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BRAIN RESEARCH

Research Report

Presence of pituitary adenylate cyclase-activating polypeptide (PACAP) defines a subpopulation of hypothalamic POMC neurons

Katrin Dürr[a], *Ebba Norsted*[a], *Burçak Gömüç*[a], *Elisabet Suarez*[a], *Jens Hannibal*[b], *Björn Meister*[a,*]

[a]*Department of Neuroscience, Retzius väg 8, Karolinska Institutet, SE-171 77 Stockholm, Sweden*
[b]*Department of Clinical Biochemistry, Bispebjerg Hospital, University of Copenhagen, 2400 Copenhagen NV, Denmark*

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ABSTRACT

Several lines of evidence support a role for pituitary adenylate cyclase-activating polypeptide (PACAP) in the regulation of energy balance. In the present study, we have used fluorescent in situ hybridization and immunohistochemistry to investigate in detail the cellular localization and chemical content of PACAP mRNA- and peptide-containing neuronal cell bodies in the mediobasal hypothalamus of the rat. PACAP mRNA-containing cell bodies were demonstrated in high numbers in the ventromedial hypothalamic nucleus (VMH) and in lower numbers in the arcuate nucleus (Arc). In colchicine-treated rats, PACAP immunoreactivity was demonstrated in many cell bodies of the VMH and several cell bodies of the ARC. Double-labeling revealed that PACAP immunoreactivity was present in approximately 20% of pro-opiomelanocortin (POMC) neurons in the ventrolateral Arc as shown by presence of α-melanocyte-stimulating hormone (α-MSH), but not in agouti-related peptide (AgRP)-containing neurons in the ventromedial aspect of the Arc. PACAP immunoreactivity was also colocalized with the vesicular acetylcholine transporter (VAChT; a marker for cholinergic neurons) in Arc POMC neurons. Brainstem POMC neurons in the commissural part of the solitary tract nucleus were devoid of PACAP immunoreactivity. However, several VAChT-positive neurons in the dorsal motor nucleus of the vagus nerve were also PACAP immunoreactive, whereas VAChT-positive neurons of the motor nucleus of the hypoglossal nerve were PACAP-negative. The results show presence of PACAP with α-MSH in a subpopulation of hypothalamic POMC neurons and point further to the neurochemical heterogeneity of hypothalamic, but not brainstem, POMC neurons.

1. Introduction

Pituitary adenylate cyclase-activating polypeptide (PACAP) belongs to the secretin/glucagon/vasoactive intestinal polypeptide family of peptides and was originally isolated for its cAMP-stimulating activity in anterior pituitary cells (Miyata et al., 1989). While PACAP has pleiotropic functions, several lines of evidence substantiate a role for PACAP in the regulation of energy balance (reviewed in Vaudry et al., 2000). Intracerebroventricular injection of PACAP leads to a

* *Corresponding author*. Fax: +46 8 30 72 08.
E-mail address: bjorn.meister@ki.se (B. Meister).

