



Neuropeptide Y: a new mediator linking sympathetic nerves, blood vessels and immune system?

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Neuropeptide Y (NPY(1-36)), a sympathetic cotransmitter and neurohormone, has pleiotropic activities ranging from the control of obesity to anxiolysis and cardiovascular function. Its actions are mediated by multiple Gi/o-coupled receptors (Y1-Y5) and modulated by dipeptidyl peptidase IV (DPPIV/cd26), which inactivates NPY's Y1-agonistic activity but generates the Y2 and Y5-agonist, NPY(3-36). Released by sympathetic activity, NPY is a major mediator of stress, responsible for prolonged vasoconstriction via Y1 receptors. Y1 receptors also mediate NPY's potent vascular growth-promoting activity leading in vivo in rodents to neointima formation. This and the association of a polymorphism of the NPY signal peptide with increased lipidemia and carotid artery thickening in humans strongly suggest NPY's role in atherosclerosis. NPY and DPPIV/cd26 are also coexpressed in the endothelium, where the peptide activates angiogenesis. A similar system exists in immune cells, where NPY and DPPIV/cd26 are coactivated and involved in the modulation of cytokine release and immune cell functions. Thus, NPY, both a messenger and a modulator for all three systems, is poised to play an important regulatory role facilitating interactions among sympathetic, vascular and immune systems in diverse pathophysiological conditions such as hypertension, atherosclerosis and stress-related alterations of immunity.

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