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The Effect of Lifelong Exercise on Canine Articular Cartilage*

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ABSTRACT

The effect of long-term exercise on canine knees was studied to determine whether an increased level of lifelong weightbearing exercise causes degeneration, or changes that may lead to degeneration, of articular cartilage. Eleven dogs were exercised on a treadmill at 3 km/hr for 75 minutes 5 days a week for 527 weeks while carrying jackets weighing 130% of their body weight. Ten control dogs were allowed unrestricted activity in cages for the 550 weeks. At the completion of the study all knee joints were inspected for evidence of joint injury and degeneration. Articular cartilage surfaces from the medial tibial plateau were examined by light microscopy, the cartilage thickness was measured, and the intrinsic material properties were determined by mechanical testing. No joints had ligament or meniscal injuries, cartilage erosions, or osteophytes. Light microscopy did not demonstrate cartilage fibrillation or differences in safranin O staining of the tibial articular cartilages between the two groups. Furthermore, the tibial articular cartilage thickness and mechanical properties did not differ between the two groups. These results show that a lifetime of regular weightbearing exercise in dogs with normal joints did not cause alterations in the structure and mechanical properties of articular cartilage that might lead to joint degeneration.

Degenerative joint disease, or osteoarthritis, is among the most common causes of pain and disability in middle aged and older people,[41] yet the cause of this disorder in joints without known abnormalities or injuries remains unknown. The incidence of degenerative joint disease increases progressively with age,[41] but it is not caused by aging alone.[12] One possible explanation for the increasing incidence with increasing age is that regular joint use over a period of years causes repetitive articular cartilage damage that exceeds the ability of the tissue to repair itself.[27] Accumulation of this unrepaired microdamage could eventually lead to degeneration of the tissue. A number of epidemiologic investigations support the concept that increased repetitive long-term joint use increases the probability of joint degeneration. They show associations between participation in physically demanding occupations and osteoarthritis, and between regular participation in selected sports and osteoarthritis.[1,6–8,11,13,14,16,29–32,46,47]

In contrast to these epidemiologic studies, investigations of the effects of running on human and animal joints do not support the hypothesis that long-term increased joint use causes degeneration. Multiple studies have found no association between regular running and an increased incidence of osteoarthritis in humans[9,23–27,38,39]; however, the conclusions drawn from these studies have been questioned because of the possibility of selection bias.[11] Critics have suggested that persons susceptible to developing joint degeneration from running do not continue to pursue regular competitive or recreational running; that is, those who chose to participate in regular running may be a self-selected group unlikely to develop joint degeneration. Randomized controlled animal studies have shown that short-term moderate or strenuous exercise does not cause cartilage erosions or osteophytes and does not have a deleterious effect on the intrinsic mechanical properties of articular cartilage of healthy joints.[19,21–23] However, these experiments have been conducted with young animals, the longest duration of exercise has been a year, and the joints were not subjected to loads greater than those produced by the animal's body weight and muscle forces. Thus, the relationship between long-term increased joint use and joint degeneration remains unclear.

If repetitive increased use of joints over a lifetime

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auses articular cartilage changes that increase the probability of joint degeneration, these changes should be detectable by evaluation of the structure and mechanical properties of the articular surface. One of the earliest morphologic changes associated with articular cartilage degeneration is surface fibrillation. Analyses of such affected cartilage surfaces have demonstrated increased water content, changes in the structure and composition of proteoglycans, and changes in the collagen fibrillar network.[34,38,48] Structural and biochemical changes have also been associated with alterations in the mechanical properties of the tissue.[2] In particular, investigators have used the indentation test to determine the material properties of normal articular cartilage[4,5,33,36] and define the associations between structural changes and altered mechanical properties in 1) the Pond-Nuki (ACL transection) model of osteoarthritis,[18,44] 2) joint disuse,[20] and 3) joint overuse.[19] The goal of this investigation was to determine whether a lifetime of exercise that places increased mechanical demands on a synovial joint will result in either joint degeneration, as demonstrated by cartilage fibrillation and erosion or osteophytes, or changes in cartilage mechanical properties that may lead to joint degeneration.