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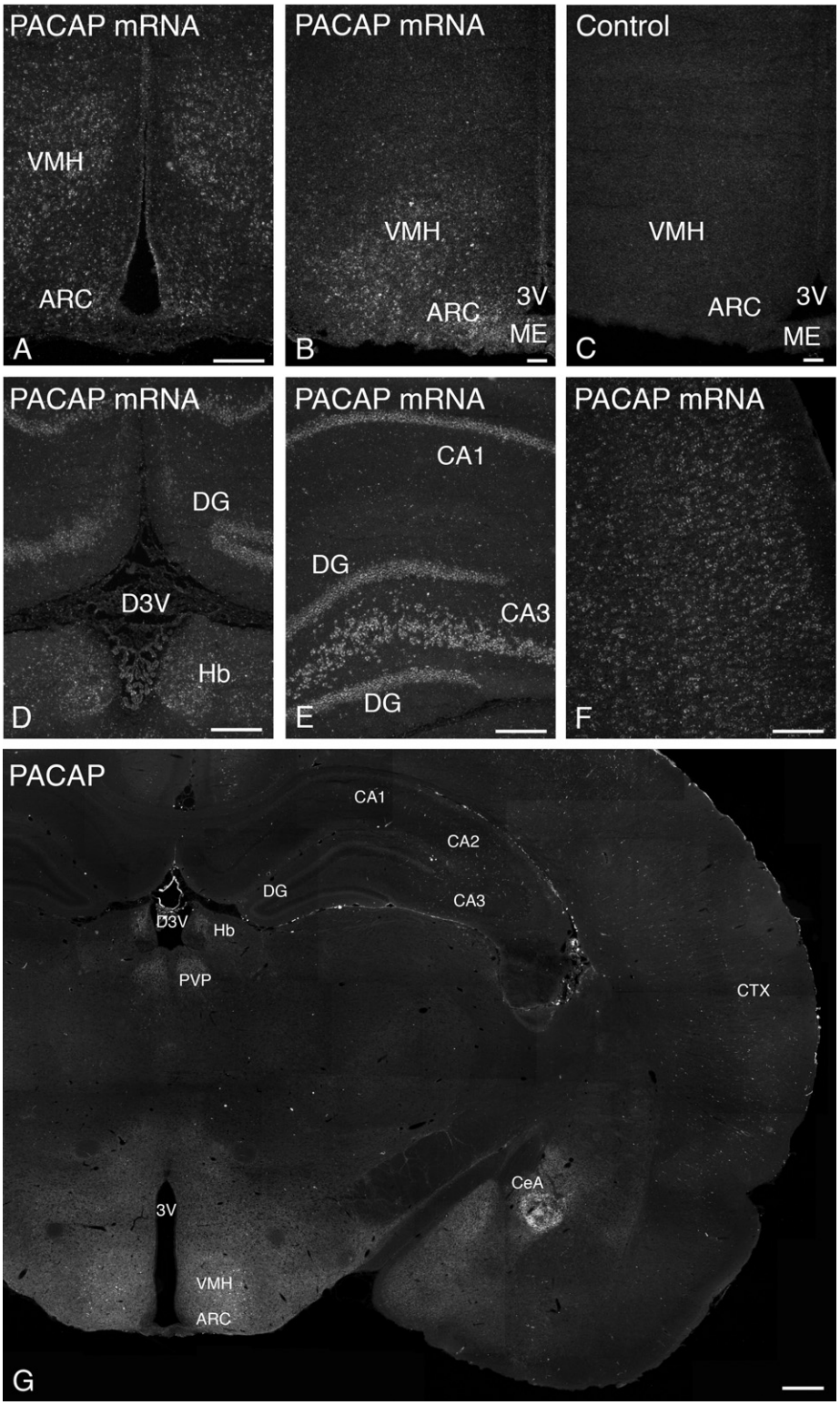

Fig. 1 – (A–G) (A, B) In situ hybridization with an antisense riboprobe detects PACAP mRNA in the ventromedial hypothalamic nucleus (VMH) and in the arcuate nucleus (ARC). (C) Parallel in situ hybridization with a sense probe as negative control does not yield any signal. (D, E, F) PACAP mRNA is also found in the habenular complex (Hb), in the hippocampus, including the dentate gyrus (DG) and the CA1 and CA3 regions, and in the cerebral cortex (F). PACAP mRNA is also detected in the cerebral cortex. (G) Immunohistochemistry of a colchicine-treated rat brain reveals PACAP immunoreactivity in cell bodies of the VMH and ARC as well as the hippocampus and cerebral cortex (CTX). Immunoreactive fibers are mostly found in the hypothalamus, amygdala, habenular complex (Hb) and the paraventricular thalamic nucleus (PVP). CA1, CA2, CA3 = fields of the hippocampus; CeA = central amygdala; D3V = dorsal third ventricle; ME = median eminence; 3V = third ventricle; Scale bars in A–F = 100 μm, scale bar in G = 500 μm.