Changes in gene expression and protein distribution at different stages of mechanically induced disc degeneration--an in vivo study on the New Zealand white rabbit

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The objective of the study was to improve the biological understanding of degenerative disc disease using a rabbit model in which different stages of disc degeneration are induced by variation of the duration of loading with an external compression-device applying 2.4 MPa. Gene expression and protein distribution were analyzed in controls and after 1, 28, and 56 days of hyperphysiologic loading. To evaluate extracellular matrix genes, quantitative real-time reverse-transcriptase polymerase chain reaction was applied for collagen I, collagen II, biglycan, decorin, fibromodulin, fibronectin, aggrecan, and osteonectin. As representatives of catabolic, anticatabolic, and anabolic factors, matrix metalloproteinase-13 (MMP-13), tissue inhibitor of matrix metalloproteinase-1 (TIMP-1), and bone morphogenetic protein-2 (BMP-2) were chosen. To evaluate protein distribution, immunohistochemistry was performed for collagen I, collagen II, and BMP-2/4. Matrix gene expression was characterized by two major developments: collagen I and II, biglycan, and decorin showed early elevation followed by later downregulation to control levels, whereas fibromodulin, fibronectin, aggrecan, and osteonectin showed continuous upregulation or remained at similar levels. Induction of MMP-13 gene expression was found in degenerated discs. TIMP-1 and BMP-2 were elevated immediately after hyperphysiologic loading and presented highest levels in the 56-day group. Immunohistochemistry showed less collagen II and BMP-2/4 positive cells after compression. In conclusion, elevated matrix gene expression represents an early cellular response to hyperphysiologic loading. As degeneration progresses, some matrix genes increase upregulation, whereas others start downregulation. Continuous upregulation of catabolic, anticatabolic, and anabolic factors indicates their important role in the degeneration process.

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