03. Psychopharmacology

03.001 Preclinical study of the effects of usnic acid on animals with Alzheimer's disease induced by Aβ1-42. Cazarin CA[1], Dalmagro AP, Gonçalves AE[1], Fátima A[2], Souza MM[1] [1]Univali, [2]UFMG

Introduction: Alzheimer's disease (AD) is the most common form of dementia and diagnoses predicted to reach 70 million people worldwide, according to World Health Organization. Extracellular and intracellular findings such as β-amyloid plaques (particularly 1-42 amino acid chains) and neurofibrillary tangles formation respectively are the main histopathological findings of the disease, all occurring simultaneously with oxidative stress events that together contribute to the cognitive decline clinically found in patients. The usnic acid (UA), $C_{18}H_{16}O_{7,}$ is a lichen metabolite, found in nature in two enantiomeric forms (+) UA and (-) UA that demonstrated anti-proliferative, neuroprotective and antioxidant activity in vitro, which led us to investigate in vivo the possible effects exhibited in an animal model of neurodegenerative disease. **Methods:** Both enantiomeric forms of UA were isolated from Cladonialecanora species. Pharmacological tests were performed according to the ethical principles analyzed by the Ethical Commission for the Use of Animals (CEUA) number 070/17p. Swiss female mice were divided into 10 groups with N of 8-10 animals per group. 1) (-) UA25 mg/kg; 2) (-) UA50 mg/kg; 3) (-) UA100 mg/kg; 4) (+) UA25 mg/kg; 5) UA50 mg/kg; 6) UA100 mg/kg; 7) Donepezila 2mg/kg; 8) DMSO; 9) SHAM (surgery control) and 10) Naive, and the treatment was made per oral. The mice were anesthetized and submitted to an intracerebroventricular (i.c.v.) administration of $Aβ_{1-42}$. An incision for exposure of the cranial cap was made and through a micro syringe inserted in the region of intersection of bregmawas injected 3µl of$Aβ_{1-42}$(400 pmol/mice). After recovery of the animals (twenty-four hours after), atwenty-four days of treatment started. On the fourteenth day of treatment began the behavioral tests: Open Field Test (OFT) to rule out locomotors changes, novel object recognition test (ORT)to evaluated the emotional memory of the animal's recognition, Morris water maze (MWM) to evaluate spatial memory and the emotional aversive memory was evaluated using the inhibitory-avoidance test (IAT). The statistical analysis performed using GraphPad Prism® 6 adopting Tukey's and Dunnett's post hoc tests when necessary. **Results:** Both enantiomers of UA treatment did not compromise the locomotors activity of the animals evaluated on the OFT. In the ORT, the treatment with every dose of (-) UA and (+) UA was able to increase the recognition index of the animals. In the MWM, both UA enantiomers doses treatment decrease the latency scape of the animals in the training session, except (+) 50mg/kg. In the test session, the treatment with 25 mg/kg and 100 mg/kg of both enantiomers increased the time in the platform quadrant on the Probe trial session of MWM. Lastly,in the IAT, the enantiomers treatment shown an increase of the step-down latency with every doses used. **Conclusion:** Both enantiomeric forms of UA exhibited a similar effect on the behavioral tests. They were able to reverse thecognitive decline caused by $Aβ_{1-42}$i.c.v. administration improving the learning and memory of the treated animals without change the locomotors parameters, demonstrating a pharmacological interest to neurodegenerative disorders, in particular AD. **Financial Support:** CAPES.

03.002 Effects of a post-conditioning treatment with ibogaine on the reinstatement of ethanol-induced conditioned place preference in mice. Henriques GM, Santos AA, Reis HS, Dias Júnior BC, Cerqueira NA, Jesus NMS, Marinho EAV, Berro LF UESC **Introduction:** Alcohol use disorder is one of the leading causes of death and disabilities among young adults and adults. Although treatments for alcohol use disorder exist, the current available pharmacotherapies are only partially effective, and rates of relapse remain high. Evidence suggests that ibogaine (IBO), a psychoactive alkaloid derived from the plant *Tabernanthe iboga*, may have therapeutic effects on drug abuse. The aim of the present study was to investigate the effects of a post-conditioning treatment with IBO on the reinstatement of ethanol-induced conditioned place preference (CPP) in mice. **Methods**: Three groups (N=8) of adult Swiss male mice were conditioned with saline (i.p.) in the non-drug-paired compartment and ethanol (1.8 g/kg, i.p.) in the drug-paired compartment for 8 alternating sessions. Starting on the day after a drug-free post-conditioning test and for 8 consecutive days, on even days animals were treated with vehicle (oral) or ibogaine (10 or 30 mg/kg, oral) and placed in the ethanol-paired compartment. On odd days, animals were treated with saline and placed in the saline-paired compartment. On the day following a drug-free post-treatment test, all animals were treated with ethanol and placed in the ethanol-paired compartment (ethanol re-exposure), with a drug-free post-reexposure test (reinstatement test) being conducted the next day. This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol #006/2017). **Results:** All groups conditioned with ethanol expressed preference for the ethanol-paired compartment ($p<0.0001$) and extinguished ethanol-induced CPP after the treatment phase (post-treatment test), regardless of vehicle or IBO treatment. However, only animals treated with vehicle expressed ethanol-induced CPP after an ethanol re-exposure ($p= 0.0040$) indicating that treatment with IBO at both doses prevented the reinstatement of CPP to ethanol. **Conclusion:** IBO blocked the reinstatement of ethanol-induced CPP in mice at both doses tested in the present study. Our findings are in agreement with previous studies suggesting that IBO may have therapeutic effects on drug abuse by showing that IBO can block the expression of the rewarding effects of ethanol in an animal model. **Financial support:** UESC, FAPESB, CNPq and CAPES.

03.003 Impact of *Lactobacillus plantarum* **administration in the acquisition of preference in ethanol-induced conditioned place preference extended protocol in mice**. Santos TB[1], Silva KSO[1], Lins JF[1], Kisaki ND[1], Rocha VN[1], Farias CJ[1], Uetanabaro APT[1], Marinho EAV[1], Nicoli JR[2] [1]UESC, [2]UFMG

Ingestion of microorganisms able to systemically influencing the host has the view as a viable supplement to health care. Previous studies have shown that bacteria *L. plantarum* strains Lp286 and Lp81, extracted from the fermentation of cocoa (*Theobroma cacao*; Lp286) and cupuaçu (*Theobroma grandiflorum*; Lp81), are potentially probiotic and Lp286 has anxiolytic and antidepressants effects. Considering the psychobiotic potential, this study aims to verify the influence of *L. plantarum* administration in the acquisition of preference in the ethanol-induced Conditioned Place Preference (CPP) in Swiss mice. For this, in experiment 1 (exp 1), 3 animal groups (N=8) were treated in the morning (8-9:00) with vehicle (0.1 mL of 0.85% saline + 15% skim milk) or vehicle + 10^9UFC Lp286 or vehicle + 10^9UFC Lp81 (gavage) by 7 days. The animals were submitted to the CPP protocol induced by 1.0g/kg of ethanol (gavage) in the afternoon (13-15:00). All animals were pre-conditioned (1 day), conditioned with saline in the non-drug compartment (even days) and with ethanol in the drug compartment (odd days) for 30 days. In the next day, the animals were submitted to the post-conditioning test: they had free access to the compartments previously conditioned to the drug or saline. The tests were analyzed with the Anymaze® software. Experiment 2 (exp 2) followed exp 1 guidelines but there was reversal in probiotic (16-17:00) and CPP (8-10:00) treatment. This study was approved by the Institutional Animal Care and Use Committee of UESC (CEUA/UESC #012/2017). In the exp 1, the paired t test analysis of the pre and post tests for the Compartment Time of Permanence (CTP) did not indicate significance for the group treated with Lp286 ($p>0.05$) but there was for the vehicle and Lp81 ($p<0.05$). In the post-conditioning analysis, ANOVA indicated a difference between groups for CTP. The Bonferroni test indicated that the group treated with Lp286 had a significant reduction of CPP (Vs. vehicle and Lp 81). Regarding the analysis for the Number of Entries in Compartments (NCE) and Distance Traveled in Compartments (DTC), the t test indicated statistical difference between the pre-test and the vehicle group only for DTC. In the post-conditioning analysis, no difference was observed in NCE and DTC. In the exp 2, for the CTP, the paired t-test indicated significance among all groups. In the t test analysis for the NCE and DTC there was difference only between the pre and post test of the vehicle group. ANOVA showed no difference between groups for all parameters. Taken together, our data suggest that the treatment with Lp286 strain was useful to prevent impulse search by the ethanol associated compartment resulting in the absence of the ethanol-induced CPP. Considering that alcoholism is a public health problem and that *Lactobacillus* species present themselves as excellent intestinal barrier protectors, these results could represent a preventive or therapeutic strategy for the clinic in the future. Probiotics; CPP; Ethanol. **Financial support:** FAPESB.

