

## Poster Abstracts (by alphabetic order)

---

### **SENSITIVITY TO ETHANOL STIMULATION AND ETHANOL INTAKE IN ADOLESCENT AND ADULT RATS**

*Acevedo Ma. Belén, Spear Norman E, and Pautassi Ricardo Marcos.* Instituto Ferreyra (INIMEC - CONICET). Friuli 2434, Córdoba, CP 5016, 351-481465 int.218, Argentina. Córdoba, CP 5016, 351-4334064. SUNY at Binghamton, NY, 13902, USA. sallycaboo@gmail.com

**Background:** It is important to analyze age-related differences in sensitivity to ethanol, as they can underscore vulnerability factors for the development of alcohol-related problems. The present experiment examined ethanol-induced behavioral stimulation and alcohol intake in adolescent and adult rats. **Methods:** Adult and adolescent male Wistar rats were tested for ethanol-induced behavioral activation (2.5 g/kg, i.g.) in an open field and were then assessed for ethanol intake (vehicle: 1% sucrose) using a 16-day-long ethanol intake protocol. The protocol had four phases, each one 4 days long. Daily, two-bottle choice tests [ethanol vs. vehicle, test duration: 120 min] were conducted in Phase 1,

whereas in Phase 2 animals were given 24 h access to ethanol as the only fluid. Phase 3 (alcohol deprivation) involved standard access to water and food and Phase 4 repeated the procedure of Phase 1. **Results:** Ethanol induced locomotor activation, which was fairly similar in adolescent and adults. Acute ethanol exposure did not alter later ethanol intake. Under conditions of limited access to the drug (i.e., Phases 1 and 4), adults drank significantly more ethanol than did adolescents. On the other hand, ethanol intake under the continuous, 24-h access condition (i.e., Phase 2) was significantly greater in adolescents than in adults. Both ages exhibited a significant increase in ethanol self-administration after the ethanol deprivation phase. **Conclusions:** Our expectation of greater ethanol-induced stimulation in adolescents than in adults was not corroborated. Both ages exhibited similar drug-induced motor stimulation. Patterns of voluntary alcohol consumption seemed to depend on the nature of testing conditions. Adolescents exhibited significantly greater ethanol intake than adults under conditions of continuous, 24-h access to ethanol. This pattern reversed when the drug was offered in a 2-h two-bottle intake test.

Proceeding of the 2011 Meeting of the Latin-American Society for Biomedical Research on Alcoholism  
RACC, 2011, Suplemento (Marzo), 4-51

Grants: PIP CONICET 2010-2012; PICT-PRH  
UNC 2009; SUNY at Binghamton.

**INTRA NUCLEUS ACCUMBENS  
ADMINISTRATION OF 5-HT<sub>2C</sub> RECEPTOR  
ANTAGONIST BLOCKS THE EXPRESSION  
OF ETHANOL-INDUCED BEHAVIORAL  
SENSITIZATION.**

A. L. M., Andrade; K. P., Abrahao; F. O.,  
Goeldner; M.L.O., Souza-Formigoni.  
Departamento de Psicobiologia, Universidade  
Federal de São Paulo-UNIFESP, São Paulo (SP)  
Brazil. andremonezi@gmail.com

Behavioral sensitization to the stimulant effects of ethanol (EtOH) or other drugs, observed in mice as an increase in locomotor activity (LA) after repeated drug administration, has been associated with neuroadaptations in the dopaminergic reward system (mesocorticolimbic pathways). In the nucleus accumbens (Nacc), dopamine release can be modulated by serotonergic 5-HT<sub>2C</sub> receptors. Some studies have reported that its direct administration in the Nacc reduces LA. However, no studies were developed on 5-HT<sub>2C</sub> specific antagonists effects on the behavioral sensitization to EtOH. In the current study we evaluated if Nacc administration of a 5-HT<sub>2C</sub> antagonist (SB-242084) affects the expression of behavioral sensitization to EtOH. Swiss albino male mice received daily i.p. administrations of 2.2 g/kg EtOH or saline for 21 days, having their locomotor activity (LA) weekly evaluated. According to their LA levels on the 21st day of

treatment, EtOH-pretreated mice were classified into 3 subgroups: sensitized (higher levels), intermediate and non-sensitized (lower levels). After the classification process, mice in Experiments 1 and 2, were submitted to surgery for the implantation of a cannulae on the Nacc. Two weeks after the 21st day of treatment, mice were submitted to a set of four pharmacological challenges, 48h apart: 1) Saline Nacc (0.2 µl) + saline i.p.; 2) saline Nacc + EtOH 2.2 g/kg i.p.; 3) SB-242084 1,0 µg/side or 2,0 µg/side Nacc + EtOH i.p. and 4) SB-242084 1,0 µg/side or 2,0 µg/side + saline i.p. The first drug was administered 15 min before the second one, after which mice LA was immediately evaluated for 15 minutes. At both doses, the direct administration of SB-242084 (1.0 or 2.0 µg/side) into the Nacc blocked the expression of behavioral sensitization to the stimulant effect of EtOH. These findings suggest that the expression of behavioral sensitization depends on the integrity of the serotonergic system. If behavioral sensitization proves to be a good animal model of human euphoric effects of EtOH, specific antagonists of 5-HT<sub>2C</sub> receptor could have a potential therapeutic use.

Supported by FAPESP (2008/07203-6), AFIP, CNPq (3067462008-3).

## **EFFECTS OF PRENATAL ETHANOL EXPOSURE ON NEUROBLASTS MIGRATION IN THE FETAL CEREBRAL CORTEX**

*Aronne MP, Guadagnoli T, Evrard SG, Brusco HA.* Instituto de Biología Celular y Neurociencias “Prof. Eduardo De Robertis”, Facultad de Medicina, Universidad de Buenos Aires. Paraguay 2155 3rd fl (C1121ABG). Buenos Aires, Argentina. hbrusco@fmed.uba.ar

Prenatal ethanol exposure (PEE) induces morphofunctional alterations in the developing central nervous system. The orderly migration of neuroblasts is a key process in the development of a layered structure such as the cerebral cortex (CC). From initial stages of corticogenesis, the transcription factor *Pax6* is intensely expressed in neuroepithelial and radial glia cells and is involved on the continual regulation of cell surface properties responsible for both cellular identity and radial migration. In this work, PEE model was developed in Wistar rats feeding with a liquid diet containing 5.9% (w/w) ethanol since one month before mating until finish lactation (PEE-W-r), rendering moderate blood ethanol concentrations. Brain sections of fetal CC obtained at G12, G14, G16 and G18 were morphologically studied by means of digital image analysis after immunocytochemical experiments using reelin, N-cadherin, R-cadherin, *Pax6* and doublecortin primary antibodies. In PEE fetuses, we found

alterations in the N-cadherin and R-cadherin expression and a significant reduction in the number of reelin-ir cells, in all prenatal stages. The migration distance through the CC and the number of postmitotic doublecortin-ir neuroblasts in germinative zones were decreased. Results showed significant decrease on these adhesion molecules exposure, a marked migratory process delay, a decreased number of neuroblasts and of *Pax6*-ir cells in the developing CC of PEE fetuses. All these alterations could be contributing factors to the establishment of cortical dysplasias in the offspring of alcoholic mothers, such as those seen in the human fetal alcohol syndrome. Grants: PIP00074, UBACYT M-004.

### References:

- N. Chi & J.A.Epstein, 2002. Getting your Pax straight: Pax proteins in development and disease. *Trends Genet.* 18, 41-47.
- M.W. Miller, 1986. Effects of alcohol on the generation and migration of cerebral cortical neurons. *Science* 233, 1308-1311.
- J.L. Eriksen, R. Gillespie & M.J.Druse, 2000. Effects of in utero ethanol exposure and maternal treatment with a 5-HT(1A) agonist on S100B-containing glial cells. *Dev. Brain Res.* 121 (2), 133-143.

**EFFECTS OF ETHANOL IN THE DEVELOPMENT AND LEARNING IN RATS**

*Arruda, Thais Volpiano* Universidade Metodista de São Paulo (UMESP). Rua Dom Jaime de Barros Câmara, 1000, Planalto, CEP 09895-400, (55) 11 - 2464-2222, Brazil. thaisvolpiano@hotmail.com

Many studies have shown the protective effect of maternal milk in the children's development and learning. Its nutritional functions and protective effects are important for the adequate development of the central nervous system. Many substances can arrive to baby through maternal milk. One of these substances is ethanol, considered the drug most used in the world. The present study verified the ethanol's effects in the development and learning in rats that drink ethanol during the period of lactation. The mothers and rats were divided into: Control (rats that had received water as source from liquid), Manipulated (rats that received water as source from liquid) and Ethanol (rats that received ethanol). Parameters of physical development had been evaluated from second day of lactation until day 14. When the rats were 2 months and 15 days, they had been submitted to the modeling of the level bar and two different reinforcement schedules: fixed rate and fixed interval. It was observed that the rats received ethanol during the lactation presented differences in the reflex's development, but did not present statistical significant differences in physical development. The results showed that the effect of

ethanol in learning of the adult rat are very subtle, not being evidenced in the reinforcement's schedules used in this study. The data showed that the differences in the learning had been caused by the manipulation's history of the rats and not the ingestion of ethanol.

**RIMONABANT MODULATES THE ANXIOLYTIC-LIKE EFFECT, BUT NOT LOCOMOTOR ACTIVITY OF ALCOHOL IN MICE**

*Batista, Luciano Conceição; Takahashi, Reinaldo Naoto.* Department of Pharmacology, Center of Biological Sciences, Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil, 88049-900 takahashi@farmaco.ufsc.br

There is considerable evidence that blocking CB1 receptors may reduce alcohol intake in alcohol-dependent individuals. However, there is still limited knowledge that CB1 receptor antagonists may also be beneficial in the attenuation the anxiolytic property of alcohol, an important motivational factor for its consumption and the development and expression of alcoholism. Here we have examined whether the CB1 receptor antagonist rimonabant (SR141716) can alleviate the behavioral symptoms elicited by acute alcohol exposure in male Swiss albino mice. In this direction the effects of acute administration of the rimonabant (SR141716, cannabinoid CB1 receptor antagonist) and an aminoalkylindole derivative (WIN55,212-2, CB1/CB2 receptor agonist), and their interaction with ethanol in the elevated plus maze test and open-field test were studied. The prior administration of non-anxiogenic doses of

SR141716A (0.5 or 1.0 mg/kg, i.p.) significantly reduced the anxiolytic-like effect of alcohol (1.2 g/kg, i.p.) in the elevated plus maze test [F(4,37)=5,38; p<0,002], without changing locomotor activity in mice tested in the open-field apparatus (p=0,47). Moreover, anxiolytic-like response was observed by the co-administration of non-anxiolytic doses of CB1 receptor agonist WIN (0.3 mg/kg, i.p.) and alcohol (0.6 g/kg, i.p.) [F(1,28)=11.64; p<0,001]. These results reinforce the involvement of endocannabinoid mechanisms in anxiety and suggest that the activation of cannabinoids CB1 receptors mediate the anxiolytic-like effect, but not ethanol-induced locomotor activity in mice.

**ETHANOL-PROMOTED CELL INJURY IN THE RAT UTERUS. ROLE OF ITS BIOTRANSFORMATION IN SITU.**

*L.R. Buthet; S.L. Fanelli; C.R. de Castro; M.H. Costantini; F.M. Bietto; J.A. Castro; G.D. Castro*  
CEITOX (CITEFA/CONICET). Email: larabuthet@yahoo.com.ar

It is known that alcohol drinking can lead to impairment in reproductive function in women. In this study we analyze the possibility that part of these effects were mediated through alterations of uterus function related to ethanol oxidation to acetaldehyde occurring in that tissue. We found that biotransformation in the cytosolic fraction is mediated by xanthine oxidoreductase (XOR), required a purine cosubstrate and was inhibited by allopurinol and pyrazol. By histochemistry XOR activity was detected in the epithelium and aldehyde dehydrogenase activity was detected in the muscular layer and the serosa. The microsomal process did not require NADPH but was of enzymatic nature, sensitive to oxygen and was inhibited by diethyldithiocarbamate, diphenyleneiodonium and partially by esculetin and nordihydroguaiaretic acid.

Both, cytosolic and microsomal fractions from uterus showed the ability to generate hydroxyl radicals in the presence of alcohol, as detected by GC-MS of the adducts formed with the spin trap PBN. Ultrastructure of uterus from rats treated with standard Lieber & De Carli liquid diet for 28 days

revealed extensive vacuolization in cytoplasm and loss of cell content. In addition we observed the promotion of oxidative stress as evidenced by increased response in the t-butylhydroperoxide induced chemiluminiscence and the depletion of the protein sulfhydryl content. Results suggest that in the rat uterus, metabolism of ethanol to acetaldehyde may play a role in alcohol effects on female reproductive function.

Grants: ANPCyT (PICT 2004 25354) and CONICET (PIP 5158).

