

Estrogen-Withdrawal Increases the Mechanosensitivity of Bones to Loading

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Estrogen, the primary non-mechanical regulator of female bones, has been suggested to enhance the mechanosensitivity of bones to loading¹. In this virtually life-long experiment, we evaluated whether the estrogen-status of the rats modulates the skeletal responsiveness to loading.

A total of 105 growing [5-17-week-old, normal estrous cycle (E+)], adult [47-59-week-old, normal estrous cycle (E+)] and senescent [90-102-week-old, menopausal (E-)] female Sprague-Dawley rats were used. At entry, rats were randomly assigned into 6 groups; 3 control groups (n=15/group) and 3 exercise groups (n=20/group). In the exercise groups, rats were subjected to an identical, 12-week period of progressive treadmill training. At each time point, a comprehensive structural analysis of the femoral neck was performed (peripheral quantitative computed tomography and mechanical testing). The menopausal status of the senescent rats was confirmed by microscopic examination of the ovaries and uterus (the absence of functional follicles in the ovaries and uterine atrophy denoting the menopausal status) in age-matched control rats prior to the execution of the exercise period.

In comparison to their age-matched controls, twelve weeks of treadmill training resulted in significant increases in femoral neck total bone mineral content (tBMC) in growing

(E+) and senescent (E-) rats. In addition, a significant exercise-induced increase in the total cross-sectional area of the femoral neck (tCSA) was observed in senescent (E-) rats. These changes resulted in significantly increased breaking load of the femoral neck (Fmax) in growing (E+) and senescent (E-) rats. In contrast, no exercise-induced benefits were observed in femoral neck parameters in the adult (E+) rats.

In conclusion, these findings are in perfect agreement with both experimental and clinical studies², as we observed an estrogen-induced packing of mechanically excess mineral into fertile (adult) female skeleton, and consequent damping of the mechanosensitivity of these bones. At menopause, this extra "bone stock" was shed, and consequently, the mechanosensitivity of bones to loading was regained.

1. Lee K, Jessop H, Suswillo R, Zaman G, Lanyon L. Endocrinology: bone adaptation requires oestrogen receptor-alpha. *Nature* 2003;424(6947):389.
2. Jarvinen TL, Kannus P, Sievanen H. Estrogen and bone--a reproductive and locomotive perspective. *J Bone Miner Res* 2003;18(11):1921-31.

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