02. Neuropharmacology

02.001 Long and short-term effects of WIN55,212-2 and nicotine exposure during adolescence in mice. Gonçalves PFR, Nunes LED, Andrade BDS, Frederico N, Borges G, Castro NG, Neves GA UFRJ

Introduction: Adolescence is a neurodevelopmental critical period especially vulnerable to the influence of environmental factors and susceptible to the onset of neuropsychiatric disorders such as schizophrenia. Among the environmental factors particularly associated to the pathogenesis of this disorder is the abusive use of psychoactive drugs. In this context, the prevalence of schizophrenic patients who use cannabis and tobacco is high. The abuse of these drugs is a comorbidity found not only in individuals already diagnosed with schizophrenia, but also in patients in first psychotic episode or even in the prodromal phase. The importance of endocannabinoid and cholinergic systems in the development of psychiatric disorders is well established, as is the modulation of these systems by cannabis and tobacco, but little is known about the interaction between these two drugs. Thus, we aimed to investigate the short and long-term consequences of a repeated exposure to a synthetic cannabinoid, nicotine or to the combination of both drugs during adolescence in mice. **Methods:** Male Swiss mice (ICB/UFRJ breeding colony) were exposed to WIN 55,212-2 (WIN) 2 mg/kg/daily i.p., nicotine (NIC) 3 mg/kg/daily s.c. or both (NIC+WIN) from post-natal day (PND) 28 to 47. Changes in locomotor activity, core temperature and weight gain were evaluated during drug exposition. Animals' behavior was assessed in two moments after drug discontinuation: 24 h (short-term) and after PND 70 (long-term). Spontaneous alternations, open field, novel object recognition (NOR), social approach, social recognition and prepulse inhibition (PPI) tasks were used. **Results:** After first drug administration, WIN, NIC and the drug combination (NIC+WIN) reduced mice core temperature. A small but significant reduction in the hypothermic effect was observed after 10 and 20 days of exposure, showing a mild development of tolerance. NIC administration induced a hyperlocomotor effect during the first 2 minutes in the open field, followed by a marked hipolocomotion in the last 4 minutes of test. On the other side, WIN-exposed mice showed a sustained hyperlocomotion that take place 4 minutes after injection. Mice co-exposed to WIN+NIC showed a locomotor profile similar to that observed after NIC injection, showing a possible interference of NIC in WIN-induced hyperlocomotion. No tolerance was observed to drugs effects on locomotion. There was no difference on weight gain between groups throughout the exposure period. Exposure to WIN, NIC or to drug combination did not impair spontaneous alternations nor PPI response regardless of the drug discontinuation interval. Open field, NOR, social approach and social recognition data are under analysis. **Conclusion:** Results show that a repeated exposure to WIN, nicotine or the combination of both during adolescence affect mice core temperature and locomotion during exposure. By now, no persistent short and long-term effects in working memory or in the sensorimotor gating were observed. **Financial support:** CAPES, CNPq, FAPERJ and ISN.

02.002 Antioxidant and neuroprotective effects of Plumieride in the Hippocampus and Prefrontal Cortex of mice chronically exposed to corticosterone. Dalmagro AP[1], Camargo A[2], Zeni ALB[2], Silva RML[1], Malheiros A[1], Souza MM[1] [1]Univali, [2]Furb
Introduction: Some studies have investigated the pharmacological potential of iridoids as anti-inflammatory, antioxidants, and antidepressants agents. Significant events have been reported as typical in the pathophysiology of depression, such as oxidative damage, and glutamatergic excitotoxicity.Therefore, this research aimed to investigate the antidepressant-like, antioxidant and neuroprotective effects of plumieride – an iridoid, in the hippocampus and prefrontal cortex of mice submitted to a chronic model of stress induced by corticosterone. **Methods:** Male *Swiss* mice (30-40 g., n=8-10) were orally treated for 21 days with (1) Vehicle, (2) Plumieride 2 µg/kg - PLU, (3) Fluoxetine 20 mg/kg - FLU, (4) Corticosterone 20 mg/kg - CORT, (5) CORT+PLU and (6) CORT+FLU. Twenty-four hours after the last gavage, mice were submitted to the Tail Suspension Test (TST) and Open-Field Test (OFT); then, they were euthanized and the hippocampus and prefrontal cortex quickly removed. These structures were evaluated for lipid peroxidation (TBA-RS), nitrite level, carbonylated protein (PC) and non-protein thiol group (NPSH). Moreover, the cell viability in hippocampal and cortical slices was also evaluated through the MTT reduction assay. Data were analyzed statistically through two-way ANOVA, followed by the Tukey's test. Results were considered significant with $p < 0.05$. **Results:** The chronic administration of PLU and FLU were capable of reversing the increase of immobility time triggered by CORT ($p<0.001$) in the TST and these treatments did not alter the locomotor capacity of the animals ($p>0.05$) in the OFT. Also, CORT exposure increased the TBA-RS ($p<0.0001$), nitrite ($p<0.01$), carbonylated protein ($p<0.0001$) and decreased NPSH ($p<0.05$) in the hippocampus; and the iridoid was able to restore these damages ($p>0.05$). FLU only decreased the PC content ($p<0.001$) and augmented NPSH level ($p<0.001$). Corticosterone also decreased hippocampal viability ($p<0.0001$) and increased the susceptibility of glutamatergic excitotoxicityin hippocampal slices ($p<0.01$); however, these effects were reversed by PLU. Regarding the prefrontal cortex, CORT triggered the elevation of TBA-RS ($p<0.0001$) and PC ($p<0.0001$), besides decreasing NPSH ($p<0.0001$). In this structure, both plumieride and fluoxetine were capable of restoring the oxidative damages ($p<0.05$). Contrary to the hippocampus, CORT did not decrease cell viability in the cortical slices ($p>0.05$) but increased their susceptibility to glutamate ($p<0.01$). PLU promoted neuroprotection *per se* in the cortical slices ($p<0.001$) and against glutamatergic excitotoxicity ($p<0.001$). **Conclusion:** Chronic administration of PLU was able to restore the harmful effects evoked by CORT exposure, that include behavioral alterations, oxidative damages in the hippocampus and prefrontal cortex of mice, besides the decrease of cell viability in hippocampal slices. Further investigations have been conducted by our research group to study the mechanismsinvolved in the antidepressant-like, antioxidant, and neuroprotective effects of plumieride. **Financial Support:** UNIVALI, FURB, CAPES. **CEUA Protocol Number:** FURB010/2018.

02.003 Cannabidiol attenuates the conditioned place aversion induced by naloxone-precipitated morphine withdrawal in mice. Souza AJ, Morais B, Gomes FV, Guimarães FS FMRP-USP

Introduction: The misuse of and addiction to opioids, such as morphine, have become a serious public health problem in some countries, such as the USA. In general, addiction, including opioid addiction, is a chronic and relapsing medical condition that involves motivational and memory-related processes due to the strong associations between drugs and abuse-related stimuli. These stimuli usually trigger continuous and compulsive use and contribute to relapses after periods of withdrawal. Several factors contribute to relapse, including withdrawal-induced affective changes, such as a susceptibility to stress and increased anxiety. Thus, drugs that attenuate affective alterations induced by withdrawal could be useful alternative treatments for preventing relapse. Cannabidiol (CBD), a non-psychotomimetic component present in the *Cannabis sativa* plant, has anti-anxiety and anti-stress properties and can be seen as an alternative for the treatment of mental disorders, including drug addiction. In this study, we evaluated if CBD would attenuate aversion induced by morphine withdrawal precipitated by the opioid receptor antagonist naloxone. **Methods:** Negative state associated with naloxone-precipitated morphine withdrawal was examined by using conditioned place aversion (CPA) paradigm. Male C57BL/6 (20-25g) mice were placed individually in a CPA box to freely explore all 3 compartments (pre-test). On the next day, animals started receiving increasing doses of morphine (30, 50, and 70 mg/kg; i.p.) or saline (control) for 3 days. To precipitate morphine withdrawal, animals received an i.p. injection of naloxone (1.5 mg/kg) and were then kept confined in one side of the conditioned place aversion (CPA) for 18 min. Twenty four hours later, animals were treated with CBD (15, 30, or 60 mg/kg) or vehicle (2% Tween 80 in saline) 30 min before the re-exposure to the CPA box (test). The time that animals spent exploring all CPA compartments during the pre-test and test were recorded and used to evaluate the effects of CBD on aversion induced by naloxone-precipitated morphine withdrawal. Results: In the test, as expected, morphine-treated animals spent less time exploring the compartment paired with the naloxone-induced withdrawal compared to the other compartment, indicating a CPA induced by naloxone-precipitated morphine withdrawal. This was not observed in animals treated with CBD at 30 and 60 mg/kg, indicating that CBD attenuated the CPA induced by naloxone-precipitated morphine withdrawal. Conclusion: Our findings suggest that CBD may be able to reduce the aversion induced by morphine withdrawal. Therefore, CBD may be a therapeutic alternative for the treatment of opioid addiction by decreasing withdrawal/abstinence-induced negative affective changes and, therefore, helping to prevent possible relapse. We are now investigating the possible mechanisms of action in which CBD produces its effects. **Financial support**: IBRO and FAEPA. Ethical committee: CEUA/FMRP 100/2019.

02.004 TRPV1 receptor antagonism induced a neuroprotective effect and rescued episodic and aversive memories in an animal model of Alzheimer's Disease. Silva EMF, Lagatta DC, Domingos LBD, Assis AB, Veras FP, Resstel L FMRP-USP

Introduction: The neurotoxic process of Alzheimer's disease (AD) is caused by the deposition of beta-amyloid protein around neurons of central nervous system areas such as the medial prefrontal cortex (MPFC) and hippocampus (Hpc). This protein accumulation leads to glutamatergic excitotoxicity, which in turn induces an exaggerated increase in the intracellular concentrations of calcium. Calcium, in these conditions, is related to the activation of neurotoxic pathways that culminate in cell death. Calcium can permeate the cell through other receptors such as TRPV1 channels in order to activate such pathways. It has been demonstrated in *in vitro* studies that these receptors contribute to increased expression of inflammatory and oxidant markers induced by application of beta-amyloid protein in cortical astrocyte culture. Such data suggest that these receptors may contribute to the neurotoxic process during disease development. However, the effect of a TRPV1 antagonist in an animal model of Alzheimer's disease has not yet been verified. Therefore, the hypothesis of the present project is that the TRPV1 receptors present in MPFCand Hpc can exert a neurotoxic effect and impair synaptic plasticity processes during the evolution of the disease. **Methods**: To induce AD-like pathological and cognitive impairments, C57 mice at 7 weeks of age were microinjected with $A\beta_{1-42}$ (i.c.v.) after stereotaxic surgery. Subsequently, 24 hours after $A\beta_{1-42}$ microinjection the animals underwent a 14 days repeated treatment with a TRPV1 receptor antagonist, SB366791 or vehicle (0.15mg / kg, i.p). Then, 24 hours after the end of the treatment, they were submitted to the object recognition test and to sound or contextual fear conditioning models. After the behavioral tests, MPFC and Hpc were dissected for molecular analysis. The experimental procedures were carried out following protocols approved by the Ethical Review Committee of the School of Medicine of Ribeirão Preto 034/2018. **Results:** Treatment with SB366791 significantly prevented short-term ($F_{(3,27)}$ = 12,86; $p<0.05$) and long-term memory impairment ($F_{(3,28)}$ = 9,67; $p<0.05$) in the object recognition test. Similarly, in the context- or sound-conditioned fear test, repeated treatment with SB366791 was able to preclude $A\beta_{1-42}$ induced damage of aversive memory consolidation($F_{(3,27)}$ = 10,47; $p<0.05$; $F_{(3,26)}$= 9,095; $p<0.05$). However, in the sound-conditioned fear test, animals with $A\beta_{1-42}$ presented a greater expression of conditioned fear when compared to the control group ($F_{(3,26)}$ = 4,263; $p<0.05$). In addition, in this model the animals showed an increase in the proinflammatory cytokines IL-1β and TNFα both in cortex ($F_{(3,19)}$ = 4,882; $p<0.05$; $F_{(3,\ 22)}$ = 7,968; $p<0.05$) and in hippocampus ($F_{(3,23)}$ = 5,217; $p<0.05$; $F_{(3,23)}$ = 3,312; $p<0.05$)which has also been prevented by repeated TRPV1 receptor antagonism. **Conclusion:** Our findings suggest that TRPV1 receptor antagonism has a neuroprotective effect by decreasing cognitive deficit in the $A\beta_{1-42}$-induced AD model. In addition, it decreased proinflammatory cytokines IL-1β and TNFα in MPFC and Hpc. Thus, the pharmacological manipulation of TRPV1 receptors could offer a new approach for the treatment of AD. **Financial support:** CAPES, CNPq, FAPESP

