Baroreceptors and Hypertension

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Despite considerable research, the role played by the sympathetic nervous system in the pathogenesis of essential hypertension remains poorly understood. In virtually all forms of chronic hypertension, the principal hemodynamic fault is an elevation in systemic vascular resistance. Because sympathetic vasomotor outflow normally is under tonic reflex restraint by sinoaortic and cardiopulmonary baroreceptors, impairments in this baroreflex restraint are hypothesized to play a permissive role in the pathogenesis of essential hypertension. The important study by Rea and Hamdan in this issue of Circulation sheds new light on this hypothesis.

Sinoaortic Baroreceptors

The carotid sinus and aortic arch baroreceptors are mechanically sensitive nerve endings that respond to deformation of their receptive fields. Baroreceptors buffer acute elevations in arterial pressure by evoking reflex decreases in both heart rate and vascular resistance. During chronic elevations in arterial pressure, however, the baroreflex is reset; a given increase in blood pressure evokes smaller decreases in heart rate in hypertensive than in normotensive animals or humans.

Baroreflex resetting is due to alterations either in the discharge properties of the baroreceptors themselves or in the central processing of the afferent input. An unanswered question is whether baroreflex resetting can be the cause as well as the consequence of chronically elevated blood pressure. In young hypertension-prone rats and humans, attenuated baroreflex inhibition of heart rate frequently precedes the onset of hypertension, suggesting that this reflex attenuation is genetic and plays a permissive role in the subsequent development of hypertension. In rabbits with renal hypertension, however, arterial baroreflex control of lumbar sympathetic nerve activity and hindlimb vascular resistance is well preserved even though baroreflex control of heart rate is severely impaired. Because vascular resistance, not heart rate, is the main hemodynamic determinant of chronic hypertension, the pathophysiological importance of an isolated attenuation of only the heart rate component of the arterial baroreflex is unknown. The ability to record peripheral sympathetic nerve traffic with intraneuronal micro-electrodes offers the opportunity to address these issues in conscious humans.

Cardiopulmonary Baroreceptors

In many animal species, the tonic reflex restraint on sympathetic vasoconstrictor outflow is shared rather equally by sinoaortic baroreceptors and by vagal afferents with mechanoreceptor endings that are scattered throughout the cardiopulmonary region. Whereas sinoaortic ("high pressure") baroreceptors are stimulated by an elevation in systemic arterial pressure, most cardiopulmonary ("low pressure") baroreceptors are stimulated by an elevation in central venous pressure. These different afferents are thought to converge on some of the same central neurons in the solitary tract nucleus, producing considerable redundancy in the regulation of vascular resistance by sinoaortic and cardiopulmonary reflexes. Thus, the sensitivity, or gain, of either reflex mechanism is augmented when the influence of the other mechanism is either reduced or eliminated. When sinoaortic and cardiopulmonary afferents are unloaded simultaneously, as with assumption of upright posture, their reflex effects on vascular resistance are synergistic.

Decreases in central venous pressure with graded levels of simulated orthostatic stress [lower body negative pressure (LBNP)] have been shown to cause much larger reflex increases in forearm vascular resistance in borderline hypertensive than in normotensive young men. From this observation, two concepts were advanced. First, in the supine position, the tonic cardiopulmonary baroreflex restraint on sympathetic vasomotor outflow is augmented in individuals with borderline hypertension. Second, this reflex augmentation results from reduction in sinoaortic baroreflex restraint on cardiopulmonary baroreflex function. Rea and Hamdan provide neurophysiological evidence that supports the first concept but refutes the second.
Findings and Importance of Present Study

The major new observations from this study are twofold. First, a given decrease in central venous pressure (produced by nonhypotensive LBNP) evoked increases in muscle sympathetic nerve activity that were almost threefold larger in young men who had intermittent, borderline elevations in blood pressure than in those with totally normal blood pressures. This finding is consistent with the previous forearm vascular data and strengthens the concept of cardiopulmonary baroreflex augmentation in borderline hypertension. In the present study, the majority of the borderline hypertensive subjects had a family history of essential hypertension. Thus, their enhanced cardiopulmonary baroreflex may be inherited rather than acquired and may represent one of the earliest physiological markers of a genetic predisposition for the subsequent development of essential hypertension. In these individuals, cardiopulmonary baroreflex augmentation occurred in the absence of attenuated arterial baroreflex control of heart rate, which was previously considered one of the earliest reflex abnormalities in hypertension. The second major finding is that the augmented sympathetic responses to nonhypotensive orthostatic stress were accompanied by surprisingly normal, not attenuated, sympathetic responses during pharmacologic perturbations in arterial pressure. Thus, in contrast to what was previously assumed, augmented cardiopulmonary baroreflex function in borderline hypertension is not dependent on an impairment of either the heart rate or the sympathetic vasoconstrictor component of the sinoaortic baroreflex.

These findings in borderline hypertensive humans are remarkably parallel with previous findings in the spontaneously hypertensive rat (SHR), a genetic model of hypertension in which cardiopulmonary baroreflex inhibition of sympathetic nerve activity and vascular resistance also is augmented. This augmentation is particularly evident in young SHR (compared with young normotensive Wistar-Kyoto rats) and is accompanied by a normal arterial baroreflex. The mechanism responsible for cardiopulmonary baroreflex augmentation in the early stage of experimental and human hypertension is unknown. Further studies are needed to examine several mechanistic hypotheses, including 1) increased mechanical deformation of cardiac afferent endings due to increased central venous pressure (resulting from decreased peripheral venous distensibility) in the setting of normal cardiac distensibility, 2) sensitization of afferents by tonic or humoral factors, 3) alteration in the central processing of the afferent input, and 4) facilitation of ganglionic transmission. Regarding the last two possibilities, it would be of interest to determine whether borderline hypertension is accompanied by normal or augmented sympathetic responses to a nonbaroreflex stimulus such as the cold pressor test.

Pathophysiological Speculation

Although the role of altered baroreceptor reflexes in the development of hypertension remains unclear, a potential role for the responses described in the study by Rea and Hamdan can be postulated. In individuals with borderline hypertension, enhanced cardiopulmonary baroreflex restraint on sympathetic vasoconstrictor outflow would be expected to promote vasodilation and to lower blood pressure during the increases in central blood volume that occur with nocturnal recumbency. This enhanced baroreflex restraint eventually may be lost when the deformation of cardiac mechanoreceptors becomes impaired due to ventricular diastolic dysfunction, left ventricular hypertrophy, or administration of β-adrenergic blockers. Indeed, when cardiac afferents are transected by orthotopic cardiac transplantation, the normal nocturnal decline in blood pressure is lost. Loss of the nocturnal dip in blood pressure has also been observed recently in some patients with essential hypertension and left ventricular hypertrophy. Thus, longitudinal studies are needed to determine whether a progressive decline in (and eventual reversal of) the cardiopulmonary baroreflex augmentation that characterizes borderline hypertension leads to abnormal nocturnal maintenance of blood pressure in patients with fixed essential hypertension.

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References

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