A Pain Related Behavior and Intervertebral Disc Degeneration After Lumbar Facetectomy in the Rat – A New Animal Model for Degenerative Disc Disease

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Introduction
Intervertebral disc degeneration is thought to contribute to low back pain, however, the pathophysiologic mechanisms are still controversial. Despite the reports of many experimental animal models with regard to intervertebral disc degeneration, it is still unknown if these models show evidence of pain in the animals. We developed and published a rat model of intervertebral disc degeneration induced by chronic mechanical compression to tail, and demonstrated that application of the degenerated nucleus pulposus tissues to the lumbar nerve roots enhanced hyperalgesia [1]. Pain in this model is radicular pain but not low back pain in degenerative disc disease seen in human. In addition, animal models utilizing researches for intervertebral disc degeneration have been achieved by injury or invasion to the intervertebral discs such as punctures and direct compression [1 - 4]. Considering clinical relevancy and pathophysiology of discogenic pain, these experimental models are thought to be quite different from patients with degenerative disc diseases. To elucidate mechanisms of low back pain due to degenerative disc disease, it is necessary to develop an animal model, in which the intervertebral disc does not receive direct invasion, and which shows evidence of pain. The purpose of the present study was to introduce an experimental animal model of intervertebral disc degeneration with possible pain behavior induced by lumbar facetectomy.

Materials and Methods
The experimental protocol was reviewed and approved by the Institutional Animal Care and Use Committee in our institute. Twenty male Sprague-Dawley rats, each weighing about 250 g were used. All surgical procedures were performed with the rats anesthetized by an intraperitoneal injection of sodium pentobarbital (50 mg/kg). Rats were divided into three experimental groups. In the sham group (n = 6), only exposure of bilateral facet joints at the L4-5 level was performed. Ten rats underwent complete resection of bilateral L4-5 facet joints on the right side to induce intervertebral disc degeneration after lumbar facetectomy. In the experimental group, there was no translational instability such as slippage of the vertebral body at the L4-5 level. In the histological and immunohistochemical analysis, the existence of diffuse nucleus pulposus cells in the matrix was found in these groups. The occurrence of the nucleus pulposus was decreased in the experimental group. Decrease in extracellular matrix content and increase in ADAMTS4, MMP13, IL-1β and TNF-α immunoreactivities were seen in the experimental group, compared with the control and sham groups.

Discussion
In the present study, we found that lumbar facetectomy resulted in abnormal walking patterns 7 weeks after the surgery and degeneration and expression of inflammatory cytokines in the intervertebral disc at the facetectomy level. This is a first report of the animal model in which the intervertebral disc has no surgical invasion directly at the operation, and which shows evidence of abnormal walking pattern. In addition, we considered the possibility that there were relationships between the gait abnormalities observed by the walking analysis system and radiological changes of intervertebral disc in the experimental group. Changes of the disc height and an increase in the extension ratio seen in radiological examination suggest segmental instability of the lumbar spine and might result in biomechanical and biological abnormalities of the intervertebral disc among abnormal walking patterns. A decrease in optical density of posterior feet observed in the experimental group is thought to be a pain related behavior observed in neuropathic pain models [6]. A clinical study demonstrated that an etiology of chronic low back pain might be neuropathic pain [7]. Collectively, the intervertebral disc abnormality after lumbar facetectomy might induce neuropathic pain. This finding suggests that we consider pain secondary to intervertebral disc degeneration in no relation to nerve root irritation. In future, it is necessary to perform quantitative molecular biological analysis of degenerative intervertebral disc and to make clear pathophysiologic mechanisms of abnormal walking pattern in this model. This animal model may be useful to elucidate mechanisms of degenerative disc disease with chronic low back pain seen in human.

Conclusions
We developed an animal model, in which lumbar facetectomy resulted in delayed intervertebral disc degeneration and abnormal walking pattern in the rat. This model has no direct invasion to the intervertebral disc and might show evidence of neurogenic pain without nerve root irritation.

References

Significance: We developed a rat model, in which the intervertebral disc did not receive direct invasion, and which showed evidence of pain, to elucidate mechanisms of low back pain due to degenerative disc disease. In this animal model, we suggest that delayed intervertebral disc degeneration results in neurogenic pain without nerve root irritation.