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VGF-peptides in the Siberian hamster

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vgf is one of the few genes selectively induced in the hypothalamus of Siberian hamsters upon their typical change from an obese phenotype (long day adaptation, during summer) to a lean, catabolic phenotype (short day, or winter adaptation). In fact, the i.c.v. injection of the VGF-derived peptide TLQP-21 caused hypophagia and a decrease in body weight in long day hamster. Hence, we studied VGF multi-peptide profiles in brain cortex and hypothalamus of (male) Siberian hamsters, in the long day (LD) versus short day (SD) adapted state. Specific antisera were produced against short sequences at the C- or N-termini of VGF, and of several known/predicted VGF-derived products: TLQP, NERP-1, and PGH peptides, and used in immunohistochemistry (IHC) and ELISA. Hamsters were perfused with 4% paraformaldehyde (n= 4/group) for IHC or used for tissue sampling and extraction (n= 7/group). In IHC, VGF C- and N- terminus peptides were brightly labelled, as well as most abundant. They were found in both perikarya and axons, in different layers of brain cortex and in multiple hypothalamic areas, including the paraventricular (PVN), suprachiasmatic (SCN), supraoptic (SON) and arcuate nuclei, the lateral and anterior hypothalamic areas, and the median eminence (ME). TLQP peptides were largely restricted to SCN perikarya, and ME axons, while PGH and NERP-1 peptides were revealed in perikarya of the brain cortex, in ME axons, and certain perikarya of PVN and SON (NERP-1 only). Most VGF peptides studied were well represented in tissue extracts of hypothalamus and cortex, VGF C- and N- terminus peptides being again most abundant (hypothalamus: 1.8±0.3 and 10.9±0.6; cortex: 0.7±0.1 and 5±0.3 nmol/g, mean±SEM, C- and N-terminus, respectively, LD animals). A selective decrease in certain VGF peptides was revealed in SD animals, compared to LD ones, so that NERP-1 peptides were decreased in hypothalamus and cortex (61.3±12.7% and 45.8±11.1% of LD animals, respectively, mean±SEM, $p<0.04$), PGH peptides were reduced in hypothalamus (24.8±12.7% of LD group, mean±SEM, $p<0.02$), and both TLQP and N-terminus peptides in the brain cortex (31.8±10.9% and 41.5±10.8% of LD animals, respectively, mean±SEM, $p<0.02$). In conclusion, VGF peptides were well represented in the Siberian hamster brain, with a distinct, apparently selective modulation in the hypothalamus and brain cortex. A regionally specific, differential post-translational processing of the VGF precursor may be implicated.

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Keywords: VGF peptides, Siberian hamster, hypothalamus