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A Joint Computational/Experimental Study of Hypothalamic-Pituitary Interactions

(NIDA R01- DA19356 FY 04)

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In response to either a sterile or a fertile mating, the female rat secretes two surges of prolactin from its pituitary gland each day: one early in the morning and the other early in the evening. These surges require a reduction of the inhibitory input to the pituitary gland by dopamine of hypothalamic origin. We have shown that oxytocin of hypothalamic origin is also released in response to mating and may act as a prolactin-releasing factor (Endocrinology, 145:3386-3394, 2004). The time of day during which these events occur is transduced by vasoactive intestinal polypeptide originating from the suprachiasmatic nucleus. We have found that injection of ovariectomized rats with a single bolus of oxytocin will initiate this unique pattern of prolactin secretion (American Journal of Physiology, 290:E566-E572, 2006). Prolactin, in turn, feeds back upon dopamine neurons to increase their activities and upon oxytocin neurons to decrease their activities. Support for these roles for prolactin and vasoactive intestinal polypeptide is the presence of their receptors on both dopamine and oxytocin neurons. The net result of prolactin on dopamine neurons is delayed feedback inhibition of prolactin secretion. We have developed a mathematical model in which this feedback inhibition drives the rhythm in prolactin secretion (American Journal of Physiology, 290:E573-E582, 2006). Also, in the model we hypothesize that injection of oxytocin initiates the prolactin rhythm by activating a population of bistable dopamine-sensitive hypothalamic interneurons. Predictions from this model are currently being tested in the lab.

Project (or PI) Website

<http://www.math.fsu.edu/~bertram>

Publications

1. M. Egli, R. Bertram, M. T. Sellix, and M. E. Freeman, *Rhythmic Secretion of Prolactin in Rats: Action of Oxytocin Coordinated by Vasoactive Intestinal Polypeptide of Suprachiasmatic Nucleus Origin*, Endocrinology, 145:3386-3394, 2004.
2. M. Egli, R. Bertram, N. Toporikova, M. T. Sellix, W. Blanco, and M. E. Freeman, *Prolactin Secretory Rhythm of Mated Rats Induced by a Single Injection of Oxytocin*, American Journal of Physiology, 290:E566-E572, 2006.

3. R. Bertram, M. Egli, N. Toporikova, and M. E. Freeman, *A Mathematical Model for the Mating-Induced Prolactin Rhythm of Female Rats*, American Journal of Physiology, 290:E573-E582, 2006.
4. M. T. Sellix, M. Egli, M. O. Poletini, D. T. McKee, M. D. Bosworth, C. A. Fitch, and M. E. Freeman, *Anatomical and Functional Characterization of Clock Gene Expression in Neuroendocrine Dopaminergic Neurons*, American Journal of Physiology, 290:R1309-R1323, 2006.
5. R. Bertram, J. Tabak, N. Toporikova, and M. E. Freeman, *Endothelin Action on Pituitary Lactotrophs: One receptor, Many GTP-Binding Proteins*, Science STKE, 2006(319):pe4, 2006.