International Behavioral Neuroscience Society

Annual Meeting

Program and Abstracts

Rio de Janeiro, Brazil

June 12-16, 2007

Abstracts of the International Behavioral Neuroscience Society, Volume 16, June 2007

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IBNS CENTRAL OFFICE

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PRESIDENTIAL WELCOME

Dear Colleagues,

It is my great pleasure to welcome you to the 16th Annual Meeting of the International Behavioral Neuroscience Society (IBNS). Hopefully, those of you from afar will have the opportunity to explore also other parts of this magnificent country and to establish a relationship to this fascinating continent – South America. We have a high calibre program, with presentations that cover most of the fields in our discipline, and attendees will represent an array of scientific approaches and countries of origin. Our meeting should provide an outstanding opportunity for cross-disciplinary and cross-cultural exchange. Our colleagues from Brazil on the Local Organizing Committee, under the leadership of Marcus Brandão, have arranged excellent conference facilities. We thank them for their warm hospitality in hosting our conference, as well as the Brazilian Neuroscience Society and CNPq for their generous support. Special thanks is due to Andrew Holmes and his Program Committee for the exciting and diverse program comprising 6 symposia, 2 oral sessions, 2 keynote speakers, and our 2 Wayner/NNOXe awardees. In total, we have about 210 scientific contributions, representing the breadth of research within behavioral neuroscience. We highly appreciate the organization of attractive Satellite Meetings, in Curitiba by Claudio da Cunha, in Joao Pessoa by Carlos Tomaz and Marillia Barros, and in Rio de Janeiro by Robert Blanchard. Special thanks also to Marianne Van Wagner, IBNS Executive Coordinator, who again performed a great job in managing the many issues related to running our Society, and to Melanie Paquette for her informative Newsletter, which helped us to prepare for the journey to Rio. There are many others, whom I cannot list here, but hope to thank personally, for their efforts and contributions to the success of this meeting.

If you have not yet become a member of IBNS, you are cordially invited to sign up at the registration desk here at the Congress or after the meeting through the IBNS website (www.ibnshomepage.org). In closing, it has indeed been an honor to serve as your IBNS President this year. Our Society is strong and is growing - moreover, with its focus on behavioural and functional analysis, it occupies a critical niche in the neuroscientific community. We hope that you will profit from our meeting in beautiful Rio de Janeiro, not only scientifically, but also personally, and hope to welcome you again to future IBNS meetings.

With best wishes,

Joseph P. Huston
IBNS President

OFFICERS

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..... Paul Rushing

We are pleased to announce the recipients of the IBNS Travel Awards for the 2007 meeting in Rio de Janeiro, Brazil. These awards will be presented at the Awards Banquet on Friday evening. Award winners will receive a cash award, certificate, and waiver of registration and banquet fees. Congratulations to all.

TRAVEL AWARDS

(listed alphabetically)

Presentations given by the Travel Awardees are indicated in the program by the symbol †.

Michal Arad, Tel Aviv University, Israel

Catalina Cervantes, The University of Texas at Austin, TX, USA

Kelly L. Conrad, Rosalind Franklin University, Chicago, IL, USA

James Doherty, Georgia State University, Atlanta, GA, USA

Jermaine D. Jones, American University, Washington, DC, USA

Amanda C. Kentner, University of Ottawa, Canada

Noam Y. Miller, University of Toronto, Canada

Rupshi Mitra, Stanford University, CA, USA

Christian P. Müller, University of Düsseldorf, Germany

Nupur Nag, Wellesley College, Wellesley, MA, USA

Jeffrey Parrilla, Universidad del Este, Puerto Rico

Susanna Pietropaolo, ETH, Switzerland

Holger Russig, ETH Zurich, Switzerland

Student Travel awardees are presenting orally in the Travel Award Blitz and will also have their research presented in a poster session.

SPONSORS

The IBNS would like to express our gratitude to the following organizations who have given financial support to the 16th International Behavioral Neuroscience Society Conference. This financial support enabled many students to attend the conference and also allowed recruitment of excellent special symposium speakers.

National Institute of Mental Health

Grant Number: 2R13MH065244-06

We also very much appreciate the efforts of the Local Organzing Committee, Chaired by Marcus Brandão, in raising funds locally to help support the IBNS meeting and its participants.

CNPq- National Council for Research Funding
Graduate Program in Psychobiology Instituto de Neurociencias & Comportamento - INeC

CORPORATE SPONSORS

The IBNS would like to express our gratitude to the following corporate sponsors that are attending the meeting as booth exhibitors and/or have given special financial support to the International Behavioral Neuroscience Society.

Elsevier Science, Inc.
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EXHIBITORS

We would also like to thank the following companies that are supporting the IBNS by attending the meeting as booth exhibitors.

Clever Sys. Inc.
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ACKNOWLEDGMENTS

The Society would like to extend our deep appreciation to the following that are responsible for the success of this meeting:

PROGRAM COMMITTEE:

Andrew Holmes (Chair)
Jacqueline Crawley (Co-Chair)
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Kelly Lambert
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For the mentoring initiative:

Christine Hohmann
Nancy Ostrowski

LOCAL ORGANIZING COMMITTEE:

Marcus Lira Brandão (Chair), FFCLRP- Campus USP, São Paulo,Brazil
Eliane Volchan, Universidade Federal do Rio de Janeiro, Rio de Janeiro
Claudio Cunha, Universidade Federal do Parana, Curitiba, Brazil

KEYNOTE SPEAKERS

- **John Aggleton***, Cardiff University, UK *Building brain systems for memory.*
- **Ivan Izquierdo**, PUCRS, Brazil *Memory consolidation: Beyond the bottom line?*

***Dr. Aggleton's Keynote Lecture is sponsored by Elsevier Science.**

PRESIDENTIAL ADDRESS

Joseph P. Huston, University of Duesseldorf, Germany *Behavioral despair incurred by withholding reinforcement: extinction-induced depression?*

MATTHEW J. WAYNER-NNOXe PHARMACEUTICALS AWARDS

- **William T. Greenough,** University of Illinois at Urbana-Champaign, IL, USA *Plastic brain mechanisms in Fragile X Syndrome (2006 Award)*
- **Donald G. Stein**, Emory University, Atlanta, GA, USA *The trials and tribulations of progesterone in the treatment of brain injury: Was the game worth the candle? (2007 Award)*

WORKSHOPS

Student Workshop: Organizers: Susan Powell and Vickie Risbrough. Susan Powell and Vickie Risbrough of the Education and Training Committee, in conjunction with the Mentorship Committee, will offer a student workshop geared at preparing an effective academic CV. A panel of IBNS members will provide tips on formatting and organizing the CV to communicate strengths, and will discuss what information should and should not be included. Time will be allotted for specific questions, and students may bring a copy of their current CVs to receive feedback.

