S02-5 Roles played by presynaptic P2X receptor channels in the brain

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The fast and precise neuron-to-neuron signalling at the synapses is one of the most crucial processes in the central nervous system (CNS) function. Recent advances in the functional and morphological analysis of the brain synapses have identified adenosine 5'-triphosphate (ATP), a ubiquitous and most important molecule in the intracellular functions, plays important roles also as an extracellular messenger at synapses. Lines of evidences accumulated until today indicate that ATP (1) is released into the extracellular space particularly from astrocytes through specific mechanisms, (2) activates specific receptors for extracellular ATP, which modifies synaptic transmission, and (3) is hydrolysed to adenosine by ecto-nucleotidases, which in turn activates specific adenosine receptors and also modulate synaptic transmission. We have recently shown, using the patch-clamp recording of postsynaptic membrane currents in the acute brain slice preparations in vitro, that ATP activates ATP-gated Ca^{2+}-permeable channels (P2X receptor channels) on presynaptic terminal of the primary afferents, triggering glutamate release, and (2) adenosine, produced from ATP in the extracellular milieu, activates presynaptic G protein-coupled receptors, which reduces Ca^{2+} entry through voltage-dependent Ca^{2+} channels and suppresses action potential-dependent transmitter release. These distinct mechanisms operate in synergy in various CNS structures and form "purinergic regulatory complex" of the synaptic transmission.