Smooth Muscle Tone and Rapid Resetting of Rat Aortic Baroreceptors

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Changes in conditioning mean arterial pressure (cMAP) selectively alter the set point of arterial baroreceptors and baroreflexes without affecting gain. Changes in smooth muscle tone at constant cMAPs shift the pressure–discharge curves of aortic baroreceptors in a similar manner. Using an in vitro preparation of the rat aortic arch, we tested whether near maximal changes in smooth muscle tone affect rapid resetting in single regularly discharging aortic baroreceptors. Discharge, pressure, and aortic diameter were simultaneously measured. By using vasoactive drugs (phenylephrine, angiotensin II, Bay K 8644, and nitroprusside), rapid resetting to cMAP changes was tested during different smooth muscle tone conditions (control, constricted, and dilated). Baroreceptor discharge–response curves were periodically assessed with slow ramps of increasing pressure at each of three different cMAP levels (10–15 minutes each). Rapid resetting relations were constructed for pressure threshold (Pth) and diameter threshold (Dth) plotted against cMAP and conditioning diameter (cD), respectively. Vasoconstriction decreased Pth in all baroreceptors (n=13, p<0.05). Baroreceptor resetting ability as indicated by the slopes of the resetting relations (pressure- or diameter-resetting ratios, ΔPth/ΔcMAP or ΔDth/ΔcD, respectively) was unaffected by large increases in smooth muscle tone (p>0.12). Vasoconstriction, however, offset the pressure-resetting relation, shifting the linear relation in a parallel manner to higher Pth values. In contrast, Dth values during vasoconstriction were not offset but instead fell along a single diameter-resetting relation coincident with the control relation for each baroreceptor. This last result suggests that acute alteration of vessel mechanics by vasoconstriction does not alter the basic rapid resetting process. These new results reinforce the notion that changes in the prevailing degree of baroreceptor distortion are the direct stimulus for a rapid resetting and that modulation of distortion threshold and baroreceptor performance are similar whether conditioning is produced passively by changes in cMAP or actively by altering local smooth muscle tone. (Circulation Research 1992;70:116–122)

The operating pressure range of arterial baroreceptors is strongly dependent on the short-term history of local pressure conditions.1–5 Thus, the pressure–discharge curves of baroreceptors rapidly shift (reset) within minutes after sustained changes in the conditioning mean arterial pressure (cMAP). This rapid resetting process selectively and reversibly affects baroreceptor pressure threshold (Pth) without altering suprathreshold pressure sensitivity (gain). Thus, rapid resetting is qualitatively different from the chronic resetting of baroreceptors during hypertension, where gain is markedly reduced and threshold is increased.6 These changes in afferent discharge characteristics importantly affect reflex function.4,7 The mechanism for rapid resetting is unknown.6,8 Since baroreceptors are mechanoreceptors and transduce changes in vessel wall distention, one hypothesis suggests that a reversible change in vessel wall mechanics might reduce the distortion of baroreceptor endings at a given pressure and, therefore, induce rapid resetting of the Pth.2,9 Measurements of vessel wall and baroreceptor discharge properties during changes in cMAP have generally found that increases in cMAP do indeed cause a long-lasting dilation of the baroreceptor region of the vessel wall.5,9,10 The changes in vascular mechanics, however, are often only slowly reversible and poorly correlated to the rapid reversal of changes in Pth.5,10,11 Structural changes in vessel wall during chronic hypertension decrease distensibility but also fail to affect the rapid resetting process.12

We have recently shown that changes in the smooth muscle tone of the aortic arch at constant

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cMAP shift the pressure–discharge curves of aortic baroreceptors in a parallel manner along the pressure axis. For example, vasoconstriction selectively increased Pth without affecting pressure gain.\textsuperscript{13} The families of baroreceptor pressure–discharge curves at successive increases in vasoactive drug concentration (see Figure 1 in Reference 13) were remarkably similar to those found during rapid resetting to cMAP changes. Early on in studies of rapid baroreceptor resetting, a possible role of local vasomotor smooth muscle was considered,\textsuperscript{2} but such a prerequisite was ruled out by the presence of rapid resetting in preparations fully dilated by nitroprusside (NP)\textsuperscript{10} and in adventitial baroreceptor preparations stripped of their smooth muscle layers.\textsuperscript{14} Nonetheless, increases in smooth muscle tone by changing the pressure–diameter relation for the vessel wall might alter the quantitative relations between cMAP and Pth. The present experiments were designed to directly compare and contrast the effects of sustained passive and active diameter changes on baroreceptor discharge properties and to test whether changes in active smooth muscle tone affect the rapid resetting process.