02.005 Pharmacological validation of a new animal model of depression in mice: **A single subconvulsant dose of pilocarpine**. Souza FMA[1], Neto JGS[1], Vieira MPS[1], Barros O[1], Souza GF[1], Correia WBZGB[1], Duarte FS[2], Lima TCM[3], Duzzioni M[1] [1]UFAL, [2]UFPE, [3]UFSC

Introduction: Our research group showed that a single subconvulsant dose of pilocarpine (PILO) triggered short- and long-term anxiogenic-like and depressive-like behavior in mice, suggesting a new experimental model for studying anxiety and depression. In this study, we validate that new proposed model of depression with the administration of psychoactive drugs, as well as we measured the serum corticosterone (CORT) levels. Methods**:** Female Swiss mice were treated with scopolamine methylbromide (1 mg/Kg, s.c.) followed 30 min later with saline (SAL, NaCl 0.9%, i.p.) or PILO (75 mg/Kg, i.p.). After 24 h, animals were treated with SAL (i.p), diazepam (DZP; 1.5 mg/Kg, i.p) or fluoxetine (FLU; 10 mg/Kg, i.p). Another group was treated daily for 30 days with the same drugs and doses. And, in both groups, 30 min after the last treatment the animals were submitted to the forced swim (FST) and open field (OFT) tests. Animals were euthanized and the blood was collected for CORT analysis. **Results:** After 24 h or 30 days, animals treated with PILO+SAL increased immobility time in FST, indicating a depressive-like behavior ($F_{3,25}$=10.16; P<0.05; $F_{3,28}$=18.64; P<0.05). Acute or chronic treatment with DZP (PILO+DZP) did not alter the depressive-like behavior induced of the PILO. On the other hand, chronic treatment with FLU (PILO+FLU) prevented PILO-induced depressive-like behavior ($F_{3,28}$=1.04; P<0.05). No changes were found in the OFT. In addition, PILO+SAL group increased CORT levels ($F_{3,3}$=2.26; P<0,05) after 24 h. **Conclusions:** Our data provide pharmacological validation showing that standard antidepressant drug prevented PILO-induced depressive-like behavior. In addition, this model can be used to identify new compounds with antidepressant properties.

02.006 Neuroplasticity of the endocannabinoid system is associated with CBD anticonvulsant effects along a chronic protocol of epileptic seizures. Lopes WL, Silva Júnior RMP, Silva RAVS, Leite JPL, Cairasco NG USP

Cannabidiol (CBD) is a compound present in *Cannabis* and has been implicated in the treatment of many neurological and neuropsychiatric diseases, such as epilepsies. However, little is known about the endocannabinoid system and its interaction with CBD mechanisms of action associated with neuropathological alteration, especially in chronic protocols of epilepsies. The Wistar Audiogenic Rat (WAR) is a rodent strain capable of developing epileptic seizures in response to intense sound stimulation (audiogenic seizures, AS). Along the chronic protocol of AS (audiogenic kindling, AuK) the initially brainstem-dependent seizures give rise to forebrain-dependent seizures through a process called limbic recruitment. Therefore, the aim of this study was to evaluate the effects of chronic CBD treatment over the endocannabinoid system and its relationship with the potential anticonvulsant and a tiepileptogenic CBD effects in a chronic protocol of epileptic seizures. WARs and Wistars (n=9-11/group; CEUA: 057/2017) were submitted to the AuK (20 acoustic stimuli, twice a day). Animals were placed in an acrylic box and sound (120 dB) was applied for 1 minute, or until the development of tonic seizures. Seizure behaviour was analyzed during 3 minutes (1 before, 1 during, and 1 after) in each stimulus. CBD treatment (25 mg/kg; i.p.) or vehicle were initiated 24 h before the first stimulus and were maintained along the whole protocol (1 h before each stimulus). At the end of the AuK protocol, CB1 receptors expression were measured in limbic brain structures by immunostaining. Chronic CBD treatment attenuated brainstem seizures ($p<0,05$) and prevented the development of limbic seizures ($p<0,05$)in WARs. Wistars did not present seizures, confirming the specific effect of the acoustic stimulation in WARs. By immunostaining protocol, WARs present a significant increase in the CB1 receptor expression in limbic structures (hippocampus, cortex and amygdala), compared to Wistar. Moreover, the AuK increases CB1 expression in WARs ($p<0,05$).CBD chronic treatment reduces CB1 expression in non-stimulated WARs, while the CB1 increased expression induced by AuK was attenuated by chronic CBD treatment ($p<0,05$). Curiously, in Wistars, chronic CBD treatment induced an increase in CB1 expression ($p<0,05$).Our results showed that CBD attenuated brainstem seizures and prevented limbic recruitment along the AuK, indicating an anticonvulsant activity and suggesting antiepileptogenic effects. CBD protective effects may be related with a decrease in hippocampal CB1 immunostaining in WARs, suggesting CBD anticonvulsant effects associated with neuroplasticity of the endocannabinoid system. Acknowledgements: INCT-Translational Medicine, FAPESP, CAPES, CNPq, FAEPA.

02.007 Neuroinflammatory response in NA, **K-ATPase activity in allergic lung inflammation**: **putative involvement of female sex hormones**. Lima GM, Umaña ER, Ribeiro MR, Leite JA, Lima WT, Scavone C ICB-USP

Introduction: Asthma is a chronic inflammatory disease characterized by airflow obstruction and subsequently limitation of the lung capacity. Obesity, for instance, represents a important public health issue and it's associated with changes in the immune system response, which might be a worsening factor for asthmatic patients, especially during post-menopause. Na,K-ATPase is a membrane protein and its activityisimpairedduringobesityandothermetabolic-relateddisorders. However, studies lack in data referring to the effects of ovary removal surgery on Na-K-ATPase activity in the central nervous system. We aimed to evaluate the involvement of female sexual hormones on the neuroinflammatory response in Na,K-ATPase in the cerebellum of mice with allergic lung inflammation. **Methods:** Female Balb/c mice were given high fat diet for 10 weeks to induce obesity. After obesity induction, mice were sensitized by i.p. injection of OVA and challenged 3 weeks later (OVA, 10 µg, i.n., 3 consecutive days). Ovariectomy (OVx) was performed and the allergic obese mice were OVA-rechallenged 10 days later (OVx, n=4). After 24 h of the last rechallenge, mice were euthanized, and central nervous system tissues were collected. The research was approved by the Committee on Ethics in Animal Use (5288160218). Budesonide (100 µg/kg, intranasal) was given to obese OVxallergic mice (OVxBud, n=2) 4 h before each OVA-rechallenge. As control were also used OVx non-allergic mice challenged with PBS (OVxC, n=4). Na,K-ATPase activity (NKA) was measured in cerebellar tissue homogenates. Data were expressed as a percentage of the mean. **Results:** Na,K-ATPase total activity was measured and it was observed an increase of 6.82% ± 3.89 (1.06x) in its activity in OVxgroup, compared to OVxC. On the other hand, budesonide-treated group has shown a reduction of 7.57% ± 2.40 (1.07x) in NKA, in relation to OVxC. Similarly, when measured Na,K-ATPase α-2,3 subunits activity, it was observed an increase of 9.07% ± 15.41 (1.09x) in its activity in OVx group and a decrease of 35.51% ±7.99% (1.35x) in OVxBud, when compared to OVxC. Nevertheless, both groups, OVx and OVxBud, have shown an increase of 5.62% ± 5.60 (1.05x) and 7.75% ± 0.66 (1.02x), respectively, in Na,K-ATPase α-1 subunit activity. **Conclusion:** Our preliminary results may suggest that there's no change in Na,K-ATPase activity in the cerebellum of oophorectomized mice with allergic lung inflammation. However, budesonide treatment may reduce Na,K-ATPase α-2,3 subunits activity. **Financial support**: FAPESP, CAPES, CNPQ.

02.008 Cannabinoid microdoses reduces Alzheimer Disease symptoms in a 75 years old patient: **A case study**. Nascimento F[1], Martins-Gomes AC[1], Cury RMC[1], Soares FAS[2], Maia BHNS[2], Pamplona FA[1], Gomes-da-Silva E[1] [1]Unila, [2]UFPR

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive decline of memory associated to other cognitive symptoms. Currently, there is no effective treatment to prevent the progression and to reduce the symptoms of the disease. On this way, the pharmacotherapy based on cannabinoids has emerged as a potential treatment for AD. The objective of this study was to evaluate the effects of microdoses of exogenous cannabinoids given to a patient diagnosed with Alzheimer's disease. The evaluation tools used were the Mini-Mental State Examination (MMSE) and the Alzheimer-Cognition Disease Assessment Scale (ADAS-Cog). The patient studied is male, 75 years old, with a two years AD diagnosis. Before our study, the patient was receiving memantine hydrochloride 10 mg since the diagnosis. Besides memantine treatment he had rapid progression of symptoms of AD and suffered with some adverse effects. After assessing the baseline condition that indicated that the patient was in stage 2 (moderate) of the disease, the pharmacological intervention consisted of the administration of an extract with 500µg of THC in the first 150 days of treatment. After this period, 750µg of THC was administered in the next 60 days, 1mg of THC for 30 days, 650µg of THC in the subsequent 30 days and 325µg of THC in the last 150 days of intervention. Administration of the extract induced an increase in the MMSE scores and a concomitant decrease of the ADAS-Cog scores in a rapid and effective manner, demonstrating a marked improvement of patient condition. The most effective results were found with the second lowest dose tested (500µg THC). Besides the results showed using the protocols tools the reports of the patient and his caregiver demonstrated improvement also in his quality of life. Then, this study demonstrates that microdoses of cannabinoides are a very potential treatment for AD. More studies are in progress to extend and to confirm these results. Keywords: THC, Cannabinoids, Alzheimer Disease, Memory, Cognition

02.009 Mental and neurological disorders as risk factors for periodontal diseases in institutionalized people. Ávila TV, Rabelo CC, Corrêa FOB, Pontes AEF, Oliveira DM, Silva BAA, Gomes MA, Reis DR, Lana VLR, Dias TLM UFJF

Introduction: The accumulation of bacterial biofilm in the dental plaque structure predisposes the individual to periodontal diseases (PD) (Loe, Journal of Clin. Periodontology, v. 13, p. 431, 1986). PD, on the other hand, has been associated with the pathogenesis of systemic diseases (SD)such as systemic arterial hypertension (SAH), diabetes and cardiopathies. (Kinane, Journal of Clin. Periodontology, v. 35, p. 333, 2008). Individuals with special needs are at particular risk for SD and PD (Anders, Spec. Care in Dentistry, v. 30, p. 110, 2010). The Santa Luzia Association (Gov. Valadares/MG) houses 107 patients with multiple disabilities that includes neurodegenerative diseases (ND), psychological disorders or brain injury. All the individuals are under psychoactive drug treatment and most of them under drug treatment for SD as well. In this study we evaluated the PD manifestation and the effects of drugs on modulating the PD in institutionalized people with special needs (IPWSN). **Methods:** This research was approved by UFJF ethics committee, #1,868,206. The epidemiological survey has diagnosed PD evaluating probing depth and clinical attachment level (CAL) in 6 sites per tooth. Searches were carried out in the medical records to identify pathologies, comorbidities, use of drugs and a degree of autonomy through the criterion of Braden (Bergstrom, Nurs Res., v. 51, p. 398, 2002) used by the nursing team. The software Prism 5 (GraphPad Software Inc., La Jolla, CA, USA) was used for statistical analysis and differences were consider significant when $p<0,05$. **Results:** ND such as Parkinson's and Alzheimer's were associated with severity of PD. ND individuals were under l-DOPA plus benzerazide or Rivastigmine treatment and in both therapeutic schemes the manifestation of PD was similar. SD such asSAH and diabetes were also associated with a worse manifestation of DP in IPWSN. Interestingly, individuals under Angiotensin II receptor blockers (ARB) or AAS treatment presented marked DP with high probing depth(2.42± 0.26 and 2.83± 0.22, respectively)and CAL means(3.6± 0.67 and 4.31± 0.61, respectively) when compared to non-ARB (2.03± 0.1 and 2.2 ± 0.09, respectively)ornon-AAS users(2.2± 0.16 and 2.36 ± 0.3, respectively). On the other hand, metformin users presented lighter PD with less probing depth (2.39± 0.15) and CAL means (2.63± 0.43) when compared to non-metformin users (2.98± 0.11 and 4.78± 0.51, respectively). **Conclusion:** We have shown that ND is involved in a more severe manifestation of PD independent of the psychoactive drug the patient is using. Co-morbidities, such as diabetes and SAH are also involved in a worse manifestation of PD in IPWSN. ARB and AAS were associated with worse manifestation of DP, while metformin was associated with lighter manifestation of PD. More clinical studies are needed to establish the biological plausibility of the association between the presence or not of drugs and PD manifestation. Acknowledgments: PROEX and PROPP/UFJF.

