A tale of two hormones: stimulus-secretion coupling in magnocellular hypothalamic neurons

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Release of the peptide hormones vasopressin (AVP) and oxytocin (OXT) in the mammalian posterior pituitary gland strongly depends on the pattern of action-potential stimulation. Release of AVP, for example, peaks at mean intra-burst frequencies around 10-15 Hz before tapering off. The cellular mechanisms underlying this pronounced, frequency-dependent modulation of excitation-secretion coupling have remained unclear.
Using high-speed optical recordings and fluorescent indicator dyes, we determined the spatio-temporal dynamics of calcium- and voltage changes in the intact mammalian neurohypophysis during trains of action-potentials between 1 and 40 Hz.
Action-potential induced Ca^{2+} transients display large and systematic modulation of their tissue-averaged amplitudes. The interplay of frequency-dependent Ca^{2+} transients and residual calcium levels correlates well with the observed levels of AVP release. This raised the question of what factors regulate the prominent facilitation and depression of ΔCa^{2+} transients? Ca^{2+} influx in individual terminals might decline due to Ca-channel inactivation. Alternatively, changes in either the waveform of the action potential or its spatial invasion might alter the tissue-averaged Ca^{2+} response. To distinguish between these latter two possibilities, we have monitored the spatial pattern of action potential invasion with a voltage-sensitive dye and an ultra high-speed CMOS camera recently developed by one of us (M. Ichikawa). The results of our optical measurements, together with existing electrophysiological observations, suggest that the local excitability of secretory terminals/varicosities is dramatically depressed after repeated stimulation, while global action-potential invasion is maintained. We have named this new mechanism for generating depression "stuttering conduction" due to the significant, localized retardation of the action-potential after passing through the inactivated varicosities.
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