Behaviorally Selective Cardiovascular Hyperreactivity in Spontaneously Hypertensive Rats
Evidence for Hypoemotionality and Enhanced Appetitive Motivation

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SUMMARY Spontaneously hypertensive rats (SHRs) and Wistar Kyoto controls (WKYs) were chronically instrumented for computer-assisted recording of arterial pressure (AP) and heart rate (HR) and examined during classically conditioned emotional (fear) reactions or during the performance of a repertoire of natural behaviors, including eating, drinking, grooming, exploring, and resting. The purpose of the study was to determine whether exaggerated cardiovascular reactivity in SHRs during aversive stimulation: 1) can be coupled to stimuli that before conditioning elicited negligible changes in AP and HR; 2) is accompanied by a proportionately enhanced level of emotional arousal; and 3) is specific to aversive emotional arousal or is also present during natural behaviors. The conditioned blood pressure response (in mm Hg) was greater (p < 0.01) in SHRs (peak response, 20 ± 3) than in WKYS (peak response, 7 ± 1). While the conditioned pressure response was accompanied by bradycardia in WKYS (peak response, -13 ± 5 bpm), tachycardia was present in SHRs (peak response, 17 ± 7 bpm). Behavioral tests indicated reduced emotional reactions in SHRs: SHRs showed less (p < 0.05) drink suppression (75 ± 17 sec) than WKYS (111 ± 10 sec) and SHRs showed less (p < 0.01) suppression of exploratory activity (201 ± 40 sec) than WKYS (499 ± 70) in the presence of the conditioned emotional stimulus. The magnitude of blood pressure changes (in mm Hg) above resting baseline was not different in SHRs and WKYS during eating (SHR, 28 ± 2; WKY, 14 ± 2), or exploring (SHR, 17 ± 2; WKY, 18 ± 2), but was greater (p < 0.01) during drinking in SHRs (48 ± 4) than in WKYS (32 ± 2). The amount of time (sec) spent grooming (SHR, 55 ± 23; WKY, 38 ± 15) and exploring (SHR, 187 ± 33; WKY, 165 ± 42) did not differ between the strains, but SHRs spent more time (p < 0.01) eating (SHR, 1103 ± 88; WKY, 800 ± 114) and drinking (SHR, 115 ± 18; WKY, 32 ± 12). These findings demonstrate that: 1) exaggerated cardiovascular reactivity in SHRs is readily coupled through conditioning to otherwise benign stimuli; 2) conditioned cardiovascular hyperreactivity is accompanied by a reduced not an enhanced level of conditioned emotional arousal; 3) cardiovascular hyperreactivity is not specific to aversive arousal but is nevertheless a behaviorally-specific mode of response; and 4) SHRs and WKYS differ in the performance of natural as well as emotional behaviors.

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KEY WORDS  • blood pressure  • natural behavior  • conditioned emotional responses  • spontaneously hypertensive rats  • classical conditioning

ARTERIAL pressure (AP) changes associated with aversive emotional arousal are exaggerated in spontaneously hypertensive rats (SHRs) when compared with strain-matched Wistar-Kyoto controls (WKYS): during the acute or chronic presentation of aversive stimuli, such as electric footshock, cage vibration, loud noises, or bright flashing lights, SHRs exhibit greater increases in blood pressure than do WKYS. However, a number of questions remain unanswered concerning the conditions that elicit the mechanisms that underlie the exaggerated AP responses.

First, since past studies of SHRs have primarily been concerned with the effects on the AP of stimuli that naturally elicit profound autonomic adjustments, it is not known whether the exaggerated blood pressure changes can be coupled through conditioning to stimuli that prior to conditioning elicit negligible or inconsistent cardiovascular responses. In other words, is the enhanced elevation of the AP in SHRs a response to physical discomfort or is it instead susceptible to con-
control by a potentially infinite range of otherwise benign environmental cues? That this is not a trivial question is indicated by the observation that the magnitude of blood pressure changes in SHRs and WKYs were similar when the animals were placed in a chamber in which they had previously received footshock.  