02.010 *In vitro* **effects of memantine and cannabidiol in Alzheimer´s disease**. Monteiro BO, Quintella ML, Romariz SA, Affonso D, Filev R Unifesp

Introduction: Alzheimer's disease (AD) is the most common type of dementia and has become a frequent cause of death in several countries. One drug commonly used in the treatment of AD is the memantine, a moderate N-methyl-D-aspartate receptor (NMDAR) antagonist that improves the patient's cognitive state. Memantine presents potential in reducing synaptic loss, and therefore dendritic spine loss. Cannabidiol (CBD), one of the major cannabinoids present in *Cannabis sativa*, acts as an inverse agonist at the CB2 receptors, which may explain some of its anti-inflammatory properties. CBD has the ability to reduce reactive gliosis and the neuroinflammatory response as well as reverses and prevents the development of cognitive deficits present in AD. **Methods:** In order to investigate the influence of these compounds in culture of neuroprogenitor cells (NPC) from transgenic mice for AD (2xTg-AD) and in neurons from neuroblatoma (N2A) (CEUA nº 9268250618), NPC were obtained from the telencephalic vesicles of 2xTg-AD embryo mice (E13), were cultured and after 2 weeks of differentiation, they were stained with DiI dye for labeling cell extensions. Likewise, murine neuroblastoma cell line (N2A) was thawed and cultured and treated with Memantine and/or Canabidiol (CBD). The CBD used in this study comes from NIH USA and was kindly provided by Prof. Elisaldo Carlini. Dendritic spines were quantified by Neurolucida 360 software (MBF Bioscience) and neuronal labeling with beta-tubulin III. **Results:** After 72h of differentiation, dendritic spines could be identified in N2A cells detectable by DiI staining (n=3, triplicate experiments), and 4 morphologic types of spines was observed in these cells. Memantine treatment was not able to alter the dendritic spine density ($p>0,05$, ANOVA one way). However, the treatment with CBD modified the pattern of dendritic and neuritic arborization. In NPC, cells obtained from wild type animals (CTRL) was compared with AD cells treated or not with memantine (n=8 wells), and the statistical analysis indicated that, although the neurite length of was different between AD and CTRL, there was no difference in memantine treated groups ($p>0,05$, ANOVA two way). In order to evaluate the neuronal differentiation, N2A cells non-treated or treated with CBD in concentrations of 1μM or 5μM was stained with β-tubulina III and quantified by ImageJ NeuriteTracer, and the length was measured (n=3, triplicate experiments). The results showed a significant reduction of neurit lengh and cell quantification in CBD 1μM and 5μM compared with CTRL ($p<0,05$, one-way ANOVA). **Conclusion:** These results indicate a negative interference of the CBD in the dendritic arborization and in neuritic length, even in low doses. Memantine did not interfere in morphology or in the quantity of dendritic spines, and thus could not indicate synaptic alterations in AD cells culture. The results demonstrate the importance of understanding the mechanisms involved in these compounds, and show that *in vitro* studies may clarify important aspects about degenerative process and point out regenerative possibilities in AD. Acknowledgments: FAPESP and CNPq for the **Financial support**.

02.011 Participation of neurokinin NK1 receptors in the streptozotocin-induced memory deficit in an animal model of Alzheimer's disease. Mendonça PDS, Leal JC, Duarte FS UFPE

Introduction: Substance P (SP) is one of the endogenous neurokinins that presents several physiological and pathological functions through the activation of its NK_1 receptors, widely distributed throughout the central nervous system. SP is involved in the modulation of learning and memory, as well as in the neuroinflammation underlying to neurodegenerative processes. **Objectives**: To evaluate the possible participation of NK_1 receptors in the streptozotocin (ETZ)-induced behavioral changes in rats evaluated in tests of learning and memory. Methods**:** Adult male Wistar rats (N = 80, three months old, 350g), were previously anesthetized with ketamine and xylazine and cannulated by stereotaxic surgery in the lateral ventricle (AP = - 0,8mm, ML = +/- 1,5mm, DV = -2,5mm). During five consecutive days, after the surgeries, animals received the central treatments through a microinjection (4µl) of vehicle (control, C), ETZ (0.1mg), NK_1 antagonist (L-733,060; 100pmol) or ETZ (0.1mg) + NK_1 antagonist (L-733,060 100pmol). On the 6th day, animals were evaluated in the inhibitory avoidance (IAT) and object recognition (ORT) tests. For statistical comparisons, one-way ANOVA was used followed by the Newman-keuls post-hoc test. All experiments were approved by the l*ocal ethics committees* (CEUA, process number 0014/2018). **Results:** In the IAT, STZ significantly reduced the latency to step-down from theplatform in test sessions evaluating working memory (WM), short (STM) and long-term (LTM) memories. Central administration ofNK_1 antagonist (L-733,060) *per se* did not affect the WM, STM and LTM. However, L-733,060 prevented the STZ-ind*uced memory impairment on the* three types of memories evaluated (WM: C = 139.33 ± 14.75; STZ = 35.77 ± 8.027; L-733,060 = 88 ± 20.68; L-733,060 + STZ = 114.1 ± 22.90; STM: C = 128 ± 17.31; STZ = 53.88 ± 17.53; L-733,060 = 91.5 ± 19.76, L-733,060 + STZ = 122.1 ± 24.02, LTM = C = 116.91 ± 16.96, STZ = 28.22 ± 6.538, L-733,060 = 62.1 ± 15.48, L-733,060 + STZ = 94.7 ± 21.41). In the ORT, STZ-treated group had lower recognition index of novel objects, effect that was reversed by NK_1 antagonist. **Conclusion:** Our results suggest that SP and NK_1 receptors seems to be critically involved in the modulation of memory impairment induced by STZ in rats. **Financial support**: CNPq, FACEPE, CAPES.

02.012 New GABAergic compound: **Acute toxicity and anxiety-like behavior in adult Zebrafish** (*Danio rerio*). Mendes B[1], Clementino-Neto J[1], D'Oca MGM[2], Ximenes-da-Silva A[1] [1]UFAL, [2]UFRGS

Introduction: Dysregulation of GABAergic signaling occurs in various neurologic and psychiatric conditions, like anxiety, pain and epilepsy, as well as Alzheimer and schizophrenia. Search for new blood-brain-barrier penetrating drugs has a pivotal role in determining the selection of drugs acting on Central Nervous System (CNS). Zebrafish (*Danio rerio*) has increasingly being used as an experimental model for toxicity assay and screening of new drugs in both, embryos and adult animals. Measuring few centimeters long, adult animals allow screening drugs test in a whole organism using a few amount of compounds. This study aimed to investigate the toxicity and the anxiolytic effect of a new GABAergic compound, N-Methyl Palmitoyl Butanoate (NMPB), a fatty-*N*-acyl amino ester, in adult zebrafish. **Methods:** A total of 80 animals, male and female, were used to acute toxicity (N=35) and anxiety-like behavior test based on light/dark tasks (N=45). Procedures were approved by local Ethic Committee (#46/2018). To perform acute toxicity test, fasting fishes were immersed in a 7L/tank and continuously exposed to different NMPB concentrations, 10.65 mg/L, 23.43mg/L, 51.58mg/L or 113.41mg/L during 96 hours. Control group animals (CTRL) were kept in drug-free water. Behavioral changes were recorded with a camera on a daily basis. Light/dark task was performed in a glass aquarium (19.5×9.3×15cm) divided by a partition (9.3×15cm) in two equally sized dark and white compartments. At first, animals were individually placed in a beaker (height 10 cm and diameter 8.5 cm at the top) and treated for 10 minutes with NMPB or diazepam (DZP) in different concentrations: 0.08mg/L, 0.16mg/L and 0.32mg/L. After, fishes were individually placed on the white side of the test-tank and locomotion was recorded for 300 seconds. The behavioral parameters analyzed were: 1) latency for the first entry into the dark compartment, 2) time spent in each compartment and, 3) number of crossings between the compartments. Videos recordings were analyzed by researchers and two blinded raters. **Results:** NMPB showed no toxicity (100% survival rate) for all tested concentrations. A limit test was performed at 100 mg/L in order to demonstrate that the LC_{50} is greater than this concentration, confirming the non-toxicity of the substance at highest concentration. Analyses of anxiety-like behavior in animals showed NMPB treatment at 0.16mg/L significantly increased time spent in the white zone (CTRL 163.6 x NMPB 197.9 sec; ANOVA one-way; $p<0.05$). Average numbers of crossings between light and dark compartments have not changed with NMPB treatment. DZP significantly reduced number of crossings at the highest concentration tested (0.32mg/L; 28.8 x 55.2 CTRL; $p<0.05$). Latency time to crossing compartments was not changed by any compounds tested. **Conclusion:** NMPB had no toxic effect in adult Zebrafish and demonstrated a potential GABAergic drug acting on the CNS, reducing anxiety-like behavior, here demonstrated by increased time spent in the white zone of the test-tank. **Financial Support:** Researchers own funding

02.013 Involvement of Neurokinin Nk3 Receptors from Nucleus Accumbens Shell (NAshell) and Prefrontal Cortex (PEC) in the positive and negative-like symptoms of Schizophrenia in Rats. Silva GVD, Pinho CCES, Duarte FS UFPE

Introduction: Schizophrenia is a severe psychiatric disorder that has a profound impact on the individual's quality of life. The main manifestations of schizophrenia are the "positive" symptoms (e.g. hallucinations and delusions), "negative" symptoms (e.g. social withdrawal, apathy) and "cognitive" symptoms. Treatments of schizophrenia is still limited for decades. In the search for molecules with better efficacy and side-effect profiles, modulators of neurokinin NK_3 receptors have been investigated as a new target for schizophrenia. **Objectives:** to investigate the involvement of neurokinin NK_3receptors from nucleus accumbens shell (Nashell)and prefrontal cortex (PFC)in the positive- and negative-like symptoms in rats. **Methods:** Adult male Wistar rats were stereotaxically cannulated in the Nashell(AP=+1.7mm, ML=±2.9mm and DV=-6.3 mm), and after 5 days, were treated with apomorphine 2mg/kg (i.p.), and 5min later, received a microinjection into the NAshellof vehicle or NK_3 receptors antagonist SR146477 (100pmol). After 1min, the climbing behavior was evaluated during 1 h. Other animals were stereotaxically cannulated in the PFC (AP=+3.0mm, ML=±0.8mm and DV=-3.0mm) and then submitted to *a* 6-days period of *social isolation*, being that in the fifth day the animals were submitted to the open field test during 5min (habituation). After 24h, animals were treated with vehicle or ketamine 25mg/kg (i.p.), and, 30min later, received a microinjection into the PFC of vehicle or NK_3 receptors agonist senktide (100pmol). Social behavior was assessed in pairs in the open field test, using the following behavioral parameters: number of social interactions and the total time of social interaction (Ethics Committee CEUA/UFPE n°. 0035/2018). **Results:** SR146477 (100 pmol) administered intoNAshell reduced the apomorphine-induced stereotyped behavior, with the total blockage achieved at 60 min (vehicle=5.96±0.4; SR146477 = 0.03±0.03). In the social interaction test, ketamine reduced the number of social interactions, effect that was reversed by the administration into the PFC of senktide (vehicle/vehicle = 36.78±2.32; ketamine/PBS = 25.78±3.16; ketamine/senktide=34.89±2.50). Moreover, senktide removed the ketamine-induced impairment in the total time of social interaction (vehicle/vehicle = 176.70 ± 29.84s; ketamine/PBS = 89.33 ± 15.02s; ketamine/senktide=124.10 ± 21.30s). ConclusionsOur findings suggest that the NK_3 receptors from NAshell modulate the apomorphine-induced stereotypy, with the blockageof this signaling pathway leadingto an antipsychotic-like activity profile against the "positive"-like symptoms. On the other hand, the activation of NK_3 receptors ofPFC plays a protective role against the "negative"-like symptoms. Together, our findings indicate that the NK_3 receptors represent a potential target for pharmacological intervention in the future treatment of schizophrenia. **Financial support:** FACEPE, CNPq.

