LEPTIN AND BMI IN OA DEVELOPMENT

The role of body weight in the pathogenesis of osteoarthritis (OA)—previously considered the sole factor in the association between obesity and OA—is being re-evaluated as the contribution of adiposity to this process becomes clearer. A new study by Pallu *et al.* indicates that chondrocyte responsiveness to leptin varies depending on BMI in patients with OA. “Obesity is associated with a defect in the central action of leptin,” explains Nathalie Presle, the study’s lead investigator, “which raises the question as to whether or not peripheral tissues, including cartilage, also become resistant to the effects of leptin.”

The investigators isolated chondrocytes from articular cartilage samples obtained from the knees of 25 patients with OA, who were classified as either nonobese (BMI ≤ 30 kg/m²) or obese (BMI > 30 kg/m²). Stimulation of the cells from nonobese individuals with 100 ng/ml leptin induced upregulation of type 2 collagen and insulin-like growth factor 1 (IGF-1) mRNA. However, 500 ng/ml leptin was required for a similar type 2 collagen and IGF-1 mRNA induction in chondrocytes from obese patients. In addition, the gene encoding metalloproteinase inhibitor 2 (TIMP-2) was identified as a target of leptin in chondrocytes from nonobese patients. By contrast, leptin stimulated production of matrix metalloproteinase 13 (MMP-13) mRNA, and not TIMP-2 mRNA, in cells from obese individuals.

Overall, these findings suggest that the BMI-dependent effects of leptin on TIMP-2 and MMP-13 expression in chondrocytes might alter the degenerative process during OA and enhance cartilage damage in obese patients. “Further investigations of intra-articular administration of leptin in animals with a high-fat diet will be helpful to determine whether chondrocytes change their response to leptin during the development of obesity,” says Presle.

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RESEARCH HIGHLIGHTS