## **EMOTIONAL PERCEPTION IN ALCOHOLISM**

*M. Carmona-Perera (1), X. Sumarroca-Hernández (2), A. Santolaría-Rossell (2), A. Verdejo-García (1,3), M. Pérez-García (1,3), A. Pilatti (4).*

(1) Faculty of Psychology. University of Granada  
(2) Unity of behavioral drug abuser (UCA), Hospital Nostra Senyora de Meritxell. (3) Institute of Neuroscience. University of Granada. (4) Laboratory of Psychology. Faculty of Psychology. National University of Cordoba, unadelaseu@hotmail.com

**Introduction.** Studies of emotion emphasize the central role of emotional perception in social life of people, allowing a correct interpersonal interaction. Drug dependent patients have showed a dysfunction in the ability to perceive emotions from facial expressions of other people (Kemmis, Hall, Kingston & Morgan, 2007; Verdejo-García et al., 2007); however there is no research on emotional perception in alcoholism. **Objective.** Therefore, the aim of this study was to investigate possible alterations in the emotional perception of patients with alcoholism and determinate if this dysfunction depends on the type of emotion perceived. **Methods.** The preliminary sample involved 15 alcoholics and 15 non-alcoholics equal in age and gender variables. We administered Ekman 60 Faces Test (Perrett, Calder, Sprengelmeyer & Etcoff, 2002) in which a set of faces expressing one of the six basic emotions

postulated by Ekman (happiness, sadness, fear, anger, surprise and disgust) are shown and the participants must identify them. We conducted a t-test for dependent samples analysis including group (alcoholics vs. non-alcoholics) as factor, and the score on the Ekman's test as dependent variable. **Results.** Results showed significant within-group differences in the total score [F (30, 26 639) 1180, p <0.000] as well as the partial scores of anger [F (30, 21 708) 5890, p <0.001], disgust [F (30, 26 308) 4214, p <0.000], fear [F (30, 29 756) 0.424, P <0.001] and surprise [F (30, 19 517) 13 943, P <0.007], drinkers obtaining significantly lower scores. With regard to the emotions of sadness and happiness, both groups scored very similar and the differences were not significant. **Conclusions.** In conclusion, this research is an evidence of perceptual disturbance of emotions in alcohol consumers, showing a difficulty to perceive anger, disgust, fear and surprise. This dysfunction in emotional perception may be related to social interaction problems presented in alcoholism.



**CONDITIONED PLACE PREFERENCE TO ALCOHOL MAY BE PREVENTED SINCE MICE ARE NOT EXPOSED TO ETHANOL IN ADOLESCENCE**

*Carrara-Nascimento, PF; Camarini R.* Instituto de Ciências Biomédicas, Universidade de São Paulo Av. Prof. Lineu Prestes, 1524; CEP 05508-000; São Paulo – SP; Brasil  
pricarrara@bol.com.br

Adolescence is a period of neurobehavioral adaptation; an individual may be more vulnerable to drug abuse. Conditioned Place Preference (CPP) may be used to examine the rewarding effect of ethanol. Animals prefer to stay in the compartment paired with ethanol due to the reward associated clues. Repeated exposure to addictive drugs promotes progressive increase in locomotor activity (LA) in rodents; a phenomena called behavioral sensitization. The aim of this study was to examine the preference of adult animals for a compartment paired with the ethanol rewarding effects when treated with ethanol injections during adolescence. Adolescent (PND30) and Adult (PND60) male swiss mice were used. Behavioral Sensitization (LA): Adolescent (J) and adult animals (A) were treated with 2.0g/kg intraperitoneal injections of ethanol (Et) or control solution (CTR) for 15 consecutive days. LA was quantified (“Day 1”; “Day 8”; “Day 15”). CPP: 5 days later the CPP paradigm started. On “Day 1” animals were allowed to explore the whole

apparatus in order to habituate to it. Conditioning sessions lasted 8 days (4 CTR conditioning sessions alternated with 4 Et sessions). Animals were confined to a single compartment paired with CTR or Et. On the test day animals were allowed to explore the whole apparatus again and time spent in each compartment (one paired with CTR; the other paired with Et) was quantified. Behavioral Sensitization (LA): On “Day 8” and “Day 15” A-Et and J-Et presented significant increase in LA compared to “Day 1”. Although, in the last treatment day A-Et presented increased LA compared to J-Et. CPP: On the test day J-Et spent more time in the compartment paired with ethanol. The A-CTR group also exhibited increased time spent in the ethanol paired compartment. In conclusion, Et exposure in adolescence promoted preference for the compartment that was associated to the ethanol rewarding effect. This effect may be prevented since animals are not exposed to ethanol during adolescence. The finding that A-CTR also presented preference for the compartment paired with the ethanol effects suggests that naive adult subjects are still susceptible to the association of the environmental clues with the ethanol rewarding effect.

## **DEVELOPMENT OF ALCOHOL DEPRIVATION EFFECT IN A SWISS MICE ADDICTION MODEL**

*Correia, Diego; Villas Boas, Gustavo Roberto; Boerngen-Lacerda, Roseli.* Department of Pharmacology, Universidade Federal do Paraná, Jardim das Américas, Curitiba, Paraná, CEP 81531-990; Brazil. diegocorreia@ufpr.br

The alcohol deprivation effect (ADE) is characterized by transient enhanced alcohol consumption upon reinstatement of ethanol following a period of forced ethanol deprivation. ADE is proposed to be a measure of relapse behavior. Although it is a very robust phenomenon in most rat strains, it is more inconsistent in mice. Furthermore, the neurochemical pathways that modulate the ADE are not well understood. In the addiction model, swiss mice (n=60) were individually housed with ad libitum access to food and had free choice between ethanol 5% and 10%, and water in a four-phase paradigm: acquisition phase (12 weeks - free access to ethanol 10% and 5% (v/v), and water), withdrawal (W -2 weeks - only tap water was provided), re-exposure (2 weeks - free access to ethanol solutions and water), and quinine-adulteration (2 weeks- ethanol solutions were adulterated with 0.005 g/L quinine, creating an less palatable bitter-tasting solution ). Control mice (n=10) had access to water. The positions of the bottles were changed on alternate days when the fluid intake was measured volumetrically. Mice were characterized as addicted (A, ethanol preference without reducing

intake when ethanol were adulterated with quinine), heavy-drinker (HD, ethanol preference but reduced ethanol intake when adulterated) and light-drinker (LD, water preference) [Fachin-Scheit DJ, et al; J Neural Transm 2006;113:1305-21.].The addiction model was performed as described before and, in order to study the effect of multiple abstinences during the W phase we added 4 cycles (2 days with and 2 days without the ethanol solutions) of withdrawal. There was no ADE when ethanol withdrawal was sustained during 2 weeks, but when mice were submitted to multiple cycles the ADE was expressed in all groups. Nevertheless ADE did not influence the proportion of animals in each group nor the individual characterization in each group.

**LONG-TERM EMOTIONAL EFFECTS OF AN ACUTE INTERACTION WITH AN ETHANOL INTOXICATED DAM.**

*Culleré, M.E.; Spear N.E.; Molina J.C.*

Instituto de Investigación Médica M. y M. Ferreyra (INIMEC - CONICET). Friuli 2434, Córdoba, CP 5000, 351-481465, Argentina. Córdoba.  
cullere@gmail.com

Maternal ethanol exposure during the first postnatal week disrupts the behavioral repertoire linked with infantile care. These alterations impact on normal offspring development. It has been observed that pup's ultrasonic vocalizations (USV) are augmented after an acute interaction with an ethanol administered dam. Given that USVs are considered as anxiety-like responses, it is possible to argue that this increase represents a negative emotional component of the mentioned experience. The aim of the present experiment was: (i) to describe the time course of USVs emission after a single interaction with an intoxicated dam on postnatal day (PD) 3; (ii) to assess long-term emotional outcomes of this early ethanol experience. Infant rats (PD16) that had interacted with an ethanol administered dam on PD3 were evaluated in terms of water and milk intake in the presence or absence of ethanol odour, a stimulus present while interacting with an intoxicated dam.

On PD3 dams were administered with ethanol (2.5 g/kg.) or water and allowed to interact with their offspring for 2 hs. USV (Frequency range: Band 1:

22-45 kHz, Band 2: 46-100 kHz, associated with aversive and non-aversive responsiveness, respectively) were recorded in different pups at 5, 30, 60, 90 and 120 min after maternal reunion. Pups from intoxicated dams exhibited higher amounts of vocalizations than controls. Moreover, Band 1 vocalizations of pups that had interacted with ethanol-treated dams increased as a function of time, whereas Band 2 vocalizations diminished across test. These patterns were not observed in control pups. During the intake test (PD16), milk was preferred over water. In the presence of ethanol odour, animals from intoxicated dams ingested significantly less milk than controls.

The present results confirm previous observations indicating exacerbated USVs responses after an acute interaction with an intoxicated dam. Maternal care alterations and/or ethanol-induced hypothermia could be syndicated as factors involved in the origin of this effect. The impact of this early interaction persisted over time. Ethanol derived pups rejected milk in the presence of ethanol odour, a possible evidence of an aversive memory originated by the association of maternal dysfunctions with the presence of chemosensory properties of ethanol.

Grants: PICT CONICET 2008-2011; SUNY at Binghamton.

**EXPOSURE TO CAFFEINE MIXED WITH ALCOHOLIC SOLUTIONS REDUCES THE PROLONGED ETHANOL CONSUMPTION AND PREVENTS THE ALCOHOL DEPRIVATION EFFECT IN ADULT RATS**

*De Carvalho, Cristiane Ribeiro; Cruz, Jéssica Silveira; Takahashi, Reinaldo Naoto.*

Departamento de Farmacologia/Centro de Ciências Biológicas – bloco D, Universidade Federal de Santa Catarina. Campus Universitário Trindade, Caixa postal 476 – CEP 88049-900 – Florianópolis, Santa Catarina – Brasil.

[crisrcfarmacia@hotmail.com](mailto:crisrcfarmacia@hotmail.com)

There is growing evidence showing that the consumption of alcohol mixed with highly caffeinated beverages may increase the risk for heavy drinking and of alcoholism (Curry and Stasio, 2009). This study was evaluate the pattern of ethanol consumption/preference and the propensity to show an alcohol deprivation effect in rats exposed to voluntary intake of caffeinated alcoholic solutions. Male Wistar rats adult were individually housed and subjected to protocol adapted from Yoneyama *et al.*, 2008. Rats given free access to two-bottle one bottle containing tap water and a second containing solutions with increasing concentrations of ethanol (0%, 3%, 6%, 10% v/v). They were divided into four groups: ethanol; ethanol plus 0.2% saccharin; ethanol plus 1 g/L caffeine and ethanol plus 0.2% saccharin plus 1 g/L caffeine. Each ethanol concentration

was made available for 4 days to reach the 10% ethanol, which was given to the animals for 6 weeks, a total of 54 days. Alcohol deprivation effect, considered a predictive measure of relapse to alcohol (Heyser *et al.*, 1997), was assessed after an abstinence period of 7 days, when the animals were again exposed to their respective alcoholic solutions for 24 hours. It was observed that all animals drank more saccharin solution in free-choice paradigm, indicating that the presence of caffeine in the solutions did not alter the preference to saccharin. None of the experimental groups preferred to drink ethanol compared to regular tap water. However, both groups that were exposed to caffeinated alcoholic solutions can be seen a reduction of ethanol intake compared to animals that consumed alcoholic solutions plus saccharin. Only the group exposed to ethanol plus 0.2% saccharin solutions showed a slight increase in the ratio of alcohol intake/total fluid intake, when access to alcohol is reinstated. Our finding showed that presence of caffeine in alcoholic solutions did not increase ethanol consumption neither induces to the alcohol deprivation effect in rats. Sensory modalities play an important role on the acceptance or rejection of alcohol oral consumption and they also may have contributed for these results. Certainly further studies are needed to clarify whether the association of energy drinks and alcohol as a risk factor for development of alcoholism.

Financial support: CAPES and CNPq

## **E-HEALTH, A NEW PERSPECTIVE FOR HEALTH CARE IN DRUG ABUSE**

*de Oliveira, Anabel; dos Santos, Luciana Marson; Christoff, Adriana de Oliveira; Boerngen-Lacerda, Roseli.* Universidade Federal do Paraná, Departamento de Farmacologia, Centro Politécnico, Caixa Postal, nº19031, CEP: 81540-970.

The *e-health* is defined as a healthcare intervention delivered via the Internet. The advancement of this approach in health is remarkable and appears to be quite useful for disseminating information. The purpose of this study was to review the state of the art of using the techniques named as *e-health*, its applicability and benefits and also, the difficulties to its implementation. In September 2010, systematic searches of the literature were carried out in the following bibliographical databases: *PubMed, Scielo, Medline* and *Journal of Medical Internet Research* considering publications since 1990 to present. Searches were conducted with key words and text words, in which words indicative of e-health interventions (*e-health, web-based programs, medical internet*) were combined with words indicative of health problems (*cardiovascular disease, renal disease, cancer, use of tobacco, use of alcohol, diabetes, health care, health communication, respiratory disease, physical activity, nutrition*). All the 36 selected studies considered this technique very useful, valid and effective and reported the positive satisfaction of

the patient to the given information and intervention. Regarding alcohol-related problems, the studies showed positive results and concluded that the web-based intervention is an adequate approach. The use of web-based intervention allows the early alcohol-related problem detection and the monitoring of behavioral change to overcome the problems. Besides it offers the precise orientation for the individual to look for help. Some studies compared the face-to-face intervention to the web-based one and concluded that both are effective. Although all studies showed positive results, some discussed that the results have small effect size. These studies pointed up several factors affecting the result of intervention: gender, educational level, geographic location and age, among others. Due to its complexity, e-health programs have much to be explored and developed in order to standardize and improve the quality of the intervention.

