BMC Pharmacology

Poster presentation

PDE9A, PDE10A, and PDE11A expression in rat trigeminovascular pain signalling system: role in pathogenesis of migraine?

Lars S Kruse*[1,2], Morten Møller[3], Maiken Tibæk[2], Steen Gammeltoft[1], Jes Olesen[2] and Christina Kruuse[2]

Address: [1]Department of Clinical Biochemistry, Glostrup Hospital, DK-2600 Glostrup, Denmark, [2]Danish Headache Center, Department of Neurology, Glostrup Hospital, DK-2600 Glostrup, Denmark and [3]Department of Neuroscience and Pharmacology, University of Copenhagen, DK-2200, Denmark

Email: Lars S Kruse* - lakr@glo.regionh.dk

* Corresponding author

from 3rd International Conference on cGMP Generators, Effectors and Therapeutic Implications
Dresden, Germany. 15–17 June 2007

Published: 25 July 2007

BMC Pharmacology 2007, **7**(Suppl 1):P36 doi:10.1186/1471-2210-7-S1-P36

This abstract is available from: http://www.biomedcentral.com/1471-2210/7/S1/P36

Background

Activation of the trigeminovascular pain signalling system, which includes cerebral arteries, meninges, trigeminal ganglion, and brain stem, may be involved in migraine. Furthermore, stimulation of cyclic nucleotide (cAMP and cGMP) production as well as inhibition of phosphodiesterases (PDEs) induces headache and migraine [1-4]. The aim is to study the expression of the most recently discovered PDE subtypes (9A, 10A and 11A) in cerebral arteries, the dura mater, and the trigeminal ganglion and nucleus. This may give a clue to a role in pathogenesis of migraine.

Methods

The amount of mRNA and protein in the middle cerebral artery, basilar artery, dura, trigeminal ganglion, and caudal trigeminal nucleus of male Sprague-Dawley rats were investigated using real-time PCR, Western blot, and immunohistochemistry, and compared to two peripheral arteries: aorta and mesenteric artery, as well as neocortex and cerebellum.

Results

Real-time PCR of mRNA and Western blotting showed that PDE9A, PDE10A and PDE11A are expressed in components of the rat trigeminovascular pain signalling system including middle cerebral artery, basilar artery, dura mater, trigeminal ganglion and trigeminal nucleus (Fig. 1). Aorta and mesenteric artery as well as cerebral cortex and cerebellum also showed expression of PDE9A, PDE10A and PDE11A. Immunohistochemistry showed that PDE9A, PDE10A and PDE11A are localised in the cytosol of nerve cell bodies of the trigeminal ganglion (Fig. 2).

Conclusion

We here present, for the first time the expression of the three most recently discovered PDEs in the trigeminovascular pain signalling system. The functional implications are yet unknown, but their localisation indicates that PDE9A, PDE10A and PDE11A may have a role in pathogenesis of migraine.

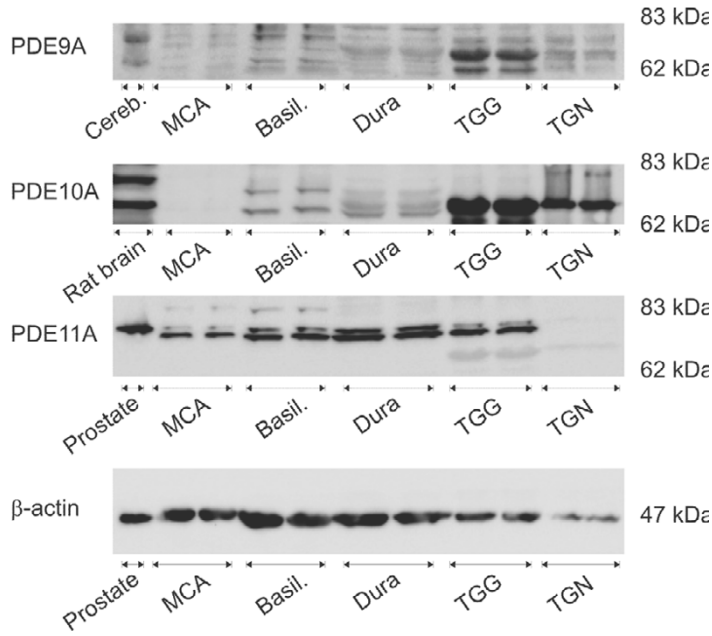

Figure 1
Western blotting of PDE9A, PDE10A and PDE11A proteins. Expression is shown in middle cerebral artery (MCA), basilar artery (Basil.), dura, trigeminal ganglion (TGG) and trigeminal nucleus (TGN). Positive controls were included: PDE9A in cerebellum, PDE10A in rat brain and PDE11A in prostate. β-actin expression was used to determine the protein loading on the gel.

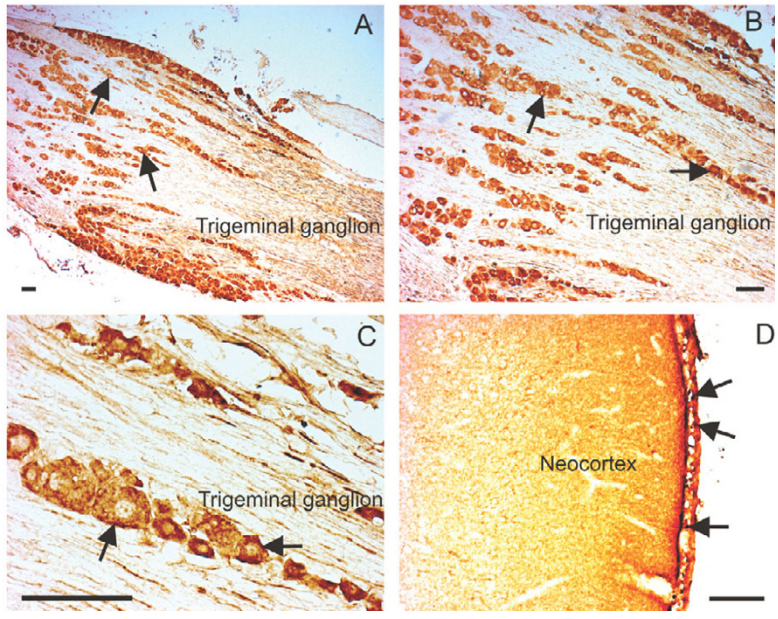

Figure 2
Immunohistochemical analysis of PDE10A in the trigeminal ganglion and dura. **A-C:** PDE10A-immunoreactive neuronal cell bodies in the trigeminal ganglion (arrows) at various magnifications. **D:** PDE10A-immunoreactive nerve cells in the cortex and cells in the dura (arrows). Bar = 100 μm.

References

1. Birk S, Kruuse C, Petersen KA, Tfelt-Hansen P, Olesen J: **The headache-inducing effect of cilostazol in human volunteers.** *Cephalalgia* 2006, **26:**1304-1309.
2. Edvinsson L: **Calcitonin gene-related peptide (CGRP) and the pathophysiology of headache: therapeutic implications.** *CNS Drugs* 2001, **15:**745-753.
3. Kruuse C, Thomsen LL, Birk S, Olesen J: **Migraine can be induced by sildenafil without changes in middle cerebral artery diameter.** *Brain* 2003, **126:**241-247.
4. Olesen J, Thomsen LL, Lassen LH, Olesen IJ: **The nitric oxide hypothesis of migraine and other vascular headaches.** *Cephalalgia* 1995, **15:**94-100.