VR-1 receptor blockade attenuates the pressor response to capsaicin but has no effect on the pressor response to contraction in cats

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VR-1 receptor blockade attenuates the pressor response to capsaicin but has no effect on the pressor response to contraction in cats. Am J Physiol Heart Circ Physiol 288: H1867–H1873, 2005. First published November 24, 2004; doi:10.1152/ajpheart.00735.2004.—Vanilloid type 1 (VR-1) receptors are stimulated by capsaicin and hydrogen ions, the latter being a by-product of muscular contraction. We tested the hypothesis that activation of VR-1 receptors during static contraction contributes to the exercise pressor reflex. We established a dose of iodoresiniferatoxoin (IRTX), a VR-1 receptor antagonist, that blocked the pressor response to capsaicin injected into the arterial supply of muscle. Specifically, in eight decerebrated cats, we compared pressor responses to capsaicin (10 μg) injected into the right popliteal artery, which was subsequently injected with IRTX (100 μg), with those to capsaicin injected into the left popliteal artery, which was not injected with IRTX. The pressor response to capsaicin injected into the right popliteal artery averaged 49 ± 9 mmHg before IRTX and 9 ± 2 mmHg after IRTX (P < 0.05). In contrast, the pressor response to capsaicin injected into the left popliteal artery averaged 46 ± 10 mmHg “before” and 43 ± 6 mmHg “after” (P > 0.05). We next determined whether VR-1 receptors mediate the pressor response to contraction of the triceps surae muscles. During contraction without circulatory occlusion, the pressor response before IRTX (100 μg) averaged 26 ± 3 mmHg, whereas it averaged 22 ± 3 mmHg (P > 0.05) after IRTX (n = 8). In addition, during contraction with occlusion, the pressor responses averaged 35 ± 3 mmHg before IRTX injection and 49 ± 7 mmHg after IRTX injection (n = 7). We conclude that VR-1 receptors play little role in evoking the exercise pressor reflex.

exercise pressor reflex; group III and IV muscle afferents; sympathetic nervous system; reflex control of circulation

DURING STATIC EXERCISE, mean arterial pressure, heart rate, and ventilation all increase. Two neural mechanisms evoke these effects, namely, central command (40) and the exercise pressor reflex (13, 22). Central command involves the activation of cardiovascular and respiratory neuronal pools in the medulla to activate autonomic and ventilatory responses in a feed-forward manner. The exercise pressor reflex is evoked by the contraction-induced stimulation of group III and IV muscle afferents (21). Group III afferents are more mechanically sensitive than are group IV afferents, but both are stimulated by metabolites, such as lactic acid, bradykinin, cyclooxygenase products of arachidonic acid, and potassium ions (15, 16, 26, 29, 32).

Capsaicin, the active ingredient in “hot” peppers, injected into the arterial supply of skeletal muscle reflexly increases mean arterial pressure, heart rate, and breathing (8, 41). Capsaicin stimulates the vanilloid receptor type 1 (VR-1), which also is responsive to increases in the concentration of hydrogen ions as well as increases in temperature (6). Hydrogen ions, dissociated from lactic acid, are by-products of anaerobic metabolism in exercising skeletal muscle and are thought to activate metaboreceptors located on group III and IV muscle afferents (26, 32). During exercise, VR-1 receptors, responding to increases in hydrogen ions concentration, may contribute in part to the contraction-induced stimulation of group III and IV muscle afferents. Iodoresiniferatoxoin (IRTX) blocks the VR-1 receptor both in vitro and in vivo (25, 39). Therefore, we used IRTX to block VR-1 receptors during static contraction of the triceps surae muscles while they were freely perfused and while their circulation was occluded to test the hypothesis that these receptors play a role in evoking the metabolic component of the exercise pressor reflex, which in turn was induced by statically contracting the triceps surae muscles.

METHODS

All procedures were approved by the Institutional Care and Use Committee of the University of California, Davis.

