BMC Pharmacology

Meeting abstract

Regulating and regulated role of the orphanin FQ/nociceptin system

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from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, **9**(Suppl 2):A46 doi:10.1186/1471-2210-9-S2-A46

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A46

Background

There is a permanent need for improvement in effective pain management that calls for implication of recent advances in the understanding of endogenous morphine-like substances. Using the technique of "reverse physiology" identification of an orphan, opioid-receptor-like 1 receptor (ORL1, recently named as OP4/NOP), and isolation of its endogenous agonist orphanin FQ/nociceptin (NC) opened a new era in opioid pharmacology. In recognition of the involvement of NOP-NC system in a wide range of physiological, and pathophysiological processes, the nociceptinergic system is considered an important new target for drug development in pain control, morphine-withdrawal, anxiety, depression, cognitive impairment, body mass control, cough suppression, hypertension, heart failure and ischemic brain injury.

Methods

We conceptionalized that elucidation of (patho)physiological conditions/human disorders with changes in endogenous levels of NC can give significant contribution to drug targeting. [^{125}I]NC-RIA and HPLC methods were used for measurements.

Results

In Wistar rats both in the central nervous system (CSF) and the periphery (blood plasma) NC levels reached the adult level by the age of 12 weeks. Plasticity of unmatured NOP receptors was evidenced in neonatal hormonal imprinting studies with NC. In patients with chronic liver disorders of different etiology (Wilson's disease, primary biliary cirrhosis) plasma NC was found to be elevated, and extremely high levels were observed in hepatocellular carcinoma patients compared to age-matched healthy controls. The functional role of circulating NC in primary neurovascular headaches (migraine and cluster headache patients) was also evidenced. Plasma NC levels in acute stroke and transient ischemic attack patients were found to be elevated compared to healthy controls; however, significantly lower NC levels were observed in atherosclerotic patients with chronic limb ischemia in both the plasma and blood vessels.

Conclusion

The observed changes in endogenous NC levels designate the NOP-NC system as a potential new target in therapy.

Acknowledgements

This work was supported by a grant of the Hungarian Ministry of Health (ETT 353/2006).