

THE EFFECT OF DIABETES AND EXERCISE ON KNEE JOINT STIFFNESS AND MCL STRUCTURAL PROPERTIES IN THE RAT

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INTRODUCTION

Diabetes has a myriad of symptoms and deleterious effects throughout the body. Orthopedic considerations have primarily focused on the increased stiffness and brittleness of bone tissue, due to the associated increase in fracture risk [1, 2]. However, soft tissues are also affected causing limited joint mobility [3, 4]. Increases in ligament and joint capsule stiffness may cause impaired mobility, impaired proprioception, and other functional limitations. In addition, the perception of stiff joints may cause diabetic patients to avoid physical activity that could actually improve both their overall health and their joint stiffness. Though there is some clinical evidence that diabetes increases the stiffness of soft tissues [5], and reduces joint range of motion [3, 4], recent clinical evidence indicates that there may be no significant increase in overall joint stiffness, but only range of motion [6]. The objective of this study was to determine the effect of uncontrolled type I diabetes on overall joint stiffness in the rat and the ability of exercise to modulate (prevent or reduce) any diabetes-related changes.

METHODS

Thirty-four male Sprague-Dawley rats, 225-249 g (approximately 2 months old), were acquired for the study. The rats were divided into three groups—a sedentary control group (n=10), a sedentary diabetic group (n=10) and an exercised diabetic group (n=14). Exercised rats ran on a treadmill 5 days/week, 1 hr/day, at 20 m/min. Sedentary animals were placed on the treadmill, but not exercised. After 2 weeks of training for the exercised rats, all the diabetic group animals (sedentary and exercised) were given an intraperitoneal injection of streptozotocin (65 mg/kg) to destroy islet cells, thus inducing diabetes. Over the course of the experiment, behavioral data was collected on the running aptitude and habits of the exercised group. Seven weeks after induction of diabetes (9 weeks into the study) all animals were sacrificed, at which time body weight and blood glucose level data were collected.

One leg from each animal was dissected to remove all soft tissue (except that the knee joint capsule was maintained intact). These

specimens were then tested to determine overall joint stiffness in anterior-posterior (a-p) tibial displacement and joint distraction. Tests were performed using custom fixtures (Figure 1) on a biaxial MTS 858 servohydraulic materials testing machine. The stiffness and ultimate load of each MCL was also determined. The a-p tests were designed to closely mimic a clinical Lachman's test for a-p displacement, which would normally be performed at 30° of flexion. Due to the rat knee anatomy the MCL was generally vertical at 40° of flexion, and because all knees would extend to 40° of flexion, all tests were performed with the knee at 40° of flexion. All tests were performed in displacement control. Prior to each test, the specimens were preconditioned with 10 cycles of 20% of the full displacement. For stiffness tests, knees were distracted 0.5 mm, and for a-p tests they were manually actuated to a target displacement of 2 mm. For MCL structural properties tests, preconditioning was performed for 10 cycles at 0.1 mm distraction before the knee was distracted to ligament failure.

Not all diabetic group animals contracted diabetes. The animals tested included 7 sedentary controls, 9 sedentary diabetics, and 14 exercised diabetics. The effect of animal group on each stiffness measure, MCL structural properties, body weight, and blood glucose level were statistically analyzed using analysis of variance and a Fisher's PLSD post hoc test (with a significance level of $p < 0.05$).



Figure 1. Dissected knee in custom testing fixtures. The joint capsule and the fibula are left intact. Proximal femur and distal tibia and fibula are potted in bone cement.

RESULTS

The majority of exercised rats ran well, though some needed prodding. The average blood glucose levels at the end of the study were 113 ± 15 mg/dl for the controls, 554 ± 44 mg/dl for the sedentary diabetics, and 476 ± 59 mg/dl for the exercised diabetics, for which all differences were statistically significant. The average body weights were 453 ± 50 g for the controls, 328 ± 45 g for the sedentary diabetics, and 305 ± 46 g for the exercised diabetics. Both diabetic groups had significantly lower body weight at sacrifice than the sedentary control group, but were not statistically different from each other.

