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Voltage-sensitive Calcium Channels Are Linked to P2X Purinoceptors in PC12 Cells

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Extracellular ATP is known to function as a neurotransmitter and as a modulator in the variety of cell types. In PC12 cells, extracellular ATP elevates $[Ca^{2+}]_i$ through receptor-operated Ca^{2+} channels and through the activation of phospholipase C, thereby facilitating the secretion of neurotransmitters. Voltage-sensitive calcium channels (VSCCs) are known to be controlled by a variety of hormones and neurotransmitters. This study was performed to understand the relationship between P2 purinoceptors and VSCCs in PC12 cells. UTP and 2-methylthioATP (2MeSATP) were used as preferential activators of P2X and P2Y, respectively. Simultaneous treatment with nifedipine with ω-conotoxin GVIA, L- and N-type calcium channel blockers, respectively, reduced ATP-evoked $[Ca^{2+}]_i$ to 72 % of the control, and reduced 2MeSATP-evoked $[Ca^{2+}]_i$ to 45 %, but had no effect on UTP-evoked calcium increase. Depolarization of PC12 cells with 70 mM K^+ reduced ATP- and 2MeSATP-evoked calcium increase to 69 %, and 49 % of control, respectively, but did not reduce UTP-evoked calcium increase. ATP and 2MeSATP induced membrane depolarization, detected by bisoxonol, whereas UTP did not. Nifedipine also reduced ATP- and 2MeSATP-evoked [^{3}H]norepinephrine ([^{3}H]NE) secretion to 76 % and 53 % of control, respectively, but had no effect on UTP-evoked [^{3}H]NE secretion. Taken together, these results suggest that VSCCs are activated by depolarization signal induced by ATP-gated cation entry through P2X purinoceptors in PC12 cells.