Vascular and hemodynamic effects of behavioral stress in borderline hypertensive and Wistar-Kyoto rats

LESLIE C. FUCHS, AZIZUL M. HOQUE, AND NATALIE L. CLARKE
Vascular Biology Center and Department of Pharmacology and Toxicology, Medical College of Georgia, Augusta, Georgia 30912

Fuchs, Leslie C., Azizul M. Hoque, and Natalie L. Clarke. Vascular and hemodynamic effects of behavioral stress in borderline hypertensive and Wistar-Kyoto rats. Am. J. Physiol. 274 (Regulatory Integrative Comp. Physiol. 43): R375–R382, 1998.—In borderline hypertensive rats (BHR), behavioral stress produces hypertension, which has been attributed to increases in sympathetic nervous system activity and peripheral changes in vascular structure. However, the mechanisms mediating development of stress-induced hypertension have not been well defined. Experiments were designed to determine hemodynamic effects and changes in small mesenteric artery (≈300 μm) vascular reactivity in response to 10 days of air-jet stress (2 h/day) in BHR and in Wistar-Kyoto (WKY) rats. The acute stress-induced increase in mean arterial pressure (AP) was impaired in WKY rats compared with BHR on day 1, and habituation developed to the increase in AP in BHR, but not WKY rats. Conversely, WKY rats adapted to the stress-induced tachycardia to a larger extent than BHR. The mechanisms mediating endothelium-dependent relaxation to acetylcholine (ACh) were altered in small mesenteric arteries isolated from WKY rats and BHR after 10 days of air-jet stress. Inhibition of nitric oxide synthase activity had a significantly larger inhibitory effect on ACh-induced relaxation in vessels from stressed compared with control BHR. Also, cyclooxygenase products contributed to ACh-induced relaxation of small mesenteric arteries from stressed WKY rats, but not control WKY rats. Endothelium-independent relaxation to nitroprusside was impaired in vessels from stressed WKY rats, but not stressed BHR. Finally, contraction to phenylephrine was impaired in vessels from stressed BHR, but not WKY rats. In conclusion, changes in vascular reactivity induced by air-jet stress appear to correlate with, and may contribute to, the differential hemodynamic adaptations to stress observed in WKY rats and BHR.

mesenteric artery; vascular reactivity

CLINICAL AND EXPERIMENTAL studies indicate that behavioral stress can contribute to the development of arrhythmias and hypertension (11, 12, 26, 27). The mechanisms mediating stress-induced hypertension are not well defined but are thought to involve both enhanced sympathetic nervous system activity and peripheral vascular changes leading to increased vascular resistance. During the early stages, enhanced sympathetic nervous system activity appears to contribute to the development of hypertension in several models of behavioral stress (9, 25, 29). In later stages, increased peripheral vascular resistance, without a sustained increase in autonomic nervous system activity, has been observed (31). Additionally, reduced baroreceptor sensitivity was observed after exposure to 11 wk of behavioral stress (21).

The present study was designed to determine behavioral stress-induced changes in vascular reactivity that occur before development of stress-induced hypertension in borderline hypertensive rats (BHR) and to correlate these changes with the hemodynamic responses observed during 10 days of behavioral stress. Because vasoconstriction occurs in the mesenteric circulation during the defense reaction (18) and because the mesenteric vascular bed significantly contributes to the determination of mean arterial blood pressure, changes in small mesenteric artery reactivity were determined in this study. Normotensive Wistar-Kyoto (WKY) rats, which do not develop hypertension in response to air-jet stress, were also studied.

The BHR is the first-generation offspring of a female spontaneously hypertensive rat (SHR) and a male WKY rat and has been extensively used for studies on behavioral stress because it is sensitive to several environmental challenges (26). Borderline hypertensive humans also demonstrate enhanced cardiovascular reactivity to behavioral stress compared with normotensives (5, 16). BHR exhibit a resting mean arterial pressure (AP) of ~130 mmHg and do not develop the age-related increase in AP observed in SHR (29). BHR have been shown to develop sustained hypertension in response to behavioral stressors including a shock conflict paradigm and air-jet stress, whereas WKY rats do not (7, 20).

