Skin Arteriolar Responses To Local Temperature Changes in Hypertensive Rats

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A rat skin preparation was developed to determine if the responses of the resistance vessels to local skin warming and cooling were abnormal in spontaneously hypertensive rats (SHR). A major advantage of this preparation is that all the skin resistance vessels from small arteries preceding the microcirculation to small arterioles can be studied by intravital microscopy techniques. An abdominal skin flap was reflected with intact vasculature and positioned on a temperature-controlled manifold. Diameters of small arteries and large through small arterioles were measured at normal skin temperature (35°C) and after cooling to 25°C and warming to 38°C. At 35°C, there were no differences in control diameters for comparable branching orders between normotensive (Wistar-Kyoto) and hypertensive rats; however, the maximum diameter of small arteries was 13% smaller in hypertensive rats. All arteriolar branching orders possessed vascular tone that was not altered by neural blockade with tetrodotoxin. With cooling to 25°C, all branching orders constricted (range, 12–37%). The largest and smallest vessels of hypertensive rats constricted almost twice as much as their normotensive counterparts. With warming to 38°C, only the smallest arterioles dilated (19% in normotensive versus 43% in hypertensive rats). This study demonstrates major differences in the arteriolar branching orders that respond to local warming and cooling of nonapical skin regions in both normotensive and hypertensive rats and also shows that skin arterioles in SHR are more responsive to local temperature changes. (Hypertension 1992;20:46–53)

KEY WORDS • skin • arterioles • essential hypertension • temperature

Thermoregulatory abnormalities occur in hypertensive humans as well as spontaneously hypertensive rats (SHR). Kenney found the increase in forearm blood flow, after the subjects had been performing leg exercises for 1 hour in a warm environment, to be approximately fivefold less in mildly hypertensive than normotensive men. Kenney’s data suggest that the vasodilating potential of human cutaneous resistance vessels in a warm environment is substantially reduced and that heat transfer is impaired in essential hypertension. In the SHR, core temperature is elevated and thermoregulatory responses to both heat and cold stress are abnormal. The tolerance to heat stress is so reduced that exposure to a 37°C environment for 2 hours is lethal to over 50% of SHR but is not lethal to normotensive rats. On exposure to cold, core temperature has been found to decrease more rapidly in SHR than in normotensive rats. The impairment of the thermoregulatory ability of the hypertensive animal could result from altered tissue thermal conductance due to abnormal vascular responsiveness. Alterations in vascular responsiveness are known to occur in arteries and arterioles of many tissues during the development of hypertension. An abnormal cutaneous vascularl response during thermoregulation could result from either an altered ability of the skin vasculature to respond to local temperature changes or a central alteration of cutaneous vascular control. Differences in the thermosensitivity of hypothalamic neurons in SHR have been reported, but the ability of the cutaneous vasculature in the SHR to respond appropriately to limit changes in core temperature during heat or cold stress has never been investigated by direct observation of the resistance vessels. The purpose of the present investigation was to develop a skin preparation for intravital microscopy that could then be used to identify which of the resistance vessels are primarily involved in the cutaneous vascular responses to local temperature changes and to determine if the vascular responses to local temperature changes are abnormal in SHR.

Methods

Twenty-week-old SHR and Wistar-Kyoto (WKY) rats were used in the present study so that any microvascular adaptations to hypertension would be well established. These animals were obtained from Harlan Sprague Dawley, Indianapolis, Ind. Thirteen WKY rats and 10 SHR were successfully studied. All rats were anesthetized with sodium thiopental (Pentothal, Abbott Laboratories, North Chicago, Ill.); an initial dose of 100 mg/kg was administered intraperitoneally. Supplemental doses (approximately 25% of initial dose) were given as needed. The skin on the left side of the abdomen was carefully shorn but was not shaved. Esophageal (T.) and abdominal skin (T) temperatures were measured within 10 minutes after the rats were anesthetized. A model 43TA Tele-thermometer and model 402 Ther-
were studied. A top plate (Figure 1) was positioned in the center of the skin preparation where vascular responses were to be measured. A midline abdominal incision was made from above the xyphoid process to the umbilicus. Four sutures were placed along the left edge of the midline incision, and then two lateral incisions were made. The sutures were used to reflect the skin over a second heater manifold (B) as the skin was dissected from the underlying abdominal muscles, and then to hold the skin on the manifold at in situ lengths. A top plate (C) was positioned to maintain suffusion solution over the skin. Care was taken not to compress any microvessels by the top plate as it was positioned over the center of the skin flap and sealed with petroleum jelly. A second temperature-controlled water circulator was used to alter the temperature of the heater manifolds for the skin (B) and suffusion solutions (D).