**Materials and Methods**

Male Sprague-Dawley rats (200–350 g, Harlan Sprague Dawley, Inc., Indianapolis, Ind.) were anesthetized with pentobarbital sodium (40 mg/kg i.p.). The methods for isolation and perfusion of rat aortic arch baroreceptors have been described previously.\textsuperscript{15,16} Briefly, after the left aortic nerve and aortic arch were surgically isolated, cannulas were introduced into the innominate and descending aorta, and the remaining tributary arteries were tied off. The preparation was removed from the rat and mounted in a temperature-regulated (37°C) perfusion chamber. The aortic arch was covered with warm mineral oil, and the lumen was perfused with an oxygenated, bicarbonate-buffered (pH 7.4) Krebs-Henseleit solution\textsuperscript{15} at a mean pressure of 80 mm Hg. A roller pump produced a steady mean flow of 3 ml/min. An air-filled reservoir damped pressure oscillations and regulated the mean level of perfusion pressure by a modified Starling resistor on the outflow. To measure aortic diameter, the aorta was positioned over a central glass window in the floor of the perfusion chamber, and the aortic profile was projected onto photodiode arrays connected to a custom-made, high-resolution photoelectronic caliper.\textsuperscript{17,18} Aortic diameter just distal to the left subclavian artery was measured continuously throughout all experiments.\textsuperscript{13,19,20}

**Single-Fiber Baroreceptor Characteristics**

The aortic nerve was split into fine filaments containing single active baroreceptors. Only regularly discharging baroreceptors were studied further. The discharge properties were tested with slow ramps of pressure (<2 mm Hg/sec) from 20 to 150–190 mm Hg. When a single baroreceptor was isolated, perfusion was halted, and pressure was lowered to 20 mm Hg for 30 seconds, followed by a test ramp using a shaker-bellows-driver system. We have previously shown that these slow ramp inputs evoke quasi-steady-state responses.\textsuperscript{15} Ramps allowed us to precisely and repeatedly assess the threshold, suprathreshold gain, and saturation characteristics of each baroreceptor in the shortest possible time.\textsuperscript{18} Pressure, diameter, and the electroneurogram were recorded on FM magnetic tape for later analysis. Discharge rate was measured as the instantaneous frequency (reciprocal of the interspike interval) by microcomputer. Pressure and diameter were digitally sampled by the microcomputer each 10 msec.

**Rapid Resetting**

Rapid resetting of arterial baroreceptors results in parallel shifts of both the pressure–discharge and diameter–discharge curves.\textsuperscript{5,9,10,12} For all experiments, the general procedures to assess rapid resetting were similar. After isolation of a single baroreceptor, ramp tests were repeated each 5 minutes to measure stability of the discharge properties in the initial, control state. All baroreceptors were initially conditioned with a pulseless cMAP of 80 mm Hg.\textsuperscript{21} Test ramps interrupted conditioning each 5 minutes over a period of 10–20 minutes. After completion of these initial tests, baroreceptors were conditioned at two additional cMAPs, which were not the same for every baroreceptor. Over all experiments, cMAP values ranged from 50 to 150 mm Hg. These three steps in cMAP were used to define the rapid resetting process at each smooth muscle condition. The order of cMAP presentation was random except that all experiments began at 80 mm Hg. No \(\Delta\text{cMAP}\) steps were smaller than 30 mm Hg or larger than 60 mm Hg. Within a given single-fiber baroreceptor experiment, identical testing intervals and sequences of cMAPs were tested at each smooth muscle state.

Smooth muscle tone was modified by addition of vasoactive drugs to the Krebs-Henseleit solution perfusing the lumen of the aortic arch. Vasoconstriction was induced by phenylephrine (PE, 10 nM) in a majority of experiments. However, angiotensin II (1 \(\mu\)M) and the calcium channel agonist Bay K 8644 (100 nM) were also used to ensure that the results were generally applicable and not dependent on adrenergic mechanisms of smooth muscle activation. Vasodilatation was induced by NP (1 \(\mu\)M). Each of these drugs appears to act on baroreceptors solely through their actions on smooth muscle.\textsuperscript{13,20,22} Drug concentrations were selected based on previous studies with complete concentration–response relations and represent concentrations that maximally contract or dilate the aortic arch of the rat.\textsuperscript{13,20,22}