Grant Workshop: Organizer: Paul Rushing. "NIH 101", Paul A. Rushing, National Institute of Diabetes and Digestive and Kidney Diseases. This brief "NIH 101" workshop will provide valuable information on a variety of issues from submission to funding. A large portion of the presentation will be dedicated to questions from the audience.

SPECIAL SYMPOSIA

- *Social and emotional behaviors: focus on serotonin and vasopressin receptors.* Chairs: **Rosa Maria Martins de Almeida**, UNISINOS, RS, Brazil & **Silvana Chiavegatto**, University of Sao Paulo.

- *5-HT and emotion: An appreciation of the contributions of Fred Graeff.* Chair: **Antonio Padua Carobrez,** Universidade Federal de Santa Catarina.

- *Early-life stress to model the interactions between genes and the environment: From the clinic to animal models.* Chairs: **Holger Russig**, University of Zürich/Swiss Federal Institute of Technology & **Francesca Cirulli**, Istituto Superiore di Sanità.

- *Gene-environment Interactions: animal models for mental health research.* Chairs: **Mikhail V. Pletnikov**, Johns Hopkins University, **Christine Hohmann**, Morgan State University, **Joanne Berger-Sweeney**, Wellesley College.

- *The role of genetics and genomics in understanding fear- and anxiety-like behaviors.* Chair: **Abraham Palmer**, University of Chicago.

- *Contributing factors to normal and pathological variation in social behaviors* Chair, **Sandra J. Kelly**, University of South Carolina

SATELLITES

- June 8-10. **Primate Models for Psychiatric Disorders**. Hotel Littoral in Joao Pessoa, Brazil. Organizers: **Carlos Tomaz,** Universidade de Brasília, Brazil. **Marilia Barros,** Universidade de Brasília, Brazil.

- June 10-11. **Learning and Memory, in honor of the 70th birthday of Ivan Izquierdo.** Mabu Royal & Premium Hotel, Curitiba, Brazil. Organizer: **Claudio Da Cunha**, Federal University of Parana State (UFPR), Curitiba, Brazil.

- June 12. **Predatory Odor: An Animal Model for the Study of Anxiety.** Othon Rio Palace, Rio de Janeiro, Brazil. Organizer: **Robert Blanchard,** University of Hawaii, Honolulu, HI, USA.

IBNS 2008 - CALL FOR SYMPOSIA PROPOSALS

The 2008 Annual Meeting of the International Behavioral Neuroscience Society will be held at the Frenchman's Reef & Morning Star Marriott Beach Resort on the tropical Caribbean island of St. Thomas, June 17-22. We look forward to another scientifically excellent conference in a beautiful venue.

The Program Committee is now soliciting proposals for symposia. A typical symposium includes 4 speakers and is scheduled for 2 hours. Symposium proposals should include a title, the name of the chairperson(s), a substantive description of the topic and proposed talks, the list of speakers, their affiliations, and tentative titles of their talks.

The deadline for priority consideration of symposium proposals is September 1, 2007. Please send your proposal to the Program Committee Chair, Dr. Jacqueline Crawley, Laboratory of Behavioral Neuroscience, NIMH, Bethesda, MD, USA, crawleyj@intra.nimh.nih.gov.

PROGRAM NOTES:

- All main events including Lectures, Symposia, Oral Sessions, Business Meeting, Slide Blitz, Student Workshop and Grant Workshop will be held in the ITAIPU Meeting Room.
- Breakfast is included if you are registered at the conference hotel, the Othon Rio Palace Hotel. It is served from 6:00-10:00 a.m. in the Patio Tropical Room.
- Registration, Reception, Exhibitors, Coffee Breaks and Poster Sessions will be held in the Foyer outside the Itaipu Meeting Room.
- Council Meeting will be held in the Mar Azul Room.
- The Banquet will be served in the Patio Tropical Room.
- Presenting authors are indicated in the program by **bold**type.
- † Indicates Travel Award recipient.

Tuesday, June 12, 2007

2:00-4:00 Registration - Location: Foyer of the Itaipu Meeting Room. For late arrivals only, the registration desk will be open on Wednesday morning at 7:30 a.m.

4:00-6:00 Student Social – Location: Asian Corner Room.

7:00-8:00 Registration

8:00-9:00 Welcome Reception - Location: Foyer of the Itaipu Meeting Room.

Wednesday, June 13, 2007

8:30-8:45 **President's Welcome**.

8:45-10:45 ***Symposium 1****: Social and emotional behaviors: Focus on serotonin and vasopressin receptors.* Chairs: Rosa Maria Martins de Almeida, UNISINOS, RS, Brazil and Silvana Chiavegatto, University of Sao Paulo.

8:45 SEROTONIN CELLS AND ESCALATED AGGRESSIVE BEHAVIOR: INTEGRATION OF SOMATODENDRITIC AUTORECEPTORS, PRE- AND POST-SYNAPTIC RECEPTORS AND TRANSPORTERS. **Miczek, K.A.**

9:10 5-HT1B RECEPTOR AND ESCALATED AGGRESSION IN MALE AND FEMALE RODENTS. **De Almeida, R.M.M.**

9:35 VASOPRESSIN AND THE REGULATION OF AGONISTIC BEHAVIOR. **Albers, E.**

10:05 SOCIAL ISOLATION AND GENE EXPRESSION OF SEROTONIN RECEPTORS. **Chiavegatto, S.**

10:25 TARGETING GENE EXPRESSION IN SUBREGIONS OF DORSAL RAPHE ALTERS STRESS AND ANXIETY BEHAVIORS. **Neumaier, J.F**.; McDevitt, R.; Hiroi, S.

10:45-11:00 Break & Exhibit Viewing

11:00-12:00 **Presidential lecture: Joseph Huston, University of Düsseldorf, Germany. *Behavioral despair incurred by withholding reinforcement: Extinction-induced depression?*** (Introduction: Robert Adamec)

12:00-2:00 Break

12:00-2:00 IBNS Council Meeting – Location: Mar Azul Room

2:00-3:30 **Student Travel Award Slide Blitz** - Chair: Susan Powell

FEMALES EXPOSED TO AN ANABOLIC STEROID DISPLAYED AN INCREASE IN SEXUAL MOTIVATION WITHOUT ALTERING SOCIAL DOMINANCE. †**Parrilla, J.**; Jorge, J.C.; Barreto-Estrada, J.L.

BEHAVIOURAL EFFECTS OF HIPPOCAMPAL OVEREXPRESSION OF BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) IN RATS. †**Pietropaolo, S.**; Paterna J.C.; Büeler, H.; Yee, B.K.; Feldon, J.

ESCALATION OF MORPHINE SELF-ADMINISTRATION IS ATTENUATED IN PERIADOLESCENT MALE RATS. †**Doherty, J.M.**; Ogbonmwan, Y.; Li, C.; Waldron, N.; Moffett, A.E.; Williams, B.F.; Frantz, K.J.