**PASSIVE INITIATION TO ALCOHOL  
DURING ADOLESCENCE INFLUENCE  
LATER VOLUNTARY ALCOHOL  
CONSUMPTION**

*Maria Carolina Fabio, Norman E Spear and  
Ricardo Marcos Pautassi*

Instituto de Investigación Médica M. y M. Ferreyra  
(INIMEC – CONICET), Córdoba, C.P 5000,  
Argentina; Facultad de Psicología, Universidad  
Nacional de Córdoba, Córdoba, C.P 5000,  
Argentina, State University of New York at  
Binghamton, NY, 13902,USA.  
mcfabio@immf.uncor.edu

Background: An early onset of alcohol use, which typically takes place in early adolescence, is associated with heightened probability of alcohol use disorders later in life. Moreover, adolescents often engage in intermittent, binge-like alcohol consumption that is associated with alterations in brain function. The aim of this study was to evaluate voluntary alcohol consumption in adolescents passively initiated to alcohol through an intermittent schedule. Methods: Adolescent Wistar rats received 5 [5-day exposure group, postnatal days (PDs) 28, 30, 32, 34 and 36], 2 (2-day exposure group: ethanol on PD 28 and 32, vehicle on PD 30, 34 and 36) or 0 (control group treated with vehicle on PDs 28, 30, 32 and 36) intragastric administrations of alcohol (2.5 g/kg). Locomotor activity was assessed on PDs 28, 32 and 36, 5 minutes after intubations. This passive

initiation to alcohol was followed by a 12-day-long ethanol intake protocol. During PDs 39 to 42 (two-bottle choice phase) animals had continuous, 24 h access to alcohol (concentration: 5.6% alcohol, vehicle: 1% sucrose; ad-libitum food) and water. Adolescents were then given standard access to water and food for seven days (alcohol deprivation phase, PDs 43-50). On PD 51 animals were tested in a 24 h, two-bottle choice test (5.6 % sweetened alcohol vs water). Results: Alcohol treatment at PD28 induced substantial locomotor activity, yet this effect subsided after repeated treatment. Perhaps more important, alcohol-initiated animals showed significantly greater alcohol consumption at PD 50 (i.e., after the deprivation phase) than non-initiated animals. The facilitative effect of alcohol initiation was significantly greater in animals given the longest, 5-day intermittent exposure. There was no significant association between ethanol- or vehicle-induced motor activity at initiation and ethanol intake scores. Conclusions: Altogether, these results highlight the permissive role of adolescent alcohol exposure on later alcohol preference. A brief, binge-like alcohol initiation during early adolescence significantly increased alcohol consumption at late adolescence.

Grants: PIP CONICET 2010-2012; PICT-PRH UNC 2009; SUNY at Binghamton.

**EXPRESSION OF D1 AND D2  
DOPAMINERGIC RECEPTORS AND  
DOPAMINE TRANSPORTERS IN  
ADOLESCENT MICE SENSITIZED AND  
NON-SENSITIZED TO THE STIMULANT  
EFFECT OF ETHANOL**

*Goeldner, Francine Oliveira; D'Almeida, Vânia;  
Souza-Formigoni, Maria Lucia Oliveira de*  
Departamento de Psicobiologia – Universidade  
Federal de São Paulo (UNIFESP). Napoleão de  
Barros, 925 3 andar – CEP 04024-002 – Vila  
Clementino – São Paulo – SP – Brazil  
[francinegoeldner@gmail.com](mailto:francinegoeldner@gmail.com)

Behavioral sensitization to ethanol, an important process in the development of ethanol dependence, is not observed in all ethanol-treated subjects. While some individuals present clear sensitization, others do not. The knowledge of the underlying mechanisms of behavioral sensitization, including alterations in gene expression, could be useful in the understanding of this phenomenon. In the present study, adolescent male Swiss mice received i.p. saline (control) or 2.2 g/kg ethanol, daily for 21 days and were weekly tested for locomotor activity. Ethanol-treated mice were classified into sensitized or non-sensitized groups, based on the locomotor activity at the end of treatment. Their brains were then removed and we analyzed the gene expression of dopamine transporter (DAT), D1 receptor and isoforms of D2 receptor in the mesocorticolimbic pathway. Gene expressions

were analyzed by PCR or real time-PCR assays in the medial prefrontal cortex (mPFC), nucleus accumbens (NAc), and ventral tegmental area (VTA). In the mPFC and VTA we observed lower D2 receptor expression in the sensitized than in the non-sensitized group. However, in the NAc, the D2 receptor expression was higher in the sensitized than in the non-sensitized group. Besides, in the VTA we observed higher D1 receptor expression and lower DAT expression in sensitized than in non-sensitized mice. These results suggest that the expression of D2 receptor may differentially modulate the process of development of behavioral sensitization in adolescent mice. In addition, differences in the dopaminergic neurotransmission of sensitized and non-sensitized adolescent mice, in the VTA - but not in mPFC or NAC, could also be responsible for the differential susceptibility to the development of sensitization.

Financial support: FAPESP(2009/15043-1), CNPq and AFIP.

**THE EFFECTIVENESS OF BRIEF INTERVENTION IN REDUCING CONSUMPTION OF ALCOHOL IN WOMEN: A BIBLIOMETRIC STUDY.**

*Gebara<sup>1</sup>, Carla Ferreira de Paula; Bhona<sup>2</sup>, Fernanda Monteiro de Castro; Correa<sup>2</sup>, Aline Francine Vaz; Cezário<sup>2</sup>, Ana Cláudia Ferreira; Diniz<sup>2</sup>, Mayla Vieira; Lourenço<sup>2</sup>, Lélío Moura; Noto<sup>1</sup>, Ana Regina.* 1 - Brazilian Information Center on Psychotropic Drugs (CEBRID) – Federal University of São Paulo (UNIFESP), Brazil.

2 - Social Psychology & Public Health Research Group (POPSS) - Federal University of Juiz de Fora (UFJF), Brazil. [carla\\_gebara@yahoo.com.br](mailto:carla_gebara@yahoo.com.br)

This study aimed to realize a bibliometrics survey about the effectiveness of the brief intervention's technique on reducing alcohol consumption in women. An electronic search was realized in all data bases of virtual platform *ISI Web of Knowledge* with a multidisciplinary content. The expression "brief Intervention" was associated with the terms "alcohol drinking", "alcohol consumption", "alcoholism", "alcohol related disorders" and "alcohol abuse", which also were associated with the word "women". Of the studies searched were selected the works published between the years of 2006 at 2010. Of the 70 publications found, 68 were included because had presented subjects of interest in area. The abstracts of these publications were

submitted to the content analysis technique. Regarding the type of document, the publication "article" was presented in larger quantity (60), followed by publications of "reviews" (5) and at last, "meetings" (3). The year with more articles published was 2007(19). As well as magazines "Journal of Studies on Alcohol and Drugs"(6), Alcoholism-Clinical and Experimental Research "(6) and" Addictive Behaviors "(5). The majority of studies (42) were realized in North American institutions and were on areas of "Psychology," Behavioral Sciences "and" Substance Abuse ", respectively. The authors who more appeared were "FLOYD, RL" (4), "NEIGHBORS, C (3) and" CAREY, KB "(3). The quantitative approach was the most prevalent among studies (51), and the randomized-controlled clinical trials, the most frequent (26). The consumption of the alcohol was measured in 37 articles. The Brief Intervention technique was tested in 34, being realized, mainly, in clinical ambient and health services (18). However, interventions were also found being made by the computer, Internet (4), phone (3) and in indigenous community (1). Regarding the studied population, 47% of articles had made the intervention addressed to men and women, 31% for pregnant women, 15% for college students, only 6% for women and 1% for Indians. The effectiveness of the Brief Intervention technique in lower the consumption of alcohol was confirmed in 48% of studies.



**ALCOHOL CONSUMPTION AND CHILD ABUSE: A BIBLIOMETRIC STUDY.**

*Gebara<sup>1</sup>, Carla Ferreira de Paula; Bhona<sup>2</sup>, Fernanda Monteiro de Castro; Campos<sup>2</sup>, Ana Paula Soares; Souza<sup>2</sup>, Letícia Côrtes de ; Lourenço<sup>2</sup>, Lélío Moura; Noto<sup>1</sup>, Ana Regina.* 1 - Brazilian Information Center on Psychotropic Drugs (CEBRID) – Federal University of São Paulo (UNIFESP), Brazil. 2 - Social Psychology & Public Health Research Group (POPSS) - Federal University of Juiz de Fora (UFJF), Brazil. [carla\\_gebara@yahoo.com.br](mailto:carla_gebara@yahoo.com.br)

There are theoretical and empirical evidence linking violence and alcohol consumption, however the peculiarities of this association need further research. In order to clarify how the family violence against children have been studied in its association with alcohol consumption, this study consisted of a bibliometric survey of articles indexed in the database Web of Science, available on the Platform CAPES. Electronic search was conducted with the association of the terms: "child abuse", "child maltreatment," "child neglect" and "alcohol related disorders," "alcohol abuse", "alcohol consumption", "drinking alcohol" and "alcoholism." Only empirical articles published between the years 2006 and 2010 and with the full text for consultation were selected. From reading the titles and abstracts were chosen only those that dealt with child abuse in the family context and involving the alcohol consumption as a variable in

the study, getting a final number of 35 articles. From among these, most were published in 2009 (10). The Child Abuse & Neglect (5) and Addictive Behaviors magazines (4) were the ones with more publications. Fifty-one percent (51%) publications were North American. The quantitative approach prevalent among studies, with almost 89% of publications. Most studies did not use standardized instruments to measure alcohol consumption. The Alcohol Use Disorders Identification Test (AUDIT) was used in two studies, as well as the Michigan Alcoholism Screening Test (MAST). Much of the publications (51%) indicated that the person who was a victim of violence during childhood used/abused or had alcohol dependence, whereas only 17% of the studies made reference to the aggressor consumption. Was evident among the analyzed studies that as the abuse of alcohol provides the perpetration of violence, as the victimization in childhood is related to excessive consumption of alcohol in adulthood.

## **ALCOHOL CONSUMPTION IN INTIMATE PARTNER VIOLENCE: A BIBLIOMETRIC STUDY.**

*Gebara*<sup>1</sup>, *Carla Ferreira de Paula*; *Bhona*<sup>2</sup>, *Fernanda Monteiro de Castro*; *Costa*<sup>2</sup>, *Priscila Morais*; *Lopes*<sup>2</sup>, *Larissa Machado*; *Lourenço*<sup>2</sup>, *Lélio Moura*; *Noto*<sup>1</sup>, *Ana Regina*.<sup>1</sup> - Brazilian Information Center on Psychotropic Drugs (CEBRID) – Federal University of São Paulo (UNIFESP), Brazil. <sup>2</sup> - Social Psychology & Public Health Research Group (POPSS) - Federal University of Juiz de Fora (UFJF), Brazil. [carla\\_gebara@yahoo.com.br](mailto:carla_gebara@yahoo.com.br)

In the literature about domestic violence alcohol consumption appears frequently associated with perpetration and victimization. This study aimed to carry out a bibliometric survey on intimate partner violence and its relation to alcohol consumption in order to highlight some indicators about the scientific treatment of the subject. For this it was conducted an electronic search of articles indexed in the international database Web of Science through the association of terms: "spouse abuse" and "intimate partner violence" with "alcoholism", "alcohol abuse", "alcohol related disorders" , "alcohol consumption" and "drinking alcohol". Only empirical articles published between the years 2006 and 2010 were collected, totaling 101 articles. Then they were analyzed by reading the titles and abstracts, and those that provide what the full text of both treated and intimate partner violence and alcohol consumption were selected, getting the final number of 34 articles. From this sample it was found an increase in publication

number over the years, being 2010 the year of largest number of publications, with 12 articles. The magazines that published more were the "Journal of Interpersonal Violence", with 06 articles, "Journal of Public Health" and "Journal of Family Violence", both with 03 publications each. Most of the research was developed in the United States of America, 59% of the sample, followed by Brazil with 10%. It can be observed that 88% of the articles gauged somehow the individuals' alcohol consumption, but most did not use any valid instrument, only added questions about alcohol use in research protocols. Most of the articles indicate the man as the aggressor in cases of intimate partner violence, as well as those who consume more alcohol. However it was not ignored the consumption of alcohol by women, being that it was observed that, in some cases, this consumption occurs in an attempt to escape from the aggressions of the companion.

## **ULTRASTRUCTURAL CHANGES IN RAT CORTICAL NEURONS EXPOSED TO ETHANOL**

*Guadagnoli T, Aronne MP, López, LM; Gironacci, MM, Brusco A.* IBCN (UBA-CONICET). Fac. Farmacia y Bioquímica, IQUIFIB-CONICET, UBA. Buenos Aires, Argentina Email: hbrusco@fmed.uba.ar

Previously, we have demonstrated alterations in the neuronal cytoskeleton in cerebral cortex of rats prenatally exposed to ethanol. We also showed in rat primary cortical neurons that ethanol induced neuronal death and a decrease in the elongation and branching of dendrites. The aim of the present work was to evaluate the ultrastructural changes in rat cortical neurons exposed to 50mM ethanol during 24 hours. Cortical neurons were obtained from one-day-old Wistar rats. Cells were plated at  $3.5 \times 10^6$  cells/35 mm dish and grown in Neurobasal supplemented with B-27 and 2 mM L-glutamine until complete differentiation. 12 h before treatment, cells were B-27 deprived, and exposed to 50 mM ethanol during 24 h. After that, cells were fixed with 2 % glutaraldehyde + 1% formaldehyde in 0,1M cacodylate buffer for 60 min. After washing in this buffer, cells were postfixed in 2 % OsO<sub>4</sub> containing 1 % potassium ferrocyanide for 60 min., treated with 0.1 % tannic acid for 1 min, washed and stained in block with 2 % aqueous uranyl acetate for 120 min , and embedded in Eppon 812 Ultrathin sections were

photographed in a Zeiss electron microscopy at 30000X and 50000X. Primary cortical neurons exposed to ethanol showed indented nucleus, increased number of lipidic vacuoles, lisosomes and multilamellar vesicles, dilated endoplasmatic reticulum lumen and a disorganized Golgi apparatus with a ring-shape appearance. Heterogeneous distribution with a decreased density of microtubules (MT) in neurites was also observed in cortical neurons exposed to ethanol (control:  $139.2 \pm 32.52$  vs. treated:  $105.5 \pm 31.56$  MT/ $\mu\text{m}^2$ ). The ultrastructural changes observed in primary neurons exposed to ethanol may explain some of the neuronal dysfunctions observed “in vivo”. Cytoskeleton disorganization may be result in a dendritic processes decrease. The alterations in the Golgi apparatus structure, commonly observed in autophagic process, and the increased lipidic vesicles are some of the most important features related with the cellular toxicity by ethanol exposition. Grants UBACYT M-004, B121, PIP 0774.

