Baroreflexes in Hypertension
A Mystery Revisited

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To date, most studies investigating baroreflexes in hypertension have been performed either by recording baroreflex afferents or by denervating them. In the current issue of Hypertension, Lohmeier et al. present data on the effects of chronic carotid sinus stimulation (CSS) in hypertensive animals. Striking differences were observed during CSS in dogs with angiotensin II (Ang II)–induced hypertension as compared with control conditions. In line with a previous study, baroreflex activation by CSS significantly reduced blood pressure during control. In contrast, the hypotensive effect was markedly attenuated in Ang II hypertensive dogs. This observation fits very well with today’s understanding of baroreflexes in several forms of hypertension.

Remarkably, it is still not fully understood how the autonomic nervous system acts in hypertension, although the issue dates back to the very beginnings of research on cardiovascular reflexes. During that era, it was generally held that baroreflexes continuously buffer sympathetic nervous output. Thus, dissection of the afferent nerves supplying regions of the baroreceptors (carotid sinuses and aortic arch) was thought to increase long-term blood pressure. Koch described what he termed Entzügelungshochdruck (disinhibition) in many species. Today, neurogenic hypertension is commonly used to describe hypertension following denervation of baroreceptors. The concept of neurogenic hypertension was never seriously questioned until the 1970s when Cowley et al performed long-term studies in conscious dogs. In these experiments, only slight increases in blood pressure were found after baroreceptor denervation. Neurogenic hypertension mainly seems to be observed under special experimental conditions: either in animals that are not fully at rest or in unrestrained, freely moving animals in which blood pressure is recorded over a long period of time. Although this seems to be the most representative protocol to simulate human life, movement and postural changes in baroreceptor-denervated animals lead to episodes of severe hypotension, resulting in lower mean arterial pressure (MAP) than in resting animals.

Matton was perhaps the first to find blunted baroreflexes in hypertensive animals, and only shortly thereafter McCubbin et al. directly demonstrated resetting of the baroreflex operating range in hypertension by electromyographic techniques. Thus, the past understanding was that baroreflexes are of minor importance during chronic hypertension because they will completely reset to any new MAP level. Lohmeier et al. show that under control conditions, CSS indeed lowers MAP over several days. Thus, there is no, or very little, resetting taking place. The situation during Ang II–induced hypertension is very different. Here, Lohmeier et al. observe significant long-term attenuation of CSS effects on MAP. This is in-line with a series of very recent studies, one which has shown that baroreceptors may indeed be able to influence long-term MAP. Furthermore, it has been shown that the baroreflex may not completely reset, at least not with regard to renal sympathetic nerve activity. Interestingly, Ang II–mediated sympathoinhibition to the kidney relies critically on intact baroreflexes.

With regard to the present study of Lohmeier et al., it is particularly interesting that renal sympathetic nerve activity has been assumed to be resistant to resetting in response to Ang II–induced hypertension. In the study by Lohmeier et al., effects of CSS on MAP taper off: one possibility is that there is gradual recovery of sympathetic drive to the kidney. This would not be in-line with nonresetting baroreflex response to renal sympathetic nerve activity. It rather seems that there exists a neural setpoint for long-term MAP, which is only acutely modulated by the baroreflex.

In light of these studies, our view of the baroreflex requires rethinking. The baroreflex is probably neither fully in control of MAP nor is it ever totally irrelevant for long-term MAP. Baroreflexes are one of many control elements acting in concert to provide the most appropriate response to a given challenge. Completely eliminating the reflex, as done by denervation, or maximum stimulation of the reflex provides valuable insight into cardiovascular control under extreme conditions. However, these may not fully elucidate a subtly controlled interaction between the neurohumoral mechanisms and the kidney, as seen in circulatory homeostasis. More studies of the type presented by Lohmeier et al are required.

References

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