ATP modulates Ca^{2+} channels via the pathway related to GTP-binding protein. P_1 and P_2 receptors seem to coexist in guinea-pig adrenal chromaffin cells.

In the smooth muscle tissues contracted by acetylcholine, ATP, 2-methylthio ATP (2MeSATP) and α,β-methylene ATP (α,β-meATP) each caused relaxation. Reactive blue 2 (RB2) and suramin inhibited the relaxant responses to ATP and α,β-meATP. PPADS and DIDS inhibited the relaxation caused by α,β-meATP but not by ATP. Both ATP- and α,β-meATP-induced relaxations were inhibited by apamin.

In tissues at resting tone, ATP and its related compounds caused contractions with the rank order of potency; 2MeSATP>> ATP≥UTP>> α,β-meATP. RB2 and suramin inhibited both ATP- and UTP-induced contractions. PPADS inhibited the contraction caused by UTP but not by ATP. Desensitization with UTP slightly decreased ATP-induced contraction. UTP-induced contraction was not inhibited by desensitizaiton with ATP. ATP- and UTP-induced contractions were inhibited by the removal of extracellular Ca^{2+} or the application of nifedipine. These results suggest that there are two purinoceptors mediating relaxation, and that apamin-sensitive K^+ channels are involved in the relaxant responses to these adenine nucleotide. In addition, it was suggested that ATP and UTP caused contractions via P_{2Y} receptors and pyrimidinoceptors, respectively, and that these contractions were caused by the Ca^{2+} entry through voltage-dependent Ca^{2+} channels. In summary, there are some purino- and pyrimidinoceptors in both chromaffin cells and smooth muscle cells. ATP and its related compounds may play a role as a transmitter in these tissues.

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Voltage-dependent calcium channels in porcine adrenal chromaffin cells: Channel subtypes and mechanisms of their facilitation.

Naoki KITAMURA

Laboratory of Pharmacology,
Department of Biomedical Sciences,
Graduate School of Veterinary Medicine,
Hokkaido University,
Sapporo 0600818, Japan

To study the characteristics of voltage-dependent Ca channels in porcine adrenal chromaffin cells, Ca currents (I_{Ca}), rise of intracellular Ca concentration ($[Ca^{2+}]_i$) and catecholamine release responses induced by stimulation with high K^+ (60 mM) were measured by whole-cell voltage clamp technique, microfluorometry and HPLC-ECD method, respectively. The results obtained were as follows:

Voltage-current relationship of I_{Ca} indicated that porcine adrenal chromaffin cells possess only high voltage-activated type of Ca channels. The I_{Ca} was inhibited by ω-conotoxin GVIA (ω-CgTx), nifedipine and ω-agatoxin IVA (ω-AgTx) dose-dependently, though the magnitudes of inhibition were various. The degree of inhibition

by maximal doses of these three agents was 78%, 15% and 6%, respectively. When these three agents were applied onto the same cell, I_{Ca} was inhibited additively. Rises in $[Ca^{2+}]_i$ and catecholamine release in response to stimulation by high K^+ were inhibited to about 50% by either ω-CgTx (1 μM) or nifedipine (10 μM) but not by ω-AgTx (0.1 μM). In addition, these responses were almost abolished by the combined application of ω-CgTx and nifedipine. A strong depolarizing pulse (a prepulse to +100 mV) applied prior to a test pulse caused about 20% increase of amplitude of I_{Ba} evoked by the test pulse (facilitation of I_{Ba}). The degree of the facilitation of I_{Ba} was increased with the increase in the voltage (in a range over +20 mV) and duration of the prepulses. Moreover the facilitation of I_{Ba} was decreased with increase in intervals between the prepulses and the test pulses. The application of 8-Bromo-cAMP (1 mM) or forskolin (10 μM) decreased the amplitudes of I_{Ba} without affecting the degree of facilitation of I_{Ba} by the prepulses. In addition, an intracellular application of Rp-cAMPS, an inhibitor of PKA, did not have any effects on the amplitudes of I_{Ba} and the degree of facilitation of I_{Ba}. The intracellular application of GTPγS (100 μM) decreased the amplitudes of I_{Ba}, but not affected those in the presence of prepulses. On the other hand, the application of GDPβS (100 μM) caused a slight increase in the amplitudes of I_{Ba} but had no effects on the amplitudes of I_{Ba} in the presence of prepulses. GTPγS-sensitive component of I_{Ba} was sensitive to ω-CgTx but not to nifedipine. The facilitation of I_{Ba} by the prepulses was abolished by ω-CgTx but not by either ω-AgTx or nifedipine.

Based on these results, it is clarified that porcine adrenal chromaffin cells possess ω-CgTx-sensitive N- and nifedipine-sensitive L- and ω-AgTx-sensitive P/Q-type Ca channels and that L- and N-type channels mainly contribute to the rise in $[Ca^{2+}]_i$ and catecholamine release by depolarizing the cells. N-type Ca channels are mainly involved in the depolarizing prepulse-induced facilitation of I_{Ba}. The facilitation seems to result from the prepulse-induced relief of tonic inhibition on Ca channels by G-protein but not from PKA-induced phosphorylation of channels during the prepulse.

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Effects of tacrine on catecholamine secretion from guinea-pig adrenal chromaffin cells: in comparison with the effects of a cholinesterase inhibitor, physostigmine

Takeshi Sugawara

Laboratory of Pharmacology,
Department of Biomedical Sciences
Graduate School of Veterinary Medicine,
Hokkaido University, Sapporo 060–0818, Japan

1. Effects of tacrine and physostigmine (Phys) on catecholamine (CA) secretion induced by acetylcholine (ACh) and their mechanisms were studied in perfused adrenal glands and dispersed adrenal chromaffin cells of the guinea-pig.
2. In perfused adrenal glands, tacrine and Phys