## **EFFECT OF REPETITIVE ETHANOL ADMINISTRATION ON THE ORAL HEALTH OF RATS WITH EXPERIMENTAL PERIODONTITIS**

*Maia-Dantas, Aline\**, *Rettori, Elisa<sup>†</sup>*, *Zorrilla Zubilete, María<sup>#</sup>*, *Muscará, Marcelo Nicolás\**, *Elverdin Juan Carlos<sup>‡</sup>*, *Rettori, Valeria<sup>†</sup>*, *Fernández-Solari, Javier<sup>†, ‡\*</sup>*. Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, Brazil. <sup>†</sup>Center for Pharmacological and Botanical Studies (CEFyBO-CONICET/UBA), Buenos Aires, Argentina. <sup>#</sup>Second Department of Pharmacology, School of Medicine, UBA, Buenos Aires, Argentina. <sup>‡</sup>Department of Physiology, Dental School, UBA, Buenos Aires, Argentina. li\_maiad@yahoo.com

It is known that ethanol consumption produces deleterious effects on the oral health. The aim of the present work was to study the effect of repetitive ethanol administration in healthy rats or in rats with experimental periodontitis (EP). Ethanol (2 g/Kg, 20% in water) or water were administrated by gavage, twice a day during 12 days. EP was induced by placing a cotton thread ligature around the neck of the first lower molars during 7 days. The experimental groups (5 rats/group) studied were: 1) control rats, 2) rats with EP, 3) rats that received repetitive ethanol (RE), 4) rats with EP and RE. The salivary secretion of the submandibular gland (SMG) induced by the cholinergic agonist metacholine

was reduced in all the groups in comparison to control rats. Also, both RE and EP increased inducible NOS (iNOS) activity in the SMG as compared to control rats ( $p < 0.01$  and  $p < 0.05$ , respectively), while PGE content (measured by RIA) was increased in rats with EP ( $p < 0.05$ ) and in rats with EP and RE combined. In the gum, iNOS activity was increased in RE rats ( $p < 0.05$ ) and in EP rats ( $p < 0.001$ ) as compared to controls. The expression of iNOS mRNA (measured by PCR) as well as PGE content in the gum were increased significantly in rats with EP ( $p < 0.05$  and  $p < 0.001$ , respectively) as compared to controls, but were higher in rats with EP and RE combined. These results demonstrate that RE alters inflammatory parameters in oral tissues and that it could aggravate the pathophysiological alterations produced by periodontal disease

Grants: ANPCyT PICT 14264 y CONICET PIP 6149 and CAPES.

**ACETALDEHYDE REINFORCEMENT AND MOTOR ACTIVITY IN NEWBORNS WITH OR WITHOUT A PRENATAL HISTORY OF ALCOHOL EXPOSURE**

*March, Samanta M.; Culleré, Marcela E.; Abate, P.; Hernández, José I.; Spear, Norman.E. and Molina, Juan.C.* Instituto de Investigación Médica M. y M. Ferreyra (INIMEC - CONICET). Friuli 2434, CP 5016, Córdoba, Argentina, 54 351-4681465. smarch@immf.uncor.edu

It has been observed that ethanol exposure during early development is associated with later acceptance of the drug. In humans, the development of alcohol related problems, such as abuse and dependence, is associated with prenatal and early exposure to the drug. In pre clinical studies we have observed that neonatal rats with a history of prenatal exposure to ethanol are more prone to self administer an ethanol solution than pups without such prior experience with the drug. Interestingly, this period of enhanced sensitivity to ethanol reinforcement is accompanied by a higher rate of activity in the central catalase system. The catalase system metabolizes ethanol in the brain. Acetaldehyde (ACD), the first oxidation product, has been found to share many ethanol-like effects. In the first experiment, we evaluated if a prenatal history of alcohol exposure (gestational days 17-20; 0.0 or 2.0 g/kg) modulated neonatal susceptibility to ACD's motor effects. ACD was centrally administered (0, 0.35 and 0.52 umol) and

motor activity was registered. Latency to display motor activity was higher in neonates prenatally treated with water and challenged with the highest ACD dose relative to newborns receiving a similar ACD dose but with a positive prenatal ethanol history. In experiment 2, ACD's reinforcement was tested through an associative learning paradigm. ACD (0.35 umol) and ethanol (100 mg%) were selected as unconditioned stimuli (US) and centrally administered in contingency with lemon odor (conditioned stimulus, CS). Suckling response to an artificial nipple odorized with the CS was the dependent variable. Both USs supported appetitive conditioning in the neonatal rat independently for prenatal treatments. According to these results it appears that prenatal ethanol experience results in tolerance to ACD's motor activity effects. Additionally, appetitive conditioning was successfully achieved when ACD or EtOH were directly administered in the brain. The present results argue in favor of heightened sensitivity to EtOH's reinforcing effects within a stage in development where ACD production is probably higher than latter in life.

Grants: PICT 254, SECYT UNC

**BACLOFEN BLOCKED THE ACUTE LOCOMOTOR STIMULATION INDUCED BY ETHANOL BUT HAD NO EFFECT ON SENSITIZATION IN MICE**

*Mattiello, Leticia; Arantes, Vanessa Cristina Saltarello; Peretti, Murilo Calvo; Montanhini, Priscilla; Amaral, Marlon Felipe Miotto; Borges, Julia de Martino Cruvinel; Picinini, Mayara Camila; Pilger, Camilla Gallo; Wille, Camila Marquette; Oliveira, Thais Erance; Zamboni, Camila Gadens; Lira, Rosane Carolina Paes; Villas Boas, Gustavo Roberto; Correia, Diego; Boerngen-Lacerda, Roseli.*

Universidade Federal do Paraná. Jardim das Américas, Curitiba, Paraná, 81540-970, Brazil. leticia\_mattiello@hotmail.com.

The stimulant effects of ethanol have been related to its rewarding properties as well as to the development of addiction. An increase in the locomotor stimulant effects of ethanol with repeated administration is known as behavioral sensitization being associated with development of addiction too. The gabaergic system is involved in modulation of the positive reinforcing properties of ethanol through modulation of dopamine release. The present study evaluated the acute and chronic effects of a specific GABA(B) agonist, baclofen, on the stimulant locomotor effect of ethanol. Male Swiss mice (n=90; 15/treatment) were exposed to the activity cages (AC) in a drug free situation to evaluate basal locomotor activity. Seven days later,

each animal was acutely i.p. administered with one of the following treatments: saline (S), saline+ethanol 2 g/kg (E), baclofen 1.25 mg/kg (B1) or 2.5 mg/kg (B2) + saline, ethanol + baclofen 1.25 mg/kg (EB1) or 2.5 mg/kg (EB2). They were exposed to AC 10 min after the 2<sup>nd</sup> injection and received daily the same treatment for 21 days and were evaluated again in AC in the 7<sup>th</sup> and 21<sup>st</sup> days. The ethanol-induced sensitization to its stimulant effect was not altered by both doses of baclofen. Acutely, the high dose of baclofen alone (B2) or co-administered with ethanol (EB2) showed depressant effect, but it was reverted by the chronic treatment suggesting development of tolerance to this baclofen effect. Then we tested the effect of baclofen in the expression of ethanol-induced sensitization. B2 blocked this expression maybe due to the same depressant effect observed in the acute evaluation in the sensitization development study. These data suggest that GABA(B) receptor neither influence the stimulant effect of ethanol or the ethanol-induced sensitization. As many other studies suggest that GABA(B) receptor agonists and, most recently, positive modulators inhibit the reinforcing effects of drugs of abuse through indirect modulatory effect, maybe our present data suggest that locomotor stimulation and its sensitization induced by ethanol are not related to its reinforcing properties.

**ALCOHOLIC BEVERAGE  
ADVERTISEMENTS IN THE BRAZILIAN  
TELEVISION – A QUALITATIVE SURVEY**

*Mattos, Walter Gimenez.* Universidade Federal de São Paulo – Programa de Orientação e Atendimento a Dependentes (UNIFESP - PROAD). Napoleão de Barros, 456, ZIP 04024-001, Brazil. São Paulo [walter.mattos@gmail.com](mailto:walter.mattos@gmail.com)

The use and abuse of alcohol is highly related to socio-cultural patterns, and the advertisement of alcoholic beverages take a significant role on how children and teenagers are exposed to the substance.

Several studies show that beverage advertisements can lead to a “pro-alcohol attitude” that changes how the individuals search and use this substance (Edwards G, Anderson P, Babor TF, Casswell S, Ferrence R, Giesbrecht N, et al. Alcohol policy and the public good. Oxford: Oxford University; 2004). In Brazil, as in many other countries, the advertisement of alcoholic beverages is allowed within certain limits, with constraints being applied to reduce the potential harm of beverage campaigns. Self regulation and code of ethics are usually applied by manufacturers and marketing agencies as tools to ensure the society adequate use of alcohol advertisement, but frequent use of symbols related to youth (e.g.: sex, sports, social life) indicate an opposite attitude.

Some studies show that alcohol consumption is correlated with the level of exposure to beverage campaigns (Grube JW, Waiters E. Alcohol in the

media: content and effects on drinking beliefs and behaviors among youth. *Adolesc Med Clin.* 2005). Therefore studies on how beverage ads are actually made are a critical feed for prevention policies.

This research was made aiming to examine the campaigns of alcohol beverages on Brazilian television. All beverage ads that appeared in TV in the second half of 2007 were taken and visual and verbal elements contained therein were analyzed using the qualitative categorical assessment method. The theoretical reference for evaluation was the previous research studies on the issue of alcohol advertisement. The result is a comprehensive table of elements found in the campaigns, the motifs with which the beverage manufacturers fix their brands, and the benefit the beverage is claimed for.

The conclusion is that advertising does not fit the parameters set by the rules on the self regulatory standards, are biased by using situations and contexts that stimulate consumption, enhance positive attitudes towards the habits of alcohol drinking, does not provide sufficient warnings about abusive drinking and use elements that are seductive to teenagers.

## **INFANTILE ETHANOL INTAKE PROFILE: A PARAMETRIC COMPARISON BETWEEN TWO TESTS**

*Miranda Morales, Roberto Sebastián<sup>(1,2)</sup>; Molina, Juan Carlos<sup>(1,2)</sup>; Abate, Paula.<sup>(1,2)</sup>* <sup>(1)</sup> Instituto Ferreyra (INIMEC - CONICET). CP 5016, Córdoba, Argentina. <sup>(2)</sup> Facultad de Psicología, UNC. CP 5000, Córdoba, Argentina.  
[smiranda@immf.uncor.edu](mailto:smiranda@immf.uncor.edu)

Prenatal and early postnatal experiences with ethanol seem to facilitate later appetitive responsiveness to the drug (Spear and Molina, 2005; Abate et al., 2008). In animal models, when assessing infantile ethanol consumption, parameters that define protocol employed (i.e. volume of infusion, test time, infusion rate, etc.) are determinant to promote acceptance of the drug and achieve significant levels of ethanol consumption. The main goal of this study was to compare two schemes of ethanol infusion used in infantile consumption evaluation, in order to compare the acceptance profile of the drug, levels of consumption between both tests.

Infant rats (postnatal days [PD] 14 and 15) were evaluated in ethanol 5% or water consumption. 28 animals were tested in a 15-min continue intake test –CIT– (Arias and Chotro, 2003; Miranda-Morales et al., 2010) during PD14 and 15. The volume of infusion was equivalent to the 5.5% of the body weight of the subject. Other group of subjects (31 infants) was evaluated in a 15-min

pulsatile intake test –PIT– (Pueta et al., in press).. The volume of infusion was 1.83% of the body weight of the subject. Solutions were delivered into the infant's mouth using a pulsatile mode of administration (3s on, 10s off).

As expected, infants evaluated in CIT consume higher levels of both, ethanol and water, than the ones in PIT. Of major importance, different rates of consumption between ethanol and water only were found in CIT. In addition, these higher levels of ethanol intake were observed during PD14 and 15. When analyzing intake score in PIT, only was observed increases in ethanol consumption from PD14 to 15. No other significant result could be observed.

It seems that the level of exposure to the drug (i.e., quantities of ethanol infused) is a critical factor to promote ethanol consumption. CIT allows not only significant levels of drug consumption, but also a better acceptance of the drug since the first day of evaluation. This intake test (CIT) should be a more effective paradigm of ethanol infusion to analyze infantile ethanol intake patterns.



**IMPLICATIONS OF CONTINUING EDUCATION COURSE ON ALCOHOL CONSUMPTION: A BRIEF INTERVENTION PROPOSAL CONDUCTED BY SCHOOL TEACHERS**

*Cruz, Luciana Ap. Nogueira da; Martins, Raul Aragão.* Instituto de Biologia, Letras e Ciências Exatas da Universidade Estadual Paulista (Ibilce – UNESP). Rua Cristovão Colombo, 2265, São José do Rio Preto, SP, 15054-000, Brazil.  
[lunogcruz@yahoo.com.br](mailto:lunogcruz@yahoo.com.br); [raul@ibilce.unesp.br](mailto:raul@ibilce.unesp.br)

The consumption of alcohol among teenagers has been initiated earlier and more often than ever. Therefore, we propose a study with teenagers enrolled in public high school conducted by in-house educators (not a third-party intervention as commonly occurs) supported by Unesp researchers in a public high school located in the northwest of São Paulo state. A continuing education course has been delivered to the group of educators in order to prepare them for the development of a research on teenagers' drinking behavior and to lead a Brief Intervention based on the BASICS method - Brief Alcohol Screening and Intervention for College Students. Such intervention has been conducted to decrease alcohol consumption and its harmful effects. The aim of this research is to evaluate the implications of the continuing education course on the effectiveness of the study held by school professionals, on their teaching practices, and on

the efficiency of a Brief Intervention conducted by these educators. Results show that the study benefited the educators teaching practices and their professional self-image. It's evident that the degree of closeness between educators and students was a facilitating factor for the success of the brief intervention, which achieved significant levels of alcohol-use reduction especially among freshman high school students. Therefore we may conclude that it is valid to provide educators with research background and practical knowledge on brief intervention methods and that intervention must comprise middle school and freshman students especially.

