

Estradiol increases activity of GABA afferents to GnRH neurons during the LH surge

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Gonadotropin-releasing hormone (GnRH) neurons form the final common pathway in the central control of fertility. A GnRH surge triggers the luteinizing hormone (LH) surge that causes ovulation. The GnRH surge is initiated by rising estradiol levels and a switch in estradiol action from negative to positive feedback. GABAergic afferents provide a major input to GnRH neurons and GABA can excite these cells via GABA_A receptors. In an ovariectomized estradiol-treated (OVX+E) mouse model that exhibits daily LH surges, frequency of GABA postsynaptic currents (PSCs) in GnRH neurons increases during onset and peak of the GnRH/LH surge (positive feedback); neither altered PSCs nor an LH surge occur in OVX controls. Increased frequency may be due to increased activity of presynaptic cells and/or an increase in the number of presynaptic contacts. Here we investigated the mechanism of surge-associated increases in GABA transmission to GnRH neurons. Whole-cell voltage-clamp recordings of GABA PSCs in GFP-identified GnRH neurons in acutely prepared sagittal brain slices were performed during negative feedback, surge onset, and surge peak. PSCs were recorded before and during bath application of 0.5 μ M tetrodotoxin (TTX) to block action potential firing. During surge onset and peak, TTX decreased PSC frequency in OVX+E cells that showed a baseline frequency >0.5 Hz ($p < 0.05$, $n=7$), but had no effect in cells with frequency <0.5 Hz ($n=5$). OVX cells recorded at the same times of day showed no change ($n=9$). During negative feedback, PSC frequency did not change in response to TTX in OVX+E ($n=6$) or OVX ($n=5$) cells. TTX did not affect PSC kinetic properties. These data suggest increases in GABA transmission to GnRH neurons during the surge are at least partly due to estradiol-induced increased activity of presynaptic GABA neurons; this may be part of the mechanism underlying estradiol positive feedback. Future studies will explore the sources of these estradiol-sensitive inputs and investigate if surge-associated changes in GABA signaling are influenced by, or mark co-release of, other neurotransmitters or neuromodulators.

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