Effect of resveratrol on the cartilage and nociceptive system of Osteoarthritic animals

S. Rosas¹,²,³,*, T. Aguiar¹,²,³, L. Almeida¹,²,³, D. Nascimento¹,²,³, S. Adães¹,²,³, J.M. Castro-Lopes¹,²,³, F.L. Neto¹,²,³, J. Ferreira-Gomes¹,²,³

¹ Department of Biomedicine - Experimental Biology Unit, Faculty of Medicine of the University of Porto, Portugal
² Pain Research Group, Institute for Molecular and Cell Biology (IBMC), Porto, Portugal
³ i3S - Institute for Investigation and Innovation in Health, Porto, Portugal

E-mail address: suu.rosas@gmail.com (S. Rosas).

Aim: This study aims to evaluate the effect of RV on the nociceptive behavior, histopathological alterations at the knee and DRG neurons of OA rats.

Introduction: Osteoarthritis (OA) is a common degenerative joint disease and arthritic pain is a prominent symptom associated with reduced quality of life. Peripheral pain mechanisms seem to be involved, with cartilage lesions showing a repercussion in Dorsal Root Ganglia (DRG) neurons. Resveratrol, a polyphenol with proven anti-inflammatory, anti-oxidant and neuroprotective properties, has been shown to prevent development of OA and act as an antinociceptive agent. However, its systemic effects once the disease has fully developed remain unclear.

Methods: To evaluate this, OA was induced in 18 male Wistar rats through intra-articular injection of mono-iodoacetate (MIA) (day 0). Animals were allowed to develop the disease for two weeks, after which followed a 4-week-long treatment with resveratrol or vehicle, administered intraperitoneally twice daily (10 mg/kg). Nociceptive behavior was quantified weekly using the CatWalk and Knee-Bend tests. Animals were sacrificed one week after the last treatment administration, their knees were dissected for histopathological analysis, and the DRG were dissected and processed for immunohistochecmical evaluation of activating transcription factor 3 (ATF-3) neuronal expression.

Results: Resveratrol was unable to prevent cartilage degeneration but it significantly decreased ATF-3 expression. The nociceptive behavior of OA animals treated with resveratrol decreased during the first three weeks of treatment, in comparison to day 14 (before treatment was initiated), as shown by Knee-Bend scores. However, this tendency reverted as the disease progressed.

Conclusion: These results indicate that resveratrol may have antinociceptive effects in the early stages of the disease development, but it might not play such a relevant role once the disease has progressed. Thus, further studies are needed to fully understand the possible role of resveratrol in the different stages of OA.

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PS016

Bupivacaine treatment enhances the regeneration of the lesioned external urethral sphincter of the rat

J.P. Morais¹,*, M. Torrado²,³,⁴, A. Avelino²,³,⁴

¹ Escola das Ciências da Vida e Ambiente, Universidade de Trás-os-Montes e Alto Douro
² Department of Biomedicine, Experimental Biology Unit, Faculty of Medicine, University of Porto, Portugal
³ Translational NeuroUrology Group, IBMC – Instituto de Biologia Molecular e Celular, Porto, Portugal
⁴ i3S - Instituto de Investigação e Inovação em Saúde, Porto, Portugal

E-mail address: joaopfmorais@gmail.com (J.P. Morais).

Aim: In this study we intent to verify if bupivacaine treatment can be used to enhance the repair of the lesioned urethral sphincter in rat.

Introduction: Stress urinary incontinence (SUI) is a major and frequent urinary dysfunction. It has been associated with external urethral sphincter (EUS) weakness due to several causes. Among them, ischemia and nerve lesion frequently associated with childbirth. The current treatments are mainly surgical but are far from being satisfactory. The local anesthetic bupivacaine is known to exert myotoxic action, followed by muscle regeneration with increased strength. This effect was already used in ocular muscles to treat strabismus. In the present study we evaluated the effect of bupivacaine application in the recovery of the damaged EUS.

Methods: A lesion of the external urethral sphincter (urethrolysis) was performed in adult female Wistar rats using established protocols. Two weeks after the lesion, the animals were injected in the EUS with 0.4 ml of 0.5% bupivacaine. Ten days later, the whole urethra was removed, fixed and sectioned in paraffin wax. Sections

were stained with hematoxylin and eosin, Masson’s trichrome and immunoreacted for markers of striated and smooth muscle (sarcomeric actin and smooth muscle actin, respectively).

**Results:** Two weeks after urethrolysis, a marked reduction of muscle fibers in the EUS was detected. A recovery was evident in lesioned, bupivacaine injected animals when compared with lesioned and saline-injected controls.

**Conclusion:** Our data show that bupivacaine application in the lesioned external urethral sphincter accelerates its recovery. This finding opens a therapeutic opportunity to treat stress urinary incontinence.

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**PS148**

**Anxiety-like behavior in elevated plus maze upon sleep fragmentation of one light phase of rats’ circadian cycle**

A. Lekovi´c †, A. Ademovi´c, Z. Grubač, N. Šutulovi´c, B. Knežević, M. Novaković

Institute of Medical Physiology “Richard Burian”, Belgrade University School of Medicine, Serbia

**E-mail address:** aleksa.lekovic@gmail.com

(A. Leković).

**Aim:** To assess anxiety-like behavior in rats after twelve hours of sleep fragmentation during the light phase of sleep-wake cycle, using the elevated plus maze test.

**Introduction:** Hallmark of sleep fragmentation is set of frequent, brief arousals, which modulates sleep architecture without significant diminishment of total sleep time. Anxiety is recognized as comorbidity in numerous disorders, including some of those related to sleep quality. Sleep fragmentation may be appropriate model of sleep alteration pattern in some disorders, yet its effects on behavioral alterations have not been broadly investigated.

**Methods:** Sleep fragmentation was achieved by treadmill method lasting for 12 h, during the light phase of the day (starting at 8 AM). Wistar albino male rats were randomly divided into: sleep fragmentation group (SF, n = 8, treadmill programmed to alternately work 30 s ON and 90 s OFF every 2 min); activity group (AC, n = 8, treadmill programmed to alternately work 10 min ON and 30 min OFF); and treadmill control group (TC, n = 8, rats stayed in the treadmill set to OFF mode and conditions equivalent to cages). Immediately after the sleep fragmentation regimen, elevated plus maze test was performed. To assess anxiety-like behavior, we measured time spent in the open arms, as well as number of transitions between open and closed arms.

**Results:** SF group spent significantly less time in the open arms, compared to both, AC and TC group (p < 0.001). SF rats also had significantly less number of transitions between closed and open arms of the maze, compared to AC and TC group (p < 0.05). Moreover, no significant difference was observed in any of the measured parameters between TC and AC group.

**Conclusion:** The results of our study indicate that acute 12-h sleep fragmentation induced anxiety-like behavior in rats in elevated plus maze. Further research should help us better understand impact of this phenomenon on psychiatric disorders.

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