METHODS

BHR. Female SHR and male WKY rats were obtained from Taconic Farms and bred at the Medical College of Georgia to obtain the first generation offspring BHR. In this study, male WKY and BHR (14–16 wk) were randomly divided into two groups. The stressed group was exposed to air-jet stress 2 h/day for 10 days, whereas the control group remained in its home cage for 10 days.

Hemodynamic measurements. All rats were anesthetized with ketamine (50 mg/kg im) and acepromazine (16 mg/kg im). Under aseptic conditions, a cannula (PE-50 attached to PE-10) was placed in the femoral artery and exteriorized at the nape of the neck. The cannula was flushed with heparinized saline (100 units/ml). After a 2-day recovery period, AP and heart rate (HR) were obtained from unrestrained rats in their home cage. HR was derived with a catheter that was triggered from the AP pulse on a Grass recorder.

Air-jet stress. Rats exposed to behavioral stress were positioned in Plexiglas restrainers for 20 min before initiation of air-jet stress to allow hemodynamic variables to stabilize. Chronic stress consisted of pulses of compressed air (15 lb/in.2) directed toward the face from a one-eighth-inch opening at the front of the restrainer. Animals were subjected to a random duration of pulses (5–120 s) and interpulse intervals (5–120 s) 2 h/day for 10 days. On days 1, 3, 5, and 10 of stress, AP and HR were continuously recorded while rats...
were in their home cage and during the 2 h of air-jet stress. Hemodynamic values were obtained for comparison of the response to stress on subsequent days within strains and for comparison of the response to stress between strains. A baseline measurement was made in the home cage consisting of an average of five measurements taken over 20 min. Measurements of the response to stress used for comparisons consisted of the change in AP and HR from baseline measured as area under the curve (AUC) and maximum percent change occurring during the first air-jet pulses of the 2-h stress period. To allow for accurate comparisons, the first air-jet pulse was 10 s long followed by 60 s before the next air-jet pulse on the days AP and HR were measured. AP and HR were recorded for the same period of time in unrestrained, unstressed rats that remained in their home cage.

Small mesenteric artery reactivity. On day 11, rats were anesthetized with pentobarbital sodium (50 mg/kg ip) and mechanically ventilated. Heparin (500 units) was administered into the femoral artery. A section of the small intestine was clamped to prevent leakage of intestinal contents and removed with the mesentery intact and placed in modified Krebs-Ringer bicarbonate solution (composition in mM: 118.3 NaCl, 4.7 KCl, 2.5 CaCl₂, 1.2 MgSO₄, 1.2 KH₂PO₄, 25 NaHCO₃, 11.1 dextrose) that had been chilled and oxygenated (20% O₂ and 5% CO₂). A third-order branch of the superior mesenteric artery (~300 µm diameter and 1–2 mm long) was isolated and removed microscopically.

The artery was transferred to the vessel chamber and mounted and secured between two glass micropipettes (100-µm-diameter tips) with 10–0 ophthalmic suture. The tissue bath was transferred to the stage of an Olympus inverted light microscope coupled to a monitor and video dimension analyzer (Living Systems Instrumentation, Burlington, VT). Small mesenteric artery intraluminal diameter was continuously monitored on a Grass recorder.

Oxygenated (20% O₂-5% CO₂) Krebs-Ringer solution was maintained at 37°C and continuously circulated through the tissue bath. The lumen of the vessel was filled with Krebs-Ringer solution through the micropipette and maintained at a constant pressure of 40 mmHg. The vessel was allowed to equilibrate for 1 h before the beginning of dose-response curves. To perform dose-response curves to vasodilatory agents, vessels were preconstricted to 40–50% of their resting diameter (at an intraluminal pressure of 40 mmHg) with the α₁-adrenoceptor agonist phenylephrine (PE). Constriction to PE was found to remain stable for several hours but could be quickly washed out with Krebs solution.

