Reproduction

Reproduction (or procreation or breeding) is the biological process by which new individual organisms – “offspring” – are produced from their “parents”. Reproduction is a fundamental feature of all known life; each individual organism exists as the result of reproduction. There are two forms of reproduction: asexual and sexual.

The brain is the central controller of reproduction and the menstrual cycle. Reproductive endocrinologists spend their days treating patients with perturbations in reproduction as a result of pituitary diseases and manipulate pituitary hormones to enhance fertility and quality of life. Microscopic neuroanatomical images will allow a better understanding of how a tumor in the pituitary might affect vision, or a mass in the brain might cause amenorrhea. Clinical correlations that are taught every day become much clearer once the anatomical relationships are explored. The objective of a pictorial tour of Vlasak et al., from Gainesville is to elucidate anatomical and clinical relationships while showcasing the neuroanatomy of reproduction [1)].

Mammalian reproductive function depends upon a neuroendocrine circuit that evokes the pulsatile release of gonadotropin hormones (luteinizing hormone and follicle-stimulating hormone) from the pituitary. This reproductive circuit is sensitive to metabolic perturbations. When challenged with starvation, insufficient energy reserves attenuate gonadotropin release, leading to infertility. The reproductive neuroendocrine circuit is well established, composed of two populations of kisspeptin-expressing neurons (located in the anteroventral periventricular hypothalamus, Kiss1AVPV, and arcuate hypothalamus, Kiss1ARH), which drive the pulsatile activity of gonadotropin-releasing hormone (GnRH) neurons. The reproductive axis is primarily regulated by gonadal steroid and circadian cues, but the starvation-sensitive input that inhibits this circuit during negative energy balance remains controversial. Agouti-related peptide (AgRP)-expressing neurons are activated during starvation and have been implicated in leptin-associated infertility. To test whether these neurons relay information to the reproductive circuit, we used AgRP-neuron ablation and optogenetics to explore connectivity in acute slice preparations. Stimulation of AgRP fibers revealed direct, inhibitory synaptic connections with Kiss1ARH and Kiss1AVPV neurons. In agreement with this finding, Kiss1ARH neurons received less presynaptic inhibition in the absence of AgRP neurons (neonatal toxin-induced ablation). To determine whether enhancing the activity of AgRP neurons is sufficient to attenuate fertility in vivo, we artificially activated them over a sustained period and monitored fertility. Chemogenetic activation with clozapine N-oxide resulted in delayed estrous cycles and decreased fertility. These findings are consistent with the idea that, during metabolic deficiency, AgRP signaling contributes to infertility by inhibiting Kiss1 neurons [2)].

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Vlasak AL, Schaub A, Barry MER, Rhoton-Vlasak AS. The Neuroanatomy of Reproduction: Seeing Is Believing. Semin Reprod Med. 2019 Jan 3. doi: 10.1055/s-0038-1675585. [Epub ahead of print] PubMed PMID: 30605926.
2)
Padilla SL, Qiu J, Nestor CC, Zhang C, Smith AW, Whiddon BB, Rønnekleiv OK, Kelly MJ, Palmiter RD. AgRP to Kiss1 neuron signaling links nutritional state and fertility. Proc Natl Acad Sci U S A. 2017 Feb 28;114(9):2413-2418. doi: 10.1073/pnas.1621065114. Epub 2017 Feb 14. Erratum in: Proc Natl Acad Sci U S A. 2017 Apr 25;114(17):E3584. PubMed PMID: 28196880; PubMed Central PMCID:

PMC5338482.