Studies on the divalent cation-controlled catecholamine secretion in adrenal medullary cells

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Summary

Catecholamine (CA) secretory responses were studied using the isolated rat adrenal medulla perfused with the standard krebs solution (containing 2 mM Ca^{2+}) and with Sr^{2+}- or Ba^{2+}-medium in which $CaCl_2$ in the Krebs solution was replaced by $SrCl_2$ or $BaCl_2$. The perfusate was directly led into a flow cell for continuous electrochemical detection of CA in the medium. In the standard solution, stimulation with nicotine or high extracellular K^+ concentration evoked CA secretion derived from Ca^{2+} influx through dihydropyridine-sensitive, voltage-dependent Ca^{2+} channels. On stimulating receptors with muscarine, bradykinin and histamine, Ca^{2+} release from intracellular stores caused an initial transient secretion whereas receptor-mediated Ca^{2+} influx produced a sustained secretion. Sr^{2+} could permeate both Ca^{2+} channels and the receptor-operated pathway for Ca^{2+} introduction and elicited CA secretion. However, the initial transient secretion following the receptor stimulation was largely inhibited in Sr^{2+}-medium. This may imply the absence of capability for Sr^{2+} influx to induced Ca^{2+} release from Ca^{2+} stores, which may takes place with Ca^{2+} influx in the standard solution to generate the initial phase of secretion. Unlike Ca^{2+} and Sr^{2+}, Ba^{2+} entered adrenal medullary cells without help of stimulants to cause CA secretion in Ba^{2+}-medium. This Ba^{2+} influx mainly passed through voltage-dependent Ca^{2+} channels and was inhibited by a dihydropyridine type of Ca^{2+} channel blocker, PN200-110. CA secretion evoked by exposure of adrenal medullary cells to Ba^{2+}(1 mM)-medium was suppressed by about half due to the concomitant presence of 80 μM Ca^{2+} in the Ba^{2+}-medium and almost completely inhibited by 640 μM Ca^{2+}. There might exist a Ca^{2+} binding site at a some point facing to the outer surface of the Ca^{2+} channel and Ca^{2+} occupation of this site may determine the permeability of Ba^{2+}. Ba^{2+}-induced CA secretion in the absence of other stimulants increased with a sigmoidal manner and saturated at the level which was roughly proportional to the second power of the external Ba^{2+} concentration. On replacing Ba^{2+}-medium by the standard medium, CA secretion decreased exponentially. To elucidate these characteristics of Ba^{2+}-induced CA secretion, a simple kinetic equation was proposed.