Second, it is not known whether exaggerated changes in blood pressure during aversive stimulation are associated with a proportionately enhanced level of emotional arousal. If so, the greater elevation of the AP might be secondary to strain differences in emotionality rather than a consequence of some dysfunction in cardiovascular regulation. While previous studies have suggested strain differences in emotional and other behaviors, few of the studies have recorded the AP during the performance of these behaviors.

Third, are exaggerated changes in blood pressure in SHRs specific to aversive emotional arousal, or are they also characteristic of the expression of natural behaviors such as feeding and grooming? Since studies of SHRs have focused on the changes in AP associated with aversive emotional arousal, little is known about cardiovascular changes in SHRs during such natural behaviors.

In the present study we have therefore examined SHRs and their Wistar Kyoto controls (WKYs) chronically instrumented for continuous computer-assisted recording of AP from the aorta during classically conditioned emotional (fear) responses and during the performance of a repertoire of natural behaviors, including eating, drinking, grooming, exploration, and resting. Our objectives were to determine whether the exaggerated changes in blood pressure in SHRs are: 1) susceptible to emotional conditioning; 2) accompanied by a proportionately enhanced emotional reaction; and 3) specific to emotional behavior. We shall demonstrate that exaggerated blood pressure changes in SHRs are readily coupled through conditioning to otherwise neutral stimuli; are behaviorally specific, though not restricted to emotional arousal; are associated with a reduced rather than enhanced fear response; and finally, that SHRs differ from nonhypertensive controls in the performance of natural as well as emotional behaviors.

Methods

General

Male SHRs and WKYs obtained from Taconic Farms were individually housed in clear plastic cages with a stainless steel wire top that held a water dispenser and lab chow. Cages were kept in the animal housing area, which was thermally controlled (at 20°C), sealed to sunlight, and maintained on a fluorescent light cycle (on at 0700, off at 1900). Age-matched SHRs and WKYs were instrumented for cardiovascular recording and studied during the performance of natural behaviors or following emotional conditioning, as described below. At the time of study, the animals were 12 to 16 weeks old.

Computer-Assisted Recording of Arterial Pressure and Heart Rate in Freely Behaving Animals

The techniques for chronic instrumentation for recording AP in unrestrained rats have been detailed elsewhere and will be summarized.

Animals were anesthesized with halothane (2.5% to 3% in oxygen). A plastic (Tygon) cannula (0.012 inch, i.d.) filled with saline containing heparin (50 units/ml) was inserted into the thoracic aorta via the left common carotid artery, and its tip was placed at the level of the diaphragm. With the cannula fixed to the soft tissues with sutures, the free end was passed subcutaneously behind the ear to the back of the neck and brought through the skin through a stab wound in the skin and sealed with stainless steel obturators. The neck wound was closed with sutures and the rats were returned to their home cages. The cannulas were flushed daily with 0.5 ml of 0.9% saline containing heparin (50 U/ml).

At the time of data acquisition, the obturator was removed from the cannula by way of a stainless steel connector, and the free end of the cannula was attached to extension tubing. The extension tubing was threaded through the cage top and connected to a strain gauge transducer (Statham P23Db, Statham Instruments, Hato Rey, Puerto Rico), which was placed (outside the cage) at the level of the heart. Pulsatile and mean AP were recorded from the transducer via an input coupler to the polygraph (Beckman Dynagraph Type R611, Beckman Instruments, Schiller Park, Illinois). Heart rate was derived by a cardiotachometer (Beckman 9857). In addition to being displayed on paper by the polygraph, all data were simultaneously recorded online on a microcomputer (Varian V-76 Vortex II Multitask Digital Computer) which sampled AP at a rate of 100/sec. Incoming data from each experiment were digitized, processed, and stored on disk for subsequent analysis and display.

Studies of Emotional Behavior

Emotional responses were established through classical fear conditioning. Four groups of animals were studied: conditioned (n = 8) and random control (n = 7) SHRs and conditioned (n = 9) and random control (n = 7) WKYs. The conditioning, random control, and test procedures are described below.

