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Meeting abstract

Histamine-neurotrophin-3 interactions in cultured rat astrocytes

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Background

Neurotrophin-3 (NT-3) is produced by astrocytes, in addition to neurons, and monoamine neurotransmitters play a role in controlling NT-3 synthesis [1]. The impact of histamine on the regulation of NT-3 synthesis in cultured astrocytes has not been studied in detail. Therefore, we focused our present study on the active involvement of multiple histaminergic receptor and intracellular mechanisms in the regulation of NT-3 production by histamine.

Results

Histamine (1 μM) significantly and transiently elevates NT-3 mRNA levels by 2.2-fold after 30 min of incubation following by 2.1-fold increase in NT-3 intracellular levels after 6 h. Its stimulation was partly inhibited by the H_1 antagonists triprolidine and mepyramine, the H_2 antagonists famotidin and cimetidin, and by the H_3 antagonist ciproxifan. NT-3 levels in astrocytes were increased by specific and selective H_1, H_2 and H_3 agonists, but none of the tested agonists was able to reach the level of histamine's stimulatory effect. Different activators of basic intracellular histamine receptor second messenger systems (forskolin, dibutyryl cAMP, dBcAMP; as well as calcimycin, i.e. Ca^{2+} ionophore A23187) and phorbol 12-myristate 13-acetate, TPA) markedly increase the cellular level of NT-3 protein. Histamine-induced cellular levels of NT-3 were significantly reduced by H-89 (an inhibitor of protein kinase A, PKA) and by staurosporin (an inhibitor of protein kinase C, PKC). Studying histamine receptor subtype expression in astrocytes using quantitative RT-PCR we confirmed that the expression levels of histamine H_1 and H_2 receptors (already shown in radioligand binding) as well as of H_3 receptors are high.

Conclusion

Our study confirmed that the synthesis of NT-3 in astrocytes is regulated by the histaminergic system and indicate the possible involvement of multiple, complex histamine H_1, H_2 and H_3 receptors and corresponding intracellular mechanisms involving the cAMP/PKA pathway, as well as mobilisation of Ca^{2+} ions and activation of PKC.

References

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