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REGULATION OF CALCIUM UPTAKE IN NEUROBLASTOMA OR HYBRID CELLS - A POSSIBLE MECHANISM FOR SYNAPSE PLASTICITY.

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Thirteen neuroblastoma or hybrid cell lines with or without defects in stimulus-dependent acetylcholine release and synapse formation (Wilson, S., *et al.* (1978) Fed. Proc. 37, 2819) were tested for K^+-dependent $^{45}Ca^{2+}$ uptake. NBr10A hybrid cells (synapse$^+$) grown for days with 1 mM dibutyryl cAMP (Bt_2cAMP) and incubated with 5.4 or 85.4 mM K^+ accumulate 2.5 and 5.0 nmoles of $^{45}Ca^{2+}$/5 min/mg protein, respectively. Methoxy-verapamil inhibits K^+-dependent $^{45}Ca^{2+}$ uptake >95% (IC_{50} = $2x10^{-7}$ M) but has no effect on basal $^{45}Ca^{2+}$ uptake. $^{45}Ca^{2+}$ uptake also is inhibited by 10 mM La^{3+}, Co^{2+}, Ni^{2+}, Mn^{2+} or Sr^{2+} but not by 10 μM tetrodotoxin, 20 mM tetraethylammonium or 1 mM 3,4-diaminopyridine. Logarithmically dividing NBr10A cells grown without Bt_2cAMP do not respond to K^+ by accumulating $^{45}Ca^{2+}$ but can be shifted to a responsive state by treatment for 7 days with Bt_2cAMP or 10 μM PGE_1 (an activator of adenylate cyclase) and 1 mM theophylline. Examination of 12 other cell lines grown with Bt_2cAMP revealed 2 classes of synapse defects: (1) defects in K^+-dependent $^{45}Ca^{2+}$ uptake and (2) defects in another unidentified step required for synapse formation. These results show that the Ca^{2+} uptake is regulated and that cell lines with or without defects in Ca^{2+} uptake can be generated. The results suggest that cAMP is required for the acquisition of K^+-dependent Ca^{2+} uptake thereby regulating synapse formation and efficiency.