THE CARDIOVASCULAR ADJUSTMENTS to exercise constitute well-coordinated responses throughout the body. Virtually every organ system is required to do more (e.g., skeletal muscle, the respiratory pump, and the cardiac pump) or to do the same as at rest while receiving less blood flow. Of all the organ systems, perhaps only global brain activity and blood flow are not modulated in some manner. The enormous demands for skeletal muscle blood flow imposed by dynamic exercise with a large muscle mass likely constitute the greatest challenge that is regularly imposed on the cardiovascular control mechanisms. The challenge of graded dynamic exercise is met by graded increases in cardiac output that make more flow and oxygen delivery available to active tissues and by graded reduction in the blood flow to inactive regions, which frees up additional oxygen delivery for active sites. The increase in calculated total systemic conductance permitted by the cardiovascular control mechanisms is well matched to the rise in cardiac output such that arterial pressure is well maintained or rises modestly. Some responses to isometric exercise differ. Owing to the sustained mechanical impingement of the muscle vasculature imposed by sustained muscle contraction, the cardiovascular response to this form of exercise has been characterized by the failure of the cardiovascular control systems to secure adequate blood flow for the contracting muscle. The resultant progression of muscle fatigue requires progressive increments in volitional effort to maintain force output until output can no longer be sustained. Heart rate and cardiac output rise progressively throughout the period of activity. Because a concomitant rise in vascular conductance is lacking, arterial pressure rises progressively as well. Although there are long-recognized similarities and dissimilarities between static and dynamic exercise (2), the cardiovascular neuroregulatory systems that bring about these adjustments likely share the same neurophysiological substrates with the substrates being activated in different patterns and/or at different levels of stimulation between the two forms of exercise.

A longstanding challenge to cardiovascular physiologists has been the unraveling of the signals that produce the cardiovascular responses to exercise. Two overall regulatory schemes with long, rich histories continue to dominate present day research: 1) classical, negative-feedback control provided by afferents from active muscle (e.g., a fall in blood flow leads to an accumulation of metabolites that stimulate sensory nerve endings, which elicits a rise in arterial pressure in an effort to restore blood flow), and 2) feedforward control provided by motor outflow from the cerebral cortex. Zuntz and Gebbert (cited in Ref. 4) established the basic idea of the importance of a feedback regulatory scheme provided by afferent neural signals from the muscles themselves. Critical early work was contributed by Alam and Smirk (1), who employed the trapping of nerve-activating chemical substances within previously active muscle by postexercise circulatory arrest, a powerful investigative tool, the use of which persists to the present day. The reflex nature of the responses was later more broadly defined by Coote et al. (3) and by McCloskey and Mitchell (9), whereas identification and characterization of the afferent fiber types involved has been provided by Kaufman et al. (7).

Zuntz and Geppert and also Johansson (all cited in Ref. 4) appear to be the first to postulate the importance of motor command signals in evoking cardiorespiratory responses to exercise. Krogh and Lindhard (8) wrote of “irradiation of impulses from the motor cortex” that activated cardiovascular responses, a concept that later morphed into “central command,” the idea that descending motor command signals activate cardiovascular centers in a parallel, feedforward regulatory scheme (4, 5).

Recently, the role of the arterial baroreceptor reflexes in governing cardiovascular responses to exercise has been succinctly reviewed by Rowell (11), and a complete review of the topic of baroreflex resetting during exercise is provided by Raven et al. (10). In brief, from early ideas that the baroreflex was “shut off” during exercise, our understanding has progressed to the realization that not only is baroreflex function preserved during exercise, but also the operating point of the baroreflexes is actually “reset” to higher operating pressures in proportion to work intensity, and there is evidence that both central command and peripheral feedback from muscle can reset the baroreflex (10). Much of the recent work on this topic has focused on the influence of steady-state dynamic exercise on overall baroreflex control of arterial pressure.

In this issue of the American Journal of Physiology-Heart and Circulatory Physiology, Ichinose et al. (6) add to a fine series of mechanistic studies that shed considerable light on how the cardiovascular responses to isometric exercise are regulated. Their present study (6) provides important tests of some longstanding ideas about the potential role of arterial baroreceptor reflex resetting during exercise. These investigators measured muscle sympathetic nerve activity (MSNA) in subjects at rest, during 3-min isometric handgrip at 30% of maximal voluntary contraction force, and during a 4-min period of postexercise muscle ischemia. Sympathetic activity was quantified as mean burst strength, burst incidence, (bursts per 100 heart beats), and total activity (the product of mean burst strength and incidence). Arterial baroreflex modulation of sympathetic activity was assessed beat-by-beat by relating spontaneous changes in diastolic arterial pressure to burst strength, burst incidence, and total activity, taking into account the latency from the R-wave of the electrocardiogram and the sympathetic burst. They found that baroreflex control of burst strength, burst incidence, and total activity were all modulated in a time-dependent manner during isometric exercise. In the first minute of exercise, when central command predominates (with input from muscle mechanoreceptors), the linear relationship of all three measures of MSNA to diastolic pressure...
was shifted rightward without a significant vertical shift or change in sensitivity (slope), implicating central command as the cause of this resetting. Resetting of the operating pressure of the baroreflex in this way would enable MSNA to be maintained at the resting level despite an increase in pressure produced by a rise in heart rate and cardiac output. By minute 2, when muscle metaboreceptors are likely to be activated, the curves were shifted rightward and upward, and the sensitivity of the control of total activity was increased. Similar further changes were seen in minute 3. These observations suggest that the muscle metaboreflex (or muscle chemoreflex) could account for both an upward and rightward shift of baroreflex curves, as well as the increase in sensitivity of baroreflex control of total activity. During postexercise muscle ischemia (which isolates muscle metaboreflex activity), the burst strength and total activity relationships were shifted leftward and downward (i.e., back toward control levels). Interestingly, the burst incidence relationship was only shifted leftward (i.e., no downward shift resulted from the withdrawal of central command and muscle mechanoreceptor stimulation), indicating that its upward shift was mediated entirely by the muscle metaboreflex. Thus Ichinose et al. (6) provide compelling evidence that baroreflex control of MSNA is modulated in a time-dependent manner during isometric exercise and that resetting of the arterial baroreflex control of sympathetic activity represents an important mechanism mediating the progressive increase in arterial pressure and sympathetic activity during isometric exercise.

GRANTS

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REFERENCES