Effects of intervertebral disc cells on neural tissue

In vitro and *in vivo* experimental studies

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av

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Avhandlingen baseras på följande delarbeten:

I. **Effects of intervertebral disc cells on neurite outgrowth from dorsal root ganglion explants in culture**
K. Larsson, E. Runesson, K. Junevik, B. Rydevik, H. Brisby.
SPINE 2011; 36(8): 600-606

II. **Electron microscopy analysis of neurites extending from dorsal root ganglia in vitro following exposure to intervertebral disc cells**
K. Larsson, H. Brisby, B.R. Johansson, E. Runesson, B. Rydevik
Cells Tissues Organs, 2012;196:82-89

III. **Evoked thalamic neuronal activity following DRG application of two nucleus pulposus derived cell populations: an experimental study in rats**
E. Nilsson, K. Larsson, B. Rydevik, H. Brisby, I. Hammar.
European Spine Journal, 2013; Jan 24, [Epub ahead of print]

IV. **Neuropathological investigation of spinal nerve tissue following exposure to notochordal cells and chondrocyte-like cells: an experimental study in rats**
K. Larsson, C. Örndal, C. Nordborg, N. Sasaki, E. Runesson,
H. Brisby, B. Rydevik.
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Introduction: Lumbar disc herniation and sciatica are common conditions that involve interactions between intervertebral discs (IVDs) and neural tissue. The nucleus pulposus (NP) of an IVD contains at least two cell populations, notochordal cells and chondrocyte-like cells. The NP can affect nervous tissue, but the biological mechanisms behind these effects are incompletely understood. The overall aim of this thesis was to investigate the effects of the two cell populations derived from NP, notochordal cells and chondrocyte-like cells, on neural tissue in the spine.

Methods: Sprague-Dawley rats were used for both *in vitro* and *in vivo* studies. In studies I and II, dorsal root ganglia (DRGs) from newborn rats were harvested and cultured. The cells in the NP were sorted by size into two cell populations, one comprising large (25-85µm), highly vacuolated notochordal cells and one comprising small (17-23µm), chondrocyte-like cells. After 24 hours culture notochordal cells and/or chondrocyte-like cells were applied to the DRG culture. After another 24 hours´ of culture neurite outgrowth was measured microscopically, using light microscopy (Study I) and electron microscopy (Study II). In Studies III and IV cell effects were evaluated using a rat disc herniation model. The cell populations were applied to L4 DRG (Study III) and to L4 DRG/nerve root (Study IV) and compared with different control systems. The analyses were performed with acute electrophysiological recordings (Study III) and with blinded light microscopic analyses (Study IV).

Results: Notochordal- and chondrocyte-like cells inhibit neurite outgrowth and reduce the diameter of neurites *in vitro* in a dose-dependent manner. Moreover, the two cell populations affect evoked neuronal thalamic activity differentially. There were pronounced neuropathological changes in both DRG and nerve roots following mechanical nerve root displacement in combination with the application of NP. The application of NP and/or the cell populations induced more discrete changes, e.g. nerve fibers with enlarged outer Schwann cell compartments.

Conclusion: The results of this thesis show that the cells in NP, notochordal cells and chondrocyte-like cells, can affect neural tissue in various ways. The findings indicate that complex mechanisms are involved in the interaction between the components of nucleus pulposus and neural tissue.

Keywords: Intervertebral disc, nerve damage, nucleus pulposus, notochordal cells, chondrocyte-like cells

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