

ACTIVATED PRESYNAPTIC P2X₇ RECEPTORS FUNCTION AS CALCIUM CHANNELS LINKED TO EXOCYTOTIC GLUTAMATE RELEASE

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The P2X₇ is a purinergic receptor that can be activated by high concentration of adenosine 5'-triphosphate (ATP). After immediate activation by agonist it allows the passage of small cations. In the present investigation glutamate release and the Ca²⁺ accumulation induced by presynaptic P2X₇ receptor activation were studied in purified rat cerebral cortex nerve terminals. **Experimental procedures:** Adult male Sprague-Dawley rats were sacrificed and cerebral cortex removed. Purified synaptosomes were prepared and the synaptosomal pellet was incubated with [³H]D-aspartate and BAPTA AM (50μM) when used, transferred in superfusion system and exposed to BzATP (2',3'-O-(4-Benzoylbenzoyl)-adenosine5'-triphosphate; 2 min). The effects of voltage-operated calcium channel (VOCC) toxins, DL-TBOA (selective non-transportable inhibitor of glutamate transporters) or niflumic acid (anion channels inhibitor) were evaluated. Ca²⁺ free EGTA (0.5mM)-containing medium was added 18 min before agonist. [³H]D-aspartate efflux was determined by liquid scintillation counting and endogenous glutamate by HPLC; endogenous glutamate release was expressed as picomoles per milligram of synaptosomal protein. The Ca²⁺ accumulation was evaluated via microflurimetric techniques in synaptosomes loaded with FURA2-AM (5μM). **Results:** The BzATP (100μM)-evoked [³H]D-aspartate and endogenous glutamate efflux from synaptosomes were reduced when extracellular calcium was removed (42 and 55% respectively n=3-7) or when synaptosomes were exposed to BAPTA-AM (about 50% inhibition n=3). These effects were not additive. Blockade of VOCC did not affect the BzATP-evoked [³H]D-aspartate or endogenous glutamate efflux. DL-TBOA (30μM) or the niflumic acid (300μM) did not affect the calcium-independent BzATP-evoked endogenous glutamate or [³H]D-aspartate efflux. **Conclusions:** It is concluded that activation of the P2X₇ receptor appears allows Ca²⁺ entry and excites glutamate efflux from rat cerebral cortex nerve endings. Activation of P2X₇ receptor can evoke vesicular exocytosis of glutamate, dependent on extracellular calcium entry. We therefore propose that presynaptic P2X₇ receptor can play a role as potential-independent Ca²⁺ channels linked to neurotransmitter exocytosis. About 50% of the P2X₇-evoked glutamate efflux was Ca²⁺-independent; ineffectiveness of blockade of glutamate transporters or anion channels on the Ca²⁺-independent neurotransmitter efflux indicates that these modes of exit are not involved in the P2X₇-evoked Ca²⁺-independent glutamate efflux.