UP-REGULATION OF ACID-SENSING ION CHANNEL 3 IN DRG NEURONS FOLLOWING APPLICATION OF NUCLEUS PULPOSUS ON NERVE ROOT IN RATS

Purpose.
Radicular pain is a common symptom of lumbar disc herniation in humans. Acid-sensing ion channel 3 (ASIC3), a depolarizing sodium channel gated by protons during tissue acidosis, is specifically expressed in sensory neurons. It has been associated with cardiac ischemic and inflammatory pain. We often perform spinal nerve root block for radicular pain using a sodium channel blocker such as lidocaine; however, it has been unclear whether the effective period of this treatment is usually longer than the expected duration of efficacy. The duration of efficacy of sodium channel blocker such as lidocaine is about 2 hours. However, after administration of lidocaine to spinal nerves affected by disc herniation, some patients experienced relief from pain for a few weeks or months. The precise reason for such a prolonged effect of lidocaine in such patients has not been clarified. In this report, we describe changes in ASIC3 immunoreactivity in dorsal root ganglion cells, and the effect of injection of lidocaine on ASIC3 expression and pain in the rat model of lumbar disc herniation.

Methods.
For the lumbar disc herniation model, nucleus pulposus was harvested from the tail and applied to the L5 nerve root, and the nerve roots were pinched. We evaluated mechanical allodynia in sham-operated animals, and in a disc herniation model. ASIC3 expression in L5 dorsal root ganglia was examined by immunohistochemistry. Finally the effect of lidocaine on pain and ASIC3 expression in the disc herniation model was examined.

Results.
Animals exposed to the lumbar disc herniation model exhibited allodynia for 8 days, and ASIC3 immunoreactivity was up-regulated in dorsal root ganglion neurons. After administration of lidocaine to spinal nerve roots affected by disc herniation, ASIC3 immunoreactivity was down-regulated in dorsal root ganglion neurons for 12 days and the level of mechanical allodynia was significantly decreased for 8 days.

Conclusions.
Our results suggest that ASIC3 in dorsal root ganglion neurons may play an important role in nerve root pain caused by lumbar disc herniation. Lidocaine decreased ASIC3 expression in dorsal root ganglion neurons and pain associated with the disc herniation model. In the current study, ASIC3 expression decreased for at least 12 days after administration of lidocaine. We believe that in humans, the ASIC3 inhibition is effective in patients suffering from lumbar disc herniation, and the mechanism of pain relief by spinal nerve block using lidocaine may be through partial blockade of ASIC3 production in the dorsal root ganglion cells.