MATERIALS AND METHODS

Twenty-one male beagles were obtained as puppies with immature skeletal physiology. On arrival, they were screened for general health, acclimated to the laboratory cage environment and to the carousel treadmill. There were two animals that were not included in the study because they could not adjust to the treadmill. Subsequent to this screening, radiographs, rib biopsies, and densitometer measurements were obtained. The initial measurements of the densitometer showed rapidly increasing values indicative of immaturity, confirming the long bone radiographs. The experimental period was not begun until the skeletal markers were that of a young adult skeleton. The animals were then randomly assigned either to an experimental (11 animals) or a control (10 animals) group.

Throughout the study all dogs were fed identical diets, housed in equivalent cages, and cared for and given personal attention on a daily basis. The only treatment difference between the two groups was that the experimental group (runners) was exercised 5 days per week for 75 minutes per day, at an average speed of 3.3 km/hr, on a motor-driven treadmill while carrying an average load of 11.5 kg (approximately 130% body weight). Lead weights were added to a saddle on each dog assigned to this experimental group. The limit for each animal was determined by observing what added weight they could comfortably support while standing and while running on the treadmill. The intent was to maximize this weight with a gradual increase. The amount of weight tolerated increased steadily for each dog over the first few months but did not change significantly thereafter for the duration of the project.

The exercise group followed this program for 527 weeks. The control group was limited to normal cage activity in dog runs that allowed 4.0 square meters of running area. For the experimental group, running ability was assessed on a scale of 1 to 8, or qualitatively from poor to excellent. This rating was based on the criteria of the number of days per week the dog was able to exercise on the treadmill, the maximal load carried, and running speed. All runners used for this investigation were assessed at a level of 7 or 8.

All animals were sacrificed and their hindlimbs were disarticulated 550 weeks after the study began. All joints were inspected for evidence of ligamentous or meniscal damage, cartilage fibrillation, cartilage erosion, and osteophytes. The left hindlimbs were used for mechanical testing, and tissue from the right hindlimbs was used for the light microscopy study.

For the light microscopy study, samples were immersed in 10% phosphate buffered formalin (pH = 7.3), decalcified in CAL EX (Fisher Scientific, Pittsburgh, Pennsylvania) containing 10% formalin, and dehydrated in alcohol. Embedded longitudinal sections were mounted on glass slides and stained with hematoxylin and eosin or safranin O. Three to five sections were examined from the central region of each tibial plateau of each animal.

The method reported by Mow and others[5,36] was used to evaluate the mechanical properties of the biphasic, viscoelastic articular cartilage. The intrinsic material properties, obtained from this theory by curve-fitting the experimental creep curves, categorize the ability of the cartilage to respond to different loading environments.[35] Any difference in these intrinsic material properties between the control and exercised dogs indicated a change in the ability of the cartilage to respond to load. Therefore, the determination of the mechanical properties served as a way to quantitatively measure the effects of long-term exercise on the articular cartilage of the dog.

The medial tibial plateau of each specimen used for mechanical testing was wrapped in gauze soaked with 0.15 M sodium chloride plus protease inhibitor (1 mM phenylmethylsulfonyl fluoride, 2 mM ethylenediaminetetraacetic acid (EDTA), 5 mM benzamidine, 10 mM N-ethylmaleimide), placed in sealed containers, and stored at −80°C. On the day of testing, each specimen was thawed in a warm water bath for 45 minutes.

The medial tibial plateau was mounted in a specimen bath chamber that was oriented in a six degrees of freedom jig so that the indentation site was perpendicular to the axis of a porous, permeable indentor tip with a radius of 0.75 mm. The specimen was completely submerged in the bathing solution and allowed to equilibrate for 15 minutes, after which a tare load of 3.5 g was applied for 950 seconds. A tare load was applied to minimize experimental artifact and to ensure that the tissue response was in the linear region,[17] as required by the biphasic curve-fitting algorithm used to obtain the cartilage material properties. At the end of the tare period, a 10.0-g test step load was applied to the specimen for 90 minutes. The test load was then lifted, with the tare load remaining on the surface for an additional 90-minute recovery period. The surface deformation of the tissue was recorded for the entire duration of the experiment.

