ABSTRACTS

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03. Psychopharmacology

03.001 Tactile stimulation prevents cocaine-induced depressive behavior in rats. Roversi KR, Antoniazzi CTD, Burger ME UFSM – Fisiologia e Farmacologia

Introduction The use of psychostimulant drugs such as cocaine has increased in the last years, leading to social and health problems [1]. Cocaine addiction can be associated to medical and psychiatric morbidities, including mood disorders, such as anhedonia, anxiety and depression. In rodents, depressive-like symptoms development was shown during withdrawal period. Antidepressant drugs have shown some efficacy in reducing anxiety and depression-like symptoms related to cocaine withdrawal in animal models [2]. Neonatal tactile stimulation (TS) is a positive approach which has been useful in reducing anxiety, stress and depressive-like behaviors in a range of situations. The present study aimed to evaluate the influence of TS in association with a sub-therapeutic dose of sertraline (SERT) on anhedonia and depression-like symptoms consequent to cocaine withdrawal. **Methods** Wistar male pup's rat were submitted to TS from postnatal day (PND) 8 to 14. Unhandled (UH) group was used as control for TS. In PND 40, experimental groups were designated to 4 groups: UH-Vehicle, TS-Vehicle, UH-Cocaine, TS-Cocaine. During 14 days, the animals received three daily administrations of cocaine (15 mg/kg, i.p.) or vehicle (NaCl 0.9%, i.p.) with 1h interval between each one, totalling 45 mg/kg of drug per day [3]. Seven days after drug withdrawal (DPN 60), anhedonia was assessed by sucrose preference quantification, while depressive behavior was assessed by forced swimming test (FST). All animals received 0.3 mg/kg of SERT 30 min before performing FST. Animals were euthanized to determine striatal dopamine receptor (D2) and glucocorticoid receptor (GR) immunocontent by western blotting. Two-way ANOVA followed by Tukey's test was used for statistical analysis. **Results** Our findings showed that after a sub-therapeutic dose of SERT, TS *per se* and after exposure to cocaine, increased sucrose intake while cocaine decreased this consumption only in UH group. In the FST, TS *per se* increased climbing and decreased immobility times, while cocaine reduced swimming time only in UH group. Molecular analysis showed that TS decreased striatal D2 immunocontent *per se* and in cocaine injected group, while UH cocaine-injected animals presented an increase in this parameter. TS increased *per se* GR immunoreactivity, and decreased after cocaine exposure, while in UH group, cocaine increased this immunoreactivity. **Conclusion** Our outcomes are showing that while cocaine withdrawal was related to anhedonia- and depression-like symptoms, TS in association with a sub-therapeutic dose of SERT reduced or prevented these deleterious effects of cocaine. Considering this and the molecular influences observed in the striatum, we hypothesize that TS can promote molecular adaptations in both GR and D2 receptors, reducing or preventing the harmful behavioral effects of cocaine withdrawal. Based on this, we propose that neonatal TS in association with low doses of antidepressant drug is able to prevent withdrawal symptoms consequent to use of psychostimulant drugs, preventing relapse episodes in drug addiction situations. **Acknowledgment** Authors are grateful to CNPq, CAPES and PRPGP (PROAP) for the fellowships and financial support. The experimental protocol was approved by the Comissão de Ética no Uso de Animais (CEUA-UFSM, nº 7928301115/2015), which is affiliated to the Council for Control of Animal Experiments (CONCEA). [1] Abdala et al., Addict. Behav., 39:297, 2014. [2] Buffalari et al., Psychopharmacology, 223:179, 2012. [3] Alves et al., Neuroscience, 277:343, 2014.

03.002 Cannabidiol treatment reverses behavioral changes in a model of schizophrenia based on antagonism of NMDA receptors: **possible involvement of 5-HT1A**, **but not CB1 or CB2 receptors**. Rodrigues NS[1], Sonego AB[1], Silva NR[1], Gomes FV[2], Guimarães FS[1] [1]FMRP-USP – Farmacologia, [2]University of Pittsburgh – Pharmacology

Introduction: Preclinical and clinical data indicate that cannabidiol (CBD), a non-psychotomimetic compound in the Cannabis sativa plant, induces antipsychotic-like effects without producing extrapyramidal effects[1]. Studies conducted by our group show that co-administration of CBD attenuated the behavioral changes induced by repeated treatment with MK-801, an NMDA receptor antagonist in the object recognition (OR) and social interaction (SI) tests[2]. These models were employed to investigate the impairment of cognitive functions and the negative symptoms of schizophrenia, respectively. The behavioral changes induced by NMDA antagonists are observed up to 6 weeks after treatment, and they are reversed by atypical antipsychotics such as clozapine and aripiprazole, but not by haloperidol, a typical antipsychotic[3]. Although several studies have shown possible antipsychotic-like effect of CBD, the mechanism of action by which it exerts this effect has not yet been elucidated. It is believed that the endocannabinoid system and/or the serotoninergic system may be involved considering that CBD modulates these systems and both systems are involved with the neurobiology of schizophrenia[4,5,6]. Thus, in the present study, we evaluated whether repeated 7-day treatment with CBD would be able to reverse changes in the IS and RO models after the end of MK-801 treatment for 14 days. In addition, it was assessed whether the effect of cannabidiol on reversing impairments in the IS and RO would be blocked by pretreatment with AM251, a CB1 receptor antagonist, AM630, a CB2 receptor antagonist, or WAY100635, a 5-HT1A receptor antagonist. **Methods:** C57BL/6J mice received i.p. injections of MK-801 (0.5 mg/kg) for 14 days. CBD (15, 30 or 60 mg/kg) treatment began 24h after the end of the MK-801 treatment and lasted for 7 days. Forty-eight hours after the last injection animals were submitted to SI and, 1 day later, to the OR test. In another experiment the same protocol was used but the animals received an injection of AM251 (0.1 or 0.3 mg/kg), AM630 (0.1 or 0.3 mg/kg) or WAY100635 (0.1 or 0.3 mg/kg) 10 min before CBD. **Results:** CBD (15 and 30 mg / kg) attenuated the impairments in the IS and RO tests induced by MK-801. This effect was blocked by WAY100635, but not by AM251 or AM630. **Conclusion:** These data suggest that CBD has antipsychotic properties by activating 5HT1A receptors and indicate that CBD could be an interesting alternative for the treatment of negative and cognitive symptoms of patients with schizophrenia. **Financial support:** CAPES, CNPq and FAPESP. **Animal research ethical committee:** process number 145/2015 **References:** 1.Campos, A. C, *et al., Philos Trans R Soc Lond B Biol Sci*, 2012. 2. Gomes, F. V, *et al., Schizophr Res.* 2015. 3.Hashimoto, K, *et al., Eur J Pharmacol***,** 2005. 4.Campos, A. C, *et al***.,** *Pharmacological Research***,** 2016. 5.Zuardi, A. W, *et al.*, *Curr Pharm Des*, 2012. 6.Fakhoury, M, *Mol Neurobiol***,** 2017.

03.003 Anandamide signaling neuromodulation in the dorsomedial hypothalamus attenuates the defensive behaviour displayed by mice threatened by rainbow Boidae wild snakes. Anjos-Garcia T[1], Falconi-Sobrinho LL[1], Coimbra NC[1]
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Introduction: The endocannabinoid system plays an important role in the organisation of defensive behaviour evoked during threatening situations. These threatening situations recruit some brain areas like dorsomedial (DMH) hypothalamus, which is also involved in fear-induced reactions. Findings from our research team suggest a panicolytic-like effect of anandamide, a cannabinoid receptors endogenous ligand, when microinjected in mesencephalic structures during threatening situations. However, there is a lack of studies addressing the role played by endocannabinoids on DMH neurons. Thus, the aim of this work was to verify the effect of increasing doses of anandamide microinjected in DMH on panic-like defensive behaviours evoked in a prey-versus-predator paradigm. We also aimed to determine the localisation of cannabinoid receptor type 1 (CB1) and transient receptor potential vanilloid type-1 channel (TRPV1) in DMH. **Methods**: Male C57BL/6 mice (n=6-9/group) underwent stereotaxic surgery to implant a guide cannula in DMH. After habituation in a polygonal arena with a burrow, the rodents were designed for intra-DMH microinjections of vehicle or anandamide (0.5, 5 and 50pmol/100nl). Five minutes after the microinjection, each mouse was placed in the polygonal arena. As a source of aversive stimuli, it was used South American rainbow Boidae snakes (*Epicrates cenchria assisi*). After a 5-min confrontation, each mouse was moved to its cage and the panic attack-like defensive behaviour was quantified as behavioural index (BI) and duration of defensive immobility and escape. At the end of the experiment, each animal was perfused for confirmation of each brain injection site. Data were analysed by one-way ANOVA followed by Tukey's post hoc test, considering $p<0.05$ as statistically significant. Inhibition dose-effect curves were generated by nonlinear regression analyses. Immunofluorescence assay was made in an independent group of animals to determine the localization of CB1 and TRPV1 receptors in diencephalic slices. **Results**: Mice exposure to a snakes increased the BI and duration of defensive immobility [BI, $F_{(4,26)}=3.69$; duration, $F_{(4,26)}=4.99$] and escape [BI, $F_{(4,26)}=14.12$; duration, $F_{(4,26)}=12.20$] when compared with the no-threat group ($p<0.05$). DMH-anandamide (5pmol) treated-group trends toward decreasing BI of defensive immobility and significantly diminished the duration of defensive immobility ($p<0.01$). Anandamide at the intermediate dose also decreased the BI and duration ($p<0.01$) of escape compared to vehicle treated-group. Inhibition curves showed a bell-shaped dose-response curve with no effect of low and high doses and significant panic-like responses inhibition for intermediated dose. In addition, the immunofluorescence assay showed that CB1 receptors were identified mainly on axonal fibers, and TRPV1 receptors were found almost exclusively surrounding perikarya. **Conclusion**: The present results suggest a panicolytic-like effect played by anandamide on dorsomedial hypothalamic nucleus with morphological correlates. **Financial Support**: CNPq Research approval by the Animal Research Ethical Committee: CONCEA nº 227/2014

03.004 Cannabidiol prevents impaired processing of conditioned fear in a rat model of ptsd: **involvement of nitrergic and serotonergic systems**. Vila-Verde C[1], Lisboa SF[1], Uliana DLM[1], Restel LBM[1], Guimarães FS[1] [1]FMRP-USP – Farmacologia

Introduction: Life-threatening traumatic events could lead to the development of Post-Traumatic Stress Disorder (PTSD), a chronic psychiatric condition usually associated with abnormalities in fear processing. Psychological stressors can activate the nitric oxide (NO) system, an effect that has been related to PTSD. Cannabidiol (CBD), a non-psychotomimetic derivative from *Cannabis sativa*, attenuates behavioral consequences of stress in clinical and preclinical studies. Multiple mechanisms are involved in therapeutic effects of CBD, including facilitation of 5-HT1A-mediated neurotransmission. Moreover, anxiolytic-like effects mediated by drugs acting via 5-HT1A receptors seems to depend on inhibition of neuronal NO synthase (nNOS) enzyme in the brain[1]. **Methods:** This study aimed to test if CBD could prevent the changes in fear processing induced by severe trauma, and if this effect involves 5-HT1A receptors. Moreover, we tested if the trauma-induced impairment in fear processing is associated with modifications in the NO system. Male Wistar rats were exposed to the single prolonged stress (SPS), a well-known model of PTSD[2,3,4]. Fear sensitization and impaired extinction of conditioned fear were evaluated one week later. Two-h after SPS the animals were treated with vehicle, Paroxetine (5-20mg/kg) or CBD (2.5-10mg/kg). The injections were administered daily for 7 days. In a second experiment, the 5-HT_{1A}-receptor antagonist WAY100635 (0.3 mg/kg) was administered 30 minutes before CBD (5 mg/kg). Twenty-four-h after the last drug injection the rats were submitted to a contextual conditioned fear procedure (three random electric footshocks, 0.35 mA/2s). Fear sensitization and extinction were assessed in two distinct sessions in the next 48 h. The brain levels of phosphorylated neuronal NO synthase enzyme (pnNOS) were measured at different time points after stress. **Results:** SPS-induced fear sensitization (increased freezing behavior in the first re-exposure to the aversive context) and impaired fear extinction (repeated measures two-way ANOVA followed by Duncan posthoc test, $p<0.05$). These effects were attenuated by paroxetine (10 mg/kg) and CBD (5 and 10 mg/kg). CBD effects were abolished by pre-treatment with WAY100635. Increased pnNOS expression in the ventral hippocampus was observed 1h after SPS ($p<0.05$), but not after the fear extinction evaluation. **Conclusion:** Our results indicate that CBD attenuates stress-induced impairment in fear processing by facilitating 5-HT1A-mediated neurotransmission. Moreover, it suggests that trauma-induced changes in behavioral responses could be partially related to the early modifications in the nitrergic system. The possibility that CBD effects in this model involve modulation of nNOS via 5-HT1A receptors still needs to be addressed. Funding: CAPES/CNPq/FAPESP. Animal Research Ethical Committee Process number: 152/2014 1-Zhang, J. Neurosci. 30,2433,2010. 2-Liberzon, Psychoneuroendocrinol. 22, 443,1997 3-Liberzon, J. Neuroendocrinol.11, 11, 1999 4-Kohda, Neurosci.148, 22, 2007

03.005 Effect of scopolamine on persistence of object location memory in rats. Rohde BZ, Souza LB, Ramos D, Porto GP Unifra

Introduction: The persistence of memory is a feature of long-term memory (BEKINSCHTEIN et al., 2007). Previous study had suggested that scopolamine induces impairment of the persistence of avoidance memory (PARFITT et al., 2012). The role of scopolamine on maintenance of memories induced by neutral stimulus has not yet been demonstrated. This study investigated the effects of Scopolamine on persistence of object location memory in rats. **Methods**: Rats were habituated for 4 consecutive days into open field with two objects for 5 min and then were submitted to a training session for seven consecutive days, which were exposed to the two objects in a different position from that of the day of habituation. Saline (control) or Scopolamine at doses of 0.5, 1, 2, 3 and 6 mg/kg, were injected intraperitoneally two days after last training session and memory retention for object location was tested 1 or 5 days after the injections. In the test session, one object was moved to a different location and the crossings and the time that the animals spent exploring new and old locations of objects was observed. It was calculated the exploration ratio, defined as the relative time the animal spends exploring the novel stimulus relative to the total time the animal engaged in exploratory behavior. **Results:** Scopolamine at 3 mg/kg promoted reduction of exploration ratio and did not affect the number of crossings during the test session. Because the amnesic effect occurred in the test performed 1 day after infusion and remained being watched also in 5 days, it is suggested that this drug interfered in the persistence of memory in object location recognition task. **Conclusion**: Scopolamine might represent a valid tool for discovery of promnesic compounds useful in diseases where there is impairment of spatial recognition memory. More experiments will be needed to elucidate the molecular mechanism of action of scopolamine to generate this amnesic effect. **References**: Bekinschtein. P. et al. Persistence of long-term memory storage requires a late protein synthesis- and BDNF-dependent phase in the hippocampus. Neuron. v. 53. p. 262. 2007. Parfitt, G. M.et al. Participation of hippocampal cholinergic system in memory persistence for inhibitory avoidance in rats. Neurobiol Learn Mem. v. 7. p. 183. 2012. **Financial Support**: Franciscan University Center Process Number of Animal Research Ethical Committee: 02/2015

03.006 Investigation of the possible antipsychotic effect of HU-910, **a selective Type-2 cannabinoid receptor** (**CB2**) **agonist**. Cortez IL[1], Rodrigues NS[1], Silva NR[1], Mechoulam R[2], Guimarães FS[1] [1]FMRP-USP, [2]Hebrew University

Introduction: Schizophrenia is a chronic psychiatric disorder that afflicts around 180 thousand people worldwide (Mcgrath et al., 2008). The available pharmacological treatments improve mainly the positive symptoms of the disease and are associated with a low clinical tolerance and high levels of treatment discontinuity (Lieberman et al., 2005). The acute or chronic administration of MK-801, a NMDA receptor antagonist, was proposed as a useful model to investigate new substances with potential antipsychotic properties (Tsai e Coyle, 2002). Recent evidence has suggested that the endocannabinoid system might be an important target for the treatment of this disorder (Ortega-Alvaro et al., 2011). Although the pathophysiology of schizophrenia is not completely understood, pro-inflammatory factors have been associated with this disorder (Palazuelos et al., 2008). CB2 agonists can inhibit microglia activation and HU-910, a CB2 receptor selective agonist, attenuated the increase of pro-inflammatory cytokines in a model of hepatic ischemia (Horváth et al., 2012). Therefore, in the present study, we evaluated whether HU-910 would reverse the behavioral changes induced by repeated treatment with MK-801 without producing the cannabinoid tetrad (an indicator of CB1 activation). **Methods:** Male mice C57BL/6 were intraperitoneally injected with HU-910 (0.3; 1; 10; 30 mg/kg) followed by MK-801 (0.25 mg/kg) and, 20 minutes later, locomotion was evaluated in an open arena. To evaluate the cannabinoid tetrad, the animals received vehicle, HU-910 (30 mg/kg) or WIN55,212-2 (5 mg/kg) and were submitted to the tests of catalepsy, hot plate, open field and tail temperature. **Results:** HU-910 (30 mg/kg) prevented the hyperlocomotion induced by MK-801. As expected, WIN55,212-2 produced the cannabinoid tetrad effects (catalepsy, antinociception, hypolocomotion and hypothermia) while HU-910 had only antinociceptive activity and did not produce the other effects. **Conclusion**: These data corroborate the hypothesis that HU-910 has potential antipsychotic-like properties without inducing the cannabinoid tetrad effects. **Financial support:** CAPES, CNPq e FAPESP**.** **Approval by the animal research ethical committee:** 127/2017 **References:** Lieberman, J. A.; Stroup, T. S.; McEvoy, J. P.; Swartz, M. S.; Rosenheck, R. A.; Perkins, D. O.; et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med, v. 353, n. 12, p. 1209-23, 2005. McGrath, J.; Saha, S., Chant, D., Welham, J. Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. Epidemiol Rev; 30 (1): 67-76, 2008. Horváth, B. et al. A new cannabinoid CB 2receptor agonist HU-910 attenuates oxidative stress, inflammation and cell death associated with hepatic ischaemia/reperfusion injury. Br. J. Pharmacol. 165, 2462–2478 (2012).

03.007 The combination of sub-effective doses of escitalopram and cannabidiol accelerates the onset of antidepressant effects in chronically stressed mice. Scarante FF[1], Fusse EJ[1], Aguiar RP[2], Duarte-Souza PC[1], Detoni VL[1], Scomparin DS[1], Guimarães FS[1], Campos AC[1] [1]FMRP-USP – Farmacologia, [2]UEM – Ciências Farmacêuticas

Despite their widespread use, antidepressant drugs show a series of limitations on the clinical practice, such as delayed onset of action (at least four weeks) and important side effects. Cannabinoid drugs, such as the phytocannabinoid cannabidiol (CBD) and the anandamide degradation inhibitor URB597 (URB), showed antidepressant- and anxiolytic-like effects in different animal models. In the present study, we evaluated whether the combination of sub-effective doses of the antidepressant escitalopram (ESC) and cannabinoid drugs would prevent chronic stress-induced behavioral changes in mice. Male C57Bl6 mice (10 months old) were submitted to social defeat stress (SDS) or chronic unpredictable stress (CUS) for ten days. Animals were divided into experimental groups (n=6-10; Control (non-stressed); Vehicle (Veh), ESC 10 mg/kg; CBD 7.5 mg/kg; URB597 0.1 mg/kg; ESC/CBD and ESC/URB) and treated during seven days (i.p., from the 4th to the 10th day of the stress protocol). After the end of the SDS protocol, animals were tested in the tail suspension test (TST). On the other hand, mice submitted to CUS were tested in Novelty suppressed feeding (NSF). Our results suggested that the Veh-treated SDS group exhibited lower latency for the first episode of immobility when compared to the control group (p=0.014). Repeated treatment with ESC or CBD alone did not prevent the effects of SDS. However, when in combination, sub-effective doses of CBD and ESC increased the latency for the first immobility episode of the stressed mice. URB597, on the other hand, neither alone nor in combination with ESC significantly alter the response of stressed animals in the TST. No changes in the total immobility time in the TST or basal locomotor activity measured in open field test were detected. Regarding the CUS protocol, stressed animals exhibited an increased latency to eat in the new environment when compared to the non-stressed group (although it did not reach statistical significance; p=0.191). Similar to the SDS protocol, neither ESC nor CBD treatment decreased the behavioral response induced by stress. Nonetheless, the combination ESC/CBD decreased the latency to eat in the new environment, an anxiolytic-like effect. URB597 alone or in combination with ESC did not significantly affect the response of stressed animals in the NSF. Besides, the exposure to CUS induced hyperlocomotion in the open field in comparison with the control group. In conclusion, our results suggest that the combination of sub-effective doses of antidepressant and CBD prevents stress-induced behavioral effects in mice after short-term treatment. **Financial Support**: CNPq, FAPESP and L'oreal-UNESCO-ABC. Animal Research Ethics Committee Approval Number: 032/2015-1.

03.008 Effect of allopregnanolone on depressive-like behavior of selectively-bred rats with high and low immobility profiles. Almeida FB[1], Fonseca AR[1], Heidrich N[1], Silva FFS[1], Costa LB[1], Fernandes PR[1], Freese L[1], Nin MS[2,1], Barros HMT[1] [1]UFCSPA – Farmacociências, [2]Centro Universitário Metodista IPA – Farmácia

Introduction: Depression is a highly incapacitating disorder known to have a multifactorial etiology, including a hereditary genetic background. Current treatments of choice for depression are focused in the use of monoamine reuptake blockers/antagonists and offer incomplete efficacy, as well as undesirable side effects. This generates the need to study the role of different pathways on depression such as the GABA system. The neurosteroid allopregnanolone (ALLO) interacts with the $GABA_A$ receptors as a positive modulator and has been shown to have an antidepressant-like effect in animals. This study aimed to assess its effect in animals with different backgrounds of depressive-like activity. **Methods:** An initial population (F0) of 40 male and 40 female Wistar rats was submitted to the Forced Swim Test (FST) for screening of the immobility behavior. Rats that scored one standard deviation above or below the mean were selected for the High Immobility (HI) group and Low Immobility (LI) group, respectively. Males and females were bred inside their groups and the subsequent generation F1 was submitted to the FST screening process. The selected animals were bred to give origin to the third generation (F2), which was also evaluated in the FST to confirm behavioral selection. Subsequently, F2 males were submitted to stereotaxic surgery for right lateral ventricle cannulation and infusion of either a dose of 5 µg/rat of ALLO, 5 µg/rat of imipramine (IMI) or vehicle (CTR). The intracerebroventricular infusions occurred 24, 5 and 1 hour prior to test sessions of the FST. Student's t-test was used to compare immobility scores of HI and LI rats on F2 and One-Way ANOVA was used to compare treatment groups. Tukey test was used when appropriate. Results are shown as Mean ± S.E.M. Statistically different when $P < 0.05$. Results Rats from the HI and LI groups had significantly different ($P < 0.001$) immobility scores in the pre-drug FST. In the HI, a significant difference in immobility was found between treatments ($P < 0.001$), showing that both IMI (167.5±6.5 s; $P < 0.001$) and ALLO (220.4±12.1 s; $P = 0,018$) reduced immobility when compared to the CTR group (265.2±11.8 s). IMI rats also showed a lower immobility than the ALLO group ($P = 0.008$). In the LI rats, however, no difference in immobility was found between treatment groups (CTR = 204.1±19.7 s; ALLO = 175±17.5 s; IMI = 166.2±18.1 s; $P = 0.341$). **Conclusion**: In this work, two strains of rats with significantly different immobility profiles in the FST were obtained in a relatively short time, after only three generations. In High Immobility rats, an antidepressive-like effect of both ALLO and IMI was found. No antidepressive-like effect was observed in the Low Immobility animals, which corroborates with the clinical understanding that antidepressants are generally unable to improve mood in non-depressive subjects. Follow-up studies should be performed to evaluate the neurochemical aspects of HI and LI rats and how the treatment with ALLO and IMIP affect these parameters. **Financial Support**: CAPES; CNPq; UFCSPA Approved by the Animal Research Ethical Committee (CEUA) of UFCSPA (process number: 15-161).

03.009 Antidepressant-like activity of *Colletia paradoxa Sprengel* mediated by monoamines and sodium channel, changes Na(+),K(+)-ATPase activity in cortex and hippocampus of mice. Stein DF[1], Machado CP[1], Holtermann AR[2], Linares CEB[2], Giacomelli SR[2], Santos KF[2], Carvalho F[3], Gutierrez J[3], Cenci L[2], Driemeier D[4], Stein AC[2] [1]UFRGS – Ciências Farmacêuticas, [2]URI – Ciências Farmacêuticas, [3]UFSM – Bioquímica Toxicológica, [4]UFRGS – Patologia

Depression affects 5.5% of the world population (WHO, 2017). Lack of full knowledge under their neurobiology makes treatment impossible in some cases, and 33% of patients relapse. Studies with natural products aim to discover new drugs and expand the possibilities of treatments. *Colletia paradoxa*, known as quina-de-porto-alegre, is a plant that presents promising effects for this pathology. This study demonstrates its activities on monoaminergic pathways, sodium channels, acute and oral toxicity studies (OECD 423 and OECD 407). In the acute toxicity study the extract as safe and classified category 5. Different groups of mice received doses of 10, 50, 100mg/kg (p.o.) of hexanic extract for the dose response curve and evaluated immobility time in tail suspension test (TST) (Steru et al., Psycopharmacolgy, v.85 p.367-370, 1985). For the monoaminergic action study, protocols are described by Stein et al. (Behavioral Brain Research, v. 228, p.66-73, 2012). Mice are treated (i.p.) with D1 (SCH23390, 0.015mg/kg) and D2 antagonist (sulpiride, 50mg/kg), α1 (prazosin antagonist 1mg / kg) and α2 (yohimbine antagonist, 1 mg/kg) and serotonin synthesis inhibitor (ρCPA, 100mg/kg). The effect of the extract on sodium channels, veratrine opener channel (0.250mg/kg, i.p.), was administered. After administration of this antagonists, C. paradoxa (50 mg/kg, p.o.) was administrated, and then, evaluated in the TST. Na+/K+ATPase (ex vivo) enzyme activity was performed in acute and repeated treatment (3 days) in the cortex and hippocampus (Carvalho et al. European Journal of Pharmacology, v.684, p.79, 2012). The results of behavioral tests, the extract showed specificity for dopaminergic receptor D2 Fpre-treatment (Fpt) (1:30)= 67,296, p<0,001; Ftreatmet (Ft) (1:30)= 9,974, p=0,004; Finteraction (Fi) (1:30)= 16,913, p<0,001) and noradrenergic α1 (Fpt (1:44)= 1,81, p=0,186; Ft (1:44)=16,033, p<0,001; Fi (1:44)=8,219, p=0,007), in addition it is dependent on serotonin levels (Fpt (1:42)=5,272, p=0,027; Ft (1:42)=4,226, p=0,047; Fi (1:42)=2,6, p=0,115) and sodium channels (Fpt (1:44)=9,764, p=0,002; Ft (1:44)=5,676, p=0,017; Fi (1:44)=3,1 p=0,095). Repeated toxicity was tested at doses of 50, 250 and 500 mg/kg, and showed a slight change of heart and liver, which had a reduction of mass when compared to the vehicle group. We also found basopenia in all groups treated with C paradoxa, but without significant damage, and we don't found histologicals alterations. These results showed an effect of *C. paradoxa* on the monoaminergic system, acting on the sodium channels, as well as the enzyme Na, K-ATPase. The mechanism of action is possibly linked to sodium dependence for release of monoamines or link to your receptors (Xhaard et al., J. Chem. Inf. Model v.48, 1423-1437, 2008). Toxicity studies have demonstrated that this extract has minimal adverse effects, characterizing it with a safe profile. **Support**: CAPES, CNPQ and URI-FW. **Ethics committee** (CEUA 003/2015)

03.010 Purinergic receptors p2x7 are involved in extinction but not reconsolidation of contextual fear conditional responses in rodents. Domingos LB[1], Hott SC[2], Terzian ALB[1], Resstel LBM[1] [1]USP – Farmacologia, [2]UFES – Ciências Farmacêuticas

Introduction: Several anxiety disorders are associated with alterations in the processing of aversive situations. The activation of purinergic (P2R) receptors in the brain seems to modulate such responses. However, few studies investigate the role of purinergic system on threatening situations, such as those observed on contextual fear conditioning (CFC). **Objective:** Considering the above mentioned, we aimed to investigate the participation of purinergic receptors P2X7R on the expression, extinction and reconsolidation of aversive memories. **Methods:** Male mice (8-10 weeks) were used. P2X7 Knockout (P2X7 KO) mice (C57BL/6 background) and wildtype (WT) mice were submitted to contextual conditioning session. According to each protocol, 3 footshocks (750-850μA; 1-2s) were triggered for conditioning. After 24h, the animals were reexposed to the context by 3 (reconsolidation) or 21min (extinction), and the next day the test session was performed. The freezing behavior was evaluated during the reconsolidation, extinction and test phases. **Results:** As results, we observed increased contextual fear expression ($F_{2,17}$=5.5,P<0.05) and impaired acquisition of extinction ($F_{2,17}$=6.2,P<0.01) after treatment with the higher dose of the nonselective P2R antagonist. Similar results were observed with the selective P2X7 antagonist, A438079 ($F_{2,98}$=29.6,P<0.05), but not after treatment with the selective P2Y1 antagonist MRS2179 (P>0.05). Additionally, P2X7 KO mice showed increased contextual fear expression (t_{16}=2.84,P<0.05) and impaired acquisition of extinction ($F_{1,105}$=25.5,P<0.01) compared to mice WT, corroborating the data obtained by pharmacologic P2X7 antagonism. No effect was observed on reconsolidation or after selective P2Y1R antagonism. .**Conclusion:** We suggest that the pharmacological or genetic blockade P2X7 receptors promote anxiogenic-like effects and impairment in aversive extinction learning processes in the CFC protocol. Therefore, the activation of these receptors presents an alternative for treatment of psychiatric disorders. **Financial support:** FAPESP, FAEPA, CAPES, CNPq. Ethical Committee approval (Process no. 043/2013).

03.011 Cocaine oral self- administration by ADHD male and female rats with neonatal injury with 6-OHDA. Fernandes PR, Umpierrez LS, Barros HMT UFCSPA – Farmacologia

Introduction Attention deficit / hyperactivity disorder (ADHD) is associated with a failure of the dopaminergic system (DA) in different brain areas, which leads to hyperactivity and attention deficit and to lower academic level, behavioral difficulties, psychosocial difficulties and increase in risk behaviors. ADHD has also been associated with cocaine abuse (COC) the reinforcing effects of psychostimulants are typically modulated via the dopaminergic system, In COC self-administration the response requirement to earn the reinforcement is a determinant in the reinforcement effects. The objective of this work was to evaluate the frequency of active lever presses and oral reinforcements in hyperactive male and female rats with 6-hydroxydopamine (6-OHDA) prenatal lesion. **Methods** We used 38 animals, divided into 4 groups: Male 6-OHDA, Male Sham, Female 6-OHDA, Female Sham. At 4 days of age the animals were lesioned with 6-OHDA via intracisternal (0.1%). 30 min before desipramine was administered via i.p. (20mg / kg) for the protection of noradrenergic neurons. At 53 days, they began training in operant conditioning with 1.5% sucrose solution. At 60 days of life, cocaine solutions were added to sucrose (0.2mg / mL - 0.3mg / mL - 0.4mg / mL; each week). Each lever press on the active bar was analyzed according to the time after the reward, to evaluate the frequency of responses. **Results** SHAM females have a higher initial response than SHAM males to receive cocaine + sucrose oral infusions. At 23min the females accumulate more than 30 reinforcements and the males less than 15 reinforcements ($P < 0.0007$). At 30 min there was a match in frequency of responses. The 6-OHDA females use a longer time to reach the 50 reinforcements in comparison to the 6-OHDA males, both of which present irregularities in the curves ($P < 0.0008$) The speed of 6-OHDA males in bar press is greater than of SHAM males, at 22 mins 6-OHDA males accumulated more than 25 reinforcements while the SHAM males posed 13 reinforcements. In 30 min the groups began to show a similarity ($P < 0.0248$) The greatest difference between the groups of females is at 16min in which the SHAM females have 25 reinforcements and the 6-OHDA females have only 5 reinforcements. The final time is also different, the SHAM females reached the 50 reinforcements in 51min and the 6-OHDA females took 1h15min. ($P < 0.0001$) **Conclusion** Males with ADHD-like behaviors tend to be more hyperactive and may even be targeted as a risk group, their increased hyperactivity is associated with faster and more intense cocaine use. A slower frequency of drug seeking shows opposite results from normal females, with a slower reaction in the search for drugs in respect to males. This study explains why 6-OHDA male rats, who usually are hyperactive, produce more bar press for cocaine reinforcements, while 6-OHDA-lesioned female rats who are not hyperactive are also slower in bar presses for cocaine. CAPES, CNPQ, FINEP CEUA - UFCSPA: 13-122

03.012 Fluoxetine facilitates consolidation of fear memory extinction through BDNF/TrkB hippocampal. Diniz CRAFD, Antero LS, Resstel LBM, Joca SRL

Purpose: Animal fear conditioning and PTSD depend on an association of the aversive stimulus with a previous neutral stimulus producing an intense conditioned fear response. PTSD patients have decreased hippocampus and impaired hippocampal-dependent cognitive functions, as well as impaired extinction of the conditioned fear response. Selective serotonin reuptake inhibitors are the first line pharmacological treatment for PTSD. In animals, chronic fluoxetine (FLX) treatment impairs renewal, reinstatement and spontaneous recovery of the conditioned response. These effects seem to depend on hipocampal BDNF. Besides, impaired extinction of fear-potentiated startle is observed in conditioned hipocampal BDNF knockout animals. The hippocampus can be divided into ventral hippocampus (VH), more closely related to anxiety and fear response, and dorsal hippocampus (DH), related to cognitive processes of learning and memory. Little is known about a possible distinct participation of DH and VH BDNF content in FLX-induced effects on fear extinction. **Methods:** Male Wistar rats (250 g) were used. Animals were submitted to conditioning procedure (day 1). Animals were treated with FLX (10mg/kg) or vehicle for twelve days. Chronic FLX, acute FLX and vehicle treatment groups were obtained. One day after the last injection animals were exposed to the extinction protocol (day 14) and in the next day to the extinction memory retention protocol (day 15). Independent group of animals were submitted to the conditioning procedure and treatment as outlined above, but euthanized rather than exposed to extinction protocol for brain BDNF protein analysis (ELISA). In another experiment K252 (TrkB functional blocker) or vehicle were infused into the DH or VH soon after extinction protocol in chronic FLX or vehicle i.p treatment. After, BDNF was infused into DH or VH soon after extinction protocol and reinstatement and spontaneous recovery was observed **Results:** Only chronic FLX treatment facilitated the extinction memory retention ($F_{2,29}$ = 2.881; $p<0.05$). Chronic FLX treatment increased BDNF in DH ($F_{2,21}$ = 5,198; $p<0.05$) while acute treatment increased BDNF in VH ($F_{2,16}$ = 5.796; $p<0.05$). k252 administered into DH or VH prevented chronic FLX-induced effects on memory consolidation ($F_{3,41}$ = 4.166; $p<0.05$) and ($F_{3,13}$ = 3.533; $p=0.056$), respectively. Chronic FLX treatment increased pTrkB levels in the DH ($F_{2,17}$=5,421) and decreased in the VH ($F_{2,21}$=4,821), with animals euthanized after extinction protocol. BDNF infused into DH increased conditioned response of fear during test (t_{11}=2,604) and reinstatement protocol (t_{11}=2,491), whereas BDNF infused into VH impaired spontaneous recovery of conditioned response (t_{12}=2,406). **Conclusion:** FLX effect from chronic treatment depend on hippocampal BDNF/TrkB. Although a dorso-ventral different functional role along hippocampal axis was observed, probably DH and VH support each other in order to favor a better decision making from more complex environmental and emotional contingences. **Financial Support:** FAPESP (2011/02746-4) and CNPq (471382/2011-6).

03.013 Physical exercise alters saccharin and ethanol self-administration learning and reward. Engi SA[1], Crestani CC[2], Planeta CS[2], Cruz FC[1] [1]Unifesp-EPM – Farmacologia, [2]FCFar-Unesp-Araraquara – Princípios Ativos Naturais e Toxicologia

Alcohol is the licit drug most abused (NIDA, 2017). Physical exercise is used as a therapeutic approach in drug abuse; however, there are many controversial results about these results (Engi et al., 2016). **Aim:** Investigate the effects of moderate treadmill running upon intermittent ethanol consumption and upon operant saccharin and ethanol self-administration reward. **Methods:** Wistar rats underwent moderate treadmill running (trained groups) or not (sedentary group) and water or intermittent 20% ethanol access during 8 weeks. All animals were transferred to operant self-administration boxes for 5 days to evaluate the impact of moderate treadmill running and ethanol intermittent consumption upon saccharin operant self-administration learning. After the learning phase, animals underwent to saccharin and ethanol operant self-administration to evaluate the number of rewards. At the end of the experiment, animals had theirs brains removed and nucleus accumbens (NAc) dissected to BDNF and D1 expression analysis using RT-PCR assay. (Protocol CEUA/FCF/Car nº41/2012). **Results:** Our results demonstrate that sedentary animals that consumed 20% ethanol in the intermittent access (during 8 weeks) showed deficit in saccharin self-administration learning when compared to all groups ($q=14.98$, $p<0.05$). This deficit was reversed when compared to the group that also consumed 20% ethanol in the intermittent access but underwent to moderate treadmill running. Our results demonstrated that the group trained + water showed significant differences in the number of rewards of saccharin when compared to other groups. The group trained + ethanol showed significant difference in the number of rewards when compared to control group - ANOVA 3-way (Training: $F(7,40)= 4.02$, $p=0.05$; Self-Administration: $F(7,40)= 15.23$, $p<0.05$ and Interaction: $F(7,40)= 4.82$, $p<0.05$). Our molecular results demonstrated increased expression of dopaminergic receptor D1 in the NAc of trained + ethanol animals that self-administrated saccharin when compared to controls groups. We also observed increased expression of D1 in the NAc of trained + ethanol animals that self-administrated ethanol when compared to all groups - ANOVA 3-way (Training: $F(7,30)=5.48$, $p<0.05$; Previous Consumption: $F(7,30)=13.21$, $p<0.05$, Self Administration: $F(7,30)=11.56$, $p<0.05$ and Interaction: $F(7,30)=8.36$, $p<0.05$). The NAc of animals that self-administrated saccharin showed no significant differences in the expression of BDNF but there were significant differences in the sedentary + ethanol animals that self-administrated ethanol when compared to all groups - ANOVA 3-way (Training: $F(7,26)=1.05$, $p>0.05$; Previous Consumption: $F(7,26)=3.02$, $p>0.05$, Self Administration $F(7,26)=1.64$, $p>0.05$). Significant Interaction between previous consumption and self-administration: $F(7,26)=5.38$, $p<0.05$. **Conclusion:** High doses of ethanol can cause deficits in the learning of sedentary animals that can be reversed by physical exercise. Our results also demonstrated that trained animals showed higher number for saccharin and ethanol rewards with significant differences in the expression of D1 receptors, indicating a possible central interaction between physical exercise and saccharin/ethanol consumption. **Financial Support:** Fapesp nº 2012/14723-1 and nº 2013/09715-2.

03.014 Adolescent exposition to a synthetic cannabinoid WIN55,212-2 modulates the cocaine-reward in mice. Gobira PH[1], Silote GP[1], Joca SRL[1] [1]FCFRP-USP – Farmacologia e Toxicologia de Produtos Naturais

Introduction: Cannabis is the most commonly used illicit drug worldwide, and use is typically initiated during adolescence. The endocannabinoid system has an important role in formation of the nervous system, from very early development through adolescence. Cannabis exposure during this vulnerable period might lead to neurobiological changes that affect adult brain functions and can increase the risk of psychiatric disorders such as anxiety, depression and addiction. The aim of this study was to investigate whether exposure to WIN55,212-2, a synthetic analogue of THC, in adolescent mice might modulate reinforcing effects of cocaine in adulthood. **Methods:** Swiss mice received intraperitoneal injections of WIN55,212-2 (3.0 mg/kg) or vehicle (0.9% NaCl with 3% Tween 80) every third day (eight injections) during adolescence (postnatal days 28–49). One week following the last injection of cannabinoid agonist, animals were submitted to cocaine-induce hyperlocomotion. A different experimental group of animals were submitted to cocaine-induced place preference paradigm. We also evaluated anxiety-like behaviour in the elevated plus maze (EPM) and depressive-like behaviour in the forced swim test (FST). The distance travelled in arena, immobility time in FST as well as frequency EPM were analyzed by student t test, comparing animals that received WIN55,212-2 with animals that receive vehicle. The conditioned place preference (CPP) score was analyzed by ANOVA followed by Newman-Keuls test. **Results:** Interestingly, we found that adolescence exposition to cannabinoid did not modifies behaviour related to anxiety and depression. Regarding cocaine effects, we did not observe difference in hyperlocomotion induced by cocaine between tested groups. On the other hand, differently from vehicle group, animals treated with WIN55,212-2 during adolescence did not shown cocaine-conditioned place preference indicating a possible modification in reward effects promoted by this psychostimulant. **Conclusion:** Our present data demonstrated that a chronic exposure to cannabinoids during adolescence alters the susceptibility to acquire cocaine place preference. These finding suggest that exposition to WIN55,212-2, during this vulnerable period, leaded to neurobiological changes which might change reward circuitry, modulating cocaine effect. Faced with this interesting behavioural data, more studies are necessary to understand how the exposition of cannabinoids during adolescence change brain circuits involved in cocaine-reward. **Financial support:** CNPq and FAPESP. The Institution’s Animal Ethics Committee approved housing conditions and experimental procedures (process number: 13214/2016).

03.015 Context-induced reinstatement of alcohol seeking is associated with unique molecular alterations in prelimbic cortex neuronal ensembles Cruz FC[1], Palombo P[1], Bianchi PC[2], Engi SA[1], Planeta CS[2], Leão RM[3] [1]Unifesp-EPM – Farmacologia, [2]PANT-FCFar-Unesp-Araraquara, [3]UFBA – Biorregulação

Context-induced reinstatement of drug seeking is a big problem for addiction treatment. ABA rewal is an animal model for assessing the neural mechanisms underlying context-induced drug relapse. Prelimbic neuronal ensembles have been shown to contribute to context-induced reinstatement of alcohol seeking. Here, we assessed whether context-induced reinstatement of alcohol seeking was associated with molecular alterations selectively induced within context-activated neuronal ensembles. We used fluorescence-activated cell sorting to isolate reinstatement-activated Fos-positive neurons from Fos-negative neurons in prelimbic cortex and used quantitative PCR to assess gene expression within these two populations of neurons. Long - Evans rats were first given home - cage access to 10% ethanol. Using a saccharin fading technique, rats were first trained to self - administer 10% ethanol in one context. Next, lever pressing in the presence of the discrete cue was subsequently extinguished in a different context. Subsequently, context-induced reinstatement of drug seeking was assessed by re-exposing rats to the drug - associated or extinction context under extinction conditions. Re-exposure to the alcohol - associated context reinstated alcohol seeking (lever press in Context B: 6.75±2.26 and Context A: 21.5±3.72) and increased the expression of the GABA-A receptor subunit gene GABAα5 (Fos positive vs negative neurons: 3.04 ±1.09, and 1±1.15) and decreased the expression of MNDA receptor subunit gene Glur1 (Fos positive vs negative neurons: 0.16±0,65 and 1±0.33) and GluR2 (Fos positive vs negative neurons: -0.3±1,41 and 0.99±0.89). Our results demonstrate an important role of prelimbic cortex in context-induced reinstatement of alcohol seeking and that this reinstatement is associated with unique gene alterations in Fos-expressing neurons. CEUA 1592270616 **Financial Support**: FAPESP 2013/24986-2

03.016 Vapor Inhalation of alcohol reduces the resilience of Wistar rats to context-induced the reinstatement of alcohol seeking. Leão RM[1], Palombo P[2], Bianchi PC[3], Oliveira-Carneiro PE[4], Planeta CS[3], Cruz F[2] [1]UFBA – Biorregulação, ICS, [2]Unifesp-EPM – Farmacologia, [3]PANT-FCFar-Unesp-Araraquara, [4]UFSCar

Evidence indicates that drug relapse in humans is often provoked by exposure to the self-administered drug-associated context. An animal model called “ABA renewal procedure” has been used to study context-induced relapse to drug seeking. However, Wistar rats have been shown resilient to context-induced reinstatement of alcohol seeking. In this way, Wistar rats exposed to the alcohol vapor inhalation model (a procedure that was developed to induce a state of alcohol dependence in rats) seem to be more vulnerable to alcohol effects. Here, we tested whether the exposure to alcohol vapor chamber could decrease the Wistar rats’ resilience to context-induced the reinstatement to alcohol seeking. Wistar Rats were first trained to self-administer drug in one context. Once a stable baseline of alcohol intake was reached, the rats were made dependent by chronic intermittent exposure to alcohol vapor. They underwent cycles of 14h on (blood alcohol levels during vapor exposure ranged between 150 and 250 mg%) and 10h off. The self-administration sessions were performed during the abstinence phase, until the animals show an escalation in alcohol intaking and lever presses. Next, drug-reinforced lever responding was extinguished in a different (non-drug) context. Subsequently, rats were re-exposed to the drug-associated context to assess context-induced reinstatement of alcohol seeking. The control group underwent to the same procedure except for alcohol inhalation. Context induced the reinstatement of alcohol seeking in Wistar alcohol dependent rats (Lever presses Context B: 4.12□1.86 and Context A: 11.1□2.6; $p<0.05$), but not in the control animals (Lever presses Context B: 1.5□0.9 and Context A: 5.7□0.9; $p>0.05$). All experiments were approved by ethical committee for research on laboratory animals of Federal University of Bahia (no. 95A/2016). Our result suggests, that vapor inhalation is necessary for studying the effects of context in the reinstatement of alcohol seeking. **Financial Support**: FAPESP 2013/24986-2

hypothalamus causes antinociception. Falconi-Sobrinho LL[1], Anjos-Garcia T[2], Coimbra NC[2] [1]FMUSP – Neurociências, [2]FMUSP – Farmacologia

Introduction: It has been established that the excitatory imbalance in the hypothalamus of laboratory animals provokes panic attack-like defensive reactions. In addition, these defensive reactions elaborated by hypothalamic neurons may cause an antinociceptive response. There is evidence that nitric oxide (NO) donor microinjected in limbic structures can evoke defensive responses. However, there is lack of investigations showing the effects of NO donor administered in the anterior hypothalamus (AH) nucleus on fear-related defensive mechanisms and on pain control. Thus, the purpose of this study was to investigate the role of nitrergic neuromodulation in AH through of AH-intra microinjections of NO donor SIN-1 on fear-related behavioural and nociceptive response. **Methods:** The experiments were performed using male C57BL/6 mice (n=6 per group) weighing 30-35g. A guide-cannula was stereotaxically implanted in the AH. Before the experiment the rats were submitted to three baseline measurements of the control tail-flick latencies. The animals received injection of vehicle (0.9%NaCl/0.1µL) or 75, 150 and 300nmol/0.1µL SIN-1 into the AH. Immediately after the AH treatment with vehicle or SIN-1, each animal was placed in a polygonal arena and quantitative analysis of defensive behaviour (freezing and escape) was performed for 10 min, followed by the nociceptive threshold recording at each 10 min for 60 min. At the end of the experiment, each animal was perfused for confirmation of injection sites. **Results:** According to one-way ANOVA followed by Newman-Keuls´post hoc test, there was a significant effect of the treatment on number ($F_{3.20}$=7.721/p<0.01) and duration ($F_{3.20}$=9.483/p<0.001) of freezing and on number ($F_{3.20}$=10.77/p<0.001) and duration ($F_{3.20}$=11.07/p<0.001) of escape. The treatment of AH with SIN-1 at higher doses elicited freezing behaviour (Newman-Keuls´post hoc test; p<0.05, regarding number and duration of freezing events). Intra-AH microinjections of SIN-1 at different doses caused escape behaviour. There was an increased the number (p<0.05) and duration (p<0.05) of escape caused by SIN-1 at the higher doses, in comparison to control group and to SIN-1 at the lower dose. According to two-way ANOVA, there was statistically significant effect of treatment ($F_{3.20}$=34.28/p<0.001), time ($F_{3.20}$=66.39/p<0.001) and treatment versus time interaction ($F_{3.20}$=34.28/p<0.001). SIN-1 microinjections into the AH at higher doses produced antinociception during 20 min, when compared to the control group (Newman-Keuls´ post hoc test p<0.05). **Conclusion:** Our findigns suggest that both panic attack-like defensive reactions and unconditioned fear-induced antinociception are under influence of nitrergic neuromodulation in AH neurons network This research was supported by CNPq (process 145258/2015-7). The experiments were performed in accordance with the recommendations of the Commission of Ethics in Animal Experimentation of the FMRP-USP (process 0187/2015). **References:** Ullah F. Behav. Brain Res. 319, 135 (2017). Falconi-Sobrinho, L.L. Neuropharmacology 113, 367 (2017). Moreira, F.A. Psychopharmacology 171, 199 (2004).

03.018 Acute stress impairs the extinction of conditioned fear memory: **participation of glucocorticoid receptors in the prefrontal cortex**. Rosa J, Uliana DLM, Resstel LBM FMRP-USP – Farmacologia

Introduction: Has been proposed that a brief exposure to stress led to deficits in extinction fear memory. The learning of extinction is used in the psychotherapy (for treatment of phobias or posttraumatic stress disorder, for example) under the name of exposure therapy. It consists of the learned inhibition of retrieval of a previously acquired memory. One very important region of the brain for retrieval of the extinction memory is the ventral portion of medial prefrontal cortex (vmPFC), which is also involved in the modulation of neuroendocrine and behavior responses in stressful situations. Additionally, there is a high expression of glucocorticoid receptors in this area. Thus, in the current study we investigated the effect of acute stress, along with the role of glucocorticoid receptors present in the vmPFC in the memory extinction learning. **Methods:** Male Wistar rats with infusion cannulae stereotaxically implanted in the prelimbic (PL) or infralimbic (IL) regions of the vmPFC were divided in two groups: 1) Stressed group (restraint stress for 1 hour); 2) Control group (without restraint stress). After 7 days, both groups were exposed to extinction of contextual fear conditioning protocol. **Results:** The stressed animals have an increase of the expression of contextual fear conditioning. Both groups, underwent to a stress or control manipulation, extinguished fear responses over the time during extinction session. However, one day later, the stress group demonstrated significantly less extinction retrieval than not stressed group. This suggest that the acute stress not impaired the acquisition, but promoted a deficit in the consolidation of extinction fear memory. Interestingly, the glucocorticoid receptor antagonist (RU 486; 10ng/side) microinjected into the PL or IL, immediately after the extinction session, attenuated such deficit promotes by restraint stress. **Conclusion:** Our results revel that a brief and single episode of stress induced before a training of contextual fear conditioning leads to extinction deficit. Together, our data suggest that the glucocorticoid receptors are necessary in vmPFC for the establishment of impaired of extinction memory promoted by acute stress. This study is important to characterizing how stress affects the extinction memory and can offer new insights about the extinction-based exposure therapy. Acknowledgments: FAPESP, CAPES and CNPq for **Financial Support**. This study was approved by a research ethics committee (CEUA-FMRP/USP 69/2015).

03.019 Antidepressant-like effect induced by Cannabidiol (CBD) is dependent on serotonin levels. Sales AJ[1], Guimarães FS[1], Joca SRL[2] [1]FMRP-USP – Farmacologia, [2]FCFRP-USP

Introduction: Cannabidiol (CBD) is a compound of *Cannabis sativa* with relevant therapeutic potential in several neuropsychiatric disorders, such as depression. CBD treatment induces antidepressant-like effects in preclinical rodent models (mice forced swimming test –FST - and the olfactory bulbectomy model; Zanelati et al., 2010 and Linge et al., 2015, respectively). However, the mechanisms involved in CBD-induced antidepressant effects have been poorly understood. Therefore, this work aimed at investigating the participation of serotonin and/or noradrenalin in CBD-induced antidepressant-ilke effects in the FST by: 1) testing if CBD co-administration with serotonergic (fluoxetine) or noradrenergic (noradrenaline) antidepressants would have synergistic effects; 2) investigating the effects of serotonin or noradrenalin depletion in CBD effects. **Methods:** Male *Swiss* mice received systemic injections of CBD (3, 7 and 10 $mg.kg^{-1}$), fluoxetine (FLX; 1, 5 and 10$mg.kg^{-1}$), desipramine (DES; 2.5 and 5$mg.kg^{-1}$) or vehicle and were submitted to the FST or to the open field test (OFT). Additional groups received a combination of subeffective dose of CBD with subeffective doses of FLX or DES. Independent groups received injections of 4-chloro-DL-phenylalanine (PCPA, an inhibitor of serotonin synthesis: 150$mg.kg^{-1}$, i.p., once per day for 4 days, i.p.) or N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine hydrochloride (DSP-4, a noradrenergic neurotoxin: 1µg/µl, i.c.v., 24h before the test). Thirty minutes before the test, the animals received systemic injections of CBD (10$mg.kg^{-1}$) or vehicle. Furthermore, in order to investigate if treatments used could induce any significant exploratory/motor effect, which would interfere in the FST results, all animals were submitted to the open field test (OFT). **Results:** CBD, FLX and DES induced antidepressant-like effects at the doses (CBD and FLX: 10$mg.kg^{-1}$, DES: 5$mg.kg^{-1}$). Subeffective dose of CBD (7$mg.kg^{-1}$) in association with subeffective doses of FLX (5$mg.kg^{-1}$) or DES (2.5$mg.kg^{-1}$) induced significant antidepressant-like effects. The behavioural effect induced by CBD is blocked by PCPA, but not DSP-4, indicating the participation of sertonergic mechanisms. None of the treatments induced locomotor effects in the OFT. The treatment effects were compared using one-way ANOVA followed by Dunnett's test for *post hoc* comparisons. Data from OFT were analyzed by a two-way ANOVA with the factors being treatment and injection. Probability less than 0.05 was accepted as significant. **Conclusion:** The antidepressant-like effect induced by CBD in the FST is dependent on serotonin levels in the CNS. **Financial support:** CAPES, CNPq and FAPESP. **Process number:** 072/2014.

03.020 Cannabidiol reduces haloperidol-induced orofacial dyskinesia and neuroinflammation in mice. Sonego AB, Prado DS, Guimarães FS FMRP-USP – Farmacologia

Introduction: Cannabidiol (CBD) is the major non-psychotomimetic compound of *Cannabis sativa* plant and exhibits anti-inflammatory and antipsychotic properties (1). CBD attenuates the extrapyramidal side effects induced by typical antipsychotics (2) and may be a potential therapy for tardive dyskinesia, a movement disorder that appears after chronic use of drugs that block dopaminergic receptors. Its pathophysiology is unknown but could involve neuroinflammatory mechanisms (3). To investigate this possibility, in the present study we evaluated if CBD would reduce the haloperidol-induced orofacial dyskinesia and if this effect would be associated with changes in levels of cytokines in the striatum. **Methods:** Male Swiss mice received an injection of CBD (60mg/kg, ip) or vehicle 30 min prior to haloperidol (3mg/kg, ip) or vehicle, during 21 days. Twenty-four hours after the last injection, the frequency of vacuous chewing movements (VCM) was evaluated for 10 min. After that, the animals were placed in the open field for 5 min. After that, the striatum was dissected to measure cytokine levels (IL-1β, TNF-α, IL-6 and IL-10) by ELISA. Data were analyzed by two-way ANOVA. In case of interaction between the evaluated factors, data were analyzed by one-way ANOVA followed by Sidak-Neuman-Keuls test. **Results:** Haloperidol induced orofacial dyskinesia by increasing the frequency of VCM, an effect that was reduced by repeated treatment with CBD. No treatment altered the locomotion of the animals. Furthermore, CBD attenuated haloperidol-induced increased levels of proinflammatory cytokines IL-1β and TNF-α in the striatum. Whereas IL-6 levels were not altered by any of the treatments, the levels of the anti-inflammatory cytokine IL-10 was increased by combined treatment of haloperidol and CBD in the striatum. **Conclusions:** CBD reduced haloperidol-induced orofacial dyskinesia and the increased levels of proinflammatory cytokines, suggesting that antidyskinetic effect of CBD could be related to an attenuation of neuroinflammation. **References:** 1. ZUARDI, A.W. *Rev. Bras. Psiquiatr***.**, v. 30, p. 271, 2008. 2. SONEGO, A.B. *Behav. Brain Res***.,** v. 309, p. 22, 2016. 3. BISHNOI, M. *Eur. J. Pharmacol***.,** v. 590, p. 241, 2008. **Financial Support:** CNPq, CAPES and FAPESP **Number process of ethical committee:** 090/2015

03.021 Anxiolytic-like effect of 2,6-di-tert-butyl-4-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)phenol mediated by GABAergic and monoaminergic pathway in mice. Moreira LKS, Brito AF, Silva DM, Cardoso CS, Siqueira L, Menegatti R, Costa EA UFG

Introduction: Anxiety is considered to be a normal physiological and psychological state necessary for human survival. However, excess anxiety can be debilitating and damage the quality of life, being considerate a pathological state demanding treatment. Anxiolytic drugs have various adverse effects, among them, sedation, muscle relaxation, amnesia, dependence and delay therapeutic. Consequently, the need for newer, better-tolerated, and more efficacious treatments remains high. In this way, was synthesize a new piperazine derivative, *2,6-di-tert-butyl-4-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)phenol* (LQFM212). This compound showed anxiolytic-like effect in mice in elevated plus maze test (EPM). Moreover, the aim this study is to investigate the mechanism of action of anxiolytic-like effect of LQFM212. **Methods:** It was evaluated mechanism of action of LQFM212 in the EPM using pharmacological antagonists of $GABA_A$/benzodiazepine site and antagonist of monoaminergic pathway. The experiments were conducted using adult male Swiss mice, weighing approximately 30-50 g (6-8 weeks old), with 8/group, according to the Ethical Principles in Animal Research and approved by the Comissão de Ética no Uso de Animais da Universidade Federal de Goiás (no. 021/13). The animals were pre-treated, 30 minutes before, with saline 0.9 % (10 mL/Kg, i.p.), flumazenil, benzodiapine antagonist (6.6 µmol/kg, i.p.), NAN-190, 5-HT_{1A} unspecific antagonist (1.3 µmol/kg, i.p.) or WAY-100635, 5-HT_{1A} specific antagonist (0.7 µmol/kg, i.p.). After the pre-treatments the animals were treated with vehicle (2% Tween 80, 10 mL/kg, p.o.) or LQFM212 (54 µmol/kg, p.o.). To assess the participation of endogenous serotonin the animals were pre-treated, once a day, for 4 days consecutives with saline 0.9 % (10 mL/kg, i.p.) or PCPA, a depletor of serotonin synthesis (500 µmol/kg, i.p.). One hour before the last pre-treatment, the animals were treated with vehicle or LQFM212 (54 µmol/kg, p.o.). Sixty minutes after the treatments, mice were submitted to EPM. The results were expressed as mean ± standard error of the mean (SEM). Statistical analyses were performed using Student's Test-t. Statistical difference was considerate when $p \leq 0.05$. **Results:** In the EPM, the treatment with LQFM212, when compared with vehicle, increased percentage of time in the open arms in 27%. However, the anxiolytic-like effect of LQFM212 was reverted by pre-treatment with antagonists in 22% (flumazenil), 73% (NAN-190), 27% (Way-100635) and 29% (PCPA). The percentage of time in center platform was decreased in 29%, when compared LQFM212 with vehicle. This effect was reverted by pre-treatment with antagonists in 91% (NAN-190), 28% (Way-100635) and 51% (PCPA). **Conclusion:** All the pre-treatment were able to prevent the anxiolytic-like effect of LQFM212 in EPM, suggesting that the anxiolytic-like effect of LQFM212 has the participation of $GABA_A$/benzodiazepine site and monoaminergic pathway. These results may be due to modulation of the monoaminergic system under GABAergic neurotransmission, but this hypothesis needs to be better evaluated by investigation of noradrenalin and dopamine involvement. **Financial Support:** The authors are grateful to CAPES and CNPq.

03.022 Chronic stressed mice treated with cannabidiol for 7 days shows attenuation in anxiogenic-like effect in the novelty suppressed feeding test. Detoni VL[1], Scarante FF[1], Aguiar RP[2], Fusse EJ[3], Guimarães FS[1], Campos AC[1] [1]FMRP-USP – Farmacologia, [2]UEM – Farmacologia e Terapêutica, [3]FMRP-USP – Neurociência e Ciência do Comportamento

Introduction: Chronic stress exposure is a factor that can culminate in the emergence of neuropsychiatric disorders such as anxiety and depression. In this meaning, the chronic unpredictable stress (CUS) paradigm can be used experimentally in animals to study the impact of chronic stress exposure. Evidences indicate that the chronic administration of antidepressants may attenuate the appearance of behavioral responses related to stress in animals submitted to CUS, although there is a latency to the positive effects of treatment. Recently, cannabidiol (CBD) has emerged as a novel drug with therapeutic potential for the treatment of psychiatric disorders, such as anxiety and depression, potentially reducing the latency observed for classic antidepressants. Therefore, the objectives of this work was to investigate whether the exposure to CUS for 7 days is able to promote the appearance of anxiogenic-like responses and if so, investigate whether treatment with CBD for 7 days is able to attenuate this behavioral. **Methods:** C57BL / 6 males mice (n = 4-5/group) were divided into 6 groups. The animals in each group received CBD (30mg / kg), escitalopram (20mg / kg) or saline daily as intraperitoneal (i.p) injection for 7 days, 2 hours after the daily stressor. The control group remained on the home cage and received the same treatment as the stressed group. One day after the last treatment, the animals were submitted to the Novelty Supressed Feeding (NSF) behavior test in a 10 minutes test session to evaluate anxiety behaviors and for 5 minutes in the home cage to evaluate food consumption. The latency was recorded for the animal to eat in the new environment and home cage. The statistical analysis used was one-way ANOVA and Kruskal-Wallis followed by Mann-Whitney. p values <0.05 were considered significant. **Results:** There was no significant statistical difference in latency to eat in the new environment among control animals and CUS exposed animals (p>0.05). There is a trend for CBD to attenuate the stress response compared to animals submitted to CUS and treated with vehicle (p<0,05). **Conclusion:** An increase in the number of animals may confirm the effect of the 7-days CUS on the anxiogenic-like effects. Preliminary results indicate that CBD treatment may be able to prevent the effects of CUS in the NSF and promote a reduction in latency when compared to animals treated with classical antidepressants. Further experiments are needed to investigate the trend observed in this protocol. **Financial Support**: CAPES, FAEPA, FAPESP. Protocol in the Ethics Committee of the Faculty of Medicine of USP/RP: 56/2017.

03.023 Effects of acute and chronic administration of agomelatine on anxiety and panic behavior in rats submitted to elevated T Maze Gomes ACCN[1], Medeiros AC, Bortolin RH[2], Gavioli EC[1], Soares-Rachetti VP[1] [1]UFRN – Biofísica e Farmacologia, [2]UFRN – Ciências Farmacêuticas

Introduction: Agomelatine is used for treating depression and it has been shown efficient in relieving the symptoms of anxiety. The Elevated T maze (ETM) is based on innate aversion of rodents to open and high spaces, allowing the observation of inhibitory avoidance and escape responses in the same animal [1]. Such responses have been associated, respectively, with generalized anxiety and panic [2]. The aim of present study was to evaluate if administration of agomelatine alters anxiety and panic-like responses in female rats. **Methods:** Female Wistar rats (n=58) were treated with Agomelatine by gavage. Agomelatine was acutely administered at doses of 25, 50 and 75 mg/kg/2mL, and chronically administered at a dose of 50 mg/kg/2mL for 25 days. In the latter group liver histology was evaluated. To evaluate the locomotor activity of the rats we used the open field test. **Results:** The results demonstrate that both acute and chronic administration of agomelatine in females do not significantly alter the locomotion of the rats. Regarding the inhibitory avoidance response, there were no changes in this response for both acute and chronic treatments. A trial effect was observed, suggesting acquisition of inhibitory avoidance in all cases. A decrease in the escape response latency was observed after acute, but not chronic administration of agomelatine (25 mg/Kg/2mL). Regarding hepatic histology after chronic administration, no changes were observed when compared to the control group. **Conclusion:** Data here obtained suggest a panicogenic-like effect of acute administration of agomelatine and the absence of both behavioral and hepatic toxicity effects after chronic administration in females. Reference: [1] GRAEFF, F G. Braz J Med Biol Res., v. 26, p.67, 1993. [2] ZANGROSSI, H Jr. Neurosci Biobehav Rev., v. 46, p.397, 2014. **Financial Support**: CNPq and UFRN; CEUA (Prot. Number 007/2012). Keywords: Agomelatine. Anxiety. Elevated T maze. Acute treatment. Chronic treatment. Panic.

