Recovery of Hindlimb Bone Mass Following Prolonged Disuse

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ABSTRACT

Bone is a dynamic tissue that responds to mechanical loads placed on it. For populations with extensive periods of disuse, like those in prolonged bed rest and astronauts during long-duration spaceflight, significant bone loss can occur. **PURPOSE**: The purpose of this study was to determine the effects of prolonged disuse on weight-bearing bones and the length of time needed to recover disuse-induced bone loss utilizing the hindlimb unloading (HU) method in young rodents. We hypothesized that hindlimb bone mass would partially recover to age-matched control levels by 14 days of recovery following prolonged disuse and fully recover by 90 days of recovery. **METHODS**: Male Sprague Dawley rats underwent 90 days of HU. Additional groups (n=5-7 rats/group) were allowed to recover (with weightbearing cage activity) for either 14 days or 90 days following 90 days of HU. Each time point had age-matched control rats with normal cage activity (CON). In HU, rats were suspended by their tails so their hindlimbs did not have any weight-bearing. Peripheral Quantitative Computed Tomography (pQCT) of the right proximal tibiae was completed to determine the total (cancellous + metaphyseal cortical bone) volumetric bone mineral density (vBMD), cancellous vBMD, and metaphyseal cortical vBMD for each bone. **RESULTS**: Total (cancellous + metaphyseal cortical) vBMD was statistically lower in HU animals after 90d HU ($p=0.001$). Both cancellous vBMD and cortical shell vBMD were lower than CON following 90 days of HU ($p=0.003$, $p=0.001$, respectively). At 14 days of recovery after 90 days of HU, these vBMD mean values for all 3 bone compartments showed no sign of recovery with total ($p< 0.0001$), cancellous ($p=0.001$) and cortical shell ($p=0.001$) vBMD still significantly lower than controls total. The HU rats were no different from CON at 90 days of recovery in all measures. **CONCLUSION**: Our data demonstrate that young rats had significant loss of bone density following prolonged disuse. Additionally, this bone loss persisted into the early phases of recovery. The same duration of weightbearing activity as the 90 days of disuse was required to recover bone mass to age-matched control levels. This study helps to simulate similar scenarios encountered by astronauts in long-duration space missions who experience bone loss in weight-bearing sites. There is some evidence that, upon return to Earth's gravity, bone density in humans declines further in the initial weeks of recovery before reversing. Future studies should address if the use of anti-resorptive medications during flight improves or worsens this recovery pattern for bone mass following prolonged disuse.