Each medial tibial plateau was tested at both an uncov-

ered site (UNC) and at the site normally covered by the posterior section of the medial meniscus (POST), as shown in Figure 1. The sequence of testing, UNC or POST, was randomized to avoid experimental bias. After each test, the thickness of the testing site was measured using the needle probe method.[36]

The creep data were collected at a variable rate, with a rapid collection rate during the initial loading and unloading phases. Creep equilibrium was usually observed at 1200 seconds for the uncovered site and 300 seconds for the covered site. Load control and data collection were performed with an IBM XT computer (IBM, Armonk, New York) with data acquisition and control software (LABTECH Notebook, Laboratory Technologies Corp., Wilmington, Massachusetts). Experimental results were used to compute the intrinsic material properties of the tested articular cartilage using the biphasic theory of Mow and coworkers.[36,37] Curve-fitting of the experimental data to the theoretical solution[5,33,36] yielded values for the hydraulic permeability, the aggregate modulus, and the shear modulus in compression.

The results were statistically analyzed to determine the effects of long-term exercise on the articular cartilage mechanical properties and tissue thickness. A two-way, multivariate analysis of variance, with exercise as one factor (control versus trained) and site as the second factor (UNC versus POST), was performed. Based on data from previous studies on osteoarthritic cartilage showing altered mechanical properties of the tissue,[19,44] a power analysis was done using a one-tailed t-test at $\alpha = 0.1$. Statistical analyses of the data were performed using the SAS statistical software package (SAS Institute, Cary, North Carolina).

RESULTS

None of the knee joints from trained or control animals had ligamentous or meniscal damage, cartilage fibrillation, cartilage erosion, or osteophytes (Fig. 2). Light microscopic examination of articular cartilage from trained and control animals also demonstrated no evidence of cartilage fibrillation, chondrocyte cloning, or loss of safranin O staining from the matrix (Fig. 3). Table 1 lists the numerical values of the four parameters measured to evaluate the cartilage mechanical properties. The uncovered tibial articular cartilage had significantly greater permeability ($P < 0.001$) and thickness ($P < 0.001$), but the two sites did not differ in aggregate modulus or shear modulus. Aggregate modulus, shear modulus, permeability, and cartilage thickness did not differ between control and trained animals at either the UNC or POST site. The power values for aggregate modulus, shear modulus, permeability, and thickness were 90%, 80%, 67%, and 80%, respectively (effect size of 0.80, $\alpha = 0.05$), confirming that the aggregate and shear moduli of the control and the trained groups are similar.

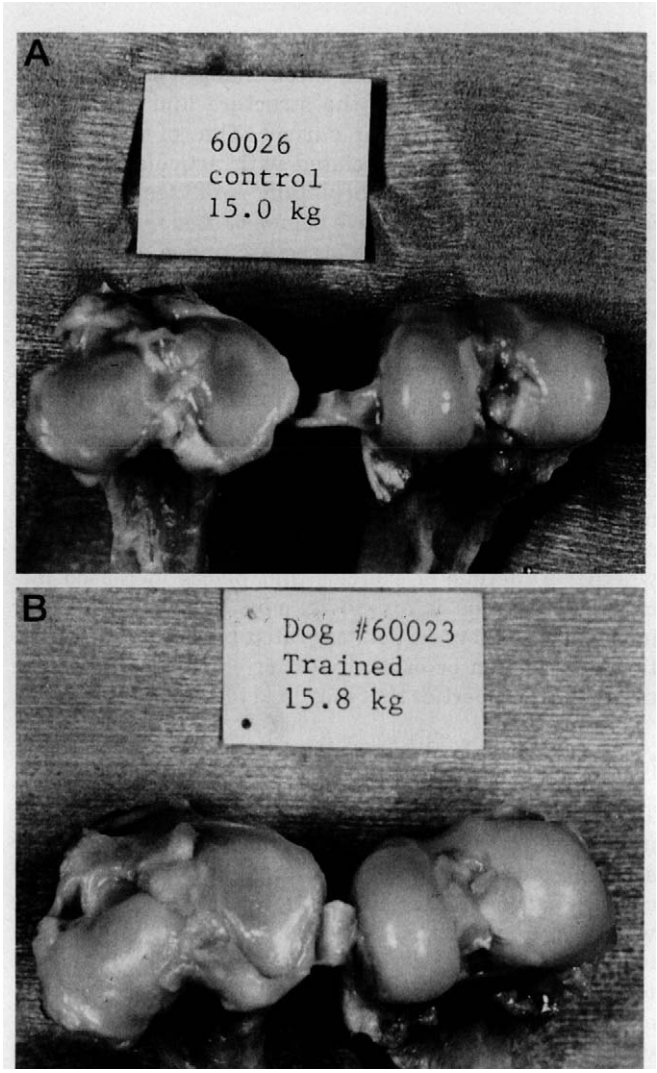

Figure 2. Gross photographs of both a representative control (A) and a trained (B) specimen. The tibial plateau and femoral condyle of each specimen had neither osteophytes nor degenerative changes.

