

## Parkinson's disease: changes in TLQP and related peptide/s in 6-OHDA treated rat and in human plasma

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VGF peptides are selectively expressed in neurons and endocrine cells, and were found to be modulated in the cerebrospinal fluid of patients affected by certain neurodegenerative diseases, as well as decreased in parietal cortex from Parkinson's disease (PD) patients. We used Sprague-Dowley rats treated with 6-hydroxydopamine (6-OHDA) in the right hemisphere to destroy dopaminergic neurons. Samples of cortex, hypothalamus and substantia nigra (SN) were collected. Human blood samples were obtained from patients affected by PD (n=6) and age-matched controls (n=6, not affected by neurodegenerative disease/s). Specific ELISA were used, as appropriate for rat tissues and human plasma. These were set up with antibodies to: (i) the C- and N-terminal sequences of human / rat VGF precursor, and: (ii) the internal cleaved products: PGH-, TLQP-, and NERP-1 peptides. Preliminary immunohistochemical experiments (IHC) were carried out on control rats, using antibodies to the same VGF-peptides listed above. TLQP peptides were largely represented in the normal brain, within the cortex (167 pmol/g), SN (152 pmol/g) and hypothalamus (250 pmol/g), with measurable, though lower values of the other peptides studied. In human plasma, VGF C-terminus peptides were richly represented (2000 pmol/g), followed by TLQP peptides (90 pmol/g). In the 6-OHDA treated brain, TLQP peptides were decreased in both cortex and SN ( $p < 0.01$  and  $0.04$ , respectively), while VGF N-terminus peptides decreased in the SN only, and PGH peptides only in the cortex. In IHC, the various VGF antibodies labelled neurons and/or axons in hypothalamus, cortex and SN, TLQP peptides being apparently most abundant in Tyrosine Hydroxylase-labelled neurons of both SN and cortex. In human plasma, a decrease in TLQP- ( $p < 0.0001$ ), PGH and VGF C-terminus peptides was shown in PD patients, compared to controls. In conclusion, the selective loss of TLQP peptide/s found in PD warrants their investigation in the physiology and pathophysiology of dopaminergic neurons.

Keywords: VGF peptides, Parkinson's disease, dopaminergic neurons.