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Top-down regulation of the hypothalamo-pituitary-adrenal axis by the forebrain. In the light of the observation that several genes and proteins expressed in the developing mammalian forebrain are known to be involved in the endocrine functions of the hypothalamo-pituitary-adrenal (HPA) axis, it is possible to think that the function of the mature HPA axis may be more dependent on changes in forebrain gene expression than on direct activity of the hypophyseal-adrenal system. The actual volume of the nucleus which contains the hypophyseal-adrenal system is however still relatively large compared with that of the cerebral cortex and hypothalamus. In the present study we have explored the possibility that forebrain gene expression may play an active role in the regulation of the HPA axis. To do this we have taken advantage of the fact that the preoptic area and anterior hypothalamus are interconnected. In the adult rat preoptic area is a very important site of HPA axis regulation. This is at least in part due to the role of the anteroventral third ventricle-preoptic area neuropeptide Y system. We have therefore studied the possibility that the preoptic area and anterior hypothalamus interact with the rest of the brain. We used a strategy that allowed us to develop an inverse model of gene expression in the adult rat. We combined de novo gene expression by the stereotaxic injection of a plasmid DNA construct with detection of the protein expressed by the gene. We detected the presence of a peptide related to the gene product of the plasmid by immunocytochemistry. This approach allowed us to determine the number of cells in the preoptic area and anterior hypothalamus that express the plasmid construct. We also studied the effects of the microinjection of the plasmid construct into the preoptic area on the expression of mRNA for vasopressin and corticotropin-releasing factor in the paraventricular nucleus of the hypothalamus. The results showed that expression of the plasmid construct in the preoptic area was sufficient to cause a change in the number of 2d92ce491b