

Neural stem cells improve cognition via BDNF in a transgenic model of Alzheimer disease.

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Public Summary:

Our findings demonstrate that neural stem cells can ameliorate complex behavioral deficits associated with widespread Alzheimer disease pathology via BDNF.

Scientific Abstract:

Neural stem cell (NSC) transplantation represents an unexplored approach for treating neurodegenerative disorders associated with cognitive decline such as Alzheimer disease (AD). Here, we used aged triple transgenic mice (3xTg-AD) that express pathogenic forms of amyloid precursor protein, presenilin, and tau to investigate the effect of neural stem cell transplantation on AD-related neuropathology and cognitive dysfunction. Interestingly, despite widespread and established A β plaque and neurofibrillary tangle pathology, hippocampal neural stem cell transplantation rescues the spatial learning and memory deficits in aged 3xTg-AD mice. Remarkably, cognitive function is improved without altering A β or tau pathology. Instead, the mechanism underlying the improved cognition involves a robust enhancement of hippocampal synaptic density, mediated by brain-derived neurotrophic factor (BDNF). Gain-of-function studies show that recombinant BDNF mimics the beneficial effects of NSC transplantation. Furthermore, loss-of-function studies show that depletion of NSC-derived BDNF fails to improve cognition or restore hippocampal synaptic density. Taken together, our findings demonstrate that neural stem cells can ameliorate complex behavioral deficits associated with widespread Alzheimer disease pathology via BDNF.

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