Available online at www.sciencedirect.com

SCIENCE DIRECT

Developmental Brain Research 156 (2005) 193–201

DEVELOPMENTAL BRAIN RESEARCH

www.elsevier.com/locate/devbrainres

Research report

Pituitary adenylate cyclase-activating polypeptide (PACAP) can act as determinant of the tyrosine hydroxylase phenotype of dopaminergic cells during retina development

Juliana Carrazzoni Borba[a,1], Isabela Pereira Henze[a,1], Mariana Souza Silveira[b], Regina Célia Cussa Kubrusly[c], Patrícia Franca Gardino[a], Maria Christina Fialho de Mello[a], Jan Nora Hokoç[a,*], Fernando Garcia de Mello[a,*]

[a]*Laboratórios de Neuroquímica and Neurobiologia da Retina, Instituto de Biofísica Carlos Chagas Filho-UFRJ, Centro de Ciências da Saúde-Bloco G, Universidade Federal do Rio de Janeiro, Ilha do Fundão, Rio de Janeiro, RJ 21949-900, Brazil*
[b]*Laboratório de Neurogênese, Instituto de Biofísica Carlos Chagas Filho-UFRJ, CCS, Ilha do Fundão, Rio de Janeiro, RJ 21949-900, Brazil*
[c]*Departamento de Fisiologia e Farmacologia, Instituto de Ciências Biomédicas, UFF, Niterói, Brazil*

Accepted 27 February 2005
Available online 7 April 2005

Abstract

In the chick retina, dopaminergic cells are generated between embryonic days 3 and 7 (E3/E7). However, the expression of tyrosine hydroxylase (TH), the first enzyme in the catecholamine synthetic pathway, is only detected after E11/E12. During the interval comprising E7 to E12, signals conveyed by cAMP are important to determine the TH phenotype. The present study shows that pituitary adenylyl cyclase-activating polypeptide (PACAP), via cAMP, is a major endogenous component in defining the TH phenotype of retina dopaminergic cells during development. PACAP type 1 receptor and its mRNA were detected in retinas since E6. PACAP was also immunodetected in cells localized in the inner nuclear layer of retinas since E8. This peptide promoted greater than 10-fold increase in cAMP accumulation of retinas obtained from embryos since E8, an effect that was blocked by PACAP6-38 (PAC1 receptor antagonist). In cultured retina cells from E8 and E9, maintained for 6 days in vitro with 10 nM PACAP (for 5 days), the number of dopaminergic cells expressing tyrosine hydroxylase increased 2.4-fold. The cAMP analog, 8-Br-cAMP and 3-isobutyl-1-methylxanthine (IBMX, a phosphodiesterase inhibitor) also increased the number of tyrosine hydroxylase-positive cells by 4- to 6-fold. IBMX plus PACAP treatment resulted in 17-fold increase in the number of cells positive for tyrosine hydroxylase. Under this condition the amount of tyrosine hydroxylase expression, as detected by western blot analysis, was also increased. The protein kinase-A inhibitor, rp-cAMPS, significantly reduced the effect of PACAP. Our data show that this peptide is an important factor influencing the definition of the tyrosine hydroxylase phenotype of retina dopaminergic cells within a narrow window of development.
© 2005 Elsevier B.V. All rights reserved.

Theme: Development and regeneration
Topic: Neurotransmitter systems and channels

Keywords: cAMP; Differentiation; Catecholaminergic phenotype; CNS; Development

1. Introduction

During development of the central nervous system sequential events are responsible for the definition of the number and distribution of neurons that will compose the mature tissue. Cumulative evidence indicates that cell fate

* Corresponding authors. Fax: +55 21 2562 6594.
E-mail addresses: jnora@biof.ufrj.br (J. Nora Hokoç), fgmello@biof.ufrj.br (F. Garcia de Mello).
[1] Both authors contributed equally to this work.

0165-3806/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.devbrainres.2005.02.016