03.004 Effects OF Nociceptin/Orphanin FQ receptor antagonist on inescapable electric footshock stress-induced anxiety-like behaviors in mice. Barbosa AIS[1], Holanda VAD[1], Soares-Rachetti VDP[1], Ruzza C[2], Calo G[2], Gavioli EC[1] [1]UFRN, [2]Universidade de Ferrara

Introduction: Nociceptin/orphanin FQ (N/OFQ) is an endogenous peptide that displays affinity for the NOP receptor. The peptide and its receptor are widely expressed in the brain, mainly in areas implicated in the control of emotions [1]. Evidence supports the view that the activation of NOP receptors with agonists elicits anxiolytic-like effects, while its blockade with NOP antagonists promotes antidepressant-like actions [2]. Of note, NOP antagonists are effective in reversing the inescapable electric foots hocks-induced depressive-like behavior [3]. However, the effects of NOP antagonists on stress-induced anxiety are still unclear. This study aims to investigate the effects of the blockade of NOP receptor on stress-induced anxiety in mice. **Methodology:** Male Swiss mice were exposed to inescapable electric foot shocks (180 shocks, 1 mA, 20 s interval) on day 1. On day 2, animals were screened in an escapable electric footshock session (30 shocks, 1 mA, 30 s interval) based on their behavior: “helpless” - failed to escape from the shock more than 20 trials (in 30), and “non helpless” - failed to escape less than 20 trials. On day 3, non stressed controls, helpless and non helpless mice were exposed to elevated plus-maze test (EPM), and on day 4, mice were exposed to the open field test (OF). Animals were treated with vehicle, diazepam (a benzodiazepine, 1 mg/kg, ip) or SB-612111 (0.1, 1 and 10 mg/kg, ip) 30 minutes prior to the EPM and OF. All the experiments were approved by ethics committees from UFRN (N° 061/2016). **Results:** Inescapable electric footshock induced anxiogenic-related behaviors only in helpless mice. In fact, a significant reduction in the percentage of time and entries into open arms of the EPM was detected in helpless, but not in non helpless, mice compared to non stressed ones. Diazepam significantly increased the percentage of time and entries into open arms of all animals tested (ie., helpless, non helpless, and non stressed mice). However, the treatment with the NOP antagonist SB-612111 (1 mg/kg) was able to selectively reverse anxiogenic-related behaviors of helpless mice. No significant differencesinthe spontaneous locomotion were observed in helpless and non helpless mice compared to non stressed animals. Additionally, neither SB-612111 nor diazepam affected the locomotor activity of mice. **Conclusion:** Under our conditions, helpless mice were significantly more anxious than non stressed animals. Despite being inactive in non stressed and non helpless mice, the treatment with the NOP antagonist successfully reversed the anxiogenic-like behavior of helpless mice. Ultimately, these data support the view that NOP antagonists can be interesting drugs for the treatment of anxiety in depressed individuals. **References:** [1] Witkin et al. PharmacolTher. 141(3):283, 2014.[2] Gavioli et al. Handb Exp Pharmacol., *In press*, 2018 (doi: 10.1007/164_2018_188). [3] Holanda et al. Psychopharmacology (Berl). 233(13):2525, 2016. **Acknowledgments:** CNPq (Pq No. 302302/2015-8, Universal No. 401837/2016-5 to ECG) and CAPES (MSc and PDSE fellowship).

03.005 The anti-stress effects of the combination of Escitalopram and Cannabidiol in mice depends on anandamide levels in the prefrontal cortex. Scarante, FF[1], Vicente MA[1], Fuse EJ[1], Lopes VD[2], Aguiar RP[3], Scomparin DS[1], Guimarães FS[1], Campos AC[1] [1]FMRP-USP, [2]FCFRP-USP, [3]UEM

The late-onset of action antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs) is one of the main limitations in the psychiatric practice. A possible strategy to overcome this limitation is to combine SSRIs with agents that could accelerate the efficacy of the treatment. Here, we hypothesized that the combination of the SSRI escitalopram (ESC) with a subeffective dose of the phytocannabinoid cannabidiol (CBD) would accelerate the behavioral and neuroplastic effects of the treatment in stressed mice. Male C57Bl6 mice (10-12 weeks old) were submitted to a 10-day protocol of repeated unpredictable or social defeat stress and were treated with Vehicle or ESC (10mg/kg) in combination with Vehicle or CBD (7.5mg/kg) during 7 days. While previous study from our group indicated that ESC alone would induce an anxiolytic-like effect at the dose of 20mg/kg after 14 days of treatment in stressed mice, our results have shown that combining half this dose with a subeffective dose of CBD induced an anxiolytic-like effect evidenced in the novelty-suppressed feeding test after only 7 days of treatment in stressed o animals. The ESC+CBD treatment also induced a significant increase in the expression of the pre-synaptic marker synaptophysin in the prefrontal cortex (PFC), indicating that the behavioral effects were accompanied by an increased synaptic plasticity in this region. Since the facilitation of the anandamide (AEA) signaling has been proposed as a response induced by both CBD and repeated ESC treatment, we addressed whether disrupting the synthesis of this endocannabinoid in the PFC would prevent the behavioral effects induced by the drug combination. In order to address that, mice were submitted to stereotaxic surgery to receive via intra-PFC a viral vector containing a construct that directs the CRISPR-Cas9-mediated deletion of the AEA synthesis enzyme N-acyl phosphatidylethanolamine-specific phospholipase D (NAPE-PLD). A construct containing a scramble sequence was injected via intra-PFC in the control wild-type (WT) mice. After 15 days of recovery, the animals were submitted to the 10-day repeated stress and 7-day treatment with the drug combinations. In the WT control group, as shown before, ESC and CBD, when combined, induced an anxiolytic-like effect. However, this effect was absent in the mice in which the expression of NAPE-PLD was deleted in the PFC, indicating that the deletion of AEA synthesis in the PFC prevents the anxiolytic-like effect of the combination of ESC and CBD in stressed mice. In conclusion, our results show that the AEA signaling in the PFC is required for the accelerated behavioral outcomes induced by the combination of ESC and CBD. Ongoing experiments are investigating the role of the signaling mediated by the endocannabinoid 2-arachidonoyl-glycerol (2-AG) in the response to the drug combination as well. CEUA number: 032/2015-1; CEUA number: 47/2019. Financial support: CNPq, FAPESP and L'Oreal Institute.

03.006 MK801 pharmacogenetics effects in two models of attention-deficit/hyperactivity disorder. Granzotto N, Caneppa S, Voltz L, Izídio GS UFSC

Introduction: The locomotor hyperactivity is one of the most important endophenotypes of Attention-Deficit/Hyperactivity Disorder (ADHD). Although there are pieces of evidence explaining the neurobiological basis of this trait, it remains not fully understood in the literature. Currently, the most used animal model in ADHD research is the Spontaneously Hypertensive Rat (SHR). However, the translational value of SHR's studies has some limitations, and new models are necessary. We recently proposed a congenic strain named SLA16, which is a strain derived from SHR and Lewis rats (part of chromosome 4 from Lewis rats was inserted in the SHR genetic background). SLA16 rats present higher hyperactivity/impulsivity and lower emotionality and basal blood pressure, than SHR strain. Here, we administered MK801 in SHR and SLA16 rats to evaluate the participation of NMDA receptors in the differences observed in the hyperactivity and emotionality. **Methods:** SHR and SLA16 male rats (4 months) received MK801 in the doses 0.01 mg/kg; 0.03 mg/kg; 0.1 mg/kg; 0.3 mg/kg; or saline. The animals (6 animals/strain/dose) were tested in the open field(OF) 30 minutes after injections, and then in the elevated plus maze(EPM). All procedures were carried out in accordance with the guidelines of the local committee for Animal Care in Research (CEUA/UFSC) and had the permission PP00903. The financial support was guaranteed by CNPQ and CAPES resources. **Results:** In the OF, ANOVA showed a treatment effect ($F(4, 42)=4.306$, $p=0.005$) on the total distance and Duncan's post hoc test showed that the MK801 0.3mg/kg decreased locomotion. There was an interaction between strain and treatment for the entries into the center ($F(4, 42)=8.051$, $p<0.001$). Duncan's post hoc test showed that the SLA16 saline visited more the center than SHRsaline; both strains have similar scores in the 0.01; 0.03 and 0.1mg/kg groups; and only the SLA16 decreased their entries after MK801 0.3 mg/kg.For the % of inner locomotion, there wasan interaction between strain and treatment($F(4, 42)=3.588$, $p=0.012$).Duncan's post hoc test showed that SLA16 saline presented higher percentage of inner locomotion than SHR saline; no differences between strains were found in the two lower doses; and only in SLA16 decreased % of inner locomotion in the two higher doses. At the EPM there was an interaction between strain and treatment($F(4,42)=7.564$, $p<0.001$) for the number of entries in the open arms. Duncan's post hoc test showed that SHR 0.03 and 0.1mg/kg groups increased their number of entries. On the other hand, the SLA16 0.01mg/kg group decreased and the 0.1 and 0.3mg/kg groups increased their entries into the open arms. For the time spent in open arms there were significant effects of strain ($F(4,42)=9.200$, $p<0.001$; SLA16>SHR) and treatment ($F(4,42)=4.155$, $p=0.012$; MK0.1mk/kg>MK0.01mg/kg). **Conclusion:** Our data corroborate that SLA16 rats are even more hyperactive than SHR, and also have a lower index of emotionality. Furthermore, there is some pharmacogenetic effect that appears to make the SLA16 more sensitive to MK801 effects', when compared with the SHRstrain, suggesting that NMDA receptors play a role on the neurobiological basis of ADHD.

