

S. Valcheva-Kuzmanova<sup>1</sup>, M. Todorova<sup>1</sup>, I. Belcheva<sup>2</sup>, S. Belcheva<sup>3</sup>, R. Tashev<sup>4</sup>

<sup>1</sup>Department of Pharmacology and Clinical Pharmacology and Therapeutics, Medical University-Varna, Bulgaria

<sup>2</sup>Institute of Neurobiology, Bulgarian Academy of Sciences, Sofia, Bulgaria

<sup>3</sup>Department of Pre-school and Primary School Education, Sofia University, Bulgaria

<sup>4</sup>Department of Pathophysiology, Medical University-Sofia, Bulgaria

## Background and purpose

The olfactory bulbectomized (OBX) rat is widely used as an animal model of depression. Studies have reported decreased sensitivity to pain of depressed animals [1]. Chlorogenic acid (CGA) and gallic acid (GA) are abundant biologically active polyphenols in human diet with antinociceptive effects in painful conditions [2,3].

The aim of this study was to investigate the effects of CGA and GA on pain sensitivity threshold to mechanical pressure on the uninflamed hind paw in OBX rats.

## Methods

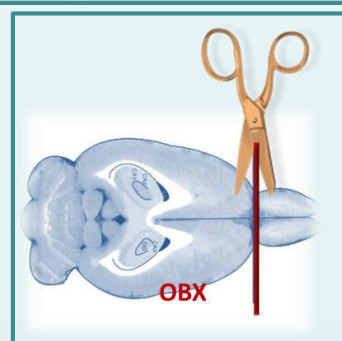
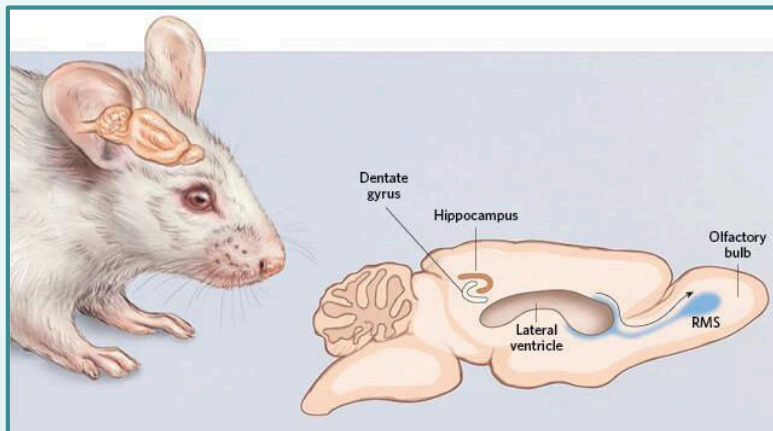
**Animals:** male Wistar rats (200-220 g)

**Experimental substances:**

CGA and GA purchased from Sigma Aldrich (Germany)

### Experimental design:

- ❖ 4 groups (n=6):
  - Sham operated (SO)
  - OBX
  - OBX+CGA
  - OBX+GA
- ❖ Bilateral OB according to the method of Kelly et al. [4]
- ❖ 15-days recovery period
- ❖ **Treatment: 14 days**



SO	OBX	OBX+CGA	OBX+GA
Distilled water 10 ml/kg	Distilled water 10 ml/kg	Chlorogenic acid 20 mg/kg	Gallic acid 20 mg/kg

