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The mechanism of GnRH pulse generation in primates: Unresolved questions

Ei Terasawa

University of Wisconsin-Madison, USA

Abstract

The pulsatility of GnRH release is essential for reproductive function. The key events in reproductive function, such as puberty onset and ovulatory cycles, are regulated by the frequency and amplitude modulation of pulsatile GnRH release. Abnormal patterns of GnRH pulsatility are seen in association with disease states, such as polycystic ovarian syndrome and anorexia nervosa. Recent studies with physiological, track-tracing, optogenetic and electrophysiological recording experiments in rodents indicate that a group of kisspeptin neurons in the arcuate nucleus (ARC) of the hypothalamus are responsible for pulsatile GnRH release. Thus, the kisspeptin neuron in the ARC, which also contains neurokinin B and dynorphin, has been called the "GnRH pulse-generator." However, a few pieces of evidence in primates do not quite fit into this concept. For example, unlike in rodents, not all kisspeptin neurons express NKB in the primate hypothalamusand our studies in rhesus monkeys indicate that pulsatile release of neuropeptide Y (NPY) occurs synchronously with GnRH pulses and modulations of NPY release by its agonists and antagonists or gonadal steroids also alter pulsatility of GnRH release. Moreover, a report shows that LH pulses can be induced by kisspeptin-10 or the opioid antagonist, naloxone, in human patients due to mutation in NKB receptors. Finally, we have extensively shown that interactions between agonists and antagonists of kisspeptin, NKB, NPY, and opioids modifying the GnRH release occur in the median-eminence neuroterminal region, rather than in the ARC where perikarya of kisspeptin, NKB, NPY and dynorphin neurons are present. Therefore, it is premature to conclude that the kisspeptin neuron in the ARC is the GnRH pulse-generator and there are several unresolved issues with the mechanism of GnRH pulse generation in primates.

Biography

Ei Terasawa is from Department of Pediatrics and Wisconsin National Primate Research Center, University of Wisconsin-Madison Joined ERP Program: 1997TeachingNeuroscience Training Program 675: Special Topics in NeuroendocrinologyCommitteesMember – Endocrinology & Reproductive Physiology Program NIH Predoctoral Training Grant Steering CommitteeMember – Endocrinology & Reproductive Physiology Program Admissions CommitteeERP T32 Faculty Trainer.

Publications

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