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Pharmacology connecting Islands: Post-Pandemic challenges and opportunities

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ONLINE EVENT

PRÊMIO JOSÉ RIBEIRO DO VALLE – 2021

O prêmio José Ribeiro do Valle, oferecido a cada ano pela SBFTE, visa identificar a cada ano os melhores trabalhos científicos desenvolvidos por jovens investigadores na área da Farmacologia. Entre os trabalhos inscritos para esta vigésima segunda edição do prêmio, foram selecionados cinco finalistas, que fizeram apresentações de seus respectivos trabalhos perante comissão julgadora, em sessão pública durante o 53º Congresso Brasileiro de Farmacologia e Terapêutica Experimental, no Formato Online – Plataforma InEvent. O resultado foi o seguinte:

Primeiro prêmio

Rianne Remus Pulcinelli

02.018 **Taurine restores extracellular GABA levels in the nucleus accumbens reduced by alcohol withdrawal and decreases voluntary alcohol intake in withdrawal rats.** Pulcinelli RR[1], Caletti G[1], Izolan LR[1], Eller S[2], Nin MS[3], Oliveira TF[2], Gomez R[1]. [1]UFRGS Porto Alegre, PPG Farmacologia e Terapêutica (PPGFT), Brazil; [2]UFCSPA Porto Alegre, Dpt de Farmacociências, Brazil; [3]FURG Rio Grande, Dpt de Ciências Biológicas, Brazil

Introduction: Taurine is an abundant amino acid in the brain and shows a neuromodulatory effect on GABAergic and glutamatergic systems, both related to neuroadaptive changes in progression from occasional alcohol intake to dependence. Previously, we found that chronic taurine administration increases voluntary alcohol intake in rats. Here we investigated the effect of repeated taurine administration during alcohol withdrawal and re-exposure, as well as *In Vivo* extracellular GABA levels in the nucleus accumbens (NAcc) of rats. **Methods**: Adult male Wistar rats were allowed to choose from two bottles containing 20% alcohol and vehicle solution (AL group) or two bottles containing vehicle solution (CT group), 24 h/day, for four weeks. On day 22nd, half of the AL rats had their alcohol bottle substituted for another containing vehicle solution (WH group). Then CT, AL, and WH groups were subdivided to receive 100 mg/kg taurine or saline i.p. (CTS; CTT; ALS; ALT, WHS, WHT; n=6/group), once a day, for five days. Before starting this treatment (day 20th), a stereotaxic surgery was conducted to insert a guide cannula in the NAcc for the microanalysis study. After seven days from the stereotaxic surgery, microdialysis was performed along 2.5 h, with samples collected every 30 min. The perfusates were analyzed by a UFLC system coupled to a triple quadrupole mass spectrometer to determine GABA efflux in the NAcc. Later, the rats from WH groups received an additional taurine/saline administration and were re-exposed to the voluntary alcohol intake model and allowed to drink for 24 h. Daily alcohol voluntary intake was monitored throughout the experiment. **Results**: Taurine treatment (WHT group) prevented the lower baseline GABA levels in the NAcc of rats found in the WHS group compared with CTS and ALS groups. Moreover, taurine decreased GABA levels in alcohol-exposed rats (ALT group) compared to the ALS group. Replaying previous studies, taurine increased twice as much alcohol intake in the ALT group on days 4th and 5th of the treatment. However, taurine during withdrawal prevented the increased alcohol consumption seen in the WHS group, decreasing by 64% the alcohol intake of the WHT group during re-exposure ($P = 0.010$). Pearson test indicated an inverse correlation ($r = -0.51$; $P = 0.0216$) between the GABA levels and alcohol consumption considering AL and WH groups. **Conclusion**: Taurine produces an alcohol anti-addictive effect dependent on the abstinence condition. This effect may be related to the

restoration of extracellular GABA levels in NAcc impaired by alcohol withdrawal that, indirectly, modulates alcohol-related reward pathways. Taurine treatment during alcohol withdrawal could be beneficial as an adjuvant therapy to prevent alcohol relapse in abstinent alcohol-dependent. **Financial Support**: CNPq, CAPES, Propesq-UFRGS Approval by Animal Research Ethical Committee: CEUA-UFRGS # 36606 **License number of ethics committee**: CEUA-UFRGS # 36606