Grants: FAPESP 2007/04849-0; Capes 2009 – 2011

## ROLE OF iNOS IN THE ANXIOTIC EFFECT INDUCED BY WITHDRAWAL FROM CHRONIC ETHANOL CONSUMPTION

Padovan, D.<sup>1</sup>, Silva, K.<sup>1</sup>, Tirapelli CR<sup>2</sup>, Padovan CM<sup>1</sup>. <sup>1</sup>Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto - USP - Psicologia e Educação; <sup>2</sup>Escola de Enfermagem de Ribeirão Preto - USP – Farmacologia 26731380

**Introduction:** The abstinence from chronic consumption of ethanol (CCE) leads to the development of different pathophysiological changes. Among them, changes in the functioning of the central nervous system appear to involve processes of neurodegeneration which are triggered by inflammatory processes due to CCE. Nitric Oxide (NO) has been considered an important factor in the onset of neurodegenerative disorders and CNS, and mainly synthesized by microglial cells induced by the enzyme nitric oxide synthase (iNOS), which are activated by various inflammatory factors. Furthermore, NO is also involved in the pathophysiology of anxiety disorders, which can be observed in the CCE abstinence. The objective of this study is to investigate whether inhibition of iNOS in the Dorsal Raphe Nucleus (DRN), one of the structures within the neural substrate of anxiety, is able to attenuate the effects of anxiety induced by withdrawal of CCE. **Methods:** After 48 hours of abstinence from CCE, the animals were injected intra-DRN of 1400W (selective inhibitor

of iNOS; 1nmol/0,2ml) or saline (0,2ml) and were submitted to the Elevated Plus-Maze, analyzing the percentages of frequency (%FA) and time spent (%TA) in open arms (two-way ANOVA followed by Duncan's test, considering the following factors: treatment (TREATY) and drink consumed (DRINK)). The experimental protocol was submitted and approved by the Ethics Committee on Animal Use (number of protocol: 07.1.992.53.2). **Discussion:** The anxiety induced by withdrawal from chronic consumption of ethanol involves an increase in NO production by action of iNOS, and the administration of a selective inhibitor of the enzyme inducible nitric oxide synthase in the dorsal raphe nucleus attenuates the effects resulting from alcoholic abstinence.

**Financial support:** CAPES

## **ETHANOL CONSUMPTION AND PINEAL MELATONIN DAILY PROFILE IN RATS**

*Peres<sup>1</sup>, Rafael; Amaral<sup>1</sup>, Fernanda Gaspar do; Madrigano<sup>1</sup>, Thiago Cardoso ; Scialfa<sup>1</sup>, Julieta Helena; Bordin<sup>1</sup>, Silvana; Afeche<sup>2</sup>, Solange Castro; Cipolla-Neto<sup>1</sup>; José.* 1: University of São Paulo, Institute of Biomedical Sciences, Department of Physiology and Biophysics, Av. Prof. Lineu Prestes, 1524, 1st floor, room 118, São Paulo, SP, CEP 05508-900, Brazil 2: Laboratory of Pharmacology, Butantan Institute, Av. Vital Brasil, 1500, São Paulo, SP, CEP 05503-900, Brazil  
[peresrafaelperes@gmail.com](mailto:peresrafaelperes@gmail.com)

It is well known that melatonin participates in the regulation of many important physiological functions as sleep-wakefulness cycle, motor coordination and neural plasticity and cognition. However, as there are contradictory results regarding the melatonin production diurnal profile under alcohol consumption, the aim of this paper was to study the phenomenology and mechanisms of the putative modifications on the daily profile of melatonin production in rats submitted to chronic alcohol intake. The present results show that rats receiving 10% ethanol in drinking water for 35 days display an altered daily profile of melatonin production, with a phase-delay and a reduction in the nocturnal peak. This can be partially explained by a loss of the daily rhythm and the 25% reduction in tryptophan hydroxylase activity and,

mainly, by a phase-delay in arylalkylamine N-acetyltransferase gene expression and a 70% reduction in its peak activity. Upstream in the melatonin synthesis pathway, the results showed that noradrenergic signalling is impaired as well, with a decrease in  $\beta 1$  and  $\alpha 1$  adrenergic receptors mRNA contents and in vitro sustained loss of noradrenergic-stimulated melatonin production by glands from alcohol-treated rats. We also show an altered expression of the clock-genes in the suprachiasmatic nucleus. Together, these results confirm the alterations in the daily melatonin profile of alcoholic rats and suggest the possible mechanisms for the observed melatonin synthesis modification.

Grants: This work was supported by São Paulo State Research Foundation (FAPESP), grant No 04/06767-2, 09/052920-0 and by fellowship no. 07/01416-5 from FAPESP.

**ETHANOL, ANXIETY AND BACLOFEN:  
CAN THIS SPECIFIC GABA<sub>B</sub> AGONIST BE  
SAFELY USED IN TREATMENT OF  
ALCOHOLISM? AN ANIMAL STUDY**

*Arantes, Vanessa Cristina Saltarello; Peretti, Murilo Calvo, Mattiello, Leticia; Brandalise, Liana; Ferrarini, Mariana Pfau; Robl, Marcela; Saito, Laura Rialto; Azevedo, Rodrigo; Saraceni, Ana Flavia; Soares, Alessandra Medeiros Rodrigues; Raldi, Nadia Cristina; Figueiredo, Fernanda; Villas Boas, Gustavo Roberto; Correia, Diego; Boerngen Lacerda, Roseli.* Universidade Federal do Paraná. Jardim das Américas, Curitiba, Paraná, 81540-970, Brazil.  
[murilo.peretti@gmail.com](mailto:murilo.peretti@gmail.com).

The anxiolytic effect of ethanol has been related to its negative reinforcing properties as well as to the development of addiction. This effect has been consistently observed in animal models of anxiety. The gabaergic system is involved in both anxiety and ethanol-induced anxiolytic effect having the GABA<sub>B</sub> receptor a modulatory action. The present study evaluated the acute and chronic effects of a specific GABA<sub>B</sub> agonist, baclofen, on the anxiolytic effect of ethanol. Male Swiss mice (n=90; 15/treatment) were evaluated in the elevated plus-maze (PM) in a drug free situation, using percent open arm time (%TA) as indicative of anxiety. Seven days later, each animal was acutely i.p. administered with one of the following treatments: saline (S), saline+ethanol 2 g/kg (E),

baclofen 1.25 mg/kg (B1) or 2.5 mg/kg (B2) + saline, ethanol + baclofen 1.25 mg/kg (EB1) or 2.5 mg/kg (EB2). They were exposed to PM 10 min after the 2<sup>nd</sup> injection and received daily the same treatment for 21 days and were evaluated again in PM in the 7<sup>th</sup> and 21<sup>st</sup> days. The anxiolytic effect of ethanol was observed both acutely and chronically. Acutely, baclofen alone showed dose-dependent anxiogenic effect and chronically, tolerance was observed. B1 co-administered with ethanol, both acutely and chronically, did not interfere in the anxiolytic effect, while the higher dose (B2) reduced this effect acutely, but chronically, B2 did not interfere on it. These data suggest that the GABA<sub>B</sub> receptor has little effect on the anxiolytic properties of ethanol. The use of baclofen in the treatment of alcoholism could be unsafe because this substance induces anxiety which could lead to relapse to alcohol use.

## **A MOTIVATIONAL MODEL OF ALCOHOL MISUSE IN ADOLESCENTS**

*Pilatti, Angelina<sup>1-2</sup>; Acuña, Ignacio<sup>1</sup>; Lamas, Luciana<sup>1</sup>; Godoy, Juan<sup>1</sup> & Brussino, Silvina<sup>1-2</sup>.* <sup>1</sup>. Facultad de Psicología. Universidad Nacional de Córdoba. Córdoba. Argentina. -Enrique Barros y Enfermera Gordillo s/n. Ciudad Universitaria, Córdoba, CP 5000, 351-4333054. <sup>2</sup>. Consejo Nacional de Investigaciones Científicas y Técnicas. CONICET. [angepilatti@gmail.com](mailto:angepilatti@gmail.com)

There is substantial support that excessive alcohol use is associated to an increment in the likelihood of experiencing alcohol related problems (Cranford et al., 2006; Hingson et al., 2009; Perkins, 2002; Wechsler & Nelson, 2008). Consequences of heavy drinking comprised academic problems, unintended pregnancies, sexually transmitted diseases, health problems, non fatal and fatal injuries (Hingson et al., 2002). According to that, researchers have been studying which factors are associated with an increase in the likelihood that adolescents would engage in a heavy drinking episode, which lead to a recognition of a broad range of factors including biological, social, and psychological aspects (Baer, 2002; Dowdall & Wechsler, 2002; Ham & Hope, 2003). The motivational drinking model postulates a person makes a decision about whether or not to drink based on a combination of actual and historical factors, where, drinking motives are visualized as

the final common pathway to alcohol use (Kuntsche et al., 2005). Historical aspects (such as personality), current aspects (such as being exposed to peer's drinking) are the basis for the development of alcohol expectancies, which are defined as the probability held by a person that a specific reinforcement (positive or negative) will follow alcohol use. However, alcohol expectancies are not sufficient to explain why a person decides to drink and it seems that to have a motive to drink is necessary in order to engage in this particular behavior. According to that, the proposed model of the present study includes antecedents factors (personality, peer's drinking), mediators (positive and negative expectancies and drinking motives), and an outcome variable (drinking behavior). Self report data obtained from an Argentinean sample of high school students (N= 343, mean age= 15.17, DS= 1.4) were analyzed with structural equation modeling. The general model fit was adequate, and it was supported the proposed personality and peer's drinking → positive and negative expectancies → drinking motives → alcohol use indirect effects. Results sustain the motivational model, where alcohol expectancies mediates between antecedents (personality and peer's use) and drinking motives, and finally, positive alcohol expectancies and drinking motives mediate the relation between antecedents and drinking use.

## **UNDERAGE DRINKING: PREVALENCE AND RISK FACTORS ASSOCIATED WITH DRINKING EXPERIENCES AMONG CHILDREN**

*Pilatti, Angelina<sup>1,2</sup>; Godoy, Juan<sup>1</sup> & Brussino, Silvina<sup>1,2</sup>. Facultad de Psicología. Universidad Nacional de Córdoba. Córdoba. Argentina. - Enrique Barros y Enfermera Gordillo s/n. Ciudad Universitaria, Córdoba, CP 5000, 351-4333054. Consejo Nacional de Investigaciones Científicas y Técnicas CONICET. [angepilatti@gmail.com](mailto:angepilatti@gmail.com)*

**Introduction:** Although high prevalence of alcohol use among adolescents claims for a better understanding of the progression of drinking in children and adolescents, there is a scarcity of information on underage drinking (Donovan, 2007; Donovan & Molina, 2008). In this context, it seems adequate to explore children drinking experiences and factors related to alcohol use at this developmental stage. Since adolescents and children differ in their drinking behaviors, more appropriate measures are needed to assess alcohol use within children. According to that, sipping, the lowest extreme of drinking behavior, represents an important measure in children's drinking research (Donovan & Molina, 2008). **Goal:** to describe drinking experiences and contexts of alcohol use of children, and to analyze the predictive utility of risk factors associated to alcohol use among children. Risk factors evaluated in the present

study were alcohol expectancies, peer's alcohol use, personality traits, impulsivity, and childhood behavior problems. **Participants:** self report data was obtained from a sample of 362 children aged 8 to 12 year olds (M= 10.44; SD= 1.213; 61.9% female). **Measures:** Demographic information; Alcohol consumption; Peer's alcohol use; Big Five Questionnaire for Adolescents (Cupani & Ruarte, 2008); Alcohol Expectancy Questionnaire for Children (Pilatti et al., 2010); an ad-hoc measure of Impulsivity, Aggressive and Antisocial Behaviors. **Data analyses:** A univariate and bivariate description of the data was performed. Then, a hierarchical multiple regression analysis was carried out to examine the unique contribution of each risk factor. **Results:** 59% of children tasted alcohol beverages at least once, and 34% reported to drink alcohol sometimes. Among the most prevalent contexts of alcohol use are drinking when allowed by adults, due to curiosity motives and when peers are present. At bivariate level, gender, age, personality traits, impulsivity, aggression, antisocial behavior, peer's alcohol use and positive alcohol expectancies were associated to drinking experiences. The hierarchical regression analysis showed gender, age, extraversion, impulsivity, female peer's alcohol use and expectancies regarding social improvement from alcohol were the best predictors of drinking experience within this sample of children. These results underscore the high prevalence of children with direct drinking experiences, giving support to a developing model of understanding drinking

behaviors.

