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### The role of nonneuronal neurotrophins in the brain

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#### Background

Neurotrophins (nerve growth factor, NGF; brain-derived neurotrophic factor, BDNF; neurotrophin-3, NT-3) are involved in various CNS functions from differentiation and neuron survival to synaptogenesis and synaptic plasticity. They are synthesized in neurons and also in nonneuronal cells (astrocytes), which therefore represent an important local source of trophic support in normal and diseased brain. Their synthesis in astrocytes is susceptible to up-regulation by cytokines, hormones, drugs and synaptically released neurotransmitters. They all show significant but diverse regulatory effects on neurotrophin levels in astrocytes with differences in dose-dependency and short-term kinetics. Cytokines are the most effective stimulators of NGF synthesis and/or secretion, whereas the monoaminergic neurotransmitters noradrenaline, adrenaline, 5-HT, dopamine and histamine differentially affect synthesis of all three neurotrophins. Their stimulatory effect is a specific receptor-mediated process involving either cytokine (IL-1), adrenergic ( $\alpha_1$ ,  $\beta_1/\beta_2$ ), dopaminergic ( $D_1$ ) or histamine ( $H_1$ ,  $H_2$ ,  $H_3$ ) receptors and corresponding intracellular mechanisms.

#### Summary

In conclusion, the studies on the mechanisms of astrocytic neurotrophin regulation suggest the importance of positive cooperation between the excitatory monoaminergic neuronal activity and astrocytic neurotrophic support (neuron–astrocyte crosstalk) in the developing, mature and diseased brain.