Generally, the baroreceptor pressure– and diameter–discharge curves from different cMAPs or smooth muscle conditions could be completely superimposed by simply shifting the relation along the x axis. Therefore, we used two previously described methods to measure these x axis shifts in the baroreceptor discharge curve\textsuperscript{4,12,23}: 1) comparison of the
location of the entire pressure–discharge curve or 2) threshold values. In the location method, the shift in the discharge curve along the x axis necessary to completely superimpose two relations was measured using the first control curve as the standard of comparison for all successive control and experimental curves. The location method, by using the entire curve of over 1,000 points, was less susceptible to small, apparently random changes in the frequency of discharge at threshold (Figure 1). When threshold frequency was very constant, Pth values were used by averaging the first 10 points; this method avoids basing this measure on the occurrence of a single spike.18 Equivalent comparisons were made on the basis of diameter–discharge curves using the diameter at threshold (Dth) and the mean diameter during conditioning (cD). These threshold or location values were then plotted against cMAP (or cD), and these resetting relations were fitted with a linear function by least-squares regression. Resetting relations were well described by this linear function (r² exceeded 0.9 in all cases except one). The slope of the line fit to the rapid resetting relation (ΔPth/ΔcMAP or ΔDth/ΔcD) was used as a measure of the ability of a given baroreceptor to rapidly reset.12

Experimental Protocols

The protocols were designed to compare the rapid resetting of baroreceptors in response to prolonged changes in passive distending pressure (cMAP) during two diverse experimental states of smooth muscle tone: near maximal contraction and near maximal dilation. Complete rapid resetting curves were tested in each smooth muscle contractile state. We used three basic protocols. In the most extensive tests, rapid resetting was measured in three conditions of smooth muscle tone in the following order and all in the same single-fiber baroreceptor: 1) control (“en-dogenous”) tone only, 2) maximum vasoconstriction, and 3) maximum vasodilation. In addition, we used two abbreviated protocols by testing resetting only during two smooth muscle tone states: maximum constriction and dilation, or control (no drug) and maximum constriction. Thus, all baroreceptors were tested at maximum constriction and either control or dilated or both minimum tone states. Only one baroreceptor was tested in each preparation (i.e., one baroreceptor per rat), and time permitted only a single protocol to be tested in each experiment.

To be accepted for analysis, each baroreceptor had to successfully complete identical resetting sequences for at least three different cMAP levels in at least two different smooth muscle conditions. To complete the rapid resetting protocol in any given smooth muscle condition required a minimum of six measurements of the complete baroreceptor discharge curve over ~40 minutes. Baroreceptors completing all three smooth muscle conditions required a minimum of 18 measurements of the pressure–discharge curve over more than 2 hours. In individual experiments, rapid resetting relations were compared within experiments at maximum and minimum smooth muscle tones by analysis of covariance to compare the slopes and x axis locations of the regression lines.24 For groups of animals, reduced data in the form of resetting ratios (the slopes of the resetting relations) were compared by analysis of variance.24 The results of both individual protocols and summary means pooled across like protocols (e.g., all experiments with constrictor drugs compared with no-drug controls) are presented. Results are generally reported as mean±1 SD. Values of p<0.05 were considered significant.

Results

Tests of the effects of vasoconstriction on rapid resetting relations were completed on a total of 13 single-fiber baroreceptors, each from a different rat. The pressure–discharge relations of most of the baroreceptors studied generally had very linear initial portions in response to slow ramp pressure stimulation (Figure 1). Under control conditions, spontaneous smooth muscle tone in these in vitro preparations was usually minimal. Administration of 1 μM NP resulted in little or no dilation of the aortic arch (an average diameter change to 99.5±0.01% of control,
maximum dilations ranged to 105% of control) and often no effect on baroreceptor properties (authors' unpublished results). Changing cMAP in control conditions shifted the pressure–discharge relation in the direction of the new cMAP when measured after 5 minutes of exposure (Figure 1). The frequency of discharge at threshold and the slopes (gains) of the pressure–diameter–discharge relations were unaffected by NP (p>0.45). The curve shifts with changes in cMAP produced a family of parallel pressure–discharge curves for each baroreceptor over the range of cMAPs tested. Plots of Pth against cMAP showed the very linear dependence of threshold on the prevailing pressure that is characteristic of rapid resetting (Figure 2).\textsuperscript{3,12} For changes in cMAP when smooth muscle tone was at unstimulated, “endogenous” levels, the slope of these resetting relations (the pressure-resetting ratio, ΔPth/ΔcMAP) averaged 0.31±0.08 (n=10, mean±SD).

