Neuropeptide AF and FF modulation of adipocyte metabolism. Primary insights from functional genomics and effects on beta-adrenergic responsiveness.

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Résumé en anglais	The presence of a neuropeptide AF and FF receptor (NPFF-R2) mRNA in human adipose tissue (Elshourbagy, N. A., Ames, R. S., Fitzgerald, L. R., Foley, J. J., Chambers, J. K., Szekeres, P. G., Evans, N. A., Schmidt, D. B., Buckley, P. T., Dytko, G. M., Murdock, P. R., Tan, K. B., Shabon, U., Nuthulaganti, P., Wang, D. Y., Wilson, S., Bergsma, D. J., and Sarau, H. M. (2000) J. Biol. Chem. 275, 25965-25971) suggested these peptides, principally recognized for their pain modulating effects, may also impact on adipocyte metabolism, an aspect that has not been explored previously. Our aim was thus to obtain more insights into the actions of these peptides on adipocytes, an approach initially undertaken with a functional genomic assay. First we showed that 3T3-L1 adipocytes express both NPFF-R1 and NPFF-R2 transcripts, and that NPAF binds adipocyte membranes with a nanomolar affinity as assessed by surface plasmon resonance technology. Then, and following a 24-h treatment with NPFF or NPAF (1 microm), we have measured using real-time quantitative reverse transcriptase-PCR the mRNA steady state levels of already well characterized genes involved in key pathways of adipose metabolism. Among the 45 genes tested, few were modulated by NPFF (approximately 10%) and a larger number by NPAF (approximately 27%). Interestingly, NPAF increased the mRNA levels of beta2- and beta3-adrenergic receptors (AR), and to a lesser extent those of beta1-ARs. These variations in catecholamine receptor mRNAs correlated with a clear induction in the density of beta2- and beta3-AR proteins, and in the potency of beta-AR subtype-selective agonists to stimulate adenylyl cyclase activity. Altogether, these data show that NPFF-R1 and NPFF-R2 are functionally present in adipocytes and suggest that besides their well described pain modulation effects, NPAF and to a lesser extent NPFF, may have a global impact on body energy storage and utilization.
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