Capsaicin Injection

Surgery. In 11 cats, anesthesia was induced with 5% halothane and oxygen. The right carotid artery, right jugular vein, and trachea were cannulated while the cats breathed a mixture of 3% halothane and oxygen. The lungs were then ventilated mechanically with the gas mixture. The right popliteal artery and vein, as well as the right saphenous vein, were isolated so that bulldog clamps could be placed on them. In addition, a snare made of umbilical tape was placed around the outside of the right thigh. The left popliteal artery also was isolated. The cervical phrenic nerve was cut and placed on a recording electrode. A midcollicular decerebration was performed, and all tissue rostral to the inferior colliculi was removed. Subsequently, the lungs were ventilated mechanically with room air. The cats were paralyzed with vecuronium bromide (0.6 mg/kg iv).

Protocol. We injected 10 μg of capsaicin into the popliteal artery of the right leg to evoke a reflex pressor response. Ten minutes later, we injected 10 μg of capsaicin into the popliteal artery of the left leg as a control. We then waited 15 min, tightened the snare placed around the right thigh, and placed bulldog clamps on the right popliteal artery and vein as well as on the right saphenous vein. To block VR-1 receptors, we injected 100 μg of IRTX into the popliteal artery of the right leg. After the injection, the snare and clamps were maintained for 10 min and then released. We allowed the right leg to be freely perfused for 5 min before reinjecting 10 μg of capsaicin, a maneuver that allowed us to challenge the effectiveness of the blockade by IRTX. We immediately repeated the capsaicin injection (10...
µg) into the left leg as a control. We repeated these capsaicin injections at 30-min intervals until recovery was apparent. All injections were made with a 30-gauge needle that was inserted with its tip pointed downstream into the popliteal artery.

This protocol was performed in 11 cats, and data from 8 of these cats were used in the data analysis shown in Fig. 1 (see RESULTS). One of the cats was excluded from the analysis because even though IRTX attenuated the reflex pressor response to capsaicin injection into the right popliteal artery, the response did not recover over time. As a consequence, any attenuation of the reflex by IRTX could be attributed to deterioration of the preparation. A second cat was excluded because IRTX attenuated the reflex pressor response to capsaicin injection into the popliteal arteries of both legs. As a consequence, the attenuation could be attributed to circulation of IRTX to the spinal cord or brain stem. Finally, a third cat was excluded because even though IRTX attenuated the reflex pressor response to capsaicin injection into the right popliteal artery, it displayed a large upward shift in baseline mean arterial pressure (i.e., 50 mmHg). As a consequence, the IRTX-induced attenuation could be attributed to a ceiling effect.

We measured arterial blood pressure by connecting the carotid cannula to a Statham pressure transducer (model 23 XL). Heart rate was calculated beat to beat from the arterial pressure pulse (Gould). Phrenic nerve activity was recorded from a bipolar recording electrode; the phrenic signals were amplified (Grass P511) and then integrated (Gould) with a sample-and-hold function that reset every 100 ms. This method of integration of phrenic nerve discharge has been shown to strongly correlate with tidal volume (11). The maximum “phrenic breath” was obtained by stopping the ventilator. This maximum was then given an arbitrary value, and all other phrenic breaths were scored with respect to it. Peak phrenic breaths were summed both for 60 s immediately preceding a maneuver and for 60 s starting from the onset of a maneuver; these sums are the neural equivalent of minute volume of ventilation (11).

**Freely Perfused Contraction With IRTX Blockade**

**Surgery.** In eight cats, the surgical preparation was the same as that described for the eleven cats receiving capsaicin injections except for the following modifications. First, the triceps surae muscles of both legs were isolated, and the calcaneal bones were cut to allow measurement of tension development of the triceps surae muscles. The free ends of the calcaneal tendons were attached to a force transducer (model FT-10C, Grass). Second, a laminectomy was performed to expose spinal segments L5 to S1. The L7 and S1 ventral roots leading to both legs were isolated, cut, and placed on stimulating electrodes. Third, all visible branches of the sciatic nerves innervating the thighs and the femoral nerves were cut in both legs.

**Protocol.** We set baseline resting tension of the triceps surae muscles at 0.5 kg. We stimulated the ventral roots (40 Hz, 0.1 ms, 60 s) at 2× motor threshold to statically contract the triceps surae muscles. Once we recorded suitable pressor, cardioaccelerator, and phrenic neural responses to contraction, we statically contracted the opposite or left leg as a control. We next injected 100 µg of IRTX into the popliteal artery of the right leg, again trapping it for 10 min. Next, we allowed the leg to be freely perfused for 5 min. We statically contracted the right triceps surae muscles (40 Hz, 0.1 ms, 60 s, 2× motor threshold) and recorded the pressor, cardioaccelerator, and phrenic neural responses. We repeated the contraction of the left triceps surae muscles. If we recorded any changes in the above responses, we repeated the contractions until recovery was attained.

