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COMMENTARY

Effects of physical training on autonomic cardiac modulation in hypertension: assessment by heart rate variability analysis

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The autonomic nervous system is the primary mechanism for short-term blood pressure (BP) regulation on a beat-by-beat basis. In normal physiological conditions, very precise control of BP levels is achieved through a complex combination between central neural and reflex influences, leading to a continuous modulation of efferent sympathetic and parasympathetic nerve activity and the associated activity of neurohormonal systems primarily regulated by the hypothalamus. Several studies using direct methodologies for the assessment of overall and regional sympathetic cardiovascular (CV) drive have demonstrated the association between chronic activation of the sympathetic nervous system and the development, establishment and progression of essential hypertension.[1] Most studies supporting this concept have consistently confirmed an increase in central sympathetic drive in essential hypertension through the use of dedicated techniques for the direct assessment of sympathetic activity (that is, regional noradrenaline spillover or the direct recording of efferent postganglionic muscle sympathetic nerve activity via microneurography).[1–3] An indirect assessment of the alterations in cardiovascular autonomic modulation accompanying essential hypertension is also possible through the analysis of BP and heart rate (HR) variability (BPV, HRV), which represent a simple, non-invasive means to quantify the amplitude of BP and HR fluctuations occurring at specific frequency regions, which are known to reflect BP and HR modulation by neural autonomic influences.[4–9] Most studies have focused on HRV only, mainly because of its ability to reflect both sympathetic and parasympathetic cardiac modulation and because its beat-by-beat fluctuations are easily recorded though the use of one electrocardiographic lead. In the frequency domain, current spectral analysis techniques allow for quantification of the power of HR variations in the very-low (VLF, 0.025–0.05 Hz), low (LF, 0.05–0.15 Hz) and high frequency (HF, 0.15–0.5 Hz) regions of the HR spectra, as well as calculation of other autonomic indices by normalizing these powers *vs.* total variance or by computing the ratio between the powers reflecting sympathetic and vagal drive (that is, LF/HF ratio).[4–8] These indices have proven to be useful in characterizing the alterations in cardiac autonomic modulation occurring in essential hypertension and even in pre-hypertensive states,[10] and have also demonstrated their prognostic value in predicting the development of CV disease and events in large population-based studies[11] or in specific clinical settings (that is, post-myocardial infarction and heart failure patients).[12] The spectral analysis of HRV has also been proposed as a tool to quantify changes in autonomic cardiac modulation in response to treatment. Indeed, significant improvements in indices of autonomic cardiac modulation derived from the analysis of HRV (reflecting increases in cardiac vagal modulation) have been reported after the achievement of BP control with antihypertensive treatment[13,14] and in response to non-pharmacological interventions such as regular physical training.[15–17] Thus, the analysis of HRV appears to represent a simple means to assess autonomic cardiac modulation and a valuable tool to track the autonomic adjustments in the CV system, induced by a number of pharmacological and non-pharmacological interventions, although its specificity should not be taken for granted.[9]

Further information on the clinical applicability of HRV analysis in the assessment of the effects of physical exercise is provided by the paper by Cozza *et al.*[18] published in the current issue of *Hypertension Research.* This study assessed the effects of a 15-week protocol of aerobic physical training (45-min treadmill exercise, three times a week) on autonomic cardiac modulation (as assessed by means of spectral analysis of HRV) in a group of sedentary, non-treated subjects with mild essential hypertension. Aside from considering a group of normotensive subjects as controls, researchers also included a third group of hypertensive subjects under active treatment with the angiotensin-converting enzyme inhibitor enalapril (10–20 mg day^{-1}) to determine whether physical training would provide any further improvement in cardiac autonomic modulation beyond that already expected to be conferred by pharmacological BP lowering.

During the follow-up, physical training promoted significant reductions of resting HR in all study subgroups and a reduction of mean BP levels in both treated and non-treated hypertensive subjects. However, significant improvements in HRV autonomic indices in the resting supine position (increase in HF and decrease in LF and LF/HF ratio) were only observed in the group of non-treated hypertensive subjects, who had reported the largest impairment in sympathovagal balance (lowest HF and highest LF and LF/HF ratios) before starting the physical training protocol.

