

LEPTIN INDUCES NEUROGENESIS AND NEUROPROTECTION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disease associated with senile b-amyloid (Ab) plaques and cognitive decline. Neurogenesis in the adult hippocampus, which is heavily affected by progressive neurodegeneration and Ab pathology, is implicated in regulating learning and memory, and is increased in human postmortem brain of AD patients and APP/PS1 double transgenic mice. Leptin, an adipose-derived hormone, promotes neurogenesis in the adult hippocampus but the manner in which these effects may interact in the AD brain is still unknown.

Aims: We examined the possibility that leptin stimulates the proliferation of neuronal precursors in doubly transgenic APP/PS1 mice.

Methods: We measured proliferating hippocampal cells after intracerebroventricular administration of a lentiviral vector encoding leptin.

Results: Leptin treatment for 3 months increased BrdU labeling of cells in the subgranular zone of the hippocampal dentate gyrus (DG). This increase in

BrdU labeling after the administration of leptin was caused by an increase in cell proliferation, but also a decrease in neurodegeneration, as revealed by Fluoro Jade staining.

Conclusions: Taken together, the above results suggest that in APP/PS1 mice leptin exert an acute neuroprotective effect in stimulating neurogenesis, and they suggest the possibility that modulating leptin AD neurodegeneration may be recovered.