02.014 Chrysin prevents memory impairment induced by aluminum in mice. Campos HM, Costa MD, Neri HS, Moreira LKS, Costa EA, Santos FCA, Ghedini PC UFG

Introduction: Chrysin (CHR) is an important natural phenolic compound found in plants, passionfruit, propolis and honey. Studies have shown that this compound presents anti-inflammatory effect, inhibiting pro-inflammatory cytokines expressions (Goes et al. 2018). In addition, CHR protects against oxidative stress and apoptosis in neuronal cells that were related with the improvement of cognitive deficits and brain damage in chronic cerebral hypoperfusion and in the aged related in mice (He et al. 2012, Souza et al. 2014). Considering this information, the purpose of this study was to evaluate the CHR neuroprotective effect in an experimental model of Alzheimer's disease.

Objective: Evaluate the protective effects of CHR treatment on the memory impairment induced by aluminum chloride ($AlCl_3$) in mice. **Methods**: Male Swiss mice (10 – 12 weeks old) were randomized into four groups (n = 8): Control (C); aluminum chloride 100 $mg.kg^{-1}$ ($AlCl_3$); CHR 10 $mg.kg^{-1}$ (CHR_{10}) and CHR 100 $mg.kg^{-1}$ (CHR_{100}). The C group received water, while all other groups received $AlCl_3$ for 90 days. At the 46^{th} day, the C and $AlCl_3$ groups received water while all others groups received CHR until the 90^{th} day. All treatments were administered daily by gavage at volume of 10 $mL.kg^{-1}$. At the 90^{th} day, animals were submitted to chimney and open field tests for locomotive and exploratory activities evaluation, respectively. In the 91^{th} and 92^{th} days, animals were submitted to step-down task for memory evaluation. Twenty-four hours after the last test, animals were anesthetized with ketamine and xylazine and euthanized for brain dissection and hippocampus obtention for biochemical analysis (carbonyl protein and malondialdehyde levels, acetyl- and butyryl-cholinesterase activities). All protocols were approved by the Animal Research Ethical Committee from Federal University of Goias (process Nº 053/2016). The statistical analysis was performed by one-way ANOVA followed by Tukey's post-hoc when appropriated or Student T-test, the value of $p < 0,05$ was considering. **Results**: No differences in locomotive ($F_{3,28} = 0.146$; $p = 0.970$) and exploratory ($F_{3,28} = 0.087$; $p = 0.084$) activities between the groups were observed. The CHR 10 $mg.kg^{-1}$treatment prevented from the memory impairment ($F_{3,28} = 6.190$; $p = 0.013$) induced by $AlCl_3$ ($p = 0.001$ compared with the C). At the same dose, CHR prevented from the increase carbonyl protein level ($T_{5,5} = 1.450$; $p = 0.001$) induced by $AlCl_3$ ($T_{7,5} = 1.736$; $p = 0.023$ compared with the C). The malondialdehyde level increased by $AlCl_3$ ($F_{3,28} = 3.899$; $p = 0.022$compared with the C) was prevented by the CHR 10 $mg.kg^{-1}$ ($p = 0.033$) and CHR 100 $mg.kg^{-1}$ ($p = 0.023$) treatments. The CHR 10 $mg.kg^{-1}$dose prevented the increase of acetylcholinesterase ($F_{3,28} = 3.811$; $p = 0.024$) and butyrylcholinesterase ($F_{3,28} = 4.912$; $p = 0.015$) activities induced by $AlCl_3$ ($p = 0.035$ and $p = 0.012$ compared with the C, respectively). **Conclusion**: Our results showed that the CHR treatment protects against the memory impairment induced by $AlCl_3$ in mice. However, further studies should be performed to confirm these preliminary findings. **Financial Support**: FAPEG, CNPQ and CAPES.

02.015 Brain glucose administration attenuates neuronal death in hippocampus, subiculum and thalamic nuclei after pilocarpine-induced status epilepticus. Melo IS[1], Santos YMO[1], Santos JF[1], Pacheco ALD[1], Costa MDA[1], Oliveira KB[1], Brito IRR[1], Duzzioni M[1], Sabino-Silva R[2], Borbely AU[1], Castro OW[1] [1]UFAL, [2]UFU

Introduction: Glucose is the main source of energy for the brain and its lack can leadto neuronal dysfunction. During status epilepticus (SE), the neurons become overexcited, increasing energy consumption. Glucose uptake is increased via the sodium/glucose cotransporter 1 (SGLT1) in the hippocampus under epileptic conditions. In addition, a supply of glucose can prevent neuronal damage caused by SE. We evaluatedthe effect of increased glucose availability inbehavior of limbicseizures, neurodegenerationprocess and SGLT1 expression. **Methods:** Experimental procedures were approved by the Ethical Committee for Animal Research of UFAL (04/2016). Male Wistar rats (n=12 [240-340g]) were submitted to stereotaxic surgery for cannula implantation in the hilus of dentate gyrus of hippocampus. Animals PILO+VEH (P+V) and PILO+GLU (P+G)received microinjections of pilocarpine (PILO) (1.2mg/μL) in hippocampus to induce SE, followed 5 minutes later by vehicle (VEH, saline 0.9%, 1μL) or glucose (GLU, 3mM [diluted in saline]). Behavioral analysis of seizures was performed for 90 minutes during of SE, according to Racine scale (1972). Animals were perfused after 24 hours of SE and neurodegeneration was evaluated by histochemistry of Fluoro-Jade (FJ). FJ positive neurons (FJ+) were counted (ImageJ–NIH) in hippocampus, subiculum and thalamicnuclei. Results were expressed as mean±SEM, compared by unpaired t test. **Results:** The administration of glucose (3 mM) after PILO reduced the severity of seizures (P+V, 0.69±0.02; P+G, 0.57±0.03), as well as the number of limbic seizures classes 3 (P+V, 1.1±0.1; P+G, 0.5±0.2), 4 (P+V, 1.2±0.08; P+G, 0.6±0.1), and 5 (P+V, 1.5±0.2; P+G, 0.6±0.2).Similarly, glucose after SE attenuated the number of FJ+ neurons in hippocampus [CA1 (P+V, 335.7±36.9; P+G, 51.7±25.2), CA3 (P+V, 300.9±39.4; P+G, 82.2±49.0) and hilus (P+V, 161.3±31.9; P+G, 25.0±9.4)], subiculum (P+V, 1.2±0.08; P+G, 0.6±0.1) and thalamic nuclei [lateral posterior (P+V, 175.1±68.2; P+G, 5.3±1.1), centrolateral (P+V, 134.1±47.6; P+G, 5.33±1.5) and posterior paraventricular (P+V, 197.9±44.9; P+G, 10.0±6.0)]. Finally, SGLT1 expression was elevated in hippocampus [CA1 (P+V, 1.5±0.2; P+G, 2.3±0.2), CA3 (P+V, 1.5±0.3; P+G, 3.0±0.3) and hilus (P+V, 1.3±0.2; P+G, 2.3±0.2)] after increasing glucose levels. **Conclusion:** These preliminary data suggest that possibly the administration of intrahippocampal glucose protects brain in the earlier stage of epileptogenic processes via an important support of SGLT1.

Financial Support: FAPEAL, CNPQ, CAPES. **Acknowledgements**: To all those involved in the Laboratory of Neuropharmacology and Integrative Physiology.

02.016 Antidepressant-like potential of solidagenone isolated from *Solidago chilensis*. Alves BO, Miorando D, Zilli GAL, Ernetti J, Alievi K, Zanotelli P, Locateli G, Dalla Vecchia CA, Müller LG, Roman Júnior WA Unochapecó

Introduction: Characterized by a set of physical and psychological symptoms, depression has an uncertain etiology. It is assumed that changes in the immune-inflammatory pathways may be involved in the genesis of disease. The aerial parts of *Solidago chilensis* Meyen (Asteraceae) are popularly used as anti-inflammatory, however, their activity at the level of the central nervous system has not been evaluated. The objective of this study was to evaluate the solid age none isolated from *S. chilensis* in a biological model of the antidepressant-type. **Methods:** The aerial parts of *S. chilensis* were collected, dried, and macerated with dichloromethane (300 ml). Subsequently, the extract was filtered, concentrated, lyophilized, and fractionated in chromatographic column, which resulted in the isolation of solid agenone. In the experimental protocol, 48 mice (CEUA 016/17) were divided into 7 treatment groups: normal (N), who only received saline; Vehicle (Veh); solid agenone in concentrations of 1, 10 and 100 mg/kg (SDG 1, 10 and 100); per se (who only received SDG 100 mg/kg); and fluoxetine (Flu, 30 mg/kg). Initially these animals received LPS (600 µg/kg, i.p.), except for the normal and per se group and, after 5 h oral treatments, according to each group. After 1h, all animals were evaluated in the open field test (TCA) for 6 minutes. After 24 hours of LPS application, the animals were again submitted to TCA and then evaluated in the tail suspension test (TSC), also for 6 minutes. Subsequently they were anesthetized and euthanized. **Results:** The groups treated with LPS caused a significant reduction ($p < 0.05$ and $p < 0.01$) in the locomotor activity of mice at 6 hours after administration, which was prevented by fluoxetine in their respective group. 24 hours after LPS application, locomotor activity returned to baseline levels. However, in the SDG 10 and SDG 100 groups, the immobility time decreased significantly ($p < 0.01$ and $p < 0.001$) compared to the Veh group. **Conclusion:** Our results demonstrate the antidepressant-like potential of solid agenone in an animal model that associates immunoinflammatory activation with the etiology of depression. **Acknowledgements**: This work was supported by the Universidade Comunitária da Região de Chapecó and Programa de Bolsas Universitárias de Santa Catarina – Uniedu[Art. 170].

02.017 Effects of metal complex derived of the Diazepam [(DZP)PdCl]2 in the behaviors related to fear, **anxiety and memory in mice**. Silva OBS, Souza FMA, Souza GF, Vieira MPS, Correia WBZGB, Neto JGS, Silva AV, Meneghetti MR, Duzzioni M UFAL

Introduction: The challenge in the therapy of anxiety disorders is to identify effective alternative medicines with better tolerability. Some studies have shown that the synthesis and semi-synthesis of metal compounds derived from benzodiazepines (BDZs) exhibit these desirable characteristics of the novel anxiolytic drugs. The objective of this work was to evaluate the effects of intraperitoneal (i.p.) administration of metal complex derived from diazepam $[(DZP)PdCl]_2$ on fear, anxiety and memory related behaviors in female *Swiss* mice. **Methods**: Female *Swiss* mice were treated (i.p.) with vehicle [0.5% Tween 80 in saline solution (0.9% NaCl)] or $[(DZP)PdCl]_2$ (0.015, 0.025 and 0.15 mg/kg). After 30 min, animals were submitted to anxiety [elevated plus maze (EPM) or light-dark box (LDB)], locomotor activity [open field (OF)] and memory [step-down (SD)] tests. The role of the $GABA_A$ receptor in the anxiolytic-like effect of the $[(DZP)PdCl]_2$ complex was evaluated after pretreatment with flumazenil (2 mg/kg, i.p)+$[(DZP)PdCl]_2$ (best anxiolytic dose). This work was approved by the Committee on Ethics in the Use of Animals (CEUA) of federal university of Alagoas, Protocol No. 29/2018. **Results**: In the EPM, $[(DZP)PdCl]_2$ (0.15mg/kg) significantly increased the percentage of time spent in the open arms and the percentage of entries into the open arms, when compared to the control group, indicating an anxiolytic-like behavior. This anxiolytic-like effect was not observed in the LDB. No locomotor activity change was found in the OF, as well as no amnesic change in the SD. Flumazenil *per se* did not alter any of the parameters evaluated in the EPM, but was able to block the anxiolytic-like effect of $[(DZP)PdCl]_2$, indicating that this compound bindto the benzodiazepine site on the $GABA_A$ receptor complex. **Conclusion**: Our results demonstrated for the first time that $[(DZP)PdCl]_2$ presents an anxiolytic-like effect in EPM test without alteration in locomotor activity and impair learning-memory processes. In addition, the anxiolytic-like effect of $[(DZP)PdCl]_2$ is mediated by benzodiazepine site on the $GABA_A$ receptor complex. Further studies are necessary to evaluate the safety of $[(DZP)PdCl]_2$.