03.007 Role of medial prefrontal cortex subregions in the impairing effects of cannabidiol on contextual fear memory reconsolidation. Bertoglio LJ[1], Stern CAJ[2], Reichmann HB[1], Gazarini L[3], Guimarães FS[4] [1]UFSC, [2]UFPR, UFMS[3], [4]FMRP-USP

Introduction: Dysfunctional aversive memory processing contributes to the development of posttraumatic stress disorder. The traumatic memory impact can be attenuated by targeting its reconsolidation, which is differentially controlled by subregions of the medial prefrontal cortex. The major non-psychotomimetic component of the *Cannabis* plant, cannabidiol (CBD), is able to disrupt fear memory reconsolidation through cannabinoid type-1 (CB1) receptor signaling in the brain. The objective of the present study was to investigate whether CB1 receptors in the anterior cingulate (ACC), prelimbic (PL) and/or infralimbic (IL) cortices are involved in CBD-induced reconsolidation disruption. **Methods:** The University Animal Research Ethical Committee approved all experimental procedures in this study (CEUA nº 9263110516). Adult male Wistar rats were fear conditioned to the Context A. In order to induce memory labilization, a 3-minContext A re-exposurewas conducted on the next day, with alltreatments performed immediatelyafter that reactivation session. In experiment 1, animals were systemically treated with vehicle (VEH) or CBD (10 mg/kg) post-reactivation and, 1 h later, theirbrains were removed for posterior evaluation of Zif268/Egr-1 expression along the medial prefrontal cortex (ACC, PL and IL) by immunohistochemistry. Results were expressed as the number of Zif268/Egr-1 positive cells/0.1 mm^2. Based on experiment 1 results, in experiment 2 theanimals were treated with VEH or the CB1 receptor antagonist AM251 (50 pmol) into the PL and with VEH or CBD systemically post-reactivation. In experiment 3, animals were treated with VEH or AM251 into the ACC and with VEH or CBD systemically. In experiment 4, rats were infused with VEH or CBD (30 pmol) directly into the ACC or PL.To assess the drug effects onmemory reconsolidation, animals were once more re-exposed to Context A one day later (Test A) and freezing time was scored. **Results:** In experiment 1, VEH-treated animals had more Zif268/Egr-1 positive cells in PL (41 ± 2) and ACC (34 ± 2) than inIL(12 ± 4) following memory reactivation. Systemic CBD treatment prevented these differences (PL: 22 ± 4; ACC: 23 ± 4; IL: 16 ± 2). In experiment 2, CBD-treated animals presented less freezing time than controls during Test A(VEH/VEH: 75 ± 9%; VEH/CBD: 43 ± 8%). The CBD effects were prevented by PL CB1 receptor antagonism (AM251/VEH: 74 ± 8%; AM251/CBD: 70 ± 8%). In experiment 3, the ACC CB1 receptor antagonism also prevented the CBD effects on reconsolidation (VEH-VEH: 78 ± 5%; VEH/CBD: 53 ± 5%; AM251/VEH: 83 ± 5%; AM251/CBD: 80 ± 7%). In experiment 4, animals treated with CBD intra-ACC or intra-PL presented less freezing time during test A than controls (ACC-VEH: 86 ± 5%; ACC-CBD: 42 ± 10%; PL-VEH: 79 ± 9%; PL-CBD: 29 ± 8%). **Conclusion:** The present results support the PL and ACC involvement in fear memory reconsolidation. They also indicate these two medial prefrontal cortex subregions as sites in which the CBD impairs the reconsolidation process. **Financial support:** CNPq, CAPES and FAPESP

03.008 Nociceptin/Orphanin FQ receptor signaling modulates resilience to stress in mice. Holanda VAD[1], Salvatore P, Azevedo JG[2], Finetti L[2], Calo G[2], Ruzza C[2], Gavioli EC[1] [1]UFRN [2]Universidade de Ferrara

Introduction: The peptide nociceptin/orphanin FQ (N/OFQ) and its receptor (NOP) are largely implicated in the modulation of emotional states [1]. Clinical and preclinical findings support antidepressant effects due to the blockade of NOP receptor signaling [2]. However, it is unclear the involvement of the endogenous N/OFQ – NOP receptor system in mediating stress coping strategies. The present study investigated the effects of activation or blockade of the NOP receptor signaling before exposure to acute stress. **Methods**: Male CD-1, female Swiss mice and male NOP receptor knockout mice (NOP (-/-)) were used in this study. Mice were treated before stress exposition with the following drugs: nortriptyline, NOP agonists (Ro 65-6570 and MCOPPB) and NOP antagonist (SB-612111). Inescapable electric footshock (2 sessions; 180 cycles, 1 mA, 1-10 s shock duration, 1-20 s interval) and forced swim (2 sessions: 15-min training session + 5-min test session) were used as acute stressors. Mouse behavior was evaluated by assessing percentage of helpless phenotype (<20 escapes/30 trails) in the inescapable footshocks and time spent immobile in the forced swim. All the experiments were approved by ethics committees from UFRN (N° 059/2015) and UNIFE-IT (Nº 302/2017). Results: The activation of the NOP receptor signaling with the agonists Ro 65-6570 (0.01-1 mg/kg, ip) and MCOPPB (0.1-10 mg/kg, ip), before inescapable footshocks and swim stress, increased percentage of mice developing helpless behavior and facilitated immobile posture, respectively. In contrast, the blockade of NOP receptor with the antagonist SB-612111 (1-10 mg/kg, ip) reduced acquisition of depressive-like phenotypes, and similar resistance to develop helpless behaviors was observed in mice lacking the NOP receptor. Under the same stressful conditions, administration of the antidepressant nortriptyline (20 mg/kg, ip) did not change acquisition of helpless behavior and immobile posture. **Conclusion:** These findings support the view that NOP agonists during acute stressful events facilitate depressive-related behaviors, whereas NOP antagonists have a protective outcome. The present study showed for the first time that the N/OFQ - NOP receptor system is a relevant player in controlling resilience to stress and development of depressive states. [1] Witkin et al. Pharmacol Ther. 141(3):283, 2014. [2] Gavioli & Calo, Pharmacol Ther. 140(1):10, 2013.

03.010 Treatment with synthetic cannabinoid WIN55,212-2, during adolescence, alters the susceptibility to cocaine-induced conditioned place preference. Gobira PH, Joca S FCFRP-USP

Introduction: Cannabis is the most commonly used illicit drug worldwide, and use is typically initiated during adolescence. Adolescence is a critical phase for cerebral development, and environmental influences on this period seems to be determinant for adult behaviour. In this way, cannabis exposure during this period, and as well as to synthetic cannabinoids, might lead to neurobiological changes that affect adult brain functions modulating the risk of psychiatric disorders such as anxiety, depression and addiction. The aim of this study was to investigate whether exposure to synthetic cannabinoid, WIN55,212-2, 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, 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), depressive-like behaviour in the forced swim test (FST) and memory in the object recognition test (ORT).The distance travelled in arena, immobility time in FSTas well as frequency EPM were analysed by student t test, comparing animals that received WIN55,212-2 with animals that receive vehicle. The conditioned place preference (CPP) score was analysed 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. This effect was not secondary to a change in memory as we did not observe differences between groups in animals submitted to ORT. **Conclusion:** Our present data demonstrated that a chronic exposure to cannabinoids during adolescence alters the susceptibility to acquisition of cocaine-conditioned place preference. These finding suggest that early exposition to WIN55,212-2leaded to neurobiological changes which might alter reward circuitry, modulating cocaine effect. 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).

03.011 Effect of pre-treatment with metadoxine on the development of ethanol-induced conditioned place preference and re-exposure to ethanol in mice. Dias Júnior BC, Santos AA, Coimbra JPSA, Santana MCE, Jesus LOS, Brito ACL, Marinho EAV, Lima AJO UESC

Introduction: Alcohol is one of the most commonly used psychoactive substances in the world, which has effects on mood, thought and behaviour and its chronic and indiscriminate intake can lead to addiction. Treatment of alcohol dependence is still limited, and adverse effects contribute to cessation of treatment by dependents. Metadoxine is a drug that acts to accelerate the metabolism of alcohol and few adverse reactions have been reported, but there are few studies that present the therapeutic potential of this drug in addiction. Thus, the aim of this study was to verify the effect of pre-treatment with metadoxine (META) on the development of ethanol-induced conditioned place preference (CPP) and re-exposure to ethanol in mice. **Methods:** Thus, 3-month-old male Swiss mice were submitted to a preconditioning test followed by conditioning with saline (control group) or META at doses of 100, 200, 400, 600 and 800 mg/kg followed by ethanol at 1.8 g/kg on odd days or with saline (Sal) on even days for 8 daily sessions, and CPP was quantified in one session of postconditioning. Then the abstinence phase was started, where the animals remained 8 days in the home cage without drug administration and CPP was quantified in a post abstinence session. On the following day the animals were re-exposed to Sal (control group) or META (all doses) followed by ethanol (1.8 g/kg) and CPP was quantified twenty-four hours later in a post-re-exposure session. This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol#012/2018). **Results:** No significant differences were found in the preconditioning tests for the scores of spending time, number of entries and distance travelled. In the postconditioning there was a statistical difference between the groups[$F(6, 99) = 17{,}25$; $P<0.0001$],and only pre-treatments with META600 and 800 mg/kg were able to block the development of ethanol-induced CPP when compared to control group ($p<0.05$). In post-abstinence session there was a statistical difference between the groups[$F(5, 42) = 5{,}069$; $p=0{,}0010$] and the groups treated with META 400, 600 and 800 mg/kg presented statistical difference when compared to control group ($p<0.05$). None of the doses of META were able to prevent reinstallation of ethanol-induced CPP. No significant differences were found in the postconditioning and post-abstinence tests fornumber of entries and distance travelled [One-way ANOVA/Bonferroni post hoc – $p<0.05$]. **Conclusion:** Our results suggest that only highest dose tested of metadoxinecan block the expression of CPP sustainably, but none of the doses are able to prevent the reinstallation of ethanol-induced preference behaviour. In view a lack of pre-clinical studies about the therapeutic effects of metadoxine on ethanol dependence, our study suggests that META as a promising treatment drug to block the development of the rewarding effects of ethanol in animal models.

