by NO donors of glucose-induced $[Ca^{2+}]_c$ dynamics.

4. A K^+_{ATP} channel inhibitor, tolbutamide (300 μM), caused a $[Ca^{2+}]_c$ rise and this increase was also inhibited by NOR3 (200 μM). The inhibition by NOR3 was restored by oxyhemoglobin. A high K^+ (50 mM)-induced transient $[Ca^{2+}]_c$ rise was not influenced by NOR3 (400 μM). These results suggest that NO has no direct action on voltage-dependent Ca^{2+} channels, but it opens K^+_{ATP} channels directly or indirectly, resulting in cessation of glucose-induced $[Ca^{2+}]_c$ dynamics in mouse pancreatic islet cells.

5. It has been shown that NO causes damage on DNA strands, which initiates an ATP-consuming repair process by activation of poly(ADP-ribose) synthetase (PARS), causing a reduction of cytosolic ATP concentration ($[ATP]_c$). There would be a possibility that this reduction of $[ATP]_c$ might be related to NO-induced inhibition of $[Ca^{2+}]_c$ dynamics. This possibility was examined by using 3-aminobenzamide (3-AB), a PARS inhibitor. In the presence of 3-AB (1 mM), the inhibitory effect by NOR3 on glucose-induced $[Ca^{2+}]_c$ dynamics was not affected. This result suggests that the ATP-consuming PARS cascade is not directly involved in the NO-induced inhibition. In conclusion, it is implied that NO but not peroxynitrite interferes with glucose-induced closure of K^+_{ATP} channels probably via reduction of mitochondrial ATP production in mouse pancreatic β cells.

Ca^{2+} CHANNEL SUBTYPES IN GUINEA PIG ADRENAL CHROMAFFIN CELLS

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1. The effects of selective Ca^{2+} channel blockers on Ca^{2+} currents and 60 mM K^+-induced catecholamine release were examined to investigate the subtypes of Ca^{2+} channels and their contribution to catecholamine release in isolated guinea pig adrenal chromaffin cells.

2. Application of nifedipine (3 μM) for 4 min, an inhibitor of L-type Ca^{2+} channel, ω-conotoxin GVIA (1 μM), an inhibitor of N-type Ca^{2+} channel, ω-agatoxin IVA (0.1 μM), an inhibitor of P-type Ca^{2+} channel and ω-conotoxin MVIIC (3 μM), an inhibitor of N/P/Q-type Ca^{2+} channel, inhibited peak amplitude of Ca^{2+} current by 33%, 15%, 23%, 33%, respectively.

3. When nifedipine, ω-conotoxin GVIA, ω-agatoxin IVA and ω-conotoxin MVIIC were applied sequentially onto the same cell, Ca^{2+} current was inhibited additively. This result suggests that guinea pig adrenal chromaffin cells possess at least L-, N-, P- and Q-type Ca^{2+} channels.

4. Even after L-, N-, P- and Q-type Ca^{2+} currents were inhibited by selective Ca^{2+} channel blockers (nifedipine (3 μM), ω-conotoxin GVIA (1 μM), ω-agatoxin IVA (0.1 μM) and ω-conotoxin MVIIC (3 μM), Ca^{2+} currents, with the amplitude of about 23% of control curents, were evoked by the depolarizing pulses to +10 mV for 50 ms from a holding potential −70 mV.

5. The Ca^{2+} current insensitive to these Ca^{2+} channel blockers was considered to be mediated through R-type Ca^{2+} channel (one of high voltage activated Ca^{2+} channels) or T-type Ca^{2+} channel (typical low voltage activated Ca^{2+} channel).

The voltage-current relationship of this current resembled that of T-type Ca^{2+} current but not R-type Ca^{2+} current. However, the rapid inactivation, one of the properties of T-type Ca^{2+} current, was not observed in the present experiment.

6. This residual current, insensitive to Ca^{2+} channel blockers, was inhibited by low concentrations of Ni^{2+} (0.01–0.1 mM), and was not suppressed by ATP (500 μM).

7. Catecholamine release induced by 60 mM KCl was significantly inhibited by nifedipine (3 μM), ω-conotoxin MVIIC (3 μM) and mixture of four blockers, but neither ω-conotoxin GVIA (1 μM) nor ω-agatoxin IVA (0.1 μM).

8. These results suggest that guinea pig adrenal chromaffin cells possess L- and N- and P- and Q-type Ca^{2+} channels and other subtypes of Ca^{2+} channel insensitive to these blockers, and that L- and Q-type channels and the unidentified Ca^{2+} channels mainly contribute to the catecholamine release by stimulation with high K^+. Some properties of unidentified Ca^{2+} channel currents were different from those of both T-type and R-type Ca^{2+} channel currents. As we can not identify the subtype of this Ca^{2+} channel, further studies are required to identify these Ca^{2+} channels.

MECHANISMS OF CATECHOLAMINE SECRETION BY Ca^{2+}-REINTRODUCTION AND Na^+ REMOVAL IN ADRENAL CHROMAFFIN CELLS OF THE GUINEA-PIG

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1. We investigated the mechanisms of increases in catecholamine (CA) secretion evoked by reintroduction of Ca^{2+} after removal of extracellular Ca^{2+} (Ca^{2+}-reintroduction) and removal of extracellular Na^+ in chromaffin cells of the guinea-pig.

2. CA secretion was increased with increasing the concentration of Ca^{2+} (0.1–10 mM) reintroduced. This secretory response was not affected by 1 μM atropine, 100 μM hexamethonium and 1 μM tetrodotoxin.

3. In the presence of 1 mM $CoCl_2$ or 1 mM $MgCl_2$, Ca^{2+}-reintroduction failed to increase CA secretion. The secretory response to Ca^{2+}-reintroduction was significantly inhibited by 10 μM methoxyverapamil (D600) and 1 μM nifedipine, but not by 1 μM ω-conotoxin GVIA and 0.1 μM ω-agatoxin IVA, and was greatly potentiated by 1 μM Bay K 8644.

4. Ca^{2+}-reintroduction caused an increase in the intracellular free Ca^{2+} concentration ($[Ca^{2+}]_i$) which was inhibited by D600 in isolated chromaffin cells loaded with fura-2.

5. CA secretion evoked by high K^+ (56 mM) which directly depolarizes the cell membranes was also inhibited only by nifedipine, and was greatly potentiated by Bay K 8644. However, the rate of inhibition in CA secretion evoked by high K^+ was much smaller than that by Ca^{2+}-reintroduction.

6. CA secretion was evoked by the removal of extracellular Na^+ in the absence of Ca^{2+} but not in its presence. This secretory responce was also significantly inhibited by D600, and was