02.018 Effects of metal complex derived of the Diazepam [(DZP)PdOAc]2 in the behaviors related to fear, **anxiety and memory in mice**. Souza GF, S OBS, Vieira MPS, Souza FMA, Correia WBZGB, Neto JGS, Silva AV, Meneghetti MR, Duzzioni M UFAL

Introduction: Anxiety disorders should be treated with psychological therapy, pharmacotherapy, or a combination of both. However, some of the patients do not respond satisfactorily to the available pharmacotherapy. Studies have shown that palladium (II) organometallic complexes derived from diazepam - $[(DZP)PdOAc]_2$ and $[(DZP)\ PdCl]_2$ had a potent antiepileptic effect in mice. The current study was designed to investigate the effects of metallic complex derived of the diazepam $[(DZP)\ PdOAc]_2$ in the behaviors related to fear, anxiety and memory in mice. **Method**: Female Swiss mice were intraperitoneally (i.p.) treated with $[(DZP)\ PdOAc]_2$ (0.025, 0.15 or 0.25 mg/Kg) or Saline (NaCl 0.9%) and, 30 min later, submitted to different anxiety [elevated plus maze (EPM) and light-dark box (LDB)], locomotor activity [open field (OF)], and memory [step down (SD)] tests.This work was approvated by Animal Ethics Committee of the Federal University of Alagoas (CEUA: 30/2018). **Results:** Our results demonstrated that the $[(DZP)\ PdOAc]_2$ compound significantly increased both the percent time spent in open arms of the EPM (0.15 mg/Kg) and latency to enter in the dark compartment of the LDB (0.25 mg/Kg), indicating an anxiolytic-like effect. No locomotor activity change was found in the OF as well as no amnesic change in the SD. **Conclusion:** Our results demonstrated for the first time that $[(DZP)\ PdOAc]_2$ presents an anxiolytic-like effect in EPM and LDB tests without alteration in locomotor activity and impair learning-memory processes. Further studies are needed to investigate the safety of this compound. This work had **Financial support** from CNPq.

02.019 Participation of Auraptene and Isoquercetin in the sedative effects promoted by hydroethanolic extract (**HE**) **of polygala altomontana in rats**. Leal JC[1], Silva JMD[1], Tizziani T[1], Brighente IMC[1], Duarte FS[1] [1]UFPE, [2]UFSC

Introduction: The genus Polygala is the main representative of the plant family Polygalaceae that shows several pharmacological properties, among them neuropharmacological actions. In previous studies we showedstrong evidences that HE is capable of producing anxiolytic, hypnosedative, and anticonvulsive effects, as well to reverse the streptozotocin (STZ)-induced memory impairment in rats. Phytochemical analysis revealed the presence of auraptene (4.93 mg/g) and isoquercetin (6.25 mg/g), suggesting that these bioactive substances could be responsible, at least in part, for the central actions seen for HE. However, so far, the underlying mechanisms for these central effects have not been elucidated. **Objectives:** To evaluate the possible participation of auraptene (AUR) and isoquercetin (ISO) in the profile of central action ofHE from *P. altomontana*in rats evaluated in the open-field test (OFT) and k*etamine or isoflurane*-induced hypnosis. Methods**:** Adult male Wistar rats (N = 100; three months old; 300g) were orally treated with HE, ethyl acetate (EA), or ethanolic (ET) (300 mg/kg) fractions of the *P. altomontana*. One hour later, the behavior was evaluated in the OFT and k*etamine or isoflurane*-induced hypnosis. Other animal groups were intracerebroventricularly(i.c.v.) cannulated by stereotaxic surgery, and six days later, each rat received AUR or ISO (40 ng/4ul, i.c.v.) and, 5min later, were evaluated in the OFTand k*etamine or isoflurane*-induced hypnosis. All experiments were approved by the local Committee for Animal Use and Care in Research (CEUA) (number 0004/2016). All results are presented as mean ± S.E.M. and analyzed by a one-way analysis of variance (ANOVA) followed by the post-hoc Student Newman-Keuls' test, with treatment being the independent variable. Differences between treated and control groups were considered statistically significant when $P \leq 0.05$. **Results:** In the OFT, HE reduced the total movements (TM = 20.50 ± 3.34) and the number of rearings (REA = 7.50 ± 1.43), when compare to control group (TM = 47.55 ± 7.03, REA = 23.45 ± 2.77). Both EA and ET fractions were not able to promote any significant changes in the behavioral parameters evaluated in the OFT.The administration i.c.v. with AUR increased the total movements (TM = 64.90 ±5.29) but did not modify the number of rearings (REA = 11.00 ± 1.97), while ISO were not able to promote any significant changes in the OFT(TM = 54.25 ± 3.89; REA = 12.33 ± 1.42).In the k*etamine*-induced hypnosis test, EA (94.37 ± 3.66s) or ET (71.88 ± 5.34s), but not HE (57.28 ± 4.20s), significantly increased the total duration of the hypnosis when compare to control group (53.26 ± 3.92s), a sedative effect similar to that produced by diazepam (DZP) (87.44 ± 8.84s). In the isoflurane-induced hypnosis, all fractions significantly increased the duration of the hypnosis in a similar way to AUR, ISOand DZP(C=106.7 ± 6.69s;HE=160.4 ± 18.44s;EA=169.8 ± 15.35s;ET=141.9 ± 11.87s;AUR = 215.9 ± 26.53s; ISO = 254.8 ± 32.37s; DZP=212.9 ± 21.09s). Conclusions: Our data provides evidence for the involvement of AUR and ISO in the sedative effects promoted by HE from *P. altomontana.* **Financial support:** FACEPE, CNPq.

02.020 The role of interferon-γ in L-DOPA-induced dyskinesia in Parkinson's disease. Ferrari DP[1], Bortolanza M[2], Bel ED[2] FMRP-USP, FORP-USP

Introduction: The development of L-DOPA-induced dyskinesia (LID) is apredictable complication in Parkinson's disease (PD) patient's duo to the chronicity of the treatment. The LID is characterized by abnormal involuntary movements (AIMs). Our group demonstrated that inflammatory mechanisms play a role in the pathophysiology of LID. We demonstrated the presence of activated microglia, astrocyte and increased expression of inducible nitric oxide-synthase (iNOS) in the lesioned striatum of dyskinetic rodents. Since iNOS transcription is dependent on pro-inflammatory cytokines, including interferon-γ (IFN-γ), it might be interesting to evaluate if the absence of IFN-γ has any influence on LID development. **Objective**: The aim of this study was to analyze the participation of IFN-γ in LID development in mouse model of PD. **Methodology**: Adult male IFN-γ knockout (IFN-γ/KO) and wild-type (WT) mice, with lesion of dopaminergic neurons induced by unilateral 6-hydroxydopamine microinjection in the striatum, received daily administration of L-DOPA (25mg/kg; i.p.) or saline during 21 days. The mice were evaluated for AIMs. At the end of the experiment animals were deeply anesthetized and sacrificed by perfusion. After fixation of the brains, they were cut and immunostained for tyrosine hidroxilase (TH) in the striatum and substantia nigra compacta (SNc). For statistical analysis, we used Student's t-test and Two-way ANOVA, followed by Tukey's post-hoc test (n=5-7 per group). The project was approved by Ethical Committee (2017.1.369.58.4). **Results**: L-DOPA chronic treatment induced AIMs in both IFN-γ/KO and WT lesioned mice. These dyskinetic movements appeared after the first L-DOPA injection and were stable after 3 weeks of treatment. IFN-γ/KO presented lower levels of AIMs scores (55.67±19.15) compared to WT group (88.56 ±18.11). No AIMs were observed in lesioned mice that received saline. There was no difference between IFN-γ/KO and WT mice in the lesion intensity demonstrated by TH immunoreactivity. The optical density analysis showed massive loss of dopaminergic neurons in SNc (87.16% ±3.55 IFN-γ/KO and 84.42% ±2.78 WT) and fibers in striatum (95.03% ±0.97 IFN-γ/KO and 95.48% ±2.73 WT) when compared to unlesioned hemisphere. TH immunorreactive neurons arise within completely lesioned striatum of mice treated with L-DOPA. Higher number of these neurons were found in dyskinetic IFN-γ/KO mice (10.3 ±3.5 neurons) compared with WT (5 ±2.3 neurons) dyskinetic mice. **Conclusion**: Our results indicate that IFN-γ is noteworthy to the development of LID. Nonetheless its absence did not block LID development in IFN-γ/KO mice. The difference in the dyskinesia was due to the genotype and not to the lesion extention. Further analyses are in progress to investigate the relationship between IFN-γ absence and the inflammatory reaction in the brain of mice with LID. **Funding:** FAPESP, CNPq.

02.022 Involvement of the hypocampal colinergic system in the depressive-like behavior induced by the withdrawal of crack/cocaine in mice. Santos Neto JG[1], Souza FMAD[1], Silva NKGT[2], Pacheco ALD[1], Nicácio DCSP[1], Cavalcante GTS[1], Correia WBZGB[1], Vieira MPS[1], Souza GF[1], Silva OBS[1], Silva VC[1], Brito IRR[1], Castro OW[1], Duzzioni M[1] UFAL[1], USP[2]

Introduction: Crack/cocaine when withdrawal abruptly after repeated administrations is associated with physical and psychological disorders, such as depression. The hippocampal cholinergic system has been implicated in drug addiction and in anxiety and depression disorders. The current study was designed to investigate the involvement of the hippocampal cholinergic system in depressive-like behaviors associated with crack/cocaine withdrawal in Swiss male mice. Methods**:** Swiss male mice (CEUA nº 48/2013 and nº 39/2018) were exposed to crack/cocaine smoke (burning 200 mg) once a day, for 5 min, and for 5 consecutive days. Twenty-four or 48h after the last exposure, mice were submitted to the forced swim test (FST). Also 24 h after the last exposure, serum corticosterone levels and the enzyme acetylcholinesterase (AChE) activity in the hippocampus were analyzed. And the role of hippocampal M1 receptors was evaluated with the administration of pirenzepine(0.06 nmol; M1 selective muscarinic receptor antagonist),5 min before the animals were submitted to FST. **Results:** Our results demonstrated that 24h or 48h after the last exposure to crack/cocaine smoke animals showeda depressive-like behavior in FST; they also showed an increased serum corticosterone levels (only 24 h). Pirenzepine was able to reverse the depressive-like behavior induced 24 h after the last exposure to crack/cocaine smoke. However, AChE activity and the concentration of total proteins in the hippocampus did not change. **Conclusion:** Our results demonstrated that 24 h after the last exposure to crack/cocaine smoke (1) the animals showeda depressive-like behavior; and (2) this behavior depends on the activation of M1 receptors in the hippocampus; or (3) activation of the HPA axis.

02.023 Evaluation of the effects of moderate aerobic exercise on PTEN/AKT pathway in mice cerebellum. Matumoto AM, Kawamoto EM, Andreotti DZ ICB-USP

Introduction: Physical exercise has been extensively studied through the last forty years and its therapeutic effects have been consistently reported for a number of diseases, from cardiovascular disease to psychiatric disorders, such as depression and autism spectrum disorder. Albeit a vast number of studies have focused on the effects of physical exercise on the hippocampus, there is still a paucity on other brain areas, such as the cerebellum. Currently, the cerebellum has left the position of being solely a motor region and has begun to be comprised to the limbic region for its key role in many motor, cognitive and emotional processes, and its implication in some psychiatric disorders, such as autism spectrum disorder, bipolar disorder and major depression disorder. Hence, there is an urge to collect more data about the mechanisms of physical exercise on the cerebellum, in order to improve therapies and enlightenment of its correlations to improvement in social behavior, memory and cognition. **Aim:** Thus, this project was designed to evaluate the effects of chronic moderate physical exercise on the cerebellum of mice, through the PTEN/AKT/mTORC signaling pathway. PTEN is known by its action in suppressing the AKT and, consequently, its downstream signaling pathway, which is involved in synaptic plasticity and cellular growth, survival, proliferation and is directly correlated to the exercise AMPK/mTORC pathway. **Methods:** This project was approved by the Animal Research Ethical Committee (nº129/2017). Animals were divided into two groups: sedentary (Sed) and exercised (Exe). Three-month-old mice were previously familiarized to the treadmill and their weight and individual maximum velocity were acquired before and after the training protocol. The aerobic physical exercise protocol was done by using the mice treadmill for four weeks, the velocity and time of sessions were increased per week, resulting in 50% of maximum velocity per 60 min session by the end of the protocol. Then the groups were subjected to the following behavioral tests: marble burying, elevated plus maze, open field, novel object recognition, social interaction and the inhibitory avoidance task, followed by euthanasia and cerebellar protein expression was evaluated by Western blotting. Samples from other brain regions were also collected for further assays. **Results:** The results presented here were analyzed by Student's T test or One-Way ANOVA, followed by Tukey's post-hoc test, considering significant the results where $p \leq 0,05$. Exe had increased mobility (n=10/group; p=0,03) and velocity (n=10/group; p=0,01) in the open field and showed more interest in social interaction than the Sed group (n = 10/group; $F(6,36)=7.302$; $p<0,001$). The western blotting was performed with cerebellum protein extract and PTEN protein was increased in the Exe group (n=5/group; p=0,02), probably due to the increase in PPARγ induced by the physical training. **Conclusion:** Therefore, the effects of the physical exercise have impact on both cognition and on protein synthesis. Next steps include verifying plastic synapse related proteins, such as NMDA and AMPA glutamate receptors and PSD95, and also other brain regions in order to compare our results to the literature. **Financial Support:** FAPESP (processo nº 2017/20938-4).

