and stimulus lights. The exercise levers were four 1/2-inch diameter metal rods and projected approximately 1 inch from the wall. Two of the levers were located 1-1/2 inches from the top of the

box and centered on the wall approximately 5 inches apart; the other two were centered on the wall 5 inches apart and 1-1/2 inches from the grid floor. The top levers were actuated by pressing up and the bottom levers were actuated by pressing down. Stainless-steel tubes 3/4 inch in diameter, split lengthwise and blocked at one end, served as food and water receptacles. The water receptacle was centered on the rear wall 11 inches from the grid floor with the water reinforcement button centered 2 inches beneath it. The food receptacle was also located in the middle of the rear wall 3 inches beneath the water button. The food reinforcement button was 2 inches beneath the food receptacle. Both food and water receptacles projected approximately 1-1/2 inches into the box. Food reinforcement was a 0.60-gram Purina Monkey Chow Pellet and water reinforcement was 2.0 cc. The stimulus lights were a blue jewel pilot light centered on the rear wall approximately 1-1/2 inches from the top and another blue light centered between the lower exercise levers approximately 1-1/2 inches from the grid floor.

The experimental box was placed in a large metal chamber that was sound attenuated, temperature insulated, and contained speakers for white masking noise and fans for air circulation. The ceiling of this metal chamber contained the houselights and a glass port over which was mounted a television camera for remote observation of the animal. Two photocell beams projected through the walls of this chamber and provided indications of general activity when they were interrupted. Feeding and watering devices were attached outside to the top of the metal chamber.

A dipole antenna was arranged around the experimental box and connected through conduit to a receiver, amplifier, and demodulator circuit located in a shielded container on the top of the large metal chamber. The telemetry system was similar to that developed by NASA Ames Research Center (4). Recording and control equipment were located in an adjacent room.

Electrocardiogram transmitters provided by NASA Ames were chronically implanted in the monkeys in the following manner: typically, a midline abdominal incision was made, followed by an incision in the subcutaneous and muscle layers, which allowed visual observation of the peritoneum. The transmitter was placed in the deep muscle layers beneath the rectus abdominis muscle sheath. Two incisions, on the left and right lateral thorax, were made and the ribs exposed. The two ECG leads were passed through the subcutaneous tissue by using a "crochet hook" instrument. The periosteum was then incised on the right third and left fifth ribs for a distance of 1 cm and elevated to the anterior and posterior margins. The leads were incised at the proper length, tied in figure-eight knots at the terminal end, and attached beneath the periosteum with three simple interrupted 3-0 cardiovascular silk sutures. Muscle layers and subcutaneous tissue were closed in a simple continuous pattern with 2-0 chromic gut, and a subcuticular closing of the skin was accomplished with the same suture material. The entire operation, including anesthesia, took approximately 2 hours.

After surgical recovery, the animals began training, during which time they were maintained at 90 per cent of their ad libitum body weight. They were introduced to the experimental box and trained to push the food button whenever a 13.5-Hz clicker sound,

the discriminative stimulus (S^D) for food, was present. The animals were then trained to push the two top exercise levers up simultaneously and then to push the two bottom levers down simultaneously in either order. This task comprised the exercise response. The stimulus light near the pair of exercise levers that were to be pushed next was always illuminated. A chain of either top-bottom or bottom-top lever presses produced the S^D. In the presence of S^D a food-button response delivered a pellet of monkey chow and terminated S^D. The number and rate of exercise responses required for food pellet delivery were varied throughout the duration of the experiment, and these response requirements are referred to as schedules of reinforcement (6).