Figure 1. Illustration of preparation of abdominal skin flap used in this study. Rat was placed on a heater manifold (A) to maintain a constant core temperature. A midline abdominal incision was made from above the xyphoid process to the umbilicus. Four sutures were placed along the left edge of the midline incision, and then two lateral incisions were made. The sutures were used to reflect the skin over a second heater manifold (B) as the skin was dissected from the underlying abdominal muscles, and then to hold the skin on the manifold at in situ lengths. A top plate (C) was positioned to maintain suffusion solution over the skin. Care was taken not to compress any microvessels by the top plate as it was positioned over the center of the skin flap and sealed with petroleum jelly. A second temperature-controlled water circulator was used to alter the temperature of the heater manifolds for the skin (B) and suffusion solutions (D).

To begin preparation of the skin for intravital microscopy, a midline abdominal incision was made through the skin from a point cephalad to the xyphoid process to the umbilicus as illustrated in Figure 1. Four sutures were attached to the left side of the skin incision to reflect the skin as it was dissected from the rat's abdomen. Lateral incisions were made, and the skin and connective tissue were dissected from the underlying abdominal muscles. Sustained bleeding from the cut edges of the skin was stopped by suture ties or microcautery at the bleeding site, but such procedures were seldom necessary. The skin was reflected from the animal's body with vasculature and innervation intact and positioned at in situ lengths on a transparent manifold (see Figure 1) heated by circulating water. Before positioning the skin on the heater manifold, four thermocouples were attached to the manifold with cellophane tape at locations that would be near the center of the skin preparation where vascular responses were studied. A top plate (Figure 1) was positioned above the reflected skin to maintain a pool of suffusion solution over the skin. A watertight seal was made between the plate, skin, and heater manifold with petroleum jelly. Most of the connective tissue over skin and cutaneous maximus muscle was carefully removed by dissection to improve the clarity of the microvessels for in vivo microscopy. In addition, some of the muscle tissue overlying two to three small arterioles (3A) was removed to permit diameter measurements of this arteriolar branching order. During this initial surgery, the skin was constantly bathed with Normosol-R (Abbott Laboratories, Chicago, Ill.), a physiological Ringer's solution.

After the skin preparation was completed, the rat was moved to a custom-built intravital microscopy station that included an Olympus BHMJ microscope (Olympus Corp., Lake Success, N.Y.). The skin preparation was transilluminated with light transmitted from the illuminator (model I-150, Cuda Products Corp., Jacksonville, Fla.) through a flexible light guide (3 x 1.500 mm, American Volpi Corp., Auburn, N.Y.) to a long focal length condenser (model LSD, Olympus Corp.) positioned beneath the small animal microscope stage. A bicarbonate-based suffusion solution (g/l: NaCl 6.90, KCl 0.46, NaHCO₃ 2.10, with 3.75 ml/l of 10% CaCl₂) equilibrated with 5% CO₂-95% N₂ was pumped (Masterflex LS peristaltic pump, Cole-Parmer Instrument Company, Chicago, Ill.) through a stainless steel heater (Figure 1) then over the tissue at a rate of 6 ml/min. The Po2 and Pco2 of the suffusion solution were approximately 40-45 mm Hg. Throughout the experiment, core temperature was monitored with a digital thermometer (model DP-11, Omega Engineering, Inc., Stamford, Conn.) and thermistor temperature probe and maintained at 37±0.5°C by a heater underneath the animal. The temperature of the suffusion solution over the skin and the manifold beneath the skin was regulated by a separate temperature-controlled water circulator (Fisher Isotemp Circulator model 910, Fisher Scientific, Pittsburgh, Pa.). The skin temperature was monitored by the four 30-gauge Copper/Constantan thermocouples (special-limits-of-error wire, 5TC-TT-K-30, Omega Engineering) attached to the manifold directly underneath the skin. The thermocouples were individually calibrated and accuracy was better than ±0.5°C over the range from 25°C to 40°C. The temperature measurements with the thermocouples were made with data acquisition software (LABTECH NOTEBOOK v6.0, Laboratory Technologies Corporation, Wilmington, Mass.) and an IBM-compatible 80386 20 MHz computer with a high resolution 16-bit,16-channel data acquisition card (WB-AA1, Omega Engineering) that included a thermal board with isothermal block for thermocouple input. In initial experiments, thermocouples were positioned on the skin surface as well as on the manifold. Since no difference was detected between these temperatures, all thermocouples were attached to the manifold for convenience in all subsequent experiments.