Because the mesenteric circulation is regulated by several factors including the endothelium and the sympathetic nervous system, vascular responses to endothelium-dependent and -independent vasodilators, in addition to α₁-adrenoceptor-mediated contraction, were studied. Dose-response curves were performed to the endothelium-dependent vasodilator acetylcholine (1 × 10⁻⁸–1 × 10⁻⁵ M) and an exogenous donor of nitric oxide, nitroprusside (NP) (1 × 10⁻⁸–3 × 10⁻⁴ M). Mechanisms mediating endothelium-dependent relaxation were assessed with an inhibitor of nitric oxide synthase activity, Nα-nitro-L-arginine (L-NNA, 0.1 mM), and a cyclooxygenase inhibitor, indomethacin (10 µM). To determine the role of K⁺ channels in mediating relaxation to acetylcholine (ACh), a dose-response curve to ACh was performed in the presence of high extracellular K⁺ (25–50 mM KCl). This concentration of K⁺ effectively blocks K⁺ efflux and prevents relaxation mediated by opening of K⁺ channels. A dose-response curve to PE was also performed in vessels at resting diameter. Two dose-response curves were performed in a single vessel only if the resting intraluminal diameter was restored after washing with Krebs solution for 15 min. Additionally, each experiment was performed only once per rat. All chemicals used in this study were obtained from Sigma Chemicals, dissolved in nanopure water, and diluted in Krebs solution.

Data analysis. Data obtained from small mesenteric arteries were expressed as intraluminal diameter in micrometers. Responses to vasodilatory agents were expressed as percent relaxation after preconstriction with PE, and contractile responses to PE were expressed as percent contraction from baseline. Baseline diameter (diameter at 40 mmHg intraluminal pressure) was the maximal diameter and was used to calculate percent relaxation to vasodilatory agents after preconstriction. In experiments in which vessels were pre-treated with L-NNA or indomethacin, only one dose-response curve was performed per vessel. Otherwise, the order of dose-response curves was randomized. AP and HR were measured in millimeters mercury and beats per minute, respectively. Data are reported as change in AP and HR from baseline measured as AUC and maximum percent change from baseline occurring during the first air-jet pulse of the 2-h stress period. All data were reported as means ± SE. Statistical differences were determined by analysis of variance for repeated measures followed by the Student’s modified t-test with Bonferroni correction for multiple comparisons. The criterion for significance was P < 0.05.

### Table 1. Baseline measurements in BHR and WKY rats

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Stress</th>
<th>Control</th>
<th>Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP, mmHg</td>
<td>Day 1</td>
<td>105 ± 5</td>
<td>108 ± 3</td>
<td>126 ± 2*</td>
</tr>
<tr>
<td>Day 3</td>
<td>103 ± 4</td>
<td>108 ± 2</td>
<td>120 ± 5*</td>
<td>128 ± 5*</td>
</tr>
<tr>
<td>Day 5</td>
<td>108 ± 4</td>
<td>109 ± 3</td>
<td>124 ± 6*</td>
<td>123 ± 3*</td>
</tr>
<tr>
<td>Day 7</td>
<td>107 ± 3</td>
<td>112 ± 2</td>
<td>125 ± 4*</td>
<td>124 ± 4*</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>Day 1</td>
<td>338 ± 14</td>
<td>346 ± 11</td>
<td>335 ± 12</td>
</tr>
<tr>
<td>Day 3</td>
<td>340 ± 11</td>
<td>351 ± 7</td>
<td>325 ± 15</td>
<td>340 ± 19</td>
</tr>
<tr>
<td>Day 5</td>
<td>328 ± 12</td>
<td>346 ± 7</td>
<td>340 ± 11</td>
<td>329 ± 10</td>
</tr>
<tr>
<td>Day 10</td>
<td>346 ± 16</td>
<td>358 ± 8</td>
<td>332 ± 9</td>
<td>342 ± 13</td>
</tr>
</tbody>
</table>

Values are means ± SE. BHR, borderline hypertensive rats; WKY, Wistar-Kyoto; AP, mean arterial pressure; HR, heart rate. *P < 0.05 vs. WKY.
by PE or KCl before dose-response curves to relaxing agents were performed is shown in Table 2.

