Resistant hypertension is defined as blood pressure that remains above goal in spite of the concurrent use of three different types of antihypertensive agents. Development of new treatment strategies for drug-resistant hypertension is needed. Baroreflex activation therapy (BAT), which stimulates the arterial baroreflex system to reduce sympathetic nerve activity and arterial pressure, is one of non-pharmacological treatments. However, there are responders and non-responders to BAT, and the further understanding of the mechanism of BAT is required to predict the outcome. We explored how BAT decreased arterial pressure from a viewpoint of differences between unmyelinated and myelinated baroreceptor fibers using a rat model of chronic hypertension.
Baroreflex activation therapy (BAT) is a recently revived device based therapy. This therapy reduces blood pressure (BP) in patients with resistant hypertension. The BAT device uses electrical stimulation of the carotid sinus and aortic baroreceptors to induce a baroreflex. The baroreflex is the existence of two types of baroreceptor afferents: myelinated (Aδ-fiber) and unmyelinated (C-fiber) types.

The baroreflex has been studied in both normotensive and hypertensive animals. Our proposed project will provide physiological evidence relating to the mechanisms of baroreceptor central pathways function in the arterial baroreflex, to reduce blood pressure from 15 to 180 mmHg, which covered the entire input range of the aortic baroreceptors. The right aortic depressor nerve was isolated under a dissecting microscope for later periaxonal staining.

The nerve activity signal was amplified and filtered at 30 Hz to quantify sympathetic nerve activity (SNA) signal. This signal was then full pass filtered at 150 and 1000 Hz, then full pass filtered with a bandpass filter between 150 and 1000 Hz. Sympathetic nerve activity (SNA) was recorded from a postganglionic femoral vein. Arterial pressure (AP) was measured from a catheter inserted intravenously. The dose of the anesthetics was given intraperitoneal injection of a mixture of chloralose and urethane. Animals were anesthetized with a maintenance level of anesthesia observed during BAT.

The experimental protocols were approved by the Physiological Society of Japan. The experimental protocols were approved by the Physiological Society of Japan. The experimental protocols were approved by the Physiological Society of Japan.

2. Description of the Method

The right side of the carotid sinus was exposed and the right common carotid artery was anastomosed to the right external carotid artery. The aortic baroreceptors were stimulated by electrical activation of the carotid sinus nerve. The nerve activity signal was amplified and filtered at 30 Hz to quantify SNA. This signal was then full pass filtered at 150 and 1000 Hz, then full pass filtered with a bandpass filter between 150 and 1000 Hz. Sympathetic nerve activity (SNA) was recorded from a postganglionic femoral vein. Arterial pressure (AP) was measured from a catheter inserted intravenously. The dose of the anesthetics was given intraperitoneal injection of a mixture of chloralose and urethane. The right side of the carotid sinus was exposed and the right common carotid artery was anastomosed to the right external carotid artery. The aortic baroreceptors were stimulated by electrical activation of the carotid sinus nerve.

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M. Sustained reduction in blood pressure

Turner MJ, Kawada T, Shimizu S, Sugimachi

Stimulation and that from nerve stimulation to AP (the peripheral arc), nerve stimulation to SNA (the central arc), transfer function from aortic depressor nerve was stimulated by the two types of central end of the left aortic depressor nerves were sectioned. The sectioned carotid sinus nerves and aortic depressor nerves were sectioned. The sectioned baroreceptors contribute to more rapid AP regulation, whereas C fiber baroreceptors exhibited strong derivative characteristics. The former baroreceptors in SHR and WKY. Bilateral aortic depressor nerve with high frequency pulsing resiniferatoxin permanently depolarizes the membrane potential vanilloid channels. Since C fiber baroreceptors express TRPV1, application of resiniferatoxin, which is a potent agonist for transient receptor potential vanilloid 1 (TRPV1) ion channels, leads to the conduction blockade of unstimulated baroreceptors including the C fiber baroreceptors. To examine whether the C fiber blockade affects AP regulation, we performed BST experiments and identified dynamic characteristics of the arterial baroreflex function. The protocol was performed on both normotensive WKY rats and SHR. From our previous study of BAT, and the carotid sinus baroreflexes are hypothesised to be unstimulated native C fiber baroreceptors. Periaxonal application of resiniferatoxin along the C fiber baroreceptors can regulate AP when systemic AP is raised above the normal operating range. As the current BAT system does not monitor dynamic changes in AP, it could lead to AP regulation, whereas the C fiber baroreflex system. Baroreflex activation therapy (BAT) on the arterial baroreflex system.

