[*J. Neurosci. Res.*, **50**, 1023-1029 (1997)] [Lab. of Molecular Biology]

Lipopolysaccharide Enhances Synthesis of Brain-derived Neurotrophic Factor in Cultured Rat Microglia.

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Expression of neurotrophins in pure micriglia cultured from embryonic rat brain and the effects of lipopolysaccharide (LPS) on the expression were investigated. In untreated cultures nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin (NT)-4/5 mRNAs were detected by use of the reverse transcriptase-polymerase chain reaction, but NT-3 mRNA was not. LPS stimulation causd a marked increase in BDNF mRNA expression in addition to a slight increment of the NT-4/5 mRNA level; however, the NGF mRNA level was not affected. LPS also increased BDNF-like immuinoreactivity in cultured microglia, an action consistent with an elevation of BDNF mRNA. These results demonstrate that LPS stimulates synthesis of BDNF and probably NT-4/5, specific ligands for tyrosine kinase receptor TrkB, suggesting that activated microglia, which appear in the damaged brain, participate neuronal regeneration via production of such neurotrophins.

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Administration of Corticosterone Alters Intracellular Localization of Brain-derived Neurotrophic Factor-like Immunoreactivity in the Rat Brain.

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We investigated the distribution of immunoreactivity for brain-derived neurotrophic factor (BDNF) in rat brain after peripheral administration of corticosterone or vehicle. In the immunohistochemical study, BDNF-like immunoreactivity (LI) was observed predominantly in the nucleus of the cortical and hippocampal neurons in the brain of vehicle-treated rats. In corticosterone-treated rats, BDNF-LI was markedly reduced in the nucleus and concomitantly increased in cytoplasm. Western immunoblot study also demonstrated that corticosterone significanlty reduced BDNF-LI in the nuclear fraction of the cerebral cortex and hippocampus . These results indicate that corticosterone regulates the intracellular localization of BDNF and/or its derivatives in the rat brain.

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Stimulation of NGF Production by Tryptophan and Its Metabolites in Cultured Mouse Astroglial Cells.

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Effects of various amino acids and tryptophan metabolites on the synthesis of nerve growth factor (NGF) in cultured mouse astroglial cells were evaluated. L-Tryptophan stimulated NGF producion in a dose-dependent manner. Serotonine and quinolinic acid slightly increased NGF synthesis. L-Kynurenine had a marked stimulatory effect on NGF production at a dose of 10 micromole. In contrast, kynurenic acid had no effect on the reaction. L-Glutamine, L^glutamic acid, L-phenylalanine and L-methionine produced no significant change in NGF synthesis. These results were discussed in relation to the treatment of Alzheimer's disease.

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Continuous Infusion of β-Amyloid Protein into the Rat Cerebral Ventricle Induces Learning Impairment and Neuronal and Morphological Degeneration.

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To investigate the toxicity of β-amyloid protein, a component of the senile plaques in Alzheimer's disease, it was infused into the cerebral ventricle of rats by a mini-osmotic pump. Performances in the water maze and passive avoidance tasks in β-amyloid protein-treated rats were impaired. ChAT activity significantly desreased in the hippocampus both immediately and 2 weeks after the cessation of the infusion. These results suggest that β-amyloid protein produces some damage in the central nervous system in vivo.