PREGNANCY AND AGING

Two Model Systems with Altered Release Patterns of Oxytocin and Vasopressin within the Hypothalamus

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The hypothalamo-neurohypophysial system (HNS) as well as the hypothalamo-pituitary-adrenal (HPA) axis adapt to various physiological and pathophysiological conditions. The period of late pregnancy, for instance, is characterized by an attenuated responsiveness of the HPA axis to emotional and physical stressors (8), whereas, in contrast to lactation (6), the activity of the oxytocinergic system as part of the HNS is only slightly reduced (1, 8). The process of aging, on the other hand, is accompanied by an increased activity of the vasopressinergic system, mostly revealed by immunohistochemical studies on human brain tissue (9) and by in situ hybridization in aged rats (4). This could cause dysregulation of the HPA axis not only in aged rats (2), but also in aged subjects and patients suffering from psychiatric diseases (3). However, results on vasopressin (AVP) secretory responses of the HNS to various stimuli are rather contradictory.

In addition to the secretion of oxytocin (OXT) and AVP from neurohypophysial terminals, microdialysis studies provided evidence for neuropeptide release within the hypothalamic supraoptic and paraventricular nuclei (PVN) from dendrites and perikarya in response to a variety of physiological and pharmacological stimuli including exposure to emotional (12) as well as rather complex stressors like forced swimming. Such local, intrahypothalamic release was shown to be independently regulated of terminal, i.e. neurohypophysial, secretion and, thus, different physiological functions of these neuropeptides should depend upon the site of release. OXT and AVP released within these nuclei were shown to be involved in local feedback mechanisms (7, 11) and in the regulation of the HPA axis (12), respectively. Here we studied by means of microdialysis within the PVN the release patterns of OXT and AVP under basal conditions and in response to forced swim stress in two physiological model systems: pregnancy and aging.
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Virgin (n=7) and day 18/19 pregnant Wistar rats (n=8) were fitted with a microdialysis probe with its U-shaped tip located within the PVN. Two days later consecutive 30-min microdialysates (100 µl) were sampled in their home cage under basal conditions and during and after exposure to 10 min of forced swimming (19°C). In lyophilized microdialysates, OXT was quantified by radioimmunoassay. The basal release of OXT within the PVN tended to be higher in day 20/21 pregnant rats (5.55±2.12 pg/dialysate) compared to virgin controls (1.77±0.73 pg/dialysate, p<0.09, n.s.). In response to the swim stress, there was a significant increase in intra-PVN release of OXT only in virgin (2.8-fold, p<0.015), but not pregnant rats (0.7-fold, n.s.). The intranuclear release of OXT found in virgin rats accompanies the well-described release of OXT into blood in response to swim stress (5) also in pregnant rats (1, 8). Although the precise function(s) of intra-PVN-released OXT in the regulation of the basal or stress-induced activity of the HPA axis and/or the HNS have to be revealed, the increased local release of OXT in pregnant rats under basal conditions may be involved in pregnancy-related adaptations. This is supported by findings of Windle et al., describing significant effects of icv OXT on stress-induced ACTH secretion (10).

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Young adult (3 to 4 months, n=9) and aged (22 to 24 months, n=8) male Wistar rats were fitted with a chronic jugular vein catheter and with a microdialysis probe within the PVN. Two days later, basal plasma concentrations of both AVP and OXT were significantly higher in aged compared to young rats (p<0.05 both, Fig. 1). This was accompanied by an increased release of AVP (p<0.01), but not OXT, within the PVN under basal conditions (Fig. 1).

In both aged and young rats, there was a significant increase in the secretion of OXT into blood in response to the swim stress, although the response in aged rats being signifi-

![Figure 1](image-url)