INTRODUCTION

Chronic pain is recognized as a worrying public health problem and the role of epigenetics in chronic pain at the supraspinal level is yet to be fully characterized.[1; 2]

Evidence has shown that TET1-3 and DNMT1/3a/3b genes are implicated in several nociceptive pathways in various locations.

AIMS

✓ To replicate altered (de)methylation genes expression patterns already shown for chronic pain at the spinal level in the brain.
✓ To evaluate if these expression patterns correlate with changes previously demonstrated for other pathological conditions and in KO models.

METHODOLOGY

14 adult Sprague-Dawley male rats were either submitted to the Spared Nerve Injury (SNI) model of pain (7), or to a sham intervention (7). 21 days after surgery, rats were euthanized and several brain regions contralateral to the lesion/sham intervention were dissected and processed. These included the dorsal hippocampus, medial prefrontal cortex, caudate-putamen, amygdala, medial thalamus and lateral hypothalamus.

RNA extraction, RNA reverse transcription and RT-qPCR were performed.

For each animal, the average Ct values for each sample were calculated and samples were grouped by SNI against control in each brain area. For each sample, the semi-quantitative expression of the gene of interest was performed according to the delta Ct method, using GAPDH as housekeeping gene. Statistically significant differences were assessed using a parametric student t-test through Prism 8.0 software, GraphPad. All averaged values are given as the mean ± SEM.

RESULTS

TET1 was downregulated in the amygdala and caudate-putamen and upregulated in the medial prefrontal cortex, congruent with the pattern of reduced global methylation elsewhere observed. In the amygdala and mPFC, the opposite variation of TET1 and DNMT mRNA levels emphasizes the need to further study the involvement of epigenetics in the functional modulating effects of the amygdala in mPFC function in chronic pain.

We found TET2 to be upregulated in the medial thalamus and TET3 to be downregulated in the medial thalamus and caudate-putamen.

We found a decrease in DNMT1 expression in the caudate-putamen and medial thalamus, but no evidence of altered DNMT3a expression was evidenced.

CONCLUSIONS

• Our results evidence a clear role for these genes in the epigenetic regulation of neuropathic pain at the supraspinal level.
• Further studies ought to be undertaken to better characterize the complex, cell-type and time-dependent specific dynamics of methylation and demethylation in the brain.

REFERENCES