THE PROFOUND THERAPEUTIC EFFECT OF EXOGENOUS HSP70 ON ALZHEIMER'S TYPE DEGENERATION IN OLFATORY BULBECTOMIZED MICE

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Brain deterioration resulting from “protein folding” diseases, such as the Alzheimer’s disease (AD), is one of the leading causes of morbidity and mortality in the aging human population. Heat shock proteins (HSPs) constitute the major cellular quality control system for proteins that mitigates the pathological burden of neurotoxic protein fibrils and aggregates. However, the therapeutic effect of HSPs has not been tested in a relevant setting. Here we report the dramatic neuroprotective effect of recombinant human Hsp70 in the bilateral olfactory bulbectomy (OBE) mouse model. We show that intranasally administered Hsp70 rapidly enters the afflicted brain regions and mitigates multiple AD-like morphological and cognitive abnormalities observed in OBE animals. In particular, it normalized the density of neurons in the hippocampus, which correlated with the diminished accumulation of amyloid b (Ab) peptide. Consistently, Hsp70 also fully protected spatial memory, which remained at the level of control animals for at least eight months following treatment. The long-lasting therapeutic effect of Hsp70 suggests a novel mechanism of action and establishes it as a practical and potent agent for treatment of neurodegenerative diseases associated with abnormal protein biogenesis and cognitive disturbances, such as AD, for which neuroprotective therapy is urgently needed.

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