Sex Difference in Glucocorticoid Regulation of Vasopressin mRNA in the Paraventricular Hypothalamic Nucleus

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SUMMARY

1. Arginine vasopressin (AVP) is synthesized in specific brain regions including the magnocellular and parvocellular divisions of the paraventricular nucleus (PVN). Whereas magnocellular AVP responds to osmotic stimuli and functions mainly—although not exclusively—as an antidiuretic hormone, that produced in the parvocellular region controls the hypothalamus–pituitary–adrenal (HPA) axis, in conjunction with CRF.

2. In view of the reported sex differences in control of the HPA axis, we studied if these also pertain to AVP mRNA in the PVN of ovariectomized–estrogenized female rats and male rats determined by in situ hybridization. AVP mRNA was measured in intact rats, adrenalectomized (ADX) rats and ADX receiving dexamethasone (DEX) of both sexes.

3. Computerized autoradiography showed that in both sexes, AVP mRNA levels in the parvocellular division of the PVN increased after adrenalectomy and decreased following DEX. However, the reduction by DEX was more pronounced in female rats. No changes were found for the magnocellular region.
Grain counting analysis of the medial–medial (MMP) and medial–lateral (MLP) subdivisions of the parvocellular region showed that the average number of grains per cell area in the MMP region of adrenally intact female rats was higher than that in males. However, in females there was no clear-cut effect of adrenalectomy on AVP mRNA levels, although the reduction after DEX treatment was again greater than that in male rats. Frequency histograms constructed by plotting the number of cells vs the number of grains per area substantiated the enhanced glucocorticoid negative control of AVP mRNA in the MMP and MLP of female rats.

4. The results indicated a sexual dimorphism in the glucocorticoid-dependent plasticity of AVP mRNA levels in the PVN. Because AVP mRNA expression differs between sexes under basal levels, after adrenalectomy, and after DEX treatment, these plastic changes may differentially condition the response to stress. Taking into consideration that stress and AVP may play a role in neurogenic hypertension, the possibility of sexual dimorphisms in AVP control may be important to assess the role of sex hormones in stress and steroid-derived hypertension.

INTRODUCTION

Arginine vasopressin (AVP) is a vasoactive peptide synthesized in several anatomical nuclei of the brain. In the magnocellular cells of the paraventricular hypothalamic nucleus (PVN) and the supraoptic nucleus (SON), AVP is produced and axonally transported, via the hypothalamic neurohypophysial tract, to the posterior pituitary (Swaab et al., 1975; De Vries et al., 1985). This system responds to osmotic changes whereby AVP acts mainly as an antidiuretic hormone peripherally (Van den Pol, 1982), although evidence that the magnocellular AVP system from the PVN and SON also influences ACTH release is also strong (Antoni, 1993). In the parvocellular region of the PVN, AVP is colocalized with CRF in a subpopulation of neurons intimately related to control of ACTH release from the anterior pituitary (Davis et al., 1986). Besides these nuclei, large groups of vasopressinergic cells are found in the bed nucleus of the stria terminalis (BNST), medial amygdala, diagonal band of Broca, and locus coeruleus (De Vries et al., 1985). Some of these areas are sexually dirmorphic. In the BNST and diagonal band of Broca, for example, sex hormones, in particular, testosterone and, on a minor scale, estradiol, increase mRNA for AVP (De Vries et al., 1994).

AVP biosynthesized in the medial parvocellular subdivision of the PVN, a stress-responsive area, shows considerable plasticity in response to changing glucocorticoid levels. Thus, increased AVP mRNA and immunoreactivity accumulate after adrenalectomy and after acute or chronic stress (Sawchenko et al., 1984; Angulo et al., 1991; Bartanuz et al., 1993; Makino et al., 1995; Herman, 1995). Conversely, down-regulation of AVP mRNA expression results from glucocorticoid negative feedback impinging upon the PVN (Davis et al., 1986;