Sympathectomy Attenuated the Excitability of Dorsal Root Ganglion Neurons in a Lumbar Radiculopathy Model

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INTRODUCTION:

Lumbar radicular pain associated with lumbar disc herniation and lumbar spinal canal stenosis is one of the most common symptoms treated by orthopaedic surgeons. Recently, the existence of sympathetically maintained pain improved by sympathetic nerve block is known, and some reports showed that a sympathetic nerve block is effective for a refractory lumbar radicular pain.

In our previous studies, we reported that spinal nerve root constriction induced sympathetic sprouting around dorsal root ganglion (DRG) neurons, and norepinephrine released from postganglionic neurons in the sympathetic nervous system enhanced the excitability of DRG neuron in the root constriction. Furthermore, we revealed that surgical sympathectomy attenuated allodynia by behavioral study with root constriction model rat.

The purpose of the present study is to examine the effects of sympathectomy on the excitability of DRG neurons originated in the spinal nerve root constriction electrophysiologically using patch clamp recordings.

MATERIALS & METHODS:

The experimental protocols used in this study were approved by the Sapporo Medical University Animal Care and Use Committee. We used a total of 30 adult male Sprague-Dawley rats weighing 150-200g at the beginning of the study. We divided these animals into 3 experimental groups: root constriction group (RC, n=10), root constriction with sympathectomy group (RC+Syx, n=10), and control group (n=10).

In the RC group, the left L5 spinal nerve root was exposed and tightly ligated with 8-0 nylon suture just proximal to the DRG. Just after root constriction, only exposure of the sympathetic nerve without sympathectomy was received. In the RC+Syx group, the L2-5 sympathetic ganglions and chains on both sides were resected through transperitoneal approach. In control group, any procedures were not performed.

At 10-14 days after surgery, we used the DRG neurons for whole-cell patch clamp recordings. The ipsilateral L5 DRG neurons were excised and enzymatically digested with collagenase.

To evaluate the excitability of DRG neurons, we examined the threshold current, resting membrane potential (RMP), action potential amplitude, afterhyperpolarization, threshold voltage, APD50, and dv/dt max by the short stimulation protocol (depolarizing currents of 0.2-4.0nA, 0.5ms duration). Also, we counted the number of the maximum spikes in each current (Max spike) by the long stimulation protocol (depolarizing currents of 0.01-0.39nA, 1000ms).

In order to compare the 3 groups (RC, RC+Syx, control), statistical analysis of the data was performed by ANOVA and Tukey-Kramer test. P<0.05 was statistically considered significant.

RESULTS:

RC neurons significantly exhibited lower threshold current, more depolarized RMP, prolonged APD50 and greater Max spike when compared to controls (Fig. 1-5). These hyperexcitable changes were inhibited by surgical sympathectomy, and there were no significant differences between RC+Syx and control group. For RC+Syx neurons, the mean value of Max spike was 5.0±1.5, which was significantly smaller than the mean of 13.7±1.7 for RC neurons (Fig. 4, 5).

There were no significant changes found in the other parameters measured such as action potential amplitude, afterhyperpolarization, threshold voltage, dv/dt max.

DISCUSSION:

The present study showed that lumbar sympathectomy attenuated the development of the hyperexcitability of DRG neurons caused by spinal nerve root constriction. These mechanisms may be based on changes of expression and functions, such as sodium and potassium channel. Controlling activity of the sympathetic nerve may lead to a new strategy of lumbar radiculopathy treatment.

REFERENCES:


Fig.1. Threshold current. ** P<0.01
Fig.2. RMP. * P<0.05
Fig.3. APD50. * P<0.05
Fig.4. Max spike. ** P<0.01
Fig.5. The responses of DRG neurons in long stimulation protocol
(A) RC, (B) RC+Syx, (C) Control