

Determinants of Disc Degeneration and Pathology: A Major Paradigm Shift

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INTRODUCTION: The traditional view over much of the last century was that disc degeneration was primarily a result of mechanical insults and injuries imposed on normal aging. However, in 2002, conducting a review of “degenerative disc disease”, incorporating recent research, Ala-Kokko concluded, “Even through several environmental and constitutional risk factors have been implicated in this disease, their effects are relatively minor, and recent family and twin studies have suggested that sciatica, disc herniation and degeneration may be explained to a large degree by genetic factors.” This represents a major shift in the understanding of determinants of disc degeneration. My research group’s work which has contributed to this dramatic shift will be presented.

METHODS: Initially, we conducted a series of studies investigating the influences of commonly suspected environmental and behavioral risk factors on disc degeneration and back symptoms using monozygotic twins highly discordant for the factor of interest, selected from the population-based Finnish Twin Cohort. Exposures were verified and data on potentially confounding factors were gathered in an extensive structured interview. Disc degeneration was assessed both qualitatively and quantitatively from MR imaging using a 1.5 Tesla scanner. The data from these studies were aggregated to allow multivariable analysis to examine the relative effects of lifetime exposures and familial aggregation on disc degeneration. Familial aggregation represents the effects of genetic and other shared family influences (e.g., shared childhood environment). Analogous data were later collected of dizygotic twins to allow classic twin studies of genetic and environmental influences. We currently have data on 600 twins. DNA analysis using a candidate gene approach and haplotypes is being conducted in search of genotypes associated with disc degeneration and back pain.

RESULTS & DISCUSSION: Our findings indicate that while physical loading involving materials handling, bending, and twisting appear to influence disc degeneration, the effect size is modest, which helps explain the inconsistent results of previous studies of the effects of occupational loading. No effects of occupational driving on disc degeneration were found. Conversely, disc degeneration was explained to a great degree by familial aggregation. In the multivariable analysis, 43-61% of the variance in disc degeneration, depending on lumbar region, was explained by familial aggregation, whereas age and occupational physical loading together explained 11-16%. The identification of gene forms associated with disc degeneration, such as TaqI and FokI of the VDR gene, each explaining 6.5% of the variance in nuclear signal intensity, allow investigations of gene forms as modifiers of environmental effects.

The degenerative findings of outer annular tears and disc height narrowing were consistently associated with history of back-related symptoms, and thus are of particular interest. Preliminary results of a classic twin study bivariate analysis revealed that the variance in the lifetime back pain variables explained by genetic influences was accounted for by the genetic correlation with disc height, suggesting such disc findings as one possible pathway through which genes influence back symptoms.

CONCLUSIONS: Disc degeneration and pathology as currently seen in developed countries appears to be largely genetically determined. Environmental factors do appear to play a role, but the identification of these factors and the estimation of their effect sizes is much more complicated than once thought and likely involves complex interactions.

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