

LEPTIN REGULATES BONE FORMATION VIA THE SYMPATHETIC NERVOUS SYSTEM

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We previously showed that leptin inhibits bone formation by an undefined mechanism. Here we show that hypothalamic leptin-dependent antiosteogenic and anorexigenic networks differ, and that the peripheral mediators of leptin antisteogenic function appear to be neuronal. Neuropeptides mediating leptin anorexigenic function do not affect bone formation. Leptin deficiency results in low sympathetic tone, and genetic or pharmacological ablation of adrenergic signaling leads to a leptin-resistant high bone mass. α -adrenergic receptors on osteoblasts regulate their proliferation, and a α -adrenergic agonist decreases bone mass in leptin-deficient and wildtype mice while a β -adrenergic antagonist increases bone mass in wildtype and ovariectomized mice. None of these manipulations affects body weight. This study demonstrates a leptin-dependent neuronal regulation of bone formation with potential therapeutic implications for osteoporosis.