# Does a high inherent aerobic capacity protect the cartilage, subchondral bone, and Hoffa's fat pad in the knee joint from degeneration in a pre-clinical model of obesity?

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## Summary

This study was aimed at investigating the combined effects of aerobic capacity and diet on the cartilage, Hoffa's fat pad, and subchondral bone properties in the knee joint, critical in understanding osteoarthritis (OA) development. Thirty-five rats bred for high (HCR) or low (LCR) running capacity were fed either a high fat/sucrose (HFHS) or a standard chow diet for 12 wks. An inherent high aerobic capacity appeared to have a protective effect against knee joint degeneration in HCR rats fed a the HFHS diet, unlike the distinct degeneration seen in the LCR rats. The study demonstrates that rats with high aerobic capacity are less susceptible to knee joint damage induced by an obesity-inducing HFHS diet compared to those with low aerobic capacity.

## Introduction

Obesity and associated metabolic syndrome are risk factors in the development of knee joint osteoarthritis and other musculoskeletal degeneration in humans and pre-clinical animal models such as rats[1]. In obese animals, muscle fibrosis and fat infiltration were observed primarily in Type II muscle fibers, which have limited aerobic capacity[2]. Furthermore, previous studies showed that aerobic training in Sprague Dawley rats had a protective effect in knee joint integrity in rats exposed to a high fat/high sucrose (HFHS) diet compared to rats exposed to the HFHS diet but not undergoing aerobic activity[3]. Based on this evidence that aerobic capacity may play a role in metabolic and musculoskeletal disease, we used an animal model of selective breeding for high and low aerobic capacity, hereafter referred to as high-capacity runners (HCR) and low capacity runners (LCR). It has been shown that HCR rats have lower weight gain when exposed to a high fat and/or sugar diets, less metabolic complications, a reduced insulin resistance, less diabetes, and a decreased risk of cardiovascular disease when compared to the LCR rats[4]. The aim of this study was to test if inherent aerobic capacity protects the knee joint from degeneration in an established pre-clinical rat model of diet-induced obesity and metabolic syndrome.

## Methods

Thirty-five 24-week-old male N:NIH rats (18 LCR and 17 HCR) were randomly assigned to either an HFHS diet or a standard chow diet for 12 weeks. Following the intervention, knee joints were harvested, formalin-fixed, and scanned using micro-computed (μCT 35, Scanco Medical). with a resolution of 30 μm. After scanning, knee joints were decalcified in Cal X II, processed in paraffin wax and serial sagittal sections were cut at 10um and stained sequentially in Gills 2 Hematoxylin, Fast green and Safranin O. Sections were evaluated by two independent and blinded scorers using a modified Mankin OA scoring system. Sections were also used to quantify hypertrophy in cells of Hoffa's fat pad using Fiji software[5,6]. Subchondral bone parameters, including bone volume, bone surface, trabecular thickness, and bone mineral density, were quantified. All procedures were conducted in compliance with the University of Calgary's Life and Environmental Sciences Animal Care Committee.

## Results and Discussion

Both LCR and HCR rats fed a HFHS diet had increased body fat compared to their chow-fed counterparts. LCR rats had significantly higher Modified-Mankin scores, indicating greater knee joint degeneration, suggesting that high inherent aerobic capacity may protect against metabolically induced OA. LCR rats exhibited significantly higher subchondral bone volume compared to HCR rats, a trait associated with metabolic OA. Trabecular thickness was significantly greater in LCR rats fed a chow diet than in their HCR counterparts, indicating microarchitectural changes linked to metabolic OA. No significant differences were found in other subchondral bone parameters. The HFHS diet caused a shift in adipocyte size distribution towards increased cell size in Hoffa's fat pad. While both groups showed this trend, LCR rats had a higher proportion of larger adipocytes than HCR rats, suggesting a greater susceptibility to adipocyte hypertrophy, inflammation, and metabolic dysfunction. In contrast, HCR rats exhibited a more balanced adipocyte remodeling response, indicating greater metabolic flexibility and resistance to diet-induced obesity.

## Conclusion

We conclude from the results of this study that high inherent aerobic capacity may protect against knee joint degeneration in the presence of a HFHS diet. The unique metabolic profiles in the LCR and HCR strains might point to crucial metabolic factors responsible for the metabolically induced degeneration of the musculoskeletal system. Furthermore, this pre-clinical research might inform clinical trials studying patients with obesity and at risk of knee joint osteoarthritis by providing better understanding of the mechanistic pathways linking obesity with joint degeneration, and provide insight into treatment modalities through aerobic capacity training.

## References

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