



## A new anatomical-functional model: effect of topiramate on capsaicin-induced mast cell degranulation in rat dura mater (Abstract)

*Um novo modelo anatômico-funcional: efeito do topiramato sobre a degranulação de mastócito induzida por capsaicina na dura-mater de rato (Resumo)*

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### Introduction

Migraine is an extremely disabling neurological disease due to its related symptoms, but the pathophysiological mechanisms involved in the activation of a migraine crisis are still unknown. Experimental models mimic the pathophysiology through chemical and electrical stimulations. Topiramate is an important drug used to prevent migraine, but its mechanism of action is still not well known. A sterile inflammation of the dura mater is believed to trigger pain in the migraine.

### Objective

Understand the effect of topiramate on sterile inflammation of the dura mater that triggers migraine.

### Method

We created an experimental model for the action mechanisms of topiramate and capsaicin in mast cell degranulation. 35 male (n=28) and one group of females (n=7) 60-day-old rats were divided in 2 groups: topiramate (20mg/kg/day, gavage/10 days) and topiramate in situ on the dura mater ( $10^{-3}$  M, 20 $\mu$ l). The animals were anesthetized and cranial windows between the suture coronal and the lambda in the hemispheres were performed with a drill, to bilaterally expose the dura mater. Capsaicin  $10^{-3}$  M (80 $\mu$ l) was placed on the right side and synthetic interstitial fluid (SIF) (80  $\mu$ l) on the left side. The percentage of degranulated mast cells was quantified after removal of the dura mater, by staining toluidine blue (0.1%). Statistical analysis was performed using the Kolmogorov-Smirnov test, t-test and ANOVA.

### Results

There was a greater amount of degranulated mast cells in the dura mater of the hemispheres stimulated with capsaicin when compared to the contralateral control side, both in females ( $18.43 \pm 3.00\%$  versus  $73.11 \pm 2.67\%$ ;  $p = 0.001$ ) and in males ( $27.21 \pm 1.91\%$  versus  $75.00 \pm 2.55\%$ ;  $p < 0.001$ ) as there was no statistic, we used only males. In the group treated with topiramate for 10 days, there was a smaller amount of degranulated cells by capsaicin ( $22.80 \pm 1.17\%$  versus  $77.00 \pm 1.32\%$ ,  $p < 0.001$ ). The topiramate placed in situ concomitantly with capsaicin also reduced the mast cell degranulation process in the dura mater ( $35.74 \pm 1.69\%$  control versus  $44.52 \pm 0.82\%$  capsaicin + topiramate;  $p < 0.001$ ).

### Conclusion

This study was able to demonstrate that capsaicin is a chemical method of inducing and stimulating mast cells and that topiramate reduces the effect of capsaicin.

#### Keywords:

Topiramate  
Mast cell  
Dura mater  
Rat  
Capsaicin