03.012 Ayahuasca and methylphenidate induce conditioned place preference: **behavioral and Fos protein expression evaluations**. Rodrigues IRS[1], Reis HS[1], Santos TB[1], Serra YA[1], Machado EBO[1], Lima AJO[1], Yokoyama TS[2], Cruz FC[2], Berro LF, Marinho EAV[1] [1]UESC, [2]Unifesp

Introduction: Addiction is an important public health problem. Thus, studies have shown that Methylphenidate (Mph) has the potential to cause addiction. Evidence suggests that *Ayahuasca* (Aya), hallucinogenic beverage derived from the decoction of the plants *Banisteriopsis caapi* and *Psychotria viridis*, may have beneficial effects for individuals experiencing substance use disorders. The aim of the present study was to evaluate the potential rewarding effect of Aya and Mph, analyzing the expression of Fos in specific structures of the brain that are involved in drug seeking behaviors. **Methods:** Using Conditioned Place Preference (CPP) paradigm, twenty-four adult Swiss male mice were subdivided into three groups with eight animals each. They were submitted to the pre-conditioning test followed by the conditioning phase in which the animals were treated with vehicle via orally (v.o.) or Aya 100 mg/kg (v.o), or Mph 10 mg/kg intraperitonial (i.p). Ninety minutes after perform the post-conditioning test, the animals were anesthetized and perfused aiming to remove their brains to subsequently submitted to immunohistochemistry procedures to quantify Fos expression. The brain structures analyzed were medial prefrontal cortex: anterior cingulate (Cg1); prelimbic (PrL); infralimbic (IL) and orbitofrontal (OFC) areas); nucleus accumbens (NAc) both core and shell areas; ventral tegmental area (VTA); dorsal striatum (DS); and basolateral amygdala (BLA). This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol #11/2016). **Results:** Animals treated with both Aya and Mph presented significantly higher levels of CPP score in the post-conditioning test compared to the pre-conditioning test. Conditioning with Mph, but not with Aya, showed significantly lower levels of Fos expression in the post-conditioning test compared to the pre-conditioning test group for the following regions: Cg1 [$F(2, 15) = 5.445$; $p = 0.0222$]; PrL [$F(2, 15) = 20.67$; $p < 0.0001$] and OFC [$F(2, 15) = 6.850$; $p = 0.0223$]. Conditioning with Mph, but not Aya, also induced increased levels of Fos expression in the NAc Shell [$F(2, 15) = 9.198$; $p = 0.0029$] and DS [$F(2, 15) = 16.91$; $p = 0.0017$]. Conditioning with both Aya and Mph induced increased levels of Fos expression in the IL [$F(2, 15) = 21.32$; $p < 0.0001$] and the NAc Core [$F(2, 15) = 16.77$; $p = 0.0001$]. For the BLA [$F(2, 15) = 30.51$; $p < 0.0001$], conditioning with Aya, but not Mph, decreased Fos expression levels compared to the pre-conditioning group. Fos expression levels were not altered in VTA [$F(2, 15) = 1.459$; $p = 0.2637$] following conditioning with either Aya or Mph. **Conclusion:** At the doses used, Aya and Mph induced CPP in mice, however, the magnitude of Mph-induced CPP was higher than that induced by Aya. This assumption is corroborated by Fos protein findings showing that while Aya had limited effects on Fos protein expression while Mph altered Fos protein expression in several brain regions associated with effects of drugs of abuse. **Financial Support:** FAPESB, CAPES and CNPq.

03.013 Effects of previous and concomitant administration of *Lactobacillus plantarum* 286 and *Lactobacillus plantarum* 81 on the development of ethanol-induced conditioned place preference in mice. Silva KSO[1], Santos TB[1], Serra YA[1], Lins JF[1], Coimbra JPSA[1], Santos ML[1], Uetanabaro APT[1], Nicoli JR[2], Marinho EM[1], Marinho EAV[1], Tamura EK[1] [1]UESC, [2]UFMG

Introduction: Recent studies have reinforced the importance of the microbiota-gut-brain axis with regard to mental health and ethanol dependence. The treatment with *Lactobacillus plantarum* 286 (Lp286) extracted from the fermentation of cocoa (*Theobroma cacao*) and *L. plantarum* 81 (Lp81) extracted from cupuaçu (*Theobroma grandiflorum*), could systemically influence the host and positively modulate the mood of Swiss mice. Thus, this study aims to verify whether administration of the strains Lp286 and Lp81 were useful to influence the reward behavior of ethanol in Swiss mice in the Conditioned Place Preference (CPP). **Methods:** Therefore, 3 groups animals (N=8) were pre-treated in the morning (8-9:00h) with vehicle (0.1 mL of 0.85% saline + 15% skim milk) or vehicle + 10^9UFC Lp286 or vehicle + 10^9UFC Lp81 (gavage) by 7 days. The animals were submitted to the CPP protocol induced by 1.0g/kg of ethanol (gavage) in the afternoon (13-15:00h) and continued to receive either vehicle or probiotic treatments. Thus, all animals were pre-conditioned (1 day), followed by conditioning phase with saline in the non-drug compartment (even days) and ethanol in the drug compartment (odd days) for 8 days. In the next day, the animals were submitted to the postconditioning test: in absence of the drug, they had free access to the compartments previously conditioned to the drug or saline. The tests were filmed and analyzed with the Anymaze® software. This study was approved by the Institutional Animal Care and Use Committee of UESC (CEUA-UESC; protocol 012/2017). **Results:** Regarding the paired analysis of the pre and post tests for the Compartment Time of Permanence (CTP) and Number of Compartment Entries (NCE), the t test did not indicate significance for the groups treated with Lp286 and Lp81 ($p>0.05$), but there was for the vehicle ($p<0.05$). In the post-conditioning analysis, ANOVA indicated difference between groups for CTP [$F(2,21)=7.93$, $p=0.002$] and NCE [$F(2,21)=3.97$; $p=0.03$]. The Bonferroni test indicated that the groups treated with Lp286 and Lp81 had a significant reduction of CPP when compared to the vehicle treated group ($p<0.05$). Finally, in the distance traveled parameter (DTC), the paired t-test showed a significant difference between the pretest and the post-conditioning test for the groups treated with vehicle and Lp81 ($p<0,05$), but not for Lp286. In the post-conditioning in the comparison of the DTC parameter, the ANOVA showed no difference between the groups [$F(2,21)=0.007$; $p=0.99$]. The results indicate that the Lp286 and Lp81 strains were able to prevent ethanol-induced CPP. **Conclusion:** In conclusion, there is a bi-directional communication between the microbiotagut-brain as showed by another groups and additional studies are required to validate the potential of Lp286 and Lp81 strains in the prevention or treatment of ethanol dependence. **Keywords:** Probiotics; Conditioned Place Preference; Ethanol. **Financial support:** FAPESB.

03.014 Effects of chronic administration of agomelatine on biochemical parameters in female rats. Costa JAM, Moura NPS, Santos LC, Gomes ACCN, Lima FMS, Silva Júnior ED, Gavioli EC, Soares-Rachetti VDP UFRN

Introduction: Anxiety disorders and depressive disorders are increasingly prevalent, and a single individual simultaneously presents both conditions (WHO, 2017), and for the pharmacotherapy of anxious and depressive disorders there is agomelatina, an agonist of MT1 and MT2 receptors and a 5-HT 2C receptor antagonist (LIU et al., 2016)The aim of the present study was to evaluate if agomelatine chronically administered in clinical doses of 25mg, 50mg and 75mg/Kg alters biochemical parameters related to both liver and kidney functions in female rats. This work was previously approved by local ethics committee (007/2012-UFRN). **Methods:** Female *Wistar* rats (n=30) were submitted to the administration of agomelatine or saline by gavage at doses of 25, 50 and 75 mg/Kg for 25 consecutive days. Sixty minutes after the last administration, the animals were submitted to the decapitation to collect blood, which was then centrifuged to obtain the serum, that was used to perform the biochemical analysis. BioPLUS 2000 analyzer was employed to assess alanine aminotransferase(ALT), aspartate aminotransferase(AST), alkaline phosphatase (ALP), creatinine and urea levels. **Results:** Results show that administration of agomelatine(25 days) at a dose of 75 mg/Kg increased ALT levels (mean±SEM: control = 52.59 ± 2.55; 75 mg/Kg = 72.01 ± 7.58, while AST, ALP, creatinine and urea levels were not modified, when compared to control group (ANOVA followed by Duncan's test). **Conclusion:** Data here obtained suggest that chronic use of agomelatine was related to increasing level of ALT, without altering other parameters associated with both liver and kidney functioning in female rats. Histological data are needed to better understand a possible hepatotoxicity caused by the long-term use of agomelatine. References: WHO. WORLD HEALTH ORGANIZATION. Depression and Other CommonMental Disorders: Global Health Estimates. Genebra, Suíca, 2017. Liu, Jiabei et al. "MT1 and MT2 Melatonin Receptors: A Therapeutic Perspective." Annual review of pharmacology and toxicology vol. 56 (2016):

03.015 The *in vitro* effect of the antipsychotic quetiapine on inflammation is dependent on the initial state of macrophages. Turra BO[1], Nerys DAO[1], Braun LE[1], Azzolin VF[1], Teixeira CF[1], Lima PASP[2], Chitolina B[1], Ribeiro EE[1], Motta JR[1], Praia RS[1], Cruz IBM[1], Barbisan F[1] [1]UFSM, [2]PUC-RS

