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Simultaneous Expression of Brain-derived Neurotrophic Factor and Neurotrophin-3 in Cajal-Retzius, Subplate and Ventricular Progenitor Cells during Early Development Stages of the Rat Cerebral Cortex.

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To identify production sites and action targets of neurotrophins during neurogenesis, we investigated immunoreactivities of neurotrophins and their tyrosine kinase receptors in the cerebral cortex of rat embryos. Two sets of ligand-receptor systems, brain-derived neurotrophic factor/TrkB and neurotrophin-3/TrkC, were expressed simultaneously in Cajal-Retzius, subplate neurons and ventricular multipotent stem cells at embryonic days 13 and 15. Intraventricular administration of brain-derived neurotrophic factor or neurotrophin-3 at embryonic day 16 markedly modulated microtubule-associated protein II and/or Hu protein expression in different ways in the cortical plate cells by embryonic day 20. These observations indicate the involvement of autocrine and/or local paracrine action of brain-derived neurotrophic factor and/or neurotrophin-3 during formation of the cerebral cortex.

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Reduction in Brain-derived Neurotrophic Factor Protein Level in the Hippocampal CA1 Dendritic Field Precedes the Delayed Neuronal Damage in the Rat Brain.

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Utilizing a specific polyclonal antibody against a peptide unique for brain-derived neurotrophic factor (BDNF), we investigated the regional and temporal profiles of immunoreactivity of the BDNF protein in the rat hippocampus after transient forebrain ischemia. The pattern of immunoreactivity for the BDNF receptor (TrkB) was also examined and compared with that for BDNF. In the early phase after ischemia, we observed a distinct regional difference in immunoreactivity between the pyramidal cell layer and the stratum radiatum of the CA1 subfield. In the pyramidal cell layer, there was a rapid and transient increase in the positive immunostaining for both BDNF and TrkB. By contrast, in the stratum radiatum there was a marked decrease in BDNF immunoreactivity, but not one in that of TrkB. One week after ischemia, high immunoreactivity for both BDNF and TrkB was observed in the reactive astrocytes in the dendritic field of the CA1 subfield. These findings suggest that a transport of BDNF from the neuronal soma to the dendrites of the stratum radiatum might be ceased after the ischemic insult. Thus, a dysfunctional autocrine mechanism of BDNF within the CA1 neuron may be involved in the pathogenesis of selective neuronal damage after ischemia.

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Nerve Growth Factor Levels in the Cerebrospinal Fluids Are High in the Inflammatory Neurological Disorders.

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Nreve growth factor (NGF) is one of neurotrophic agents, which promote differentiations or support survivals and functions of some populations of neurons, influencing its effects not only on the peripheral sensory and sympathetic neurons. Patients with acute MS, traumatic injury or hypertensive cerebral hemorrhage show higher NGF levels in the CSF. These results suggest that NGF in the human CSF is linked to neurological disorders.

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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, brain-derived neurotrophic factor, and neurotrophin-3 in the peripheral nerves, we examined the levels of proteins and messenger RNAs in the sciatic nerve of adult rats following transection. Neurotrophin-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 neurotrophin-3 transported from the periphery toward the neuronal cell bodies, because the neurotrophin-3 messenger RNA level was not changed in any sciatic segments during this experimental period. An increase in brain-derived neurotrophic factor protein was observed simultaneously in both the distal and proximal stumps three days after transection. Brain-derived neurotrophic factor messenger RNA was elevated in the same stumps two days after transection. These observations demonstrate that neurotrophin-3, like nerve growth factor, is retrogradely transported in the sciatic nerve but that brain-derived neurotrophic factor is not. This suggests that neurotrophin-3 plays a role in the conveyance of trophic signals from target organs to neurons.