[*Neuroscience*, **82**, 653-670 (1998)] [Lab. of Molecular Biology]

Brain-derived Neurotrophic Factor-like Immunoreactivity in the Adult Rat Central Nervous System Predominantly Distributed in Neurons with Substantial Amounts of Brain-derived Neurotrophic Factor Messenger RNA or Responsiveness to Brain-derived Neurotrophic Factor.

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Distribution of brain-derived neurotrophic factor-like immunoreactivity was investigated in the adult rat brain using two types of antibodies against peptides, V2 and V4, unique to the brain-derived neurotrophic factor. Both antibodies recognized an identical precursor form in lysates of COS7 cells transfected with brain-derived neurotrophic factor gene. These indicated that both antibodies recognized identical precursor protein(s) or its derivative(s). Immunochemical studies showed that anti-V2 predominantly stained the cytoplasm of cells; whereas the anti-V4 bound to the nucleus. Cell populations with the immunoreactivity were similar in most brain sections stained with either anti-V2 or anti-V4 antibodies. These results suggest that brain-derived neurotrophic factor-like immunoreactivity distributes in neurons responding to brain-derived neurotrophic factor and in neurons expressing abundant brain-derived neurotrophic factor messenger RNA. These provide additional information to elucidate the function of brain-derived neurotrophic factor in the rat central nervous system.

[*J. Neurol.*, **245**, 781-793 (1998)] [Lab. of Molecular Biology]

Histological Investigation of Spinal Cord Lesions in the Spinal Hyperostotic Mouse (*twy/twy*): Morphological Changes in Anterior Horn Cells and Immunoreactivity to Neurotrophic Factors.

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We examined the morphology of spinal accessory motoneurons and immunoreactivity to neurotrophins, brain-derived neurotrophic factor (BDNF) and neurotrophin (NT)-3, as well as the presence of reactive astrocytosis in 70 tiptoe walking Yoshimura (twy) mice that develop calcification at C1-C2 vertebral level compressing the spinal cord. At the level of compression, the area of neuronal soma and total length of dendrites of wheat germ agglutinin-horseradish peroxidase (WGA-HRP)-labelled accessory motoneurons in the medial cell pool decreased significantly with decrement in motoneuron population, relative to the control. In contrast, at sites rostral to the compressive lesion, a significant enlargement of the neuron soma and dendritic elongation were noted. At this site, enhanced BDNF and NT-3 immunoreactivities were evident in the anterior horn cells. In mice with a more severe degree of compression, astrocyte-like cells showing BDNF immunoreactivity became abundant and axons in the anterior column demonstrated a marked NT-3 immunoreactivity. We speculate that the presence of BDNF and NT-3 in neurons and astrocyte-like cells is proportionate to the severity of chronic mechanical compression and may contribute to the heterotrophic neuronal reserve and survival.

[*Jpn. J. Pharmacol.*, **76**, 321-323 (1998)] [Lab. of Molecular Biology]

Repeated Injections of Nicergoline Increase the Nerve Growth Factor Level in the Aged Rat Brain.

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We studied whether nicergoline, clinically active in chronic cerebrovascular insufficiency, influences nerve growth factor (NGF) levels in the rat brain. In young Fischer rats, repeated intraperitoneal injections of nicergoline (0.3 and 1.0 mg/kg body weight) did not show any effects on frontal NGF contents determined by a highly sensitive enzyme immunoassay. In aged rats, 22-month-old, however, repeated injections of nicergoline (1.0 mg/kg body weight) induced a significant increase in the NGF level in the frontal region.

[*NeuroReport*, **9**, 1661-1665 (1998)] [Lab. of Molecular Biology]

Neurotrophin Switching in Spinal Motoneurons of Amyotrophic Lateral Sclerosis.

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To clarify the roles of neurotrophins in the human spinal motoneurons, with special reference to amyotrophic lateral sclerosis (ALS), we studied the immunohistochemical localizations of neurotrophins and their receptors in spinal cords of patients with ALS and compared them with controls. In the controls, the majority of motoneurons showed BDNF-, NT3-, trkB- and trkC-like immunoreactivity (-LI) suggesting that the motoneurons receive an autocrine regulation by both BDNF and NT3. In ALS patients, about three-quarters of the motoneurons had degenerated and the remaining motoneurons showed significantly decreased BDNF-LI, increased NGF- and trkA-LI. These findings indicated neurotrophin-switching in the remaining spinal motoneurons of ALS patients from BDNF and NT3 responsive to NGF responsive.