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Norepinephrine acts as D_1-dopaminergic agonist in the embryonic avian retina: Late expression of β_1-adrenergic receptor shifts norepinephrine specificity in the adult tissue

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Abstract

Dopamine is the main catecholamine found in the chick retina whereas norepinephrine is only found in trace amounts. We compared the effectiveness of dopamine and norepinephrine in promoting cyclic AMP accumulation in retinas at embryonic day 13 (E13) and from post-hatched chicken (P15). Dopamine (EC_{50} = 10 μM) and norepinephrine (EC_{50} = 30 μM), but not the β_1-adrenergic agonist isoproterenol, stimulated over seven-fold the production of cyclic AMP in E13 retina. The cyclic AMP accumulation induced by both catecholamines in embryonic tissue was entirely blocked by 2 μM SCH23390, a D_1 receptor antagonist, but not by alprenolol (β-adrenoceptor antagonist). In P15 retinas, 100 μM isoproterenol stimulated five-fold the accumulation of cAMP. This effect was blocked by propanolol (10 μM), but not by 2 μM SCH23390. Embryonic and adult retina display β_1 adrenergic receptor mRNA as detected by RT-PCR, but the β_1 adrenergic receptor protein was detected only in post-hatched tissue. We conclude that norepinephrine cross-reacts with D_1 dopaminergic receptor with affinity similar to that of dopamine in the embryonic retina. In the mature retina, however, D_1 receptors become restricted to activation by dopamine. Moreover, as opposed to the embryonic tissue, norepinephrine seems to stimulate cAMP accumulation via β_1-like adrenergic receptors in the mature tissue.

Keywords: Norepinephrine; Dopamine; Cyclic AMP; Retina; β_1 adrenergic receptor

1. Introduction

The catecholamines dopamine (DA), norepinephrine (NE) and epinephrine (E) are synthesized from the L-amino acid tyrosine and are present in several areas of the nervous system. While DA is the main catecholamine found in the vertebrate retina, present in a subtype of amacrine cells (Gardino et al., 1993; reviewed in Witkovsky, 2004), NE and E are present in limited amounts in retinas of most studied species (Hadjiconstantinou et al., 1983; Hadjiconstantinou et al., 1984; Ehinger and Seinbusch, 1985; Nguyen-Legros et al., 1999). In mammals, NE fulfills many of the criteria to function as a retinal synaptic neurotransmitter (Osborne, 1981). However, in chick retina the production of NE and E is uncertain and most of them are likely to stem from sympathetic nerve fibres (Ehinger and Seinbusch, 1985). Previous studies have shown that NE can interact with bovine D_1 (Vanderheyden et al., 1986) or cat D_2 dopaminergic receptors in the retina (Robbins et al., 1988).

DA activates D_1- and D_2-types of dopaminergic receptors that show differential ontogenesis in the chick embryo retina. D_1 receptors promote activation of adenylyl cyclase and are expressed since embryonic day 7 during development (De Mello, 1978), while D_2 receptors are detected several days later (Ventura et al., 1984). NE or E are not normally found in the embryonic chick retina but some reports suggest that under certain circumstances, increased levels of circulating NE or E can reach the CNS and act on catecholaminergic receptors (Moron et al., 2002). Most of the NE found in the retina arrives

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