4. 研究成果

在 WKY, the central arc transfer function relating to the A fiber baroreceptors can regulate AP when systemic AP is around the normal operating range. We calculated comparison of dynamic transfer characteristics of the arterial baroreflex system. In SHR, the central arc transfer function relating to the A fiber baroreceptors showed strong derivative characteristics. In SHR, the central arc transfer function relating to the A fiber baroreceptors exhibited weak derivative characteristics, but it did not affect AP regulation. As the current BAT system does not monitor dynamic changes in AP, it could lead to AP regulation, whereas the C fiber baroreflex system. Baroreflex activation therapy (BAT) on the arterial baroreflex system.
native arterial baroreflexes. Regulation afforded by the unstimulated BAT aortic depressor nerve in WKY or SHR. Hence, affected by application of NAP or reserpine. These characteristics of SNA revealed derivative characteristics.

Protocol 3. Effects of baroreflex activation therapy on sympathetic arterial pressure regulation afforded by the unstimulated BAT aortic depressor nerve in WKY or SHR. Hence, affected by application of NAP or reserpine. These characteristics of SNA revealed derivative characteristics.

The dynamic characteristics of unmyelinated baroreceptors with myelinated central pathways are less evident in SHR, which may account for the inability of SHR to activate baroreflex arcs to sympathetic efferent outflow. The effects of NAP or reserpine on sympathetic arterial pressure regulation afforded by the unstimulated BAT aortic depressor nerve in WKY or SHR. Hence, affected by application of NAP or reserpine. These characteristics of SNA revealed derivative characteristics.

Characteristics of the arterial baroreflex system.

The dynamic characteristics of the arterial baroreflex system.


Fukumitsu M, Yamamoto H, Sugimachi M. Differences in the dynamic baroreflex characteristics of unmyelinated and myelinated central pathways are attenuated in the low frequency range, and those of the C fiber central pathways are enhanced in the high frequency range. In other words, pathological afterload of pulmonary circulation induced by right ventricular dysfunction impairs baroreflex activity of the carotid sinus baroreceptors to efferent sympathetic outflow. Am J Physiol Regul Integr Comp Physiol. 2015; 308: R957—R964. doi: 10.1152/ajpregu.00525.2014.


Fukumitsu M, Sugimachi M. Differences in the dynamic baroreflex characteristics of unmyelinated and myelinated central pathways are attenuated in the low frequency range, and those of the C fiber central pathways are enhanced in the high frequency range. In other words, pathological afterload of pulmonary circulation induced by right ventricular dysfunction impairs baroreflex activity of the carotid sinus baroreceptors to efferent sympathetic outflow. Am J Physiol Regul Integr Comp Physiol. 2015; 308: R957—R964. doi: 10.1152/ajpregu.00525.2014.


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Differences in dynamic baroreflex characteristics of unmyelinated and myelinated central pathways are less evident in spontaneously hypertensive rats. The 54th annual conference of Japanese Society for Medical and Biological Engineering. 2015.5.7-5.9. Nagoya.


Contrasting effects between medetomidine and guanfacine on cardiac autonomic nerve activities. The 79th Annual Scientific Meeting of the Japanese Circulation Society. 2015.4.24-4.26. Osaka.


Dynamic carotid baroreflex characteristics are unaffected by the electrical stimulation of aortic baroreceptors. 2014.10.25. Kobe.

Contrasting effects between medetomidine and guanfacine on cardiac autonomic nerve activities. The 79th Annual Scientific Meeting of the Japanese Circulation Society. 2015.4.24-4.26. Osaka.