Types of Baroreceptor Afferent Neurons

The results reported by Seagard et al.1 and van Brederode et al.2 provide important new insights into the characterization of the different types of baroreceptor neurons and the mechanisms of baroreceptor activation.

The authors describe two types of neurons (type I and type II) in the carotid sinususes of dogs based on differences in the shape of the arterial pressure–discharge frequency relation.3,4 Type I receptors are inactive at low pressures and increase their activity abruptly as the pressure “threshold” is reached with a rise in pressure. Type II receptors show a low level of spontaneous discharge even at zero pressure and increase their activity gradually in a sigmoid manner with increases in pressure. Baroreceptors are often classified as myelinated or nonmyelinated (C fibers) based on measurement of conduction velocity. The classification described by the authors may provide an additional, useful means of classification. Because of the differences in discharge characteristics of the two receptor types, Seagard et al.1 and van Brederode et al.2 suggest that the type I and type II receptors may subserve different reflex functions.

The second major finding by the authors is that 4-aminopyridine, a blocker of the transient K+ channel,3 converts the pattern of discharge of type I receptors to that of type II with a minimal effect on the discharge of type II receptors. The results suggest that activation of the K+ channel reduces the rate of depolarization and suppresses the activation of type I baroreceptors at pressures below or near threshold.

We would like to comment on two important aspects of these new findings: 1) the physiological significance of the type I versus type II receptors and 2) the suggestion that the activity of the K+ channel accounts for the difference in discharge characteristics of the type I and type II receptors.

Physiological Significance

Influence of static versus pulsatile pressure on the pattern of activation of baroreceptors. In the studies by Seagard et al.1 and van Brederode et al.2, the different discharge characteristics of type I and type II receptors have been demonstrated when the baroreceptors are stimulated with a slow increase in nonpulsatile pressure. In a recent study, the responses of carotid sinus baroreceptors to nonpulsatile versus pulsatile pressures were contrasted.4 The relation between nonpulsatile pressure and the discharge frequency of the single fibers studied was of the type I pattern, that is, a discontinuous increase in activity with increases in pressure with abrupt activation and high frequency of discharge at threshold. When the same neurons were exposed to the physiological condition of pulsatile pressure, the type I pattern of discharge was converted to a type II pattern, that is, a lower pressure threshold and lower discharge frequency at threshold and a continuous increase in activity with increases in mean pressure. Thus, the same receptor may have two different patterns of discharge depending on the nature of the pressure stimulus. The demonstration that the discharge characteristics of type I baroreceptors are converted to that of type II receptors during pulsatile pressure suggests that the pattern of activation of the two receptor types may not be very different in vivo when pressure is pulsatile. This raises a question as to the physiological significance of the two types of responses observed during stimulation with static pressure.

Prevalence of type I versus type II receptors. Another important consideration is the relative number of type I versus type II receptors. In the study by Seagard et al.,1 74% of the fibers were type I and only 26% were type II, suggesting that the type II receptors may be less prevalent and possibly less important than the type I receptors. Alternatively, as the authors suggest, the fewer type II receptors examined may reflect a greater difficulty in isolating these single fibers. Although this may be true for the nonmyelinated type II neurons that have thinner axons and slower conduction velocities and compose 15% of the fibers studied, it does not appear to be true for the myelinated type II neurons that have larger axons but compose only 11% of the fibers studied.

Reflex function of type I versus type II baroreceptors. The suggestion by the authors2,3 that type I and type II baroreceptors may subserve different reflex functions is provocative but appears to be somewhat premature. The two studies by Seagard et al.1 and van Brederode et al.2 do not examine reflex responses to baroreceptor stimulation. Preliminary results reported by the same group4 failed to detect a change in the selectivity of the baroreflex inhibition of sympathetic activity after converting the type I pattern of discharge to that of type II with 4-aminopyridine.

Clearly, more work is needed to define the physiological significance of type I and type II baroreceptors, particularly in regard to their relative prevalence, their responses to pulsatile pressure, and their influence on the reflex control of the circulation.

Does K+ Channel Activation Account for the Differences Between Type I and Type II Receptors?

van Brederode et al.2 suggest that the differences between type I and type II receptors result from differences in the effectiveness of the K+ channel in controlling the excitability of the spike initiating zone. The ability of 4-aminopyridine to lower the pressure threshold of type I receptors and trigger spontaneous discharge at very low pressures suggests that the K+ channel plays an important role in the determination of the pressure threshold. Thus, the differences in threshold in type I and type II receptors may be caused by differences in the activity of the K+ channel in the two types of neurons, with a greater activity or effectiveness of the channel in the type I receptors. It should be noted, however, that 4-aminopyridine did not reduce the discharge frequency or the slope of the pressure–activity curve of type I receptors, which remained much greater in type I compared with type II receptors. Therefore, these characteristics of the type I receptors cannot be attributed to a “more active” K+ channel. Apparently, there are additional differences in the nerve endings of type I and type II receptors and/or in the coupling of the receptors to the vessel wall.