Introduction: Chronic inflammation is related to the development of psychiatric disorders. Quetiapine (QUE) is an atypical antipsychotic drug that exerts its effects through interaction with the dopaminergic, noradrenergic and serotonergic systems. Studies demonstrate the anti-inflammatory effect of QUE and its therapeutic effects could also be associated with this property. However, patients who use QUE present greater susceptibility of weight gain and metabolic syndrome. This apparent contradiction could be related to the initial state of immune cells, in which the QUE would act as an anti-inflammatory agent in activated macrophages, and as pro-inflammatory in macrophages not activated for inflammation. Our objective was to evaluate in vitro the effect of QUE on activated and non-activated macrophages by mitogenic agent phytohemagglutinin (PHA). **Methodology**: This study was performed with the RAW 264.7 commercial macrophage cell line. Cells were plated and part of them was activated for inflammation by treatment with PHA, another part was not treated. After 24 hours, all cells were treated with 100µg / L quetiapine and then again incubated for 24 or 72 hours. Tests on cell viability and proliferation, inflammation and oxidative metabolism were carried out. The data was analyzed using the Graph Pad Prism software, using 2-way ANOVA followed by the Tukey post-hoc test. Data were considered significant at $p < 0.05$. **Results**: Results demonstrate cellular pro-proliferation action of the QUE both in the macrophage scattering evaluation, as well as the MTT test and flow cytometry, when the treatment was performed in cells not activated for inflammation. The evaluation of the proinflammatory cytokines (IL-1, IL-6, TNF-α), both protein levels via immunoassay, and gene expression via qRT-PCR demonstrated a strong pro-inflammatory effect of QUE when treatment was performed in non-activated cells. In relation to IL-10, QUE induced a decrease in the levels of this anti-inflammatory cytokine. Moreover, nitric oxide, superoxide and reactive oxygen species levels were increased in non-activated macrophages treated with QUE. However, when macrophages were previously treated with PHA, inflammation was induced prior to contact with QUE, all results were reverted, demonstrating the anti-inflammatory effect of QUE. **Conclusion**: Thus, despite the methodological limitations of in vitro studies, we demonstrated a differential effect between non activated and activated macrophages, which could clarify the dual nature of this antipsychotic in the central nervous system and peripheral tissues. **Acknowledgement and Financial Support**: Capes/CNPq. **References:** EL – SAIFI, N; JONES, C; MOYLE, W. Australas J Ageing. v. 35. p. 281, 2016. GRABOWSKI, K. Acta Clin Belg. v. 73.p.162, 2018.

03.016 Effect of the environment on the re-exposure to ethanol in mice treated with ibogaine in the ethanol-induced conditioned place preference (CPP) paradigm. Santos AA, Henriques GM, Kisaki ND, Leite JPC, Machado EBO, Macêdo LEL, Marinho EAV, Lima AJO UESC

Introduction: Alcohol is one of the most widely used licit psychoactive substances in the world, and chronic exposure to lead to addiction and even death. Treatments for alcohol dependence are still limited, low adherence and high relapse rates. Evidence suggests that ibogaine (IBO), a psychoactive alkaloid derived from the plant Tabernanthe iboga, may have therapeutic effects on drug abuse. The aim of this study was to investigate the effect of the environment on the re-exposure to ethanol in mice treated with IBO in the ethanol-induced conditioned place preference (CPP) paradigm. **Methods:** Three groups (N=8) of adult Swiss male mice were conditioned with saline (Sal) (i.p.) in the non-drug-paired compartment and ethanol (1.8 g/kg, i.p.) or saline (SalSal, i.p.) in the drug-paired compartment for 8 alternating sessions. Starting on the day after a drug-free post-conditioning test and for 8 consecutive days, on even days animals were treated with vehicle (oral) or ibogaine (10 or 30 mg/kg, oral) or Sal (Sal-Sal, oral) and placed in the ethanol-paired compartment. On odd days, animals were treated with Sal and placed in the saline-paired compartment. On the day following a drug-free posttreatment test, all animals were treated with ethanol or Sal (Sal-Sal) and placed in the middle of the apparatus with free access to the compartments (ethanol re-exposure) and CPP was quantified. Twenty-four hours later, was performed a drug-free post-reexposure test (reinstatement test) and CPP was quantified. This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol #006/2017). **Results:** No significant differences were found in the preconditioning tests for the scores of spending time [$F(3, 28) = 0.1460$; $p=0.9314$]. All groups conditioned with ethanol expressed preference for the ethanol-paired compartment when compared to Sal-Sal group in postconditioning session, and there was a statistical difference between the groups [$F(3, 28) = 8.88$; $p=0.0005$]. No difference between the groups were found in the post-treatment test, suggesting extinction of the preference behaviour [$F(3, 28) = 1.105$; $p=0.3638$]. In the reexposure session there was a statistical difference between the groups [$F(3, 28) = 8.333$; $p=0.0004$], and the groups treated whit IBO 10 or 30 mg/kg did not present preference to the ethanol-paired compartment when compared to treated with vehicle. Post-re-exposure test data are still under analysis. [One-way ANOVA/Bonferroni post hoc – $p<0.05$]. **Conclusion:** Our results suggest that IBO blocked the reinstatement to rewarding effects of ethanol in animal models independent of the environment in which ethanol was administered, suggesting ibogaine as a promising drug in the treatment of dependence and relapse to ethanol independent of context.

03.017 Early and late behavioral and biochemical consequences of ethanol withdrawal: **focus on indoleamine 2,3 dioxygenase activity**. Santos LC[1], Ayres D[1], Pinto I, Silveira M[1], Dantas R[1], Albino M[1], Lima R[1], André E[2], Tirapelli C[3], Padovan C[3], Gavioli EC[1], Rachetti V[1] [1]UFRN, [2]UFPR, [3]USP

Introduction: Anxiety and depression are among the symptoms associated with ethanol withdrawal, these symptoms leading to the relapse of the individuals (APA, 2013). In the kynurenine pathway the enzyme indoleamine 2,3 dioxygenase (IDO) is responsible for the conversion of tryptophan to kynurenine and a dysregulation of this pathway has be associated with various psychiatric disorders, such as anxiety and depression (Strasser et al., 2017). The present study aimed to evaluate the early and late behavioral and biochemical effects of ethanol withdrawal in rats. **Methods:** Protocol was approved by Ethic Committee for Animal Use of Federal University of Rio Grande do Norte (protocol number 019/2010 and 045/2016). Male *Wistar* rats (60 days old) were submitted to increasing concentrations of ethanol (2% for 3 days, 4% for 3 days and 6% for 15 days) as the only source of liquid diet and the control group received water *ad libitum*. Both groups received food *ad libitum*. In the experiment 1, control animals received water during all period and withdrawn group was submitted to a battery of behavioral tests 3, 5, 10, 19 and 21 days after ethanol discontinuation. The following tests were used: elevated plus maze (EPM, at day 3), open field test (at days 5 and 19), rota-rod (at day 10) and forced swimming test (FST, at day 21). In the experiment 2, animals were submitted to the euthanasia for decapitation 3 days (short-term ethanol withdrawal) and 21 days after withdrawal (long-term ethanol withdrawal). The brains of all groups, including both control (water *ad libitum*) and continuous ethanol intake (2% for 3 days, 4% for 3 days and 6% for 15 days) groups, were dissected at the same day and posteriorly submitted to the analysis of the concentration of kynurenine - a product of the enzyme IDO activity - in the prefrontal cortex, hippocampus and striatum. **Results:** Student's *t*-test or ANOVA followed by Duncan's test showed: in the experiment 1, decreased entries ($t=2.60$, $p<0.05$,) and time ($t=2.69$, $p<0.05$) spent in the open arms of EPM in short-term ethanol withdrawal animals (day 3); no statistical differences in the open field test 5 ($t=0.41$, $p>0.05$) or 19 days after withdrawal ($t=-0.54$, $p>0.05$) and in the rota-rod test ($F=0.26$; $p>0.05$) 10 days after withdrawal. In the FST, long-term (21 days) ethanol withdrawn rats displayed higher immobility time than control animals ($t=-6.18$, $p<0.05$). In the experiment 2, kynurenine concentrations were increased in the prefrontal cortex after a long-term (21 days), but not short-term (3 days), period of withdrawal ($F=5.93$, $p<0.05$). **Conclusion:** Short-term ethanol withdrawal produced anxiety-like behavior by reducing exploration in open arms of EPM and long-term withdrawal induced depressive-like behavior by increasing immobility in the FST. Long-term ethanol withdrawal elevated kynurenine levels in the prefrontal cortex, suggesting that the depressive-like responses observed after long-term withdrawal might be related to the increased IDO activity. The activation of this tryptophan-kynurenine pathway has been associated with the pathophysiology of several inflammation-related neuropsychiatric diseases, including depression. **References:** American Psychiatry Association. Diagnostic and Statistical Manual of Mental disorders - DSM-5. 5th.ed. p.155. Washington: American Psychiatric Association, 2013. Strasser B, et al. Mechanisms of Inflammation-Associated Depression: Immune Influences on Tryptophan and Phenylalanine Metabolisms. Curr Top Behav Neurosci. 31:95. 2017.