ASSOCIATIONS BETWEEN OFFENSIVE AGGRESSION AND IMPULSIVITY IN ADULT MALE GOLDEN HAMSTERS. †**Cervantes, M.C.**; Delville, Y.

EXPLORING THE INFLUENCE OF REWARD ON SICKNESS AND IMMUNITY IN THE FEMALE RAT. †**Kentner, A.C.**; Takeuchi, A.; Miki, T.; James, J.; Seino, S.; Bielajew, C.

THE EFFECTS OF SINGLE AND MULTIPLE MONOAMINE TRANSPORTER GENE DELETION ON COCAINE-INDUCED CONDITIONED TASTE AVERSION. †**Jones, J.**; Hall, F.; Uhl, G.; Riley, A.

OPERANT CONDITIONING IN ZEBRAFISH. †**Miller, N.**; Gerlai, R.

THE EFFICACY OF HALOPERIDOL IN RESTORING LATENT INHIBITON IN FEMALE RATS IS ESTROGEN DEPENDENT. †**Arad, M.**; Weiner, I.

AMPA AND DOPAMINE RECEPTOR TRAFFICKING IN THE NUCLEUS ACCUMBENS DURING THE INCUBATION OF COCAINE CRAVING. †**Conrad Kelly, L.**, Marinelli, M., Wolf, M.E.

VISUAL SENSORY-MOTOR GATING BY SEROTONIN ACTIVATION IN THE MEDIAL PREFRONTAL CORTEX, BUT NOT IN THE RHINAL CORTICES. †**Müller, C.P.**; Pum, M.E.; Huston, J.P.

OVEREXPRESSION OF CHIMERIC ESTRADIOL-GLUCOCORTICOID RECEPTOR (ERGR) IN BASOLATERAL AMYGDALA REDUCES ANXIETY AND INCREASES FEAR CONDITIONING IN NORMAL AND STRESSED RATS. †**Mitra, R**; Sapolsky, R.M.

DIETARY SUPPLEMENTATION AND HOUSING ENVIRONMENT ALTERS BEHAVIOR AND NEUROANATOMY IN A MOUSE MODEL OF RETT SYNDROME. †**Nag, N.**; Ward, B.; Berger-Sweeney, J.

3:30-3:45 Break & Exhibit Viewing

3:45-5:45 ***Symposium 2:*** *5-HT and emotion: An appreciation of the contributions of Fred Graeff.* Chair: Antonio Padua Carobrez, Universidade Federal de Santa Catarina

3:45 INTRODUCTION. **Blanchard, R.**

3:55 NEUROBIOLOGY OF PANIC DISORDER. **Graeff, F.**; Del-Ben, C.

4:30 THE DEAKIN/GRAEFF HYPOTHESIS: UNFOLDING THE MODEL. **Schenberg, L.C.**; Vargas, L.C.; Lugon, A.B.

4:55 IMPAIRED STRESS-COPING AND FEAR EXTINCTION AND ABNORMAL CORTICOLIMBIC MORPHOLOGY IN SEROTONIN TRANSPORTER KNOCK-OUT MICE. **Holmes, A.**; Izquierdo, A.; Wellman, C.L.

5:20 TESTS OF THE DEAKIN-GRAEFF THEORY IN HUMANS USING PHARMACO-MRI. **Deakin, J.F.W.**; Anderson, I.M.; Lythe, K.J.; Palm, M.E.; Elliott, R.

5:45-6:00 Break & Exhibit Viewing

6:00 – 8:00 ***Poster Session 1***

Nociception

1. PERIPHERAL ADMINISTRATION OF OFQ ALONE, BUT NOT IN COMBINATION WITH A PGC NANOCARRIER, PRODUCES ANALGESIA IN THE PREWEANING RAT. **Vanderlinden, B.**; Ledbetter, K.; Bolotin, E.; Castillo, G.; Ruiz Limon, E.

2. EFFECT OF THE DENDRIMER-NALOXONAZINE COMPLEX IN THE μ1-OPIOID-RECEPTOR-MEDIATED POST-ICTAL ANALGESIA. Felippotti. T.T.; Do Carmo, D.R.; Paim, L.L.; Parada, C.A.; **Bicalho, U.O.**; Coimbra, N.C.

3. IS THE PLUS MAZE-INDUCED ANTINOCICEPTION OPIOID MEDIATED? **Cornélio, A.M.**; Nunes-de-Souza, R.L.

4. CHRONIC TREATMENT WITH FLUOXETINE DO NOT REVERT THE HYPERALGESIA INDUCED BY REM SLEEP DEPRIVATION. **Damasceno, F.**; Skinner, G.; de Almeida, O.

5. BEHAVIORAL ASSAYS OF PAIN SENSITIVITY: AN ALTERNATIVE MODEL FOR ASSESSING THE IMPACT OF NON-STEROIDAL ANTIINFLAMMATORY DRUGS IN THE RODENT HOT PLATE TEST. Koch, K.; **Wiertelak, E.P.**

6. PLACENTA INGESTION BY RATS ENHANCES CENTRAL DELTA1-, BUT NOT CENTRAL DELTA2-OPIOID-MEDIATED ANTINOCICEPTION. **Neumann, A.**; Kastanenka, K.; Thompson, A.; Cheema, R.; DiPirro, J.; Kristal, M.

Ingestion-related Behaviors

7. EFFECTS OF 5-HT1A, 5-HT1B and 5-HT 2C RECEPTOR AGONISTS ON BEHAVIORAL SATIETY SEQUENCE IN RATS. **Mancilla-Díaz, J.M.**; López-Alonso, V.E.; Ecartín-Pérez, R.E.

8. EFFECTS OF CHRONIC ADMINISTRATION OF CAFFEINE AND STRESS ON FEEDING BEHAVIOR AND ABDOMINAL FAT OF MALE RATS. **Pettenuzzo, L.F.**; Noschang, C.; Toigo, E.v.P.; Vendite, D.; Dalmaz, C.

9. CLONIDINE INJECTED SUBCUTANEOUSLY REDUCES WATER AND NACL INTAKE INDUCED BY GABAERGIC ACTIVATION OF THE LATERAL PARABRACHIAL NUCLEUS. **Roncari, C.F.**; Oliveira, L.B.; Barbosa, S.P.; De Luca Jr., L.A.; Colombari, D.S.A.; De Paula, P.M.; Menani, J.V.

10. LESIONS OF COMMISSURAL NUCLEUS OF THE SOLITARY TRACT ENHANCE WATER INTAKE INDUCED BY PERIPHERAL OSMORECEPTOR ACTIVATION. **Blanch, G.T.**; Freiria-Oliveira, A.H.; Vendramini, R.C.; De Paula, P.M.; Menani, J.V.; Colombari, E.; Colombari, D.S.A.

