PRELIMINARY COMMUNICATION

EFFECTS OF CHRONIC TREATMENT WITH CLASSIC AND NEWER ANTIDEPRESSANTS AND NEUROLEPTICS ON THE ACTIVITY AND LEVEL OF CYP2D IN THE RAT BRAIN

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The aim of the present work was to study the effect of chronic treatment with pharmacological doses of selected antidepressants (imipramine, mirtazapine) and neuroleptics (thioridazine, risperidone) on the activity and level of CYP2D in the rat brain. Our previous studies carried out on the liver showed that after chronic treatment with psychotropics, the activity of CYP2D was significantly decreased by imipramine, thioridazine and risperidone, but increased by mirtazapine. Our preliminary results suggest that the same may happen in the brain, where similar tendencies in changes in CYP2D activity were observed. Imipramine, thioridazine and risperidone diminished, while mirtazapine tended to accelerate the rate of ethylmorphine O-deethylation, a specific reaction for measurement of CYP2D activity. In the case of thioridazine, the observed decrease in the enzyme activity was the most pronounced and statistically significant. The level of brain CYP2D4 was not substantially changed by the prolonged administration of the investigated drugs (imipramine 136.3 ± 14.9%, thioridazine 121.9 ± 3.5%, risperidone 113.5 ± 7.8%, mirtazapine 80.3 ± 1.5% of the control), and did not correspond positively with the measured CYP2D activity. This may imply that the observed changes in the CYP2D activity were not caused by the involvement of those psychotropics in the regulation of CYP2D4. In conclusion, our preliminary results suggest that the effects of prolonged treatment with antidepressants and neuroleptics on the activity of CYP2D found in our previous study in the liver also occur in the brain, which may have an impact on the pharmacological and clinical profile of those drugs.

Key words: CYP2D, brain, imipramine, mirtazapine, thioridazine, risperidone