

Treadmill Running and Tower Climbing Exercise Produce Genotype Dependent Responses in the Femurs of C57BL/6J (B6) and DBA/2J (D2) Aged Inbred Mice

¹Peter Gdovin, ¹Neil A. Sharkey, and ¹Dean H. Lang

¹Biomechanics Laboratory, Department of Kinesiology, The Pennsylvania State University
email: tcl133@psu.edu

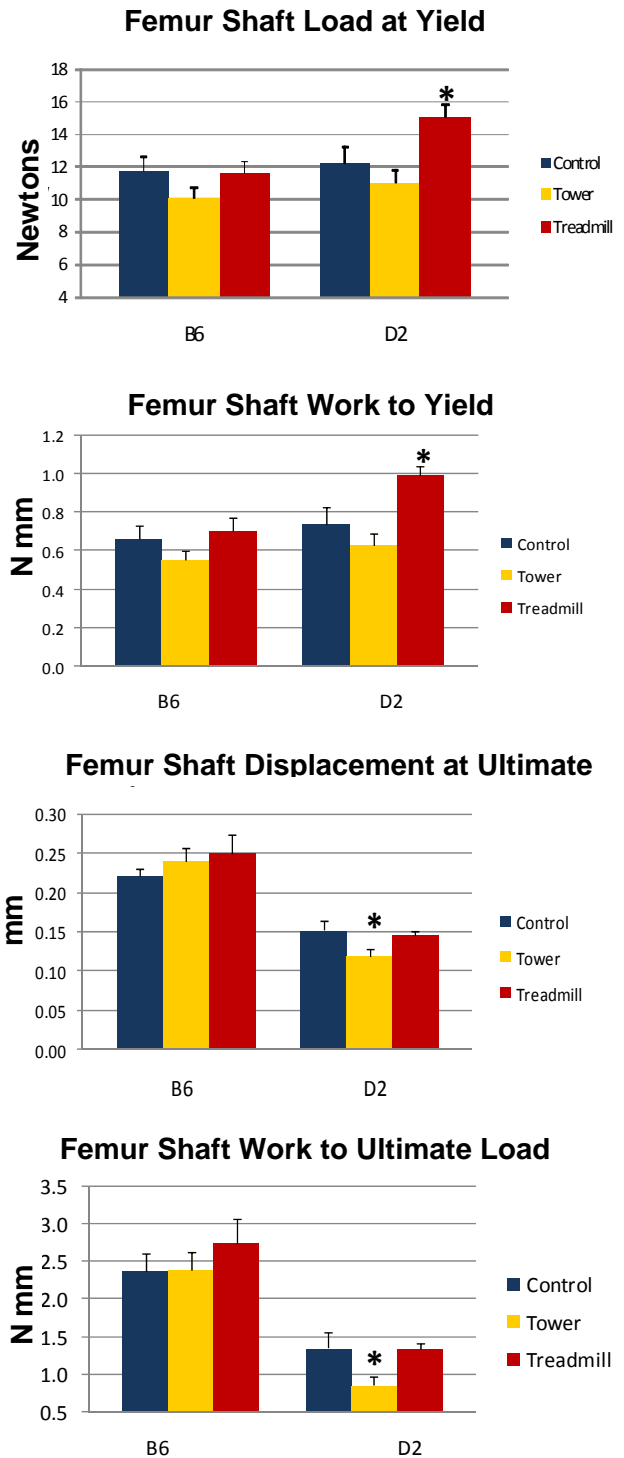
INTRODUCTION

We are interested in gene-environment interactions that influence skeletal performance. By focusing efforts on defining interactions between genes and environmental loading, therapeutic interventions may someday be designed to target specific genotypes where differential responses are anticipated. To begin to examine these issues we hypothesized that the two principal types of exercise, aerobic training and strength training will both produce differential skeletal responses in D2 and B6 inbred strain of mice.