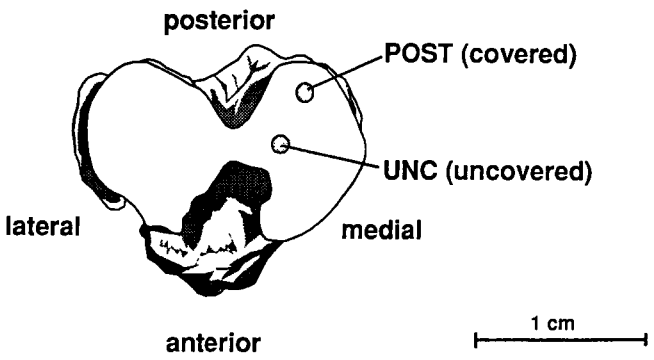

Figure 1. Indentation sites (UNC and POST) on the medial tibial plateau for both control and trained animals.

DISCUSSION

This study demonstrates that a lifetime of increased use and loading of canine knees did not cause carti-

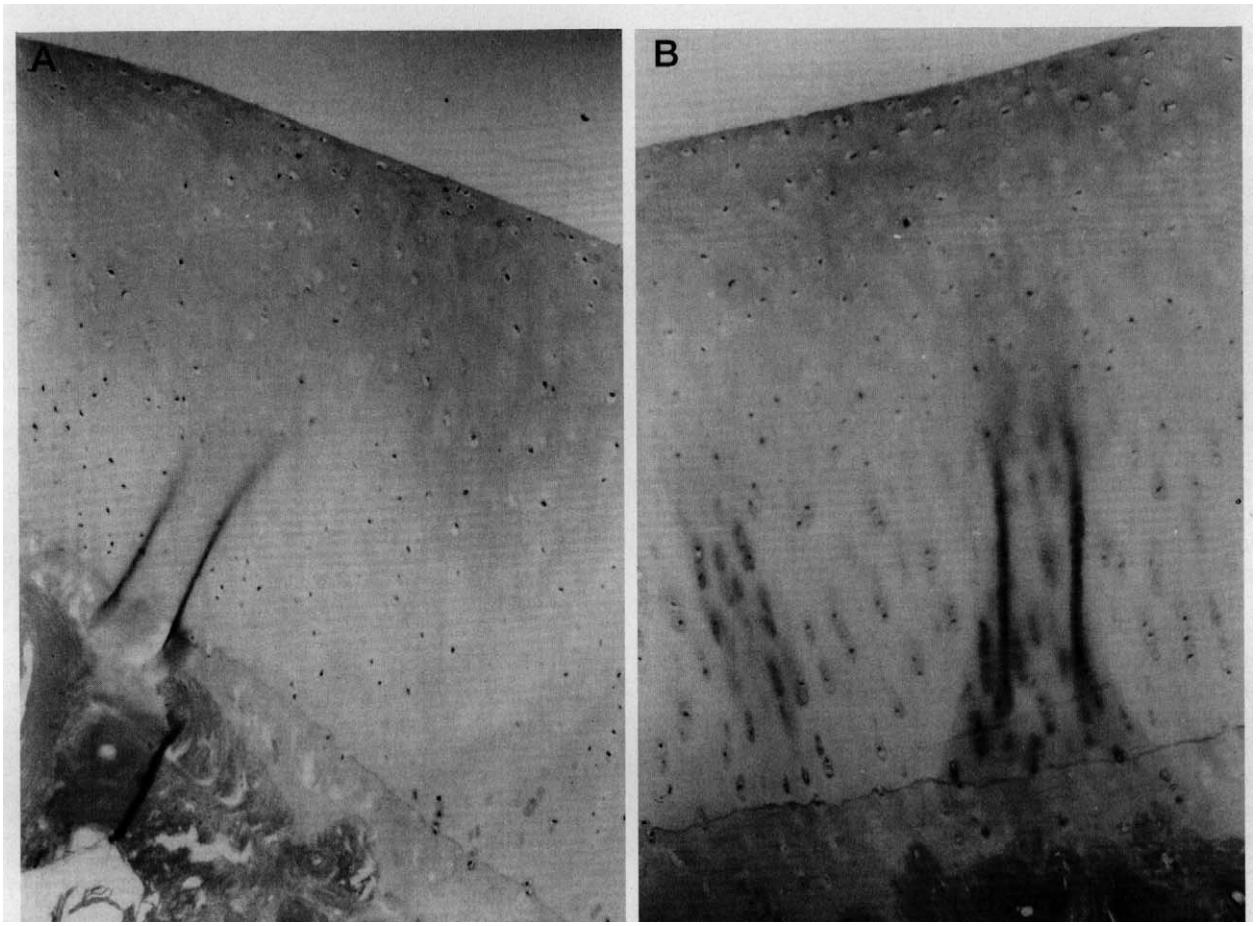

Figure 3. Hematoxylin and eosin stained histologic section of a control (A) and trained (B) specimen at ×10 magnification. Note the smooth and intact cartilage surface for both specimens.

TABLE 1
Values for the Mechanical Properties of Cartilage

Group	Aggregate modulus (MPa)	Shear modulus (MPa)	Permeability (m^4/N-s)	Thickness (mm)
Control	0.45 ± 0.17	0.20 ± 0.07	0.49 ± 0.20 E-14	0.90 ± 0.37
Experimental	0.44 ± 0.21	0.19 ± 0.08	0.50 ± 0.22 E-14	0.92 ± 0.31
UNC	0.46 ± 0.12	0.20 ± 0.05	0.62 ± 0.20 E-14[a]	1.21 ± 0.13[a]
POST	0.43 ± 0.24	0.19 ± 0.09	0.37 ± 0.14 E-14[a]	0.61 ± 0.16[a]

[a] Significant difference $P < 0.001$.

lage fibrillation and erosion or osteophytes, changes in cartilage thickness, or changes in articular surface mechanical properties. These observations extend results of previous studies showing that shorter-term moderate and strenuous running did not cause joint degeneration in young dogs[19,21–23,44] and that running is not associated with increased prevalence of osteoarthritis in humans.[11,24–28,39,40] They do not explain the reported associations between a long history of strenuous physical activity and joint degeneration in some groups of people.[1,6–8,11,13,14,16,19,29–32,44,46,47]

Previous studies using the animal model have shown that repeated or isolated joint impact loading[42,43,45] can cause degeneration of normal joints, and clinical observations suggest that traumatic impact and torsional loading of human joints can cause articular surface damage.[10] The current study provides the first evidence from a randomized controlled study that regular lifelong increased joint use, as detected by mechanical testing and light microscopy, does not cause joint degeneration. The ability of articular cartilage to withstand repetitive increased impact loading at the level used in this study may be due, in part, to the greater fluid pressurization that occurs with higher joint loading.[3,15] The design of this study did not