The experimental protocol involved a 30-minute equilibration period at 34°-35°C after all surgery was completed. The existence of vascular tone was verified by topical application of 10⁻³ M sodium nitroprusside. In all animals, the water circulating bath was then adjusted to cool the skin to 24°-25°C, return to 34°-35°C, warm to 38°-39°C, then cool to 34°-35°C. There were no statistical differences between the three diam-
eter measurements made at 34º–35ºC. Figure 3 is a representative record of the experiments and compares the corresponding changes in skin temperature and vessel diameter over time. The average time required to cool the skin from 34º to 25ºC was 15 minutes. Approximately 7 minutes were needed to warm the skin from 34º to 38ºC. The time required to return the skin temperature to 34º–35ºC averaged 10 minutes from both 38º and 25ºC. Diameter measurements at preselected vessel sites (Figure 2) were made at 34º–35ºC and approximately 1 minute after reaching 25º and 38ºC. About five to seven different vessels were measured in each animal, and the time required to complete all measurements at each temperature was approximately 5 minutes.

The next step in the protocol was the neural blockade of the preparation by the topical application of tetrodotoxin (Sigma Chemical Company, St. Louis, Mo.) at similar concentrations and incubation times used by Lombard et al.13 in the hamster cheek pouch and Falcone and Bohlen14 in the rat small intestine. Before the administration of tetrodotoxin, an electrical stimulus (8 Hz, 0.2 msec duration, 5 V) was applied to the skin preparation to verify that the innervation of the cutaneous maximus muscle overlaying the skin vasculature was functional. Tetrodotoxin was then added to the bath solution (3 x 10⁻⁶ M) and suffused over the preparation for 30 minutes. Neural blockade was verified by repeating the electrical nerve stimulation of the cutaneous maximus muscle. The sympathetic innervation of the vasculature was assumed to be blocked when contractions of the cutaneous maximus muscle during stimulation of the motor neurons were abolished. The bath solution was then replaced and diameter measurements repeated approximately 20 minutes after the tetrodotoxin had been washed out. The preparation was then maximally dilated with a dilator cocktail consisting of 10⁻¹⁴ M adenosine, 10⁻⁴ M verapamil hydrochloride, and 10⁻³ M sodium nitroprusside (Sigma).

All diameter measurements were made with a videocaliper (Microcirculation Research Institute, College Station, Tex.) from video images magnified approximately 1,000 times. MAP was measured from the right femoral artery cannula with a blood pressure display unit (BPM1, Stemtech, Inc., Houston, Tex.) and a pressure transducer (model 156PC06GW12, Microswitch, Freeport, Ill.). An individual preparation was rejected for any of the following reasons: mean arterial pressure less than 90 mm Hg for WKY rats or less than 120 mm Hg for SHR, continued bleeding of the preparation, or absence of vascular tone.