11. THE EFFECTS OF GLOBAL UNDERNUTRITION DURING FETAL DEVELOPMENT ON LEARNING IN ADULT LIFE. **Krägeloh, C.**; Davison, M.; Landon, J.; Miles, J.; Thompson, N.; Breier, B.

12. EFFECT OF ADULT-ONSET CALORIE RESTRICTION ON ANXIETY, SOCIAL AND SEXUAL BEHAVIOR AND NEUROENDOCRINE MEASURES. Levay, E.A.; Govic, A.; Penman, J.; Paolini, A.G.; **Kent, S.**

Reward and Addiction

13. CHARACTERIZATION OF THE ALCOHOL ESCALATION EFFECT IN C57BL/6J MICE. **Melendez, R.I.**

14. REWARDING AND AVERSIVE PROPERTIES OF THE CANNABINOID AGONIST WIN 55,212-2: INFLUENCE OF THE AGE AND RAT STRAIN. **Pandolfo, P.**; Vendruscolo, L.F.; Pamplona, F.A.; Prediger, R.D.; Takahashi, R.N.

15. CORTICAL AND LIMBIC MODULATION OF LOCOMOTOR ACTIVITY PRODUCED BY ACTIVATION OF DOPAMINERGIC POSTSYNAPTIC RECEPTORS IN THE NUCLEUS ACCUMBENS. **Rouillon, C.**; Abraini, J.H. and David, H.N.

16. ETHANOL SELF-ADMINISTRATION IN ß-ENDORPHIN DEFICIENT TRANSGENIC MICE. **Williams, S.**; Hollaway, A.; Allen, S.A.; Grisel, J.E.

17. ANTAGONISM OF NK3-RECEPTOR DOES NOT ALTER HORMONAL EFFECTS OF ACUTE SYSTEMIC COCAINE ADMINISTRATION IN MARMOSET MONKEYS. **Barros, M.**; Lima, D.; Spíndola, D.B.; Dias, L.O.; de Souza Silva, M.A.; Huston, J.P.; Tomaz, C.

18. CONTEXT-SPECIFIC SENSITIZATION OF LOCOMOTOR BEHAVIOUR PRODUCED BY A SINGLE ADMINISTRATION OF APOMORPHINE. **Bloise, E.**; Carey, R.J.; Carrera, M.P.

19. A NEW MODEL TO EVALUATE AFFECTIVE STATES ASSOCIATED WITH REWARD-PREDICTING CUES IN MICE. **Cagniard, B.**; Murphy, N.P.

20. EEG MAPPING IN ALCOHOL DEPENDENCE OFFENDERS. **Calzada, A.**; Alvarez, A.

21. EFFECTS OF MORPHINE WITHDRAWAL ON THE DEFENSIVE RESPONSES INDUCED BY ELECTRICAL STIMULATION OF THE MIDBRAIN TECTUM. **Castilho, V.M.**; Ávila, M.A.V., Ruggiero, R.N., Nobre, M.J.

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23. PERSISTENT INCREASES IN COCAINE SEEKING BEHAVIOR AND IN DOPAMINE NEURON ACTIVITY AFTER ACUTE EXPOSURE TO COLD SWIM STRESS. †**Conrad, K.L.**; Beales, M.; Rudick, C.N.; Unal, C.T.; Cotterly, L.M.; Marinelli, M.

24. NEUROKININ3-RECEPTORS MODULATE THE NEUROCHEMICAL AND BEHAVIORAL EFFECTS OF COCAINE IN RATS AND NON-HUMAN PRIMATES. **De Souza Silva, M.A.**; Jocham, G., Müller, C.P.; Barros, M.; Tomaz, C.; Huston, J.P.

25. DIFFERENCIAL EFFECT OF LIDOCAINE IN THE DORSAL AND VENTRAL HIPPOCAMPUS ON THE EXPRESSION OF BEHAVIORAL SENSITIZATION TO AMPHETAMINE. **Degoulet, M.**; Abraini, J.H.

26. 'PROPHYLACTIC' NPY TREATMENT DECREASES OPERANT ETHANOL RESPONDING BY DEPENDENT AND NON-DEPENDENT RATS. **Gilpin, N.W.**; Koob, G.F.

27. COCAINE MICROINJECTIONS INTO THE NUCLEUS ACCUMBENS SHELL, BUT NOT MEDIAL PREFRONTAL CORTEX, PRODUCE APPROACH AVOIDANCE BEHAVIOR IN A RUNWAY MODEL OF SELF-ADMINISTRATION. **Guzman, D.**; Ettenberg, A.

28. EXAGGERATED EMOTIONAL RESPONSES FOLLOWING WITHDRAWAL FROM HYPNOTIC-SEDATIVE DRUGS OR STRESS ARE ASSOCIATED WITH THE LACK OF FEED-BACK INHIBITION ON RAT BASOLATERAL AMYGDALA. **Isoardi, N.A.;** Rodríguez Manzanares, P.A.; Bertotto, M.E.; Martijena, I.D.; Carrer, H.F.; Molina, V.A.

29. ESCALATION OF MORPHINE SELF-ADMINISTRATION IS ATTENUATED IN PERIADOLESCENT MALE RATS. †**Doherty, J.M.**; Ogbonmwan, Y.; Li, C.; Waldron, N.; Moffett, A.E.; Williams, B.F.; Frantz, K.J.

30. EXPLORING THE INFLUENCE OF REWARD ON SICKNESS AND IMMUNITY IN THE FEMALE RAT. †**Kentner, A.C.**; Takeuchi, A.; Miki, T.; James, J.; Seino, S.; Bielajew, C.

31. THE EFFECTS OF SINGLE AND MULTIPLE MONOAMINE TRANSPORTER GENE DELETION ON COCAINE-INDUCED CONDITIONED TASTE AVERSION. †**Jones, J.**; Hall, F.; Uhl, G.; Riley, A.

Learning and Memory

32. NEUROGENESIS IN THE MEDIAL PREOPTIC AREA (MPOA), AFTER THE ADMINISTRATION OF AN AROMATASE INHIBITOR OR AN ANDROGEN RECEPTOR ANTAGONIST. **Medina, J.P.**; Dominguez Salazar, E.; Paredes, R.

33. LEVELS OF NORADRENALINE IN THE INSULAR CORTEX DURING NOVEL AND AVERSIVE TASTE MEMORY FORMATION. **Miranda, M.I.**; Romero, M.; Reyes-López, J.

34. ENVIRONMENTAL ENRICHMENT PREVENTS OBJECT RECOGNITION MEMORY DEFICIT CAUSED BY HYPOXIA ISCHEMIA. **Nabinger, P.M.**; Orlandi Pereira, L.; Strapasson, A.C.P.; Netto, C.A.

