Sensory transduction of the ischemic myocardium

Jeffrey L. Ardell
Department of Pharmacology, East Tennessee State University, Johnson City, Tennessee

Ischemic-sensitive dorsal root ganglion afferent neurons likely subserve the perception of angina in addition to their reflex effects on cardiovascular function (1, 3, 12). It is unclear as to the function of the nonischemic-sensitive afferents. These data point to the heterogeneity of afferent transduction of the ventricular milieu, even within a single population of cardiac sensory neurons in dorsal root ganglia. This diversity of transduction capability is even more pronounced when one includes the differential static and dynamic transduction characteristics of nodose and intrathoracic (extracardiac and intrinsic cardiac) afferent neurons (1, 2). Future studies should consider how second-order neurons within the central and peripheral aspects of the cardiac nervous system process this time-varying afferent neuronal input that ultimately modulates effenter autonomic activity. Similarly, future studies should consider whether the dynamic characteristics of sensory transduction of an ischemic event impacts the perception of that event (c.f., angina vs. silent ischemia).

Afferent neuronal transduction of myocardial ischemia exhibits both phasic and lower-level static activity components. Antagonists to various potential mediators discussed above preferentially influence different aspects of this time-varying afferent signal. In this article, preemptive P2 blockade attenuates the phasic component at occlusion onset, with minimal effects on the steady-state response during the later stages of the 5-min occlusion. These data indicate that ATP may preferentially affect the early phasic response. In contrast, histamine likely exerts preferential effects on afferent neuronal activity in the later stages of myocardial ischemia, while endothelin similarly affects early and late-phase afferent responses (4, 8). Such data point to the time-varying components of the afferent neuronal signals provided to processing centers within the cardiac neuronal hierarchy.

Furthermore, differential reflex responses are evoked by afferent neurons transducing events within the anterior versus posterior parts of the left ventricle. Within this study, exogenous ATP induced pressor responses in 50% of animals and depressor responses in the remaining 50%. Future studies should consider what contribution differential afferent transduction plays in these opposing hemodynamic responses. Correspondingly, the neurochemical diversity exists among cardiac afferent neurons that transduce signals from the ventricular milieu, with horseradish peroxidase-identified ventricular neurons in T3 dorsal root ganglion staining for substance P, calcitonin gene-related peptide, or neuronal nitric oxide synthase, either alone or with two markers colocalized (9). These data indicate that cardiac sympathetic afferent neurons transduce a variety of neurochemicals. In addition, the activity profile of each affected afferent neuron during the course of myocardial ischemia-reperfusion is likely reflected in the combination of neurotransmitters released at second-order neurons.

In conclusion, the study by Lu and Longhurst (6) supports the underlying hypothesis that different mediators can affect...
cardiac afferent neuronal activity during ischemia-reperfusion in an interactive and multifactorial manner. Future studies to elucidate these interactions at the level of sensory neurites, the information content provided to second order neurons, and in the integrated reflex responses to such inputs should provide critical data for understanding not only cardiovascular control but also the perception of pain.

DISCLOSURES

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

REFERENCES