### Table 1. Comparison of Body Weight, Mean Arterial Pressure, and Esophageal and Skin Temperatures

<table>
<thead>
<tr>
<th>Group</th>
<th>Body weight (g)</th>
<th>Mean arterial pressure (mm Hg)</th>
<th>Esophageal temperature (°C)</th>
<th>Skin temperature (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WKY</td>
<td>336±7.2</td>
<td>105±2.7</td>
<td>37.3±0.14</td>
<td>35.1±0.16</td>
</tr>
<tr>
<td>SHR</td>
<td>340±6.2</td>
<td>166±3.7*</td>
<td>38.1±0.14*</td>
<td>35.8±0.26*</td>
</tr>
</tbody>
</table>

WKY, Wistar-Kyoto; SHR, spontaneously hypertensive rat.

*SHR/WKY; p≤0.05.

**Calculations and Statistical Analysis**

Comparisons were made between WKY rats and SHR in body weight, MAP, and esophageal and skin temperatures. Maximum and control inner arteriolar diameters, percent vascular tone, percent control diameter after neural blockade, and percent increase and decrease from control diameter with warming and cooling were also compared between WKY rats and SHR for each arteriolar branching order. Changes in diameter were expressed as percentage of control diameter to decrease variation. Percent vascular tone was calculated from the equation:

\[
\text{Percent vascular tone} = \left( \frac{\text{maximum diameter} - \text{control diameter}}{\text{maximum diameter}} \right) \times 100\%
\]

One-way analysis of variance was used to test for statistical significance (p≤0.05) for these comparisons. A statistical analysis software program (STAT-PACKETS, Walonick Associates, Minneapolis, Minn.) was used with a data spreadsheet (LOTUS 123 R2.3, Lotus, Cambridge, Mass.) to perform these statistical evaluations. Data are reported as mean±SEM.

**Results**

The body weight, MAP, and esophageal and skin temperatures for the SHR and WKY rats are reported in Table 1. The average MAP of the SHR was more than 60% greater than the average of 105 mm Hg for the WKY rats (p≤0.05). Esophageal and skin temperatures averaged 0.8° and 0.7°C higher in the SHR than the 37.3° and 35.1°C measured in WKY rats (p≤0.05).

The photomicrograph and line drawing in Figure 2 illustrate the branching orders of cutaneous resistance vessels studied in this investigation. The feed artery to the preparation is the lateral thoracic artery and is designated as the small artery (SA). The largest arterioles that branch directly from the SA and penetrate the cutaneous maximus muscle to lie between this muscle and the skin are referred to as first-order arterioles (1A). Second-order arterioles (2A) are arcade arterioles that do not arise directly from the SA and have smaller diameters than 1A. These intermediate-diameter arcade vessels branch from a 1A or another 2A and form interconnections between adjacent 1A or 2A, or both. Although not visible in the photomicrograph, small arterioles branch from the 2A and penetrate the dermis to form the beginning of the terminal microvasculature of the skin. These small arterioles do not form interconnections and are referred to as third-order arterioles (3A). They have inner diameters that are approximately one-half those of the 2A.

In preliminary experiments, arteriolar diameters were found to return to the control diameter at 34º–35ºC when the local skin temperature was not increased to more than 39ºC or decreased below 25ºC. When local skin temperatures exceeded 39ºC, intense vasomotion developed in all branching orders, especially in the SHR. If the local skin temperature was sustained above 39ºC, the skin became blanched as profound vasoconstriction occurred that could not be reversed by vasodilators (10⁻⁴ M adenosine or 10⁻⁵ M sodium nitroprusside) or cooling to 34ºC. For these reasons, the ranges of 24º–25ºC and 38º–39ºC were selected to compare vas-
FIGURE 2. Top panel: Photomicrograph shows arteriolar network of the rat abdominal skin flap. Feed artery of this preparation is the lateral thoracic artery and is designated as the small artery (SA) (see bottom panel). Large arterioles (1A) branch directly from the SA and give rise to the intermediate diameter arcade arterioles (2A). Small arterioles (3A) branch from the 2A and penetrate the dermis to form the terminal microvasculature of the skin. The SA, 1A, and some of the interconnecting 2A are apparent in the photograph. The 3A cannot be seen at this magnification (x10). The particular skin flap shown in the micrograph was fixed with 10% formalin at the end of an experiment, and many of the venules were dissected from the tissue so the small arterioles could be seen more readily. Bottom panel is a line drawing made from tracing over the SA, 1A, and all of the 2A of a video image of the same tissue with an image analysis system. Lines representing 1A are filled solid black to distinguish the 1A from the SA and 2A. Open circles indicate typical sites where diameter measurements were made on SA, 1A, and 2A.

