Exercise in hypertension: do skeletal muscle reflexes make this a dangerous proposition?

Scott A. Smith  
Departments of Physical Therapy, Internal Medicine, and Bioengineering, University of Texas Southwestern Medical Center, Dallas, Texas

The benefits of exercise and exercise training are numerous, varying from increasing skeletal muscle strength to enhancing cardiovascular and respiratory fitness. These attributes of exercise are key elements to the maintenance of good health and the improvement of athletic performance. But are there certain conditions in which exercise is not recommended and may actually do more harm than good? One potential patient population in which the answer to this question may indeed be “yes” is hypertensive individuals. In established hypertension, the response to moderate-to-high-intensity exercise is often characterized by exaggerated increases in blood pressure, heart rate, and vascular resistance (11). These potentially dangerous elevations in circulatory hemodynamics increase the risk for adverse cardiac (e.g., acute myocardial infarction, arrhythmia, and cardiac arrest) and cerebrovascular (e.g., stroke) events during or immediately after a bout of exercise (6, 10). As such, the prescription of exercise as a viable therapeutic option in hypertensive patients is often limited. However, if the cause(s) of this cardiovascular hyperexcitability could be determined and successfully treated, these patients could benefit greatly from a relatively safe, regular physical activity regimen. For this to be a realistic goal, however, we must first understand the basic pathophysiology of the abnormal cardiovascular response to exercise in this disease.

The cardiovascular response to both dynamic and static exercise is regulated by three distinct neural mechanisms: 1) the arterial baroreflex, 2) central command, and 3) the exercise pressor reflex. The arterial baroreflex (with afferent fibers originating in the carotid sinus and aortic arch) functions to tonically regulate blood pressure on a moment-to-moment basis by inducing autonomic adjustments in sympathetic and parasympathetic activity (8). The reflex is “reset” to functionally operate around the elevated blood pressures that manifest during exercise (12). Central command is a feed-forward neural drive originating in higher brain centers (e.g., insular and anterior cingulate cortices) that simultaneously recruits motor units for volition as well as activates cardiovascular control centers within the brainstem to modulate sympathetic and parasympathetic nerve activity (3). The exercise pressor reflex is a feedback peripheral drive originating in skeletal muscle (9). In this reflex, somatosensory signals from contracting skeletal muscle are transduced via thinly myelinated group III and unmyelinated group IV afferent fibers. Most group III afferents are activated abruptly at the onset of muscle contraction with associated receptors responding primarily to mechanical distortion (i.e., the muscle mechanoreflex), whereas the majority of group IV fibers subserve chemically sensitive receptors activated by the by-products of skeletal muscle metabolism (i.e., the muscle metaboreflex) (5). Stimulation of these skeletal muscle afferent fibers during contraction induces hemodynamic changes predominately via the activation of the sympathetic nervous system (4). Given their essential roles in cardiovascular regulation, each of these inputs serves as a potential candidate for mediating the enhanced circulatory response to exercise in hypertension.

Emerging evidence from animal models of essential hypertension suggests that of the three mechanisms actively engaged in cardiovascular regulation during physical activity, it is the skeletal muscle exercise pressor reflex that is the primary culprit behind the aforementioned exaggerated circulatory response. For example, it has been recently demonstrated in spontaneously hypertensive rats that selective activation of the exercise pressor reflex elicits markedly exaggerated increases in blood pressure and heart rate compared with normotensive controls (17). Using the same animal model, it has further been demonstrated that both the mechanically and metabolically sensitive components of the reflex contribute to its overactivity (7). Such findings produced from animal research serve to advance our understanding of altered cardiovascular control during exercise in hypertension. However, for the findings to be of considerable impact, they must be translated into the human condition.

