

Oral Abstract

ORI6

Endorphins alter bone material properties by actions through dynorphin

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The dynorphins, part of the endorphin family, regulate leptin and neuropeptide Y, both of which mediate powerful sympathetic links from the hypothalamus to bone. Dynorphins are predominantly expressed within the CNS, regulating pain, addiction and depression through the kappa opioid receptor. In the hypothalamus, dynorphin is expressed in leptin-responsive neurons and pre-prodynorphin is co-expressed with neuropeptide Y.

Dynorphin knockout mice (Dyn^{-/-}), which lack the pre-prodynorphin gene and thus all five dynorphin peptides, were examined for skeletal change.

In Dyn^{-/-} central NPY expression was reduced, with no change in serum leptin or body weight.

Cancellous bone volume was greater in Dyn^{-/-} compared to wildtype (11.9% ±1 vs 8.8 ±0.6 p<0.02), consistent with greater mineral apposition rate in Dyn^{-/-} (2.4µm/d ±0.2 vs 1.6 ±0.1, p<0.02). Bone resorption was greater in Dyn^{-/-} mice, as indicated by both osteoclast surface (11.9% ± 0.7 vs 7.9 ±0.7, p<0.01) and number.

Cortical bone volume, in contrast, was reduced in Dyn^{-/-} without change in bone length. Femoral BMD by DXA was reduced 20% (60mg/cm² ±2 vs 72 ±4, p<0.05) and BMC by 30% (23mg ±1 vs 30 ±2, p=0.05). By pQCT, cortical BMD and BMC were reduced across the femur without changes in bone dimensions, cortical thickness or area suggesting altered material properties.

Loss of dynorphin signalling resulted in a marked change in bone material properties not explained by the neuropeptide Y or leptin pathways. This study identifies a novel central mechanism for regulation of bone, with potential links to higher brain functions.