Classical Fear Conditioning

On the day after cannulation (see above), the rat was removed from its home cage and placed in a standard conditioning chamber enclosed by a sound attenuating cubicule (Coulbourn Instruments, Lehigh Valley, Pennsylvania). After a 5-minute acclimation period, the rat was subjected to 10 habituation trials. During habituation, the conditioned stimulus (CS), a 10-second, 600 Hz, 80 db tone, was presented through a speaker mounted in the test chamber at an average intertrial interval of 150 seconds (range = 100 to 200 sec). After habituation, the animals received either 30 conditioning or 30 random control trials. For all animals receiving conditioning trials, the final 0.5 sec-
ond of the CS was coextensive with the unconditional stimulus (US), a 0.5-second, 1.2 mA electric foot-shock distributed across the grid floor of the conditioning chamber. Random control animals received the exact same CS sequence as conditioned animals, but with the US randomly programmed in relation to the CS.

Following the conditioning sessions, which lasted approximately 2 hours, the animal was returned to its home cage and allowed access to food and water for 2 hours. Subsequently, the animals were deprived of food and water overnight.

**Conditioned Response Tests**

Conditioned responses (CRs) were assessed during extinction trials (CS presented without US) administered the day after conditioning to the animal while it was at rest in its home cage.

The animal’s home cage was transferred to the observation chamber and the cannula connected to the transducer (as described above). After a 15-minute period of acclimation, the three extinction trials were administered by the computer, which also simultaneously recorded AP and HR from the polygraph. Following these trials, the computer generated a table that listed the average value (mean) and variability (standard deviation) of AP and HR during the following time periods: preCS (averaged over 10 seconds); CS (averaged over 10 seconds); and preCS average subtracted from each second of CS. In this way, the absolute value of AP and HR during the preCS and CS periods and the change from baseline of AP and HR during each second of the CS were computed.

After assessment of AP and HR responses to the CS, conditioned emotional behavior responses (CERs) were tested. This order of assessment was employed since we observed in pilot work that the behavioral responses were less subject to diminution during extinction testing.

The CER was assessed in two ways. The first consisted of the drink suppression test.21 A drinking tube was lowered into the cage following the third extinction trial, which gave the water-deprived animal free access to tap water. Once the animal had completed 5 consecutive seconds of drinking, a 120-second CS was presented. The latency to resume drinking served as a measure of emotional arousal.

Previous studies of normal rats have demonstrated that drink suppression compares favorably with other appetitive and nonappetitive measures of conditioned fear.22 Nevertheless, we included a nonappetitive CER measure because of possible differences in appetitive motivation between SHRs and WKYs suggested by the results of the behavioral experiment (see Results). The nonappetitive measure involved the suppression of activity by the CS following transfer to a new cage.

On the day following conditioning, SHRs (n = 6) and WKY’s (n = 6) were placed in a clean cage in the observation chamber, and after a 10-second delay the CS was presented for 10 consecutive minutes. The total amount of freezing behavior (all four paws motionless) was recorded using a stopwatch.

**Data Analysis**

Statistical analysis involved analysis of variance (ANOVA) and the Newman-Keuls post-hoc test. A separate ANOVA comparing SHR and WKY (experimental and control) groups was performed for preCS (baseline) AP and HR, for the change from baseline of AP and HR during each second of CS, and for the two CER measures.

**Studies of Natural Behavior**

Following overnight food deprivation, normal rats exhibit a relatively stereotyped repertoire of behaviors when presented with lab chow.23 We thus placed SHRs (n = 7) and WKYs (n = 7) on a limited access feeding schedule and recorded AP and HR during the performance of the repertoire of natural behaviors elicited by food presentation. In this way, we could determine whether there are strain differences in cardiovascular responsivity during natural behavior as well as determine any differences in the performance of natural behavior.

**Feeding Schedule**

Following cannulation (see above), the animals were deprived of food for overnight. The following day, a 3.5 g pellet of rat chow was placed on the floor of their home cage. One hour later, the animals had free access to food for 3 consecutive hours. This procedure was continued for 2 to 3 days before data acquisition.