There is a strong need to examine the contribution of the exercise pressor reflex, and its individual components, to altered cardiovascular hemodynamics during exercise in hypertensive patients. Delaney and colleagues (2) have done just that in their well-designed and executed study in this issue of the American Journal of Physiology-Heart and Circulatory Physiology. In the investigation, older hypertensive (mean age, 63 yr) and normotensive (mean age, 60 yr) adults performed static handgrip exercise at 30 and 40% of their maximal voluntary contraction followed by a period of postexercise ischemia (PEI). The latter maneuver was designed to isolate the metaboreflex contribution to the cardiovascular response by “trapping” the metabolites produced during muscle work in the limb of origin. This procedure has the added advantage of examining metaboreflex function at a time period when the muscle mechanoreflex and central command have been disengaged (i.e., after exercise has been terminated). Handgrip exercise at both intensity levels produced enhanced increases in blood pressure and muscle sympathetic nerve activity in hypertensive compared with normotensive subjects. In agreement with a previous report from this group (15), the blood pressure response remained greater in hypertensive subjects during PEI. The key finding from this study, however, was that the sympathetic response elicited by exercise also remained greater in the hypertensive subjects during the period of PEI. This finding suggests for the first time that the metaboreflex-mediated regulation of sympathetic nerve activity is altered in hypertensive...
patients in an exaggerated manner. Importantly, the work represents a significant advance in our understanding of sympathetically mediated cardiovascular control during exercise in hypertensive humans, expertly translating previous findings reported in animal models of human disease.

These findings are not without controversy, however. A previous study in which middle-aged hypertensive (mean age, 42 yr) and normotensive (mean age, 38 yr) men and women performed a similar handgrip exercise protocol suggested that muscle metaboreflex control of sympathetic activity may actually be reduced in hypertension (14). The reasons for the discrepancies between these questions. But is it worth the effort? When you consider the patient populations’ ages and the length of time the subjects had been afflicted with the disorder may be the key to reconciling the apparent conflicting results. Hypertension is a progressively developing disease, worsening over time. It is quite possible that metaboreflex sensitivity is decreased in the initial stages of hypertension. Speculatively, this decrease in function could compensate for increases in the sensitivity of other neural inputs important to cardiovascular control during exercise (e.g., the muscle mechanoreflex). As the disease worsens, this compensatory tendency may be reversed such that the metaboreflex becomes overactive. For example, it has been shown that skeletal muscle arteriolar and capillary rarefaction progressively develops in hypertension and is associated with increases in vascular resistance and reductions in skeletal muscle blood flow (13, 16). Reductions in flow could impede the removal of exercise-induced metabolites leading to enhanced stimulation of the metaboreflex. Other factors such as muscle deconditioning or hypertension-induced transformations in skeletal muscle fiber type (e.g., from slow-oxidative to fast-glycolytic fibers) could also play a role (1). Given our current knowledge base, it is impossible to know the true time course for the genesis of metaboreflex dysfunction in hypertension or the factors that mediate these changes. Thus there is a clear need for further research in this area.

The studies described represent a good starting point for increasing our understanding of altered neural cardiovascular control during exercise in hypertension. However, many questions remain to be answered. For example, is muscle mechanoreflex function altered in hypertensive humans? What are the molecular and cellular mechanisms underlying skeletal muscle reflex dysfunction in hypertension? Is skeletal muscle reflex dysfunction related to changes in the activity of its receptors, afferent fibers, or central processing centers? Furthermore, the possible involvement of central command and the arterial baroreflex to the abnormal circulatory response to exercise cannot be ignored. The use of animal models of human hypertension as well as the conduction of studies in patient populations will aid in providing answers to these questions. But is it worth the effort? When you consider the fact that hypertension is a major risk factor for the development of heart disease and stroke (both leading causes of death in Western civilization) and that numerous clinical investigations have indicated that the prevention of poor cardiovascular health and development of disease is greatly enhanced by the treatment of hypertension, then the expenditure of effort to develop any and all safe treatments for this malady is a worthwhile endeavor. To this end, the effective treatment of dysfunctional skeletal muscle reflexes could minimize the risks associated with exercise in hypertension by reducing or eliminating the cardiovascular hypertensive-ness to physical activity characteristic of this disease. As a result, physical activity of a longer duration and greater intensity could become a viable and safe therapeutic option for hypertensive patients, maximizing the benefits of exercise training.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES