02 Neuropharmacology

02.001 Choline reduces the neuromuscular transmission at 50 Hz triggering α_7 - nicotinic receptor, thereby inducing presynaptic activations of A_{2A} and M_2 receptors. Castellão-Santana LM[1], Ambiel CR[2], Correia-De-Sá P[3], Alves-Do-Prado W[1]
[1]UEM – Farmacologia e Terapêutica, [2]UEM – Ciências Fisiológicas, [3]UP – Ciências Biomédicas

Introduction: We have previously shown that choline (Chol, 1.0 µM) might activate alfa$_7$ neuronal nicotinic receptors in perisynaptic Schwann cells of motor nerve to cause inhibitory effect on neuromuscular transmission when the motor nerve is submitted at tetanizing frequency (50 Hz). In current study we investigate: i) if part of inhibitory effect caused by 1.0 µM Chol in neuromuscular transmission might origin from interaction of drug with postsynaptic nicotinic receptors and ii) if the presynaptic facilitatory-A_{2A} and/or inhibitory-M_2 receptors might have roles keys in the effect caused by Chol in the phrenic nerve diaphragm muscle preparations indirectly stimulated at 50 Hz, as exist a interplay between such receptors in motor nerve terminal (Oliveira L. Signal Transduction 6:19, 2006). **Methods:** Phrenic nerve–diaphragm muscle preparations of rats were set up as described by (Bülbring. J Pharmacol Chemother 1:38, 1946). Each preparation was immersed in a 30 mL chamber containing Krebs' buffer solution, maintained at 37°C and aerated. The phrenic nerve was stimulated through a bipolar platinum electrode. Preparations were indirectly stimulated at 0.2 Hz and six tetanic stimuli (50 Hz) were applied at 20 min intervals. T= 45 min was the instant selected to analyze of data. Muscular contractions were recorded on Chart Software. In some preparations, a polyethylene catheter was introduced in the thoracic inferior vena cava to permit retrograde injections of ACh. The ratio between the initial tetanic tension at the beginning (A) and tension at the end (B) of the tetanic stimulus (after 5 s; B) was analyzed as ratio (R) (R=A/B). Chol or PNU 282987 (PNU) were administered separately or 20 min after addition of other agents in the bath containing Krebs-buffer solution. Data were submitted to ANOVA, followed by Bonferroni post-hoc test at $P<0.05$ significance level. **Results:** 1.0 µM Chol or PNU caused similar ($P> 0.05$) percentage of reduction in R-values (-8.00±1.81%, Chol, -7.00±1.73%, for PNU). The amplitudes of fast twitches induced by retrogrades injections of 0.5 µM ACh were not affected by 1.0 µM Chol or PNU in the bath. The reductions in R-values caused by 1.0 µM Chol and PNU were diminished by previous administration of metylcaconitine (40 nM) (from -8.00± 1.81% to -0.34± 0.61% for Chol, from -7.00± 1.73% to -0.29± 0.45% for PNU), of ZM 241385 (10 nM) (from -8.00± 1.81% to -2.84± 0.09 for Chol, from -7.00± 1.73% to -0,28± 0,14% for PNU), of metoctramine (0.1µM) (from -8.00± 1.81% to -0.19± 1.19% for Chol, from -7.00± 1.73% to 0.08± 0.82% for PNU), or of McN-A-343c (3.0 µM) (from -8.00± 1.81% to -4.05± 0.32% for Chol, from -7.00± 1.73% to 0.37± 0.57% for PNU). **Conclusion:** It is unlikely that inhibitory effect caused by 1.0 µM Chol or PNU has been determined by a direct action of such agents with postsynaptic nicotinic receptors. In contrast, it is possible to suppose that other actions of Chol besides the activation of α7-CnNR in Schwann cells might have participation in the inhibitory effect caused by this agent at 50 Hz. **License number of ethics committee**: 7227300915 **Financial support**: fadec-UEM

02.002 Thalamic nucleus reuniens activity during consolidation influences fear memory specificity, **long-term maintenance and plasticity in the hippocampus and pre-frontal cortex**. Troyner F, Bicca MA, Bertoglio LJ UFSC – Farmacologia

Nucleus reuniens (NR) is recognized as a hub for networks which support fear memory processes, especially those dependent on cortico-hippocampal interactions. Therefore, its activity could be decisive for memory consolidation. We investigated whether temporary NR inactivation immediately after fear memory acquisition would modulate fear memory features such as specificity and long-term maintenance. We also investigated if NR temporary inactivation would interfere with the expression of plasticity-related Arc protein in areas necessary for fear memory consolidation. Male Wistar rats (CEUA/ 2012PP00766) were fear conditioned to context A with three shocks of 0.8 mA and then infused intra-NR with vehicle (VEH) or the $GABA_A$ receptor agonist muscimol (MUS - 4 nmol/ 0.2 µL). Animals were re-exposed to the paired context A (Test A) and to a novel and unpaired context B (Test B) at recent (days 1 and 2) or at remote (days 21 and 22) time points. In both cases, MUS-treated animals presented a significant increase in freezing time during Test B in comparison to VEH-treated, indicating impaired contextual specificity. MUS-treated animals also spent significantly more time freezing than VEH-treated during Test A at the remote time point, which indicates increased fear memory persistence over time. We questioned whether augmented freezing during Test B resulted from changes in anxiety-related behaviors and/or general exploratory activity. To investigate that, additional groups were infused with VEH or MUS into the NR immediately after contextual fear conditioning. On day 1, both groups performed Test A. Twenty-four hours later they were tested in the elevated plus-maze (EPM) to coincide with the temporal window used to assess freezing time during Test B. Behavioral assessment in the EPM revealed no significant MUS treatment effects on inhibitory avoidance, risk assessment or general exploratory activity, suggesting that increased fear expression during Test B is not related to altered levels of anxiety and general exploratory activity. Lastly, animals were divided in 5 groups: surgery home-cage, non-conditioned VEH, non-conditioned MUS, conditioned VEH and conditioned MUS. Conditioned and non-conditioned animals were euthanized, and brains collected 90 minutes after intra-NR injection of VEH or MUS. We analyzed the CA1 of dorsal and ventral hippocampus, nucleus reuniens, pre-limbic, infralimbic and anterior cingulate cortices. MUS-conditioned animals expressed a significant decrease in Arc+ cells in the ventral hippocampus and infralimbic cortex when compared with VEH-conditioned group. An elevated number of Arc+ cells were found in the dorsal hippocampus and pre-limbic cortex of MUS-conditioned animals. No differences were observed between groups in the anterior cingulated cortex. MUS induced a decrease in Arc+ cells in NR in both conditioned and non-conditioned groups. Overall, our results indicate that NR activity is decisive for fear memory consolidation, providing control over fear memory specificity and long-term maintenance which is accompanied by plasticity changes in the dorsal and ventral hippocampus and pre-limbic and infralimbic portions of the prefrontal cortex. **License number of ethics committee**: CEUA/2012PP00766 **Financial support**: CNPQ / CAPES / PPG FMC - UFSC

02.003 Dorsal Hippocampal kappa opioid receptors modulate contextual fear memory consolidation in rats. Jesse AC[1], Vanz F[1], Bobinski F[2], Bertoglio LJ[1], de Lima TCM[1] [1]UFSC – Farmacologia, [2]UNISUL – Ciências da Saúde

Introduction: The kappa opioid receptors (κORs) and their endogenous ligands are expressed in brain regions regulating fear learning and memory processing, including the dorsal hippocampus (DH) (GALL et al., 1981; MANSOUR et al., 1994; MCLEAN et al., 1987; SIMMONS, 1996). However, the role of DH κORs in consolidation of fear memories with intensity moderate is still uncertain. The present study aimed to investigate this question using pharmacological agents in rats subjected to a moderate contextual fear conditioning (CAC) protocol. **Methods:** Adult male Wistar rats (approved protocol n. 9771250417 CEUA/UFSC) were conditioned to the context A with one shock (0.7 mA, 3 s and 60 Hz - CAC moderate) and received a bilateral infusion into the DH of vehicle (VEH) or the selective κOR antagonist nor-Binaltorphimine (nor-BNI 1, 3 or 10 nmol/0.5 µL/hemisphere) 0 or 6 h later (experiment 1 and experiment 2, respectively). In certain experiments, nor-BNI was infused immediately after an unpaired shock (immediate shock - experiment 3). Test session was performed one (test A1) and seven (test A2) days after the conditioning day. Freezing behavior was measured as an index of memory retention. In experiment 4, to κORs immunoblotting analysis animals were conditioned (except the naive group) and the DH was dissected 0, 1, 3 or 6 h later. In experiment 5, animals were conditioned (context-shock pairing) or just exposed to contextual (context no-shock) or aversive (immediate shock) components, and the DH was dissected 1 h later. Finally, in experiment 6 BDNF levels were measured by ELISA in animals that received nor-BNI infusion in DH 90 min after CAC moderate. **Results:** In experiment 1, infusion of nor-BNI 3 or 10 nmol immediately after conditioning increased freezing time in both tests A1 and A2 when compared with respective VEH groups (Test A1: VEH = 40 + 5%, nor-BNI 3 = 80 + 5%, nor-BNI 10 = 68 + 6%; Test A2: VEH = 36 + 4%, nor-BNI 3 = 69 + 3%, nor-BNI 10 = 65 + 4%). Moreover, nor-BNI 3 nmol infused 6 h after the conditioning session (experiment 2) or immediately after the immediate shock (experiment 3) had no effect on freezing behavior ([VEH= 38 + 9% vs. nor-BNI 3 = 39 + 6%] and [VEH = 11 + 2% vs. nor-BNI 3 = 12 + 2%], respectively). In experiment 4, contextual conditioning induced an increase in DH κORs immunoblotting content in groups 1 and 3 h when compared with naive or 0 h groups (Naive = 100 + 11%, 0 h = 101 + 12%, 1 h = 163 + 21%, 3 h = 171 + 17%). In experiment 5, shock-context group, but not context or immediate shock groups, showed DH κORs immunoblotting content increased 1 h after training session (Naive = 100 + 13%). Context no-shock = 147 + 13%, Context-shock pairing = 171 + 24%, Immediate shock = 114 + 8%). Finally, in experiment 6 nor-BNI infusion increased BDNF levels in DH 90 min after CAC moderate, suggesting a possible mechanism by which DH κOR blockage leads to the potentialization of memory consolidation. **Conclusion:** These present results suggest that DH κORs are up-regulated during an associative fear experience and its activation plays a modulatory inhibitory role in the consolidation of a contextual fear memory. **References:** GALL C. J Comp Neurol., v. 198(2), p.335, 1981. MANSOUR A. Brain Res., v. 643, p. 245, 1994. MCLEAN S. J Comp Neurol., v. 255, p. 497, 1987. SIMMONS M.L. Int Rev Neurobiol., v. 39, p. 145, 1996. **License number of ethics committee**: 9771250417 CEUA/UFSC **Financial support**: CNPq, CAPES, UFSC and PPG Farmacologia/UFSC

02.005 The effects of intranasal administration of the cerebral dopamine neurotrophic factor (CDNF) in an animal model of Parkinson's disease Lopes SC[1], Lopes MW[2], Portes MAM[1], Roversi K[1], de Souza BS[1], de Oliveira PA[1], Prediger RDS[1]
[1]UFSC – Farmacologia, [2]UFSC – Bioquímica

Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and the presence of Lewy bodies. Pharmacotherapeutic options for PD have grown considerably in the last decades. Even so, to date, PD remains incurable, with therapeutic strategies limited to symptomatology and effectiveness for a certain period; nevertheless, neurodegeneration remains unchanged. The exact molecular mechanisms associated with the progressive neurodegeneration seen in PD remain unknown but some basic research studies indicate the involvement of neurotrophic factors (NTFs), leading to increased immunoreactivity of TH and dopaminergic projections, such as substantial improvement in motor deficits. However, the evaluation in clinical trials does not demonstrate such efficacy, which is speculated to be involved with the delivery systems used for the NTFs. In the year 2007 was characterized the CDNF, cerebral dopamine neurotrophic factor, as having a greater specificity for protection and restoration of dopaminergic neurons, especially in PD models (than NRTR and GDNF, e.g.). Thus, the major focus of our work is to evaluate the effect of CDNF when administered by the intranasal route (i.n.) in a 6-OHDA animal model of PD. For this, an extensive behavioral study has been done and the CDNF (i.n.) was effective in alleviate the overall performance of the animals. CDNF (i.n.) was able of restoring weight loss after injury, improve motor dysfunction when evaluated in the rota-rod, cylinder, footprint and adhesive-test, as well as showing positive effects under the memory evaluated through the Y-maze and the anhedonic-like behavior when evaluated by the splash test. Taken together, these results suggest that the strategies we are adopting through an effective and non-invasive delivery system for the CDNF - able of modifying the course of the disease, bringing functional benefits; and provides new evidence of CDNF potential for the PD. **License number of ethics committee**: PP830 **Financial support**: CNPq; CAPES; FAPESC

02.006 Sex influence on PTEN expression in embryonic primary neuronal culture from conditional PTEN knockout mice. Mello NP, Scavone C, Kawamoto EM USP – Farmacologia

Introduction: PTEN (Phosphatase and Tensin homolog on chromosome ten) is a protein related to growth, proliferation and cell survival. Due to its importance in cell development, PTEN deletion results in neuronal morphological alterations and has been related with several neurological illnesses such as Autism Spectrum Disorder, Parkinson and Alzheimer's disease. Since most of these pathological conditions are more prevalent in men than in woman, understanding how gender differences influence on PTEN expression and on the PI3K-AKT pathway could contribute to identify possible female neuroprotective responses and to generate new pharmacological strategies. **Methods:** PTEN conditional knockout mouse was obtained by the Cre-LoxP system. Heterozygous animals were mated in order to get the homozygous (HO) and wild-type (WT) embryos. Embryo (E16.5) cortex was used in the primary neuronal culture and the tail was used for genotyping the Cre-LoxP system and the embryo sex. Cells were fixed after 7 and 14 days *in vitro* (DIV) before performing immunofluorescence. **Results:** According with the obtained data, considering the time during the cell development, the highest increase in PTEN expression in WT mice seems to occur at the period between DIV7 and DIV14. Regarding the gender, neurons from female WT mice demonstrated to have higher PTEN expression than the male one at the same period of the time. However, besides that, no difference was found in the pAKT (Thr308) expression between the WT embryo cells from both sexes. **Conclusion:** Compared with the male WT embryo, the highest PTEN expression and the unaltered pAKT (Thr308) expression in female WT embryo can indicate a possible balance mechanism present in the last one. Besides, it is important to notice that sex difference can influence the development of the cell even in embryonic culture. In this way, studies using embryos must considering the animal sex in order to not miss valuable information. **Animal Research Ethical Committee:** n° 57/2016. **Financial Support:** FAPESP. **License number of ethics committee**: n° 57/2016 **Financial support**: FAPESP

02.007 The response of swiss mice to the forced swim test under acute, **subacute and chronic treatment with ketamine**. Bezerra MA, Zerbinatti N, Suman PR, Lino de Oliveira C UFSC – Ciências Fisiológicas

Introduction: One of the drugs most recently studied for the treatment of depression is ketamine, widely used as a general anaesthetic. The mechanism of ketamine action is based on the blockade of NMDA receptors for glutamate indicating the critical participation of this neurotransmitter in the aetiology of the disease (Murrough et al., 2013). The aim of this study is test different doses of ketamine in acute (1 day), subacute (7 days) and chronic (14 days) periods of time. **Methods:** This research was approved by CEUA at UFSC, with approval number 8080/17. Forced swim test (FST) was used to evaluate the effect of ketamine on mice behaviour when placed individually in a cylindrical tank (24 cm height x 14 cm diameter) containing water at temperature of 24 ± 1°C, for six minutes. Ketamine was administered through intraperitoneal route at doses of 0 (saline), 5, 10, 20, 40 mg/kg. Mice of the acute, subacute or chronic treatments were tested in the FST 30 minutes after the last administration. The FST was recorded using VirtualDub and immobility time in the final four minutes of FST was scored using Ethowatcher (Suman et al., 2017). Results were analysed using ANOVA followed by Duncan (if applicable) to evaluating statistical significance ($p<0.05$). **Results:** Parameters of immobility in mice treated subacutely or chronically with ketamine in the doses of 5, 10 and 20 mg/kg were not significantly different from acute treatment or control. Acute treatment with ketamine 40 mg/kg reduced significantly (Duncan $p<0.05$) duration (17.8± 10.7 s) and frequency (1.8 ± 1.2 bouts) of immobility as compared to control (154.9 ± 23.3 s, 5.3 ± 0.9 bouts). Subacute treatment with ketamine 40 mg/kg reduced significantly (Duncan $p<0.05$) duration (58.3 ± 26.9) and frequency (2.8 ± 1.1 bouts) of immobility as compared to control group (171.4 ± 21.4 s, 6.3 ± 0.4 bouts). Chronic treatment with ketamine 40 mg/kg a reduced significantly (Duncan $p<0.05$) duration (47.4 ± 24.2) and frequency (2.6 ± 0.9) of immobility as compared to control group (170.5 ± 21 s, 5.1 ± 0.5 bouts). Latency for immobility after acute, subacute and chronic treatment with ketamine 40 mg/kg did not differ significantly from control. Interestingly, the effect size of ketamine 40 mg/kg on the duration of immobility decreased with the lengthening of the treatment. **Conclusion:** In contrast with lower doses, ketamine 40 mg/kg was able to decrease significantly duration of immobility in all periods of treatment. **License number of ethics committee**: 8080/17 **Financial support**: CNPq

02.009 BDNF mRNA expression influence in the prefrontal cortex of the cocaine-conditioning behavior. Freese L[1], Zavarie L[2], Almeida FB[1], Heidrich N[1], Fernandes P[1], Gomez R[3], Barros HMT[1] - [1]UFCSPA – Ciências da Saúde, [2]UFCSPA – Farmacociências, [3]UFRGS – Farmacologia

Introduction: psychostimulants effect has been shown to be associated with the alterations in the brain-derived neurotrophic factor (BDNF) expression. Evidence from animal and clinical studies suggests that increased central BDNF activity may be implicated in the pathogenesis of cocaine addiction (McGinty, J.F. et al, Brain Res. Vol. 1314, Pag. 193, 2010). According some studies, BDNF regulates cocaine-induced behaviors in a highly complex manner that varies depending on the brain region, the nature of cocaine exposure, and the addiction phase examined (see Li and Wolf, Brain Res. Vol. 1314, Pag. 183, 2015 for a review). Although most studies demonstrate that increased levels of BDNF reduce the rewarding effects of cocaine, when the pre-frontal cortex was analyzed, the role of BDNF seems to be singular (Berglind et al, Eur J Neurosci. Vol. 26, Pag. 757, 2007). Here we aim to evaluate if the role of BDNF mRNA levels change according the conditioning response in the cocaine-induced CPP. **Method**: forty-nine Wistar male rats were divided in two groups of CPP: classical CPP - cocaine versus saline; and choice CPP - cocaine versus saccharine. The score of the time spent in each compartment defining if the rats were conditioned or unconditioned to cocaine (15mg/kg; i.p.). After the end of the CPP, the rats were sacrificed, and the PFC was dissected. After, the BDNF mRNA levels in the prefrontal cortex (PFC) were determined by real-time polymerase chain reaction (PCR). For the statistical analysis, was used a two-way ANOVA (CPP and cocaine-conditioning response). The study was approved by Ethical Committee for Research of UFCSPA (#224/13). **Results:** as expected, the behavior results showed a preference for the cocaine-paired compartment only in the classical CPP ($p = < 0.05$). The BDNF mRNA level in the PFC was significantly increased in the unconditioned rats from cocaine versus saline CPP ($p < 0.05$) and there was an interaction between CPP and the cocaine-conditioned behavior ($p < 0.05$). **Conclusion:** the present results support the hypothesis that BDNF mRNA levels in the PFC are critical in conditioning behavior of the classical CPP paradigm. Our findings thus provide novel evidence demonstrating that, different from other regions, in the PFC the high BDNF expression can protect the rat to cocaine-conditioning behavior. **License number of ethics committee**: #224/13 **Financial support**: CAPES

02.011 Plumieride, **an iridoid isolated from** *Allamanda cathartica* **flowers**, **exert antidepressant and anxiolytic effect after acute oral administration**. Dalmagro AP[1], Camargo A[2], Zimath PL[1], Bonomini TJ[1], Malheiros A[1], Zeni ALB[2], Souza MM[1] [1]Univali – Ciências Farmacêuticas, [2]Furb – Ciências Biológicas

Introduction: Plumieride, an iridoid isolated from the *Allamanda cathartica* flowers, has demonstrated pharmacological effects in inflammation and oxidative stress modulation in studies developed by our research group. These findings have been strongly correlated to the anti-depressant and anxiolytic capacity of the molecules, therefore the aim of the research was to evaluate the plumieride antidepressive-like and anxiolytic-like effect in mice, after acute oral administration. **Methods:** Female Swiss mice aged 60-90 days, were used, and all administrations were oral and acute - 60 minutes before the behavioral tests. For the antidepressant-like effect, five groups were used (n=8-10): CON (vehicle – destilled water), Plu 0,5 (0,5 µg/Kg), Plu 1 (1 µg/Kg), Plu 2 (2 µg/Kg) and Flu 10 (10 mg/Kg). The treated mice were submitted to the Tail Suspension Test (TST) and the immobility time was registered for six minutes. The investigation of the anxiolytic-like effect was performed through the Elevated Plus Maze Test (EPM), and the spent time and number of entries in the open and closed arms were counted for six minutes. For this purpose, the same groups were used, except for the reference drug, which was diazepam 1 mg / kg. The locomotor, exploratory and emotional capacity of the animals was also evaluated through the Open Field Test (OFT). The results were evaluated through one-way ANOVA and considered significant as $p<0.05$. **Results:** Plumieride was able to reduce immobility time in TST at all administered doses: 0.5; 1 and 2 µg / kg ($p<0.001$, $p<0.01$, $p<0.001$, respectively), as well as fluoxetine ($p <0.001$); however, there was no statistical difference between doses. In the EPM, animals treated with Plu 1 and Plu 2 stayed longer in the open arms ($p <0.05$; $p <0.01$), as well as mice given diazepam ($p <0.001$). There was no statistically significant difference between the effective doses in EPM, however, only the treated mice with Plu 2 ($p<0,01$) and diazepam ($p<0,0001$) spent less time in the closed arms. There was no interference from any treatment given in the locomotor, exploratory or emotional capacity of the animals (OFT – $p>0,05$). **Conclusion:** The plumieride antidepressant-like and anxiolytic-like effects, even after acute and orally administration by gavage, were demonstrated in extremely low doses when compared to reference drugs for the treatment of depression and anxiety. In addition, the good solubility and reduced toxicity of plumieride support the need for more research involving its action in the CNS. **Financial Support:** UNIVALI, FURB, CAPES. **CEUA Protocol Number:** 035/2016 - UNIVALI. **License number of ethics committee**: CEUA/UNIVALI 035/2016. **Financial support**: UNIVALI, FURB, CAPES.

02.013 Biperiden: **Potential drug for addiction**. Palombo P[1], Maeda RA[1], Zaniboni CR[1], Yokowama TS[1], Santos PCJL[1], Galduroz JC[2], Cruz FC[1] [1]Unifesp – Farmacologia, [2]Unifesp – Psicobiologia

Recent studies suggest that nicotinic and muscarinic cholinergic receptor mediate dopamine release in the mesolimbic system and can alter the drug's reinforcing value. It was demonstrated that systemic treatment with the biperiden, a muscarinic cholinergic (*M1)* antagonist receptor blocked the expression of cocaine conditioned place preference (CPP) in mice. Here, we examine the effect of systemic biperidene injection (1, 5 and 10mg / kg ip) on alcohol conditioned place preference. The CPP procedure consisted of the following phases: habituation, conditioning and testing. It was used a three-chamber 'unbiased' apparatus. During the habituation, each male Swiss mouse was placed in the neutral compartment with the guillotine doors removed to allow access to the entire apparatus for 15 min for 3 days. On day 3, mice were placed in the apparatus the time spent in each compartment was recorded. For conditioning, mice were randomly paired to alcohol or saline administration. Conditioning was performed using a protocol consisting of 8 injections of 2.0 mg/kg i.p. of alcohol or saline over 8 alternate and consecutive days. The test was conducted 24 h after the last conditioning session. Thirty minutes before the test mice were grouped in 4 groups and were injected with biperiden at the doses of 1 or 5 or 10 mg/kg and were placed in the neutral compartment with the guillotine doors removed to allow access to the entire apparatus. The time spent in each compartment was recorded for 15 min. Biperiden 10 mg/kg blocked the alcohol CPP expression (Saline: pretest - 35.20% ± 0.02; test - 59.61 ± 0.04; Bip 1mg/Kg: pretest - 34.55% ± 0.03; test - 48.71% ± 0.14; Bip 5 mg/Kg: pretest - 35.17% ± 0.02; test - 50.51% ± 0.03; Bip 10 mg/Kg: pretest - 33.18% ± 0.03; test: 45.28% ± 0.02; p□0.05). Our results add to growing evidence that biperiden might be a promising drug for drug addiction treatment. **License number of ethics committee**: 8583220517 **Financial support**: Fapesp 2013/24986-2 and 2017/262250

02.015 Aging process impacts epigenetic markers in hippocampal Brain-Derived Neurotrophic Factor (BDNF) gene promoter: Effect of exercise modalities.

