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Meeting abstract

Monoamine neurotransmitters modulate NT-3 levels in astrocytes

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Background

Neurotrophin-3 (NT-3), a member of the neurotrophin family of neurotrophic factors, displays profound neuromodulatory functions in the normal and in the diseased brain. Under physiological conditions, NT-3 is produced by neuronal cells and also by local glial cells. We focused our investigation on the ability of astrocytes to synthesize NT-3 and, additionally, on the active involvement of the neurotransmitters noradrenaline, adrenaline, dopamine, histamine and serotonin (5-HT) in the regulation of NT-3 production in neonatal rat cortical astrocytes.

Results

Our study confirms the ability of neonatal rat cortical and cerebellar astrocytes in primary culture to express and synthesize significant amounts of NT-3. The examined monoamines, with the exception of 5-HT are able to potently and transiently increase NT-3 mRNA and NT-3 protein cell levels; their action is dose- and time-dependent. Screening different activators of basic intracellular second messenger systems which can participate in the possible monoamine receptor mediated stimulation of NT-3 by examined monoamines revealed that forskolin, dibutyryl cAMP (dBcAMP), as well as calcimycin (Ca^{2+} ionophore A23187) and phorbol 12-myristate 13-acetate (TPA), markedly increase the cellular level of NT-3 protein. Neurotransmitter-induced NT-3 is susceptible (to varying degrees) to inhibition by H-89 (an inhibitor of protein kinase A, PKA) or staurosporin (an inhibitor of protein kinase C, PKC), which led us to conclude that downstream signaling responsible for the stimulation of NT-3 synthesis by monoamines in astrocytes is a receptor-mediated process consisting of multiple, complex intracellular mechanisms involving the cAMP/PKA pathway, activation of PKC, as well as mobilization of Ca^{2+} ions.

Conclusion

In conclusion, our study indicates for the first time that monoaminergic neurotransmitters play an important role in the regulation of neurotropic NT-3 activity in cultured rat astrocytes.