In summary, the results reported by Seagard et al.1 and van Brederode et al.2 provide important new information that should stimulate further research that may clarify the physiological significance of type I and type II baroreceptors and the role of the transient K+ channel in the mechanoelectrical transduction processes of baroreceptors.

Mark W. Chapleau, PhD
The Cardiovascular Center and the Department of Internal Medicine
University of Iowa College of Medicine and The Department of Veterans Affairs Medical Center
Iowa City, Iowa
References


Reply to the Preceding Letter

We appreciate the comments and insights offered by the above authors regarding our two recent articles.1,2 The following comments are offered both as responses to the above points and as additional information that may help to clarify certain areas.

Physiological Significance

Influence of static versus pulsatile pressure on the pattern of activation of baroreceptors. As indicated above, a slow sinus pressure ramp was used to stimulate baroreceptors in the cited papers. However, additional studies have been3 and are currently being performed that examine the effects of changes in rates of pressure stimulation on both type I and type II baroreceptors. In these studies, with pressure ramps from 1–2 to 60–80 mm Hg/sec, we have not seen the conversion of type I to type II baroreceptors. Preliminary results suggest that while changes in rates of pressure stimuli may change baroreceptor sensitivity and threshold pressure, they do not cause conversion of the hyperbolic discharge pattern to a sigmoidal one. In addition, constant pressure perfusion of the isolated carotid sinus before ramp stimulations has been done using both pulsatile and nonpulsatile pressures, and no difference has been observed in the shape of the resulting stimulus–response curve of either type I or type II baroreceptors. The role of static versus pulsatile stimulation and resulting effects on baroreceptor discharge is complex and remains an area of investigation.

Prevalence of type I versus type II baroreceptors. We believe that the smaller number of type II baroreceptors studied reflects the difficulty to record from smaller diameter axons and does not suggest a smaller number of type II versus type I baroreceptors. Even though 11% of the baroreceptors studied were type II receptors with myelinated axons, the diameters of these fibers, as suggested by conduction velocities, were not much greater than C-fiber diameter. Single-fiber activity from any fiber of this size, regardless of the presence or absence of myelin, is more difficult to locate and record because of the fragile nature of the small axon.

Reflex function of type I versus type II baroreceptors. Unlike the perception stated by the above authors, our ongoing studies in which we examine the reflex effects of activation of type I versus type II baroreceptors do indicate that each type of receptor may preferentially contribute to different areas of blood pressure control. As indicated above, preliminary results with 4-aminopyridine (4-AP) to “convert” type I baroreceptors to type II sigmoidal patterns indicated no change in sensitivity of baroreflex inhibition or sympathetic inhibition.1 However, there was a decrease in ongoing sympathetic tone during constant pressure perfusion of the sinus after baroreceptor exposure to 4-AP. This suggests that the sensitivity of the baroreflex was not altered by 4-AP (shown also by no change in sensitivity [slope] of the stimulus–response curves of type I baroreceptors after exposure to 4-AP) but that “conversion” to a sigmoidal curve did result in information that helped to regulate tonic levels of sympathetic activity and blood pressure (increased input from type I curves after 4-AP exposure caused by lowering of Pa and appearance of spontaneous subthreshold activity).3 We have also initiated preliminary (unpublished) studies with anodal block of the intact carotid sinus nerve to sequentially eliminate afferent baroreceptor input first from A-fiber baroreceptors (predominantly type I) and progressively from smaller A and C fibers (predominantly type II). These studies have shown that elimination of large A-fiber baroreceptors results in a decrease in sensitivity of baroreflex inhibition of sympathetic activity, followed by a loss of tonic inhibition of sympathetic activity caused by blockade of small A- and C-fiber baroreceptors. While these data provide indirect evidence for differential roles for type I versus type II baroreceptors, these are preliminary studies and more investigation is needed to evaluate this possibility.

Finally, as suggested in our paper,3 we certainly agree that the transient potassium current (or A current) blocked by 4-AP is only one of many possible factors that could help to regulate baroreceptor discharge. However, the finding that 4-AP selectively affects only type I and not type II baroreceptor discharge indicates that the electrophysiological properties of the two types of baroreceptors are not identical. Both our experimental results and modeling studies suggest that the differences in the A current are most effective in setting the firing threshold of baroreceptors without much effect on the sensitivity or maximum discharge rate. Other electrophysiological characteristics and coupling mechanisms could certainly contribute to differences in the other firing characteristics between type I and type II receptors, as noted in our studies.

We hope that the studies and possibilities suggested by these results initiate many studies investigating the functional characteristics and possible differential roles played by different baroreceptor types. Stimulation and exchange of comments and ideas as outlined above are part of an important process that could lead to new and valuable information on baroreceptor control of blood pressure.

J.L. Seagard   J.F.M. van Brederode   C. Dean   F.A. Hopp   L.A. Gallenberg   J.P. Kampine
Veterans Administration Medical Center and Departments of Anesthesiology and Physiology
The Medical College of Wisconsin
Milwaukee, Wis.

References

Types of baroreceptor afferent neurons.
M W Chapleau

Circ Res. 1991;68:619-620
doi: 10.1161/01.RES.68.2.619

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/68/2/619.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org//subscriptions/