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Introduction: Exercise has been related to neuroprotection and epigenetic regulation of *Bdnf* gene (1). Although BDNF is considered an important neurotrophin associated with neuroplasticity (1,2), its precursor, proBDNF, may have opposite effects in brain specifically in aging process (2). The aim of this study was to investigate the effects of the aging process and exercise modalities on epigenetic marks in hippocampal *Bdnf* gene promoter, such as H3K9ac, H3K4me3, H4K8ac and H3K9me2. **Methods:** Male Wistar rats of 2 and 22-month-old were submitted to aerobic, acrobatic, resistance or combined exercise modalities for 20 minutes, 3 times a week, for 12 weeks. In resistance training, animals scaled the ladder in series of 8 repetitions with a weight attached to their tails. The acrobatic training consisted of 6 repetitions of a circuit with 5 activities that stimulated multiple motor skills. The aerobic training consisted of running sessions at 60% of VO2max. In the combined modality animals performed 6 minutes of each modality mentioned previously. Hippocampi were collected one hour after the last exercise session and used to evaluate epigenetic marks at the promoter region of the *Bdnf* gene through chromatin immunoprecipitation (ChIP) assay. Student t-test and One-Way ANOVA followed by Dunnet's were used. In all tests, $p \leq 0.05$ was considered to indicate statistical significance. The project was approved by Comissão de Ética no Uso de Animais/UFRGS (29818). **Results:** Aged sedentary rats showed increases on activating epigenetic marks, H3K4me3 and H4K8ac, and decrease the repressive mark, H3K9me2, at hippocampal Bdnf gene promoter, comparing to adult ones. Exercise impacts hippocampal epigenetic marks in an age- and modality-dependent manner. Interestingly, aerobic and resistance modalities decreased H3K4me3 levels in aged rats, attenuating the impact of the aging process on this mark. While aerobic, acrobatic and resistance modalities increased the H4K8ac levels at hippocampal Bdnf gene promoter of adult rats. **Conclusion:** Our results demonstrated aging-induced changes in epigenetic marks favoring Bdnf expression in the hippocampus; it can be involved with previous findings about hippocampal proBDNF levels in the aging process. Besides, aerobic and resistance modalities reversed age-induced increases in H3K4me3, suggesting a reduction of *Bdnf* transcription. On the other hand, active epigenetic markers were increased in adult exercised rats submitted to aerobic, acrobatic and resistance modalities. **References:** 1. Buhusi, M., Etheredge, C., Granholm, A.-C., Buhusi, C.V., 2017. Increased Hippocampal ProBDNF Contributes to Memory Impairments in Aged Mice. Front Aging Neurosci 9, 284.1 2. Gomez-Pinilla, F., Zhuang, Y., Feng, J., Ying, Z., Fan, G., 2011. Exercise impacts brain-derived neurotrophic factor plasticity by engaging mechanisms of epigenetic regulation. Eur J Neurosci 33(3), 383-390 **License number of ethics committee**: 29818 **Financial support**: Financial support: CNPq, PIBIC.

02.018 GlyT1 inhibitor promotes neuroprotection against quinolinic acid-induced excitotoxicity in the striatum. Pinto MCX[1], Lima IVA[1], Lima OCO[1], Gomez MV[2], Gomez RS[3], Oliveira ACP[4] [1]UFG – Farmacologia, [2]Ensino e Pesquisa da Santa Casa de Belo Horizonte – Farmacologia, [3]UFMG – Cirurgia, [4]ICB-UFMG – Farmacologia

