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Expression Patterns of BDNF with Central Anorexigenic Signaling Pathways Involving PACAP in the Hypothalamic Ventromedial Nuclei

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Presentation Abstract

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Abstract: Pituitary adenylate cyclase-activating polypeptide (PACAP) is a 38-amino acid polypeptide belonging to the secretin super family of peptides. PACAP binds to its type 1 receptor (PAC1R) with greater affinity than for the receptors for vasoactive intestinal polypeptides (VIP), VPAC1 and VPAC2. Although mRNA for PACAP and its receptor PAC1R are found throughout the central nervous system, they are abundantly expressed in the hypothalamic ventromedial nuclei (VMN). In male Sprague Dawley rats, infusions of PACAP into the VMN produce a robust decrease in food intake with concomitant increased energy expenditure, decreased body weight, and significantly elevated brain-derived neurotrophic factor (BDNF) mRNA expression in the VMN. This latter effect of PACAP on BDNF mRNA expression has been shown to occur in other brain regions. Exogenous BDNF in the VMN regulates energy homeostasis in a manner similar to that of PACAP with decreased feeding and increased metabolism. Although the physiological responses to individual PACAP and BDNF infusions in the VMN lead to decreased feeding behavior and body weight loss, the

anatomical distribution of these two cell signals in the VMN has not been established. PACAP-induced changes in BDNF mRNA expression in the VMN may reveal an important interaction with PACAP signaling in the control of feeding behavior. In the present study, we have employed double-labeled fluorescent in-situ hybridization (FISH) to examine the expression patterns of PACAP, PAC1R and BDNF mRNA containing neuronal cells. In the VMN, PACAP mRNA expressing cells co-express BDNF, PAC1R, and VGLUT2. BDNF mRNA expressing cells co-express PAC1R and PACAP. Coupled with previous behavioral data demonstrating PACAP- and BDNF-induced changes in feeding behavior, the co-expression of BDNF with PACAP and PAC1R mRNA in the VMN suggest a potential functional relationship between the two signaling peptides in the regulation of energy homeostasis. The specific and integrated contributions of PACAP and BDNF in the VMN towards regulating energy homeostasis and feeding behavior still remain to be studied.

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