

## Publication

Activation of brain serotonergic system by repeated intracerebral administration of 5-hydroxytryptophan (5-HTP) decreases the expression and activity of liver cytochrome P450

### JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

**ID** 4617711

**Author(s)** Rysz, Marta; Bromek, Ewa; Daniel, Władysława A.

**Author(s) at UniBasel** [Rysz, Marta Anna](#) ;

**Year** 2016

**Title** Activation of brain serotonergic system by repeated intracerebral administration of 5-hydroxytryptophan (5-HTP) decreases the expression and activity of liver cytochrome P450

**Journal** Biochemical Pharmacology

**Volume** 99

**Pages / Article-Number** 113-22

**Keywords** Antidepressants; Brain serotonin; Intraventricular 5-hydroxytryptophan; Liver cytochrome P450; Neuroendocrine regulation

**Mesh terms** 5-Hydroxytryptophan, administration & dosage; Animals; Brain, drug effects, metabolism; Cytochrome P-450 Enzyme System, biosynthesis; Drug Administration Schedule; Injections, Intraventricular; Liver, drug effects, metabolism; Male; Rats; Rats, Wistar; Serotonin, metabolism

Our recent studies suggest that brain serotonergic system may be involved in the neuroendocrine regulation of cytochrome P450 expression. Intracerebral injection of the serotonergic neurotoxin 5,7-dihydroxytryptamine affected serum hormone concentration and increased the expression and activity of the hormone-dependent isoforms CYP1A1/2, CYP2C11 and CYP3A1. Therefore, the aim of the present study was to investigate the effect of stimulation of brain serotonergic system on cytochrome P450 expression in the liver. The serotonin precursor 5-hydroxytryptophan (5-HTP) was injected for 5 days to the lateral ventricles of rat brain. Afterwards, the brain concentrations of serotonin and its metabolite 5-hydroxyindoleacetic acid 5-HIAA, serum hormone levels and liver cytochrome P450 expression and activity were measured. 5-HTP potently increased the concentration of serotonin and its metabolite 5-HIAA in all the brain structures studied including the hypothalamus. The brain concentrations of noradrenaline or dopamine and its metabolites were not changed in that structure. At the same time, a significant decrease in the serum concentration of the growth hormone and an increase in that of thyroxine were observed. In the liver, the activity of CYP1A, CYP2A, CYP2B, CYP2C11 and CYP3A was diminished, which positively correlated with a decrease in the respective CYP protein levels and a reduction in the mRNA levels of CYP1A2, CYP2A2, CYP2C11, CYP3A1 and CYP3A2. The obtained results provide evidence to prove that brain serotonergic system negatively regulates liver cytochrome P450 expression via endocrine system and suggest mechanisms by which this enzyme may be regulated by drugs with a serotonergic profile such as antidepressants.

**Publisher** Elsevier

**ISSN/ISBN** 0006-2952 ; 1873-2968

**edoc-URL** <https://edoc.unibas.ch/82366/>

**Full Text on edoc** No;

**Digital Object Identifier DOI** 10.1016/j.bcp.2015.11.014

**PubMed ID** <http://www.ncbi.nlm.nih.gov/pubmed/26581122>

**Document type (ISI)** Journal Article