The initial schedule was a differential reinforcement of high rate (DRH), which required the animals to produce an exercise response within a fixed period of time; typically, the DRH time was 5 seconds. With further increases in the number of sessions the fulfillment of the DRH requirement sometimes produced S^D and food availability, and sometimes a different stimulus, a 49.5-Hz clicker of 1-second duration. In the presence of this latter stimulus (S^Δ), food-button depressions were never reinforced. The ratio of the S^D frequency to S^Δ frequency varied randomly and was manipulated during the experiment in attempts to increase response rate. Initially, the DRH schedule alternated with a schedule of water reinforcement; i.e., a period of DRH schedule was in effect for 15 minutes followed by a 5-minute period in which the animal could obtain the 2.0-cc allotment of water for each water-button press. During the 5-minute water period, a 1-Hz click was presented. Water was not available during the 15-minute DRH schedule component nor during the other schedules of reinforcement.

The next schedule of reinforcement was an animal-initiated fixed interval (FI). A fixed interval of time, typically 1 minute, elapsed following an exercise response, and the first exercise response that occurred after the interval timed out was reinforced with S^D. Each exercise response produced either S^D or S^Δ. Later sessions on the FI did not require the animal's response to start the interval timing. Instead, the FI began when the experimental session began and after each reinforcement.

The final schedule required the animal to emit a fixed number of exercise responses to produce food reinforcement. This schedule was set at a fixed ratio (FR) of 10; 10 responses were necessary to produce S^D and, hence, food availability. The ratio requirement was increased to 40 near the end of the experiment. During a portion of the experiment under the FR schedules, exercise responses that did not produce S^D did produce S^Δ.

Experimental sessions occurred daily except on weekends and generally lasted 4 hours. The animals were transported in an enclosed cart between the colony building and the research building. The body weights of the animals were varied from 80 to 100 per cent of their ad libitum weights. During experimental sessions ECGs were recorded whenever possible, depending upon signal reception, animal activity, and the animal's location within the experimental box. Heart rates were determined from the ECG recordings.

RESULTS AND DISCUSSION

The recorded heartbeat rates from the three monkeys particularly during resting were lower than those previously reported as normal rates in rhesus monkeys (8, 13, 14). However, virtually all the previous studies had been conducted with restrained or anesthetized animals. Table I presents a summary of the heartbeat data obtained during our experiment. The experiment was interrupted numerous times because of transmitter failure; with one exception, failure was due to broken leads on the transmitter. Each failure required that the transmitter be removed and another implanted. One transmitter had to be relocated because it had broken through the muscle layers. Generally, an interruption of approximately 1 month occurred with each transmitter replacement. The highest heart rates were seen in 4Z8 and 0Z0 who were trained on the exercise task. Differences in heart rates were not related to the different schedules of reinforcement imposed. In most instances heart rates were double those of resting heart rates for 5 minutes or longer. Occasionally, heart rates were triple those of resting heart rates for 2 minutes continuously. When heart rates were triple their resting rates, continuous recording was unreliable due to difficulty in receiving the transmitted ECG signals.

Table I

Heart Rates as a Function of the Experimental Conditions

Subject	Number of Trans- mitter Implants	Range of Heart Rate (BPM)		
		Resting	Pacing	Exercise
2334	3	70-120	150-200	
4Z8	3	76-180		150-250
0Z0	5 (1 relocated)	72-150		140-270

As 2334 never acquired the exercise task, she was a control subject. However, numerous heartbeat samples were obtained from this animal during sitting and pacing from end to end in the box. Her resting heart rate ranged from a low of 70 beats per minute (BPM) to 120 BPM, and her rate during pacing activity ranged from 150 BPM to a high of 200 BPM. These data were consistent and no noticeable trends were observed in 48 training sessions.

The training of 4Z8 and 0Z0 on the exercise task was accomplished within five or six sessions. The response was relatively difficult for the rhesus monkey because the top levers had to be pressed upward, and the monkeys invariably would hang on the levers during

4

training. The top response after training was completed typically consisted of a grasping jerk downward, followed by a releasing press upward. The extra effort required on the top levers produced a seemingly more difficult task than originally intended, and the greater degrees of continuous exercise performance seen in an earlier study (5) were not obtained.