Segundo prêmio

Naiara Ayako Satori

08.011 **Relaxation of airway smooth muscle induced by classical phosphodiesterase (PDE) inhibitors involves inhibition of ecto-PDE**. Satori NA[1], Pacini ESA[1], Jackson EK[2], Godinho RO[1]. [1]Division of Cellular Pharmacology, Dpt of Pharmacology, Escola Paulista de Medicina, Univ Federal de São Paulo (EPM/Unifesp), São Paulo, Brazil [2]Dpt of Pharmacology and Chemical Biology, Univ of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Introduction: β_2-adrenoreceptor agonists and phosphodiesterase (PDE) inhibitors are effective bronchodilators drugs used for asthma treatment, due to their ability to increase intracellular 3',5'-cyclic AMP (cAMP) levels and induce airway smooth muscle (ASM) relaxation. Interestingly, we have shown that increases in intracellular cAMP levels in ASM is followed by cAMP efflux, leading to an increase in extracellular cAMP levels and constriction of ASM (Pacini et al., J. Pharmacol. Exp. Ther. 366; 75, 2018). Assuming that in many tissues extracellular cAMP is converted to adenosine by ectoenzymes (ecto-PDEs and ecto-nucleotidases), we evaluated whether classical inhibitors of intracellular PDEs 3-isobutyl-1-methylxanthine (IBMX) and aminophylline could also inhibit ecto-PDEs, and as consequence affect the contracting effects of extracellular cAMP in the ASM. **Methods**: Isolated tracheal segments from adult male rats (Wistar, 3–4-month-old; 250-350 g) were pre-contracted with carbachol in order to measure the relaxing effects of these PDE inhibitors using an isometric force transducer. In another set of experiments, isolated tracheal segments were incubated for 60 min with exogenous cAMP (30 µM) in the presence of IBMX (non-selective PDE inhibitor), and the concentrations of extracellular 5'-AMP, adenosine and inosine were measured using ultraperformance liquid chromatography–tandem mass spectrometry (UPLC-MS/MS). All values were expressed as mean ± S.E.M. **Results**: The PDE inhibitors induced a concentration-dependent relaxation of tracheal segments (pEC_{50}: IBMX = 5.5 ± 0.1; aminophylline = 4.0 ± 0.1; n= 5-6). Pretreatment of tracheas with 20 µM CGS-15943, a nonselective adenosine receptor antagonist, did not change the relaxation curve of PDE inhibitors but shifted to the left the relaxation curve of the β2-adrenoceptor agonist salbutamol (pEC_{50} = 6.9 ± 0.1 versus pEC_{50} = 7.4 ± 0.1). Preincubation of tracheal segments with 1 mM IBMX reduced the extracellular conversion of cAMP to 5'-AMP by 42% (17.15 ± 1.30 versus 9.92 ± 1.42 ng/mL), to adenosine by 42% and to inosine by 57% (n=6, $p < 0.05$). **Conclusion**: These results indicate that inhibitors of intracellular PDEs could also be acting as ecto-PDE inhibitors, thus preventing extracellular degradation of cAMP to the contracting metabolite adenosine. **License number of ethics committee**: CEUA #1021240519 and #9987150714

Menção Honrosa

Anderson Romério Azevedo Cerqueira

04.017 **Antioxidant effect of mitochondrial H2S donor (AP39) in topical treatment for burn injury**
Cerqueira ARA[1], Teixeira SA[1], Coavoy-Sanchez SA[1], Oliveira JP[1], Wood ME[2], Whiteman M[3], Muscará

MN[1], Lopes LB[1], Costa SKP[1]. [1]USP São Paulo, Inst of Biomedical Sciences, Dpt of Pharmacology, Brazil; Univ of Exeter Exeter, [2]Dpt of Biosciences, [3]College of Medicine and Health, UK

Matheus Leite de Medeiros

04.016 **Methylglyoxal aggravates lipopolysaccharide-induced mouse lung inflammation**. Medeiros ML, Oliveira AL, Oliveira MG, Mónica FZ, Antunes, E. Dept de Farmacologia, Faculdade de Ciências Medicas, Univ de Campinas, Campinas, Brasil

Roberta Giusti Schran

05.011 **Nociceptive effect of TLR2 on a mice model of postoperative pain** Schran RG, Ferreira MDA, Silva AMD, Martins F, Ferreira J Department of Pharmacology, Federal University of Santa Catarina, Florianópolis, SC, Brazil

Comissão Julgadora

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