Effect of Dopamine on Calcium Uptake in Renal Proximal Tubule Cells

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It has been known that dopamine (DA) increases intracellular calcium ($[Ca^{2+}]_i$) level, inducing various physiological effects such as cell proliferation or modulating renal transport functions. In this study, we examined the effect of DA on $[Ca^{2+}]_i$ level and its related signal pathway in proximal tubule cells (PTCs). PTCs were grown in D-MEM/F-12 supplemented with three growth supplements (5 μg/mL insulin, 5 μg/mL transferrin, and 50 nM hydrocortisone). PTCs were incubated with dopamine of different time or dosage and Ca^{2+} uptake, cAMP assay, Western blotting, and electrophoretic mobility shift assay (EMSA) were performed. DA increased $[Ca^{2+}]_i$ in a time- (>8 hr) and dose- ($>10^{-10}$ M) dependent manner. DA-induced increase of $[Ca^{2+}]_i$ was blocked by nifedifine and methoxyverapamil (L-type Ca^{2+} channel blockers). SKF 38393 (DA1 agonist) but not Quinpirole (DA2 agonist) increased $[Ca^{2+}]_i$. DA increased cAMP level, and DA-induced increase of $[Ca^{2+}]_i$ was blocked by PKI (PKA inhibitor), PTX (Gi protein inhibitor), SQ 22536 (adenylate cyclase inhibitor). In addition, U 73122 or neomycin [Phospholipase C (PLC) inhibitors] suppressed DA-induced increase of $[Ca^{2+}]_i$. The pretreatment of staurosporine or bisindolylmaleimide I [Protein kinase C (PKC) inhibitors] blocked DA-induced increase of $[Ca^{2+}]_i$, suggesting the involvement of PKC. SB 203580 (p38 MAPK inhibitor) or PD 98059 (p44/42 MAPKs inhibitor) also inhibited DA-induced increase of $[Ca^{2+}]_i$, consistent with the phosphorylation of p38 MAPK or p44/42 MAPKs. DA significantly increased H_2O_2 release, and the level of NF-κB p65, which was prevented by SQ 22536, neomycin, or staurosporine. DA-induced increase of $[Ca^{2+}]_i$ was indeed blocked by N-acetyl-l-cysteine (NAC) or taurine (antioxidant). In conclusion, DA incrases Ca^{2+} uptake through cAMP, PLC/PKC, MAPKs, oxidative stress via DA1 receptor in renal proximal tubule cells.