Huntington's disease (HD) is a complex and severe disorder characterized by the gradual and the progressive loss of neurons, predominantly in the striatum. The brain preconditioning is a protective mechanism, which can be activated by NMDA receptor (NMDAR) stimulation and be used to achieve neuroprotection in experimental models of neurodegenerative diseases. Glycine transporter type 1 inhibitors modulate glutamatergic neurotransmission through NMDAR, suggesting an alternative therapeutic strategy of brain preconditioning. The aim of this work was to evaluate the effects of brain preconditioning induced by NFPS, a GlyT1 inhibitor, against quinolinic acid-induced excitotoxicity in mouse striatum, a model of Huntington's disease, as well as to study its neurochemical mechanisms. C57BL/6 mice (male, 10-weeks-old) were preconditioned by intraperitoneal injection of NFPS at doses of 1.25, 2.5 or 5.0 mg/kg, 24 h before intrastriatal injection of quinolinic acid (QA). We examined the treatment effects in the animal behavior, neuron viability and brain neurotrophins expression. We observed that NFPS preconditioning reduced neuronal death in striatum submitted to QA-induced excitotoxicity. NFPS preconditioning has also led to improvements in motor behavior. Striatum neurotrophins assessment revealed a significant increase of NT4 expression, a neurotrophin that acts in TrKB receptor. Our study demonstrated that NFPS preconditioning increases neurotrophin expression and induces protective effects in striatum from mice submitted to Huntington's disease experimental model. **License number of ethics committee**: CEUA/UFMG nº. 182 / 2013 **Financial support**: CAPES; CNPQ; FAPEMIG

02.020 The Pancuronium-induced tetanic fatigue of the neuromuscular transmission is attenuated, *in vitro*, **in a mouse model of multiple sclerosis**. Pestana RRF[1], Serra CSM[1], Teixeira NB[2], Picolo G[2], Munhoz CD[1], Oliveira AC[1] [1]USP – Farmacologia, [2]IBu – Dor

Introduction: Multiple sclerosis (MS) is a demyelinating disease that affects the Central Nervous System. It is characteristic of the disease the presence of a number of signs and symptoms, either of a sensorial or motor nature. Among these, muscle paralysis is the most important. In the present work pharmacological studies were performed, *in vitro*, using isolated nerve-muscle or muscle preparations of animals displaying muscle paralysis, in a model of MS known as experimental autoimmune encephalomyelitis (EAE). **Methods**: The EAE was induced immunizing mice (adult, female, C57BL6 strain) with the myelin oligodendrocyte glycoprotein (MOG) used in conjunction with the complete Freund adjuvant (CFA) and pertussis toxin (PT). Animals in this group are referred to as “EAE”. To compare with EAE animals, two types of controls were employed: a) “Naïve” animals, that did not undergo any treatment; b) “CFA+PT” animals, that were treated with the adjuvants, only. The animals were daily examined as regards motor impairment and classified using a conventional disease score of four levels (0 to 3). Pharmacological experiments were performed *in vitro* using the isolated sciatic nerve-extensor digitorum longus (EDL) muscle or the isolated EDL muscle preparations. Indirect tetanic contractions (evoked at 100 Hz for 3 seconds) or twitches (evoked at 0.2 Hz) were recorded in the absence or presence of the neuromuscular blocker pancuronium. Direct tetanic contractions or twitches were generated at 100 Hz for 3 seconds or 0.2 Hz, respectively. The fatigue of the tetanic contraction was quantified expressing, percentually, the fall of the amplitude value of the tetanic contraction measured 1 second apart from the peak amplitude with respect to the value of the peak amplitude. The “EAE” animals included in this work were within score 3 of the disease: they displayed hemi-paresis or total paralysis of the hind-limb(s). In all groups of animals studied in this work, each sample encompassed 4 to 8 animals. This research was approved by the local Animal Research Ethical Committee. **Results**: In the presence of pancuronium ($5x10^{-8}$M) the percent fall of the indirect tetanic contraction, a quantitative indication of the fatigue of the neuromuscular transmission, was 75.0±12.5% in Naïve, 70.8±6.8% in CFT+PT and 23.6±2.2% in EAE animals. ANOVA followed by Tukey’s tests indicated a significant 5% difference between the EAE group with respect to the other two groups. The directly evoked tetanic contractions were not affected, being well sustained in the three groups of animals. The pancuronium IC_{50} for the block of indirect twitches were $1.76x10^{-7}$M in Naïve, $1.62x10^{-7}$M in CFA+TP and $1.89x10^{-7}$M in EAE animals. These values did not differ significantly. **Conclusion:** The EAE animals are more resistant than Naïve and CFA+TP animals to the fatigue of the indirect tetanic contraction induced by pancuronium. **Financial support**: FAPESP (11/50119-9), CNPq and CAPES. **License number of ethics committee**: Protocolo No. 99, fls. 03, livro 09. **Financial support**: FAPESP (11/50119-9), CNPq, CAPES