35. SPATIAL MEMORY IMPAIRMENTS CONSEQUENT TO NEONATAL HYPOXIA-ISCHEMIA ARE PREVENTED BY ENVIRONMENTAL ENRICHMENT HOUSING. **Orlandi Pereira, L.**; Nabinger, P.M.; Strapasson, A.C.P.; Netto, C.A.

36. INTERACTION OF ANGIOTENSINERGIC, SEROTONERGIC SYSTEM AND K-ATP CHANNEL ON WATER INTAKE BEHAVIOR IN ADULT MALE WISTAR RATS. **Oryan, S.**; Alemi, S.; Ebrahimi, A.

37. HIPPOCAMPUS, NEURONAL NITRIC OXIDE SYNTHASE AND SPATIAL LEARNING IN PIGEONS. **Ferrari, E.A.M.**; Silva, M.I.; Canova, F.; Langone, F.; Toledo, C.A.B.

38. FOS-LIKE IMMUNOREACTIVITY IN THE RAT BRAIN ASSOCIATED WITH PLACE CONDITIONED AVERSION INDUCED BY INHIBITION OF GLUTAMIC ACID DECARBOXYLASE IN THE DORSAL PERIAQUEDUCTAL GRAY. **Zanoveli, J.M.**; Ferreira-Netto, C.; Brandão, M.L.

39. EFFECT OF EMOTIONAL CONTENT ON EXPLICIT MEMORY: A STUDY CONDUCTED ON MIGRAINE HEADACHE PATIENTS. Gasbarri, A.; Arnone, B.; Pompili, A.; **Pacitti, C.**; Di Fabrizio, P.; Marini, C.; Tavares, M.C.; Tomaz, C.

40. EFFECTS OF ANISOMYCIN INFUSIONS INTO INSULAR CORTEX ON MEMORY CONSOLIDATION OF INHIBITORY AVOIDANCE. Huchín-Ramírez, T.C.; Quirarte, G.L.; Medina, A.C.; **Prado–Alcalá, R.A.**

41. PHYSOSTIGMINE MITIGATES WORKING MEMORY LOSS DURING HYPOBARIC HYPOXIA THROUGH CHOLINERGIC SYSTEM. **Muthuraju**, S.; Singh, S.B.; Panchanan, M.; Sharma, A.K.; Barhwal, K.

42. EMOTIONAL AROUSAL ENHANCES DECLARATIVE MEMORY IN ALZHEIMER'S DISEASE. **Satler, C.**; Martínez Garrido, L.; Prada Sarmiento, E.; Leme, S.; Conde, C.; Tomaz, C.

43. EFFECTS OF GABAERGIC TRANSMISSION IN THE DENTATE GYRUS ON ACQUISITION, CONSOLIDATION AND RETRIEVAL OF PASSIVE AVOIDANCE LEARNING AND MEMORY TASK IN RAT. **Shahidi, S.**; Komaki, A.; Nourbakhshnia, M.; Akbari, M.M.; Shooshtari, R.

44. AMNESIC ACTION OF UROCORTIN 3 IN PASSIVE AVODANCE LEARNING IN MICE. INVOLVEMENT OF NEUROTRANSMITTERS. **Telegdy, G.**, Adamik, A.

45. THE SONGSYSTEM OF SONGBIRDS: STRICTLY FOR THE SONG? **Tokarev, K.I.**; Tiunova, A.A.; Scharff, C.; Anokhin, K.V.

46. AUTONOMIC AND BEHAVIORAL RESPONSES DURING ENCODING AND REMEMBERING OF EMOTIONALLY AROUSAL AUDIOVISUAL STIMULI. **Uribe, C.**; Conde, C.; Botelho, S.; Tomaz, C.

47. EVALUATION OF ATTENTION, LANGUAGE AND EMOTIONAL MEMORY IN LOBECTOMIZED PATIENTS. **Botelho, S.**; Acevedo, L.M.P.; Conde, C.; Franky, J.F.; Tomaz, C.

48. WORKING MEMORY AND VARIABILITY OF REACTION TIME EVALUATED IN UNIVERSITY STUDENTS UNDER DIFERENTS STIMULI'S TIME EXPOSITION USING "MEMONUM" SOFTWARE. Albarracin, A.P.; **Conde, C.**

49. TEMPORARY INACTIVATION REVEALS AN ESSENTIAL ROLE OF THE DORSAL HIPPOCAMPUS IN CONSOLIDATION OF OBJECT RECOGNITION MEMORY. **de Lima, M.N.M.**; Luft, T.; Roesler, R.; Schröder, N.

50. DISSOCIATION BETWEEN CORTICAL ACTIVATION AND COGNITIVE PERFORMANCE FOLLOWING PHARMACOLOGICAL BLOOD PRESSURE ELEVATION IN CHRONIC HYPOTENSION. **Duschek, S.**; Hadjamu, M.; Schandry, R.

51. ENHANCEMENT OF DECLARATIVE MEMORY ASSOCIATED WITH EMOTIONAL CONTENT IN MAJOR DEPRESSION PATIENTS. **Garcia, R.G.**; Zarruk, J.G.; Arenas, W.; Reyes, L.; Ruiz, S.; López-Jaramillo, P.; Tomaz, C.

52. CARDIOVASCULAR AUTONOMIC FUNCTION IN RESPONSE TO PSYCHOLOGICAL STRESS TESTS IN MAJOR DEPRESSION PATIENTS. **Garcia, R.G.**; Zarruk, J.G.; Barrera, C.; Trillos, E.; Quintero, D.; Lopez-Jaramillo, P.; Tomaz, C.

53. DIFFERING EFFECTS OF ECS ON CONSOLIDATION OF TRACE VS. DELAY FEAR CONDITIONING. **Glover, E.M.**; Paschall, G.Y.; Davis, M.

54. BLOCKADE OF NMDA RECEPTORS IN ROSTRAL AND CAUDAL DORSOLATERAL PERIAQUEDUCTAL GRAY REVEAL DIFFERENT CONTRIBUTIONS TO THE INNATE AND TO THE CONTEXTUAL FEAR CONDITIONING. **Souza, R.R.**; Cavalli, J.; Carobrez, A.P.

55. DORSAL PERIAQUEDUCTAL GRAY GLUTAMATERGIC MEDIATION OF THE DEFENSIVE BEHAVIOR OF RATS EVALUATED IN THE ELEVATED PLUS MAZE. **Kincheski, G.C.**; Moraes,C.L.K.; Carobrez, A.P.

56. BRAIN LEVELS OF CELLULAR PRION PROTEIN AFFECT LEARNED AVERSION IN MICE. **Lobão-Soares, B.**; Calvo, F.; Martins, V., Bianchin, M.M.; Walz, R.

