Abstract

The magnocellular neurosecretory cells (MNCs) of the hypothalamus project axons from the supraoptic nucleus to the posterior pituitary gland, where they secrete either oxytocin or vasopressin into the circulation. Oxytocin is important for delivery at birth and is essential for milk ejection during suckling. Vasopressin primarily promotes water reabsorption in the kidney to maintain body fluid balance.

The profile of oxytocin and vasopressin secretion is principally determined by the pattern of action potentials initiated at the cell bodies in the hypothalamus. MNCs principally secrete hormones from terminals in the pituitary, but the secretion also occurs from their dendrites in the supraoptic nucleus, where they diffuse and affect the neighbouring cells. Mechanisms controlling the oxytocin and vasopressin secretion from MNCs have been extensively studied over the last decades and it is assumed that the relationship between Ca^{2+} signalling, secretion from dendrites, and the firing patterns is essential in understanding the magnocellular neurosecretory system.

In this project, we combine mathematical analysis and experimental measurements of Ca^{2+} activity of MNCs of transgenic rats expressing an arginine vasopressin-enhanced green fluorescent protein (AVP-eGFP) or oxytocin-monomeric red fluorescent protein (OT-mRFP1). We report a detailed analysis of the spontaneous $[Ca^{2+}]_i$ oscillations and depolarization-induced $[Ca^{2+}]_i$ elevations in MNCs in isolated conditions. We show how these oscillations are affected by the physiological state of the animal (dehydration, lactation) and by exposure to extracellular stimuli (osmotic change, exposure to vasopressin). In terms of mechanisms underlying the oscillations, we show that they do not require action potentials but are rather mediated by intrinsic mechanisms driven by the action of Ca^{2+} channels and the membrane Na^+/Ca^{2+} exchanger. Furthermore, we prove that vasopressin has autoregulatory feedback on oscillating neurones similar to the autocrine signalling described for electrical activity. For depolarization-induced $[Ca^{2+}]_i$ elevation, we show, in detail, how the $[Ca^{2+}]_i$ responses are modulated by the filling state of the intracellular Ca^{2+} stores. Taken together, this study covers important Ca^{2+} signalling mechanisms in MNCs that have not yet been sufficiently described and are essential for understanding the physiology of oxytocin and vasopressin secretion.