MUCH information has been collected over the past few years on the main features of neuroadrenergic abnormalities that characterize cardiovascular disease. We learned, eg, that in a number of pathological states adrenergic influences lose their homeostatic regulatory function and become “less sympathetic,” not only favoring the development of the disease itself but also contributing to its clinical progression. We also learned that elevated circulating plasma norepinephrine levels do not invariably reflect sympathetic activation and that complex but accurate methodologic approaches to quantify neuroadrenergic drive should be of help in dissecting the peripheral (reduced clearance and or reuptake of norepinephrine) versus the central (increased in central sympathetic outflow) origin of the sympathetic activation characterizing a given physiological or pathophysiological condition. Other key findings of recent investigations in the field of neural cardiovascular control should not be forgotten. They include, eg, the evidence that sympathetic influences on cardiac, renal, thermoregulatory, and metabolic function are not independent entities but rather complex phenomena integrating each other in a “neurally exchanging network.” They also include the evidence that, in several cardiovascular and noncardiovascular diseases, therapeutic counterbalance of adrenergic overdrive may be clinically relevant for reducing cardiovascular risk, improving cardiovascular function, and possibly retarding the progression and favoring the regression of the end-organ damage. This therapeutic goal is based on a well-documented rationale, namely the evidence that in a number of diseases (heart failure, acute myocardial infarction, stroke, and renal failure) sympathetic activation characterizing a given physiological or pathophysiological condition. Other key findings of recent investigations in the field of neural cardiovascular control should not be forgotten. They include, eg, the evidence that sympathetic influences on cardiac, renal, thermoregulatory, and metabolic function are not independent entities but rather complex phenomena integrating each other in a “neurally exchanging network.” They also include the evidence that, in several cardiovascular and noncardiovascular diseases, therapeutic counterbalance of adrenergic overdrive may be clinically relevant for reducing cardiovascular risk, improving cardiovascular function, and possibly retarding the progression and favoring the regression of the end-organ damage. This therapeutic goal is based on a well-documented rationale, namely the evidence that in a number of diseases (heart failure, acute myocardial infarction, stroke, and renal failure) sympathetic activation characterizing cardiometabolic disease. Indeed, for many years investigators in the field of neural cardiovascular control have attempted to define whether and to what extent a given cardiac, metabolic, or renal disease was characterized by an increase in sympathetic cardiovascular drive. Although successful, the approach has been regarded with time as a limited one because of the inability to assess the multifaceted aspects of the basic neurogenic abnormalities. One of the first attempts to overcome these limitations has been the definition of the regional behavior of the sympathetic activation in the various cardiovascular districts, such as the cutaneous, coronary, renal, and cerebral circulation. The evidence collected so far clearly indicates that almost invariably the adrenergic overdrive characterizing cardiometabolic disease is not homogeneously distributed along the cardiovascular tree, but it rather heterogeneously affects different circulatory districts. It has been shown, eg, that in hypertension and in heart failure muscle sympathetic nerve firing rate is markedly potentiated at variance from skin sympathetic neural outflow, which still remains within the reference range. It has also been shown that the sympathetic overdrive occurring in obesity affects the renal, as well as the muscle, circulation but spares the coronary and the cutaneous ones.

A further attempt to understand the role of the neurogenic mechanisms in the pathophysiology of the hypertensive disease has been founded on the assessment of the neural bursts amplitude spectra, which has been suggested in a variety of conditions to represent a qualitative marker of an altered sympathetic drive that is more sensitive than traditional methods. This approach has been implemented re-
cently by the analysis of the minute-to-minute sympathetic nerve traffic variability both of rest and during autonomic challenge.7 The main feature of the approach is represented by the definition of whether and to what extent sympathetic nerve firing rate undergoes spontaneous or reflex alterations within a given temporal window. This may have relevant clinical implications, taking into account that blood pressure variability, which is under sympathetic influences, has been demonstrated to be closely related in hypertension with development and progression of target organ damage.8

The approach used by Lambert et al in their study2 to qualitatively characterize the sympathetic overdrive in obesity-related hypertension, as well as in normal-weight hypertension, has both strengths and limitations. The strengths are represented by the following: (1) the direct quantification of the nerve firing patterns provided by the method, (2) the short- and long-term reproducibility of the microneurographic nerve recording, and (3) the computerized software approach used to define the single-unit nerve fiber firing rate. The limitations are basically represented by the fact that if 2 different fibers have identical morphology and, thus, firing characteristics, then the erroneous attribution to a single sympathetic nerve may occur, and the approach has been thus far applied exclusively to conditions characterized by sympathetic activation, and whether its use may be feasible and sensitive also in states in which sympathetic tone is reduced remains to be seen. Furthermore, as properly recognized by the authors, the methodology used in the present study cannot be regarded as a new endeavor, because previous investigations have already delineated the behavior of multiunit and single-unit nerve fiber recording in heart failure or in hypertension complicated by left ventricular hypertrophy.9,10 The innovative aspect of the study, however, stands not only in the application of the approach to obesity-related hypertension but also in the intriguing interpretation that the authors provide for explaining the qualitative differences in the sympathetic activation in lean and obese hypertensive subjects, as well as their potentially different clinical outcomes. As far as the causes of the different patterns of sympathetic activation are concerned, it is likely that, as also suggested by the authors, baroreflex mechanisms are involved, an impairment in the baroreceptor modulation of sympathetic drive being described in obesity-related hyperten-
sion but not in uncomplicated hypertension.1 The potentially different clinical impact may be represented by the possibility that sympathetic activation originating from recruitment of new fibers firing at a normal rate (such as occurs in obesity-related hypertension) might be less dangerous in terms of cardiovascular risk than that characterized by a true increase in the nerve firing rate, such as what happens in hypertension. This intriguing possibility, although already based on a solid background,9,10 will require confirmation by future prospective studies, which will also hopefully allow us to define the impact of different therapeutic regimens on these 2 different types of adrenergic overdrive.

Disclosures

None.

References

Qualitative Assessment of Sympathetic Neural Drive in Cardiometabolic Disease: A New Challenge
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