Figure 1 contains a section (A) of a cumulative record, illustrating performance of 4Z8 on a DRH 10-second schedule wherein he was required to complete an exercise response within 10 seconds to produce reinforcement. The exercise component is indicated in each set of records with the lower horizontal line by downward deflections of the event pen. During the portion of record denoted by A, each exercise component was in effect for approximately 12 minutes; in records B and C each exercise component was in effect for 15 minutes. The water component was of 5-minutes' duration in all three records and is indicated by upward deflection of the event pen. The response pen stepped each time when either a top or bottom response occurred. Bottom responses were approximately four times more frequent than top responses, and the cumulative record shows all responses within the DRH contingency but does not give an indication of alternating responses alone. The B portion of Figure 1 shows later performance on a DRH 5-second schedule wherein, on the average, 40 of 100 completions resulted in food reinforcement. Again, more bottom responses occurred than top responses, but the overall behavior was pause and run as seen earlier. This pattern of responding was predominant whenever the DRH schedule was in effect. The C portion of Figure 1 illustrates behavior wherein, on the average, 1 of 10 DRH 5-second completions resulted in reinforcement. Response rates were higher in this condition, but the pattern of responding previously seen still prevailed.

Figure 2 illustrates similar performance for 0Z0 on various DRH 3-second schedules. Record A shows behavior when each DRH 3-second completion was reinforced. Record B was produced when, on the average, 2 of 10 completions were reinforced; and record C was produced when 1 of 10 DRH 3-second completions was reinforced. The response rates of 0Z0 seem lower than those of 4Z8, but 0Z0 alternated his top and bottom responses each time and thereby produced a higher density of reinforcement than did 4Z8. Yet, the pause-and-run response pattern was also predominant with 0Z0.

Samples of ECG recordings for the three animals during sitting and activity are shown in Figure 3. These records were not taken during the lowest or highest rates observed but are merely some of the more reproducible recordings; however, they are comparable to those obtained with restrained or anesthetized animals (8, 11, 12). The reversed waveform for 0Z0 and 2334 was due to a reversal of the ECG leads during implantation. An ECG anomaly can be observed in the records of 4Z8 but the records appear to be normal for the other two animals.

