

VGF and Type II Diabetes: decrease of VGF fragment levels in adipose tissues of diet-induced obese mice

Filomena D'Amato¹, Cristina Cocco¹, Barbara Noli¹, Roberta Pilleri¹ and Gian-Luca Ferri¹

¹ Dep. of Biomedical Science, Cagliari University, 09043 Monserrato, Italy

VGF encodes a precursor protein processed in various neuropeptides, one of these involved in metabolic mechanisms and named TLQP-21, stimulates the autonomic activation of adipose tissue and reduces the early phase of diet-induced obesity in mouse. In immunohistochemistry (ICC) and ELISA, we used antisera to short sequences at C-/N-terminus of the VGF precursor, and of several VGF-derived peptides. Plasma of type II diabetes (DMII) was taken from patients with different body mass index (BMI): (i) BMI =18-24, (ii) BMI=25-29, (iii) BMI=30-39, in parallel with samples from healthy subjects (iiii) matched with BMI of group "i" (n=10 samples/group). Male CD1 mice were fed with standard chow (group-a: controls), or with standard chow plus 36% lard (group-b: obese) for 16 weeks (n=24 animals/group). For glucose tolerance test, 12 mice from groups a and b, respectively, received i.p. injection of glucose (3g/kg), and were sacrificed after 120 minutes. White and brown adipose tissues (WAT and BAT, respectively) were extracted (n=9 animals/group) while for ICC, mice (~4/group) were perfused with 4% paraformaldehyde. In plasma of DM II patients, we found a clear decrease of VGF C-t, in parallel with the increase of BMI (iiii=1200±70, i=1100±85, ii=760±60, iii=550±40 pmol/ml, mean±SEM). In WAT, through ELISA, we found a significant decrease for VGF C-t in group-b respect to group-a (2±0.5 vs. 5±2*, pmol/g, mean±SEM, *p<0.03). A similar trend was observed in BAT, not only for VGF C-t, but also for N-t, TLQP, and RVW peptides (groups b vs. a, respectively: 10±3 vs. 22±7**, 9±3 vs. 18±4**, 210±75 vs. 420±95**, and 38±11 vs. 70±10*, pmol/g, means±SEM, *p<0.007, **p<0.02). Moreover, exclusively in BAT of group-a but not of group-b, we measured a great increase of VGF C-t, N-t and RVW peptide levels after glucose load (values taken before and after glucose load, respectively: 22±7 vs 35±5**, 18±4 vs. 30±7 **and 70±10 vs. 95±10*, pmol/g, means±SEM, *p<0.02, **p<0.04). In pancreas, BAT and WAT tissues was showed an extended colocalization of VGF C-t peptides with sympathetic fibers, while TLQP peptides were largely restricted to noradrenergic perikaria in celiac ganglia of both control and obese mice. In conclusions, more than one VGF fragment could be important for peripheral activation of autonomic nervous system.

Key words

VGF, Type II Diabetes, BAT, WAT, autonomic nervous system.