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

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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 ATPγS (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 µM ATP (20.3±2.5%, n=7) and a more pronounced inhibition was observed at a concentration of 100 µM ATP (77.8±3.3%, n=7). The apparent EC_{50} value of ATP on fEPSP inhibition was 59 µM. 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 A_1 adenosine antagonist, completely blocked the ATP-mediated reduction of fEPSP. An increase of 6.6±3.8% and of 12.3±7.2% in fEPSP amplitude was observed at the highest stimulus intensity tested after 30 µM and 100 µM ATP application, respectively. The potentiation induced by 30 µM ATP was blocked in the presence of 100 µM suramin. At somatic level ATP induced a 66±7.1% decrease in PS amplitude (n=8) that was reversed after few minutes' washout. The apparent EC_{50} value of ATP on PS inhibition was 7 µM. ATPγS evoked a concentration-dependent decrease in fEPSP amplitude. The apparent EC_{50} value for ATPγS on fEPSP inhibition was 22 µM. After 15 minutes ATPγS application, a significant potentiation of fEPSP (n=12) was observed at the highest stimulus intensity tested, an effect prevented in the presence of 30 µM PPADS. The inhibitory effect of ATPγS on fEPSP amplitude was significantly reduced both in the presence of 30 µM PPADS and 10 µM MRS 2179, a selective P2Y1 receptor antagonist. In order to discern if the ATP and ATPγS 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). ATPγS and ATP significantly increased PPF, an effect blocked in the presence of DPCPX. Our results indicate that the inhibitory effects observed during ATP or ATPγS 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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