## **THE ROLE OF NONSPECIFIC AND SPECIFIC RISK FACTORS IN THE PREDICTION OF ADOLESCENT DRINKING.**

*Pilatti, Angelina<sup>1,2</sup>; Godoy, Juan<sup>1</sup> & Brussino, Silvina<sup>1,2</sup>*. Facultad de Psicología. Universidad Nacional de Córdoba. Córdoba. Argentina. - Enrique Barros y Enfermera Gordillo s/n. Ciudad Universitaria, Córdoba, CP 5000, 351-4333054. CONICET. angepilatti@gmail.com

**Introduction:** A broad range of risk factors increase the likelihood of alcohol use and abuse in children and adolescents. These risk factors can be categorized in two big groups: nonspecific risk factors (those that may influence many forms of problems behaviors) and specific risk factors (those that are directly related to alcohol use and abuse).

**Goal:** to assess the predictive utility of two nonspecific risk factors (personality traits and antisocial behaviors) and two specific risk factors (peers' alcohol use and alcohol expectancies) over frequency and quantity of alcohol use.

**Participants:** A sample of 249 adolescents (Mean age= 14.77, SD= 1.37; 56.6% female) attending three private high schools within Cordoba, Argentina took part of the study. **Measures:** Demographic information; Alcohol consumption; Peer's alcohol use; Big Five Questionnaire for Adolescents (Cupani & Ruarte, 2008); Alcohol Expectancy Questionnaire for Adolescents (Pilatti

et al., 2010); an ad-hoc measure of Impulsivity, Aggressive and Antisocial Behaviors. **Data analyses:** A univariate and bivariate description of the data was performed. A series of hierarchical multiple regression analyses was carried out to examine the unique contribution of each risk factor. **Results:** Positive associations were found between frequency and quantity of drinking and extraversion, peers' alcohol use, impulsivity, aggressive and antisocial behaviors, and two of positive alcohol expectancies' scales. Negative associations were found between drinking measures and responsibility, and all negative alcohol expectancies' scales. Extraversion, antisocial behaviors, peers' alcohol use and negative mood alcohol expectancies were the best predictors of drinking quantity while age, extraversion, antisocial behaviors, peers' alcohol use and relaxation alcohol expectancies were the factors that better predicted drinking frequency. These results support previous studies that highlighted the utility of personality traits, externalizing disorders, and alcohol expectancies in predicting drinking behavior among adolescents. However, opposite to what was expected, alcohol expectancies regarding an improvement in social relationships didn't uniquely predict drinking frequency and quantity. In fact, although previous studies with Argentinean adolescents (Pilatti et al., 2010; Pilatti et al., 2011) supported the reported association between alcohol expectancies regarding social improvement, this result wasn't found in the present study.

**REWARD AND CONDITIONING: FULL DISSOCIATION BY GENE ADMINISTRATION IN AN ANIMAL MODEL OF ALCOHOLISM.**

*Quintanilla, María Elena<sup>1</sup> Tampier Lutske<sup>1</sup>, Karahanian Eduardo<sup>2</sup>, Rivera Mario<sup>1</sup>, Herrera-Marschitz Mario<sup>1</sup>, Israel Yedy<sup>1,3,4,5</sup>.* <sup>1</sup>Program of Molecular and Clinical Pharmacology. Independencia 1027, Santiago, CP 70000, 56-2-9786908 equintanilla@med.uchile.cl, <sup>2</sup>Center of Biomedical Research, Universidad Diego Portales, Chile, <sup>3</sup>Department of Pharmacological and Toxicological Chemistry, Chile, <sup>4</sup>Institute for Cell Dynamics and Biotechnology, University of Chile, and <sup>5</sup>Thomas Jefferson University, Philadelphia PA.

It is well established that alcohol and drug dependent individuals often fail to cease consuming their drug of dependence without psychotherapeutic or pharmacological treatment. There are two main elements likely involved in the perpetuation of the addictive behavior: (i) the drug rewarding effects and (ii) cues (olfactory or visual or situational) associated with the presence or use of the drugs, which act as motivational incentives, becoming “conditioned reinforcers”. Not known, however, is the relative strength of these two elements in the perpetuation of the addictive behavior. We recently showed (Karahanian et al., In press) that the voluntary self-administration of

ethanol by rats bred as high alcohol consumers (UChB) can be virtually abolished (-95%  $p < 0.001$ ) by the injection of a gene vector that inhibits the synthesis of catalase (the main enzyme that transforms ethanol into acetaldehyde) in the ventral tegmental area (VTA). In the present studies we allowed naïve rats to voluntarily self-administer ethanol (10% choice or water) on a 24-hour basis for 60 days, reaching consumption levels of 7-8 g ethanol/kg/day (equivalent to 500 g of ethanol/70kg). Subsequently, after achieving such consumption level, we injected the anticalase gene vector into the VTA. Under this paradigm the anticalase vector was fully inactive in altering the high levels of ethanol intake, suggesting a marked effect of conditioning most likely by the ethanol flavor and smell cues. We reasoned that a period of complete abstinence would blunt the conditioning. This was indeed observed; after a 28-day period of ethanol abstinence the anticalase group now showed the inhibitory effect on ethanol intake, although the effect was only 50% of that observed in naïve rats. We believe this is the first study suggesting that after chronic ingestion of a drug of abuse, conditioning constitutes a more important element of craving than the rewarding effects of the drug, conditioning which should be first extinguished to achieve any successful therapy.

Grants: FONDECYT 1095021, FONDECYT 1080447, ICM P05-01-F and NIAAA R01 AA015421.



**PLASTICITY OF THE DOPAMINERGIC MESOCORTICOLIMBIC PATHWAY UNDERLIES THE INCREASED RESISTANCE TO ETHANOL ADDICTIVE PROPERTIES IN CELLULAR PRION PROTEIN (PrP<sup>C</sup>) NULL-MICE.**

*Rial, Daniel.<sup>1</sup>; Pandolfo, P.<sup>1</sup>; Bitencourt, R.M.<sup>1</sup>; Pamplona, F.A.<sup>1</sup>; Moreira, E.L.G.<sup>1</sup>; Moreira, K.M.<sup>2</sup>; Hipolide, D.C.<sup>2</sup>; Dombrowski, P.A.<sup>3</sup>; Da Cunha, C.<sup>3</sup>; Walz, R.<sup>4</sup>; Martins, V.R.<sup>5</sup>; Takahashi, R.N.<sup>1</sup>; Prediger, R.D.S.<sup>1</sup>.* <sup>1</sup>Depto. de Farm., Univ. Federal de Santa Catarina, Florianópolis-SC. <sup>2</sup>Depto. Psicobiologia, Univ. Fed. de São Paulo, São Paulo-SP. <sup>3</sup>Depto. de Farmacologia, Univ. Federal do Paraná, Curitiba-PR. <sup>4</sup>Depto. de Clínica Médica, Univ. Federal de SC, Florianópolis-SC. <sup>5</sup>Instituto Ludwig de Pesquisa para o Câncer, São Paulo-SP, Brazil. [rialdaniel@gmail.com](mailto:rialdaniel@gmail.com)

We investigated the role of the cellular prion protein (PrP<sup>C</sup>) in ethanol addictive phenotypes, the dopaminergic (DA) content and DA receptors density. Wild-type (Prnp<sup>+/+</sup>) and PrP<sup>C</sup>-null female mice (Prnp<sup>0/0</sup>) were submitted to behavioral paradigms: climbing behavior, spontaneous locomotor activity (SLA), rapid tolerance (RT), conditioned place preference (CPP) and oral self-administration. DA content was evaluated by HPLC in the olfactory bulb (OB), prefrontal cortex (PFC), striatum (STR) and hippocampus (HIP). STR D<sub>1</sub>-receptor density was measured by

autoradiography. C57BL/6 mice were evaluated in ethanol induced-SLA and in ethanol oral self-administration after i.c.v. treatment with anti-prion protein antibody. The absence of PrP<sup>C</sup> increased the climbing behavior, which was blocked when Prnp<sup>0/0</sup> mice were treated (i.p.) with SCH-23390 (D<sub>1</sub>-antagonist) or sulpiride (D<sub>2</sub>-antagonist). Alterations of DA levels were observed in the OB and PFC of Prnp<sup>0/0</sup> mice, but not in the STR and HIP, when compared to wild-type mice. Prnp<sup>0/0</sup> mice also showed increased SLA after 1, 7, 14 and 21 days receiving ethanol. The impact of PrP<sup>C</sup> on ethanol SLA alteration was confirmed by the blockade of PrP<sup>C</sup> after i.c.v. infusion of anti-prion protein antibody in C57BL/6 mice. Prnp<sup>0/0</sup> mice were not susceptible to acquire rapid tolerance. In CPP the lowest ethanol dose tested (0.5 g/kg, i.p.) induced rewarding effects only in Prnp<sup>0/0</sup> mice, while the highest ethanol dose tested (2 g/kg, i.p.) induced rewarding effects only in Prnp<sup>+/+</sup> mice. Prnp<sup>0/0</sup> mice showed decreased ethanol (10 and 20% solutions) consumption when compared to control group. Treatment with SCH-23390, but not with sulpiride, blocked the ethanol intake in Prnp<sup>0/0</sup> mice. Pretreatment with anti-prion protein antibody reduced ethanol intake in C57BL/6 mice. Autoradiography for D<sub>1</sub> receptors showed diminished receptor density in the STR of Prnp<sup>0/0</sup> mice when compared to Prnp<sup>+/+</sup>. The results indicate the participation of PrP<sup>C</sup> in ethanol addictive properties, probably related with the blockade of plasticity processes and DA modulation at the mesocorticolimbic pathway.

Grants: FAPESC, CNP, CAPES e FAPESP.

## **ENERGY METABOLISM ON THE BRAIN: CAUSE OR CONSEQUENCE FROM ETHANOL EXPOSURE**

*Ribeiro, Andrea Frozino<sup>1</sup> Correia, Diego<sup>2</sup> Boerngen-Lacerda, Roseli<sup>2</sup> Brunialti-Godard, Ana Lúcia<sup>1</sup>.* <sup>1</sup>Department of General Biology, Universidade Federal de Minas Gerais, Pampulha, Belo Horizonte, MG, CEP 31270-901, Brazil [brunialti@icb.ufmg.br](mailto:brunialti@icb.ufmg.br)

<sup>2</sup>Department of Pharmacology, Universidade Federal do Paraná, Jardim das Américas, Curitiba, PR, CEP 81531-990, Brazil [boerngen@ufpr.br](mailto:boerngen@ufpr.br)

Proteins and enzymes, that act on energy metabolism show several regulatory functions on brain, whose effects interfere on signal transduction and neuroplasticity. In another words, these molecules are essential for maintaining equilibrium of cells, neurotransmission and consequently the equilibrium of mental cognitive and emotional process. Therefore, we investigated the relationship between genes responsible for energy metabolism of the brain and alcohol dependence. We used non-inbred, Swiss mice exposed to three-bottle free-choice model (between water and ethanol 5% or 10% v/v) during a long period consisting of four phases: acquisition (AC, 10 weeks), withdrawal (W, 2 weeks), reexposure (RE, 2 weeks), and quinine-adulteration (AD, 2 weeks). Based on their individual ethanol intakes, mice were classified into three groups: persistent

heavy drinker (PH; preference for ethanol and maintenance of high ethanol consumption in AD), heavy-drinker (HD; preference for ethanol and reduction in AD), and light-drinker (LD; preference for water during all phases). For the molecular analysis, total RNA was extracted from the extended amygdala area dissected from both cerebral hemispheres. Then, mRNA was quantified using real-time polymerase chain reaction assays. Only in mice behaviorally classified as PH was observed a negative correlation ( $p < 0.05$ ) between transcript levels of *Hadh* and *Acaa2*, *Acat1*, *Hadhb* and *Slc27a2* (genes involved on metabolic pathways). Similar result was observed between *Hadh* and *Kcnn3* (potassium conductance calcium-activated channel) in PH mice. These data suggest that the energy metabolism pathway could be altered in a cerebral area important to emotional process and thus it may contribute to addictive behavior in PH mice. Although more studies are necessary to understanding the role of metabolic process in alcohol addiction, these results reveal the new insight of studying cerebral energy metabolism to better clarification of neuronal mechanisms associated with ethanol addiction.

Grants: FAPEMIG EDT Universal 01/2010 APQ-02054-10

**REDUCTION OF ETHANOL CONSUMPTION IN ALCOHOL DEPENDENT RATS BY GENE THERAPY: MIMICKING THE FULLY-PROTECTED ORIENTAL GENOTYPE**

*Rivera-Meza, Mario; Quintanilla, María Elena; Tampier, Lutske.* Program of Molecular and Clinical Pharmacology, Faculty of Medicine, University of Chile, Santiago, CHILE.  
[mariorivera@med.uchile.cl](mailto:mariorivera@med.uchile.cl)

There is ample evidence that individuals bearing some polymorphisms in genes coding for enzymes involved in the metabolism of ethanol show protection against the development of alcoholism. In humans, ethanol is metabolized mainly by hepatic alcohol dehydrogenase (ADH) to acetaldehyde, which is oxidized to acetate by mitochondrial aldehyde dehydrogenase (ALDH2). In some East Asians, a point mutation in the ALDH2 gene (ALDH2\*2) abolishes the activity of this enzyme which upon ethanol consumption results in marked elevations of blood acetaldehyde. This increase in blood acetaldehyde levels lead to marked dysphoric effects that deter individuals to continue drinking. Another important polymorphism is that carried by individuals bearing a fast variant of ADH (ADH1B\*2; Arg47His) which also show a marked protection against alcoholism. Recently, we demonstrated that rats transduced with an engineered rat ADH

(rADH<sup>47His</sup>) gene equivalent to the fast human ADH1B\*2 showed high levels of arterial acetaldehyde and reduced in 50% their ethanol intake. Studies in Oriental populations have showed that individuals carrying both protective genes (ADH1B\*2 /ALDH2\*2) are virtually abstainers. The aim of this work was to mimic by gene transfer this protective phenotype in a rat model of alcoholism and studies its effect on the voluntary ethanol intake of the animals. For this purpose, we developed a bicistronic adenoviral vector encoding both: the fast rADH<sup>47His</sup> and an antisense RNA against rat ALDH2 (AdV-rADH<sup>47His</sup>-asALDH2). This vector was administered (dose:  $3 \times 10^{12}$  pv/kg) to UChB alcohol-preferring rats that were rendered alcohol dependent by a previously 2-month period of voluntary ethanol intake. Liver ADH activity in UChB rats transduced with AdV-rADH<sup>47His</sup>-asALDH2 was increased 176% ( $p < 0,001$ ) whereas liver ALDH2 activity was reduced 24% ( $p < 0,01$ ). Upon the administration of a dose of ethanol (1 g/kg, i.p.) rats that had received AdV-rADH<sup>47His</sup>-asALDH2 showed a peak in arterial acetaldehyde level that were 400% higher ( $P < 0.001$ ) than those of control animals. Rats that received AdV-rADH<sup>47His</sup>-asALDH2 showed a marked reduction of 60% ( $p < 0,001$ ) in their voluntary ethanol intake. These results showed that simultaneous increase of ADH and decrease of ALDH activity in the liver could be a strategy to develop a gene therapy for alcoholism.

