Plasticity in neuroendocrine circuits controlling prolactin secretion: changing patterns of secretion to meet physiological demand

D.R. Grattan, Centre for Neuroendocrinology and Department of Anatomy, University of Otago, Dunedin 9054, New Zealand.

Prolactin secretion from the anterior pituitary gland is inhibited by the hypothalamus by means of dopamine released from tuberoinfundibular dopamine (TIDA) neurons. In a classical negative feedback system, prolactin stimulates the synthesis and release of dopamine from TIDA neurons, thereby inhibiting its own secretion by short-loop negative feedback. This negative feedback pathway is essential for establishing the normal patterns of prolactin secretion. Prolactin action on the TIDA neurons is mediated through the prolactin receptor, a member of the cytokine receptor family. As such, the predominant mode of signalling is through the JAK/STAT pathway, particularly involving STAT5b. This is a transcriptional regulatory pathway, and appears to be essential for the regulation of TIDA neurons by prolactin, likely through the regulation of tyrosine hydroxylase (TH) gene expression. In addition to this transcriptional regulation, however, prolactin also regulates phosphorylation of TH and induces very rapid actions on the spontaneous firing rate of these neurons, mediated through less well-defined pathways. These signaling pathways exhibit remarkable plasticity during late pregnancy and lactation. While the TIDA neurons continue to express prolactin receptors and remain responsive to prolactin, they no longer produce dopamine and they begin to synthesize the opioid peptide enkephalin. This adaptation involves a change in the balance of signalling through the JAK/STAT and through a MAP kinase pathway involving ERK1/2. This hormone-induced plasticity in the TIDA neurons overcomes the normal homeostatic processes limiting prolactin secretion, allowing a marked change in the pattern of prolactin secretion, providing the significant elevation in circulating prolactin that is critical for milk production and maternal behaviour.