ROLE OF P2 PURINERGIC RECEPTORS IN SYNAPTIC TRANSMISSION UNDER NORMOXIC AND ISCHEMIC CONDITIONS IN THE CA1 REGION OF RAT HIPPOCAMPAL SLICES

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In this study we investigated the role of ATP and P2 purinergic receptors in rat hippocampal neurotransmission under normoxic conditions and during oxygen and glucose deprivation (OGD). Field excitatory postsynaptic potentials (fEPSPs) from the dendritic layer or population spikes (PSs) from the soma were extracellularly recorded in the CA1 area of rat hippocampus.

Exogenous application of ATP (10-100 μM,) or stable analogue ATPγS (adenosine-5'-o-(3-thio) triphosphate, 1-100 μM) reduced fEPSP and PS amplitude. In both cases the inhibitory effect was blocked by the selective A_1 adenosine receptor antagonist DPCPX (8-cyclopentyl-1,3-dipropylxanthine). The inhibitory effect of ATP on fEPSP amplitude was potentiated by different ecto-ATPase inhibitors: ARL 67156 (6-N,N-diethyl-D-β,γ-dibromomethylene, n=5); BGO 136 (1-hydroxynaphthlene-3,6-disulfonate) and PV4 (hexapotassium dihydrogen monotitanoundecatungstocobaltate(II, n=6) tridecahydrate, $K_6H_2[TiW_{11}CoO_{40}]\cdot 13H_2O$, n=5). ATPγS-mediated inhibition was significantly reduced by the P2 antagonist suramin (8-(3-benzamido-4-methylbenzamido)naphthalene-1,3,5-trisulfonate) at somatic level, and by other P2 blockers, PPADS (pyridoxalphosphate-6-azophenyl-2',4'-disulfonate) and MRS 2179 (2'-deoxy-N^6-methyladenosine 3',5'-bisphosphate), at dendritic level.

The role of P2 receptors may become relevant during pathological conditions such as ischemia. The first demonstration that ATP outflow increases *in vivo* during the induction of focal ischemia in the rat was reported by Melani *et al.* (1). A 7-minute OGD induced tissue anoxic depolarisation and was invariably followed by irreversible loss of fEPSP. The P2 antagonists PPADS, suramin, MRS 2179 or BBG (Brilliant Blue G) significantly prevented the irreversible failure of neurotransmission induced by 7-minute OGD. Furthermore, in the presence of these P2 antagonists, the development of anoxic depolarisation was blocked or significantly delayed.

Our results indicate that P2 receptors modulate CA1 synaptic transmission under normoxic conditions by eliciting both inhibitory and excitatory effects. In the same brain region, P2 receptor stimulation plays a deleterious role during a severe OGD insult.

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1. Melani A, Turchi D., Vannucchi M.G., Cipriani S., Gianfriddo M. and Pedata F. (2005) Neurochem Int, 47(6):442-448