There was a significant increase in both anterior and posterior stiffness of the knee for the exercised diabetic group, compared to the control group (Table 1 and Figure 2). The sedentary diabetic group was not statistically different from either the control group or the exercised diabetic group, and the mean joint stiffness for the sedentary diabetic group approximately fell midway between the other two groups for both testing modes. For distraction, no significant differences were found in knee joint stiffness, though there was a trend toward higher stiffness in both diabetic groups (Table 1).

Table 1. Joint Stiffnesses (N/mm) for the Rat Knee as mean (stdev)

	Control	Diabetic	Exercise
Anterior	8.4 (1.9)	9.7 (2.2)	10.3 (1.7)
Posterior	7.5 (1.6)	8.8 (1.4)	9.8 (1.1)
Distraction	51.8 (17.3)	57.4 (21.9)	62.5 (20.9)

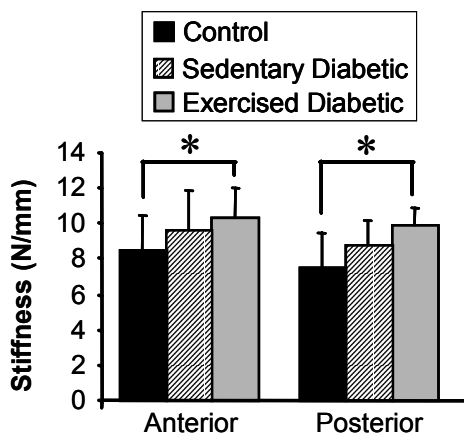


Figure 2. Anterior and Posterior Knee Joint Stiffness

The structural testing of the MCL ligament revealed no significant differences between animal groups (Table 2). Average ligament stiffness was nearly identical in all three groups, and there were only minor (insignificant) differences in ultimate load.

Table 2. Stiffness (N/mm) and Ultimate Load (N) for the Rat MCL as mean (stdev)

	Control	Diabetic	Exercise
Stiffness	19.6 (3.7)	19.1 (2.0)	19.5 (2.4)
Ult Load	36.6 (5.8)	33.9 (5.5)	35.0 (6.7)

DISCUSSION

In a clinical setting, medical interventions for patients with diabetes include oral hypoglycemic medication, insulin injections, diet and exercise. Exercise can have positive effects on both blood glucose levels and cardiovascular health. Conversely, stiff joints may discourage diabetics from getting the exercise that would help them. For the musculoskeletal system, exercise would be expected to have a positive effect by 1) stretching and loosening tight or stiff joint tissues through motion to the joints, and 2) increasing bone tissue properties.

There were clear effects of the streptozotocin induced type I diabetes on the blood glucose levels, body weight and structural properties of the knee joint. Exercise reduced blood glucose levels, but they remained well above normal (with no supplemental insulin). Exercise did not increase body mass, but the trend indicates it actually reduced body mass—consistent with additional caloric expenditure.

Running was expected to have lowered joint stiffness through repetitive joint motion stretching and loosening the tissue. Instead, it appears exercise may have actually increased joint stiffness, relative to sedentary diabetics. Presumably this could occur through an adaptive response to increased mechanical loading. However, the increased loading in the exercise group did not change the stiffness or ultimate load of the MCL. It could be that increased joint stiffness in diabetics with exercise (if the trend is to be believed), is due to increased local blood flow than actually increases stiffness through higher rates of glycation of the joint capsule tissue.

The results of this study indicate that though exercise has several positive effects on the health of diabetics, it does not appear to have a beneficial effect on joint stiffness. In future studies, we hope to determine the effectiveness of exercise in combination with other interventions to prevent or reduce the changes in skeletal tissue properties associated with diabetes.

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