02.024 Biological evaluation of a library of bivalent derivatives as potential theranostic tools for Alzheimer's disease. Gonçalves AE[1], Gandini A[2], Poeta E[2], Sabaté R[2], Bartolini M[2], Monti B[2], Strocchi S[2], Paglia S[2], Grifoni D[2], Bolognesi ML[2]
[1]Univali, [2]Università di Bologna

Introduction: The only way to have a definitive diagnosis of Alzheimer's disease (AD) is identifying the pathological hallmarks, β-amyloid and tau misfold proteins, postmortem by autopsy. Thus, it is of great interest searching for theragnostic small molecules, which integrate therapeutic and imaging functionalities, with potential to diagnose and treat AD [1]. In light of this, we previously synthesized a small library of 24 bivalent 2,4-thiazolidinedione derivatives, rationally designed with the aim to be anti-aggregating compounds, and able to fluorescently label misfolding proteins. **Methods:** First, to study the native fluorescence, the compounds were dissolved in ethanol, and the spectra were recorded using a spectrofluorometer. Then, to assess neurotoxicity on primary cultures of cerebellar granule neurons (CGNs), the cells were treated with the compounds at 10μM, and after 24 h the Hoechst 33342 staining was used to quantify apoptotic nuclei of cells [2]. To track Aβ aggregation we used *Escherichia coli* AD model, where the cells BL21 (DE3) carrying the DNA sequence of Aβ42 were treated with compounds and Thioflavin-S (Th-S) to quantify the aggregation by fluorescence[3].And finally, we selected the one most promisor compound to test in in vivo *Drosophila melanogaster* AD model, verifying the lifespan and climbing behavior of transgenic flies expressing Aβ42 on days 7, 14 and 21 of treatmentof one compound at 10, 20 and 50 μM concentrations [4].**Results:** Among the 24 synthesized compounds, fifteen were able to emit fluorescence, and 7 of them showed an emission wavelength higher than 500 nm.22 compounds showed not to be toxic to primary neurons. Moreover, the preliminary biological tests showed that 6 compounds were effective in inhibiting the Aβ42 aggregation process of more than 40% in the *E. coli* model, at 10 μM concentration. Taking these results together, we were able to select one compound to test on *D. melanogaster* overexpressing Aβ42, and we found that the administration of this compound did not changed their lifespan, but it was able to slow the progression of their locomotor deficits, especially on the 21st day of treatment at the lowest dose. **Conclusions:** Further studies must be done to correlate these in vivo effects with in vitro observations verifying their fluorescence properties when interacting with Aβ aggregates and tau protein to prove the thermostatic capacity of this selected compound to diagnose, treat and monitor the progression of the AD. **References**: [1] Bolognesi, M. L. "From Imaging Agents to Theranostic Drugs in Alzheimer's Disease." Reference Module Chemistry Mol Sc&CHem Eng. p. 74, 2017. [2] Espargaró, A., et al. "Ultrarapid in vivo screening for anti-Alzheimer anti-amyloid drugs." Sci Rep. v. 6, 2016. [3] Uliassi, E., et al. "A Focused Library of Psychotropic Analogues with Neuroprotective and Neuroregenerative Potential." ACS chem neurosci. v. 10, p. 279, 2018. [4] Costa, R., et al. "Testing the Therapeutic Potential of Doxycycline in a Drosophila melanogaster Model of Alzheimer Disease." J Biol Chem.v. 286, p. 41647, 2011. **Acknowledgments:** Part of this work was conducted during a scholarship of A.E.G supported by the International Cooperation Program CAPES/PDSE at the University of Bologna. Process #88881.187586/2018-01.

02.025 SUMOylation: **A new neuroprotective target for Parkinson's disease?** Soares ES, Junqueira SC, Zanella CA, Mansur DS, Prediger RDS, Cimarosti HI UFSC
Introduction: SUMOylation-mediated neuroprotection is emerging as an important new field of investigation. In this post-translational modification, SUMO (small ubiquitin-like modifier) is conjugated to target proteins on a 3-step enzymatic pathway and deconjugated by sentrin-specific proteases (SENPs). Recent discoveries suggest that protein SUMOylation might play a neuroprotective role in neurodegenerative diseases, such as Parkinson's disease (PD), representing a potential therapeutic strategy. The present study aims to investigate whetherSUMOylationis altered in PD models and the effects of manipulating SUMO levels on neuroprotection. **Methods:** Adult male Wistar rats (Animal Research Ethical Committee approval: Protocol 830, 104 - CEUA/UFSC) received 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)or 0.9% NaCl (vehicle) through intranasal administration (i.n.),at a concentration of 1 mg/nostril. Then, the olfactory bulb, striatum and hippocampus were collected for analysis at the following times: 1, 6 and 24 hours, 7, 14 and 21 days. As an in vitro PD model, SH-SY5Y cells maintained in Dulbecco's Modified Eagle's Medium (10% fetal bovine serum) were exposed to 1-methyl-4-phenylpyridinium (MPP^+) (1.5 mM) or phosphate buffered saline (vehicle) for 24 and 48 hours. Levels of SUMO-1, SUMO-2/3, Ubc9 and SENP-3 were quantified by Western blotting. In order to modulate SUMOylation, lentivirus to knockdown SENP3 (shRNA constructs, with the following sequence: 5'-ACTGGCTCAATGACCAGGTGATGAACATG-3')was produced. This virus is currently being testedin the in vitro PD model, and will be subsequently tested in vivo in the MPTP-administered rats. **Results:** Levels of SUMO-2/3 conjugated proteins decreased in the striatum at 14 days post-MPTP i.n. administration, a time point that corresponds to the onset of motor changes. In the hippocampus, a decrease in global SUMO-1 conjugation was observed at 7 and 14 days, whereas Ubc9, the only SUMO conjugating enzyme, decreased at 21 days. Differently from these structures, global SUMOylation levels remained constant in the olfactory bulb. In the in vitro model, MPP^+ decreased global SUMO-2/3 conjugation at 24 and 48 hours and caused about 20%cell death in SH-SY5Y cells. **Conclusion:** So far, our results suggest that SUMOylation is decreased in both in vivo and in vitro models of PD. Using lentivirus to knockdown SENP3, and thus increase SUMO-2/3 conjugation, will help to clarify whether SUMOylation plays a neuroprotective role. This study will contribute to understand critical molecular mechanisms involved in the pathogenesis of PD and might identify SUMOylation as a potential target for the development of new therapies. **Financial support**: CNPqand CAPES. **Acknowledgements**: UFSC Central Animal House, Post-graduate Program in Pharmacology - UFSC.

02.026 Nicotinic α7 receptor controls acetylcholine spillover from the rat motor endplate during high frequency nerve firing. Santana LMC, Silva CRA, Prado WA, Matos JBAGN, Sá PC UEM

Introduction: Alfa 7 neuronal (n) nicotinic (N) receptors (Rs) (α7-nNRs) are present in Schwann cells (SC) and skeletal muscle. Despite α7 nAChR can sense and control ACh spillover from the neuromuscular synapse the mechanisms underlying communication between SCs and the nerve terminal are not entirely understood. Here, we investigated whether adenosine could be the gliotransmitter mediating inhibition of transmitter release following α7 nAChR activation. **Methods:** The Ethics Committee for Experimental Animals Studies of the State University of Maringá approved (ECEAS7227300915) this study. Rat phrenic hemidiaphragms were used to measure nerve-evoked (i) myographic recordings and (ii) [^{3}H]ACh release. The phrenic nerve-diaphragm preparations of rat were mounted as described elsewhere (Bülbring, Brit. J. Pharmacol. 1: 38, 1946). The muscular tension (A/B) registered at the beginning of high frequency (50 Hz) elicited by electric indirect stimulation was the parameter analyzed. The tetanic (T) stimulation was applied each 20 min intervals, during 10s. A/B-value control was obtained after the muscular tetanic contraction to be stable. The 3H]ACh release was evoked by two periods of electrical stimulation of the phrenic nerve, starting at the 12th (S1) and 39th (S2) minutes after the end of washout (zero time).**Results:** The selective α7nAChR agonist, PNU282987, decreased tetanic (50 Hz-bursts)-induced muscle contractions. This effect, which was mimicked by the cholinesterase inhibitor neostigmine. The α7 nAChR antagonist, methyllycaconitine prevented the inhibitory effects of neostigmine and PNU282987. Adenosine and blockade of A_1 receptors with DPCPX prevented inhibition of PNU282987. **Conclusion:** Data suggest that α7 nAChR controls tetanic-induced ACh spillover from the neuromuscular synapse by favoring adenosine outflow from PSCs via activation of presynaptic A_1 inhibitory receptors. **Keywords:** Nicotinic α7 receptors; Acetylcholine release; Adenosine A_1 receptor; Cholinesterase inhibitors; Neuromuscular junction; Perisynaptic Schwann cells.

02.027 Structure-activity relationships, **molecular docking and biological evaluation of sulfonamides on the memory of animals with Alzheimer's disease**. Souza MM[1], Andreolla MCA[1], Souza AS[2], Ferreira LLG[3], Andricopulo AD[2], Brighente IMC[2], Yunes RA[4], Nunes R[4], Oliveira AS[4] [1]Univali, [2]Unifesp, [3]UFSCar, [4]UFSC

Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder, characterized by irreversible and progressive memory loss, which decreases daily tasks performance, reduces speech abilities and visual perception, culminating in total dementia. AD affects thousands of people worldwide regardless of ethnicity or socioeconomic conditions. As a cure of AD has not yet been developed, the disease has been the focus of major worldwide research programs. Some medicines available for the treatment of AD are acetylcholinesterase (AChE) inhibitors, such as tacrine, rivastigmine, donepezil and galantamine. AChE is an enzyme responsible for acetylcholine (ACh) hydrolysis. By inhibiting the enzyme, those drugs increase cerebral ACh levels. **Methods** The effects of five synthetic sulfonamides were evaluated on the cognitive deficits of animals with streptozotocin (STZ)-induced Alzheimer Disease (AD). Memory (inhibitory avoidance), ambulation (open field), anxiety (elevated plus maze) and oxidative stress (ex vivo) were evaluated. In vitro assays were performed to assess the inhibition of acetylcholinesterase (AChE) and the data were confronted with molecular docking for the discussion of structure-activity relationships. **Results:** The memory of animals treated with compounds derived from morpholine (1), hydrazine (3) and 2-phenol (5) was improved. 3 was the most promising, yielding excellent results in the inhibitory avoidance test. Moreover, the compounds did not exhibit any deleterious effect on the animals' ambulation in the Open Field test. Molecular docking confirmed the results obtained in the AChE inhibition assay. **Conclusions**: In short, 1, 3 and 5 can revert STZ-induced deficits and show anti-Alzheimer potential. In addition, these agents produce significant anxiolytic and antioxidant effects. **Financial Support:** CAPES/CNPq/UNIVALI

02.028 Zika virus neuroinfection impairs Dentate-CA3 hippocampal synaptic plasticity in adult mice. Neves GA, Castro NG, Figueiredo CP, Aragão FB, Neris RLS, Souza INO, Miranda IA, Clarke J, Poian AT, Ferreira ST UFRJ

Introduction: Zika virus (ZIKV) infection during gestation has been recently associated with severe neurodevelopmental abnormalities. Signs of central neurological disease have also been described in infected adults, but the underlying mechanisms are unknown. Previous data from our group show that ZIKV affects the adult mouse brain, targeting mature neurons and affecting synaptic function. Our group has found a selective regional pattern of viral replication and neuropathological changes, which, together with impaired performance in memory tasks, implicated the principal cells of the dentate gyrus (DG) and CA3 as relevant targets. Objective: We aimed at investigating whether ZIKV neuroinfection affects plasticity in synapses between DG mossy fibers and CA3 pyramidal neurons, and also whether any such changes are due to neuroinflammation. Methods**:** Brazilian (Pernambuco strain) ZIKV (or MOCK) were infused i.c.v. in adult Swiss mice and allowed to replicate for 6-10 days before euthanasia (CEUA-CCS-UFRJapproval#043/2016 and #126/2018).Dorsal hippocampal slices preserving the DG-CA3 pathway were used for field excitatory postsynaptic potential (fEPSP) recordings. **Results:** Control mossy fiber-evoked fEPSPs recorded in CA3b stratum lucidum showed marked paired-pulse facilitation (PPF) at 40 ms intervals (2.4 +/- 0.2x, n = 10), while ZIKVinfection significantly reduced PPF (1.7 +/- 0.2x, n = 8, p = 0.040). High-frequency stimulation (HFS) induced robust post-tetanic potentiation (PTP) of the fEPSP to 384 +/- 43% but infection reduced PTP to 201 +/- 22% (p = 0.003). Fourty minutes after HFS, the fEPSP was still 137 +/- 8% of baseline in control slices, showing long-term potentiation (LTP), while infection reduced LTP to 111 +/- 5% (p = 0.015). We next examined the role of microglia-derived TNF-alpha in the ZIKV-induced changes in synaptic plasticity. The microglial inhibitor minocycline (50 mg/kg i.p., 3 doses one week before, 3 doses one week after the virus injection), as well as the TNF-alpha antagonist infliximab (0.2 ug i.c.v., 4 daily doses after ZIKV injection) prevented the infection-induced impairment in synaptic plasticity. **Conclusion:** ZIKV impairs both short-term (PPF and PTP) and long-term plasticity (LTP) of the mossy fiber to CA3 synapse, which might explain the associated cognitive deficits. These changes seem to be dependent on microglial activation and may be prevented by appropriate control of neuroinflammation. **Support**: INCT Neurociência Translacional, IN Pesquisa e Inovação em Medicamentos e Novos Alvos Terapeuticos, FAPERJ, CNPq, CAPES, FINEP.

