

Sympathetic inhibition prevents but high fat, high protein diet causes bone loss during cold exposure in young C57BL/6J mice

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Cold stress upregulates the sympathetic nervous system (SNS), causing bone loss via osteoblast beta-adrenergic receptors. SNS activation also increases nonshivering thermogenesis (NST) in brown adipose tissue (BAT), which raises body temperature but is energetically costly. The goal of this study was to understand how interactions of sympathetic tone, NST, and diet mediate skeletal effects of cold exposure. We hypothesized that skeletal acquisition in cold-housed mice would increase with 1) SNS inhibition or 2) a high fat, high protein diet providing calories for NST. To test these hypotheses, we pair housed wildtype C57BL/6J male mice at 26C (thermoneutrality) and 16C (moderate cold stress) from 3-12 wks of age. Mice were fed high fat, high protein (HFHP, 40% protein, 40% fat, 20% carbohydrate) or normal diet (N, 20% protein, 10% fat, 70% carbohydrate), with or without propranolol (PRO, 0.5 mg/ML) in drinking water. Outcomes at 12 wks of age included body mass, food intake, uncoupling protein (UCP1) expression in BAT, whole body bone mineral density (BMD, g/cm²) and percent body fat (%) via PIXImus, and cortical and trabecular bone architecture at the midshaft and distal femur via μ CT. Results indicate that body mass did not differ in response to temperature or PRO, but 16C mice ate more and had lower body fat compared to 26C mice ($p < 0.05$ for both). Mice at 16C had lower BMD vs. 26C mice ($p < 0.05$), but 16C PRO mice did not. In 16C mice, distal femur trabecular bone volume fraction (BV/TV, -37%) and connectivity density (Conn. D, -40%) and midshaft femur cortical thickness (BA/TA, -8%) were lower vs. 26C mice, despite twofold higher UCP1 expression ($p < 0.05$ for all). In 16C PRO mice, trabecular and cortical bone acquisition did not differ vs. 26C mice, despite 78% lower UCP1 expression ($p < 0.05$). PRO had no effect on bone or on UCP1 protein expression at 26C. HFHP diet increased body mass and body fat at 26C ($p < 0.05$), but decreased trabecular BV/TV (-29 to -54%) and Conn.D (-47 to -135%) as well as cortical BA/TA (-7 to -10%) in all temperature and PRO groups vs. N diet ($p < 0.05$ for all). These data show that sympathetic inhibition blunts cold-induced bone loss, but high fat, high protein diet is deleterious to bone during cold exposure and at thermoneutrality. Thus sympathetic inhibition is sufficient to prevent cold-induced bone loss, but high fat, high protein diets do not protect against cold-induced bone loss, and may be detrimental to human bone health.

Disclosures: Amy Robbins, None