Meniscal tissue explants response depends on level of dynamic compressive strain

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Summary

Objective: Following partial meniscectomy, the remaining meniscus is exposed to an altered loading environment. In vitro 20% dynamic compressive strains on meniscal tissue explants has shown to lead to an increase in release of glycosaminoglycans from the tissue and increased expression of interleukin-1α (IL-1α). The goal of this study was to determine if compressive loading which induces endogenously expressed IL-1 results in downstream changes in gene expression of anabolic and catabolic molecules in meniscal tissue, such as MMP expression.

Method: Relative changes in gene expression of MMP-1, MMP-3, MMP-9, MMP-13, A Disintegrin and Metalloproteinase with Thrombospondin domain 4 (ADAMTS4), ADAMTS5, TNFα, TGFβ, COX-2, Type I collagen (COL-1) and aggrecan and subsequent changes in the concentration of prostaglandin E2 released by meniscal tissue in response to varying levels of dynamic compression (0%, 10%, and 20%) were measured. Porcine meniscal explants were dynamically compressed for 2 h at 1 Hz.

Results: 20% dynamic compressive strains upregulated MMP-1, MMP-3, MMP-13 and ADAMTS4 compared to no dynamic loading. Aggrecan, COX-2, and ADAMTS5 gene expression were upregulated under 10% strain compared to no dynamic loading while COL-1, TIMP-1, and TGFβ gene expression were not dependent on the magnitude of loading.

Conclusion: This data suggests that changes in mechanical loading of the knee joint meniscus from 10% to 20% dynamic strain can increase the catabolic activity of the meniscus.

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Key words: MMP, IL-1, Meniscus, Knee, Osteoarthritis, ADAMTS.

Introduction

Patients who undergo partial meniscectomy, a common surgical treatment for meniscal tears, often experience osteoarthritis (OA) in the underlying cartilage in long-term follow-up studies1-5. The meniscus plays a major role in load distribution and transmission in the knee joint6-8 and it has been shown to be mechanically sensitive9,10. Recently, 20% dynamic compressive strain on meniscal explants has been shown to lead to increased glycosaminoglycan (GAG) content in the culture media, an upregulation of interleukin-1α (IL-1α) expression and increased release of nitric oxide (NO)11,12. IL-1α is a pro-inflammatory cytokine involved in the etiology of OA13,14. It has been shown to increase levels of NO15 which in turn can induce gene expression of other catabolic molecules such as metalloproteinases (MMPs matrix cleavage proteins) and inhibit cell proliferation16-18. IL-1α has been shown to increase cyclooxygenase-2 (COX-2) synthesis leading to increased production of prostaglandin E2 (PGE2) in osteoarthritic cartilage14.

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