

THE CHANGES OF MATRIX METALLOPROTEINASE 2, 9 ACTIVITY AND METALLOTHIONEIN LEVEL IN RAT'S BRAIN UNDER CADMIUM INFLUENCE

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The main functions assigned to metallothioneins (MT) are the metal detoxification (heavy metals in particular) like Mercury and Cadmium, metal homeostasis including Copper and Zinc, anti-oxidation against reactive oxygen species, protection against DNA damage, oxidative stress, cell survival, angiogenesis, apoptosis, as well as increase proliferation, in the body. Matrix metalloproteinases (MMPs) are members of the proteases which share the conserved zinc-binding motif in their catalytic active site. It was originally thought that their main function is to degrade the various components of the extracellular matrix, but last data allow to appreciate their significance as regulators of extracellular tissue signalling networks. The changes of metalloproteinases activity and correlation with metallothionein level under toxic factors are not well known. The main goal of work was the investigation of the MMP2 and MMP9 activity and metallothionein level in the brain under cadmium influence at different doses. The 18 Wistar rats divided into 3 groups were used for the experiment. CdCl₂·2.5H₂O in doses 0.1 µg/kg and 1 µg/kg was given to rats intragastrically in drinking water during 36 days. The rats were decapitated under Isoflurane anesthesia according to ethical rules. The relative activity (in arbitrary units – au) of pro- and active forms of MMP9 and MMP2, total protein (TP) and metallothionein levels were studied. It was shown that low doses of exogenous cadmium (0.1 µg/kg) have not lead to changing in both gelatinase activity. But high doses of cadmium (1 µg/kg) caused a reliable increase of pro-MMP9 activity in the brain: pro-MMP9 was increased from 17.9±0.8 au/mgTP to 22.4±2.8 au/mgTP. At the same time, activity of pro- and active forms of MMP2 was decreased (12.7±1.0 au/mgTP and 13.4±1.5 au/mgTP compare to the 18.1±0.9 au/mgTP and 17.8±0.7 au/mgTP in the control rats accordingly). The intoxication of Wistar rats with small doses of Cd, over time, causes the gradual exhaustion of the levels of MT in the brain, depending on the dose administered and the time required for the accumulation of this metal. In the hippocampus, the values recorded disclosed sharp reductions in MT content; 3.4 ± 0.08 µg/100 mg of tissue under 0.1 µg Cd effect and 2.7 ± 0.1 µg/100 mg of tissue under 1.0 µg Cd effect, when compared to the controlled experiment, 4.7 ± 0.3 µg/100 mg of tissue. Obtained results indicate the dose-dependent and tissue-specific effect of cadmium on MMP-depended protein degradation and decreased level of metallothionein under intoxication in the brain.

Keywords: matrix metalloproteinases, metallothioneins, brain, Cd