MATRIX COMPOSITION AND TURNOVER IN NORMAL VERSUS SCOLIOTIC INTERVERTEBRAL DISCS

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INTRODUCTION : The modern day treatment of adolescent idiopathic scoliosis is limited by our lack of understanding of the etiologic processes that surrounds this pathology. The disc and end plates have been implicated as possible etiologic components in the pathogenesis or progression of adolescent idiopathic scoliosis. To better understand the pathophysiology of scoliosis, we characterized the matrix composition and matrix turnover in scoliotic versus normal intervertebral discs.

METHODS: Thirty two intervertebral discs, fifteen from scoliotic spines and seventeen from normal spines, were harvested from donors aged 13-15 years of age (mean 13.5). The scoliotic discs were obtained intraoperatively while the normal discs were obtained post-mortem. Water, collagen, proteoglycan, and total protein contents were determined using standard methods. Samples from defined regions were extracted with 4 M guanidinium chloride for quantitation by immunoassay of 846 epitopes (present on newly synthesized aggrecan) and of C-propeptide of types I and II collagen (markers of newly synthesized procollagen types I and II). Adjacent tissue blocks underwent alpha-chymotrypsin and proteinase K treatment to quantitate the percentage of total collagen denaturation.

RESULTS: Percent water was significantly lower in the annulus and end plates of scoliotic discs ($p<0.01$). Hydroxyproline content was significantly lower in the annulus and endplate of scoliotic discs ($p<0.01$). Glycosaminoglycan content was significantly lower in the end plates and nucleus pulposus of scoliotic discs ($p<0.01$). The total protein content was significantly higher only in the endplate of scoliotic spines ($p<0.05$). Percentage of denatured collagen was significantly elevated in the nucleus pulposus of normal discs ($p<0.05$). Synthesis of type I collagen in end-plates (CPI) were significantly lower in the end-plate of scoliotic discs ($p=0.0087$). Synthesis of type II collagen in end-plates (CPII) was significantly higher in the nucleus pulposus, annulus fibrosus and end plates of scoliotic discs (figures 1 & 2 - $p<0.01$), while synthesis of aggrecan (846) was only found to be increased in the nucleus pulposus of scoliotic disc. When comparing the concave and convex regions of the end-plates of scoliotic discs, water was the only component that was significantly different with the content on the concave side being higher than that on the convex side ($p<0.05$).

DISCUSSION: The present study identifies some clear differences between normal and scoliotic disc matrix composition. The hydroxyproline, glycosaminoglycan and percent water contents are significantly lower in scoliotic versus normal discs. Interestingly, the lower contents exist despite a higher total protein content being present in scoliotic discs. This suggests that scoliotic discs must have a higher content of non-collagenous proteins than normal discs.

More importantly, synthesis of type II collagen is higher in the nucleus pulposus, annulus and end plates of scoliotic discs. However, synthesis of proteoglycan, is only found to be increased in the nucleus pulposus of scoliotic disc. Type one collagen synthesis, although slightly elevated in normal discs, does not to seen be a significant presence in either group. Thus, elevated synthetic levels without an associated increased collagen denaturation reflects an overall synthetic response with an ineffective matrix turnover. These results also imply higher non-collagenous protein synthesis relative to collagen or proteoglycan synthesis. Given that scoliotic discs and vertebrae are small and deformed, these higher synthetic levels and lower contents per dry weight suggest that scoliotic changes are due to an altered and ineffective synthetic response to a pathologic mechanical environment without an associated increase in matrix turnover. Thus, altered synthesis does not appear to be an etiologic process. Rather, it seems to be a response to a pathologic environment. These findings are consistent with the Hueter-Volkmann law which states that growth is retarded by mechanical compression of the growth plate. This must be taken into consideration in future work attempting to determine the etiology of idiopathic scoliosis.

Figure 1

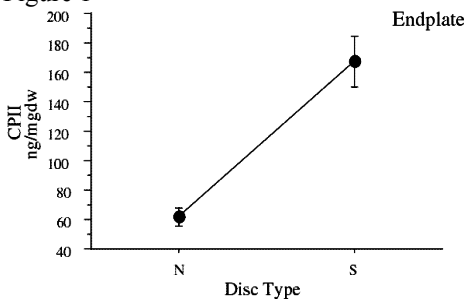
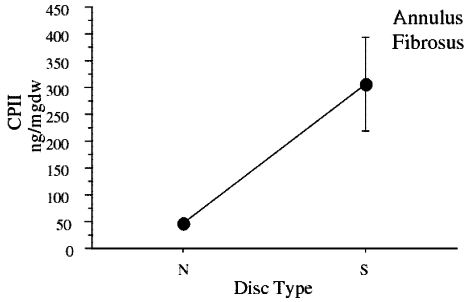


figure 2



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