**Ischemic Static Muscular Contraction With IRTX Blockade**

**Surgery.** In seven cats, the surgical protocol was very similar to that described for the eleven cats receiving capsaicin injections except for the following modifications. Third, all visible branches of the sciatic nerves innervating the thighs and statically contracted the right leg again. If we recorded any changes in the above responses to static contraction while the muscles were freely perfused.

However, in the following experiments, we prepared only the right leg. In addition, we no longer recorded phrenic nerve activity but, instead, recorded airflow using a pneumotach (Fleisch), which was attached in series to the tracheal cannula. Airflow was integrated, breath by breath, to yield tidal volume, which in turn was used to calculate minute volume of ventilation.

**Protocol.** We set baseline resting tension at 0.5 kg. We tightened the snare around the upper thigh and placed bulldog clamps around the popliteal artery, popliteal vein, and saphenous vein. After 3 min of circulatory occlusion, we stimulated the ventral roots (40 Hz, 0.1 ms, 60 s, 2× motor threshold) and maintained the occlusion for 30 s after the end of the static contraction. We next injected 100 µg of IRTX into the popliteal artery of the right leg, again trapping it for 10 min, and statically contracted the right leg again. If we recorded any changes in the cardiovascular and ventilatory responses, we repeated the contractions until recovery was attained.

The data were analyzed with either one- or two-way repeated-measures analysis of variance. When required, Student-Newman-Keuls post hoc tests were used. The criterion for statistical significance was P < 0.05.

**RESULTS**

In eight decerebrated cats, we found that IRTX (100 µg) attenuated the cardiovascular responses to capsaicin injection (10 µg) into the popliteal artery. The peak pressor response in the right leg averaged 49 ± 7 mmHg before IRTX and 9 ± 2 mmHg after IRTX (P < 0.05; Figs. 1 and 2 and Table 1). Moreover, the duration of the pressor response to capsaicin injection before IRTX averaged 176 ± 32 s, whereas the duration of the pressor response to capsaicin injection after IRTX averaged 21 ± 10 s (P < 0.05). The interval between the IRTX injection and the second capsaicin injection averaged 16 ± 2 min. In the left leg, which was not given IRTX, the pressor response to capsaicin averaged 46 ± 10 mmHg “before” and 43 ± 6 mmHg “after” (P > 0.05).

After establishing a dose of IRTX that blocked VR-1 receptors, we examined its effect on the exercise pressor reflex while the circulation to the contracting muscles was intact. We found that IRTX had no effect on the cardiovascular and ventilatory responses to static contraction while the triceps surae muscles were freely perfused (Fig. 3 and Table 2). Data from eight decerebrated cats show that during freely perfused contraction of the right triceps surae muscles, which received IRTX, the pressor response before blockade averaged 26 ± 3 mmHg, whereas after blockade it averaged 22 ± 3 mmHg (P > 0.05). Contraction of the left triceps surae muscles, which did not receive IRTX, evoked a pressor response that averaged 24 ± 3 mmHg before IRTX was injected into the right popliteal artery and 21 ± 1 mmHg after IRTX was injected. The peak cardioaccelerator response to contraction of the right triceps surae muscles averaged 13 ± 4 beats/min before IRTX injection and 14 ± 3 beats/min after IRTX injection (P > 0.05). The peak cardioaccelerator responses to contraction of the left triceps surae muscles, which did not receive IRTX, averaged 36 ± 17 beats/min “before” and 26 ± 7 beats/min “after” (P > 0.05). Tension development by the right triceps surae muscles averaged 2.7 ± 0.5 kg before IRTX and 2.4 ± 0.5 kg after IRTX (P > 0.05). Likewise, tension development by the left triceps surae muscles, which did not receive any IRTX, averaged 2.5 ± 0.3 kg “before” and 2.3 ± 0.5 kg “after” (P > 0.05).
Our next aim was to examine the effects of VR-1 receptor blockade on the responses to static contraction during circulatory occlusion. We found that IRTX had no effect (\(P < 0.05\)) on the responses to static contraction while the circulation was occluded (Fig. 4 and Table 3). Data from seven decerebrated cats show that the peak pressor response to contraction averaged 35 ± 3 mmHg before IRTX injection and 49 ± 7 mmHg after IRTX injection (\(P > 0.05\)). Likewise, the peak pressor responses to postcontraction circulatory occlusion averaged 15 ± 4 mmHg before IRTX injection and 17 ± 7 mmHg after IRTX injection (\(P > 0.05\)). The peak cardioaccelerator responses to contraction averaged 12 ± 2 beats/min before IRTX injection and 19 ± 4 beats/min after IRTX injection (\(P > 0.05\)). Heart rate was not increased over baseline levels during postcontraction circulatory occlusion. The increase in minute volume of ventilation in response to contraction averaged 61 ± 39 ml/min before IRTX injection and 125 ± 62 ml/min after IRTX injection (\(P > 0.05\)). Likewise, the ventilatory response to postcontraction circulatory occlusion averaged 91 ± 32 ml/min before IRTX injection and 92 ± 29 ml/min after IRTX injection (\(P > 0.05\)). Tension development by the triceps surae muscles was not significantly different between the two groups: before IRTX, developed tension averaged 3.0 ± 0.2 kg, and after IRTX, injection tension averaged 3.0 ± 0.2 kg.

