

COLD STRESS CHALLENGE IS ASSOCIATED WITH EARLY NERVE GROW FACTOR ACTIVITY IN BROWN FAT AND TESTIS REGULATING MRNA LEVELS OF OSTEOCALCIN AND BRAIN-DERIVED NEUROTROPHIC FACTOR IN BONE AND BRAIN OF MICE

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NGF/BDNF and osteocalcin (Ost) share pleiotropic effects regulating energy, bone mass, reproduction and neuronal functions (Camerino et al.,2016). We challenged this previous system investigating NGF and its receptors p75NTR and NTRK1, BDNF, Ost and its receptor GPRC6A mRNA from 3 months-old mice in bone, brain, BAT and testis during cold stress (CS). UCP-1 in BAT was used as positive control. Mice were divided into three groups: controls at room temperature (RT=25°C), CS for 6h and 5-days at T=4°C (N=15 mice). Mice were sacrificed and the mRNA interscapular BAT, bone, brain and testis were extracted. CS for 6h enhanced UCP-1 and NGF mRNA levels in BAT respectively by 2 and 1.5-fold vs controls, down-regulating p75NTR and NTRK1 genes. UCP-1 in BAT was up-regulated after 5-days of CS vs controls; NGF was not affected and its receptors were down-regulated. p75NTR/NTRK1 receptor genes were not affected in bone and brain, while the NGF mRNA was significantly increased in bone and unchanged in brain following 5daysCS. UCP1 increased in bone after 5 days CS. p75NTR mRNA increased by 0.76 and 0.83 folds, respectively, after 6h and 5-days of CS in testis vs controls, while NGF was unaffected. BDNF shows an opposite trend. BDNF mRNA increased by 9.5-fold in bone following 5-days of CS vs controls, and in brain by 0.6-fold after 6h, but not in BAT. BDNF decreased by 1 and 0.6 folds respectively after 6h and 5-days of CS in testis. Ost mRNA increased by 16-fold in bone and 3-fold in BAT after 5-days of CS vs controls; its receptor was unaffected. GPRC6A is upregulated by 3-fold after 6h in brain, Ost is down-regulated by 0.33-fold; these were not affected after 5-days of CS. Ost/GPRC6A mRNA levels were not significantly affected in testis following CS. Linear correlation analysis shows that the changes in the expression levels of the genes of controls mice at room temperature and mice exposed to 6 h and 5 days of CS were linearly correlated in brain, bone and testis showing positive slope and a coefficient of correlation close to 1 in all tissues, but not in BAT, suggesting that a coordinated regulation of gene expression is operative following CS. This study suggest that during cold stress in mice, UCP1 increase in BAT is associated with early NGF response in the same tissue, long-term potentiation of NGF in bone and NGF receptor in testis. UCP1 upregulation in bone is consistent with its protective effect on this organ. BDNF activity may exert bone and neuroprotective effects reducing its function on the reproductive tissue. Similarly to UCP1, Ost signaling is enhanced in bone and BAT while it may exert local neuroprotective effects through its receptor.

Camerino et al.(2016), *Front.in Physiol.*13;7:456

Nguyen et al.(2015), *Bone* 30:1551-2

Jia et al.(2016), *Acta Physiol* 17:311-24