03.024 Environmental enrichment affects emotional behavior and pharmacological response to antidepressants in CF1 mice. Speck ML, Gomes AL, Stein DF, Rojas C, Rates SMK UFRGS – Ciências Farmacêuticas

Introduction: Environmental enrichment (EE) consists of exposing animals to environments enriched with sensory stimulators (Chamove, Lab. Animals,v. 23, p 215,1989) aiming at stimulating the captive animals' natural behavior. (Frajblat, Marcel, Scie. Cult, v60, p44, 2008). Several studies have shown that EE stimulates neurogenesis in the rodent brain, especially in the hippocampus, a limbic structure important for memory formation and emotional processing, which is affected in Alzheimer's disease and mood disorders (Kempermann, Gerd et al. Nat, v386, p493, 1997). However, the influence of EE on pharmacological (PH) and behavioral responses in animal models of psychiatric diseases has not fully established yet. The aim of this study was to evaluate the effect of dams and offspring's exposure to EE on the behavioral and PH responses in the open field (OF) and forced swimming test (FST) (Porsolt et al., Eur. J. Phar., v, 47, p.379, 1978). **Methods:** Different groups of female CF1 mice (25-30g) (CEMBE-PUCRS) were exposed (EG) or not (NEG) to the enrichment schedule from the mating until offspring weaning. Then, the pups (male only) were located to receive or not the EE, and named enriched offspring (EOF) or non-enriched offspring (NEOF), therefore comprising four groups (10 – 12 mice): NEOF-NEG, EOF-NEG, NEOF-EG and EOF-EG. At P50 mice were evaluated in the OF (crossings (CR), rearings (RE), periphery time (PT) and grooming (GRO)) and FST (immobility time (IT) one hour after being treated with vehicle (saline+polysorbate 80 2%, 1mL/kg p.o.) (VHC), bupropion (30mg/kg p.o.) (BUP) or fluoxetine (30mg/kg p.o.) (FLX). **Results:** The offspring EE altered the behaviors in a different way, depending on the progenitor. The comparisons considered NEOF-NEG values as control: CR reduced in EOF-NEG; PTreduced in EOF-EG; GRO increased in EOF-EG and EOF-NEG; rearing was not affected. There was interaction between offspring and treatment factors. The comparisons considered the respective vehicle values as control. FLX: increased CR in EOF-NEG and decreased it in the NEOF-EG; decreased rearing in the NEOF-NEG and NEOF-EG and increased it in the EOF-EG; reduced GRO in EOF-NEG and increased it in EOF-EG. FLX did not affect periphery and immobility times of any offspring. BUP: did not affect CR of none of NEG offspring and increased CR in EOF-EG; increased rearing in the EOF-EG; decreased GRO in EOF-NEG and in EOF-EG. BUP reduced ITof the OEF-NEG and NEOF-NEG. BUP did not affect the ITof any EG offspring. **Conclusion:** The EE of offspring affected the emotional and PH responses. The EE seems to have anxiolytic/sedative effect, as it reduced spontaneous locomotion and PT and increased GRO. Progenitors' EE also seems to be important to the reduction of periphery time. The EE of offspring favored the stimulating effect of FLX, while the stimulating effect of BUP seems to enhance by the combination of progenitor and offspring EE. On the other hand, the progenitor exposure to the EE abolished the antidepressant-like effect of BUP, indicating an EE influence on dopaminergic and noradrenergic neurotransmission. FLX did not show antidepressant-like effect in any group, which is in agreement with the low sensitivity of immobility behavior to serotonergic drugs (Lucki et al. Behav Pharmacol. 1 v. 8(6-7), p.523, 1997) and indicates that EE is not able to stimulate this PH response. Acknowledgements: PhD scholarship from CAPES-POREX 646-2014. Ethical approval (CEUA-UFRGS (31882).

03.025 Study of the effect of daidzin and a synthetical analogue – LQB 308 – in *Caenorhabditis elegans* and primary cerebellar culture. Silva CPM[1], Stein DF[1], Goethel G[1], Costa P[2], Garcia SC[1], Rates SMK[1] [1]UFRGS, [2]UFRJ

Introduction: Daidzin is a natural isoflavone that has antioxidant and hormonal properties, (SETCHELL, 1998, and ZUANAZZI et al., 2017). In addition, it showed efficacy in reducing self-administration of cocaine in rats, attributed to its ability to inhibit the enzymes ALDH2 and dopamine β-hydroxylase (DBH) in the brain (GAVAL-CRUZ and WEINSHEIMER, 2009). Suggesting a new therapeutic use of daidzin and point to the need to investigate the safety of this compound. **Methods:** Daidzin from Biochempartner. The Bioorganic Chemistry Laboratory-UFRJ synthesized LQB 308, by catalytic arylation. Primary culture obtained from cerebellum of Wistar neonates rats were incubated for 48 hours with daidzin or LQB 308 at 0.01 to 10 µM in absence or presence of 06-OH-dopamine 30 µM, which is a toxin that is carried to the dopaminergic neuron cytoplasma by binding to the dopamine transporter (BLUM et al., 2001). Cell viability was evaluated by the fluorescein diacetate (FDA) technique. *C. elegans* N2 wild and BY 200 (dopaminergic neuronal transporters marked with GFP-green flurescent protein) strains were maintained on Nematode Growth Medium seeded with *E. coli* O P50 at 20°C. The worms synchronized by age. The drugs concentration ranged from 0.3 to 300µM, except in BY 200 which was tested only 300 µM. CL_{50} was determined by non-linear regression, the (ROS) production by the 2 ', 7'-dichlorofluorescein diacetate test (DCF-DA), The body area measured through the AxioVision LE software. Fluorescence microscope (Olympus IX-71) captured BY 200 images. All experiments, except BY 200, were performed in triplicate. **Results:** 6-OH-DA reduced the survival of the cerebellar neurons by 50%, cells treated with daidzin and LQB 308 at concentrations of 0.01µM, 0.1µM, 1.0µM and 10µM and incubated with 06-OH-DA had 82%, 72% 77%, 72% and 74%, 77%, 80%, 77% respectively of cell viability, indicating that daidzin [F (4.50) = 17.75; P <0.001] and LQB 308 protect the cells against this lesion [F (4,50) = 17, 22; P <0.001]. Survival of cultures treated with daidzin and LQB 308 did not differ from the control (p = 0.1882 / p = 0.8181). Daidzin LC50, LBQ 308 were 200 and 21 µM. Daidzin showed a bell-shaped dose-response curve over the body area (reduction in 3 µM, 10 µM, 30 µM and 100 µM [F (7,413) = 4,005; p <0.001] (one-way ANOVA / Bonferroni) And no effect at 0.3, 1 and 300 µM). LQB 308 did not affect the body area (p <0.1092). Daidzin and LQB 308 did not affect ROS production (p <0.5705; p <0.8765). Both compounds reduced BY 200 fluorescence. **Conclusions:** Daidizin and LQB 308 had a protective effect against neuronal death induced by 6-OH-dopamine, effect observed in BY200 strain indicates that these drugs compromise the dopamine neuronal transporter functioning. The effects N2 strain indicates that these drugs have low to moderate toxicity and that daidzin is less toxic than its analogue LQB-308. **References:** BLUM, D., S. Prog Neurobiol. V.65. p.135, 2001. GAVAL-CRUZ, M. Mol. Int.. V.9, p. 75, 2009. SETCHELL, K.D. American J. C. of Nutrition. V.134, p.1333S, 1998. ZUANAZZI, J. A. S.; Flavonoids. Pharmacognosy. V.2, 2017. **Acknowledgements:** PhD scholarship from CAPES-POREX 646-2014. **Ethics** Committee on the Use of Animals-UFRGS approved: 30060.

03.026 The FAAH Inhibitor, URB597, modulates anxiety-like behavior in mice depending on previous stressful experience. Fusse EJ, Turcato F, Scarante FF, Marrubia MM, Aguiar RP, Detoni VL, Guimarães FS, Campos AC FMRP-USP

Introduction: During a stressful situation, our brain orchestrates a series of events in order maintain homeostasis. However, under chronic stress circumstances, series of behavioral and physiological changes throughout the body occur that can contribute with the precipitation of psychiatric disorders, such as anxiety and mood disorders. The endocannabinoid system (ECBS) is recruited during stress-related responses. Changes in the endocannabinoid signaling are observed in key brain areas related to stress response and facilitation of ECBS induces antidepressant and anxiolytic effects in rodents. In the present work, we investigated if the facilitation of anandamide-mediated signaling by URB597, a FAAH inhibitor, prevents chronic social defeat stress (CSDS)- induced anxiogenic-like behavior in mice. **Methods:** male C57/BL6 mice (n=8-9) were submitted to a 7 days protocol of CSDS and treated daily with URB597 (i.p; 0.1, 0.3 and 1 mg/kg). On the 8th day, the animals were submitted to the Novelty Supressed Feeding test (NSFT). **Results:** Chronic stressed mice displayed a tendency to increase the latency to feed in the new environment in comparison to the non-stressed group (Two Way ANOVA, $F(3,60) = 2,33$, $p = 0,083$). The treatment with URB597 (dose 0.3mg/kg) in the stressed group exhibited a trend to reduce the latency to feed in comparison to the vehicle stressed group (One Way ANOVA, $F(3,32) = 1,846$, $p = 0,159$). In contrast, treatment with 1mg/kg URB597 in the non-stressed group produced an anxiogenic-like effect in comparison to the vehicle non stressed group, increasing the latency to eat in the NSFT (One Way ANOVA, $F(3,28) = 4,280$, $p< 0.05$). Our results suggested that under basal conditions URB facilitates anxiety-like behavior while tend to induces anxiolytic-like effects in animals exposed to chronic social defeat stress. **Financial Support**: CNPq, FAPESP, L'oreal-UNESCO-ABC. Animal Ethics Committee protocol: CEUA 144/2016