After observation during the DRH schedule, the investigators were interested in observing the development of heart rate as responding occurred from one reinforcement to another; therefore, the animals were put on the fixed interval schedule. Figure 4 illustrates typical cumulative records during the FI 1-minute schedules. Only alternating responses stepped the response pen in these records. Food reinforcement is indicated by
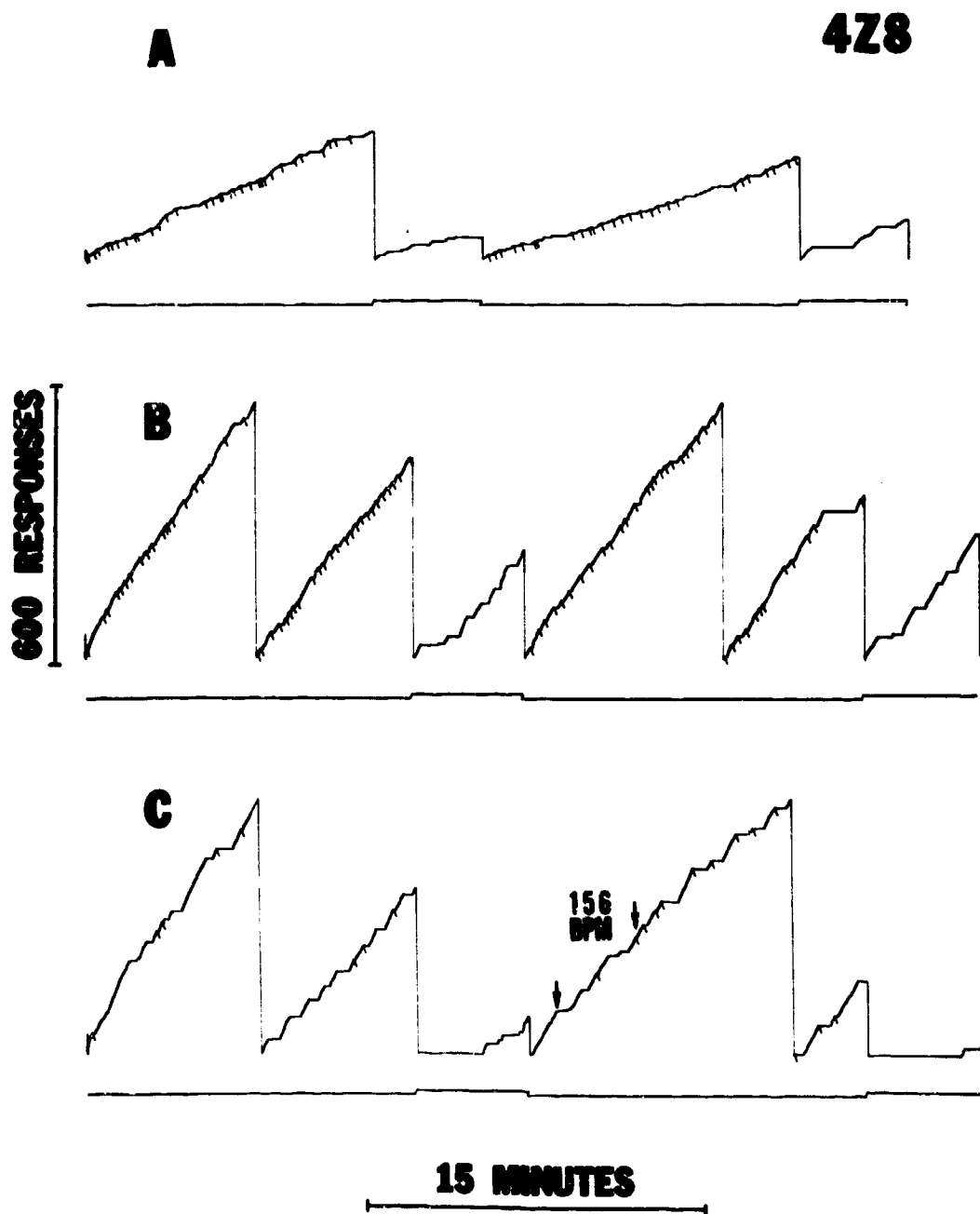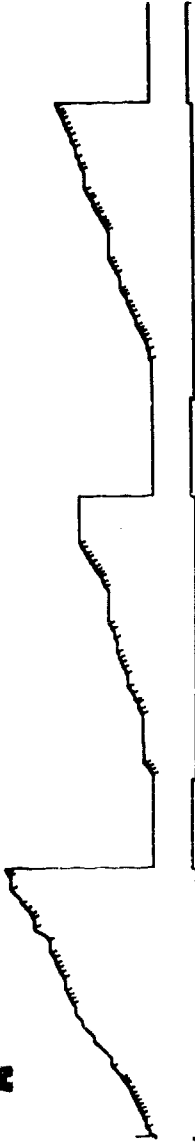
5

