Complex Interactions Between Estrogen, Strain, and Exercise-Induced Periosteal Bone Growth

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Abstract:
Understanding the relationship between bone strain and bone growth is critical for interpreting variations in skeletal robusticity. Recently we presented a model for interactions between estrogen, strain, and periosteal bone growth, in which high estrogen (E2) increases, and low (E2) decreases, osteogenic responses to strain. We compared cortical growth in expercised and sedentary sheep (Ovis aries) with higher vs. lower estrogen levels, and showed that exercised animals with high E2 added substantially more bone than those with lower E2. However, without normal controls, it was unclear whether exercise-induced cortical growth was stimulated by high E2, suppressed by lower E2, or both. Here we present a broader test of interactions between E_2 levels (normal, low, high) and loading (exercised and sedentary). Low E2 animals were vaccinated against GnRH to suppress estrogen, while high E2 animals received estrogen implants. After 45 days, periosteal bone growth was measured at hindlimb midshafts. The results support the hypothesis that estrogen upregulates strain-induced cortical bone growth: exercised, high-E2 animals grew 6-27% more bone than exercised animals with lower E2 levels, or sedentary animals ($p<.05$). The effects of the anti-GnRH vaccine on bone growth are more complex. Assays showed that vaccinated animals had normal, not decreased, E2 levels, but grew 34-39% less bone in response to exercise than normal controls ($p<.05$). This suggests the vaccine affected strain-induced bone growth without changing circulating E2, an unexpected finding. These results demonstrate that variation in E2 levels may produce differential growth response to similar mechanical loading through complex mechanisms.