Proceeding of the 2011 Meeting of the Latin-American Society for Biomedical Research on Alcoholism  
RACC, 2011, Suplemento (Marzo), 4-51

Funded by Grant: NIAAA R01-015421 (to Y.  
Israel).

**EFFECTS OF DIZOCILPINE ON NITRIC OXIDE SYNTHASE (nNOS) IN MICE FOLLOWING STRESS AND ETHANOL EXPOSURE**

*Rocha, Jaqueline Borges dos Santos; Teixeira, Simone A; Muscará, Marcelo Nicolas; Camarini, Rosana.* Department of Pharmacology. Instituto de Ciências Biomédicas, Universidade de São Paulo. Av. Prof. Lineu Prestes, 1524, Prédio Biomédicas I - Cidade Universitária, CEP. 05508-900 - São Paulo, SP, Brasil. [jaqueline.rocha@usp.br](mailto:jaqueline.rocha@usp.br)

Initiation of ethanol abuse in humans may be due to either the excitatory effects of ethanol or stress-relief properties of this drug. Nitric oxide (NO) plays an important role in regulating behavioral processes, and also in various effects of ethanol, including ethanol-induced behavioral sensitization. The involvement of glutamate NMDA receptor in the nNOS was examined after repeated stress and to a subsequent injection of ethanol. Mice were exposed to immobilization stress or received either a saline (SAL) or ethanol (ET) injection (1.8 g/kg) for 14 days. All groups were challenged with 1.8 g/kg ethanol or saline on the 15<sup>th</sup> day of treatment and the locomotor activity was measured during 10 min. Another set of mice received 0.25 mg/kg dizocilpine (DZP) 30 min before exposure to stress or the injections and were challenged with either SAL or ET on the 15<sup>th</sup> day. The animals were euthanized 3 hours later, and prefrontal cortex

(PFC) and hippocampus (HP) were extracted for nNOS activity analysis. Cross-sensitization between stress and ethanol and DZP and ethanol were found. The animals subjected to stress showed an increased activity of nNOS in HP and PFC, compared with the control group, while ethanol challenge attenuated this response. DZP pretreatment also attenuated the activation of nNOS induced by stress in HP and PFC. These results suggest that immobilization stress induces behavioral sensitization to ethanol; stress increases nNOS; attenuation of stress-induced nNOS by ethanol depends on NMDA receptor.

FINANCIAL SUPPORT: FAPESP e CNPq.

**ENVIRONMENTAL ENRICHMENT  
BLOCKS THE BEHAVIORAL  
SENSITIZATION TO ETHANOL IN MICE:  
EFFECTS ON EGR-1 AND THE BDNF  
SIGNALLING.**

cortex. EE can be considered and useful strategy to block BS effects, a phenomenon related to craving and relapse.

Financial Support: FAPESP

*Rueda, André Veloso Lima; Faria, Rulian Ricardo; Teixeira, Ana Maria Aristimunho; Alves, Adilson Silva; Yonamine, Mauricio; Britto, Luiz Roberto G.; Camarini, R.* Instituto de Ciências Biomédicas - Universidade de São Paulo. São Paulo, SP, Brazil. avlrueda@gmail.com

The use of addiction drugs can lead to long-term neuroplastic changes on the brain, such as behavioral sensitization (BS), a phenomenon related to addiction. Environmental enrichment (EE) is a strategy used to study the environmental influence on the response to several manipulations, including the treatment with addiction drugs. The aim of this work was to evaluate the effects of EE on the BS to ethanol and on the expression of proteins related to the response to drugs of abuse, as BDNF, TrkB and Egr-1. Thus, mice were exposed to EE and then repeatedly treated with a low dose (1.8 g/kg) of ethanol. Other group of mice was first submitted to the BS protocol and then exposed to EE. EE protected the mice from developing the BS to ethanol, and promoted its reversion. EE decreased BDNF levels in the prefrontal cortex and TrkB in the hippocampus, and increased Egr-1 expression in the insular

**EXPLORATORY BEHAVIOR OF  
ADOLESCENT AND ADULT RATS  
SUBJECTED TO STRESS AND  
ENVIRONMENTAL ENRICHMENT AFTER  
THE WITHDRAWAL PERIOD TO  
ETHANOL**

*Santos, Sílvia Cezar; Pierotti, Felipe Faria; Meirelles, Mônica Costa; Nakahata, Heidy de Sousa Dutra; Perez, Luciane Rodrigues N.; Mariotti, Thaís; Balbino-Junior, Mauri; Araújo, Renata; Calvente, Patrícia Renata Valester; Rocha, Jaqueline Borges dos Santos.* Health Sciences Directory. Universidade Nove de Julho, São Paulo. Av. Francisco Matarazzo, 612 - 1º Andar, Água Branca 05001-100 - São Paulo, SP, Brasil. [silvio\\_csc@hotmail.com](mailto:silvio_csc@hotmail.com)

The consumption of alcohol can lead to dependence on the individual through complex biochemical mechanisms that may or may not be associated with subjective factors of each person. Parallel dependence on ethanol is the alcohol withdrawal syndrome, characterized for the lack of this substance. Thus, this study aimed to elucidate the influence of unpredictable chronic stress (UCS) and environmental enrichment (EE) in the period of abstinence from alcohol in adult and adolescent rats. These animals (N = 12 each group) received 2.5 g / kg ethanol via intraperitoneal injection (ip) for 14 days. After the animals were subjected to abstinence for four days, leisure and stress were

performed. The UCS was: deprivation of food and water, forced swimming and sleeping with the lights on. EE was the exposure of animals for 2 hours at classic toys such as: plastic tunnels, bridges, ladders and wheel for rats. Behavioral analysis occurred after treatment with ethanol (D1) and after the period of abstinence (D2) in the open field for 5 minutes to get the number of rearings and locomotion total. The results show that adolescent subjected to stress had a higher exploratory behavior compared with adult rats. EE has kept the same behavior, comparing adolescents and adults. However, in adults showed an increased exploratory behavior, compared with the group subjected to stress. The results suggest behavioral differences on the UCS and EE in adolescent and adult rats in the ethanol abstinence period.

## **DOSE-DEPENDENT MOTOR EFFECTS OF ALCOHOL IN WISTAR RATS SELECTED BY THEIR RESPONSE TO NOVELTY**

*Herrera Sara, Reyes Cosette, Hernández-Fonseca Karla and Méndez Milagros.* Departamento de Neuroquímica, Instituto Nacional de Psiquiatría Ramón de la Fuente, Calzada México Xochimilco 101, 14370 México, D.F., México. [saraheor@imp.edu.mx](mailto:saraheor@imp.edu.mx)

Alcohol is a depressant drug that produces different behavioral effects depending on the dose. In rodents and humans, low doses produce psychomotor activation, whereas high doses induce sedation. The stimulant motor effects of alcohol have been difficult to assess in rats, since several factors alter behavior, including the dose, route of administration, duration of treatment, light-dark cycle, strain, stress or exposure to a novel environment. The aim of this work was to study the motor effects of alcohol at different doses in Wistar rats selected by their response to a novel environment in a normal light-dark cycle. Horizontal and stereotyped movements, as well as rearings were recorded at 2 min intervals in an open-field activity chamber. Rats were habituated to the chamber during 30 min and were selected as high- (HR) or low-responders (LR) depending on their activity in a novel environment. Animals received a saline injection (ip) and 30 min later were administered with saline or alcohol (0.5, 0.75,

1.0, 1.5, 2.0, 2.5, 3.0 g/kg ip). A control group was recorded but not injected (naïve). Blood alcohol concentration (BAC) was determined by an Alcohol Dehydrogenase spectrophotometric assay. Alcohol at doses of 0.75, 1 and 1.5 g/kg produced 1.7-, 2.5- and 2.1-fold increases in horizontal movements, while the 3.0 g/kg dose decreased this parameter (68%). HR and LR rats were equally responsive to the intermediate alcohol doses (1 and 1.5 g/kg), but only HR animals were sensitive to the highest dose. Stereotyped movements were not affected by alcohol, but rearings were significantly decreased by low, intermediate and high doses, versus the naïve group. Alcohol-induced decreases (55-84%) in rearings were observed in both HR and LR rats. Animals injected with 0.5, 0.75 and 1 g/kg alcohol showed mean BAC values of 96, 133 and 157 mg/dl, while the other tested doses produced BAC's in the range of 324 to 422 mg/dl. Our results show that intermediate and high alcohol doses stimulate or reduce motor activity in Wistar rats, respectively. A novel environment might be critical in determining alcohol sensitivity and the behavioral responses elicited by different drug doses.

Grants: INSTITUTO DE CIENCIA Y TECNOLOGIA DEL DISTRITO FEDERAL (ICyTDF) (PICDS 08-13) y CONSEJO NACIONAL DE CIENCIA Y TECNOLOGIA (CONACyT) (82728).



## **BASIC PERSONALITY DIMENSIONS AND RISKY ALCOHOL CONSUMPTION IN YOUNG ADULTS**

*Schmidt, V., Calero, A., Injoque-Ricle, I., y Maglio, A.* Instituto de Investigaciones - Facultad de Psicología - Universidad de Buenos Aires (UBA) y Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). [vaninaschmidt@gmail.com](mailto:vaninaschmidt@gmail.com)

Costa and McCrae's Five Factor Model (FFM; 1985, 1991, 2005) is one of the most useful personality models of the last decades. According to the FFM, personality traits can be grouped in five basic dimensions: Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness. Given the great amount of different results found in previous researches when this model is used in young adults, the present study investigates which personality dimensions contribute to risky alcohol consumption in young adults from Buenos Aires. Two-hundred and eighty six young adults participated in this study (17% male) with a mean age of 23-years-old (SD = 4.9). They participated voluntarily and their anonymity was preserved. 82% of the participants had completed their high-school studies, 14% college, and 4% university studies. The NEO-PI-R Personality Inventory (Costa & McCrae, 1992; adaptation: Leibovich & Schmidt, 2003, 2009), a socio-demographic questionnaire, and an alcohol consumption questionnaire (Cremonte, 2009) were administered.

Logistic regression analysis was conducted, considering the personality dimensions as independent variables and the presence or absence of risky consumption as dependent variable. The interaction effect of gender on the results was also tested. Significant regression models for men and women are presented, as well as some interaction effects among the variables introduced in the models. The results showed that conscientiousness is the dimension that best predicts risky alcohol consumption. The models indicate that gender has a moderator role between personality and alcohol consumption. Male models have better predictive capacity. This result is consistent with those obtained in national and international studies that use the FFM and other personality models.

**ONTOGENIC DIFFERENCES IN CREB FUNCTION AND BDNF LEVELS OF PREFRONTAL CORTEX AND HIPPOCAMPUS IN MICE TREATED WITH REPEATED ETHANOL.**

*Sabrina Lucio Soares Z.S. Ferreira; C. Scavone; R. Camarini.* Universidade de São Paulo, Department of Pharmacology, Instituto de Ciências Biomédicas, São Paulo, SP, 05508-900, Brazil; [salucios@yahoo.com.br](mailto:salucios@yahoo.com.br)

Adolescence is a period characterized by reorganization of brain regions such as the prefrontal cortex (PFC) and hippocampus (HPC), which are associated with impulse control and learning/memory, respectively. One of the ethanol's target in the central nervous system is the cyclic AMP response element binding factor (CREB), that promotes alterations in many genes, including the brain-derived neurotrophic factor (BDNF). Alterations in CREB phosphorylation and BDNF expression in several brain structures have been shown to be associated with alcohol dependence. The aim of the present study was to investigate the acute and chronic effects of ethanol on DNA/CREB binding activity; and CREB, pCREB and BDNF levels in the PFC and HPC of adolescent (ADL) and adult (AD) mice submitted to the behavioral sensitization model. Mice from both ages received saline or ethanol (2.0 g/kg) injections for 15 consecutive days. One week after

this pretreatment, mice received a challenge injection of either saline or ethanol (2.0 g/kg), constituting the groups: saline control, acute ethanol and chronic ethanol. The DNA/CREB activity was measured by Electrophoretic Mobility Shift Assays (EMSA), the pCREB/CREB levels by Western blot; and BDNF levels by ELISA assay. Adult mice developed behavioral sensitization, whereas ADL mice did not sensitize. Acute and repeated ethanol decreased substantially DNA/CREB activity in the PFC of ADL and in the HPC of AD mice compared to the saline controls. Acute ethanol increased BDNF levels in ADL and AD mice. However, there was a reduction in the capacity of ethanol to increase BDNF levels following repeated ethanol administration in ADL, but not in AD. Decreased function of cAMP-PKA-CREB signaling and BDNF levels has been involved in alcohol drinking. Taken together, the results suggest age-linked differences in drug experience-dependent plasticity, what may influence the effects of addictive drugs in adolescence.