A

4Z8

B

600 RESPONSES

C

156
BPM

15 MINUTES

Figure 1

Representative cumulative records of 4Z8's exercise behavior on various DRH schedules. Record A denotes a DRH 10-second schedule. Record B denotes the schedule wherein 40 per cent of DRH 5-second completions produced food reinforcement. Record C denotes the schedule wherein 10 per cent of DRH 5-second completions produced food reinforcement. A sample of the average heart rate during a specifiable performance is indicated in Record C. The response pen reset whenever a component terminated or whenever it reached the top of the record. The straight horizontal line in each set of records is the event pen line; when the line is down, it indicates the exercise component, when up, it indicates the water component. Reinforcement is denoted by the diagonal hash marks on the response lines.
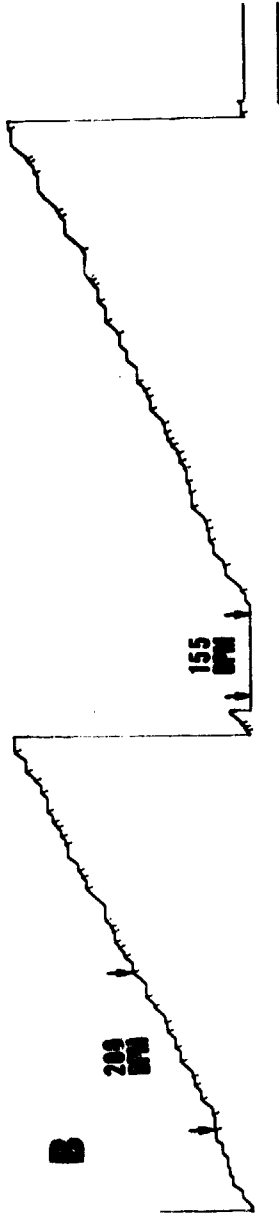
6

OZO

A

B
200
BPM
155
BPM

C
100
BPM

600 RESPONSES
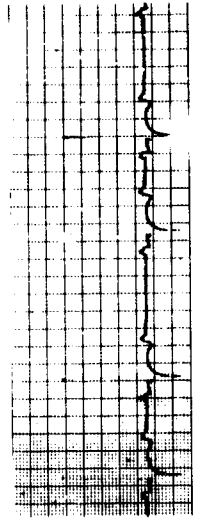
20 MINUTES

Figure 2

Representative cumulative records of OZO's exercise behavior on various DRH schedules. Record A denotes a DRH 3-second schedule. Record B denotes a schedule in which 20 per cent of the DRH 3-second completions produced food reinforcement, and Record C denotes the same schedule wherein 10 per cent of the completions produced reinforcement. Samples of average heart rates during specifiable behaviors are indicated in records B and C.
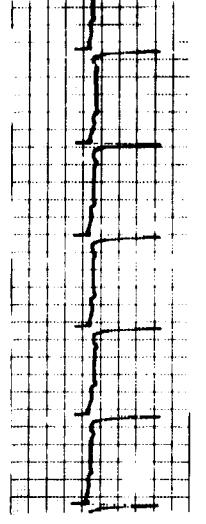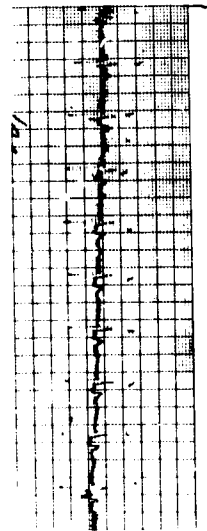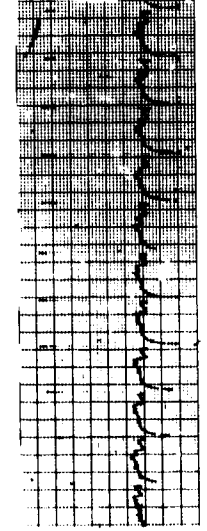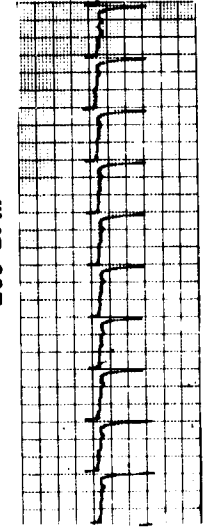
LOW

