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Neurotensin Induces Catecholamine Secretion and Calcium Rise by B2 Bradykinin Receptor Activation in PC12 Cells

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The effect of neurotensin (NT) was investigated in rat pheochromocytoma (PC12) cells. When PC12 cells were treated with micromolar concentrations of NT, [^{3}H]norepinephrine ([^{3}H]NE) secretion and elevation of cytosolic Ca^{2+} concentration ($[Ca^{2+}]_i$) were evoked in a concentration-dependent manner with an EC_{50} of 50 μM. Both cytosolic calcium release and inositol 1,4,5-trisphosphate (IP_3) production were also detected at micromolar concentrations of NT, suggesting that phospholipase C is involved in the responses. Studies with NT analogs and NT receptor (NTR) antagonists confirmed that high- and low-affinity NTRs are not involved. In addition, NT did not potentiate high K^+-induced responses. These results suggest that NTRs in PC12 cells are entirely different from high- and low-affinity NTRs in view of the effective concentration of NT and the pharmacological characteristics. Simultaneous treatment with maximal concentrations of NT and bradykinin induced [^{3}H]NE secretion and $[Ca^{2+}]_i$ rise similar to those induced by bradykinin alone. Furthermore, pretreatment with bradykinin inhibited a subsequent $[Ca^{2+}]_i$ rise induced by NT and vice versa. Finally, bradykinin- and NT-induced $[Ca^{2+}]_i$ rises were inhibited by bradykinin receptor antagonists with similar IC_{50} values. The data suggest that micromolar concentrations of NT induces NE secretion and $[Ca^{2+}]_i$ rise by acting on B2 bradykinin receptors.