PHARMACOLOGICAL ENHANCEMENT OF NEUROGENESIS AND NEURONAL PLASTICITY: A PROMISING APPROACH TO TREAT ALZHEIMER DISEASE

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Introduction: Alzheimer disease (AD) is a multifactorial disorder which is associated with abnormal levels of neurotrophic factors and is characterized by unsuccessful neurogenesis, compromised neuronal plasticity and by tau and Aβ pathologies.

Aim: The aim of this study was to test the hypothesis that enhancement of neurogenesis and neuronal plasticity can reverse cognitive impairment in the presence of tau and Aβ pathologies.

Methods: We administered intraperitoneally an 11-mer peptide, corresponding to an active region of CNTF, daily for six weeks in 6-7 month female 3xTg-AD mice and non-transgenic control animals matched for strain and genetic background, the 129/SVxC57BL/6 mice.

Results: Peptide 6 enhanced dentate gyrus neurogenesis and inhibited ectopic birth in the granule cell layer. It increased neuronal plasticity in the hippocampus and cerebral cortex as measured by increase in MAP2 and synaptophysin. The 3xTg-AD mice showed intraneuronal accumulation of Aβ1-42 and phosphotau and treatment with Peptide 6 had no detectable effect on these pathological changes. The treatment with Peptide 6 inhibited impairments in object discrimination task as well as in spatial reference memory task in 3xTg-AD mice.

Conclusions: Impairments in neurogenesis, neuronal plasticity and cognition precede the formation of neurofibrillary tangles and Aβ plaques in 3xTg-AD mice. Pharmacologically shifting the balance from neurodegeneration to regeneration of the brain can restore cognition even in the presence of tau and Aβ pathologies.

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