

healthy controls, and verify associations of these measures with brain-derived neurotrophic factor (BDNF).

Methods: Participants were 63 women, aged 18 to 75 years. Transcranial Magnetic Stimulation (TMS) was used to measure motor-evoked potential (MEP), intra-cortical facilitation (ICF), short-intracortical inhibition (SICI) and silent-period (SP). A Quantitative sensory testing (QST) assessed Heat-pain-threshold (HPT_h) and the Conditioned pain modulation task (CPM-task) assessed changes in the perception of heat pain as a measure of DPMS function. BDNF was dosed from blood samples. Validated instruments assessed other clinical outcomes.

Results: The mean of SICI was 53% larger in FM compared to MDD [1.03(0.50) vs. 0.55(0.43)] and 67% when compared to HC [1.03(0.50) vs. 0.34(0.19)]. FM patients had a mean of ICF 24% [(0.33(0.23) vs. 1.39(1.02)] lower than MDD and 29% lower than HC [(0.33(0.23) vs. 1.14(0.27)]. The inhibition of the DPMS (CPM-test) was 112.29 % lower in FM compared to MDD [0.22(1.37) vs. -0.87(1.49)]. In FM, the change in the heat stimulus during the CPM-task was inversely correlated the SICI; $\rho = -0.49$ [CI(95%) = -0.78 to -0.03]. The BDNF (adjusted-index for age and medication use) was positively correlated with the disinhibition of the DPMS ($\rho = 0.35$ [CI(95%) = 0.02 to 0.61]).

Conclusions: These findings support the hypothesis that FM has different pathological substrates from depression. They suggest that an up-regulation phenomenon of intracortical inhibitory networks associated with a disruption of the DPMS function occurs in FM.

Keywords: *descending pain system, Fibromyalgia, Pain*

A5

Forced-exercise and transcranial direct current stimulation (tDCS) provide antinociceptive effects and modulate inflammatory and neurotrophic parameters in the spinal cord in a chronic pain model: long-term effects

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Objective: Investigate antinociceptive and neuromodulatory effects of association between exercise and/or tDCS in a chronic neuropathic pain model (NP) in rats.

Methods: 78 adult Wistar rats were randomized into groups: Control; Sham-Pain; Sham-Pain+Exercise; Sham-Pain+Sedentary+Sham-tDCS; Sham-Pain+Sedentary+tDCS; Sham-Pain+Exercise+Sham-

tDCS; Sham-Pain+Exercise+tDCS; Pain; Pain+Exercise; Pain+Sedentary+Sham-tDCS; Pain+Sedentary+tDCS; Pain+Exercise+Sham-tDCS; and Pain+Exercise+tDCS. NP was induced by sciatic chronic constriction (CCI). Mechanical and thermal hyperalgesia were assessed using von Frey (VF) and Hot Plate (HP) tests at baseline, 7th and 14th days after CCI; immediately, 24h and 7days after treatment. Rats were subjected to treadmill and/or tDCS 0.5mA/20min/day/8days from 15th day. At 48h or 7days after treatments, rats were decapitated, spinal cord was collected for BDNF and IL-4 analysis. Behavioral data were analyzed by GEE/Bonferroni and biochemical data by one-way ANOVA/SNK ($P < 0.05$ considered significant). Approved by CEUA-HCPA#20170061.

Results: There was interaction between group X time upon mechanical and thermal hyperalgesia ($P < 0.05$). On 7th day after CCI, sham-pain and pain groups exhibited hyperalgesia ($P < 0.05$), and on 14th day, only pain groups exhibited hyperalgesia. Exercise and/or tDCS partially reverted mechanical hyperalgesia in pain groups immediately, 24h and 7days after treatment; tDCS+Exercise in pain group showed slightly improvement at 7days ($P < 0.05$). tDCS and/or exercise reverted thermal hyperalgesia at all times after treatments ($P < 0.05$). Pain and Pain+Sedentary+Sham-tDCS groups displayed increased BDNF levels at 48h and 7days compared to other groups ($P < 0.05$). Sham-Pain+tDCS and Pain-sedentary+tDCS groups showed an increase in IL-4 levels ration to other groups at 48h ($P < 0.05$). At 7days after treatment, IL-4 levels were reduced in Pain group ($P < 0.05$).

Conclusion: Exercise and tDCS trigger antinociceptive effect in NP model in rats, and this effect can involve modulations in the BDNF and IL-4 levels in the spinal cord.

Keywords: *exercise, tDCS, chronic pain*

Funding: CNPq, CAPES, FIPE-HCPA, FAPERGS

A6

Pain catastrophizing thought modulated by low dose naltrexone (LDN) in fibromyalgia women

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Objective: To evaluate the effects of low dose naltrexone upon pain catastrophism in women with fibromyalgia.