At a fixed cMAP of 80 mm Hg, addition of 10 nM PE evoked a near maximal vasoconstriction and caused a rapid shift in the pressure–discharge curve to a higher range of pressures (middle panel of Figure 1). The PE constriction was similar in magnitude to that found with angiotensin II or Bay K 8644, and at 80 mm Hg, the constrictors as a group produced an average aortic diameter reduction to 91.1±0.07% of the control diameter. This concentration of PE and the accompanying vasoconstriction did not affect the discharge frequency at Pth or the slope (gain) of the individual pressure–discharge curves for any unit baroreceptor (p>0.3). Thus, this concentration of PE avoids the excitatory, gain-increasing effects of higher (>100 nM) concentrations of α-adrenergic agonists on baroreceptors.\textsuperscript{20} Increases in cMAP during PE vasoconstriction resulted in further shifts of the baroreceptor pressure–discharge curve to higher pressures (middle panel of Figure 1). This pressure resetting during maintained vasoconstriction was qualitatively and quantitatively similar to that found during resetting tests at control levels of smooth muscle tone (Figure 2). Thus, the major effect of the addition of PE and vasoconstriction was to shift the family of pressure–discharge curves to higher pressures (Figure 1) and to raise the pressure-resetting relation to a higher range of Pth values (Figure 2).

Addition of 1 μM NP returned aortic diameter to near control levels and returned the baroreceptor pressure–discharge curve to a lower range of pressures (bottom panel of Figure 1). In cases such as that of Figure 2 where NP dilation after constriction did not quite return the diameter at 80 mm Hg back completely to control levels, Pth values remained somewhat elevated, perhaps because of lingering effects of PE on smooth muscle. Compared with control, NP vasodilation after vasoconstriction had no effect on the slope of the pressure–diameter–discharge relations or on threshold firing frequency (bottom panel of Figure 1, p>0.4). The similarity of the overall shape of the baroreceptor pressure–discharge relations was attested to by the completeness of their superimposition after x axis shifting (see “Materials and Methods”). Increases in cMAP resulted in pressure resetting of the baroreceptor in a manner similar to that during control or increased smooth muscle tone conditions. The slope of the pressure–rapid resetting relation (the resetting ratio) was unaffected by NP (Figure 2, p>0.2).

Vasoconstriction significantly increased Pth at any given cMAP in all cases (n=13, p<0.05), and the results were uniform regardless of the vasoconstrictor. In the most rigorous test and most successful experiments (n=4), each baroreceptor completed sequential tests of a series of three different cMAPs in each of three smooth muscle states, control (“endogenous”), PE, and NP, and these tests showed no changes in the mean pressure resetting ratio (Figure 3, p=0.233). Protocols using angiotensin II (n=3) or Bay K 8644 (n=1) showed similar degrees of aortic constriction and similar, selective parallel shifts in pressure–discharge curves as baroreceptors exposed to PE only (n=2). When the results for the control and vasoconstrictor portions of these experiments were pooled (two PE, three angiotensin II, and one Bay K 8644; total n=6), no significant changes (p=0.19) in the mean pressure resetting ratios were found during vasoconstriction (0.301±0.080) compared with control (0.341±0.093). For baroreceptors tested with maximum vasoconstriction and dilation (an additional three baroreceptors), no difference in the mean pressure resetting ratio was found (PE, 0.218±0.099; NP, 0.216±0.134; p=0.91). Thus, the results uniformly suggest that the pressure rapid resetting ratio is unaffected by changes in smooth muscle tone.
FIGURE 3. Bar graph showing average rapid resetting ratios for baroreceptors completing resetting tests at each stage of the smooth muscle sequence: control, vasoconstricted, and dilated. Four baroreceptors completed this protocol. C, Control no-drug condition; PE, 10 nM phenylephrine; NP, 1 µM nitroprusside. Bars are mean±SD. Changes in smooth muscle tone had no effect on the resetting ratio (p=0.233).

We measured aortic diameter simultaneously with pressure and the electroneurogram throughout all experiments. Dth can be used as an expression of the distortion threshold of the baroreceptor.13,25 Thus, as a complementary approach, rapid resetting can be depicted in terms of mechanical distortion as well as pressure. Plots of Dth against the cD were linear over the range of pressures tested (Figure 4). Overall, the slopes of these Dth-resetting relations (ΔDth/ΔcD) averaged 0.322±0.098 for controls and 0.355±0.105 during constriction. Within-experiment testing of replicate measures of threshold across three different cMAPs detected no slope changes in any case during vasoconstriction (p>0.12, n=13).