57. OPERANT CONDITIONING IN ZEBRAFISH. †**Miller, N.**; Gerlai, R.

Sensorimotor-gating, neurodegeneration and dopamine-related behaviors

58. THE EFFICACY OF HALOPERIDOL IN RESTORING LATENT INHIBITON IN FEMALE RATS IS ESTROGEN DEPENDENT. †**Arad M.**; Weiner I.

59. VISUAL SENSORY-MOTOR GATING BY SEROTONIN ACTIVATION IN THE MEDIAL PREFRONTAL CORTEX, BUT NOT IN THE RHINAL CORTICES. †**Müller, C.P.**; Pum, M.E.; Huston, J.P.

60. HALOPERIDOL-INDUCED CATALEPSY CAN BE REVERSED BY MK-801 MICROINJECTED INTO THE INFERIOR COLLICULUS IN RATS. **Melo, L.L.**; Ferrari, E.A.M.; Santos, P.; Maisonette, S.S.

61. ROLE OF SIGMA RECEPTORS IN L-DOPA-INDUCED DYSKINESIAS. **Paquette, M.A.**; Brudney, E.G.; Putterman, D.B.; Johnson, S.W.; Berger, S.P.

62. THE EFFECTS OF THE 5-HT2A AGONIST DOI AND THE 5-HT2A INVERSE AGONIST AC90179 ON PREPULSE INHIBITION AND LOCOMOTOR ACTIVITY IN C57 MICE. Ruderman, M.A.; **Powell, S.B.**; Geyer, M.A.
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63. NITRIC OXIDE MODULATION OF BASOLATERAL AMYGDALA DOPAMINERGIC-DISRUPTION OF PREPULSE INHIBITION. **Salum, C.**; Issy, A.C.; Brandão, M.L.; Guimarães, F.S.; Del Bel, E.A.

64. ENHANCING CENTRAL NOREPINEPHRINE TRANSMISSION DISRUPTS PREPULSE INHIBITION: RESPECTIVE CONTRIBUTIONS OF THE LOCUS COERULEUS, MEDIAL PREFRONTAL CORTEX, AND NUCLEUS ACCUMBENS. **Alsene, K.M.**; Ramaker, M.J.; Bakshi, V.P.

65. NEUROPROTECTIVE EFFECTS OF PYRUVATE AND PIROXICAM IN ANIMALS TREATED WITH MPTP. Soliman, Y.I.; **Soliman, K.F.A.**

66. QUALITATIVE CHANGES IN ULTRASONIC VOCALIZATIONS (USVS) OF THE RAT PARKINSON'S DISEASE MODEL AFTER UNILATERAL LEASION OR HALOPERIDOL. **Ma, S.T.**; Ciucci M; Fox C.; Kane J.R.; Ramig L.O.; Schallert T.

67. SLEEP DEPRIVATION DISRUPTS SENSORIMOTOR GATING IN RATS IN AN ANTIPSYCHOTIC-SENSITIVE FASHION. Frau, R.; Orrù, M.; Mereu, G.; Gessa, G.L.; Marrosu, F.; **Bortolato, M.**

68. TRYPTOPHANE-FREE DIET SENSITIZES RATS TO THE EFFECTS OF D-AMPHETAMINE IN RAT MODELS OF SCHIZOPHRENIA. **Bortolato, M.**; Carta, M.; Frau, R.; Orrù, M.; Mereu, G.; Fadda, F.; Stancampiano, R.

69. MONOAMINE OXIDASE A/B KNOCK-OUT MICE ARE HYPERSENSITIVE TO THE PSYCHOTOMIMETIC ACTIONS OF NMDA RECEPTOR ANTAGONISTS. **Bortolato, M.**; Frau, R.; Orrù, M.; Mereu, G.; Chen, K.; Shih, J.C.

70. GABA(B) RECEPTOR SIGNALING DYSREGULATIONS UNDERPIN GATING DEFICITS AND SEIZURE IN DBA/2J MICE. **Bortolato, M.**; Frau, R.; Orrù, M.; Piras, A.P.; Castelli, M.P.; Mereu, G.; Marrosu, F.

71. SPECTRAL ANALYSIS OF EEG IN PERSONALITY DISORDER SUBJECTS. **Calzada, A.**; Alvarez, A.

72. THE MPTP RAT MODEL OF THE EARLY STAGE OF PARKINSON'S DISEASE. **Da Cunha, C.**; Wietzikoski, E.C.; Kouzmine, I.; Gregorio, M.L.; Ferro, M.M.; Vital, M.A.B.F.; Canteras, N.S.

Animal Models of Behavior and Neural Function

73. INTRINSIC FACTORS ASSOCIATED WITH WILD-RUNNING SUSCEPTIBILITY IN THE COMMON WISTAR RAT. **de Paula, H.M.G.**; Aquino, S.; Miwa, M.K.; Matsunaga, Jr., M.M.

74. EFFECTS OF A NEURONAL NITRIC OXIDE SYNTHASE INHIBITOR ON HIPPOCAMPAL GENE EXPRESSION PROFILE. **Ferreira, F.R**; Joca, S.R.; Santos, A.R; Silva, Jr. W.A; Guimarães, F.S.

75. THE MULTIPLE PARTNER CHOICE ARENA: AN ANIMAL MODEL TO EVALUATE THE PREMATURE EJACULATION IN RATS. **Ferreira-Nuño, A.**; Morales-Otal, A.; Fernández-Soto, C.; Olayo-Lortia, J.; Velázquez-Moctezuma, J.

76. BIOCHEMICAL AND BEHAVIORAL EFFECT OF GLUTATHIONE DEPLETION IN RAT BRAIN. **Gonzalez Fraguela, M.E.**; Bauza, J.; Garcia, R.; Blanco, L.

77. FREQUENCY DISTRIBUTION OF THE MAO-A PROMOTER ALLELIC VARIANTS IN A MALE POPULATION SAMPLE. **Oliveira, L.L.**; Lage, C.A.C.; Melgaço, M.C.P.; Urmenyi, T.P.; Rondinelli, E.; Moura-Neto, R.; Silva, R.

78. VENDOR EFFECTS IN BEHAVIOR: KNOWING YOUR MOUSE FROM YOUR MOUSE. **Buell, M.R.**; Young, J.W.; Geyer, M.A.

79. NORMALIZING CHOLINERGIC TONE TO AMELIORATE THE MANIFESTATION OF CLINICAL SYMPTOMS IN NEUROLOGICAL PATHOLOGIES. **Paskvan, C.D.**; Edmonds, B.W.; Schulte, M.K.

80. IDENTIFICATION AND BEHAVIORAL CORRELATES OF THE UROCORTINERGIC SYSTEM IN PIGEONS. Cunha, R.P.; Cavani, J.C.; Reiner, A.; **Toledo, C.A.B.**

81. ASSOCIATIONS BETWEEN OFFENSIVE AGGRESSION AND IMPULSIVITY IN ADULT MALE GOLDEN HAMSTERS. †**Cervantes, M.C.**; Delville, Y.