03.018 Chronic treatment with venlafaxine in stressed mice up-regulates CB1 expression in the hippocampus but produces its behavioral effects in a CB1-independent manner. Araújo MR, Scarante FF, Scomparin DS, Guimarães FS, Campos AC FMRP-USP

Facilitation of monoaminergic neurotransmission is being accepted as the main mechanism of action behind antidepressant drugs (ADs). However, this mechanism does not seem to be enough to explain all the behavioral and neuroplastic effects evoked by chronic treatment with ADs. It has been demonstrated that an intact adult hippocampal neurogenesis is required for the response to Fluoxetine, a Selective Serotonin Reuptake Inhibitor (SSRI). On the other hand, ECS seems to act synergistically with the serotonergic neurotransmission to induce antidepressant-like effects in mice. Unpublished observations of our group suggest that CB1 and CB2 receptors participate of the antidepressant, but not the anxiolytic effects Escitalopram, a selective serotonin reuptake inhibitors (SSRIs). Venlafaxine (VFX) is noradrenaline-serotonin reuptake inhibitor (SNSRI), widely prescribed in clinical practice with pro-neurogenic effects. In the present work, we hypothesize that VFX exerts behavioral and pro-neurogenic effects through the modulation of ECS via CB1 activation. In order to test this, C57Bl / 6 mice (10-12 weeks) were exposed to an Chronic Unpredictable Stress (CUS) protocol and were treated daily with vehicle or different doses of VFX (10, 20 or 40mg/kg- intraperitoneal, i.p.). In a second experiment, CUS mice also received vehicle or VFX (20mg/kg), but this time, 1h before the treatment they were administered i.p. with vehicle or AM251 (CB1 receptor inverse agonist/ antagonist; 0.3mg/kg) for 21 days. Mice were submitted to the Novelty Suppressed Feeding and the Splash-test, to evaluate anxiolytic-like and antidepressant-like behaviors, respectively. Our results suggest that chronic treatment with VFX induces anxiolytic-like effects in stressed animals in a dose-dependent fashion (doses of 20 and 40mg/Kg being effective). Moreover, treatment with VFX positively modulate CB1 receptor expression in the hippocampus. However, unlike escitalopram, an SSRI, the behavioral effects of VFX seem to be independent of the CB1 activation, since the pre-treatment with AM251 was not able to block the VFX effects. Lastly, chronic treatment with AM251 was able to promote weight loss in stressed animals; however, mice treated with AM251 and VFX did not present weight loss. In conclusion, our results indicate that the behavioral effects evoked by VFX are independent of CB1 receptor activation. Ongoing experiments are testing if the proneurogenic actions of VFX are also independent of CB1 activation. CEUA nº001/2018. **Financial support** CAPES, FAPESP and Instituto L´Oreal.

03.019 Involvement of TRPA1 in a model of depression induced by corticosterone in mice. Santos BM, Pereira GCP, Bochi GV UFSM

Introduction: According to the World Health Organization, major depression disorder (MDD) affects more than 300 million people around the world. MDD is a mental illness characterized by depressive mood, sleep and appetite disorders and recurrent thoughts of suicide. Considering that the illness is related to the high suicide rate and a large part of the patients are refractory (30 - 50%) to any of the available antidepressant, it is of great importance to investigate the mechanisms involved in the pathophysiology of MDD. It was demonstrated that inflammatory and oxidative processes play an important role in its own development. It has been suggested that inflammatory and oxidative mediators contribute to neuroinflammation and suppress neurogenesis in the central nervous system. The transient receptor potential ankyrin 1 (TRPA1) is part of a broad family of non-selective ion channels and acts as a sensor for inflammatory mediators and oxidant compounds. Thus, the objective of this study was to investigate the involvement of the TRPA1 in the development of depressive-like behavior in a model of depression in mice. **Methods**:Use the animals was approved by Ethical Committee of Federal University of Santa Maria (nº7698200617). Male Swiss mice received corticosterone (20 mg/kg/10 mL s.c.) for 21 days to induce depression-like behavior. Vehicle group received saline containing 0.2% Tween 80 and 0.2% DMSO, s.c., for the same period. To evaluate the participation of TRPA1 in the depression-like behavior, the animals were treated with HC-030031 (100 mg/kg/10mL, v.o) or A-967079 (100 mg/kg/10mL, v.o), TRPA1 antagonists, 30 minutes before the behavioral tests. The positive control group were treatedwith Ketamine (10 mg/Kg/10 mL, v.o.). Open field test (OFT), tail suspension test (TST), splash test (ST) and forced swim test (FST) were performed to evaluate the depressive-like behavior. Results: The mice subjected to corticosterone administration showed higher immobility time on FST and TST when compared with vehicle group. The TRPA1 antagonists (HC-030031 and A-967079) reduced the immobility time of the mice on FST and TST after the chronic administration of corticosterone. Ketamine was also able to reduce the immobility time in the FST and TST. On the ST, the corticosterone group showed lower grooming behavior when compared to vehicle group and the administration of Ketamine improved this behavior. However, just HC-030031 was able to improve the grooming behavior. In the OFT, no locomotive alteration was observed between the groups, including in the animals treated with TRPA1 antagonists. **Conclusion:** These results demonstrated that chronic corticosterone administration induced depressive-like behavior and that both Ketamine and TRPA1 antagonists improved this condition. Therefore, it was suggested that TRPA1may be a potential target involved in the pathophysiology of the depression. This study received financial support from Capes and CNPq. **References**: ZHAO, Z., Front MolNeurosci, v. 10, p. 293, 2017. TREVISAN, G.,Free RadicBiol Med, v. 72, p. 200, 2014.

03.020 Pharmacological treatments for cocaine addiction needs a selective approach. Anesio A, Yokoyama TS, Zaniboni CR, Palombo P, Bertagna N, Cruz FC Unifesp

Introduction: Relapse is the major challenge in cocaine addiction treatment, and, in the last several decades, no effective pharmacological therapy could change it. Hence, a better understanding of the process that leads to relapse is fundamental. Exposure to environmental stimuli previously associated with drug use can induce cocaine relapse by an associative learning process [1-3]. Associative learning is encoded by a small specific pattern of activated neurons, now called neuronal ensembles [2]. Neuroplasticities are fundamental for associative learning; however, most of them, especially those related to drug addiction, are still unknown [2-3]. It was demonstrated that some of the addiction-related plasticities are modified during the abstinence period, and these modifications appear to be pivotal for the increase of the cue induced cocaine craving after prolonged abstinence. This phenomenon has been termed incubation of drug craving [1]. Our study aims to investigate molecular adaptations related to the incubation of cocaine craving in neuronal ensembles selectively activated by cocaine related cues. Further, we also aim to find an appropriate cocaine access protocol to model the incubation of cocaine craving in rats. **Methods**: Jugular vein of male Wistar rats was catheterized for cocaine self-administration. Rats were trained to self-administer cocaine 6h/day (extended access) or 1h/day (restricted access), for 12 days in a context-specific. All infusions were paired with cues. Then, we assessed relapse to cocaine-seeking under extinction conditions after 1 or 30 days of abstinence (Animal Research Ethical Committee number: 4183030918). Results: Extended access produced a higher cocaine intake normalized for the first hour of consumption and induced a more prominent escalation on cocaine consumption during the 12 days of training, mimicking the transition between occasional use to the abusive use. Only extend access rats presented incubation of cocaine craving behavior. After 1 or 30 days of abstinence, extended access rats exposed to drug context, compared with home cage group, presented a higher activation of nucleus acumbens core and shell neurons. Interestingly, the number of acumbens activated neurons following drug context exposure was not different between 1 and 30 days of abstinence. **Conclusion:** Our data indicate that extended access is a better protocol to induce incubation of cocaine craving when compared with restricted access. Besides that, our results suggest the selective involvement of nucleus accumbens neuronal ensembles on incubation of cocaine craving and not of a random population of neurons. Thus, relevant neuroplasticities for drug relapse and with therapeutical potential, should be sought in these group of neurons and not in random neuronal populations. Financial support: FAPESP 2018/15505-4 and 2018/14153-7, CAPES **References**: 1. WOLF, M. E. Nat. Rev. Neurosci., v. 17, p. 351, 2016; 2. CRUZ, F. C. Nat. Rev. Neurosci., v. 14, p. 743, 2013; 3. NESTLER, E. J. Nat. Rev. Neurosci., v. 2, p. 119, 2001; 4. PICKENS, C. L. Trends Neurosci, v. 34, p. 411, 2011.

03.021 Cannabidiol attenuates orofacial dyskinesia and cognitive impairment induced by haloperidol in mice via PPARγ receptors. Sonego AB, Prado DS, Guimarães FS FMRP-USP

