The following is the abstract of the article discussed in the subsequent letter:

Cheng, Zizi (Jack), Hong Zhang, Shang Z. Guo, Robert Wurster, and David Gozal. Differential control over postganglionic neurons in rat cardiac ganglia by NA and DmnX neurons: anatomical evidence. Am J Physiol Regul Integr Comp Physiol 286: R625–R633, 2004. First published November 26, 2003; 10.1152/ajpregu.00143.2003.—In previous single-labeling experiments, we showed that neurons in the nucleus ambiguous (NA) and the dorsal motor nucleus of the vagus (DmnX) project to intrinsic cardiac ganglia. Neurons in these two motor nuclei differ significantly in the size of their projection fields, axon caliber, and endings in cardiac ganglia. These differences in NA and DmnX axon cardiac projections raise the question as to whether they target the same, distinct, or overlapping populations of cardiac principal neurons. To address this issue, we examined vagal terminals in cardiac ganglia and tracer injection sites in the brain stem using two different anterograde tracers [1,1′-dioleoyl-3,3′,3′,3′-tetratexylicarbocyanine methanesulfonate and 4-[4-(dihexadecylamino)-styryl]-N-methylpyridinium iodide] and confocal microscopy in male Sprague-Dawley rats. We found that 1) NA and DmnX neurons innervate the same cardiac ganglia, but these axons target separate subpopulations of principal neurons and 2) axons arising from neurons in the NA and DmnX in the contralateral sides of the brain stem enter the cardiac ganglionic plexus through separate bundles and preferentially innervate principal neurons near their entry regions, providing topographic mapping of vagal motor neurons in left and right brain stem vagal nuclei. Because the NA and DmnX project to distinct populations of cardiac principal neurons, we propose that they may play different roles in controlling cardiac function.

**Differential cardiac parasympathetic innervation—what is the functional significance?**

**To the Editor:** Cheng and colleagues (4) readdressed the question of the origin of the cardiac vagal innervation. Whereas previous studies (8, 9, 12) emphasized the importance of the parasympathetic preganglionic neurons of the periambigual nucleus ambiguous (NA) in control of heart rate, the study by Cheng et al. (4) clearly indicates that the heart receives a dual parasympathetic innervation that arises from the dorsal motor nucleus of the vagus (DmnX) as well as the periambigual NA. Aside from supporting previous observations of the dual vagal premotor innervation of the heart (1, 2, 16), the study indicates that DmnX and periambigual NA vagal premotor neurons project to different principal neurons within the same cardiac ganglionic plexus. In an accompanying editorial commentary, Persson and Armour (10) speculated about the possible implications of this dual innervation.

Baroreceptor-evoked reflex bradycardia is largely abolished by blockade of ionotropic excitatory amino acid (EAA) receptors in a region of the ventrolateral medulla (VLM), which overlaps with the periambigual NA vagal premotor neurons (7). Functional studies performed by Cheng and colleagues addressed the question of the involvement of the DmnX and the periambigual NA in mediating baroreflex bradycardia. They found that domoic acid lesions of the periambigual NA (3) but not the DmnX (5) abolished baroreflex bradycardic responses. These results are consistent with the long held view of the role of periambigual NA vagal premotor neurons in mediating baroreflex bradycardia (8). In view of the findings obtained in the lesion experiments Cheng and colleagues went on to speculate that perhaps the DmnX may prove to be important for reflex bradycardia mediated by activation of other reflexes, e.g., C fiber-mediated reflexes. However, C fiber-evoked bradycardia elicited by systemic administration of 5-HT_3 receptor agonists is also markedly reduced by EAA receptor blockade in the VLM (17) suggesting an important role for periambigual vagal premotor neurons.

An alternative function for the DmnX vagal innervation of the heart may be in modulation of coronary blood flow (6). Cardiac parasympathetic vasodilatation has been demonstrated in a number of species, although its significance compared to the effects of autoregulatory metabolic mechanisms and local oxygen tension is uncertain. Coronary artery vasodilatation occurs in several species in response to intracoronary acetylcholine administration (6). Similarly, parasympathetic vasodilatation is observed in the electrically paced heart in response to vagal efferent stimulation and in response to activation of cardiac or pulmonary vagal afferents (6).

Rat atrial and ventricular microvessels receive a prominent cholinergic innervation as judged by the presence of fibers containing vesicular acetylcholine transporter immunoreactivity (14). Cholinergic vasodilatation is also well recognized in airway smooth muscle (11) and cholinergic vasodilator mechanisms may operate in some regions of the gastrointestinal tract [e.g., stomach and pancreas (13, 15)].

The challenge will be to determine whether vagal premotor neurons of the DmnX participate in cholinergic vasodilator mechanisms in the heart and other organs and to identify circumstances in which these pathways operate. This question may be examined in animals whose periambigual vagal preganglionic neurons had been destroyed by domoic acid or by a selective cholinergic neurotoxin.

**REFERENCES**


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