FIGURE 4. Rapid resetting relations expressed as pressure threshold (Pth, left panel) and aortic diameter threshold (Dth, right panel) for a single baroreceptor before and during strong vasoconstriction. Plots are of threshold versus the conditioning mean arterial pressure (cMAP) or the aortic diameter at that pressure (cD). Points represent single, periodic measurement of threshold at a given cMAP before (control, unfilled circles) and during vasoconstriction (angiotensin, filled circles). Two measurements were made under each condition, but overlap obscures some points. Lines are least-squares linear regression fits to each set of data for a given smooth muscle condition (r² was 0.982 and 0.996 for Pth fits and 0.983 and 0.994 for Dth fits before and during angiotensin, respectively). Note the offset of fits to higher Pth values in the left panel but the near identity of fits for Dth values in the right panel. Note Dth values tended to be lower during vasoconstriction, especially at the lowest cMAP (80 mm Hg).

Interestingly, there was generally no discernible offset between the diameter-resetting relations measured at different degrees of smooth muscle tone. For example in Figure 4, note that Dth values at 80 mm Hg cMAP were lower during vasoconstriction than during control. This is the opposite rank order of the corresponding Pth values and a finding similar to previous studies with vasoactive peptides at constant cMAP.13 However, expression of the conditioning stimulus as diameter shows that cD was also lower during vasoconstriction at the 80 mm Hg cMAP and that all Dth values fell along a single relation predicted by control measurements. Thus, in absolute terms, although constriction at low cMAPs shifted Dth to lower values, they fit along a common diameter-resetting relation. Differences in Dth between constricted and relaxed smooth muscle states tended to be largest at the lower cMAPs (50–80 mm Hg) and were generally smaller to absent at higher cMAPs in most baroreceptors studied (Figure 4, right panel).

Discussion

The ability of arterial baroreceptors and baroreflexes to rapidly reset after changes in the prevailing pressure has attracted considerable attention recently. Generally, these reports describe the rapid resetting process in baroreceptor afferents as a parallel shifting of the pressure–discharge curve with no change in suprathreshold gain.5,9,11 A number of techniques have been used to alter the prevailing blood pressure in several different species (rabbits,4,23 rats,1 and dogs9), and these yielded qualitatively similar results. Similar manipulations in conscious subjects show parallel shifts of baroreflex response curves for control of heart rate for rabbits,4,23 rats,26 and humans.27

The present study focused on a possible interaction between two known modulators of baroreceptor discharge properties: conditioning transmural pressure (which we equate with rapid resetting) and vasoconstriction. It should be noted that prevailing transmural pressure is indirectly related to distortion of the baroreceptor sensory ending and that the transformation of pressure into distortion depends on the state of vessel wall mechanics. When cMAP is increased, the vessel wall and all associated elements passively stretch. By contrast, changes in smooth muscle tone actively generate force within one vessel wall element and thereby change global diameter and vessel wall distension. This study examined these two modulators together to see if their actions on baroreceptors were additive or if there was a more complex interaction. Our two major new findings are as follows: 1) The degree of smooth muscle tone does not alter the resetting process. 2) A single Dth–cD relation describes the resetting process across widely disparate smooth muscle conditions. Surprisingly, the latter results suggest that the mechanisms responsible for rapid resetting may be an important determi-
nant of the net effects of smooth muscle tone on baroreceptor discharge properties.

As in previous reports,3,21 changes in cMAP at a single smooth muscle state induced parallel shifts in the entire discharge curve without affecting the general shape of the curve or the minimal and maximal discharge rates. Also as we previously found,12 application of vasoconstrictor drugs at a fixed cMAP decreased Dth and increased Pth, a finding generally similar to that of others.10,20,29-31 The major new finding was that when tested together, changes in cMAP shifted the baroreceptor discharge curves in a quantitatively similar manner whether vascular smooth muscle tone was maximal or minimal. Thus, despite constriction-induced changes in threshold, we found no evidence to suggest that the ability of these baroreceptors to rapidly reset (as measured by pressure or distortion resetting ratios, ΔPth/ΔcMAP or ΔDth/ΔcD, respectively) was affected by changes in smooth muscle tone.

