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## Endogenous Neurotrophin-3 Is Retrogradely Transported in the Rat Sciatic Nerve.

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To address the active transport of neurotrophins, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) in the peripheral nerves, we examined the levels of proteins and mRNAs in the sciatic nerve of adult rats following transection. NT-3 protein increased one day after transection only in the distal segment next to the transection site and returned to the original level two days later. This was considered to reflect accumulation of NT-3 transported from the periphery toward the neuronal cell bodies. An increase in BDNF protein was observed simultaneously in both the distal and proximal stumps three days after transection. BDNF mRNA was elevated in the same stumps two days after transection, suggesting that BDNF was produced within the transected stumps. These observations demonstrate that NT-3, like NGF, is retrogradely transported in the sciatic nerve but that BDNF is not. This suggests that NT-3 plays a role in the conveyance of trophic signals from target organs to neurons.

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## Brain-derived Neurotrophic Factor Prevents Neuronal Cell Death Induced by Corticosterone.

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Corticosterone (CORT), one of the glucocorticoids, causes neuronal damage in the hippocampus, but the mechanism(s) of action underlying its effects remains unknown. In this study, the effects of CORT on Brain-derived neurotrophic factor (BDNF) protein contents and mRNA expression were investigated in relation to neuronal survival/death of cultured rat hippocampal neurons, because BDNF may exert its putative protective and trophic effects through an autocrine mechanism in the hippocampus. Administration of CORT accelerated the neuronal death that proceeds after serum deprivation, and simultaneously reduced the levels of BDNF mRNA and intracellular BDNF content. Exogenously added BDNF actually attenuated CORT-induced neuronal death, but not in the presence of K252a, an inhibitor of the tyrosine kinase activity of Trk family receptors. These observations suggest that CORT induces damage to hippocampal neurons, at least partly, via reducing their BDNF synthesis.

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## 4-Methylcatechol Increases Brain-derived Neurotrophic Factor Content and mRNA Expression in Cultured Brain Cells and in Rat Brain *in vivo*.

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Practical use of brain-derived neurotrophic factor (BDNF) as therapy is limited by two serious problems, *i.e.*, its inability to cross the blood-brain barrier and its instability in the bloodstream. In the present study, we investigated the effects of 4-methylcatechol (4-MC) on BDNF content and mRNA expression in cultured brain cells and *in vivo* in the rat brain. 4-MC elevated BDNF content in culture media of both rat astrocytes and neurons with different dose-response relations. We also found that ventricularly administered 4-MC facilitated an increase in the BDNF content in the cerebral cortex and hippocampus in association with its diffusion into the brain parenchyma, and i.p. administration of 4-MC enhanced BDNF mRNA expression in the infant rat brain, in which the blood-brain has not yet fully been established. These results demonstrate that 4-MC, once delivered into the brain, can stimulate BDNF synthesis.

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## Induction of a Physiologically Active Brain-derived Neurotrophic Factor in the Infant Rat Brain by Peripheral Administration of 4-Methylcatechol.

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Effects of 4-methylcatechol (4-MC), a known potent stimulator of nerve growth factor (NGF) synthesis, on expression of brain-derived neurotrophic factor (BDNF) mRNA and BDNF-like immunoreactivity (BDNF-LI) was investigated in infant rat brains. A single intraperitoneal administration of 4MC caused transient increases in the levels of BDNF mRNA and BDNF-LI in neurons of the cerebral cortex from 1 to 3 h and 3 to 12 h, respectively, after the injection. Repetitive injections of 4MC to newborn rats (12-h intervals for 10 days) caused a marked and besides elevating the number of cells containing calbindin D-28 and enhancing its immunoreactive intensity in the pyriform cortex and hippocampus. These findings demonstrate that 4-MC stimulates *de novo* synthesis of BDNF in the infant rat brain, resulting in acceleration of the developmental expression of calbindin D-28.