Introduction: Tardive dyskinesia (TD) is a movement disorder that appears after chronic use of drugs that block dopaminergic receptors (1).Besides the motor symptoms, patients with TD also present cognitive deficits (2).Despite its pathophysiology being unknown, neuroinflammatory mechanisms could be involved in the development of this disorder (1). Cannabidiol (CBD), the major non-psychotomimetic compound of *Cannabis sativa* plant, exhibits antipsychotic and anti-inflammatory properties (3). Furthermore, our group demonstrated that it can attenuate catalepsy (4) and prevent orofacial dyskinesia induced by typical antipsychotics (5). In this study, we evaluate if CBD could reverse the orofacial dyskinesia and the cognitive impairment induced by haloperidol. Moreover, we investigate if CBD effects would depend on the activation of PPARγ receptors, a subtype of receptor that is involved in an anti-inflammatory pathway (6). **Methods:** Male Swiss mice received an injection of haloperidol (3mg/kg, ip) or vehicle during 21 days. In the last 7 days, they received an injection of CBD (60mg/kg, ip) or vehicle 30 min after the haloperidol injection. The frequency of vacuos chewing movements (VCM) was evaluated on day 0, 14 and 22 of treatment while the novel object recognition (NOR) test was realized on days 21 and 22. After the behavioral tests, striatum and hippocampus were dissected to measure cytokine levels (IL-1β and TNF-α) by ELISA. For evaluating the participation of PPARγ receptors in the behavioral effects of CBD, the same protocol was realized. However, the animals received an injection of GW9662 (2mg/kg, ip) or vehicle 30 min prior to CBD. **Results:** Haloperidol increased the VCM frequency on days 14 and 22 of treatment (Student-Newman-Keuls test, $p<0.05$). Furthermore, this drug decreased the discrimination index (Mann-Whitney test, $p<0.05$)in the NOR test, indicating an impairment of the long-term memory. CBD, in turn, attenuated the haloperidol-induced behavioral effects ($p<0.05$).Haloperidol increased IL-1βand TNF-αlevels in the striatum (Mann-Whitney test, $p<0.05$) and hippocampus (Student-Newman-Keuls, $p<0.05$) while CBD reverted these effects ($p<0.05$). The striatal and hippocampal levels of proinflammatory cytokines correlated with VCM frequency and discrimination index (Pearson correlation, $p<0.05$), respectively. The behavioral effects of CBD were blocked by the PPARγ antagonist GW9662 (Student-Newman-Keuls, $p<0.05$). **Conclusions:** CBD attenuated haloperidol-induced orofacial dyskinesia once it was established and improved non-motor symptoms associated with TD. These effects of CBD seem to depend on the activation of PPARγ receptors and its anti-inflammatory properties. **References:** 1. BISHNOI, M. Eur. J. Pharmacol., v. 590, p. 241, 2008. 2. KRABBENDAM, L. Schizophr. Res., v. 42, p. 41, 2000. 3. ZUARDI, A.W. Rev. Bras. Psiquiatr., v. 30, p. 271, 2008. 4. SONEGO, A.B. Behav. Brain Res., v. 309, p. 22, 2016. 5. SONEGO, A.B. Brain Behav. Immun., v. 74, p. 241, 2018. 6. ESPOSITO, G. PLoS One, v. 6, p. 1, 2011. **Financial Support:** CAPES, CNPq and FAPESP **Number process of ethical committee:** 090/2015

03.022 Cannabidiol and 7-nitroindazol reverse the behavioral changes induced by an animal model of PTSD. Lisboa SFDS[1], Vila-Verde C[2], Uliana DL[3], Resstel L[2], Guimarães FS[2] [1]FCFRP-USP, [2]FMRP-USP, [3]University of Pittsburgh

Introduction: Previous results from our laboratory showed that cannabidiol (CBD), a nonpsychotomimetic phytocannabinoid, can prevent the behavioral changes induced by single prolonged stress (SPS), a proposed model of PTSD. In addition, interference in the nitrergic system can also attenuate behavioral consequences related to PTSD in rodents. It is unknown, however, if CBD or nitrergic interventions can reverse the SPS-induced changes once they have been established. **Methods:** Male Wistar rats were exposed to SPS (consisting of consecutive exposure to restraint, forced swimming, and ether anesthesia). Fear sensitization and impaired extinction of conditioned fear were evaluated one week later. In an additional protocol, SPS consequences were evaluated in the forced swimming test (FST) 7 days later. Two-h after SPS or the FST, the animals received acute [vehicle (V), 7-nitroindazol (7-NI, a nNOS inhibitor, 30mg/kg), CBD (30mg/kg, i.p)] or repeated (V, CBD (5mg/kg i.p.) daily for 7 days). Twenty-four-h after the last drug injection, the rats were submitted to the contextual conditioning fear procedure. Fear sensitization and extinction were assessed in two distinct sessions in the next 48 h. The brain levels of phosphorylated neuronal nitric oxide synthase enzyme (pnNOS) were measured at different time points after SPS stress. **Results:** The SPS induced fear sensitization (increased freezing in the first context re-exposure), impaired fear extinction, and increased immobility time in the FST. Increased pnNOS levels were observed 1-h after SPS in the ventral hippocampus, and nine days after SPS, in the prelimbic cortex. Acute 7-NI or repeated CBD treatment prevented and reversed the behavioral effect of SPS. **Conclusion:** These results suggest that CBD or nitrergic interventions could be useful in the treatment of stress associated disorders such as PTSD. **Animal Research Ethical Committee Process number:** 152/2014 **References:** Campos Behav Brain Res. 256, 391, 2013. Vila-Verde Neurosci. 21, 30, 2016. Yamamoto Depress Anxiety, 26, 1110, 2009.

03.023 Antidepressant-like effect of beta-caryophyllene in mice. Almeida FRC, Oliveira GLSO, Lopes EM, Reis Filho AC UFPI

Introduction: *β*-caryophyllene (beta-CP) is a volatile hydrocarbon with an unusual structure, which has a trans-fused cyclobutene ring with a nine-membered ring. It has an important role in the chemistry of sesquiterpenoids and is among the major sesquiterpenes found in varying amounts in plant foods such as pepper (*Piper nigrum* L.*),* clove (*Eugenia caryophyllata* Thunb.), cinnamon (*Cinnamomum spp.*) and oregano (*Origanum vulgare* L.). Beta-CP is a food additive that exhibits various pharmacological activities in vivo, such as neuroprotective and antinociceptive. However, there is a need to clarify the molecular mechanisms involved in the central effects of beta-CP. Thus, the aim of the present study was to evaluate the antidepressive-like potential of beta-CP using the open field test, tail suspension test, forced swimming and splash test. **Methods:** Female *Swiss* mice (25-30 g) were obtained from the Central Bioterium of the Agricultural Sciences Center of the Federal University of Piauí (UFPI). The maximum effort was made to minimize both the suffering and the number of animals used, and each experiment was approved by the Ethics Committee on the Use of Animals (CEUA/UFPI: 012/15) and carried out according to the ethical principles established by the Brazilian Directive on the Care and Use of Animals in Teaching or Scientific Research Activities. Beta-CP was emulsified in 0.05% Tween 80 dissolved in 0.9% saline solution (vehicle) and given orally only once at the doses of 100, 200 and 400 mg/kg for detailed evaluation of the behavioral tests (open field, tail suspension, forced swimming and splash test). **Results:** When compared to the control in the tail suspension test, beta-CP at doses of 100, 200 and 400 mg/kg reduced the immobility time by 8.15, 48.15 and 54.74 %, respectively ($p<0.05$). In the forced swimming test, beta-CP at doses of 100, 200 and 400 mg/kg reduced the immobility time by 7.57, 50.52 and 59.94 %, respectively ($p<0.05$). Similarly, Imipramine in the tail suspension and forced swimming test significantly reduced the immobility time by 65.27 and 71.1 %, respectively ($p<0.05$). Additionally, as observed in the behavioral effect after 10% sucrose spraying, groups of animals treated with beta-CP (200 and 400 mg/kg) and imipramine showed a significant increase in total time and frequency of grooming when compared to control group ($p<0.05$). In the results described, two-way ANOVA analysis showed that pre-treatment with bicuculline, ketanserin or ondansetron did not antagonize the immobility reduction results evidenced by beta-CP (200 mg/kg) in the tail suspension test and forced swimming test. **Conclusion:** The beta-CP antidepressive-like effect evidenced did not involve the $GABA_A$, 5-HT2 and 5-HT3 receptors. This study has contributed to understand the neuropharmacological actions of this monoterpene. Financial Support: CAPES, UFPI.

03.024 Investigation of the rewarding effects of ibogaine and alcohol on a mouse conditioned place preference model. Kisaki ND, Henriques GM, Rodrigues IRS, Santana MCE, Coimbra JPSA, Moreira Júnior ECM, Marinho EAV, Berro LF UESC

Introduction: Accumulating evidence suggests that ibogaine (IBO), a psychoactive alkaloid derived from the plant *Tabernanthe iboga* and used in rituals in West Central Africa, may have therapeutic effects on drug abuse (CORKERY, J. Prog Brain Res. 242. p. 217. 2018). However, it remained unknown whether ibogaine has rewarding effects *per se*, and whether its rewarding effects would be comparable to those of other drugs of abuse. Therefore, the aim of the present study was to evaluate the rewarding effects of ibogaine and compare them to the rewarding effects of alcohol using the conditioned place preference (CPP) model. **Methods:** Following a pre-conditioning test, adult Swiss male mice (n=8 per group) were conditioned with saline (i.p.) in the non-drug-paired compartment, and IBO (3, 10, 30 or 100 mg/kg, oral) or ethanol (1.8 g/kg, i.p.) in the drug-paired compartment during 8 sessions. On the day following the last conditioning session, animals were given free access to the CPP apparatus during a drug-free post-conditioning test. This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol #006/2017). **Results:** Ethanol induced CPP in mice, shown by a significantly longer time spent in the ethanol-paired compartment compared to the saline-paired compartment ($p=0.002$). IBO, on the other hand, did not induce CPP at any of the doses tested under our experimental conditions ($p=0.9502$, $p=0.9987$, $p>0.9999$, and $p=0.0686$, respectively for the doses 3, 10, 30 and 100 mg/kg). **Conclusion:** IBO did not induce rewarding effects on its own, contrary to what was observed for the drug of abuse alcohol. Further research is needed into the effects of IBO for the treatment of substance use disorders, as this compound might have therapeutic utility without exerting abuse potential. **Financial support:** CNPq, Uesc, CAPES e FAPESB.