An interesting contrast was evident, however, in the results expressed as diameter-resetting relations compared with their pressure-equivalent relations. The pressure-resetting relations were always parallel (i.e., equal in slope), indicating an equivalent ability to reset. However, changes in smooth muscle tone produced a substantial offset between pressure–resetting relations by shifting them along the Pth axis. In contrast, diameter-resetting data tended to lie on a single relation regardless of the state of the smooth muscle. We feel that this finding suggests that this diameter-resetting relation is probably a more fundamental expression of the modulation of these mechanoreceptors by prevailing levels of stimulation. Thus, the identity of the diameter-resetting relations for a given baroreceptor across close to the full range of smooth muscle tone reinforces the notion that one of the effects of smooth muscle on baroreceptor pressure–discharge properties is secondary via mechanical effects on the vessel wall.13 A second effect of vasoconstriction is to lower distortion thresholds. Thus, a corollary suggested by the present results is that resetting mechanisms play an important part in the baroreceptor response to sustained smooth muscle stimulation by changing distortion threshold. During vasoconstriction, especially at low cMAPs, the prevailing diameter is reduced, and the mechanisms responsible for rapid resetting act to reduce distortion threshold in response to the sustained, decreased baroreceptor “loading.” This new data provides an explanation for the paradoxical, partially “compensatory” changes in Dth found in our previous study13 during changes in smooth muscle tone at fixed pressures.

The mechanisms hypothesized for rapid resetting fall into two major classes: mechanical effects involving the vessel wall and changes in the intrinsic, cellular properties of the baroreceptor itself. A very basic interpretation of the mechanical hypothesis of resetting suggests that, for example, reductions in the vessel wall distensibility reduce the stretch of baroreceptor endings and thus could account for increases in Pth during hypertension.32,33 Such a simple scheme, however, cannot account for the simultaneous changes in baroreceptor distortion threshold that occur during hypertensive resetting.6 A micromechanical version of the mechanical hypothesis is harder to evaluate.34,35 This hypothesis suggests that local mechanical changes or changes in the coupling of the baroreceptor ending to the vessel wall that are not reflected in measurements of the vessel diameter may be responsible for “unloading” the stretch on the baroreceptor during sustained increases in cMAP.5,9 Thus, a viscoelastic relaxation of some wall element might gradually reduce the distortion of the baroreceptor endings after an increase in cMAP and resetting the baroreceptor threshold.

The results of our study cannot rule out a role for potential micromechanical effects, but our experiments do suggest certain prerequisite characteristics for these mechanical elements that may raise doubts about the feasibility of this hypothesis. Since the total vessel wall can undergo relatively large absolute changes in distensibility or diameter, then offsetting changes by the micromechanical coupling element would have to be equally large. Furthermore, the linearity of the rapid resetting process and the immunity of the resetting ratio to large changes in diameter implies an extended range of linearity of operation of this coupling element, an unusual property for vascular mechanics over a range of pressures from 20 to 180 mm Hg.3 The coupling element would also need remarkable properties to effectively link dynamic changes in wall strain to discharge generation to allow for the well-known dynamic fidelity of the baroreceptor responses36 and yet still retain the proposed ability to relax over many seconds to minutes to follow the time course of rapid resetting.

Effects on the intrinsic membrane or cellular properties of the baroreceptor could be responsible for rapid resetting.3,10,37 Such properties can also only be probed indirectly, however, since intracellular access with present technologies is impossible in such fine structures (<2 μM diameter) arborized over receptive areas of several square millimeters. Among the suggested candidates has been the electrogenic sodium pump or changes in ionic distributions.10,37 Although many other cellular properties of neurons such as changes in phosphorylation state of membrane ionic channels or intracellular second messengers could be hypothesized to play a role in rapid resetting, hard evidence is lacking.

In conclusion, these studies suggest that the ability of arterial baroreceptors to rapidly reset to changes in the prevailing pressure or stretch is unaffected by the level of tone in vascular smooth muscle. Smooth muscle tone appears to act on baroreceptors indirectly through changes in global vessel wall distension, and when sustained, these changes in diameter evoke rapid resetting of baroreceptor distortion threshold. Each baroreceptor appears to have a single, perhaps fundamental relation between the
level of prevailing wall distortion and the current distortion threshold of the sensory ending that is independent of smooth muscle tone. Thus, important physiological modulators of baroreceptors such as vasoconstriction can act through changes in gross vessel wall mechanics as well as more directly on the baroreceptor neuron by altering the basic excitability mechanisms and changing distortion threshold.

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