MOTOR CORTEX STIMULATION'S ROLE IN RELEASE OF NEUROTRANSMITTERS IN THE PERIAQUEDUCTAL GRAY AREA (PAG)

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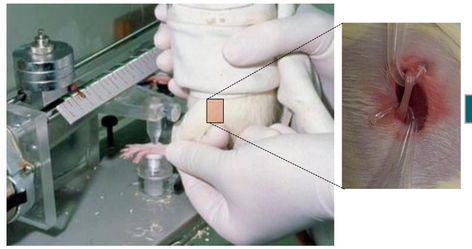
INTRODUCTION

Subthreshold stimulation of the motor cortex is a relative new technique that has been used for the treatment of patients with chronic neuropathic pain syndromes that are resistant to conventional pharmacological treatment. The motor cortex may be the most rostral structure in the neuroaxis responsible for pain modulation, and recent results obtained by our group demonstrated that motor cortex stimulation (MCS) increase the neuronal activation of periaqueductal gray (PAG) in animals models of peripheral neuropathies. The PAG is one of the main subcortical centers of the descending pain suppressor system, and receives inputs from several brain areas.

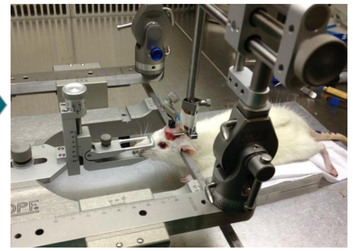
OBJECTIVES

This study investigate the effects of motor cortex stimulation on neurotransmitters release in the PAG in order to investigate the possible neurochemical mechanisms involved in this effect.

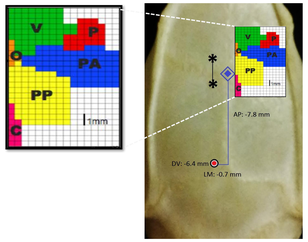
METHODS



The animals were evaluated for mechanical hyperalgesia test and subdivided into three surgical groups: **1- chronic constriction injury group (CCI); 2- a sham-operated group; 3- a non-operated animals (naïve).**

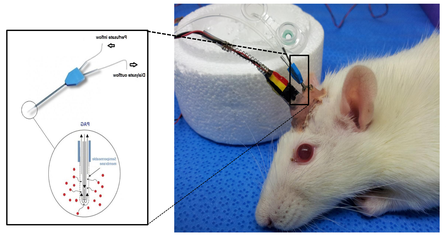


A microdialysis guide cannula was stereotaxically implanted into the PAG, according to the Rat Brain Atlas.

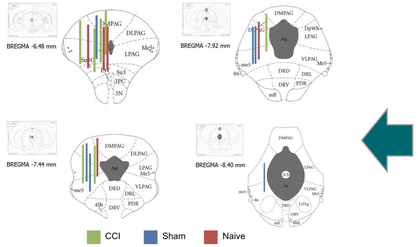


Implantation of unilateral transdural electrodes on the motor area corresponding to the right hind paw.

The rats were stimulated for 15 min and then were evaluated by the paw pressure test. The parameters chosen was: ***1,25 mA; 60Hz; 210 µs.***



The microdialyzate samples were collected and the neurotransmitters analysis was performed by a high performance liquid chromatography (HPLC).



Microdialysis sites are shown with anterior–posterior coordinates in the PAG. The probes are placed in the lateral or ventrolateral PAG.

RESULTS

Concentrations of the neurotransmitters glutamate, glycine and GABA from PAG. The neurotransmitters were collected before (t = 30 min) , during (t = 15 min) and after MCS (t = 30 min).

	Baseline			Stimulation			Post-stimulation		
	Sham	Naive	CCI	Sham	Naive	CCI	Sham	Naive	CCI
Glutamate (pg/µL)	0,015 ± 0,00022	0,001 ± 0,0002	0,001 ± 0,00007	0,002 ± 0,001	0,002 ± 0,0009	0,001 ± 0,0001	0,002 ± 0,0008	0,002 ± 0,0008	0,001 ± 0,0001
Glycine (pg/µL)	0,044 ± 0,02	0,0055 ± 0,0006	0,134 ± 0,01	0,029 ± 0,009	0,005 ± 0,0006	0,153 ± 0,106	0,028 ± 0,01	0,005 ± 0,0004	0,138 ± 0,094
GABA (pg/µL)	0,015 ± 0,003	0,0015 ± 0,0002	0,0004 ± 0,0003	0,003 ± 0,001	0,001 ± 0,0002	0,0004 ± 0,0004	0,004 ± 0,002	0,001 ± 0,0001	0,0001 ± 0,00008

Figure 1– Concentration (pg/microL) of glycine, GABA and glulatamate during microdialysis. The samples were collected before (BL= baseline), during (S = stimulation) and after MCS (PS = post stimulation). All data are presented as mean ± standard error of mean (S.E.M.).

MCS induced a significant increase in glycine levels during MCS (153 % increase) and after MCS (134% increase).

The GABA concentration increases 145 % during transdural stimulation.

Glutamate levels showed no change in PAG microdialysate after MCS.

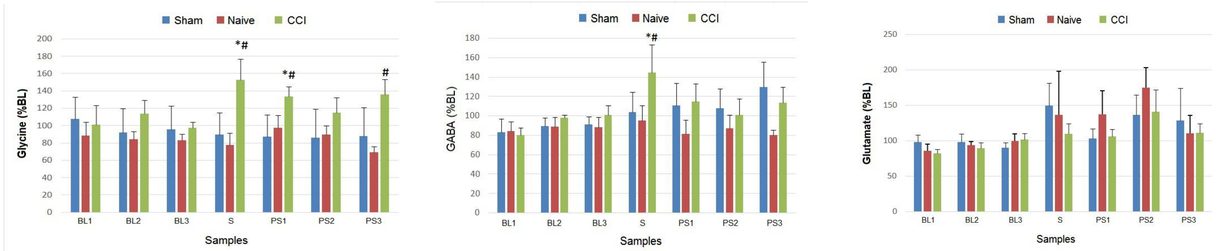


Figure 2- Changes in the neurotransmitters release (glycine, GABA and glulatamate) during microdialysis. The samples were collected before (BL= base line), during (S = stimulation) and after MCS (PS = post stimulation). All data are presented as mean ± standard error of mean (S.E.M.). Statistical comparison of more than two groups was performed using analysis of variance (ANOVA), followed by Tukey's test. In all cases, p≤0.05 was considered statistically significant.

CONCLUSION

Our results suggest that the neurotransmitters glycine and GABA, released in PAG during MCS, contribute to descending antinociceptive actions. The results of this project will contribute for the elucidation of the mechanisms of the antinociceptive effect of MCS, a phenomenon that has not been fully understood currently.

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