Muscular responses with local warming and cooling in SHR and WKY rats.

The changes in the diameter of a 1A in SHR during the experimental protocol are illustrated in Figure 3. The arteriole constricted from 75 to 65 μm during cooling from 34° to 25°C. The tracking of this vessel was interrupted for about 4 minutes while diameter measurements were made at other sites. When the diameter tracking of this vessel was resumed the diameter was 63 μm. As warming occurred, the vessel dilated to 76 μm at 34°C. The temperature was maintained at 34°-35°C for about 4 minutes, and warming to 39°C was started. As the temperature increased, the vessel first dilated, followed by the initiation of vasomotion and a decrease in diameter as the temperature approached 38°-39°C. It was not unusual for the larger vessels in the SHR to constrict somewhat as the temperature increased from 34° to 38°C. In this particular experiment, the response of the vessel was also studied after neural blockade with tetrodotoxin. The arteriolar diameter was 75 μm after neural blockade. The vessel constricted to 65 μm with cooling to 26°C and dilated to 77 μm with warming to
plotted versus time in this figure. The vessel constricted with progression to profound vasoconstriction with complete measurements were made on other vessels. As the skin was similar to the responses that occurred before neural blockade.

38°C. Because of the apparent lack of effect of tetrodotoxin on the temperature response and because the MAP was not stable in some rats during the additional time required, this portion of the experimental protocol was discontinued early in the experiments.

The average diameter of these vessels under control conditions (normal skin temperature of 35°C) was 128 ± 7.3, 85 ± 6.4, 66 ± 6.8, and 28 ± 1.1 μm in the WKY rats for SA, 1A, 2A, and 3A, respectively. As illustrated in the top panel of Figure 4, there were no differences in control diameters between WKY rats and SHR for any branching order. When maximally dilated (10⁻⁴ M adenosine, 10⁻⁴ M verapamil, and 10⁻⁵ M sodium nitroprusside), the diameters were increased to 182 ± 6.3, 109 ± 4.3, 82 ± 3.9, and 43 ± 2.1 μm in the WKY rats. The bottom panel of Figure 4 shows that in the SHR, only the SA had a maximum diameter statistically different from its counterpart in the WKY, which averaged 13% smaller.

The percent of vascular tone present in the four branching orders of vessels in SHR and WKY rats at local skin temperature of 34°–35°C is seen in Figure 5. In the WKY the vascular tone in the SA, 1A, 2A, and 3A was 30 ± 2.5%, 24 ± 3.7%, 19 ± 5.4%, and 35 ± 5.7%, respectively. Although there were no statistically significant differences between SHR and WKY rats in the percent of vascular tone for similar vessels, the average values for each branching order were lower in the SHR.

Neural blockade of the skin vasculature was accomplished by superfusion of the preparation with tetrodotoxin after the arteriolar responses to cooling and warming had been completed. In both SHR and WKY rats, the effect of neural blockade on individual vessels was variable; diameters were increased in some and decreased in other vessels. There were no statistical differences between diameters measured at the end of the 30-minute period when tetrodotoxin was administered and after tetrodotoxin was removed from the superfusion solution. Figure 6 illustrates that neural blockade did not change the average diameter (expressed as percentage of control diameter) of any arteriolar branching order in either SHR or WKY rats.

The vascular responses to local skin warming and cooling are presented in Figure 7. With warming from 34°–35°C to 38°–39°C, the arteriolar responses were limited to the smaller vessels, as seen in the top panel. In WKY rats only the 3A dilated (19 ± 5.9%) with
Figure 5. Bar chart compares percentage of vascular tone (mean±SEM) present in small arteries through small arterioles in the abdominal skin of Wistar-Kyoto (WKY) rats and spontaneously hypertensive rats (SHR). All branching orders have significant tone, but there is no statistical difference between SHR and WKY vessels for any branching order. SA, small artery; 1A, first-order arterioles; 2A, second-order arterioles; 3A, third-order arterioles.