80 BPM
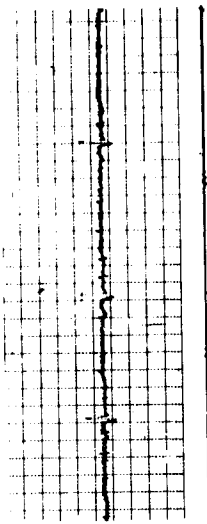
100 BPM

120 BPM

HIGH

200 BPM

220 BPM

200 BPM

2334

428

020

Figure 3

Three-second samples of the electrocardiograms of three rhesus monkeys (paper speed = 50 mm/second).
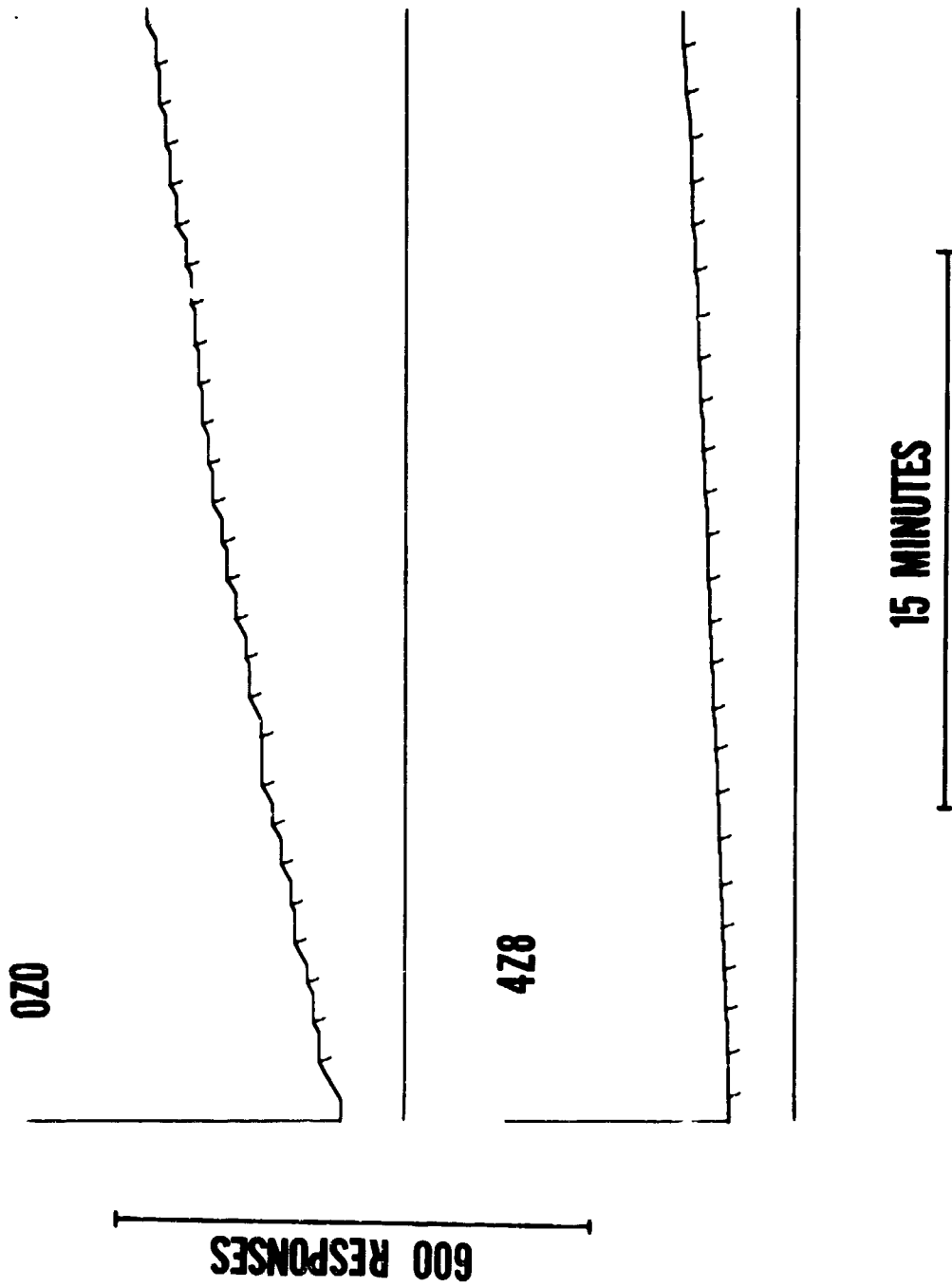
8