02.029 Study of the participation of nitrergic neurotransmission in the lateral prefrontal cortex in cardiovascular responses by acute restraint stress in rats. Alves FHF[1], Goulart MTG[1], Crestani CC[2], Busnardo CB[2], Corrêa FMA[3] [1]UFLA, [2]Unesp-Araraquara, [3]USP

Introduction: The insular cortex (IC) is a brain structure involved in the central control of the cardiovascular system. Cardiovascular responses were reported after electrical or chemical stimulation of IC. These responses could be the neural subtract by IC connections with structures that participate of the central control of the cardiovascular system, such as the nucleus dorsal vagus and the nucleus of solitary tract. Nitrergic neurotransmission in the central nervous system (CNS) is well established in the central control of cardiovascular system and its present in IC. The NO in CNS is a neuromodulator that acts by activating the guanylate cyclase (GC) cascade producing guanosine monophosphate cyclase (cGMP). Although some papers have shown the participation of some brain areas and neurotransmitters in the central control of cardiovascular activity during stress phases, the mechanisms and the possible areas of the brain that control the cardiovascular system during stress situations doesn't have totally elucidate. There are no studies showing the involvement of nitrergic systems present in IC in the modulation of cardiovascular activity during stress situations. So, the objective of the present work was to investigate the involvement of nitrergic neurotransmissions into IC modulating the cardiovascular responses during the restraint stress in rats. **Methods:** Male Wistar rats had guide cannulas bilaterally implanted in the IC for drugs injection. Polyethylene catheter was implanted in the femoral artery for mean arterial pressure (MAP) and heart rate (HR) recording using a computerized acquisition system. The restraint stress was realized putting the animals in a small plastic cylindrical restraining tube (diameter= 6.5 cm and length=15 cm) during 30 minutes ethics committee number (025/16). It was used a selective nNOS inhibitor, N-Propyl (0.4 nmol / 100nL); a NO scavenger, Carboxi-PTIO (2 nmol / 100 nL); and a specific GC formation inhibitor, ODQ (2 nmol / 100nL). The drugs were microinjected in the IC 10 minutes before the animals be submitted to acute restraint. **Results –** Acute restraint (n=28) caused significant increases in the MAP (before restraint: 92±4 and restraint: 107±6 mmHg, $t=3$, $p<0.05$) and in the HR (before restraint: 345±11 and restraint: 410±12 bpm, $t=5$, $p<0.005$). Administration of vehicle in the IC did not affect the changes in the MAP (∆ MAP: 15±2 vs 16±3 mmHg, $t=0.2$, $p>0.05$) and HR (∆HR: 72±8 vs 69±6 bpm, $t=0.6$, $p>0.05$) to acute restraint. However microinjection of drugs cited above, increase the tachycardic responses during restraint stress $F_{(3, 14)}= 4{,}106$, $P=0{,}0277$, with no changes in pressor responses $F_{(3, 14)} = 0{,}6146$, $P=0{,}6168$. **Conclusion -**In conclusion our results show that the nitrergic neurotransmission into the IC modulate the tachycardic responses during restraint stress, without significant changes in blood pressure. **Financial support:** FAPEMIG, FAPESP and CNPq

02.030 Evaluation of anti-neuroinflammatory effect of a standardized extract of *Amburana cearensis* **in a microglial cell line**. Azul FVCS, Machado de Jesus N, Araújo AB, Ferreira MKA, Norberto JN, Sousa JAC, Almeida TS, Leal LKAM UFC

Introduction: Neurodegenerative diseases are some of the greatest causes of disability in the world and are exacerbated by inflammatory processes. Microglia are part of the innate immunity and are activated in different disorders affecting the central nervous system (CNS). They release inflammatory mediators such as nitric oxide, which is produced by the enzyme inducible nitric oxide synthase (iNOS). Amburana cearensis (cumaru) is a native plant from Brazilian northeast and exerts an anti-inflammatory activity in disease models in the peripheral system. Thus, the aim of the present work was to investigate whether its anti-inflammatory activity could be applied to cells of the CNS. **Methods:** Microglial cells (BV2 line) were maintained in RPMI-1640 medium, 10% FBS, 5% CO_2. Inflammatory activity: BV2 cells were exposed to the standardized dry extract of Amburana cearensis (DEAC; 1-100 µg/mL) and stimulated with LPS (1µg/mL) for 24 h; the release of nitrite to the medium was measured by the Griess test. Cytotoxicity: BV2 cells were exposed to DEAC (5-100 µg/ml) or vehicle (DMSO 0.1%) for 24 h, MTT (0.5 mg/ml) was added for 90 min, the supernatant was withdrawn, pure DMSO added, and the absorbance measured at 570 nm. iNOS expression was evaluated by Western blot: BV2 cells were exposed to DEAC (100 µg/ml) and stimulated with LPS (1 µg/ml) for 24 h; the cells were then centrifuged, the supernatant was discarded, and total protein extracted for Western Blot analysis and labelling of iNOS. **Results:** In the cytotoxicity test, DEAC did not decrease cell viability (97% to 105% of viability of vehicle group) at any of the concentrations tested. In the Griess test (inflammatory activity), two concentrations of DEAC decreased LPS-stimulated nitrite release: 50 µg/ml (74.3 ± 2.6% of LPS control group) and 100 µg/ml (54.0 ± 2.0%). In the Western blot analysis, DEAC (100 µg/ml) reduced iNOS density by 41.6% when compared to the LPS treated group. **Conclusion:** As DEAC exerts anti-neuroinflammatory action (as measured by nitrite production and its associated enzyme iNOS) at concentrations that did not cause cell toxicity, we propose Amburana cearensis as a potential candidate for the treatment or prevention of neuroinflammatory diseases

References: Luci Maria Sant'Ana Dusse. Revisão sobre óxido nítrico. J. Bras. de Patologia e Medicina Laboratorial, Rio de Janeiro, v. 39, n. 4, p. 343-350, 2003.HilmaraHélia de Souza Amaral. Extrato seco padronizado de amburana cearensis cultivada e constituintes químicos modulam a inflamação em um novo modelo de asma exacerbada em camundongos balb/c e a resposta neutrofílica *in vitro*. Repositório UFC, 2017. Xiaobao Zhang. Dexmedetomidine inhibits inducible nitric oxide synthase in lipopolysaccharidestimulated microglia by suppression of extracellular signal-regulated kinase. Neurological Research, V.37, NO.3, p. 238-245, 2015. **Acknowledgments**: CEFAC; FUNCAP; CAPES; CNPQ; UFC

02.031 The ventral medial prefrontal cortex CRF1 receptor modulates the tachycardic activity of the baroreflex. Brufatto JPT[1], Uliana DL[2], Resstel L[3], [3]Lagatta DC, Silva EMF[3], Assis ABB[3] [1]USP, [2]University of Pittsburgh, [3]FMRP-USP

Introduction: The glutamatergic pathway of the ventral medial prefrontal cortex (vMPFC), has a facilitatory role in the cardiac activity of baroreflex, by the activation of NMDA receptors. It is already known that the vMPFCis formed by Infralimbic (IL) and Prelimbic (PL) regions. Corticotrophin Releasing Factor Receptors type1 and 2 (CRF1 and CRF2) are present in this area and it was already seen that the CRF1 receptor are colocalized in neurons with glutamate vesicles. Our hypothesis is that the IL and PL regions through CRF1 and CRF2 receptors can modulate the bradycardic and tachycardic responses of the baroreflex. **Methods**: Male Wistar rats, weighing 240-260g, had stainless steel guide cannulae bilaterally implanted into thevMPFC. Afterwards, a catheter was inserted into the femoral artery for mean arterial pressure (MAP) and heartrate (HR) recording. Baroreflex activation was induced by infusion of sodium nitroprusside and phenylephrine through a second catheter implanted into the femoral vein. **Results**: The injection of the CRF1 receptor antagonist (CP376395,4.5nmol/200nL) in the IL did not change bradycardic ($F_{(2.12)}$=2.83;p>0.05,n=7) and increased tachycardic responses ($F_{(2.12)}$=15.47;P<0.05,n=7), although a lower dose of this antagonism (0.45nmol/200nL) did not alter bradycardic ($F_{(2.15)}$=0.02;p<0.05,n=6) nor tachycardic responses ($F_{(2.15)}$=0,39;p>0.05,n=6). The injection of CRF1 receptor antagonist (CP376395,4.5nmol/200nL) in the PL did not induce changes in bradycardic ($F_{(2,14)}$=3.90,p<0.05,n=5), however, it increased tachycardic responses ($F_{(2.14)}$=1.08,p>0.05,n=5). The injection of CRF2 receptor antagonist (K41498,4.5nmol/200/nL) in the IL did not alter bradycardic ($F_{(2.12)}$=0.30,p>0.05,n=6) nor tachycardic responses ($F_{(2.12)}$=0.25;p>0.05,n=6).The injection of the CRF2 receptor antagonist (K41498,4.5nmol/200nL) in the PL did not alter bradycardic ($F_{(2.12)}$=0.03,p>0.05,n=5) nor tachycardic responses ($F_{(2.12)}$=0.73;p>0.05;n=5). The injection of the non-selective CRF receptors agonist (0.2nmol/200nL) in the IL did not alter bradycardic ($F_{(2.15)}$=0.85;p>0.05,n=7), but decreased tachycardic responses ($F_{(2,15)}$=4.52;p<0.05,n=7), although a lower dose of this agonism (0.02nmol/200nL) did not alter bradycardic ($F_{(2.12)}$=0.05;p>0.05,n=5) nor tachycardic responses ($F_{(2.12)}$=0.70;p<0.05,n=5). The injection of the CRF1 receptor antagonist (CP376395,0.45nmol/200nL) prior to injection of the non-selective agonist (Urocortin,0.2nmol/200nL) in the IL did not alter bradycardic ($F_{(2.15)}$=0.13,p>0.05,n=6) but prevented tachycardic responses to increase ($F_{(2.15)}$=0.49;p>0.05,n=6). The injection of the CRF2 receptor antagonist (K41498,0.45nmol/200nL) prior to injection of the non-selective agonist (Urocortin,0.2nmol/200nL) in the IL did not alter bradycardic($F_{(2.8)}$=2.47;p>0.05;n=5), and had continued to increase tachycardic responses ($F_{(2.8)}$=9.99;p<0.05;n=5). **Conclusions:** The results suggest that CRF1 but not CRF2 receptors in the IL and PL regions of the vMPFC have an inhibitory role on the tachycardic and not on the bradycardic activity of baroreflex.