82. FEMALES EXPOSED TO AN ANABOLIC STEROID DISPLAYED AN INCREASE IN SEXUAL MOTIVATION WITHOUT ALTERING SOCIAL DOMINANCE. †**Parrilla, J.**; Jorge, J.C.; Barreto-Estrada, J.L.

83. BEHAVIOURAL EFFECTS OF HIPPOCAMPAL OVEREXPRESSION OF BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) IN RATS. †**Pietropaolo, S.**; Paterna J.C.; Büeler, H.; Yee, B.K.; Feldon, J.

Thursday, June 14, 2007

8:15-10:15 ***Symposium 3.*** *Early-life stress to model the interactions between genes and the environment: From the clinic to animal models.* Chairs: Holger Russig, University of Zürich/Swiss Federal Institute of Technology & Francesca Cirulli, Istituto Superiore di Sanità

8:45 GENE X ENVIRONMENT INTERACTIONS: EXAMPLES IN DEPRESSION AND AGGRESSION. **Reif, A.**; Lesch, K.-P.

9:15 EARLY RISK FACTORS FOR NEUROPSYCHIATRIC DISEASES: COMPARATIVE APPROACHES TO INVESTIGATE INTERACTIONS BETWEEN GENES AND ENVIRONMENT. **Cirulli, F.**; Francia, N.; Capone, F.; Aloe, L.; Suomi, S.J.; Alleva, E.

9:45 DEVELOPING AN EARLY LIFE STRESS MODEL THAT RELIABLY ALTERS ADULT NEUROENDOCRINE AND BEHAVIORAL STRESS-REACTIVITY IN C57BL/6 MICE: NEONATAL HANDLING VS. MATERNAL SEPARATION. **Parfitt, D.**

10:15 MATERNAL SEPARATION AS A MODEL OF GENE-ENVIRONMENT INTERACTIONS IN THE MOUSE, IS MORE THAN ONE GENERATION AFFECTED? **Russig, H.**; Franklin, T.B.; Mansuy, I.M.

10:15-10:30 Break & Exhibit Viewing

10:30-11:30 **Elsevier Keynote Lecture: John Aggleton, University of Cardiff, UK. Building brain systems for memory.** Introduction: Andrew Holmes.

11:30-12:30 ***Oral session 1***: Neural substrates of behavior. Chair: Antonio Padua Carobrez

11:30 DORSAL HIPPOCAMPAL CA3 LESIONS IMPAIR EPISODIC-LIKE MEMORY IN RATS. **Li, J.-S.**; Chao, Y.-S.

11:45 REVERSION OF RECOGNITION MEMORY IMPAIRMENT ASSOCIATED WITH AGING OR BRAIN IRON ACCUMULATION BY THE TYPE 4 PHOSPHODIESTERASE INHIBITOR ROLIPRAM. **de Lima, M.N.M.**; Torres, J.P.; Garcia, V.A.; Roesler, R.; Schröder, N.

12:00 INFUSIONS OF NALOXONE INTO THE MEDIAL PREOPTIC AREA AND VENTROMEDIAL NUCLEUS OF THE HYPOTHALAMUS BLOCK CONDITIONED PLACE PREFERENCE INDUCED BY PACED MATING BEHAVIOR IN FEMALE RATS. **Garcia-Horsman, P.**; Ågmo, A.; Paredes Guerrero, R.

12:15 AMYGDALA OPIOID STIMULATION ENHANCES 'WANTING' BUT NOT 'LIKING' OF SUCROSE REWARD. **Mahler, S**; Berridge, K.

12:30-2:00 Break

2:00-4:00 ***Symposium 4***: Gene-environment Interactions: animal models for mental health research. Chairs: Mikhail V. Pletnikov, Johns Hopkins University, Christine Hohmann, Morgan State University, Joanne Berger-Sweeney, Wellesley College

2:00 EARLY ENRICHMENT SHAPES ADULT MOUSE SOCIAL PATTERNS: A COOPERATIVE ROLE FOR NEUTROPHINES. **Branchi, I.**; Alleva, E.

2:25 DIETARY SUPPLEMENTATION AND HOUSING ENVIRONMENT ALTERS BEHAVIOR AND NEUROANATOMY IN A MOUSE MODEL OF RETT SYNDROME. †**Nag, N.**; Ward, B.; Berger-Sweeney, J.

2:50 INTERACTIONS OF NEONATAL STRESS AND MATERNAL CARE BEHAVIOR: DEVELOPMENT OF THE CORTICOSTERONE RESPONSE SYSTEM AND POSSIBLE MODULATION VIA SEROTONIN. **Hohmann, C.F.;** Hodges, A.

3:15 INTERACTION OF PRENATAL INFECTIONS WITH A GENETIC RISK FACTOR FOR SCHIZOPHRENIA: MOUSE MODEL. **Pletnikov, M.**

3:40 EFFECTS OF NEONATAL HANDLING ON MATERNAL ODOR PREFERENCE IN RAT PUPS: ROLE OF NORADRENALINE/CREB PATHWAY. **Lucion, A.B.**; Raineki, C.; Lutz, M.L.; Vasconcellos, L.F.T.; Szawka, R.E.; Anselmo-Franci, J.A.; Sanvitto, G.L.; Bevilaqua, L.R.M.; Izquierdo, I.; Cammarota, M.

4:00-4:15 Break & Exhibit Viewing

4:15-5:45 *Oral Session 2:* Animal models of behavior and disease. Chair: Francisco Guimaraes

4:15 TURNING ORDER INTO CHAOS THROUGH REPETITION AND ADDITION OF ELEMENTARY ACTS IN OBSESSIVE-COMPULSIVE DISORDER (OCD). Zor, R.; Hermesh, H.; Szechtman, H.; **Eilam, D.**

4:30 ANTIDEPRESSAN-LIKE EFFECT OF RAPAMYCIN IN ANIMAL MODELS. **Einat, H.**; Linde, J.; Hiscock, K.; Cleary, C.; Belmaker, R.H.; Agam, G.

4:45 ASCENDING PROJECTIONS FROM THE ROSTRAL LATERAL PERIAQUEDUCTAL GRAY (rlPAG): A CRITICAL SITE FOR CONTOLLING FORANGING BEHAVIOR. **Mota-Ortiz, S.R.**; Bittencourt, J.C.; Elias, C.F.; Canteras, N.S.

5:00 EFFECTS OF INTRAAMYGDALOID MICROINJECTIONS OF ACYLATED-GHRELIN ON FOOD INTAKE AND LEARNING. **Lenard, L.**; Toth, K.; Laszlo, K.; Lukacs, E.; Bagi, E.