Table 1. Baseline values for capsaicin injection

<table>
<thead>
<tr>
<th>Capsaicin Injection</th>
<th>Before</th>
<th>After</th>
<th>Recovery</th>
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<tbody>
<tr>
<td><strong>Right leg, received IRTX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>132±14</td>
<td>144±12</td>
<td>122±13</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>172±10</td>
<td>159±13</td>
<td>201±33</td>
</tr>
<tr>
<td>PNA, au</td>
<td>748±109*</td>
<td>444±30*</td>
<td>549±40</td>
</tr>
<tr>
<td><strong>Left leg, control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>137±14</td>
<td>142±12</td>
<td>121±10</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>165±10</td>
<td>158±12</td>
<td>182±18</td>
</tr>
<tr>
<td>PNA, au</td>
<td>666±42*†</td>
<td>456±73*†</td>
<td>500±29†</td>
</tr>
</tbody>
</table>

Values are means ± SE; \(n = 8\). IRTX, iodoresinaferatoxin; MAP, mean arterial pressure; HR, heart rate; PNA, phrenic nerve activity; au, arbitrary units. *\(P < 0.05\), before vs. after IRTX injection. †\(P < 0.05\), recovery vs. before IRTX injection.
receptors in the right triceps surae muscles. They also suggest that IRTX did not circulate systemically to block VR-1 receptors in the spinal cord or brain stem.

In our experiments, the "ventilatory" response to contraction was modest on average and displayed a large amount of variability. These findings are consistent with those reported previously (30, 42); they are also consistent with the conclusion that the exercise pressor reflex evokes only a small increase in breathing (13). In addition, the ventilatory (i.e., phrenic) response to capsaicin did not repeat after the first injection, regardless of whether this substance was injected into the right leg, which received IRTX, or into the left leg, which did not receive IRTX. Consequently, the decrease in the phrenic responsiveness to capsaicin in our experiments cannot be attributed to VR-1 receptor blockade. Moreover, the decrease in phrenic responsiveness cannot be attributed to tachyphylaxis because the pressor and cardioacceleratory responses to capsaicin did repeat in the left leg. We speculate that the decrease in phrenic responsiveness to capsaicin injection was caused by the activation of brain stem neuronal circuits that depress ventilatory adjustments to peripheral input.

Capsaicin injected into the arterial supply of skeletal muscle of anesthetized dogs and cats stimulated ~25% of the group III muscle afferents and 75% of the group IV muscle afferents tested (14, 15). Many of the group III and IV afferents responsive to capsaicin also were responsive to static contraction (15). Moreover, circulatory occlusion amplified the responses to static contraction of these thin fiber muscle afferents as well as recruiting previously unresponsive ones (17). In part, the responses of group III and IV afferents to contraction are thought to be evoked by lactic acid production in the working muscles. Because the VR-1 receptor has been shown to be activated by hydrogen ions (6), it is a potential candidate for playing a role in stimulating the group III and IV muscle afferents responsible for evoking the reflex pressor response to contraction (i.e., the exercise pressor reflex). However, our findings suggest that VR-1 receptors play little, if any, role in the responses of group III and IV muscle afferents to hydrogen ion production by contracting muscles.