METHODS

B6 and D2 inbred female mice were subjected to treadmill running or tower climbing at 480 days of age. Ninety mice were used in a 2 x 3 experimental design with strain (B6 vs. D2), and treatment (treadmill running or tower climbing vs. control) as independent factors resulting in six groups with 13 mice per group. Treadmill running is more closely identified as an aerobic exercise while tower climbing is a more resistance type of exercise. Those mice in the aerobic exercise treatment group underwent treadmill running 30 min/day, five days a week, over a five week period with increasing speed and incline peaking at 15 m/min on a twenty five degree incline for the duration of week 5. Mice in the resistance training group were required to climb a one meter tall tower to drink from water bottles placed at the top. Mice remained in these towers 24 hours per day for five weeks. All procedures complied with and were approved by the Pennsylvania State University Institutional Care and Use Committee.

At the conclusion of the intervention the femurs were harvested and frozen at -20C until examined. Femoral shafts were loaded to failure in three-point bending using an MTS 858 Mini-Bionix apparatus (MTS Systems, MN, USA) and structural properties were derived from load-displacement data. The



Figures 1-4: These four figures illustrate the significant differences between the B6 and D2 mice.

effects of the exercise intervention were evaluated within each mouse strain separately. Exercise treatment group differences were evaluated using a one-way ANOVA. Post-hoc multiple comparisons were made using a 2-sided Dunnett test where treadmill running and tower climbing were compared to controls. Differences at the 95% confidence level were considered significant, while those at 90% were considered suggestive.

RESULTS AND DISCUSSION

Genetic strain had a significant effect on many of the skeletal measures (data not presented). Of primary interest were those skeletal measures that displayed significant effects as function of exercise treatment. Exercise effects were examined within each strain separately. The mechanical performance of femurs from D2 mice were significantly affected by exercise whereas B6 femur did not exhibit any significant differences due to exercise treatment. (Table 1)

In D2 mice, treadmill running significantly increased yield load and work to yield and produced a suggestive increase in displacement at yield compared with controls. In contrast, tower climbing reduced the mechanical properties of the femoral

shaft in D2 mice with a decrease in displacement at ultimate load and work to ultimate load. Figures 1-4 illustrate the treatment effects of treadmill running and tower climbing compared to controls within each strain separately. These results indicate that in D2 mice treadmill running produced significantly stronger bones at yield whereas tower climbing significantly reduced mechanical properties at ultimate load. Although not statistically significant, the B6 treadmill mice took longer to fail and absorbed more energy than B6 controls.

CONCLUSIONS

Clearly, these results indicate that the skeletal effects of physical activity and exercise are extremely dependent on both genetics and type of exercise. These data emphasize the importance of gene by environment interactions. Future research may provide the foundation on which to build effective means of assessing fracture risk due to osteoporosis and thereby enabling more early intervention. A more thorough understanding of genetic control will also enhance our abilities to decipher the molecular and physiological mechanisms affecting skeletal health and could lead to new treatment options that effectively target patient-specific deficits.

Table 1: Femur Shaft Mechanical Properties from Three-point Bending Test

Femur Shaft Mechanical Properties from Three-point Bending and Shear Test							
Main Effects		Treatment Effects within Each Strain Separately					
		B6			D2		
Variable	Values	Control	Tower	Treadmill	Control	Tower	Treadmill
Yield Load (N)	Mean	11.75	10.07	11.58	12.23	11.07	*15.10
	SE	0.87	0.63	0.76	1.03	0.74	0.68
	p-value	ns			p = 0.002		
Displacement at Yield Load (mm)	Mean	0.100	0.099	0.110	0.108	0.102	^0.122
	SE	0.005	0.005	0.009	0.005	0.005	0.004
	p-value	ns			p = 0.006		
Work to Yield Load (Nmm)	Mean	0.66	0.55	0.70	0.74	0.63	*0.99
	SE	0.07	0.05	0.07	0.09	0.06	0.05
	p-value	ns			p = 0.001		
Displacement at Ultimate Load (mm)	Mean	0.220	0.239	0.250	0.152	*0.118	0.146
	SE	0.010	0.017	0.024	0.012	0.010	0.005
	p-value	ns			p = 0.024		
Work to Ultimate Load (Nmm)	Mean	2.37	2.39	2.75	1.35	*0.85	1.35
	SE	0.24	0.25	0.33	0.20	0.12	0.07
	p-value	ns			p = 0.007		

Group differences from ANOVA for exercise treatment. P-values for treatment main effect; ns: not significant; * indicates $p < 0.05$ and ^ $p < 0.10$ for pairwise comparisons of individual treatment (treadmill running or tower climbing) compared to controls (Dunnett test).