**Computer-Assisted Encoding of Natural Behavior**

On the day of cardiovascular data acquisition, the extension tubing was connected to the cannula. The home cage was then transferred to the observation cubicle, a 2 x 2 x 2.5 foot sound-attenuating chamber, and the distal end of the extension tubing was connected to the transducer. After 15 minutes of acclimation to the observation cubicle, the 3.5 g pellet of rat chow was dropped through the cage top and the front door of the cubicle was closed. The experimenter then observed through a half-silvered mirror the animal’s activities and recorded these activities using a keyboard, which was monitored by the computer once each second and allowed the coding of the onset termination of five behaviors:

1. **Eating.** The animal was either manipulating the pellet with its front paws and/or its mouth was in contact with pellet, or the animal was chewing the food.
2. **Drinking.** The mouth was in contact with the tip of drinking spout, which rested approximately 3 inches above the cage floor.
3. **Grooming.** The animal was scratching, licking, or rubbing any part of its body.
4. **Exploring.** The animal was sniffing and/or moving and otherwise investigating the content of cage.
5. **Resting.** The animal was lying still with eyes either opened or closed. This category included phases of sleep.
The recording of AP and HR by the computer began when the animal commenced eating, and the session was terminated when the animal completed 3 consecutive minutes of rest. The computer segregated and scored the episodes with respect to behaviors and their duration. In this way, the cardiovascular events associated with the performance of different behaviors could be registered within and between animals and groups.

Data Analysis

Cardiovascular responsivity during behavior was analyzed by the construction of frequency-interval histograms for each behavior. The histograms of AP and HR indicate the incidence with which the cardiovascular variables assume a certain value during select time periods, in this case defined by the occurrence of natural behaviors. In this way, the average value (mean) and variability (standard deviation) of AP and HR during each behavior could be computed.

The behavioral analysis involved an assessment of several time-based variables. These included the total amount of time spent feeding, drinking, grooming, and exploring following the start of the initial feeding episode and the total time elapsed from commencement of eating to the start of 3 consecutive minutes of rest. The latency to rest served as an activity measure;

<table>
<thead>
<tr>
<th>Group</th>
<th>WKY Mean arterial pressure (mm Hg)</th>
<th>SHR Mean arterial pressure (mm Hg)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>123 ± 3 (n = 7)</td>
<td>151 ± 8 (n = 7)</td>
<td>(p &lt; 0.001)</td>
</tr>
<tr>
<td>Conditioned</td>
<td>118 ± 4 (n = 9)</td>
<td>152 ± 6 (n = 8)</td>
<td>(p &lt; 0.001)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>WKY Heart rate (bpm)</th>
<th>SHR Heart rate (bpm)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random</td>
<td>306 ± 12 (n = 7)</td>
<td>319 ± 6 (n = 7)</td>
<td>n s.</td>
</tr>
<tr>
<td>Conditioned</td>
<td>293 ± 8 (n = 9)</td>
<td>347 ± 15 (n = 8)</td>
<td>(p &lt; 0.05)</td>
</tr>
</tbody>
</table>

Values represent means ± se. Between-strain differences are indicated.
the amount of time spent eating and drinking served as measures of appetitive motivation in food-deprived animals; and the amount of time spent grooming and exploring served as indices of the strength of these responses.

Statistical analysis involved analysis of variance (ANOVA). A separate ANOVA comparing SHRs and WKYs was performed for AP, HR, and each behavioral variable described above. The locus of significant differences was determined by the Neuman-Keuls test.

Results
Do Conditioned Emotional Changes in Arterial Pressure and Heart Rate Differ in SHRs and WKYs?

Conditioned AP and HR responses were assessed over three extinction trials during which the CS (tone) was presented without the US (shock) to the animal while at rest in its home cage. With this procedure, changes in AP and HR could be assessed from a relatively low and stable baseline. Baseline AP and HR were measured as the average value during the 10-second preCS for each trial. Although this is a relatively short period, we have found this interval to be representative of longer periods (1 minute and longer) in resting animals.

Baseline AP, computed for the three trials, was higher in conditioned and control SHRs than in conditioned and control WKYs, as shown in table 1. Baseline HR was not different in control SHRs and WKYs, but was greater in conditioned SHRs than in conditioned WKYs.

