

7 ABSTRACT

Comparison of *in vivo* and *in vitro* effects of BDNF on the development of serotonergic neurons

Serotonergic neurons in the central nervous system are crucial in the control of autonomic function and behavior. Major psychiatric and neurodegenerative diseases are linked to altered functions of serotonergic neurons. Beyond Serotonin other trophic factors promoting development of the serotonergic system are brain-derived neurotrophic factor (BDNF), a member of the neurotrophin family and S100 β , a calciumbinding protein. In the present study the development of the serotonergic system in mice lacking BDNF was investigated. In addition the effects of BDNF and S100 β on mouse raphe and hippocampal primary cultures were tested.

In 16 days old mice the number of serotonergic neurons in raphe nucleus and as well as serotonergic fibers in forebrain was increased. Serotonin and its main metabolite 5-hydroxyindolacetic acid revealed a significant increase in important target areas in BDNF $-/-$ compared to BDNF $+/+$ mice. The more extensive development in mice lacking BDNF indicate that the lack of BDNF is compensated by other factors.

In raphe primary cultures of NMRI mice BDNF increased the number of serotonergic neurons of about 2-fold. In addition the number of dendrites in raphe and hippocampal neurons in cultures was enhanced. Presumably, BDNF acts on the formation of primary dendrites. By contrast, simultaneous addition of BDNF and S100 β decreased the extension of dendrites of both raphe and hippocampal neurons. The same treatment, however, promoted axon branching of raphe neurons. This indicates an interaction between BDNF and S100 β .

BDNF treatment of glial cell cultures revealed an increased S100 β synthesis in astrocytes. In BDNF deficient mice the S100 β immunoreactivity was reduced in the raphe region. These findings indicate that BDNF promotes expression or synthesis of S100 β .

In brain of BDNF $-/-$ mice a decrease of myelin was observed, determined by immunohistochemistry and Westernblot analysis. Accordingly, treatment of hippocampal primary cultures with BDNF promotes a strong enhancement of oligodendrocytes producing myelin. Thus, BDNF is important for the myelination in the central nervous system.