ACTIVATED PRESYNAPTIC P2X$_7$ RECEPTORS FUNCTION AS CALCIUM CHANNELS LINKED TO EXOCYTOTIC GLUTAMATE RELEASE

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The P2X$_7$ 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 Ca^{2+} accumulation induced by presynaptic P2X$_7$ 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 [^{3}H]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. Ca^{2+} free EGTA (0.5mM)-containing medium was added 18 min before agonist. [^{3}H]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 Ca^{2+} accumulation was evaluated via microflurimetric techniques in synaptosomes loaded with FURA2-AM (5µM). **Results**: The BzATP (100µM)-evoked [^{3}H]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 addictive. Blockade of VOOC did not affect the BzATP-evoked [^{3}H]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 [^{3}H]D-aspartate efflux. **Conclusions**: It is concluded that activation of the P2X$_7$ receptor appears allows Ca^{2+} entry and excites glutamate efflux from rat cerebral cortex nerve endings. Activation of P2X$_7$ receptor can evoke vesicular exocytosis of glutamate, dependent on extracellular calcium entry. We therefore propose that presynaptic P2X$_7$ receptor can play a role as potential-independent Ca^{2+} channels linked to neurotransmitter exocytosis. About 50% of the P2X$_7$-evoked glutamate efflux was Ca^{2+}-independent; ineffectiveness of blockade of glutamate transporters or anion channels on the Ca^{2+}-independent neurotransmitter efflux indicates that these modes of exit are not involved in the P2X$_7$-evoked Ca^{2+}-independent glutamate efflux.