Conditioned AP and HR responses were readily established in both WKYs and SHRs, as indicated by the polygraph tracings from representative animals shown in figure 1. The conditioned pressor response, which was exaggerated in SHRs relative to WKYs, was biphasic in both strains (fig. 2). Although the conditioned pressor response in both strains was different from the “nonassociative” responses of the random control groups, the SHR random control group showed a biphasic pressor response that was as large as the pressor response in conditioned WKYs (fig. 2).
The conditioned pressor response in WKYs was accompanied by a slight bradycardia, while conditioned SHRs exhibited tachycardia (fig. 3). The HR response in control WKYs was variable and did not differ from baseline. However, control SHRs exhibited a tachycardia that was indistinguishable from the HR response to the CS in conditioned SHRs.

Is Conditioned Emotional Behavior Different in SHRs and WKYs?

The enhanced elevation of the AP and HR during an aversive CS in conditioned and control SHRs could be attributable to strain differences in emotional arousal rather than to differences in cardiovascular reactivity. To test this possibility, we employed two behavioral measures of emotional arousal.

Drink Suppression

Conditioned emotional behavior was assessed first by measuring the extent of drink suppression during a 120-second CS. The typical rodent response in such situations is defensive freezing, which is thought to interfere with the appetitive response.22

Conditioned WKYs, for the most part, remained motionless throughout the 2-minute CS and thus showed almost complete suppression of drinking (fig. 4). The CS produced less drink suppression in conditioned SHRs, which when not drinking sometimes explored in the cage or assumed a resting posture, responses seldom seen in WKYs. Control SHRs, like control WKYs, were little influenced by the CS.

Activity Suppression

The lower drink suppression scores in conditioned SHRs than in conditioned WKYs could be attributable to differences in appetitive motivation. Thus, an activity suppression test, which does not depend on appetitive motivation, was employed. As shown in figure 4, activity was suppressed much less in conditioned SHRs than in conditioned WKYs. The SHRs explored

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**Figure 3.** Conditioned heart rate (HR) responses in WKYs and SHRs. HR increased during the 10-second tone (conditioned stimulus, CS) in conditioned SHRs and decreased in conditioned WKYs (significant differences indicated by asterisk). Random control animals from both strains exhibited tachycardia during the tone, although the HR increase was more pronounced in random control SHRs (significant difference indicated by asterisk). In neither SHRs nor WKYs did the conditioned HR response differ from the random control group. Data points represent a three-trial mean for each animal averaged across the group and plotted as mean ± SE (** p < 0.01; * = p < 0.05).
the new cage and rested during the CS. Although the SHR freezing scores were low, they were thus actually inflated by the periods of rest, which were coded as freezing by the criteria established. WKYs, in contrast, never rested.

Both CER tests thus indicated that an aversive CS produces less behavioral suppression (i.e., less emotional arousal) in SHRs than in WKYs. In addition, observations of the animal's activities also suggested that the emotional arousal elicited by an aversive CS is less in SHRs than in WKYs. The exaggerated changes in AP and HR elicited by an aversive CS could not thus be readily explained in terms of enhanced emotional arousal in SHRs. Similarly, the exaggerated AP and HR changes in random control SHRs could not be explained in terms of the development of conditioned emotional responses to the CS since control SHRs like control WKYs exhibited little behavioral suppression (emotional arousal) during CS presentation.

**Do Changes in Arterial Pressure and Heart Rate during Natural Behavior Differ in SHRs and WKYs?**

AP and HR were assessed in recording sessions during which five natural behavioral activities were observed and recorded: eating, drinking, grooming, exploring, and resting (quiet wakeful states or sleep). During the performance of these natural behaviors, the magnitude of the AP responses was hierarchically organized in WKYs, as shown in table 2. The average response of AP during the consummatory behaviors, eating and drinking, was greater than the response during grooming and exploration, and AP during each of these was greater than the AP while the animals were resting. This hierarchical pattern of blood pressure responsivity is identical to that which we have observed in normotensive rats of the Sprague-Dawley strain.

In SHRs, AP was greater during drinking than during eating, and AP during both of these was greater than during grooming and exploration (table 2). In addition, AP during resting was lower than AP during each other behavior.

Although AP was higher during each behavior in SHRs than WKYs, there was a hierarchical organization of AP in SHRs that resembled the pattern seen in WKYs and other normotensive rats, with one exception: in SHRs, AP during drinking was higher than during eating, but in normotensive rats, the average AP during eating and drinking did not differ.