allow for the study of chondrocyte metabolic activity; thus, it is possible that, even though the joints of trained and control animals did not differ in structure or cartilage mechanical properties, increased joint use or microdamage caused by the exercise stimulated a chondrocytic adaptive or reparative response that maintained the normal mechanical and structural properties of the cartilage. It is also possible that joints from control and trained animals differed in the macromolecular organization of the cartilage matrix. Another important consideration is that starting the training of the animals at a young developmental age and the gradual increase in loading could have resulted in adaptation of the muscles and neuromuscular stabilization of the joints, changes that may have helped prevent increased stress at the articular surfaces and prevented joint degeneration. More intensive levels of joint use, for example, increased duration of exercise periods or increased pace might have produced joint changes.

The current study suggests that a regular lifelong exercise program that includes increased joint use and loading will not necessarily cause degeneration of a normal synovial joint. Measurement of articular cartilage mechanical properties should have detected subtle alterations in the tissue that might increase the probability of degeneration, but the mechanical properties of the tibial cartilage from trained dogs were similar to the mechanical properties of the cartilage from the control group and of normal canine articular cartilage.[5] This study does not eliminate the possibility that other types of lifelong exercise could cause joint degeneration. For this reason, further work is needed to examine the effects of more intense levels of joint use and impact loading, and the possibility that joint, muscle, and neuromuscular adaptation to lifelong increased joint use and loading may decrease the risk of degenerative joint disease.

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