KIN 512 Example critique

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Trebacz, H. (2001). "Disuse-induced Deterioration of Bone Strength is not Stopped After Free Remobilization in Young Adult Rats". *Journal of Biomechanics, 34*, 1631-1636.

Summary

The aim of the present article was to examine the effects of a period of unilateral hindlimb immobilization, followed by a period of free remobilization on femora in rats. After a period of immobilization bone reaches a new steady state, and metabolism re-stabilizes at a level equivalent to the decreased bone mass and load levels. However, it had previously not been determined whether ~~extinction~~ termination of immobilization prior to the onset of a new steady state would stop the loss of bone, which was a goal of this study. Also in question was whether the osteopenia induced by immobilization is temporary or permanent, and whether complete recovery of the bone is possible.

Forty adult male rats were randomly divided into two control and two experimental groups (labeled C0, C4, E0, and E4, respectively). Posterior right legs of rats in both experimental groups were immobilized by securing the leg to the body with bandages and padded tape, while control rats were allowed to move around unhindered. The rats were housed and fed in this manner for a period of 2 weeks, after which one of the control groups and one of the experimental groups (C0 and E0) were killed. The legs of rats in the second experimental group were remobilized, and the rats were allowed to move freely about their cages. After four weeks of free remobilization, the remaining control and experimental groups (C4 and E4) were killed. Both posterior femora of all rats were removed and cleaned of their soft tissue prior to analysis.

The femora were measured for length, minimum diameter, and maximum diameter, and total cross-sectional area was subsequently calculated. Both femora were subjected to mechanical three-point bending tests, with a 15mm distance between the two supports, and a deformation rate of 2mm/min. A load-deformation curved was developed, from which the researcher was able to determine the maximum bending moment, the yield point, the amount of work to failure, and the stiffness of the bone. The researcher removed marrow from the broken femora, after which the femora were dried in heat for 24-hours and weighed. The bones were ashed in a furnace, weighed again, and the percentage of mineralization was calculated. Various types of *t*-tests were used to test mean differences between values in the corresponding groups (C0 was compared to E0, and C4 to E4). The researcher also conducted multiple tests of femoral properties amongst control (C0 vs. C4) and amongst experimental (E0 vs. E4) groups, along with comparisons of right vs. left femora in both groups. Alpha levels for all tests were set at .05. No experiment-wide alpha level was set. No Bonferroni adjustment?

Although the rats were adults at the onset of the experiment, control rats grew steadily throughout the study. Experimental rats lost weight during immobilization; after remobilization they began rapid weight gain. Tests between C0 and E0 showed that two weeks of immobilization resulted in a lower bone density in both rear femora for the experimental rats. However, there were no significant differences between these groups in mass, size, mineralization, or mechanical parameters of the femora. After four weeks of remobilization, the density of the right femora in the E4 group was still significantly lower compared to that of the control group C4, and mineralization was also significantly lower for the E4 group. Additionally, statistically significant deficits in mechanical parameters were present compared to controls (not in absolute units). The E4 rats had a lower maximum bending moment, a lower yield point, and less stiffness than the C4 rats. After remobilization, despite rapid body weight gain and an increase in mass, length and density

of both rear femora, the E4 group did not exhibit a change in mechanical parameters of the right, previously immobilized femora, while their left femora improved on these parameters.

Critique

At first glance, the results of this study seem somewhat confounding. It would seem logical that bone would be weaker after immobilization, and regain strength after mobilization. The results from this study are just the opposite, but are explained through a few subtle differences in bone characteristics. The author points out that the medullary cavity in the right femora of the E4 group increased in size after remobilization. Additionally, mineralization did not rise in this group. The author suggests that these effects are related to an increased level of resorption due to immobilization, and that the development of bone in experimental rats was either blunted, or could not equal the rate of rapid weight gain that the E4 group exhibited after remobilization. The change in medullary size and lower mineralization are thought to be the reasons for decreased mechanical parameters exhibited during three-point bending.

