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65. Corticotropin-releasing Hormone: Prenatal and Postnatal Gene Expression in the Developing Rat Hypothalamus

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Corticotropin-releasing hormone (CRH) is a neuropeptide involved in hormonal and behavioral stress responses in mammals. Being a potent convulsant, it may also play a role in infantile seizures that respond to manipulation of the CRH-ACTH-corticosteroid axis. The brain-adrenal axis and the steroid response to stress are depressed in the perinatal period; this is thought to result in protection of the brain from high toxic steroid levels generated by the stress of birth. Little is known about the role of CRH in the perinatal stress response or about the peptide's expression at hy-pothalamic and extrahypothalamic sites during that critical period. We studied the ontogeny and regulation of CRH expression in rat brain, especially in the paraventricular nu-cleus (PVN) at both mRNA and peptide levels. Immature rats (fetal days 16, 18, and 20 and postnatal days 1, 4, 7, 10, 14, 29, and 25) were used. Brains were cut into 20-micron coronal slices and relevant brain regions identified by estab-lished landmarks. Sequential slices subjected in situ were to hybridization. immunocytochemistry, and routine staining. CRH mRNA was localized by in situ hybridization using an S^{35} -labeled synthetic oligonucleotide probe complementary to codons of the 20 carboxy-terminal amino acids of CRH. A "sense" probe, similarly labeled, was used as a control. Mes-sages were first detectable on the eighteenth fetal day in the PVN and on the first postnatal day in the interstitial nucleus of the stria terminalis. Messages decreased perinatally in the PVN. concurrent with the nonresponsive period of the CRH-adrenal axis, suggesting that a decrease in CRH gene expression may contribute to this phenomenon. Better understanding of the mechanisms underlying CRH expres-sion may shed light on the long-term effects of perinatal stress and possibly on the susceptibility of the immature