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INTRANASAL ADMINISTRATION OF HSP70: MOLECULAR AND THERAPEUTIC CONSEQUENCES

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Hsp70 and other molecular chaperones function as a complex neuroprotective system, which fails in the brains of aged people and Alzheimer disease (AD)-type neuropathologies. It was demonstrated that intranasally injected exogenous Hsp70 (eHsp70) effectively bypassed the blood-brain barrier and penetrates brain regions of the model animals. It was shown that chronic administration of eHsp70 decreases beta-amyloid level and the number of Aβ-plaques in two mouse models of AD. In both cases, eHsp70 restored learning and memory parameters as well as functional state of neurons. Characteristically, eHsp70 treatment increased synaptophysin level and protects neurons in brain areas most affected in AD patients such as hippocampus and neocortex. It was also demonstrated that eHsp70 can promote longevity and life quality in male mice. The eHsp70 treatment decreased accumulation of aging marker lipofuscin and modulates the activity of UPS by increasing expression of several proteasome subunits including immunoproteasome subunit β5i. Deep sequencing studies exploring mice of brain regions of AD-model 5XFAD different age groups treated with eHsp70 revealed candidate genes and signal pathways probably underlying beneficial effects of eHsp70 treatment. Taken together, our findings established intranasal administration of exogenous human Hsp70 as a practical therapeutic approach for the treatment of various neurodegenerative diseases and aging.

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