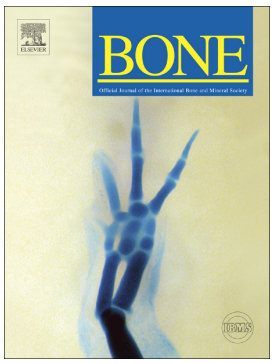

Brain to bone: What is the contribution of the brain to skeletal homeostasis?

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Brain to bone: what is the contribution of the brain to skeletal homeostasis?

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Abstract

The brain, which governs most, if not all, physiological functions in the body, from the complexities of cognition, learning and memory, to the regulation of basal body temperature, heart rate and breathing, has long been known to affect skeletal health. In particular, the hypothalamus – located at the base of the brain in close proximity to the medial eminence, where the blood-brain-barrier is not as tight as in other regions of the brain but rather "leaky", due to fenestrated capillaries – is exposed to a variety of circulating body cues, such as nutrients (glucose, fatty acids, amino acids), and hormones (insulin, glucagon, leptin, adiponectin) [1]–[3]. Information collected from the body via these peripheral cues is integrated by hypothalamic sensing neurons and glial cells [4]–[7], which express receptors for these nutrients and hormones, transforming these cues into physiological outputs. Interestingly, many of the same molecules, including leptin, adiponectin and insulin, regulate both energy and skeletal homeostasis. Moreover, they act on a common set of hypothalamic nuclei and their residing neurons, activating endocrine and neuronal systems, which ultimately fine-tune the body to new physiological states. This review will focus exclusively on the brain-to-bone pathway, highlighting the most important anatomical sites within the brain, which are known to affect bone, but not covering the input pathways and molecules informing the brain of the energy and bone metabolic status, covered elsewhere [8]–[10]. The discussion in each section will present side by side the metabolic and bone-related functions of