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Atypical effect of dopamine in modulating the functional inhibition of NMDA receptors of cultured retina cells

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Abstract

Cultured retina cells released accumulated [^{3}H]GABA (γ-aminobutyric acid) when stimulated by L-glutamate, *N*-methyl-D-aspartate (NMDA) and kainate. In the absence of Mg^{2+}, dopamine at 200 μM (IC_{50} 60 μM), inhibited in more than 50% the release of [^{3}H]GABA induced by L-glutamate and NMDA, but not by kainate. This effect was not blocked by the D_1-like dopamine receptor antagonist, *R*-(+)-7-chloro-8-hydroxy-3-methyl-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine hydrochloride (SCH 23390), neither by haloperidol nor spiroperidol (dopamine D_2-like receptor antagonists). The dopamine D_1-like receptor agonist *R*(+)-1-phenyl-2,3,4,5-tetrahydro-(1H)-3-benzazepine-7,diol hydrochloride (SKF 38393) at 50 μM, but not its enantiomer, also inhibited the release of [^{3}H]GABA induced by NMDA, but not by kainate; an effect that was not prevented by the antagonists mentioned above. (±)-6-Chloro-7,8-dihydroxy-1-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine hydrobromide (SKF 812497) had no effect. Neither 8BrcAMP (5 mM) nor forskolin (10 μM) inhibited the release of [^{3}H]GABA. Our results suggest that dopamine and (+)-SKF 38393 inhibit the glutamate and NMDA-evoked [^{3}H]GABA release through mechanisms that seem not to involve known dopaminergic receptor systems. © 1998 Elsevier Science B.V.

Keywords: Cell culture; Retina, chick; GABA (γ-aminobutyric acid) release; Dopamine; Glutamate; NMDA receptor complex

1. Introduction

Glutamate, dopamine and γ-aminobutyric acid (GABA), are widely recognized as neurotransmitters in the central nervous system, including the retina of many vertebrate species (Lam et al., 1979; Brandon, 1985; Yazulla, 1986; Massey and Redburn, 1987).

L-Glutamate is an excitatory neurotransmitter that mediates its effects through ionotropic and metabotropic receptors. The activation of the ionotropic receptors induces the release of several neuroactive substances including GABA (Miller and Slaughter, 1986; Barnstable, 1993; Hamassaki-Britto et al., 1993). A considerable number of publications have demonstrated that a substantial portion of the release of GABA induced by excitatory amino acids occurs via the activation of NMDA and non-NMDA ionotropic receptors by mechanisms independent of external calcium (Szerb, 1979; Harris and Miller, 1989; Pin and Bockaert, 1989; Dunlop et al., 1991; Duarte et al., 1993) and is present in a variety of central nervous system regions, including the retina (Yazulla and Kleinschmidt, 1983; Do Nascimento and De Mello, 1985; Schwartz, 1987; Ferreira et al., 1994).

Dopamine is the predominant biogenic amine in the retina and both, GABAergic and dopaminergic cells seem to interact in the processing of visual information at the retina level (Kramer, 1971; Araki et al., 1983; Kato et al., 1984; Dowling, 1987; Gardino et al., 1993). Until recently only two subtypes of dopamine receptors (D_1 and D_2) had been identified in the central nervous system. Both types of receptors are present in the retina (Iuvone et al., 1978; Ventura et al., 1984; Schorderet and Novak, 1990; Ventura and De Mello, 1990). With the advent of the recombinant DNA methodology, seven different dopamine receptors

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