# PACAP-mediated Regulation of Chromaffin Cell Secretion

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**Background:** The adrenal medulla is an important effector of the sympathetic nervous system in the periphery. An increase in sympathetic tone causes the medulla to release epinephrine, norepinephrine, and other hormones in the bloodstream for circulation throughout the body. The secretory units of the adrenal medulla are chromaffin cells. Chromaffin cells synthesize and store catecholamines and peptide hormones in dense core granules and release these agents as a result of exocytosis. In situ, chromaffin cell exocytosis is triggered by the neurotransmitters, acetylcholine and pituitary adenylate cyclase activating polypeptide (PACAP). However, the mechanisms by which PACAP causes exocytosis in chromaffin cells is poorly understood.

**Objectives:** The goal of this study is to further our understanding of how PACAP activation of chromaffin cells causes exocytosis.

**Methods:** We used time-resolved membrane capacitance measurements in combination with perforated patch clamp methods in primary cultured adrenomedullary chromaffin cells from adult mice to measure and determine the relationship between calcium entry and secretory activity. In addition, we used pharmacological and genetic approaches to elucidate how PACAP affects secretory output.

**Results:** We showed that PACAP treatment increased the calcium sensitivity of exocytotic activity and increased the readily releasable pool size. This PACAP-mediated enhancement of depolarization-evoked secretion is mitigated when the cell is pretreated with PKC antagonist NPC-15437, indicating that PACAP activation of PKC is critical for the enhancement of chromaffin cell secretion.

**Conclusions:** PACAP application during depolarization-induced exocytosis appears to enhance both the calcium sensitivity and the number of vesicles available for exocytotic release. This PACAP-mediated enhancement appears to rely on the activation of PKC. Understanding how PACAP affects chromaffin cell secretory activity provides new insights into how splanchnic signalling tunes the neuroendocrine stress response.

 