**Table 2. Mesenteric small artery intraluminal diameter**

<table>
<thead>
<tr>
<th></th>
<th>WKY</th>
<th>BHR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Stress</td>
</tr>
<tr>
<td>PE/ACh</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>253 ± 17</td>
<td>288 ± 10</td>
</tr>
<tr>
<td>Preconstriction</td>
<td>124 ± 6</td>
<td>140 ± 13</td>
</tr>
<tr>
<td>PE/ACh + L-NNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>295 ± 20</td>
<td>284 ± 9</td>
</tr>
<tr>
<td>Preconstriction</td>
<td>142 ± 8</td>
<td>146 ± 11</td>
</tr>
<tr>
<td>PE/ACh + Indo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>296 ± 12</td>
<td>290 ± 17</td>
</tr>
<tr>
<td>Preconstriction</td>
<td>142 ± 14</td>
<td>149 ± 10</td>
</tr>
<tr>
<td>KCl/ACh</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>301 ± 10</td>
<td>307 ± 23</td>
</tr>
<tr>
<td>Preconstriction</td>
<td>167 ± 8</td>
<td>169 ± 19</td>
</tr>
<tr>
<td>PE/NP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>287 ± 10</td>
<td>335 ± 16</td>
</tr>
<tr>
<td>Preconstriction</td>
<td>155 ± 9</td>
<td>157 ± 15</td>
</tr>
<tr>
<td>PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>281 ± 25</td>
<td>340 ± 14</td>
</tr>
</tbody>
</table>

Values represent means ± SE in µm. PE, phenylephrine; L-NNA, Nω-nitro-L-arginine; Indo, indomethacin; NP, nitroprusside.

**Fig. 1. Change in arterial pressure (AP; A) and heart rate (HR; B) analyzed as area under the curve (AUC in mm²) in response to air-jet stress on days 1 (n = 9), 3 (n = 8), 5 (n = 8), and 10 (n = 6) in borderline hypertensive rats (BHR) and on days 1 (n = 9), 3 (n = 8), 5 (n = 8), and 10 (n = 7) in Wistar-Kyoto (WKY) rats. All values represent means ± SE. *P < 0.05 vs. BHR and tP < 0.05 vs. day 1.**

Vascular responses to air-jet stress. Dose-response curves to ACh in small mesenteric arteries from stressed and unstressed WKY and BHR are summarized in Fig. 3A. Endothelium-dependent relaxation to ACh was similar in vessels from WKY and BHR and was unaltered by exposure to behavioral stress in either strain. The effect of pretreatment of mesenteric arteries from all four groups of rats with L-NNA for 20 min before the dose-response curve to ACh was performed is shown in Fig. 3B. Inhibition of nitric oxide synthase activity had a significantly greater effect on relaxation to ACh in vessels from stressed compared with control BHR, but not in stressed compared with control WKY rats. A typical tracing showing relaxation to ACh in L-NNA-pretreated small mesenteric arteries from control and stressed BHR is shown in Fig. 4. Inhibition of cyclooxygenase had a significantly greater effect on relaxation to ACh in vessels from stressed compared with control WKY rats, but not in stressed compared with control BHR (Fig. 3C). To assess the role of K⁺ channels in relaxation to ACh, vessels were preconstricted with KCl (25–50 mM) to obtain a similar percent precontraction as that produced with PE. Inhibition of K⁺ efflux with a
high extracellular K\(^+\) concentration impaired relaxation to ACh to a similar extent in all groups (Fig. 3D).

Relaxation to an exogenous nitric oxide donor, NP, was significantly greater in small mesenteric arteries from control BHR compared with control WKY rats at a dosage range of $10^{-8}$ to $10^{-5}$ M (Fig. 5). Additionally, exposure to air-jet stress impaired relaxation to NP in vessels from WKY rats, but not BHR, with maximal relaxation to NP being 94\% in vessels from unstressed WKY rats and 50\% in vessels from stressed WKY rats. The effect of behavioral stress on \(\alpha\)-adrenoceptor-mediated contraction is illustrated in Fig. 6. Small mesenteric artery contraction to PE was significantly less at a concentration of $10^{-6}$ M in vessels from control BHR compared with control WKY rats. Additionally, exposure to stress significantly impaired contraction to PE in vessels from BHR, but not WKY rats.