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Some caution is required, however, for a proper interpretation of these results because LF and HF powers, despite being considered indices of sympathetic and parasympathetic cardiac modulation, respectively, may be influenced by a number of other cardiovascular regulatory mechanisms.[6,7,19] Although changes in the HF (0.15–0.5 Hz) spectral power of HRV seem to be primarily caused by the modulation of cardiac parasympathetic efferent activity,[5,19–21] at respiratory frequencies below nine breaths per minute sympathetic modulation of respiratory-induced HR changes also occurs, together with some degree of mechanical stimulation of the sinus node by ventilation cycles. Thus, HR HF power is considered a satisfactory, but incomplete, measure of parasympathetic cardiac control. The specificity of HR LF power (0.05–0.15 Hz) in reflecting sympathetic cardiac modulation of HR has been reported to be even lower because it may also depend on vagal influences (as demonstrated by the reductions in LF HR power achieved by either parasympathetic or sympathetic pharmacological blockade)[5,20] and on a variety of other factors, including thermoregulation, atrial stretch by periodic breathing and hemodynamic instability.[22] In recognition of the limited specificity of HR LF and HF powers as respective markers of sympathetic and vagal cardiac drive and based on the assumption that sympathetic and vagal cardiac influences are normally altered in opposite directions,[6,23–25] the LF/HF ratio was proposed as an index of sympathovagal balance and has proven to be useful in providing information in a number of clinical conditions.[19] In addition, the specificity of LF and HF spectral powers in reflecting cardiac sympathetic and parasympathetic modulation, respectively, can be enhanced by laboratory stimuli that can selectively activate (that is, head-up tilting and mental stress) or deactivate (that is, sleep and alpha-adrenergic blockade) sympathetic nervous system influences.

In the study by Cozza *et al.*, the assessment of autonomic CV modulation was performed not only during supine rest but also in response to orthostatic activation by passive tilting at a 75° angle. Importantly, this simple maneuver may improve the specificity of LF and HF components of HRV as well as the LF/HF ratio by inducing sympathetic activation and deactivation of the parasympathetic branch of the cardiac baroreflex. Aside from the assessment of changes in the sympathovagal balance induced by the shift from supine to standing (a possible marker of autonomic balance rearrangement), this measure also provides information on the integrity of the reflex arc involved in the autonomic response to orthostatic stress.

By the end of the study, physical training induced significant improvements in cardiac autonomic modulation during the tilt test within each group (increase in LF power and LF/HF ratio), with no significant differences between groups. The additional significant improvement in the autonomic response to passive tilting observed in the group of treated hypertensives (who shared similar profiles of autonomic response with normotensive subjects before starting the physical training protocol) led investigators to conclude that physical exercise may provide further improvements in autonomic CV modulation even in hypertensive patients under active treatment with an angiotensin-converting enzyme inhibitor (an intervention previously demonstrated to improve autonomic cardiac modulation itself).[13,14] These findings, along with the additional reductions in BP levels induced by physical exercise in the group of treated hypertensives (who reached BP levels similar to those of normotensive subjects), reinforce the importance of implementing regular physical activity even in treated hypertensive patients, not only to favor BP control, but also to improve cardiac autonomic modulation, given the prognostic implications of an altered sympathetic and parasympathetic CV modulation for target organ damage and for the progression of CV disease.

Important as they are, the findings obtained by the study by Cozza *et al.* on the benefits of physical training on CV autonomic modulation provide only a partial perspective on this phenomenon because the protocol of autonomic assessment only considered indices of cardiac autonomic modulation derived from the analysis of HRV and disregarded concomitant changes in BPV.

Moreover, in recognition that autonomic modulation of the CV system takes place in a network of intricate interactions between several regulatory systems, a general concern has been raised that for a comprehensive assessment of autonomic CV modulation, information provided by HRV analysis might not be specific enough and should be integrated with the analysis of variability in other biological signals. An example of this is represented by the assessment of HRV along with analysis of BPV from beat-to-beat BP recordings, which complements the information provided by HRV analysis (by providing indices of vascular autonomic modulation). In addition, by applying modeling approaches which focus on the relationship between fluctuations of HR and BP (either in time or in the frequency domain),[26,27] it is also possible to assess other mechanisms of major importance for autonomic CV control such as the degree of spontaneous cardiac baroreflex sensitivity. Such an approach may provide a more comprehensive analysis of cardiovascular regulation mechanisms than that represented by the separate analysis of BP and HR variability alone.[28]

In conclusion, the data by Cozza *et al.*[18] provide further support to the concept, promoted by a number of previous studies, that exercise training in hypertensive patients may carry benefits, not only due to better BP control but also due to improved cardiac autonomic modulation. They also emphasize the usefulness of spectral analysis for dynamically tracking changes in neurally modulated HRV parameters induced by exercise over time. It should be emphasized, however, that the combination of HRV analysis with analysis of the variability of other cardiorespiratory parameters might offer deeper and more specific insights into this complex issue.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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