Control of Neurotransmitter and Hormone Release by Ca⁺⁺ and cAMP

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It has been known since the work of Katz and collaborators in the early 50s, that an increase in intracellular Ca⁺⁺ concentration ([Ca⁺⁺]) is the immediate trigger for neurotransmitter release. Later work has shown that next to Ca⁺⁺ many other signaling pathways, particularly via cAMP, modulate the release of both neurotransmitters and hormones. However, regulated secretion is a multistep process and the signaling pathways involved act at many stages. Biochemical and traditional electrophysiological techniques very often cannot dissociate between signaling actions on ion channels, vesicle trafficking and the secretory process itself. We have tried to dissect the stimulus secretion pathway by developing assays in chromaffin cells (for catecholamine release) and at a glutamatergic central nervous synapse (the Calyx of Held), which allow to study secretion in single cells under voltage clamp conditions. This enables us to clearly distinguish between influences on electrical signaling from those on the process of vesicle recruitment and on the process of exocytosis. We focus in our study on the role of [Ca⁺⁺] and cAMP.