OZO

4Z8

15 MINUTES

600 RESPONSES

Figure 4

Cumulative records of OZO and 4Z8 during the FI 1-minute schedule of reinforcement. The response pen stepped each time an alternation on the top and bottom handles was made.

diagonal hash marks. As seen in the records of both animals, no responding occurred immediately after a food reinforcement. As the interval approached temination, responding occurred more frequently until reinforcement was produced. The record of 4Z8 is somewhat different because of an added contingency. After a reinforcement, timing of the 1-minute interval did not begin until the animal's first top or bottom response. His response rates, therefore, were lower than those for 0Z0, and the intervals between reinforcements were longer, as shown in Figure 4.

Heart-rate samples were obtained simultaneously with the FI 1-minute behavior. Figure 5 shows average heart rates for 0Z0 and 4Z8 during 6-second periods from one reinforcement to the next. The graph for 0Z0 is the mean of three samples and that of 4Z8 is the mean of five samples. 0Z0's samples were obtained during an FI 1-minute schedule. Those of 4Z8 were obtained during the self-initiated FI 1-minute schedule; hence, 4Z8's records cover more than 60 seconds. The curves in Figure 5 demonstrate a relationship between heart rate and responding. That is, as responding accelerated to the next reinforcement, heart rate also accelerated, and heart rate decelerated immediately after a reinforcement when the animal was not performing the exercise response.

When the animals were placed on the fixed ratio schedules, FR 10 up to FR 40, a variety of equipment problems produced delays in continuing the experiment. Finally, after a few records during FR behavior of the ECG were obtained, the experiment was terminated. During the larger FR contingencies the animals seldom responded and produced extraordinarily long pauses following reinforcement. Moreover, heart rates during rest and responding were no different from those obtained in the earlier portions of the experiment.

