

ROLE OF P2 PURINERGIC RECEPTORS ON CA1 NEUROTRANSMISSION OF RAT HIPPOCAMPAL SLICES

Traini Chiara, Coppi Elisabetta, Pugliese Anna Maria and Pedata Felicità

Department of Preclinical and Clinical Pharmacology, University of Florence,
Viale Pieraccini 6, 50139 Florence, Italy

Extracellular nucleotides activate multiple P2 receptors in neurons and glial cells of different brain areas including hippocampus. This study was designed to assess the effects of adenosine triphosphate (ATP) and of the metabolically stable ATP analogue ATP γ S (adenosine-5'-o-(3-thio)triphosphate) on hippocampal neurotransmissions. The field excitatory postsynaptic potential (fEPSP) from the CA1 dendritic layer or the population spike (PS) from the soma in the same region were extracellularly recorded. At dendritic level, a significant and reversible inhibition was observed at a concentration of 10 μ M ATP ($20.3 \pm 2.5\%$, n=7) and a more pronounced inhibition was observed at a concentration of 100 μ M ATP ($77.8 \pm 3.3\%$, n=7). The apparent EC₅₀ value of ATP on fEPSP inhibition was 59 μ M. The inhibitory effect of ATP on fEPSP amplitude was not blocked by the P2 antagonists PPADS and suramin. On the contrary, the application of 100 nM DPCPX, a selective A₁ adenosine antagonist, completely blocked the ATP-mediated reduction of fEPSP. An increase of $6.6 \pm 3.8\%$ and of $12.3 \pm 7.2\%$ in fEPSP amplitude was observed at the highest stimulus intensity tested after 30 μ M and 100 μ M ATP application, respectively. The potentiation induced by 30 μ M ATP was blocked in the presence of 100 μ M suramin. At somatic level ATP induced a $66 \pm 7.1\%$ decrease in PS amplitude (n=8) that was reversed after few minutes' washout. The apparent EC₅₀ value of ATP on PS inhibition was 7 μ M. ATP γ S evoked a concentration-dependent decrease in fEPSP amplitude. The apparent EC₅₀ value for ATP γ S on fEPSP inhibition was 22 μ M. After 15 minutes ATP γ S application, a significant potentiation of fEPSP (n=12) was observed at the highest stimulus intensity tested, an effect prevented in the presence of 30 μ M PPADS. The inhibitory effect of ATP γ S on fEPSP amplitude was significantly reduced both in the presence of 30 μ M PPADS and 10 μ M MRS 2179, a selective P2Y₁ receptor antagonist. In order to discern if the ATP and ATP γ S mediated effects on fEPSP amplitude were due to pre- or postsynaptic mechanisms, we performed a paired pulse facilitation (PPF) protocol (40 ms inter-pulse interval). ATP γ S and ATP significantly increased PPF, an effect blocked in the presence of DPCPX. Our results indicate that the inhibitory effects observed during ATP or ATP γ S application are due to P1 (adenosine) and to P2 (ATP) receptors stimulation and that P2 receptors modulate CA1 synaptic transmission by eliciting both inhibitory and excitatory effects.

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