Activation of 5-HT; 1A; Receptors in the Hypothalamic Paraventricular Nuclei Negatively Regulates Cytochrome P450 Expression and Activity in Rat Liver

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4617709
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Year 2018
Title Activation of 5-HT; 1A; Receptors in the Hypothalamic Paraventricular Nuclei Negatively Regulates Cytochrome P450 Expression and Activity in Rat Liver
Journal Drug metabolism and disposition: the biological fate of chemicals
Volume 46
Number 6
Pages / **Article-Number** 786-793
Mesh terms 8-Hydroxy-2-(di-n-propylamino)tetralin, pharmacology; Animals; Aryl Hydrocarbon Hydroxylases, metabolism; Corticosterone, metabolism; Cytochrome P450 Family 2, metabolism; Growth Hormone, metabolism; Liver; Male; Paraventricular Hypothalamic Nucleus, drug effects, metabolism; Rats; Rats, Wistar; Receptor, Serotonin, 5-HT1A, metabolism; Serotonin, metabolism; Serotonin Receptor Agonists, pharmacology; Steroid 16-alpha-Hydroxylase, metabolism

Our recent work suggested a negative effect for the serotonergic innervation of the paraventricular nuclei (PVN) of the hypothalamus on growth hormone secretion and growth hormone-dependent expression of CYP2C11. The aim of our present research was to determine the effect of the activation of the 5-hydroxytryptamine [(5-HT) serotonin] 5-HT; 1; or 5-HT; 2; receptors in the PVN on the expression and activity of cytochrome P450 in male rat liver. The serotonergic agonists 5-carboxyamidotryptamine [(5-CT), a 5-HT; 1; receptor-type agonist], 8-hydroxy-2-(di-n-propyloamino)-tetralin [(8-OH-DPAT), a 5-HT; 1A; receptor agonist], sumatriptan (a 5-HT; 1B/D; receptor agonist), and 2,5-dimethoxy-4-iodoamphetamine [(DOI), a 5-HT; 2A/C; receptor agonist] were individually injected into the PVN. The liver cytochrome P450 activity and expression and the levels of serum and pituitary and hypothalamic hormones were measured. 5-CT and 8-OH-DPAT significantly decreased the activity and expression of; CYP2C11; at both the mRNA and protein levels, which was accompanied by an increase in pituitary and hypothalamic somatostatin levels and a decrease in the serum growth hormone concentration. The expression of; CYP3A1/23; also decreased. The serum corticosterone concentration declined after the injection of 8-OH-DPAT. The obtained results indicated that 5-HT; 1A; but not the 5-HT; 1B/D; or 5-HT; 2; receptors in the PVN are engaged in the negative neuroendocrine regulation of cytochrome P450 via the stimulation of hypothalamic somatostatin secretion and in the decreases in the serum growth hormone and corticosterone concentrations. Since the affected enzymes metabolize steroids and drugs and 5-HT; 1A; receptors are engaged in the action of psychotropic drugs, the results obtained may be of both physiologic and pharmacological meaning.

ISSN/ISBN 1521-009X
edoc-URL https://edoc.unibas.ch/82364/
Full Text on edoc No;
Digital Object Identifier DOI 10.1124/dmd.117.079632
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/29555828