**DISCUSSION**

Genetic factors, such as a family history of hypertension, and environmental factors, including exposure to behavioral stress, may contribute to the development of hypertension. Some studies have suggested that the type A behavior pattern, which consists of aggressive, competitive, and time-urgent behavior, or responsiveness to mental stress, may predict the future incidence...
of cardiovascular disease (2, 11, 23, 28). The BHR, which has been used as a model for studies on the effects of environmental stimuli on the cardiovascular system, exhibits exaggerated cardiovascular and sympathoadrenal responses to acute stress (15, 24). Prolonged exposure of BHR to air-jet stress results in sustained hypertension, which persists after removal of air-jet stress (6, 7). The present study is the first to examine functional changes in reactivity of isolated small arteries in response to behavioral stress in BHR and in normotensive WKY rats. Because borderline hypertensive humans exhibit an exaggerated response to mental stress in a manner similar to BHR, the BHR may be useful in providing a comparison to humans with a family history of hypertension and increased cardiovascular reactivity to behavioral challenges (1).

Acute hemodynamic response to air-jet stress. As anticipated, resting AP was significantly higher in BHR compared with WKY rats in both the stressed and unstressed groups. The acute response to stress consisted of a pressor response and tachycardia, which is characteristic of the defense reaction. The air-jet stress-induced increase in AP analyzed as AUC was significantly enhanced in BHR compared with WKY rats. However, in this study, the maximum increase in AP was not significantly different, indicating a similar initial response to stress followed by a prolonged increase in AP in BHR. Similar results were observed in a clinical study in which the duration, but not the magnitude, of the blood pressure response to acute stress was enhanced in subjects with a parental history of hypertension, but not in offspring with either no or one hypertensive parent (10).

A study comparing the acute response to stress in BHR and WKY rats exposed to aversive classical conditioning found that both the maximum increase in AP and the duration of the response were enhanced in
BHR compared with WKY rats (13). In agreement with the present study, they also found that stress-induced tachycardia was similar in BHR and WKY rats. While Hubbard et al. (14) found that an enhanced total peripheral resistance associated with increased release of norepinephrine mediated the larger pressor response in BHR, the results of this study indicated that α-adrenoceptor-mediated contraction of isolated small mesenteric arteries was less in vessels from BHR compared with WKY rats before exposure to behavioral stress. Therefore, it does not appear that enhanced sensitivity of mesenteric small arteries to α-adrenoceptor stimulation accounts for the increased pressor response to air-jet stress observed in BHR on day 1. Because mesenteric arteries and arterioles can show differential vascular responses, our findings do not preclude the possibility of changes in α-adrenoceptor-mediated responses in vessels of different size (16).

Sympathetic nervous system activation results in increased release of norepinephrine in BHR compared with WKY rats. Therefore, a downregulation of, or reduced sensitivity to, α-adrenoceptors may occur, even in the absence of exposure to behavioral stress. Receptor binding and signal transduction studies would have to be performed in the mesenteric arteries to confirm this hypothesis. Another possible explanation for these findings is that increased stress-induced release of norepinephrine may occur, resulting in enhanced contraction despite the reduced sensitivity of mesenteric arteries to α-adrenoceptor-mediated contraction. Finally, enhanced responsiveness to other vasoconstrictor agents or enhanced responsiveness in other vascular beds could also account for the results observed.

Conditioning to the acute hemodynamic response to air-jet stress. Conditioning to the stress-induced pressor response occurred by day 3 of stress in BHR, but not WKY rats. Habituation to stress that correlated with a reduced mesenteric resistance has been shown to occur previously in BHR after 3.5 wk of conflict stress (18). In another study, SHR were found to exhibit greater habituation to stress-induced increases in blood pressure than WKY rats, suggesting that in this regard, BHR respond similarly to SHR (30). These studies do not support the hypothesis that a genetic predisposition to the development of hypertension would be associated with an inability to habituate to the increase in sympathetic nervous system activity associated with repeated stimulation (9). Similar results were also obtained in the Lyon hypertensive rat, in which the first exposure to air-jet stress resulted in a larger increase in blood pressure compared with the Lyon normotensive rat, while subsequent exposure to stress resulted in a decreased responsiveness of hypertensive, but not normotensive, rats (17).