To compare the magnitude of changes in AP between the strains, the average AP during resting behavior was subtracted from the average AP during each behavior for each animal (fig. 5). In this way, changes in AP associated with nonresting behaviors could be represented as changes from resting AP and thus could be compared in spite of the strain differences in baseline AP. While during drinking SHRs showed greater elevations of AP above baseline than WKYs, during eating, grooming, and exploration the magnitude of changes between the two strains did not differ. Thus, changes in AP were exaggerated during drinking in SHRs relative to WKYs, but not during other behaviors.

Average HR (table 2) was slower in WKYs during resting than during each other behavior. In SHRs, HR was slower during resting than during grooming, but not during the other behaviors. There were no between group differences in HR during the natural behaviors.

**Are There Strain Differences in the Performance of Natural Behaviors?**

During natural behavior recording sessions, we have found that food-deprived normotensive (Sprague-Dawley) rats exhibit a rather stereotyped pattern of responses when presented with a single pellet of lab chow. First, they consume the pellet; second, they drink; third, they groom; fourth, they explore the cage and engage in nesting; finally, they rest. Although this is not a strict ordering, the overall pattern is reliably seen.
In the present study, we found this general pattern to hold for both SHRs and WKYs. In addition, we quantified the behavioral observations, as described in the Methods, measuring the latency to begin rest and the amount of time spent eating, drinking, grooming, and exploring. SHRs were more active during the recording sessions, as indicated by the longer latency to commence 3 consecutive minutes of rest, as shown in table 3. While no differences were obtained for the amount of time spent grooming or exploring, SHRs spent more time eating and drinking than WKYs. These latter differences, rather than general increases in motility, largely accounted for the increased rest latency and suggest strain differences in appetitive motivation. Thus, it appeared that differences between SHRs and WKYs exist in the expression of natural as well as emotional behaviors.

### Discussion

We have examined SHRs and WKYs to determine whether the exaggerated elevation of the AP in SHRs during aversive emotional arousal is: 1) susceptible to conditioning; 2) accompanied by a proportionately enhanced emotional response; and 3) specific to emotional arousal. To do this we have studied SHRs and WKYs chronically instrumented for computer-assisted recording of the AP during classically conditioned emotional arousal and during the performance of a repertoire of natural behaviors. The results demonstrate that: 1) the exaggerated elevation of the AP during aversive emotional arousal in SHRs is readily coupled through conditioning to stimuli which prior to conditioning elicited minimal changes in AP and HR; 2) conditioned cardiovascular hyperreactivity in SHRs is associated with a reduced rather than an enhanced conditioned emotional response; 3) while exaggerated changes in the AP in SHRs are not specific to aversive emotional arousal, they are nevertheless behaviorally specific; and 4) differences between SHRs and WKYs exist in their performance of natural as well as emotional behaviors.

**Vascular Hyperreactivity Can Be Conditioned in SHRs**

Previous studies demonstrating exaggerated rises of the AP in SHRs in response to stressfull stimulation have examined the effects of immobilization, exposure to cold, electric footshock, loud noises, flashing lights, cage vibrations, and other forms of unconditioned aversive arousal.¹⁴ Such conditions by nature elicit profound autonomic adjustments. In the present study, however, we have demonstrated that stimuli which themselves elicited negligible changes in AP and HR in SHRs can through association with aversive stimuli acquire the capacity to elicit large magnitude adjustments in the AP. This observation thus extends to true "psychological stressors" the capacity to elicit exaggerated blood pressure changes in SHRs.

