

Accelerated intervertebral disc degeneration in scoliosis versus physiological ageing develops against a background of enhanced anabolic gene expression

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INTRODUCTION: Molecular consequences of long term deformation and altered mechanical loading of intervertebral disc tissue (IVD) in idiopathic scoliosis have yet to be elucidated. In order to get insight into such mechanisms we studied alterations in IVD tissue from human scoliotic spines on the histological and on the molecular level. We hypothesized that disc degeneration is accelerated in scoliosis compared to normal ageing and that this is reflected by an altered gene expression profile.

METHODS: Semiquantitative histological analysis of IVDs [1], was performed in scoliotic adolescents (surgery group, age 10-22, mean 14,2 years, n=16) and compared to non-scoliotic adolescents (autopsy group, age 8-17, mean 13,3 years, n=8), normal adults after traumatic injury of vertebrae (surgery group, age 28-55, mean 35,6 years, n=7) and mature normal adults (autopsy group, age 44-77, mean 63,2 years, n=10) which served as controls. Molecular analysis was performed by a custom made cDNA array [4] which harboured 48 genes for cartilage, bone, adipose tissue, mesenchymal progenitor cells, but also genes functioning as transcription factors or morphogens. The gene expression pattern of 16 scoliotic IVDs (age 10-22, mean 14,2 years) and of 7 normal IVDs (trauma surgery, age 28-55, mean 35,6 years) was analyzed and related to the histological scoring of the same sample.

RESULTS: Histological grading revealed significantly enhanced degeneration in the scoliosis (HDS 5,3) versus age-matched control IVDs (HDS 2,25; p=0.001). Degeneration phenomena were similar to those observed in normal aging discs of older age (n=7; mean 35,6 years HDS 5,6). This shows that IVD degeneration in the scoliotic group (HDS 2–10 points, mean 5.3 points) seems to occur about 20 years ahead of time. cDNA array analysis revealed higher mRNA levels for AGC1 (mean

15-fold; p=0.002), COL11A1 (mean 9-fold; p=0.007), COL12A1 (p=0.037), biglycan (p=0.027), decorin (p=0.016), lumican (p=0.023), chondromodulin1 (p=0.012), and MIA (p=0.037) in the scoliotic than in the trauma disc tissue, while COL1A1 levels were equal. On average COL2A1 mRNA was 5.7-fold higher (p=0.057) in scoliotic discs. No differences in mRNA levels were evident for molecules involved in matrix catabolism like MMP3, MMP13, MMP17, and TIMP1.

DISCUSSION & CONCLUSIONS: This is the first study correlating histological scoring and gene expression profiling in IVDs. In conclusion, alterations in the tissue over time graded by a morphologic degeneration score were not reflected by the actual gene expression profile of the cells. Morphologic disc degeneration was accelerated by about 2 decades in scoliosis versus physiological ageing and developed against a stronger anabolic matrix metabolism at younger age or in response to the altered mechanical environment of the tissue.

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