Unlike the effect of stress on AP, habituation to stress-induced tachycardia was observed in WKY rats, but not in BHR. The finding of conditioning to the stress-induced pressor response, but not tachycardia, in BHR and conditioning to the stress-induced tachycardia, but not the increase in AP, in WKY rats indicates selective changes in autonomic nervous system regulation of the heart compared with the vasculature in response to behavioral stress. A similar finding was reported by Lane et al. (20), who found that humans with higher levels of resting parasympathetic tone demonstrated a faster adaptation of HR, but not AP, responses during behavioral stress, which suggests that increased parasympathetic nervous system activity may offset an increase in sympathetic nervous system activity to the heart. They also concluded that interactions between the sympathetic and parasympathetic nervous systems during the response to stress may involve specific target organs rather than a generalized response (20). Additionally, exposure to 12 h of acoustic stress was found to increase sympathetic innervation to the heart to a larger extent than to the aorta (3). Differential effects of stress on AP and HR have been observed in other studies. For example, foot shock stress increased AP and HR, whereas immobilization stress increased HR, but not AP, in Sprague-Dawley rats (4).

Air-jet stress-induced changes in vascular reactivity. Very few studies have examined vascular changes that occur in response to behavioral stress. In this study, exposure to 10 days of air-jet stress did not produce a sustained increase in resting AP or HR in BHR or WKY rats, allowing for the determination of vascular changes before the development of stress-induced hypertension (20). Exposure to behavioral stress significantly impaired contraction to PE in small mesenteric arteries from BHR, but not WKY rats. Another study evaluated the effects of either 7–14 or 30–35 days of social deprivation stress in Wistar rats on aortic contraction to norepinephrine (24). Although the aorta is a large artery and would not significantly contribute to determination of peripheral vascular resistance, similar results to those obtained in small mesenteric arteries in this study were observed. Aortic contraction to norepinephrine was impaired after 7–14 days of stress. Interestingly, they also found that contraction to norepinephrine was enhanced after 30–35 days of stress. Breschi et al. (3) found that aortic contraction to norepinephrine was not altered by 12 h of acoustic stress in Wistar rats. Although the mechanisms mediating the impaired contraction cannot be determined from the results of this study, receptor downregulation or a reduced sensitivity to α-adrenoceptor stimulation could contribute to this effect. These possibilities are supported by the finding of enhanced stress-induced release of norepinephrine in BHR (14).

To our knowledge, the effects of behavioral stress on endothelium-dependent vascular relaxation have not been evaluated. This study has shown that although endothelium-dependent relaxation to acetylcholine is not altered quantitatively, the mechanisms mediating relaxation are altered. Other studies have shown that several relaxing factors, including nitric oxide, endothelium-derived hyperpolarizing factor, and prostacyclin,
may be released by the endothelium (22, 32). Exposure to air-jet stress enhanced the role of nitric oxide in ACh-induced relaxation of vessels from WKY and enhanced the role of vasodilatory cyclooxygenase products in vessels from WKY rats. The role of K+ channels did not appear to be altered by stress in either strain. In another study, aortic production of prostacyclin was enhanced by exposure to behavioral stress in Sprague-Dawley rats (12). Interestingly, relaxation to NP, which releases nitric oxide independently of the endothelium, was impaired in small mesenteric arteries from unstressed WKY rats compared with BHR and was further impaired by exposure to stress in vessels from WKY rats, but not BHR. The reduced sensitivity of vascular smooth muscle to exogenous nitric oxide observed in vessels from stressed WKY rats compared with stressed BHR may partially account for the finding that nitric oxide plays a more important role in ACh-induced relaxation of vessels from stressed BHR compared with stressed WKY rats. Although the mechanism mediating stress-induced changes in vascular contraction and relaxation are not known, possibilities include changes in signal transduction and vessel morphology.

In summary, BHR exhibited enhanced arrhythmogenesis during 10 days of stress associated with an inability to adapt to stress-induced tachycardia compared with WKY rats. BHR adapted to the stress-induced increase in AP and exhibited impaired small mesenteric artery contraction to α-adrenergic receptor stimulation, whereas WKY rats did not adapt and exhibited reduced sensitivity of small mesenteric arteries to exogenous nitric oxide. Adaptation to changes in AP occurred independently of adaptation to tachycardia within strains. Additionally, air-jet stress differentially altered the mechanisms mediating endothelium-dependent relaxation between strains. In conclusion, changes in vascular reactivity induced by air-jet stress appear to correlate with, and may contribute to, the differential hemodynamic adaptations to stress observed in WKY rats and BHR.

Address reprint requests to L. C. Fuchs.

Received 22 May 1997; accepted in final form 29 September 1997.

REFERENCES