Regulation of the Bone Homeostasis, Energy Balance and Fertility by NGF-BDNF/Oxytocin and Osteocalcin Genes in Mice

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The bone mass, metabolism and reproduction require a coordinated regulation. Key players are the centrally acting neurotrophins BDNF/NGF and the oxytocin(OXT) that have effects on neuronal function, bone, metabolism and fertility. The osteocalcin (OST) is instead a peripheral regulator of bone homeostasis; but it recently emerged as a regulator of metabolism, male fertility and neuronal functions suggesting a potential interaction with neurotrophins and OXT signaling. To investigate on the neurotrophin-oxytocin and osteocalcin interaction we analyzed the mRNA levels of Ngf, Bdnf, Ost, Oxt and their receptors p75NTR/Ntrk1, Ntrk2, Gprc6a, Oxtr using RT-PCR in adipose WAT/BAT, reproductive organs, brain and bone tissues of 3 months old female and male mice.
The mRNA levels of Ngf/Ngfr gene were highly expressed in BAT, brain, ovaries/uterus, but down-regulated in bone in both genders, the Ngfr gene was expressed in testis. Conversely, the Bdnf gene was overexpressed in bone, but down-regulated in BAT/WAT and in the reproductive organs. The Ntrk2 was instead expressed in BAT/WAT. The Oxt/Oxtr genes were markedly expressed in brain and ovaries/uterus. Osteocalcin and Gprc6a genes were up-regulated in bone and brain, but down-regulated in BAT/WAT. Gprc6a was expressed in the testes, but not in the ovaries/uterus.
In conclusion, the up-regulation of NGF and related-receptors in fat is consistent with NGF as an energy regulator. The inverse correlation of NGF and BDNF in fat and bone, shows these exerting opposite effects on leptin with BDNF regulating bone. The osteocalcin, NGF and oxytocin genes and with minor extend the BDNF gene were expressed in brain in either gender; while their relative receptors were expressed in the reproductive organs showing a gender expression profile; the osteocalcin gene receptor in male vs female, the oxytocin gene receptor in female vs male, while the NGF gene receptor in either gender. These findings suggest that the regulatory signalling of fertility are released from CNS to act on the peripheral reproductive apparatus. Osteocalcin is therefore a regulator of male fertility, NGF of either female and male fertility elevating LH while Oxytocin of female fertility. The up-regulation of Ngfr in the testes match the Gprc6a expression, and can be responsible for higher LH in the Ost-/- mice.