



Exercise and Osteoarthritis in Animal Studies

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Introduction

Osteoarthritis (OA) is a major public health problem, with individual and socio-economic consequences worldwide. Not limited to humans, OA is similarly the most common joint disease diagnosed in veterinary medicine. OA is typically characterized by progressive joint degeneration leading to impaired patient function and pain [1]. Recently, the relationship between physical exercise and OA has accelerated in interest for clinicians and researchers alike. Definitive nonsurgical treatments for OA are lacking and exercise is considered one of the most effective, non-pharma logical treatments for reducing pain and improving function in patients with OA [2]. The present editorial focuses on the latest research related to OA and exercise in animal models. In addition, there are several species where OA develops spontaneously including guinea pigs, hamsters, monkeys, mice, dogs, horses and sheep [3].

Benefits of exercise for OA

An emerging number of studies consistently demonstrate the beneficial effects of exercise in subjects with OA. Hamster studies have demonstrated that weight-bearing physical activities appear to protect against development of OA [4]. Weight bearing activities reduce articular cartilage degeneration [5,6], local oxidative stress [7] and tissue inflammation [5]. Dykgraaf et al. observed an increase in chondrocyte viability in trained horses compared to untrained controls [8]. On the contrary, prolonged immobilization leads to reductions in articular cartilage thickness suggesting that there is an optimal dose of loading for joint homeostasis/health [9]. Training performed immediately after induction of chemical [7] or mechanical-induced OA [6] decreases disease progression. Eight consecutive weeks of running at a moderate pace (16 m/min for 30 min/d to 50 min/d, 3 days per week) can minimize tibiofemoral articular cartilage deterioration [7]. In addition, the duration of the session appears to be important for articular cartilage viability in ACL sectioned rats subject to treadmill training. Animals running 30 min/day demonstrated optimal chondroprotection with varying results for time periods of 15 min/day and 60 min/day [10]. Moderate physical activity and normal mechanical joint loading in elderly rats improves tribology and lubricative properties of articular cartilage, promoting lubricin synthesis and its increase in synovial fluid [11]. Lubricin is present on the surface (superficial layer) of articular cartilage and plays an important role in joint lubrication and synovial homeostasis [12]. A similar finding was observed by Guo-Xin et al. where they compared mild, moderate, and high-intensity treadmill running and effects on articular cartilage bio-composition. While high-intensity running (26.8 m/min 10° inclination, 8 weeks) accelerated development of OA, mild (15.2 m/min 0° inclination, 8 weeks), and moderate (19.3 m/min 5° inclination, 8 weeks) exercise produced a significant elevation of lubricin content and decreased Mankin's score compared to the control group [13].

Exercise as a risk factor for OA

Over exercised Wistar rats can experience chondrocyte death, matrix depletion, and increased joint inflammation [14]. The loss of cartilage matrix occurs not only at the tissue level but there is a significant fluctuation of proteoglycan fragment (keratan sulfate) s within the serum following 6 weeks of running at 25 m/min [15]. On the other hand, higher frequencies of daily loading during jumping or pivoting sports can be accompanied by aggrecan loss [16] and subsequent increased risk of OA progression. Radin and colleagues demonstrated in sheep studies those four hours of walking on a concrete surface-initiated development of OA [17]. Canine experiments by Kiviranta et al. [18,19] have shown that mild running improves articular cartilage thickness and glycosaminoglycan content, whereas heavy running reversed these positive adaptations. Similar results were reported by Pap et al. [20], who generated mice with heterozygous inactivation of the gene coding for type 2

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procollagen and subjected them to lifelong voluntary wheel-running exercise? The effects of voluntary wheel running on the incidence and severity of OA have been explored on normal mice and mice carrying either a targeted inactivation of one allele, heterozygous 'knockout', of COL2A1 gene or both alleles, homozygous 'knockout', of COL11A2 gene [21]. Exercised knockout mice had more knees OA than controls. Normal mice running, however, showed less OA of the knee than control mice. Authors suggested that voluntary wheel running had a protective effect against OA in both knockout mice lines. It has been suggested that the decrease in OA may result from the reorganization and strengthening of the articular cartilage collagen network and/or adjacent muscles due to running, or lower body weight. Furthermore, increased compliance of the articular cartilage and bones of the knockout mice may also contribute to the reduction of OA in exercised animals [21].

More recent studies showed those 6 weeks of running at 25 m/min (45 km) initiates structural changes in the cartilage surface and depletion of cartilage matrix [22]. Such changes have been accompanied by an increase in MMP 3 serum activity, which indicates accelerated cartilage collapse [22]. Guo-Xin et al. observed a similar dose-response finding of treadmill running on articular cartilage bio-composition. Running at high-intensity (26.8 m/min 10°, 8 weeks) resulted in knee OA [23].

Conclusion

There are many benefits to initiating and maintaining an exercise program - whether or not you have OA. Exercise has been shown in animal models to slow OA progression. On the other hand, it is also clear that too much exercise can be detrimental to individuals with OA. In conclusion, the optimal 'dose' of exercise as defined by duration, magnitude, and frequency remains unknown at this time and is likely highly personalized. Future studies will undoubtedly uncover the molecular pathways and initiate and propagate OA so that we may better understand the role of exercise in symptom management and ideally disease prevention and treatments.

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