02.032 Crack cocaine affects larval development, **motility and female fertility in** *Drosophila melanogaster*. Brito IRR, Santos JF, Angelo LKGA, Araújo LA, Castro OW, Silva Filho EA, Rodarte RSR UFAL

Introduction: Crack cocaine is a drug of abuse that stimulates the central nervous system. The pathophysiological and toxicity mechanisms promoted by crack cocaine use is unclear. We used Drosophila melanogaster as an experimental model to evaluate the crack cocaine toxicity *in vivo*. Our goal was to identify the damage induced by this substance over female fertility and during the normal development of Drosophila. **Methods:** Individuals were exposed to crack cocaine from the first instar larval stage (L1) to the adult stage (developmental assay), when they were transferred to control medium and the number of deaths counted over time (lifespan). We have also employed larval motility tests and fertility assays. For all experiments, animals were fed with standard Drosophila medium containing crack cocaine in different concentrations: 0.25; 0.5; 0.75, 1.0, 1.25 and 1.50 mg /ml of. For the developmental assay, the L1 larvae were transferred to standard Drosophila medium (control group) or standard medium containing crack cocaine at different concentrations. The individuals were monitored from L1 stage until adulthood, when females where collected and the Lifespan assay performed, lasting about 65 days. For the motility test, the larvae were removed from the medium at 24h of the third instar larval stage (L3), transferred to an agarose plate and recorded moving for 1 minute, allowing us to determine the travelled distance. For the fertility test, virgin females were exposed to crack cocaine for 7 days and then crossed individually to *naïve* males in vials for 4 days, then the number of viable pupae and adults resulting from these crossing was determined. The data from the lethality, motility and fertility tests were analyzed using the one-way ANOVA test followed by the Bonferroni Multiple Comparison Test; ***: $p < 0.001$ compared to control. Lifespan data were analyzed using the survival curve with log rank test. $p < 0.001$. **Results:** The samples containing higher concentrations of crack cocaine showed a significant increase in larval lethality when compared to control. Regarding the larval motility, all crack concentrations have caused a decrease in larval motility. In relation to the lifespan of adult females we did not observe any significant reduction in the survivorship of the flies that developed in standard medium containing crack cocaine. Our fertility assay showed that all concentrations caused a significant reduction in the number of viable embryos compared to control, as indicated by the number of pupae resulting from individual crosses containing single females exposed to crack. **Conclusions**: Altogether, our data showed that crack lead to deleterious effects on the larval development of *Drosophila,* evidenced by the reduced survival at this stage, as well as negatively influences the female fertility. **Financial support**: FAPEAL, CNPQ **References:** Linford, N.J. Measurement of Lifespan in Drosophilamelanogaster. J. Vis. Exp. P- 71, 2013; Nichols, C.D., Becnel, J. Methods to Assay Drosophila Behavior. J. Vis. Exp. P-61, 2012.

02.033 Increased glucose availability reduces neuronal activity in hippocampus, subiculum and thalamic nuclei after status epilepticus. Santos JF[1], Melo IS[1], Santos YMO[1], Pacheco ALD[1], Costa MDA[1], Oliveira KB[1], Brito IRR[1], Duzzioni M[1], Sabino-Silva R[2], Borbely AU[1], Castro OW[1] [1]UFAL, [2]UFU

Introduction: Status Epilepticus (SE) is defined as continuous and self-sustaining seizures, which trigger hippocampal neurodegeneration, inflammation and gliosis. SE is typically characterized by neuronal hyperexcitability and promotes a sharp increase of regional cerebral blood flow and oxygen consumption correlated with enhancement in glucose utilization. Control of glucose availability can protect neurons from hyperexcitability. In this study, we evaluated the influence increased glucose availability in neuronal activity after SE. **Methods:** Experimental procedures were approved by the Ethical Committee for Animal Research of UFAL (04/2016). Male Wistar rats (n=12 [240-340g]) were submitted to stereotaxic surgery for cannula implantation in the hilus of dentate gyrus (DG) of left hippocampus. Animals received unilateral microinjections of pilocarpine (PILO) in hippocampus (H-PILO, 1.2mg/μL, 1 μL). After 5 minutes of H-PILO, PILO+VEH (P+V) and PILO+GLU (P+G) received microinjections of vehicle (VEH, saline 0.9%, 1 μL) or glucose (3mM [diluted in saline]), respectively, in the same site of PILO. Animals were perfused after 24 hours of SE and the neuronal activity was evaluated by c-fos immunofluorescence. C-fos positive neurons (Cfos+) were counted (ImageJ–NIH) in hippocampus and thalamic nuclei. Results were expressed as mean±SEM, compared by unpaired t test. **Results:** The increase in glucose availability (3mM) after PILO resulted the same effect on neuronal activity in both hippocampi and thalamic nuclei. Increased glucose reduced the total number of cfos+ neurons in the DG hilus (PV, 0.92±0.16; PG, 0.39±0.13) and CA1 (PV, 0.83±0.21; PG, 0.2±0.09) subfield of hippocampus compared to control. Similarly, intrahippocampal infusion of glucose was able to decrease neuronal activity in thalamic nuclei[lateral posterior (PV, 1.0±0.1; PG, 0.35±0.05), centrolateral (PV, 1.0±0.2; PG, 0.3±0.08) and posterior paraventricular (PV, 1.0±0.2; PG, 0.4±0.1)]. **Conclusion:** Our preliminary findings suggest that controlling glucose availability protects the brain from the characteristic hyperexcitability of earlier stage of epileptogenic processes. FINANCIAL SUPPORT: FAPEAL, CNPQ, CAPES. **Acknowledgements**: To all those involved in the Laboratory of Neuropharmacology and Integrative Physiology.

02.034 Pharmacological validation of a new animal model of anxiety in mice: **A Single subconvulsant dose of pilocarpine**. Vieira MPS[1], Souza FMA[1], Santos Neto JG[1], Silva OBS, Souza GF[1], Correia WBZGB[1], Duarte FS[2], Lima TCM[3], Duzzioni M[1]
[1]UFAL, [2]UFPE, [3]UFSC

Introduction: Recently, our research group showed that a single subconvulsant dose of pilocarpine (PILO) triggered short- and long-term anxiogenic-like behavior in rodents, suggesting a new and useful experimental model for studying anxiety. In this study, we validate that new proposed model of anxiety with the administration of anxiolytic drugs. Methods**:** Female Swiss mice were treated with scopolamine methylbromide (1 mg/Kg, s.c.) followed 30 min later with saline (SAL, NaCl 0.9%, i.p.) or PILO (75 mg/Kg, i.p.). After 24 h, animals were treated with SAL (i.p), diazepam (DZP; 1.5 mg/Kg,i.p) or fluoxetine (FLU; 10 mg/Kg,i.p). Another group was treated daily for 30 days with the same drugs and doses. And, in both groups, 30 min after the last treatment the animals were submitted to the elevated plus maze (EPM) and open field (OFT) tests. **Results:** After 24 h, animals treated with PILO+SAL reduced the percentage of entries on the open arms (%AOE; $F_{3,25}$=1.65; P<0.05) of the EPM, indicating an anxiogenic-like behavior. This behavior was only blocked by DZP (PILO+DZP; P<0.05). The FLU (PILO+FLU) reduced the percentage of time (%OAT; P<0.05) and entries (%AOE; P<0.05) in the open arms of the EPM, indicating an anxiogenic-like behavior. After 30 days, the treatment with PILO (PILO+SAL) increased protected stretch-attend postures (pSAP) in the EPM ($F_{3,25}$= 4.71;P<0.05), indicating an anxiogenic-like behavior. However, the number of pSAP was blocked by DZP (PILO+DZP; P<0.05) and FLU (PILO+FLU; P<0.05). There were no changes in the locomotor activity of the animals submitted to OFT. **Conclusions:** Our data provide pharmacological validation showing that two anxiolytics drugs maintain their effects in the model of anxiety proposed by us. In addition, this model can be used to identify new compounds with anxiolytic properties.

02.035 Solutol® HS 15 has anticonvulsant and neuroprotective actions in an experimental model of temporal lobe epilepsy. Paulino PAT, Arroxelas-Silva CL, Conceição-Silva GF, Santos ED, Pereira-Silva W, Castro OW, Gitaí DLG UFAL

Introduction: Epilepsy is characterized by the occurrence of spontaneous and recurrent seizures that affects approximately 50 million people worldwide. Nearly 35% of patients with Temporal Lobe Epilepsy (TLE) acquire medically intractable epilepsy despite adequate antiepileptic drug (AED) treatment. Furthermore, AED therapy can lead to side effects and most TLE patients have memory and mood dysfunction that are not alleviated with the available treatment. Hence, there is an urgent need for new AEDs. Solutol® HS 15 (SOL) is a pharmaceutical excipient used clinically to solubilize drugs. Recently, studies have shown that SOL presents an inhibitory effect on neuronal calcium influx and a neuroprotective action in cerebral ischemia. Here, we investigated the hypothesis that the SOL presents an anticonvulsant and neuroprotective effects on Pilocarpine (PILO)-induced Status Epilepticus (SE), a widely used model of TLE. **Methods:** adult male Wistar rats received intrahippocampal microinjection of SOL (1.6 mg / kg, n = 10) or Saline (0.9%, n = 7) 30 minutes before SE-induction by intraperitoneal (ip) injection of PILO (30mg / kg). The action of PILO was potentiated by lithium chloride (127 mg / kg, ip) administered 16 hours prior. Immediately after PILO-injection, the animals were continuously video-monitored for the seizure counting during 90 minutes of SE, aborted by diazepam (5 mg/kg, ip).The seizure severity was assessed according to Racine´s scale. At 24hours after SE, the animals were euthanized and the brains processed for Fluoro-Jade (FJ) histochemistry to assess the neurodegeneration in hippocampal formation. Statistical analysis was performed using Student t-test (GraphPad, Prism 6.0). All experimental procedures were approved by the Ethical Committee of the Federal University of Alagoas (Protocol 37/2017). **Results:** the animals pretreated with SOL had 39% lesser seizures (stage 2 to 5) during SE compared to saline group(p=0.010). Notably, the SOL groups had a significant decrease of FJ-positive neurons inthe CA3 region of bothipsilateral (54%, p=0.026) and contralateral (48%, p= 0.010) hippocampus compared to control animals. **Conclusions:** SOLhadan inhibitory effect on seizures during SE and a neuroprotective action on hippocampus (CA3 subregion) of rats submitted to SE-induction. The data are promising to investigate the potential of SOL for antiepileptogenic and anticonvulsive role in chronic epileptic animals. **Financial Support:** CNPQ (466995/2014-8), FAPEAL and CAPES. **Acknowledgements:** To all those involved in the Laboratory of Neuropharmacology and Integrative Physiology.

02.036 Maternal crack cocaine use in rats alters depression, **anxiety-like behavior**, **memory impairment and seizure susceptibility in offspring**. Pacheco ALD, Melo IS, Santos JF, Costa MA, Souza FMA, Santos YMO, Silva BRM, Oliveira KLS, Santos Neto JG, Borbely AU, Duzzioni M, Castro OW UFAL

Rationale: Crack cocaine use is currently one of the main public health problems in many countries. Additionally, an alarming factor is the increase in the number of children intoxicated by crack cocaine during pregnancy, called crack babies. In children, the effects of crack cocaine have been associated with cognitive deficits, difficulty in verbalization, aggressiveness, depression, besides modifying the susceptibility to epileptic seizures in adulthood. Here, we evaluated the effects of crack cocaine exposure in pregnant Wistar rats on anxiety and depression, long-term memory and susceptibility of epileptic seizures in the offspring. **Methods:** Experimental procedures were approved by the Ethical Committee for Animal Research of the Federal University of Alagoas (UFAL) (protocol # 54/2017). Pregnant Wistar rats from the 5th to the 21stgestational daywere exposed to the products of crack cocaine pyrolysis. Pups were kept with their mothers until the 21stday of postnatal life. After 30 days, animals were subjected to behavioral anxiety, depressionand memory tests. At 60 days, the male and female adult animals (F1 offspring) were submitted to stereotaxic surgery for cannula implantation in the hilus of dentate gyrus of the hippocampus. Animals received microinjection of intrahippocampal pilocarpine (H-PILO) in subconvulsantdoses (sH-PILO, 0.6 mg/μL) to analyze the susceptibility of epileptic seizures. Results were expressed as mean± SEM with the unpaired t-test. **Results:** Exposure to crack during the embryonic stage led to anxiogenic behaviors in male and female animals, reducing time spent and entering open arms, as well as a lower frequency of risk assessment as measured by head diving in young male rats. Female rats exposed during pregnancy also presented depressive type behavior. In addition, maternal exposure to crack also leads to impairment of long-term memory consolidation of young rats (F1) and animals as adults (F1). Animals exposed to sH-PILO showed greater susceptibility to epileptic seizures reducing SE latency, increased seizure frequency and total seizure time. **Discussion and Conclusions:** These data suggest that exposure to crack cocaine pyrolysis products during the gestational period leads to the involvement of offspring with the presence of comorbidities such as increased propensity to anxiety and depression, long-term memory deficit and reduction of the threshold of epileptic seizures, which may predispose crack cocaine babies to develop severe clinical outcomes. **Financial Support**: FAPEAL, CAPES, CNPQ. **Acknowledgements:** Members of the Laboratory of Neuropharmacology and Integrative Physiologyof the Department of Physiology and Pharmacology, Institute of Biological Sciences and Health, Federal University of Alagoas (UFAL).