CONCLUSIONS

The heart rates produced in the present study were generally much lower than those obtained in many previous studies. This outcome was interpreted as a result of the lack of restraint on the experimental subjects and the long period of adaptation to the experimental environment. Virtually all other previous studies have used either anesthetized or restrained animals, and many studies report as normal, heart rates that are as high as the highest heart rates we obtained. Because of the telemetry system and recording devices used, we could not always ascertain the length of time the heart rates during exercise actually remained at their highest levels; and only occasionally when samples were taken, did we observe the highest heart rates for more than 2 minutes. However, on many occasions the heart rates were at least twice the resting rate for as long as 5 minutes. In other words, it was relatively easy to exercise these rhesus monkeys vigorously enough to double their heart rates rather frequently during a daily experimental session for periods longer than 5 minutes. The data, as shown in the fixed interval records, show that these heart rates were probably due to the muscular activity itself and not to autonomic factors alone. Although it is known that increases in heart rate accompany responding on reinforcement schedules (2), other investigators also conclude that these changes are primarily due to motor activity (9, 10, 15). Nevertheless, there is an investigation that shows
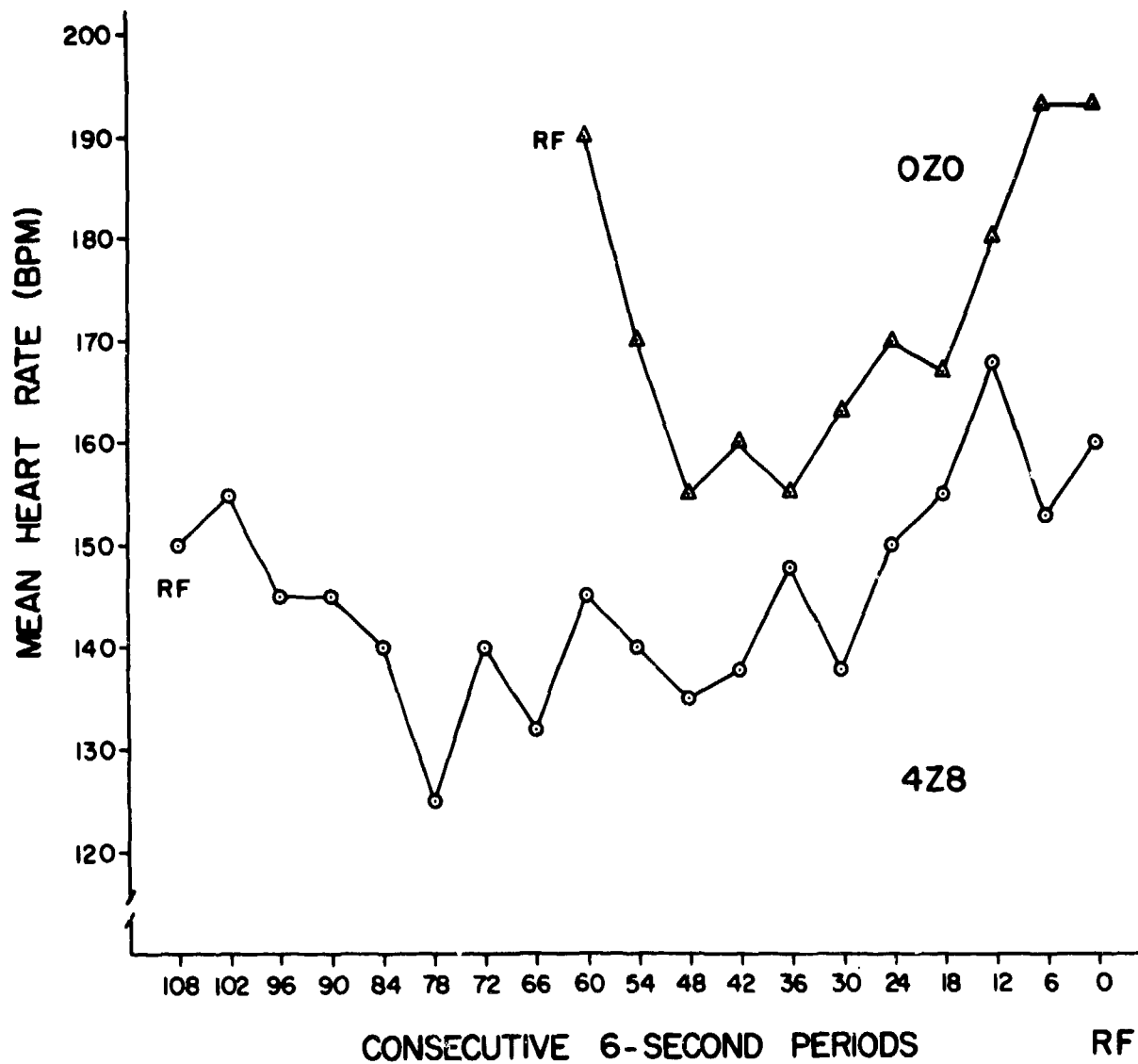
10

Figure 5

The relationship between heart rate and time during the FI schedules. 0Z0 was on an FI
1-minute schedule and 4Z8 was on a self-initiated FI 1-minute schedule. Reinforcement
occurred at the start of the curves and at the end of the 6-second periods denoted by "0"

heart-rate changes due to the emotional responses of the animal, especially when the reinforcement schedules have aversive consequences (7).

All schedules used in this study appeared to elicit similar heart rates. None of the schedules, however, was as effective in producing relatively high stable exercise rates as the random ratio schedule employed in an earlier study (5). The fault may not be with the schedules alone but is probably due to the difference in manipulanda between the two studies.

Although all the implants were originally intended to last for long durations, they consistently failed due to lead breakage which was probably caused by this specific exercise response.

There is no way we can verify the good physical health of these animals. Ergo, we cannot conclude that the exercise regimen was responsible for maintaining their good health or that it would work in a zero-g condition. However, we have demonstrated a procedure for exercising rhesus monkeys and simultaneously have shown that such exercise will reliably produce double resting heart rates for relatively prolonged periods and triple resting heart rates for relatively short periods.

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