Cell bodies in the dorsal root ganglion that do not recognize the N52 antibody have been classified as C-fiber afferents because this antibody binds a 200-kDa protein, the presence of which correlates with myelination (18). N52 negative dorsal root ganglion cells display two profiles. The first depends on nerve growth factor for postnatal survival, does not bind

**DISCUSSION**

We found that the exercise pressor reflex (22) was not attenuated by injecting IRTX, a VR-1 receptor antagonist, into the arterial supply of the right triceps surae muscles. This was found to be the case both while the contracting triceps surae muscles were freely perfused and while their circulation was occluded. We also found that IRTX had no effect on the pressor responses to postcontraction circulatory occlusion, a maneuver that is commonly used to evoke the muscle metaboreflex in both humans and animals (1, 7, 21, 28, 35). Nevertheless, IRTX injected into the right popliteal artery attenuated the pressor response to subsequent capsaicin injection into the right popliteal artery but did not attenuate the pressor response to capsaicin injection into the left popliteal artery. These latter findings strongly suggest that the dose of IRTX used in our experiments was effective in blocking VR-1

### Table 2. Baseline values for static contraction under freely perfused conditions

<table>
<thead>
<tr>
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<th>Freely Perfused Static Contraction</th>
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<tbody>
<tr>
<td><strong>Right leg, received IRTX</strong></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>123±9</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>191±20*</td>
</tr>
<tr>
<td>PNA, au</td>
<td>602±242</td>
</tr>
<tr>
<td><strong>Left leg, control</strong></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>119±8</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>199±26*</td>
</tr>
<tr>
<td>PNA, au</td>
<td>562±146</td>
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Values are means ± SE; n = 8. *P < 0.05, before vs. after IRTX injection.

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**Fig. 3.** IRTX had no effect on cardiovascular and phrenic responses to static contraction under freely perfused conditions. Summary data are presented for the changes in MAP, HR, and phrenic nerve activity from 8 decerebrated cats in response to static contraction of triceps surae muscles before and after popliteal arterial injection of 100 μg of IRTX. Values represent mean changes (± SE). Solid bars represent responses to static contraction before (B) IRTX injection, and open bars represent responses to contraction 21 ± 4 min after (A) IRTX injection. The right leg received IRTX, whereas the left leg did not and thus served as a control. There were no significant differences between any variable before and after IRTX injection. *P < 0.05, response was significantly different from its corresponding baseline.
isolectin B4, and contains neuropeptides, including substance P and calcitonin gene-related peptide (CGRP). The second profile depends on glial cell line neurotrophic factor for postnatal survival, binds isolectin B4, and is neuropeptide poor (2–4, 23). In vitro, murine dorsal root ganglion cells displaying the first profile have been shown to be more responsive to both capsaicin and hydrogen ions than have dorsal root ganglion cells displaying the second profile (9). If this in vitro finding in mice can be extended to our in vivo findings in cats, capsaicin may have exerted its reflex cardiovascular and ventilatory effects by stimulating mostly group IV muscle afferents containing neuropeptides such as substance P and CGRP.

In vivo, group IV muscle afferents responsive to capsaicin display minimal sensitivity to mechanical stimuli, such as nonnoxious probing of their receptive fields and muscle stretch (15). In contrast, group III afferents, which often do not respond to capsaicin (15), display significant sensitivity to both of these stimuli. In vitro, cultured dorsal root ganglion cells that generated inward currents in response to capsaicin displayed higher thresholds and generated lower inward currents in response to mechanical stimuli than did cell bodies that did not generate inward currents in response to capsaicin (10). These findings lead us to speculate that VR-1 receptor blockade, such as that done in our experiments, would have little, if any, effect on the pressor, cardioaccelerator, and ventilatory responses to tendon stretch, which in turn are evoked by the stimulation of group III muscle afferents (34).

