Lifelong Hyperarousal in the Spontaneously Hypertensive Rat Indicated by Operant Behavior

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Abstract—Instrumental conditioning techniques were used to obtain objective evidence of differences in behavioral arousal between the spontaneously hypertensive rat (SHR) and the normotensive ancestral Wistar Kyoto (WKY) strain. Subjective emotionality ratings previously indicated that the genetically hypertensive rats were more active and aggressive than their normotensive cousins. In a lengthy series of operant conditioning sessions using a small number of adult female SHR and WKY rats, hyperarousal in the SHR was confirmed by their significantly higher response outputs on either response contingent or time contingent schedules of reinforcement. Conditioned emotionality tests during this series of experiments also suggested hyperarousal and aggressiveness in the SHR, since the fear-conditioned stimulus suppressed bar-pressing in the SHR much less than in the WKY. Further experiments with young prehypertensive SHR rats provided the same evidence of hyperresponsivity in the SHR compared to the WKY strain. Furthermore, these young SHR failed to develop hypertension by the end of the study (14 weeks of age), while their nonconditioned SHR cousins had become clearly hypertensive by the same age. This suggests that factors related to the conditioning methods modified the development of high blood pressure in this animal model of essential hypertension.

SUBJECTIVE RATING TECHNIQUES were used in an earlier study (Schaefer, Brackett, Gunn, and Wilson, 1978) to demonstrate activity and emotionality differences in genetically-related hypertensive and normotensive rats of the Okomoto and Aoki (1963) breed. The present study was conducted to gather more objective evidence of arousal differences between the spontaneously hypertensive rat (SHR) and their normotensive ancestral strain, the Wistar Kyoto (WKY) rat. Because we previously found the SHR to be more active and aggressive than the WKY, we expected the SHR to bar-press significantly more than the WKY during operant conditioning.

Experiment 1

The first project consisted of an extensive study of a small number of animals over a period encompassing much of the rat's adult lifetime. Instrumentally conditioned bar-pressing was studied using both fixed ratio and fixed interval schedules of reinforcement. The motivation to bar-press was maintained first by food deprivation and later by water deprivation.

Methods and Materials

The subjects were female rats (5 SHR and 6 WKY) obtained from the Hypertension Division's rat colony. The animals were approxi-
mately 8 months old at the start of the study which spanned a 10-month period. During this time the rats were housed individually in metal cages with food and water available ad lib except during the intervals of behavioral testing. Body weights were recorded daily during all deprivation periods.

All operant conditioning was conducted in a BRS/LVE Rodent Test Cage enclosed in a sound-attenuating chamber. The Skinner box was equipped with a single response lever and a dipper mechanism with which liquid reinforcers (16% dextrose solution or water) were delivered to the subject in 0.02 cc amounts.

**Phase 1**

The rats were gradually reduced to 80% of their ad lib body weights by providing a limited daily ration of food pellets with unlimited access to water. Bar-pressing behavior was established by manual shaping with sugar solution reinforcers in daily 15 minute training sessions. After establishing the operant response using continuous reinforcement, the ratio of response reinforcements in daily training sessions was gradually shifted to a fixed ratio—8(FR-8) schedule.

Following five days of FR-8 training, a conditioned emotional response (CER) test was begun. First, the rats were habituated to the neutral stimulus (light flashes) during three additional days of FR-8 training. In each habituation session three 30 second periods of light flashes (2 per second at an intensity setting of 4) were presented using a Grass PS-2 photostimulator. For two consecutive days after these habituation sessions the fear response was conditioned by pairing the flash presentations with unavoidable tail shock (0.5 second pulses of 1 ma. current for 5 seconds) while the rats were immobilized in a plastic restrainer.

The CER was then measured in the final two sessions of Phase 1 when the rats were again exposed to the light flashes in the operant chamber (without the application of electric shocks). The disruptive effect of each flash series in the habituation and the CER sessions was measured by calculating suppression ratios (base period presses minus flash period presses/base period presses). A suppression ratio of 1.0 indicated total suppression of responding while zero indicated a lack of effect of the stimulus on the operant behavior.

**Phase 2**

Six weeks after the completion of Phase 1 the same subjects were tested again. This time a longer training period was used to ensure that the bar-pressing behavior of each group had stabilized at its asymptotic level under the FR-8 schedule. Following the response stabilization period, a new CER test was administered. Due to the previous exposure of these subjects to the conditioned stimulus, no habituation sessions were provided prior to CER retraining. To increase the likelihood of response suppression in this retest, the CER training was conducted inside the Skinner box this time. A single session of CER training was provided in which three series of flashes were presented during bar-pressing, with each series followed by electric shock (0.5 sec pulses of 1 ma. intensity for 5 sec) administered through the grid floor. This conditioned suppression session was followed by seven sessions of CER testing in which no shocks were delivered. Finally, Phase 2 was completed with two sessions in the Skinner box without presentation of the conditioned stimulus.

**Phase 3**

Six months after the completion of Phase 2 the rats were restested using water deprivation instead of food deprivation to see if the same group differences would be obtained under different motivational conditions. A 23.5 hour water deprivation schedule was employed in which free access to water was provided in the home cages for 30 minutes each day following behavioral testing. Food pellets were available ad lib.

An FR-8 schedule of reinforcement was used as in Phases 1 and 2 for the first seven sessions of operant conditioning using water rewards. Then, after a two day break in training, the reinforcement schedule was shifted from a response contingency to a time contingency. For five days a fixed interval—15 seconds (FI-15) reinforcement schedule was used. Finally, after another two day break, four sessions of training with an FI-30 schedule completed Phase 3, and the rats were killed.

**Results and Discussion**

The most notable result was that the SHR displayed 50 to 100% more bar-pressing behavior than the WKY over the entire ten month period studied (Fig. 1). The hyperresponsiveness of the SHR was equally striking whether the behavior was motivated by food deprivation (Phases 1 and 2) or water deprivation (Phase 3). There was no indication that the response output of the WKY would reach that of the SHR if additional training had been provided. Indeed, the results of all three phases of testing revealed a marked tendency for practice to increase the group differences in operant responding.

Figure 2 displays the mean body weights of the