A new rat model of aortic sympathetic denervation

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The sympathetic nervous system plays an important role in short- and long-term cardiovascular homeostasis. The sympathetic nervous system influences vascular function via multiple mechanisms, including alteration of vascular tone, and in turn, is influenced by arterial stiffness via baroreceptors. Consequently, imbalancs in the system could lead to maladaptive vascular function and cardiovascular disease. Indeed, the role of the sympathetic nervous system has been well-described in rat models of both renal[1] and peripheral vasculature and successfully translated in humans for treatment of resistant hypertension. However, there is a paucity in molecular-level data on how sympathetic denervation impacts abdominal aortic morphology.

In their study, Bin Jiang et al propose a new experimental rat model to study denervated abdominal aortas and explored how sympathectomy affects vascular remodeling.[2] The model employs open topical denervation of the infrarenal aorta using a one-time application of local neurotoxin, 10% phenol. Six months after treatment, the aorta show features similar to those seen in aneurysmal disease, such as changes in intima-media thickness, elastin and collagen composition, adventitial vascular density, and expression of vascular smooth muscle proteins. These results support the importance of sympathetic nervous system in vascular wall integrity. However, the study did not assess the off-target or systemic effects of phenol application, and comparison with other neurotoxins would be warranted to assess specificity of the toxicity, including effects on the parasympathetic nerves. Additionally, the authors point out that the application of the neurotoxin may result in non-uniform denervation of the aorta with predilection for its anterior surface. Nevertheless, the proposed model provides a stepping-stone for understanding the interplay between sympathetic and vascular functions.

Sympathetic denervation has been applied to treat a variety of conditions. Renal sympathetic denervation reduces both renal and central sympathetic activity, including blood pressure in patients with resistant hypertension.[3] Unlike the open direct neurotoxin injection proposed in this rat model, current technologies for human renal artery denervation apply percutaneous approaches that use different technology for denervation, such as catheter-directed radiofrequency ablation and ultrasonic ablation therapy,[4] and thus the relevance of a neurotoxin model remains to be established. Pharmacological ablation with ethanol and guanethidine monosulfate locally delivered through infusion catheters has only been described in preclinical studies. In addition, the potential for renal artery re-innervation after these procedures remains a concern. The new rat model may serve as a tool to further evaluate the role of the sympathetic nervous system in normal arterial homeostasis and may also be applied to rodent models of disease to assess novel therapeutic approaches targeting sympathetic dysfunction in vascular diseases.

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DISCLOSURES

None.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS-Vascular Science policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

JVS—Vascular Science 2024;5:100205

2666-3503

https://doi.org/10.1016/j.jvssci.2024.100205