In the SHR, the 2A dilated 9±3.5% and the 3A dilated more than twice (43±7.4%) as much as the WKY 3A. The vascular responses with cooling to 24°-25°C (Figure 7, bottom panel) were not limited to the smallest vessels as occurred with warming, but involved all branching orders. The smallest degree of constriction was observed in the WKY SA (12±3.6%), and the greatest constriction occurred in the 3A of the SHR (37±5.1%). The largest and smallest vessels (SA and 3A) of the SHR constricted almost twice as much as those of their WKY rat counterparts.

Discussion
The rat abdominal skin preparation for intravital microscopy presented in this report provides the opportunity to study skin vascular responses in a species commonly used in experimental studies of hypertension and thermoregulation. A specific advantage of the rat abdominal skin preparation over other skin models is the capability to study all of the major vessels that would be expected to participate in the control of skin blood flow. Intravital microscopy techniques can be used to observe the cutaneous vasculature from the small artery preceding the microcirculation to the small arterioles at the beginning of terminal microcirculation (Figure 2). All of these branching orders in this preparation possess vascular tone (Figure 5). The vascular responses of dilation with local skin warming (Figure 7, top panel) and constriction with cooling (Figure 7, bottom panel) are appropriate for thermoregulatory function. However, there are some limitations of this skin preparation as well as unique features of skin in general that must be considered in interpreting data related to vascular control in skin. First, the preparation of the rat abdominal
skin for intravitral microscopy requires anesthesia, which might influence both vascular tone and reactivity. Furthermore, the larger vessels of this preparation are unique in that they supply blood to both the skin and the cutaneous maximus muscle. In older animals such as those used in this study, considerable connective tissue overlies these vessels. Some of this tissue must be removed to provide adequate resolution of the larger microvessels. Even then it is not possible to resolve all of the 3A in older animals, and it is generally necessary to dissect some of the muscle tissue over selected 3A to improve clarity adequately for diameter measurements. In addition to the limitations specific to this preparation, consideration must also be given to the considerable differences in skin that occur between regions (apical versus nonapical) and species. Skin blood flow in apical regions such as the hand are characterized by much greater changes during both heating and cooling than occur in nonapical regions. Differences between species include innervation (sympathetic vasoconstrictor versus vasodilator nerve fibers), thermoregulatory reflexes, the prevalence of sweat glands, and the number of arteriovenous anastomoses.

The primary purpose of the present study was to compare the responses of the cutaneous resistance vessels with local temperature changes in SHR and WKY rats to determine if a vascular abnormality in the SHR might contribute to the impaired thermoregulation of the SHR. The top panel of Figure 4 illustrates that there are no differences in the diameters of small arteries through small arterioles at normal skin temperatures of 34°C–35°C. The maximally dilated diameters of arterioles were also similar between SHR and WKY rats, but the small arteries were significantly smaller in the SHR (Figure 4, bottom panel). Although the potential to dilate, as judged from the percentage of vascular tone at normal skin temperature (Figure 5), tended to be less in the SHR SA, there were no statistically significant differences. The smaller SA in the SHR could potentially limit maximum dilation and thereby flow, but this was not the case in the present study since the SA did not participate in the vascular response to local skin warming (Figure 7, top panel). The diameter measurements reported for arterioles in the present study are somewhat different than those reported for younger rats by Haack et al, who found the intermediate (2A) and small (3A) cutaneous arterioles to be larger in SHR than in WKY rats. The diameters in the previous study tend to be between the maximum and control diameters of the current study. It is difficult to know how to compare diameters between the two studies because, as Haack et al discuss, their technique of excising and fixing abdominal skin sections removed the vessels from normal neural and humoral influences as well as pressure.