The present study reports some findings that are contradictory to some of the previous results in the area, which are presented in Table 5 of the article. Kaneps, Stover, and Lane (1997) conducted a study on a group of 20 mongrel dogs. Utilizing a similar study design, two experimental groups, of seven dogs each, had their right forelimbs immobilized, while the other six dogs were divided into two control groups. After 16 weeks, one experimental group and one control group were euthanized. The remaining experimental group was remobilized freely for 16 weeks, after which the dogs completed an additional 16-week treadmill exercise program. Results from this study showed a nearly complete recovery of bone mechanical properties, with only the cortical bone failure point being higher in controls. This recovery of mechanical properties is in direct contrast to the findings of Trebacz (2001). Also contrasting the current

after 16 weeks of what?

results was the fact that the bones of dogs that were euthanized after 16 weeks had significantly lower values for nearly all measures, including yield point, stiffness, and bone mineral density.

These contrasting results are most likely due to the differences in duration of the studies. Since the dogs were immobilized for a period of 16 weeks, they most likely reached a new steady state of bone metabolism, causing the decreased strength at this point. Also, the dogs had a 32-week period to rehabilitate after remobilization, including a 16-week treadmill program. It would have been interesting to see the effects of a rehabilitation program on an additional group of experimental rats in the Trebacz (2001) study. This would provide a more thorough investigation of the healing properties associated with immobilization and remobilization before a new steady state of bone metabolism is reached.

One weakness of the study is the lack of description about rat behavior following remobilization. The author makes many comparisons of the right and left rear femora of the experimental rats after remobilization, showing that the left, undisturbed femur underwent normal growth, and showed normal mechanical parameters, while the right femur lagged behind. However, the only description given is that within one day of remobilization experimental rats "used all legs while moving" (p.1632). This leaves speculation as to the extent that the rats used their right hind legs. Perhaps, since they were accustomed to ambulating with only three legs, they often times refrained from using all four legs when moving, and the right hind leg did not undergo normal loading. The paper should include a more detailed description of post-remobilization movement.

Good question

A second weakness of the study is the lack of statistical power. *T*-tests are generally thought to be the weakest type of statistical test for determining significance. The author does not explain why these tests were used. It seems that one-way ANOVA's would have been

appropriate to use, and would have provided more statistical confidence. It is even possible that the author could have used regression techniques to analyze the data. Using group and time of measurement as independent variables, and multiple bone characteristics as dependent variables, regression could have given us an interesting and more detailed look at the effects of time on bone properties. Regression analysis would also help in predicting what might happen if longer periods of unloading or longer periods of remobilization were employed.

The article has some practical implications that could affect human health. The author suggests that the findings may be important in dealing with osteopenia resulting from injury. The implications of these findings suggest that the early phase of recovery (i.e., a person recovering from a tibial fracture who is freshly out of a cast and allowed to begin weight-bearing activities) could be crucial in restoring bone strength. Since free remobilization actually seemed to worsen bone strength in rats, it may be extremely important that a structured physical therapy program be employed as soon as possible. Additionally, it is important that a person adds greater loads to the injured area very gradually, since the bone is in a weakened state and may be susceptible to re-injury. However, the author does not establish the similarities between rat and human bone function or metabolism, so results from rats may not be directly correlated to results in humans.

These potential practical implications give rise to a few questions that the study does not directly answer. First, what kinds of therapy might be most beneficial for bone strength? A study by Huang et al. (2003) examined this issue. Although the rats used in this study did not undergo a period of immobilization, young rats were used in order to provide a look at how exercise helps to develop growing bone, which would presumably be similar to bone that is positively remodeling after injury. 29 male rats, 7-weeks old, were randomly assigned to a

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swimming condition, a running condition, or a non-exercise control group. The rats underwent 8-weeks of training, five days a week. The run group progressively increased running speeds throughout training, while weights were attached to the tails of the swim group in a similarly progressive manner. The bones were subjected to three-point bending in addition to other measures in this study as well. The rats in the running condition exhibited a higher bone mineral density than both the swim and control groups, while mechanical parameters were significantly higher in both exercise groups compared to control. Interestingly, the swim group exhibited significantly stronger mechanical parameters than the run group in maximal stress and energy absorbed to failure. The authors hypothesize that the superior performance of the bones in the swim group has something to do with the water content of the bones in these rats.

The findings from this study provide an interesting addition to the practical implications of the Trebacz (2001) study. Since bones may be fragile in the time period soon after remobilization, it may be beneficial to begin rehabilitation with some type of hydrotherapy. It may even be safe, and beneficial, to apply increased loads to a person underwater. Additionally, it is potentially beneficial to begin running as a form of rehabilitation, after substantial bone strength has been recovered, in order to help increase bone mineral density as well.

References

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