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Interactions of peripheral and central μ opioid systems during emotional stress

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Background

Numerous studies support an important contribution of endogenous opioid peptide systems in the mechanisms of emotional behavior. It is well known that the structure of opioid receptors (OR) and endogenous opioid peptides in the CNS and in the periphery is identical, but the central and peripheral functions of endogenous opioid systems are considered different, because the blood-brain barrier (BBB) generally prevents the entry of peptides into the brain. We hypothesize that the central and peripheral components of the endogenous opioid system function in close relationship, interacting with each other. The aim of this work was to study an influence of a peripheral administration of the μ opioid receptor ligands, which do not penetrate the BBB, on behavioral parameters as well as on extracellular levels of β-endorphin (BE) in the the cingulate cortex (CC) of rats during acute emotional stress.

Materials and methods

The behavioral parameters of male Wistar rats were estimated in the elevated plus maze (EPM) test and in the Porsolt forced swim test. Determination of BE in the CC of the midbrain of rats was performed using microdialysis technique with following immunohistochemical analysis. The agonist of μ opioid receptor agonist loperamide and the opioid receptor antagonist methylnaloxone were administered intragastrically using a special catheter 30 min before the experiments.

Results

Peripheral administration of the μ opioid receptor agonist loperamide produced mostly an anxiolytic effect, while a peripheral treatment with the antagonist methylnaloxone evoked a more depressive effect. The administration of loperamide and methylnaloxone produced opposite effects on the extracellular level of BE in the CC of rat brain. Thus, loperamide decreases, whereas methylnaloxone significantly increased output of BE from CC neurons of rats. Immobilization stress produced only slight elevation of BE release in CC. Peripheral administration of loperamide, but not methylnaloxone, significantly increased extracellular levels of the studied neuropeptide in the CC of rats subjected to immobilization stress.

Conclusions

These data support our hypothesis on reciprocal interactions between the central and peripheral components of the endogenous opioid system. The results may also explain the mechanism of anxiolytic effects of loperamide.

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