The susceptibility of the AP and HR in SHRs to environmental control, however, extends beyond the conventional development of conditioned responses to stimuli that are systematically associated with aversive arousal. When the tone and shock were randomly pro-

### Table 2. Average Magnitude of Mean Arterial Pressure and Heart Rate During Natural Behavior in SHRs (n = 7) and WKYs (n = 7)

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Mean arterial pressure (mm Hg)</th>
<th>Heart rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WKY</td>
<td>SHR</td>
</tr>
<tr>
<td>Drinking</td>
<td>133 ± 4</td>
<td>182 ± 4 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Eating</td>
<td>127 ± 4</td>
<td>166 ± 5 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Grooming</td>
<td>114 ± 4</td>
<td>149 ± 3 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Exploring</td>
<td>117 ± 3</td>
<td>151 ± 4 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Resting</td>
<td>99 ± 3</td>
<td>134 ± 5 (p &lt; 0.01)</td>
</tr>
</tbody>
</table>

Significance levels for within-group comparisons:

- Drinking & eating: ns (p > 0.05)
- Drinking & grooming: p < 0.01
- Drinking & exploring: p < 0.01
- Drinking & resting: p < 0.01
- Eating & grooming: p < 0.05
- Eating & exploring: ns
- Eating & resting: p < 0.01
- Grooming & exploring: ns
- Grooming & exploring: ns
- Exploring & resting: p < 0.01

In the present study, we found this general pattern to hold for both SHRs and WKYs. In addition, we quantified the behavioral observations, as described in the Methods, measuring the latency to begin rest and the amount of time spent eating, drinking, grooming, and exploring. SHRs were more active during the recording sessions, as indicated by the longer latency to commence 3 consecutive minutes of rest, as shown in table 3. While no differences were obtained for the amount of time spent grooming or exploring, SHRs spent more time eating and drinking than WKYs. These latter differences, rather than general increases in motility, largely accounted for the increased rest latency and suggest strain differences in appetitive motivation. Thus, it appeared that differences between SHRs and WKYs exist in the expression of natural as well as emotional behaviors.
grammed, a situation that characteristically produces inconsistent, if any, effects. 19–23 SHRs reliably exhibited AP and HR responses similar to those seen in properly conditioned animals, but showed minimal emotional behavioral responses. These AP and HR reactions, which were thus uncoupled from emotional arousal, suggest that the cardiovascular system of SHRs is hyperresponsive to both associative and non-associative environmental contingencies. This situation drastically increases the possibilities for environmental manipulation of the circulation in SHRs.

The present observations of conditioned cardiovascular hyperreactivity in SHRs are in part inconsistent with previous studies. Hutton et al. 27 found that an aversive CS-elicited bradycardia rather than tachycardia in SHRs. However, their animals were examined while tightly restrained. Under such conditions, basal HR in rodents is greatly elevated, and the typical conditioned HR response is decellerative. 28 In contrast, McCarty et al., 2 in studying freely behaving animals found that, when SHRs were returned to a chamber in which they had received footshock, HR increased. Since the chamber presumably served as an aversive CS, the finding is comparable to our observation of conditioned tachycardia in SHRs. By the same reasoning, McCarty et al.’s failure to find greater elevations of basal AP in SHRs under these conditions is not readily explained. However, proper control groups for conditioning were lacking and change in basal AP rather than stimulus-bound blood pressure reactivity was examined. The present findings, however, clearly demonstrate conditioned cardiovascular hyperreactivity in SHRs.

Behavioral Specificity of Cardiovascular Hyperreactivity Suggests Central Neural Involvement

The enhanced conditioned changes in the AP and HR in SHRs could be related to several factors. Follkow et al. 29 for example, have argued that structural changes in the vessels, involving an increased wall-lumen ratio, account for the greater total peripheral resistance30 in SHRs. Under such conditions, the same amount of neural discharge would produce a greater vascular response. However, heightened peripheral sympathetic neural activity in SHRs has also been demonstrated, through direct recordings20 31,32 and through the measurement of plasma levels of catecholamines. 2, 8–20, 33

Our observation that exaggerated changes in blood pressure are behaviorally selective is not readily accounted for in terms of strain differences in vascular conformation or differences in peripheral sympathetic activity. If the enhanced elevation of the AP in SHRs during conditioned emotional arousal and drinking were due to such differences in peripheral mechanisms alone, then all blood pressure changes should be proportionately magnified in SHRs. The demonstration that exaggerated rises of the AP in SHRs only accompany certain behaviors suggests specific strain differences, perhaps involving select central neural pathways, in the coupling blood pressure changes to the physiological demands of behavior. Indeed, strain differences have been observed in baroreceptor reflex function34 and in various neurochemical systems involved in the central regulation of the circulation.34, 35–45