03.025 Curve doses of ethanol administered orally in the conditioned place preference induction in male and female mice. Lins JF[1], Santos TB[1], Silva KSO[1], Santos ML[1], Leite JPC[1], Santana MCE[1], Rocha VN[1], Tamura EK[1], Lima AJO[1], Uetanabaro APT[1], Nicoli JR[2], Marinho EAV [1]UESC, [2]UFMG

Ethanol dependence has become a public health problem and it is necessary to develop therapeutic approaches that allow the recovery of patients and their reallocation in society (CISA, 2019). Thus, studies aimed at elucidating questions not yet answered are of great value in this field of research. Linked to this perspective, the present study sought to identify dose(s) of ethanol capable of promoting oral CPP in male and female Swiss mice. For this, 6 groups of animals male and female groups (N=8) received per gavage 0.5; 1; 1.5; 2; 2.5 or 3g/kg doses of Ethanol and were submitted to a CPP protocol. All animals were pre-conditioned (1 day), conditioned with saline in the non-drug compartment (even days) and with ethanol in the drug compartment (odd days) for 8 days. In the next day, the animals were submitted to the post-conditioning test: in absence of the drug, they had free access to the compartments previously conditioned to the drug or saline. The tests were analyzed using Anymaze® software. This study was approved by CEUA of UESC (protocol #006/2017). Regarding the analysis for the compartment time of permanence in the post-test, the two way indicated interaction between the factors gender and treatment [$F(5.84)=3.34$; $p=0.008$]. The Bonferroni test indicates that up to the 2g/kg dose the male and female animals respond in a similar way, increasing the residence time with increasing dose. However, at doses of 2.5 and 3 females continue to increase the time spent in the drug compartment significantly when compared to male animals at the same dose. The two way did not identify genders treatment interaction for the parameter number of entries in the compartments [$F(5.84)=0.99$; $p=0.4$] in the post test, but when analyzed individually, there is an effect of the gender [$F(1,84)=11,00$; $p=0.001$].Regarding the factor distance traveled in the compartments, in the post test, the two way indicated genders treatment interaction [$F(5,84)=2,7$; $p=0.02$]. The female animals present a hyperlocomotor effect in the drug compartment (doses of 2.5 and 3) suggesting a possible behavioral sensitization effect and the Bonferroni test indicates that in these doses the female animals respond more intensely than the males ($p<0,05$). In males, regardless of the dose, the locomotion in the drug compartment is not different from the saline compartment. In females the higher the dose, the greater the locomotion in the compartment drug. Finally, our results indicate the presence of CPP at doses of 1; 1.5 and 2g/kg ethanol in males and 1; 1.5; 2; 2.5 and 3g/kg of ethanol in females ($p<0.05$). Taken together, our data provide important information about the relationship between the effects of ethanol under the genders. In addition, our study makes possible the standardization of a paradigm that mimics the route of administration by which humans consume ethanol and which is widely used in the investigation of the positive reinforcing effects of ethanol. **Keywords:** Conditioned Place Preference; oral intake; Ethanol; Swiss Mice. **Financial support:** FAPESB, CAPES, CNPQ. **Reference:** CISA – Centro de Informações sobre Álcool e Drogas. CISA. p. 10. 2019.

03.026 Ayahuasca blocks the expression of methylphenidate-induced conditioned place preference in mice: **Behavioral and Fos protein expression evaluations**. Serra YA[1], Reis HS[1], Santos AA[1], Henriques GM[1], Rodrigues IRS[1], Lima AJO[1], Yokoyama TS[2], Cruz FC[2], Berro LF, Marinho EAV [1]UESC. [2]Unifesp

Introduction: Psychostimulant addiction is a chronic brain disease that affects reward, motivation and memory. The abusive and non-prescribed use of Methylphenidate (Mph) has increased significantly in recent decades. Moreover, pharmacological studies have demonstrated that Ayahuasca (Aya) can inhibit the development of drug-induced behavioral sensitization and conditioned place preference (CPP) in rodents. The aim of the present study was to evaluate the potential of Aya as a treatment for Mph abuse, analyzing the expression of Fos before and after the treatment and reexposure in specific structures of the brain that are involved in drug seeking behaviors. **Methods:** Thirty-two mice were submitted to the pre-conditioning test, Mph (10 mg/Kg, i.p.) conditioning and post-conditioning test. After the post-conditioning test, the treatment phase began. Animals received Vehicle (Veh) (v.o., n=16) or Aya (100 mg/Kg, v.o., n=16) and were confined to the compartment previously paired with Mph. This phase was followed by the drug free post-treatment test, after which half of the animals in each group was submitted to the Fos protocol. On the following day, animals were submitted to Mph reexposure and the drugfree post-reexposure test. Fos protein expression was quantified after the posttreatment and reexposure tests. Ninety minutes after each behavioral test, the animals were anesthetized and perfused. Their brains were removed and subsequently submitted to immunohistochemistry procedures to quantify Fos expression in medial prefrontal cortex: anterior cingulate (Cg1), prelimbic (PrL), infralimbic (IL) and orbitofrontal (OFC) areas; nucleus accumbens (NAc) both core and shell areas; and basolateral amygdala (BLA). This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol #11/2016). **Results:** Animals displayed a significant increase in CPP score during the postconditioning test compared to the pre-conditioning test [$t(27) = 4.824$; $p < 0.0001$]. There were no significant differences between treatment conditions (Veh *vs* Aya) during post-treatment test. During the post-reexposure test only the group treated with Veh showed a higher CPP score compared to the pre-conditioning. Aya treatment restored Fos protein expression back to baseline levels, even after Mph reexposure on the brain regions Cg1 [$F(3, 20) = 6.477$; $p = 0.0031$], PrL [$F(3, 20) = 37.15$; $p < 0.0001$] and IL [$F(3, 20) = 5.205$; $p = 0.0081$]. The treatment with Aya prevented the increase in Fos protein expression observed in the NAc Core [$F(3, 20) = 12.67$; $p < 0.0001$] and in the NAc Shell [$F(3, 20) = 8.521$; $p = 0.0008$] following Mph reexposure and significantly decreased Fos protein expression in the BLA [$F(3, 20) = 13.31$; $p < 0.0001$]. **Conclusion:** Together, the above-discussed considerations demonstrate that treatment with Aya in the compartment previously paired with Mph blocks the reinstatement of Mph-induced CPP following a Mph reexposure. Those behavioral effects were accompanied by changes in Fos protein expression patterns. Moreover, the therapeutics effects of Aya may be involved with the activation of the cortical structures related with seeking behavior and inhibitory control and shift in the rewarding effect of the environment previously paired with Mph. Nevertheless, others studies are needed to elucidate the specific mechanism of action of this psychostimulant on substance abuse. **Financial Support:** FAPESB, CAPES and CNPq.

03.027 Effects of repeated methylphenidate treatment in mice´s childhood on place preference conditioning in their adult life. Leite JPC, Campos DO, Dias Júnior BC, Silva AA, Brito ACL, Pereira JLA, Marinho EAV, Lima AJO UESC

Effects of repeated methylphenidate treatment in mice´s childhood on place preference conditioning in their adult life. Methylphenidate (MET) is a stimulant that blocks the reuptake of Dopamine (DA) and noradrenaline (NA) in areas of the central nervous system and activates mainly the prefrontal cortex, limbic regions and the striatum, thus presenting mechanisms of action similar to amphetamines and with potential for significant behavioral changes after use. The escalation in consumption has been credited, in part, to the increased diagnosis of people with Attention Deficit Hyperactivity Disorder (ADHD) and their use as a performance improvement, slimming and recreational. Some of the concerns in the use of methylphenidate are related to its inappropriate use and the development of side effects to the chronic use of this drug after exposure during childhood.In this context, an important question to be answered is: should MET exposure in childhood be able to favor compulsive behaviors in adulthood? Conditional Preference Protocol consists of a non-operative procedure to evaluate the reinforcing effectiveness of drugs of abuse using Pavlovian conditioning and was used to assess this issue. Considering all above, this work aimed to verify the effects of chronic treatment of MET during mice`s childhood on expression of place preference at their adult life.For this purpose, 22 Swiss females mice with 30 days of life were used. They were housed in groups of 5 or 6 with light and dark cycle of 12 hours, water and food *ad libidum*. The animals received an intraperitoneal injection (i.p.) of MET (10 mg / kg; N=11)or vehicle (VEH; N=11) and set back to their house cage from 30th to the 39th day of life. They remained without any intervention until their 69th day of life. After this period (Day 70) they were submitted to a Place Preference Conditioning (Place) short protocol. Instand of regular 4 drug/ 4vehicle conditioning sessions, they were submitted only to 2 drug/ 2 vehicle conditioning sessions, in order to evaluate how pre-treatment influenced on Place Preference acquisition. This study was approved by the Institutional Animal Care and Use Committee of UESC (protocol 009/2017). The difference of time spent at drug and vehicle compartments (Time Score) and total locomotion were analyzed at Pre and Post Conditioning Tests. A Two-way ANOVA analysis of Time Score revealed an interaction between Conditioning Sessions and Early Intervention [$F(1, 14) = 4.937$; $p = 0.0433$] and Bonferroni´s test revealed that MET Early Intervention Group was the only one that showed significative difference at Post Conditioning Test (*$p = 0.0301$). Same interaction appeared at a Two-way ANOVA analysis of total locomotion [$F(1, 7) = 21.44$; $p = 0.0024$] and Bonferroni´s test revealed that MET Early Intervention Group at Post Conditioning Test had a higher locomotion when compared to itself at Pre Conditioning Test (*$p = 0.0248$) and to Veh Early Intervention Group at Post Conditioning Test (#$p = 0.0226$).Our results suggest that the repeated treatment with methylphenidate during childhood favorsthe installation of CCP to methylphenidate. Thanks to FAPESB, CNPq and CAPES.