In our present experiments, we did not measure the hydrogen ion concentration of the contracting triceps surae muscles. Nevertheless, static contraction has been shown to decrease either the “intramuscular” or interstitial pH of the freely perfused triceps surae muscles of anesthetized cats (20, 27). Moreover, injections of lactic acid into the arterial supply of these muscles, which causes decreases in pH identical to those caused by contraction, evoked a reflex pressor response (20, 27). In humans, static handgrip decreased the intracellular pH of the contracting muscles, and the time course of the decrease matched the time course of the reflex increase in muscle sympathetic nerve activity (31, 38). Consequently, we are comfortable in offering the speculation that static contraction of the triceps surae muscles under freely perfused conditions increased the hydrogen ion concentration contacting group III and IV afferents in our preparation. We also speculate that this concentration was further increased by circulatory occlusion in our preparation (35). The fact that postcontraction circulatory occlusion evoked a significant pressor response in our preparation is consistent with this latter speculation.

Our findings in combination with those recently reported by Li et al. (19) may shed some light on the role played by hydrogen ions in stimulating VR-1 receptors during muscular contraction. Specifically, Li et al. reported that capsazepine, which blocks VR-1 receptors, did not prevent the reflex pressor response to lactic acid injection into the arterial supply of the gastrocnemius muscles of rats, whereas amiloride, which blocks acid-sensitive ion channels (ASIC), did prevent the pressor response. We have extended these findings by showing that VR-1 receptor blockade had no effect on the pressor responses to static contraction either while the circulation to the triceps surae muscles was intact or while it was occluded.

Table 3. Baseline values for static contraction under circulatory occluded conditions

<table>
<thead>
<tr>
<th>Static Contraction with Circulatory Occlusion</th>
<th>Before</th>
<th>After</th>
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<tbody>
<tr>
<td>MAP, mmHg</td>
<td>136±10</td>
<td>139±7</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>222±18</td>
<td>231±18</td>
</tr>
<tr>
<td>Vmin, ml/min</td>
<td>294.50</td>
<td>316±73</td>
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<tr>
<th>Postcontraction Circulatory Occlusion</th>
<th>Before</th>
<th>After</th>
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</thead>
<tbody>
<tr>
<td>MAP, mmHg</td>
<td>151±10</td>
<td>156±11</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>224±18</td>
<td>236±18</td>
</tr>
<tr>
<td>Vmin, ml/min</td>
<td>386±64</td>
<td>409±80</td>
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Values are means ± SE; n = 7. Vmin, minute volume of ventilation.
Consequently, it seems best to shift attention to the ASIC when attempting to discern the receptor on group III and IV muscle afferents responsible for signaling hydrogen ion production by contracting muscles. With respect to this last point, we find it interesting that the threshold hydrogen ion concentration needed to activate the ASIC is lower than that needed to activate the VR-1 receptor (5, 37).

One interpretation of our findings is that the reflex pressor component attributable to VR-1 receptor stimulation was compensated by stimulation of some other receptor responding to a metabolic by-product of contraction. Although we cannot exclude this possibility, we think it unlikely, because there have been several other studies that have shown that the exercise pressor reflex is reduced either by blocking other metabolic by-products or by slowing their production. For example, bradykinin receptor blockade with HOE-140 has been shown to attenuate the exercise pressor reflex in cats (24). Likewise, cyclooxygenase blockade with indomethacin and meclofenamate, agents that slow the production of prostaglandins and thromboxanes, also attenuated the reflex in cats (36). Furthermore, slowing lactic acid production with either glycogen depletions or dichloroacetate attenuated the pressor and muscle sympathetic nerve activity components of the exercise pressor reflex in humans (12, 33). Dichloroacetate also has been shown to attenuate the response of group III muscle afferents to static contraction (32).

The finding that VR-1 receptors can be stimulated by hydrogen ions prompted us to determine their role in evoking the metabolic component of the exercise pressor reflex. We made this determination in the standard animal preparation that is used to investigate the exercise pressor reflex. Specifically, we electrically stimulated the ventral roots of decerebrated cats to statically contract the triceps surae muscles while their circulation was either intact or occluded (7, 21). We found that blockade of VR-1 receptors in this muscle group had no effect on the exercise pressor reflex either while the circulation to the contracting muscles was occluded or while it was not occluded. We also found that VR-1 receptor blockade had no effect on the pressor response to postcontraction circulatory occlusion (i.e., the muscle metaboreflex) (28). Our findings lead to the conclusion that VR-1 receptors on group III and IV muscle afferents play little, if any, role in evoking any metabolic component of the exercise pressor reflex.

GRANTS

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