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Pilot study on the effect of botulinum toxin type A in rats with neuropathic pain after spinal cord

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Background
The application of botulinum toxin type A (BTX-A) has been recently explored in a number of painful neuropathic conditions. We aim to determine the changes in pain behavior after spinal cord injury, and the effects of botulinum toxin type A (BTX-A) on neuropathic pain after spinal cord injury through behavioral sensory test and electrophysiological assessments.

Methods
Twelve male Sprague-Dawley rats(300-350g) were induced to thoracic spinal cord injury by contusion method. One week after injury, BTX-A (20U/kg) or saline was administered to the plantar surface by subcutaneous injection. Behavioral tests were conducted preoperatively and weekly for 5 weeks postoperatively. Mechanical allodynia was measured using von Frey filament, and thermal hyperalgesia was measured on a hot plate analgesia meter. Sensory evoked potential was detected in the cortex by stimulating the posterior tibial nerve. Two-way analysis of variance (ANOVA) with repeated measures was used to detect statistical significance.

Results
The paw withdrawal threshold (PWT) to mechanical stimulation decreased immediately and significantly after spinal cord injury. The paw withdrawal latency (PWL) to thermal stimulation gradually decreased to the lowest level at 3 weeks after injury. Amplitude of sensory evoked potential gradually decreased after spinal cord injury (Figure 1) After subcutaneous injection of BTX-A, the PWT to mechanical stimulation was increased and higher than that of the control group. Similarly, the PWL to thermal stimulation was measured to be higher in the BTX-A injection group. Subcutaneous injection of BTX-A reversed the amplitude reduction of sensory evoked potentials, and the amplitude measured after 5 weeks of injury was higher than that of the control group. However, there was no statistically significant differences in all variables (Figure 2, Table 1).

Conclusions
Subcutaneous injection of BTX-A tended to be effective in neuropathic pain. It is necessary to evaluate the effect of BTX-A on neuropathic pain through a large sample study in the future.

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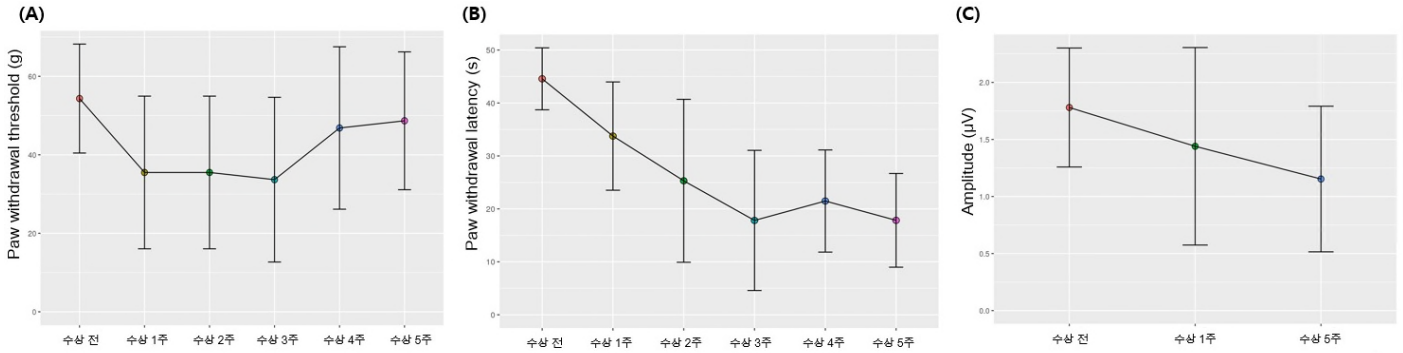

Figure 1. Change in withdrawal threshold to mechanical and thermal stimulation, amplitude of sensory evoked potential after spinal cord injury.

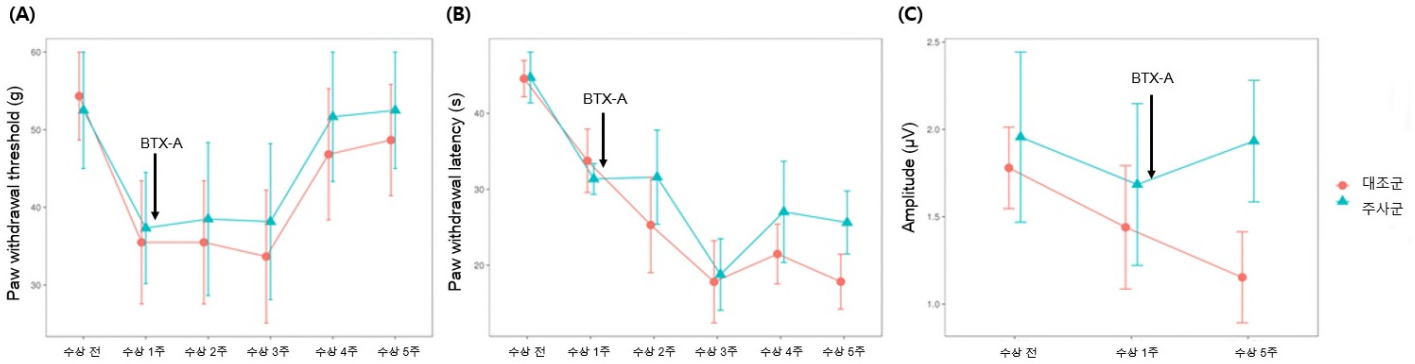

Figure 2. Comparison of withdrawal threshold to mechanical and thermal stimulation, amplitude of sensory evoked potential after subcutaneous injection of botulinum toxin type A.

Group	Before injury	Spinal cord injury 1wk	Injection 1wk	Injection 2wk	Injection 3wk	Injection 4wk
Paw withdrawal threshold (g)						
Saline(n=6)	54.3 ±13.9	35.5± 19.5	35.5± 19.5	33.7 ±20.9	46.8 ±20.7	48.7± 17.6
BTX-A(n=6)	52.5± 18.4	37.3± 17.6	38.5 ±24.1	38.2± 24.6	51.7± 20.4	52.5 ±18.4
Paw withdrawal latency (s)						
Saline(n=6)	44.6 ±5.86	33.8± 10.2	25.3± 15.4	17.8± 13.2	21.5± 9.6	17.8± 8.8
BTX-A(n=6)	44.7± 8.2	31.4± 4.9	31.6± 15.2	18.8± 11.5	27.0± 16.3	25.6 ±10.1
Amplitude of sensory evoked potential (μV)						
Saline(n=6)	1.8 ±0.5	1.6± 0.9	-	-	-	1.2± 0.7
BTX-A(n=6)	1.9 ±1.1	1.6± 1.2	-	-	-	2.1± 0.9

Data are means ± standard deviation.

Table 1. Effects of botulinum toxin type A on pain threshold and sensory evoked potential in spinal cord injury rat model.