The exaggerated cardiovascular reactivity in SHRs could thus involve disruption of the central neural mechanisms underlying the regulation of peripheral sympathetic activity, baroreceptor reflexes, or the control of the release of vasoactive substances into the

![Figure 5. Elevation of mean arterial pressure (AP) above resting baseline during natural behavior in WKYs and SHRs. While the magnitude of the average AP was similar during exploration, grooming, and eating in the two strains, SHRs showed an exaggerated elevation of the AP during drinking. Values represent means ± se (** = p < 0.01).](http://hyper.ahajournals.org/)

<table>
<thead>
<tr>
<th>Duration (sec)</th>
<th>WKY (n = 7)</th>
<th>SHR (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest latency</td>
<td>1260 ± 120</td>
<td>1980 ± 120 (p&lt;0.01)</td>
</tr>
<tr>
<td>Eating</td>
<td>800 ± 114</td>
<td>1103 ± 88 (p&lt;0.05)</td>
</tr>
<tr>
<td>Drinking</td>
<td>32 ± 12</td>
<td>119 ± 18 (p&lt;0.01)</td>
</tr>
<tr>
<td>Grooming</td>
<td>38 ± 15</td>
<td>55 ± 23 (ns)</td>
</tr>
<tr>
<td>Exploring</td>
<td>165 ± 42</td>
<td>187 ± 33 (ns)</td>
</tr>
</tbody>
</table>

Values represent means ± se. Between-strain differences are indicated.
circulation. Further studies will be required, however, to determine whether such disturbances do in fact account for the behaviorally selective alterations of vascular control which we have observed.

Strain Differences in Emotional and Natural Behaviors

The exaggerated increases in the AP during conditioned emotional behavior in the present study are accompanied by a reduced level of emotional arousal. Strain differences in emotionality thus do not readily account for the enhanced elevation of the AP during emotional arousal in SHRs.

Our finding that an aversive CS produces less drink suppression in SHRs than in WKYS is consistent with Schaeffer et al.15 observation of less conditioned suppression of food motivated lever pressing in SHRs. However, in our present study, as well as in Schaeffer et al.'s study, evidence for increased appetitive motivation in SHRs was uncovered. SHRs may thus be more inclined to eat and drink than WKYS under deprivation conditions, and these tendencies may have competed with and thus diminished the suppressive effects of the CS. Consequently, we also employed a test of response suppression that did not depend on an appetitively motivated baseline. The results of the activity suppression test, however, were even stronger than the drink suppression test in suggesting less emotional arousal in SHRs.

It should be noted that previous studies have suggested that SHRs are more active than WKYS.11, 12, 13, 14 Increased activity levels could confound the interpretation of the activity suppression test. However, SHRs did not simply replace defensive freezing with exploration. They also rested and in general appeared less fearful of the aversive CS than WKYS. Moreover, while researchers have used the observations that SHRs are more active in an environment associated with footshock,2, 3 and are more active in a novel environment4, 5 and in an open field6 to demonstrate increased activity levels in SHRs, such observations are also readily interpreted in terms of less emotional arousal.2, 6

Diminished fear responses in threatening situations may represent a more general aspect of the finding of reduced pain reactivity due to increased opioid activity in hypertensive animals.7, 11, 13 Reduced emotional arousal in the presence of actual (i.e., pain eliciting) or perceived (i.e., fear eliciting) aversive stimuli might in fact reflect compensatory mechanisms in the central nervous system which develop to counterbalance the hyperreactivity of central circulatory control in hypertension. By altering the threshold for emotional arousal, such mechanisms could reduce the frequency and intensity of emotional reactions and thus reduce the possible damaging consequences44, 45 of repeated or prolonged emotional arousal on the circulation.

References

22. Boulton ME, Bolles RC: Conditioned fear assessed by freezing and by the suppression of three different baselines. Animal Learn Behav 8: 429, 1980
BLOOD PRESSURE AND BEHAVIOR IN SHR/LeDoux et al. 863


Behaviorally selective cardiovascular hyperreactivity in spontaneously hypertensive rats.
Evidence for hypoemotionality and enhanced appetitive motivation.

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