Financial Support: FAPESP

## **ETHANOL WITHDRAWAL ACTIVATES NITRIC OXIDE PRODUCING NEURONS IN ANXIETY-RELATED BRAIN AREAS**

*Taciany Bonassoli, Rúbia M. M. W. de Oliveira, Humberto Milani.* Universidade Estadual de Maringá, Department of Pharmacology, Av. Colombo 5.790. Maringá, (55) (44) 3011-4998, Brasil. Paraná, 3011-4040  
[vivianbonassoli@yahoo.com.br](mailto:vivianbonassoli@yahoo.com.br)

Discontinuation of ethanol chronic consumption has been related to the onset of withdrawal syndrome, which is characterized by heightened anxiety. Nitric oxide (NO) has been involved in the development and expression of ethanol withdrawal syndrome as well as in the anxiety states. The present study aimed to investigate whether NO-producing neurons localized in brain areas related to anxiety are activated following ethanol withdrawal. Male Wistar rats were offered 6 e 8% (vol/vol) ethanol added to a nutritionally balanced solution (Sustagen M®) as the only source of food for a period of 21 days. Control animals received control dietary fluid for similar period of time. Twenty-four or 48 h after ethanol discontinuation, the animals were exposed to the open field for 10 min. Two hours later, the animals had their brains removed and processed for Fos immunohistochemistry and nicotinamide adenine dinucleotide phosphatediaphorase histochemistry, in order to detect activated neurons and NO-

producing neurons, respectively. Data are expressed as mean  $\pm$  S.E.M. Data obtained in the open-field test were analyzed by one-way ANOVA. For histological data, an individual ANOVA was done for each brain structure analyzed. Post hoc comparisons were made by the Tukey's test. A decreased exploratory activity was observed in animals subjected to 24-h withdrawal which was characterized by a shorter distance traveled in the open field. Additionally, increased Fos expression was detected in several brain areas, including the cingulate and piriform cortices, hypothalamic nuclei, amygdaloid nuclei, most subdivisions of the periaqueductal gray matter, and dorsal raphe nucleus. Ethanol withdrawal activated NO-producing neurons in the paraventricular nucleus of the hypothalamus, dorsolateral periaqueductal gray matter, and dorsal raphe nucleus. The present results show that ethanol withdrawal activates NO producing neurons in brain areas implicated in the modulation of emotional, autonomic, and motor expression of anxiety-like behaviors.

GRANTS: Fundação Araucária, CNPq, and CAPES

## **COCAINE TREATMENT IN ADOLESCENT MICE PRODUCES ANXIETY AND INCREASED LEVELS OF pCREB IN THE HIPPOCAMPUS**

*Rocha, Maria Cristina Valzachi; Camarini, Rosana.* Instituto de Ciências Biomédicas - Universidade de São Paulo - Av. Prof. Lineu Prestes, 1524, São Paulo/SP-  
[cris\\_valzachi@yahoo.com.br](mailto:cris_valzachi@yahoo.com.br)

The adolescence differs from adulthood in several aspects, including behavioral and neurochemical parameters. The psychomotor sensitization, measured by the increased locomotor activity, is used to study the long-term effects of molecular adaptations of prolonged use of addictive drugs. Not only psychomotor stimulation, but also the 'incentive salience' attributed to an initially neutral stimulus is progressively increased. This incentive sensitization has been proposed as a possible mechanism to explain the transition from controlled to compulsive drug-seeking and -taking behavior. The aim of this study is to evaluate the anxiety and locomotor responses after repeated administration of cocaine in adolescent and adult mice, and the protein expression in prefrontal cortex and hippocampus of a transcription factor involved in drug abuse, CREB and its phosphorylated form, pCREB. Male Swiss mice adolescents (28–30 days) and adults (58-60 days) were subjected to a daily injection of saline or

cocaine (10mg/kg i.p.) during 8 days. At 9th day of treatment, every mouse received a saline injection in order to evaluate possible environmental conditioning. After ten days without any treatment, animals received an injection (challenge) of cocaine or saline. Only adults exhibited locomotor sensitization, on the other hand, only the adolescents expressed an effect of the context, suggesting the existence of independent mechanisms to these phenomena. The adolescents treated with a daily injection of cocaine showed a decrease in the time spent in the open arms of *Plus maze* during withdrawal, furthermore, they showed increased thigmotaxis suggesting increased anxiety behavior. Analysis of protein expression by *Western blotting* showed an increased level of pCREB in the hippocampus of adolescents during withdrawal compared to animals treated with chronic or acute cocaine, suggesting organism's attempt to restore homeostasis. In conclusion, results showed different neurochemical and behavioral responses between adult and adolescent mice, suggesting the necessity of different approaches to the dependence treatment according to the age.

Grants: CNPq, FAPESP.

**BACLOFEN REDUCED ALCOHOL CONSUMPTION IN “HEAVY-DRINKER” BUT NOT IN MICE WHOSE LOST CONTROL OVER INTAKE**

Villas-Boas<sup>a</sup>, Gustavo Roberto; Zamboni<sup>a</sup>, Camila Gadens; Peretti<sup>a</sup>, Murilo Calvo; Correia<sup>a</sup>, Diego; Boerngen-Lacerda<sup>\*a</sup>, Roseli. <sup>a</sup>Department of Pharmacology, Universidade Federal do Paraná, Jardim das Américas, Curitiba, Paraná, CEP 81531-990; Brazil [gustavo.villasboas@gmail.com](mailto:gustavo.villasboas@gmail.com)

Several studies have shown that baclofen, a  $\gamma$ -aminobutyric acid-B (GABA<sub>B</sub>) receptor agonist, reduces ethanol intake in animals and humans, but others have shown the contrary. A previous study using the same model of the present study demonstrated that mice characterized to “loss of control over alcohol intake” had different *Gabbr1* and *Gabbr2* transcription levels, which express the GABA<sub>B1</sub> and GABA<sub>B2</sub> subunits, respectively, in brain areas related to addictive behavior. In the present study, we tested whether mice with “loss of control” exhibit differential ethanol consumption in response to baclofen treatment. Sixty adult male Swiss mice were individually housed and offered ethanol (5% and 10%) and water orally in a free-choice paradigm that consisted of four phases: acquisition, withdrawal, reexposure, and adulteration. Mice were characterized as “loss of control” (A), heavy (H), and light (L) drinkers. After the classification, the three groups of mice

were divided into two subgroups that received intraperitoneal injections of baclofen (0, 1.25, 2.5, and 5.0 mg/kg) or saline, being exposed to free-choice 30 min later. Ten mice whose had access only to water during the free-choice paradigm (control group) received all doses of baclofen and continued having access to water. Fluid consumption was measured for 90 min and 24 h after the injection. Baclofen reduced ethanol intake only in group H. The mice of group A, even after baclofen treatment, continued to exhibit a “loss of control” over ethanol intake. Activation of the GABA<sub>B</sub> receptor is necessary for the precise balance between the GABA<sub>B1</sub> and GABA<sub>B2</sub> subunits, so the disproportionate transcription levels observed in “loss of control” mice could account for this lack of response to baclofen treatment. These data suggest that baclofen may only be a useful treatment in individuals who have not lost their control over ethanol intake.

## **IMPACT ON MOTHER PROLE CONSUMPTION OF ETHANOL DURING LACTATION**

*Lima, V.B.V.; Carvalho, W.R.S.; Arcanjo, H.; Figueiredo, M.M.; Bellot, R.G.; Freitas, T.A.; Conceição, I.M.* Neuroscience Center - Faculty of Healthy, Methodist University of São Paulo Av. Dom Jaime de Barros Câmara, 1000, Bairro Planalto. São Bernardo do Campo, SP, Brasil CEP 09895-400. Telefone: 4366-5303 E-mail: isaltino.conceicao@metodista.br

The importance of breastfeeding is emphasized by many studies which show the protective effect of breastfeeding against infant mortality and morbidity. Besides its nutritional and immunoprotective functions, breastmilk is extremely important for central nervous system development. Many substances ingested by the mother can reach the infant through breast milk. One of these substances is ethanol; a psychotropic drug considered the most widely consumed abuse substance in the world. The prevalence ethanol addiction is the highest of all drugs of abuse. Its chronic use can lead to serious physical, social, psychological and economic problems. Studies aimed at determining the consequences for the offspring of ethanol consumption by mothers during the lactation period are of great importance, considering that the primary goal of healthcare today is the prevention. This work aimed to

identify and analyze the effects on the pups of the consumption of ethanol by their mothers during the lactation period. More specifically were investigated possible alterations on physical and reflex development. Were used 11 female mice and their pups, divided into two groups: ethanol (which received a 4% ethanol solution from day 2 to day 14 of lactation as the sole liquids source) and control group (who received filtered water throughout the experimental period). We observed that both male and female that received breast milk from mothers who drank ethanol showed alterations on reflex parameters. For example, ethanol group showed palmar reflex (mean $\pm$ SEM of time in s) deficits in days 6 ( $1.769 \pm 0.231$ ), 9 ( $1.115 \pm 0.118$ ) and 10 ( $1.108 \pm 0.096$ ) after birth, compared to control group ( $1.119 \pm 0.093$ ;  $1.740 \pm 0.281$ ;  $1.840 \pm 0.266$  for days 6, 9 and 10 respectively). For this parameters, females showed deficits on days 9 ( $1.418 \pm 0.188$ ) and 10 ( $1.073 \pm 0.065$ ), compared to control ( $2.200 \pm 0.304$  and  $1.740 \pm 0.252$ ). These results demonstrate that ethanol when ingested by mothers, during lactation may cause harmful effects for their offspring.

Financial support: Faculty of Healthy, Methodist University of São Paulo; CNPq-PIBIC.

## **THE EFFECT OF ETHANOL CONSUMPTION ON THE MATERNAL BEHAVIOR OF MICE**

*Carvalho, W.R.S.; Lima, V.B.V.; Arcanjo, H.; Figueiredo, M.M.; Bellot, R.G.; Freitas, T.A.; Conceição, I.M.* Neuroscience Center – Faculty of Health, Methodist University of São Paulo Av. Dom Jaime de Barros Câmara, 1000, Bairro Planalto. São Bernardo do Campo, SP, Brasil CEP 09895-400. Telefone: 4366-5303 E-mail: isaltino.conceicao@metodista.br

The importance of breastfeeding is emphasized by many studies which show the protective effect of breastfeeding against infant mortality and morbidity. Besides its nutritional and immunoprotective functions, breastmilk is extremely important for central nervous system development. Many substances ingested by the mother can reach the infant through breast milk. One of these substances is ethanol; a psychotropic drug considered the most widely consumed abuse substance in the world. The prevalence ethanol addiction is the highest of all drugs of abuse. Its chronic use can lead to serious physical, social, psychological and economic problems. It is of current knowing that ethanol is harmful to the growth of fetus when drunk during the pregnancy. However, few are the report about of the consequence of ethanol use during the breast feeding, specially concerning to the maternal

behavior, namely the relation of mother and your baby. The aim of this work was evaluate the effects of ethanol ingestion during the period of breast feeding in the maternal behavior of mice. Were used 11 female mice and their pups, divided into two groups: ethanol (which received a 4% ethanol solution from day 2 to day 14 of lactation as the sole liquids source) and control group (who received filtered water throughout the experimental period). In the 5, 8, 11 days of breast feeding, were performed tests to evaluate the maternal behavior of both groups. We observed disruption of the maternal behavior of that mothers that received ethanol, indicated by a poor performance in several parameters indicative of maternal behavior, ie, On day 8 of lactation the mothers in the control group (mean  $\pm$  SEM of  $177.4 \pm 53.88$ , N=5) spent significantly more time(s) taking care of their offspring than mothers who drank ethanol ( $33.83 \pm 12.68$ , N=6). These data demonstrated that even in small doses ethanol intake during lactation can be harmful to the interaction mother-baby, causing a disruption on maternal behavior.

Financial support: Faculty of Health, Methodist University of São Paulo; CNPq-PIBIC.

**HOW TO DETECT EARLY HARMFUL AND  
HAZARDOUS SUBSTANCE USE  
IN WORKPLACE: A QUALITATIVE  
ASSESSMENT**

*Zibe-Piegel, Viviane Paola; Pelissari, Raquel; Fogaça, Bruno; Bronner, Caroline; Hubner, Denise; Boerngen-Lacerda, Roseli.* Department of Pharmacology, Universidade Federal do Paraná. P.O. Box 19031, 81531-990 Curitiba, PR, Brasil. boerngen@ufpr.br

The workplace is appropriate to prevent hazardous/ harmful substance use among employees. This study evaluated the implementation process of early detection using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) and brief intervention (BI) in a City Hall workplace in a southern city of Brazil. First, meetings were held to inform the managers the importance to prevent substance-related problems in workplace. Of the 70 professionals of the occupational health service trained in a 20 h course regarding psychoactive substances, detection, and intervention, 26 applied the ASSIST and BI using systematic criteria to form a representative sample of employees. According to the ASSIST score, each employee received either general information about drugs or BI or was referred to specialized treatment. Then, focus group meetings were held with professionals. Of the 1310

interviewed employees, lifetime use was 84% (alcohol), 50% (tobacco), 17.5% (other drugs). The percentages of possible dependence and risky use were 17.8% (tobacco), 3.2% (alcohol), 0.5% (other drugs). The action research improved the implementation of early detection and intervention for substance use in their routine. The ASSIST facilitates talking about substances without prejudice or stigma, enabling earlier detection, intervention, and treatment referral.