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Structural and functional sex differences in the reproductive center of the hypothalamus in rats

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The hypothalamus is functionally and structurally different between female and male rats to control sex-specific reproductive functions. Gonadotropin -releasing hormone (GnRH) is secreted from the hypothalamus to regulate gonadal functions. GnRH and luteinizing hormone (LH) surges occur in females to induce ovulation with the positive feedback effects of estrogen, whereas normally sexually differentiated males have no surge secretion even if they are treated with estrogen in adulthood. In female rats, the anteroventral periventricular nucleus of the preoptic area (AVPvN-POA) and suprachiasmatic nucleus (SCN) are considered to play a critical role in the generation of GnRH/LH surges (1, 2). During estrogen-induced LH surge in ovariectomized rats, the expression of c-Fos, a transcription factor of immediate early gene, increased in GnRH neurons and the AVPvN-POA in the present study. c-Fos expression of the SCN increased estrogen-dependently before the initiation of the LH surge. On the contrary, in estrogen-treated castrated males, such increases in c-Fos were not observed in any of GnRH neurons, the AVPvN-POA and SCN. Thus, estrogen-dependent sex differences in neuronal activations of the hypothalamus are presumably exhibited in the surge generation. The functional sex differences could result from structural sex differences of the surge-generating system, because the AVPvN-POA is a sexually dimorphic nucleus, in which more densely cellular components are found in females than males. Sex difference in apoptotic cell death during the development is responsible for the formation of the AVPvN-POA (3). In postnatal rats of the present study, the protein expression of anti-apoptotic Bcl-2 was greater in the female preoptic region including the AVPvN-POA, whereas larger expression of Bax, a pro-apoptotic Bcl-2 family member, was found in males. Caspase-3 was more activated in the AVPvN-POA of postnatal males. These results suggest that mitochondrial apoptotic cascades are involved in the mechanisms for producing the sex difference in apoptosis of the AVPvN-POA in developing rats. Regarding the SCN, there was no significant sex difference in the nuclear volume and number of neurons in 1.6–1.9 months of age, although age-related changes in the neuronal cell number showed in a sex-specific manner in the present study (4). Significant loss of neurons was observed in males, but the female SCN still comprised enough number of neurons in 11.7–16.3 months of age.