

POSTER PRESENTATION

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Nitric oxide synthase, Calcitonin Gene-Related Peptide and inflammatory mechanisms are involved in GTN induced neuronal activation

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Introduction and objective

Infusion of glyceryl trinitrate (GTN), a nitric oxide (NO) donor in awake freely moving rats closely mimics a universally accepted human model of migraine and responds to sumatriptan treatment [1,2]. Here we analyse the effect of nitric oxide synthase (NOS) and calcitonin gene-related peptide (CGRP) systems on the GTN induced neuronal activation in this model.

Methods

The femoral vein was catheterized and rat allowed recovering for ten days before infusion of GTN (4 µg/kg/min, for 20 min, i.v.). Immunohistochemistry was used to measure Fos, nNOS and CGRP protein expression. Western blot was done to re-confirm the nNOS expression. Olcegepant (1 mg/kg) for 3 mins was given both as a pre-treatment and post treatment to analyse its effect on Fos activation. The response to pre-treatment with L-NAME (40 mg/kg) and NK-1 antagonist, L-733060 (1mg/kg) was also measured at the activation level.

Results

GTN treated rats showed a significant increase of nNOS and CGRP in dura and CGRP in trigeminal nucleus caudalis (TNC). Upregulation of the nociceptive marker Fos was observed in TNC at 2 and 4 hrs after the infusion. The activation at 4 hrs was inhibited by pre-treatment with olcegepant. However, post treatment with olcegepant could not inhibit this activation. Pre-treatment with L-NAME and L-733060 also significantly inhibited the GTN induced Fos expression.

Conclusion

The present study indicates that inhibition of CGRP, NOS and inflammatory systems all block GTN induced neuronal activation. These findings also predict that pre-treatment with olcegepant may be a better option than post-treatment to study inhibitory effect on GTN migraine models.

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