invited editorial

Invited Editorial on “Effect of arterial occlusion on responses of group III and IV afferents to dynamic exercise”

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MANY OF THE CARDIOVASCULAR and respiratory adjustments to exercise are mediated by activation of the sympathetic nervous system. This sympathetic activation has been attributed both to the central neural drive associated with the volitional component of exercise, termed “central command,” and to a reflex arising from activation of mechanically and chemically sensitive afferents in the contracting muscles, termed “the exercise pressor reflex” (13). The muscle afferents mediating the exercise pressor reflex are the slowly conducting thin-fiber group III and IV afferents, the receptors of which are paciniform corpuscles and unencapsulated nerve endings. In contrast, the fast-conducting thick-fiber group I and II afferents that mediate proprioception are not involved in the exercise pressor reflex (9).

Electron microscopic studies have localized the endings of the group III afferents to collagen structures within skeletal muscle, whereas the endings of the group IV afferents are associated with blood and lymph vessels (3). This structural arrangement corresponds well with the traditional thinking about the discharge properties of the group III and IV muscle afferents, as defined by classic experiments performed in the 1980s (5–8). In those experiments, performed on barbiturate-anesthetized cats, the activity of single-fiber afferent nerves dissected from the dorsal roots was recorded during hindlimb muscle contraction evoked by electrical stimulation of the ventral spinal roots. This work advanced the notion that the majority of group III muscle afferents appear to be mechanoreceptors, endings that respond rapidly to mechanical deformation of their receptive fields. Two properties of a rapidly adapting mechanoreceptor were demonstrated: 1) an explosive burst of activity at the onset of tetanic contraction followed by rapid adaptation and 2) bursts of activity that followed an oscillating stimulus, i.e., rhythmic twitch contractions. In contrast, the majority of group IV afferents appeared to be chemoreceptors, endings that respond to the accumulation in the muscle interstitium of some metabolic products of muscle contraction. During sustained tetanic contractions of the triceps surae muscles, two distinctive properties of muscle chemoreceptors are 1) a relatively long latency of 8–10 s from the onset of contraction to the onset of afferent activation and 2) augmentation of this response when the contracting muscles are made ischemic by vascular occlusion, a maneuver that exacerbates the mismatch between muscle blood flow and metabolism. A third property is that the activation of group IV chemoreceptor afferents is maintained during postcontraction vascular occlusion: muscular relaxation eliminates the mechanical stimulus to muscle afferents while the occluded circulation maintains the concentration of metabolites in the vicinity of the muscle afferent endings.

Although the use of this animal model unquestionably provided valuable insights regarding the afferent arm of the exercise pressor reflex during static contractions, it also has a number of potential limitations, if the goal is to understand the role played by group III and IV muscle afferents in orchestrating the cardiopulmonary responses to real dynamic exercise. These include 1) anesthetic effects, 2) a nonphysiological pattern of muscle fiber recruitment (4), 3) isometric contraction of a small muscle group rather than dynamic exercise of large muscle groups, and 4) activation of nocioceptors (as well as ergoreceptors).

In a Herculean effort to overcome many of these limitations, in this month’s issue of the Journal, Adreani and Kaufman examined the responses of group III and IV muscle afferents in an animal model that more closely mimics dynamic exercise (2). In the unanesthetized decerebrate cat, electrical stimulation of the mesencephalic locomotor region was used to cause rhythmic locomotion of all four limbs, producing a pattern of motor-unit recruitment nearly identical to that during dynamic exercise (14). Using this technically demanding model, Adreani and Kaufman measured single-fiber group III and IV muscle afferent activities during locomotion while the hindlimb muscles were freely perfused (in the present and in two prior publications from their laboratory (1, 2, 10)) and while the arterial supply to the hindlimb was occluded. The new work prompts some novel conclusions that alter significantly the thinking about the behavior of group III and IV skeletal muscle afferents. First, without muscle ischemia, mild rhythmic exercise alone is sufficient to activate group III and IV muscle afferents at firing rates (~0.5 Hz) that probably would evoke reflex effects on efferent sympathetic nerve activity and blood pressure. Second, in their response to both freely perfused and ischemic exercise, group III and IV afferents are more similar than different. The group IV afferents responded rapidly to freely perfused contrac-

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tions with a latency as short as that of the group III afferents. A proportion of the group IV afferents displayed another property of mechanoreceptors: they fired synchronously with the rhythmic pattern of muscle recruitment. The group III afferents displayed an augmented response to ischemic, compared with freely perfused, contraction, a property indicative of chemosensitivity. Taken together, these experiments provide a vivid demonstration that group III and IV skeletal muscle afferents are polymodal.

Regarding the chemosensitivity of these afferents, a number of important questions are raised by the present experiments, which utilized brief bouts of very mild dynamic exercise. For example, what is the under-lying chemical or metabolic signal responsible for muscle afferent activation during such a mild exercise stimulus? The previous experiments using electrically evoked tetanic contractions in anesthetized cats emphasized the importance of hydrogen ion and, in particular, lactic acid (11, 12). With the present model, however, the chemosensitivity of group III and IV muscle afferents could not be explained readily by muscular acidosis, since venous effluent pH and lactate concentrations were unchanged. This suggests an important physiological role for some as-yet-unidentified metabolic product of muscle contraction other than hydrogen ion.

Another important question relates to the role played by muscle afferent activation in the integrated regulation of cardiovascular and respiratory function during dynamic exercise. One preeminent view is that at the onset of exercise central command sets the basic pattern of autonomic response, which, in turn, is modulated by baroreceptor reflexes and reflexes arising in mechanoreceptive and chemosensitive skeletal muscle afferents (13). According to this formulation, the “muscle chemo-reflex” is not tonically active during the early stages of progressive exercise but, rather, it becomes engaged only during higher levels of freely perfused dynamic exercise, which are of sufficient intensity to create a mismatch between muscle perfusion and metabolism, a metabolic error signal. In the present study, even brief bouts of mild rhythmic exercise were a potent stimulus to group III and IV muscle afferents, raising the possibility that reflexes arising in these afferents may contribute importantly to the early autonomic adjustments to dynamic exercise. However, to assign specific functions to the afferent activation will require that the model be expanded to both grade the metabolic error signal by increasing the intensity and duration of the exercise and to correlate the afferent stimulus with specific effector responses.

REFERENCES