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МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

ADDITIVE PROTECTIVE EFFECT OF INSULIN AND ALPHA-TOCOPHEROL ON BRAIN CORTICAL NEURONS IN OXIDATIVE STRESS AND IN THE CONDITIONS OF TWO-VESSEL BRAIN ISCHEMIA AND REPERFUSION

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The detection of neuroprotectors increasing the protective and antioxidant effects of each other may promote the development of innovative approaches for treatment and prevention of diseases concerned with CNS damage. Insulin and alpha-tocopherol (alpha-T) significantly increased the protective effects of each other on cultured brain cortical neurons in oxidative stress. Immunoblotting, RT-PCR, flow cytomentry and other methods were used in the work. Studying the mechanism of insulin and alpha-T action it was found that their combined use activated Akt protein kinase to greater extent than the exposure of neurons to one of them. Akt activation increases the cell viability as it leads to GSK-3beta protein kinase inactivation (activation of this enzyme disrupts mitochondrial function) and to decrease of Bax/Bcl-2 ratio. Insulin elevated the formation of pGSK-3beta (Ser^9) and thus inactivated the enzyme in brain cortical neurons, alpha-T increased its effect. Insulin and alpha-T decreased Bax/Bcl-2 ratio in neurons, elevating the expression and the level of Bcl-2. The combined effects of insulin and alpha-T on ERK1/2 also promoted their additive protective effect. Two-vessel brain ischemia and reperfusion resulted in the increase of the levels of lipid peroxidation products and in oxidative inactivation of Na^+, K^+-ATPase in rat brain cortex. The combined administration of intranasal insulin (0.25 IU) and alpha-T prevented the increase of the levels of Shiff bases, di- and triene conjugates and increased Na^+, K^+-ATPase activity in brain cortex in conditions of ischemia and reperfusion to greater extent as compared to administration of one of these compounds. Thus, alpha-T is able to enhance the protective effect of insulin *in vitro* and *in vivo*.

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