The most apparent difference between the cutaneous arterioles of the SHR and WKY rats was in the magnitude of the responses to local warming and cooling. The response to warming from 34°C–35°C to 38°C–39°C was limited to the small arteries; the 3A of SHR lost essentially all of their vascular tone and were maximally dilated, whereas the WKY SA had approximately 50% of their tone remaining (Figures 5 and 7). When local skin temperature was changed from 35°C to 25°C, vasoconstriction occurred in all branching orders (SA-3A, lower panel of Figure 7). The 1A and 2A of SHR constricted the same percentage as those of WKY rats, but the SHR SA and 3A constricted about twice as much as comparable vessels in WKY rats. Increased vascular reactivity or sensitivity, as seen in the temperature-dependent responses of the cutaneous arterioles in this study, is common to both arteries (as reviewed by Muhlven and Aakjaer?) and arterioles of the SHR.

As discussed above, the results of this study reveal differences between WKY and SHR rats in the magnitude of the skin vascular response to local temperature changes. However, it seems unlikely that such differences would be responsible for the thermoregulatory abnormalities associated with hypertension. The increased vasoconstriction seen with local cooling should act to maintain core temperature rather than cause a more rapid fall in core temperature as has been reported for SHR during cold stress. The greater vasodilation with skin warming could possibly contribute to heat intolerance in the SHR when the thermal gradient is such that the environmental temperature is higher than skin temperature. But the enhanced vasodilation would not explain why blood flow in the forearm after exercise is reduced in mildly hypertensive humans or why, during heat stress in conscious rats, the rate of increase in body temperature is similar between SHR and WKY rats. Although the results show that the ability of SHR cutaneous arterioles to alter their diameters in response to local temperature changes is not impaired, the observed responses in anesthetized rats to local skin temperature changes could be quite different from those that occur with exposure of the whole body to temperature extremes that alter core temperature and activate central thermoreceptors in conscious animals.

The cutaneous vasculature does not contribute to the elevated total peripheral resistance in SHR as much as other organs, and studies are not in agreement regarding the exact contribution of the skin to the increased peripheral resistance. Studies in 4–6-month-old and 7–8-week-old SHR have found total peripheral resistance to be elevated approximately 60% without a statistically significant increase in skin resistance. However, a recent study by Thomas et al in 12–15-week-old SHR did find a significant increase in skin vascular resistance that was proportional to the increase in total peripheral resistance. If skin vascular resistance is elevated in the SHR, the hemodynamic mechanism responsible for the increase is not clear. The current study found no differences between SHR and WKY rats in either control or denervated arteriolar diameters (Figures 4 and 6). The absence of significant neural tone in the microvasculature has also been reported for intestine and cheek pouch of normotensive animals. A previous study by Haack et al did report fewer numbers of small arterioles in SHR skin, but the significance is unclear since they also found the diameters of larger arterioles to be increased in the SHR, and larger vessels generally contribute more to total peripheral resistance than smaller vessels. Based on the evidence available, the chronic adaptation of the cutaneous vasculature in the SHR seems to be similar to that of the spinotrapezius and cremaster muscles. In the cremaster, large through small arterioles in SHR and WKY rats have similar diameters when innervated,
denervated, and vasodilated. Studies in the spinotrapezius muscle have also observed similar diameters under control and vasodilated conditions for WKY rats and SHR.

In conclusion, a method is presented to prepare the rat abdominal skin for intravital microscopy that provides the capability to study the vascular responses of small arteries through small arterioles. With local skin temperature changes, major differences exist between branching orders in the response to heating versus cooling. A major question that remains to be answered concerns the mechanisms that are responsible for the temperature-induced alterations in skin vascular tone. Faber has shown in the rat cremaster muscle that cooling augments noradrenergic constriction of the microvasculature. This temperature-dependent response is more pronounced in smaller arterioles and is mediated by \( \alpha_1 \)-adrenergic receptors. If basal adrenergic tone exists due to circulating norepinephrine and epinephrine in the rat abdominal skin, this same mechanism in the rat abdominal skin could potentially mediate the responses that were observed. Other mechanisms such as myogenic and flow-dependent mechanisms could also be involved and might mediate responses in larger arterioles due to pressure or flow alterations, or both, that occur as a result of changes in the tone of the small arterioles. In the SHR, greater vasoconstriction occurs with local skin cooling, and vasodilation during skin warming is enhanced relative to the vessels in WKY rats. Such enhanced vascular responsiveness is common to the SHR but does not explain the thermoregulatory abnormalities that occur in the SHR.

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