### Test:

#### The paw pressure Randall-Selitto test

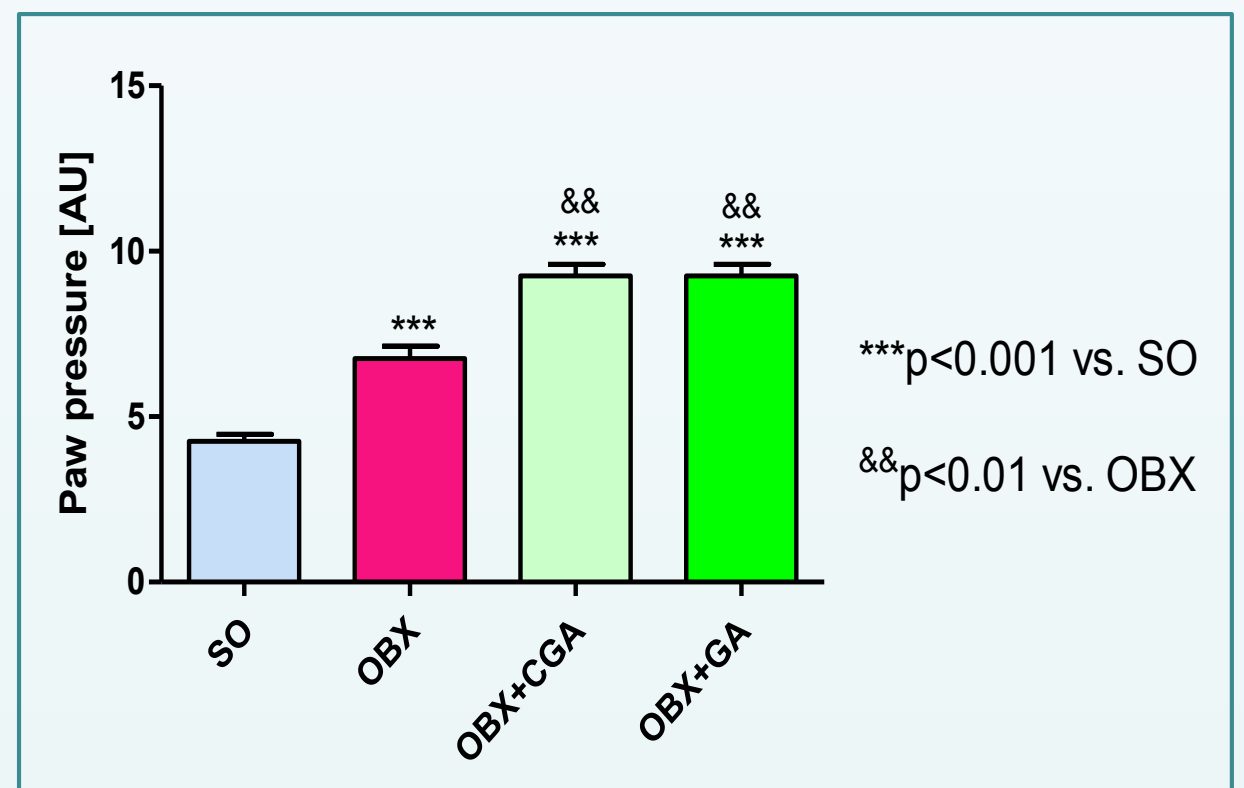
- Anagesimeter (Ugo Basile)
- Pain sensitivity – measured by the pressure at which the rat pulled back its hind paw



### Statistical analysis:

One-way ANOVA, followed by Dunnett's multiple comparison post test; GraphPad Prism statistical software

## Results



## Conclusion

CGA and GA exerted antinociceptive effects and significantly elevated the reaction threshold to pressure of an uninflamed paw in OBX rats. There are some mechanisms that could be proposed as an explanation of these results. CGA has been shown to enhance the activities in voltage-gated potassium channels and thus to decrease the excitability of neurons [2]. GA exerted antinociceptive effects in painful condition in mice acting as an antagonist of the transient receptor potential ankyrin 1 (TRPA1), thus reducing the TRPA1-mediated calcium influx [3]. TRPA1 receptor antagonism as an explanation of the observed effects is further supported by the fact that TRPA1 knockout mice have a loss of noxious mechanosensation in the paw [5].

## References

- [1] Shi, M., Qi, W.J., Gao, G., Wang, J.Y., Luo, F., 2010. Increased thermal and mechanical nociceptive thresholds in rats with depressive-like behaviors. *Brain Res* 1353, 225-233.
- [2] Zhang, Y.J., Lu, X.W., Song, N., Kou, L., Wu, M.K., Liu, F., Wang, H., Shen, J.F., 2014. Chlorogenic acid alters the voltage-gated potassium channel currents of trigeminal ganglion neurons. *Int J Oral Sci* 6(4), 233-240.
- [3] Trevisan, G., Rossato, M.F., Tonello, R., Hoffmeister, C., Klafke, J.Z., Rosa, F., Pinheiro, K.V., Pinheiro, F.V., Boligon, A.A., Athayde, M.L., Ferreira, J., 2014. Gallic acid functions as a TRPA1 antagonist with relevant antinociceptive and antiedematogenic effects in mice. *Naunyn Schmiedeberg's Arch Pharmacol* 387(7), 679-689.
- [4] Valcheva-Kuzmanova, S., Georgieva, A., Belcheva, I., Belcheva, S., Tashev, R. 2016. Investigation of the effects of chlorogenic acid, ferulic acid, gallic acid and quercetin on pain sensitivity threshold in rats. *Eur Neuropsychopharmacol* 26(Suppl. 2), S222.
- [5] Minett, M.S., Eijkelkamp, N., Wood, J.N., 2014. Significant determinants of mouse pain behaviour. *PLoS One* 9(8), e104458.

**There is no potential conflict of interests.**