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МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

EXPRESSION OF CELL DEATH MARKERS IN RAT HIPPOCAMPUS AFTER LONG-TERM FLUORIDE INTOXICATION

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Fluorine in ionic form (F^-) crosses the blood-brain barrier relatively freely and exerts numerous negative effects on the cells of nervous system, which leads to the development of neurological and cognitive disorders. Previously, we showed that long-term consumption of excessive F^- doses by the rats induces pathomorphological changes and death of hippocampal neurons, which may be one of the causes of CNS dysfunction. The aim of this work was to evaluate the level of expression of the key mediators of mitochondrial, death receptor, and TGF-β-dependent pathways of cell death in the rat hippocampal cells after prolonged F-intoxication.

Male Wistar rats received the water with 0.4 (control), 5, 20 and 50 mg/L F^- (as NaF) *ad libitum* during the year. Changes in expression of cell death markers were determined by Western blotting in hippocampal homogenates.

Consumption of 5–50 mg/L F^- by rats led to a dose-dependent increase in the content of cytochrome C in the cell cytosol, which indicates a disruption of the outer mitochondrial membrane. The cellular expression of pro-apoptotic protein Bax increased, but the activity of anti-apoptotic protein Bcl-2 decreased. An inactive pro-caspase 3 was observed to underwent proteolysis to its active form in the hippocampus of rats given 20–50 mg/L F^-. In contrast, intoxication with F^- did not affect the expression of one of the key components of receptor death pathway – membrane receptor Fas. However, the consumption of F^- excess by the rats was accompanied by a dose-dependent stimulation of transcription factor p53, which is a marker of DNA damage, as well as of multifunctional cytokine TGF-β and one of its effectors – protein kinase JNK.

Thus, excessive F^- consumption by the rats leads to activation of the mitochondrial apoptosis pathway in hippocampal cells. The toxic F^- effect can also be associated with the processes induced by DNA damage or involving stimulation of TGF-β-dependent cascades of cell death.

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