Methods: This is a randomized controlled trial (CAAE 0005317.5.0000.5307). 86 female patients aged 18 to 65 years were included according to the American College of Rheumatology (ACR) criteria. In addition, 48 patients were excluded or dropped out of the study. Patients were randomized between low doses of naltrexone (LDN) ($n = 43$) or placebo ($n = 43$). Each patient received 26 days of treatment. During the 1st and 26th day of intervention the patients did the Catastrophic Pain Thinking Scale (B-PCS), divided into rumination, magnification and hopelessness. Data were analyzed using SPSS 20.0, using t test for independent samples, with significant difference when $P < 0.05$.

Results: patients had patients had a mean age of 49.38 ± 9.05 . The placebo group showed no significant difference in total catastrophism, rumination, magnification and hopelessness scores ($P > 0.05$). However, the LDN group showed significant difference in total catastrophism, rumination, magnification and hopelessness when compared pre-intervention with post-intervention ($P < 0.05$).

Conclusions: This study demonstrated that the use of low dose naltrexone is able to significantly reduce catastrophic thinking scores in patients suffering from fibromyalgia syndrome. This result may be related to the use of low doses of naltrexone and the consequent decrease in pain thresholds.

Keywords: *fibromyalgia, catastrophism, naltrexone*

Pain perception

A7

Comparison between the effects of hypnotic suggestion and transcranial direct current stimulation on pain perception and the descending pain modulation system: a randomized crossover clinical trial

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Objective: To determine whether hypnotic suggestion and Transcranial Direct Current Stimulation (TDCS) have a differential effect on pain perception and function of the descending pain modulatory system (DPMS).

Methods: Twenty-four healthy women were included, aged 18 to 45. years, with high susceptibility to hypnosis on the Waterloo-Stanford Hypnotic Susceptibility Scale (WSGC) > 8 , in a randomized, blinded, crossover study. The women received anodal tDCS over the CFPC (contralateral supraorbital cathode) with 2mA or hypnotic suggestion for 20min. Pain threshold and pain tolerance by heat were measured using the Quantitative Sensory Test (QST), pain tolerance to the cold by the Cold Pressure Test (CPT) variation of the perception of heat pain through the conditioned modulation task. (CPM-task) as a function of DPMS. Blood samples were taken to measure brain derived neurotrophic factor (BDNF) before / after intervention.

Results: Only hypnotic suggestion produced significant changes by intervention in measures of cold pain tolerance and thresholds and heat pain tolerance ($P < 0.05$). The analysis showed a major effect on treatment when comparing CPM-task data, indicating improvement of DPMS function after TDCS ($P = 0.04$). Increases in BDNF levels were associated with worse DPMS function ($\beta = 0.04$; $P < 0.05$).

Conclusion: The results confirm that interventions have different neural effects, as hypnotic suggestion improved pain perception, while tDCS increased inhibition of the descending pain modulator system.

Keywords: *pain perception, descending pain system*

A8

Combined transcranial direct current stimulation with hypnotic suggestion in acute experimental pain: A Proof of Concept cross-over sham-controlled randomized trial

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Objective: This research evaluated the anodal transcranial direct-current stimulation (tDCS) effect over the left dorsolateral prefrontal cortex (DLPFC) combined with hypnotic suggestion (HS) on pain perception and the function of the descending pain modulatory system (DPMS) and whether these effects are related to neuroplasticity changes

Methods: Forty-eight healthy females received active (a)-tDCS (2mA, 20min) or HS in a randomized crossover sequence, considering 4 conditions: 1) a-tDCS; 2) HS; 3) a-tDCS/HS and 4) sham-tDCS/HS). Pre and post-intervention outcomes were the function of the DPMS assessed with a Conditioned pain-modulation (CPM)-task (primary outcome), Heat pain threshold (HPT), heat pain tolerance (HPTo) and cold pain tolerance (CPT). Brain-derived neurotrophic factor (BDNF) levels were evaluated in blood samples.

Results: The a-tDCS intervention increased the inhibitory function of the DPMS markedly compared to other groups ($p=0.030$). All other interventions increased the HPTo in comparison to a-tDCS ($P < 0.003$). Only the a-tDCS/HS intervention increased the CPT substantially compared to all other interventions ($P=0.007$). Also, higher baseline levels of BDNF were correlated with a larger change in CPT ($\beta=0.224$; $P=0.029$) and HPTo ($\beta=0.029$; $P=0.002$).

Conclusions: These findings indicate that a-tDCS upregulates the inhibition on DPMS, increasing it, while only HS improves HPTo and the a-tDCS/HS showed substantial effect upon the CPT. The results suggest that these inventions modulate pain processing distinctly and its combined effect did not improve the efficiency of inhibitory function in the DPMS.

Keywords: *tDCS, hypnotic suggestion*

A9

S-Ketamine's Effect Changes the Cortical Electrophysiological Activity Related to Semantic Affective Dimension of Pain: A Placebo-Controlled Study in Healthy Male Individuals

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Objective: The main purpose of this study was to evaluate the effect of S-ketamine on the affective dimension of pain through electroencephalogram (EEG) and behavioral measures. The hypothesis was that S-ketamine would be more effective than placebo, both within and between groups, to attenuate the EEG signal elicited by target and non-target words.