5:15 HYPERSENSITIVITY OF DOPAMINE TRANSPORTER KNOCKDOWN MICE TO THE EFFECTS OF THE DOPAMINE TRANSPORTER ANTAGONIST GBR 12909. **Young, J.**; Goey, A.; Geyer, M.A.

5:30 CREB IS NECESSARY FOR LONG-TERM MEMORY FOR HABITUATION AND FOR MEMORY ASSOCIATED CHANGES IN GLUTAMATE RECEPTOR SUBUNIT EXPRESSION IN CAENORHABDITIS ELEGANS. **Timbers, T.A.**; Rankin, C.H.

5:45-6:00 Break & Exhibit Viewing

6:00-8:00 ***Poster Session 2***

Fear, Anxiety and Defense

84. OVEREXPRESSION OF CHIMERIC ESTRADIOL-GLUCOCORTICOID RECEPTOR (ERGR) IN BASOLATERAL AMYGDALA REDUCES ANXIETY AND INCREASES FEAR CONDITIONING IN NORMAL AND STRESSED RATS. †**Mitra, R.**;Sapolsky, R.M.

85. CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE PERIAQUEDUCTAL GRAY ARE DIFFERENTIALLY REGULATED BY SEROTONERGIC MECHANISMS IN THE BASOLATERAL AMYGDALA. **Martinez, R.C.R.**; Oliveira, A.R.; Brandão, M.L.

86. ANXIETY-LIKE BEHAVIORS AND ANTINOCICEPTION INDUCED BY CORTICOTROPIN RELEASING FACTOR INJECTION INTO THE MOUSE PERIAQUEDUCTAL GRAY. **Miguel, T. T.**; Nunes-de-Souza, R. L.

87. FICTION OR TRUTH? DIFFERENTIAL PROCESSING OF AVERSIVE SCENES: AN ERP STUDY. **Mocaiber, I.**; Erthal, F.S.; Cagy, M.; Figueira, I.; Pereira, M.G.; Machado-Pinheiro, W.; Volchan, E.; Oliveira, L.

88. CORRELATION BETWEEN C-FOS EXPRESSION AND BEHAVIOR OF RATS TESTED IN THE ELEVATED PLUS-MAZE IN THE PRESENCE AND ABSENCE OF LIGHT. Rico, J.L.; **Morato, S.**

89. MODULATION AGGRESSION LEVELS IN THE RESIDENT - INTRUDER PARADIGM. **Motta, S.C.**; Gouveia, F.V.; Canteras, N.S.

90. IN VIVO LEVELS OF GASTRIN-RELEASING PEPTIDE AT THE BASOLATERAL AMYGDALA PREDICT FREEZING TO A FEAR-INDUCING EVENT. **Mountney, C.**; Kent, P.; Merali, Z.

91. ANXIETY INDUCED BY DIAZEPAM WITHDRAWAL REDUCES 22-kHz ULTRASOUND VOCALIZATIONS AND ENHANCES STARTLE REFLEX. De Ross, J.B.; Castilho, V.M.; **Nobre, M.J.**

92. CHARACTERIZATION OF BETA-CATENIN KNOCK-OUT MICE IN BEHAVIORAL MODELS OF MOOD DISORDERS. **O'Donnell, K.**; Picchini, A.; Manji, H.; Gould T.

93. PERITRAUMATIC TONIC IMMOBILITY PREDICTS A POOR RESPONSE TO PHARMACOLOGICAL TREATMENT IN VICTIMS OF URBAN VIOLENCE WITH PTSD. Fiszman, A.; **Rego-Rocha, V.**; Mendlowicz, M.V.; Marques-Portella, C.; Coutinho, E.F.S.; Souza, W.F.; Lima, A.A.; Volchan, E.; Oliveira, L.; Figueira, I.

94. AFFECTIVE CHRONOMETRY OF SECURITY MOTIVATION. **Hinds, A.**; Szechtman, H.; Woody, E.

95. CONDITIONED AND UNCONDITIONED FEAR ARE REGULATED BY GABAERGIC MECHANISMS IN THE DORSAL PERIAQUEDUCTAL GRAY. **Reimer, A.E.**; Oliveira, A.R.; Brandão, M.L.

96. POSTERIOR CINGULATE CORTEX HYPOMETABOLISM IMPAIRS SPATIAL MEMORY IN A FOOD SEARCH TASK. **Riha, P.D.**; Rojas, J.C., Gonzalez-Lima, F.

97. DIFFERENT CONDITIONS OF CHRONIC SOCIAL ISOLATION INDUCES SIMILAR ANXIETY-LIKE BEHAVIOR IN RATS. Faggioni, F.; Fabíola; **Rosa, M.L.**

98. FMRI IN MICE REVEALS THAT EARLY LIFE STRESS IMPAIRS SEROTONERGIC NEUROTRANSMISSION IN THE PREFRONTAL CORTEX. **Russig, H.**; Razoux, F.; Mueggler, T.; Franklin, T.B.; Rudin, M.; Mansuy, I.M.

99. INVOLVEMENT OF DORSOMEDIAL AND VENTROMEDIAL HYPOTHALAMIC NUCLEI IN CONDITIONED FEAR AS ASSESSED BY FREEZING BEHAVIOR AND FEAR-POTENTIATED STARTLE. **Santos, J.M.**; Brandão, M.L.

100. USE OF A PLATFORM IN AN AUTOMATED OPEN-FIELD TO ENHANCE ASSESSMENT OF ANXIETY-LIKE BEHAVIORS IN MICE. Pogorelov, V.M.; Lanthorn, T.H.; **Savelieva, K.V.**

101. BEHAVIORS OF WISTAR, WILD (Rattus norvegicus sp) AND HYBRID RATS IN THE RESIDENT-INTRUDER MODEL. Póvoa, R.M.F.; **Schenberg, L.C.**

102. DEFENSIVE BEHAVIORS PRODUCED BY STIMULATION OF DORSAL PERIAQUEDUCTAL GRAY MATTER (DPAG) OF WISTAR, WILD AND DERIVED RAT STRAINS. Póvoa, R.M.F.; **Schenberg, L.C.**

103. EFFECTS OF CORTICOSTEROID CENTRAL INJECTIONS (ICV) ON DEFENSIVE BEHAVIORS PRODUCED BY STIMULATION OF DORSAL PERIAQUEDUCTAL GRAY MATTER (DPAG) OF THE RAT. Rangel, T.C.; **Schenberg, L.C.**

104. HYPOTHALAMUS-PITUITARY-THYROID (HPT) FUNCTION IN PERIAQUEDUCTAL GRAY (PAG)-EVOKED DEFENSIVE BEHAVIORS. Siqueira, C.C.; Tiengo, A.N.C.P.; **Schenberg, L.C.**

105. DEFENSIVE BEHAVIORS INDUCED BY INTENSITY- OR FREQUENCY-VARYING STIMULATION OF PARS DIFUSA (DMD) AND PARS COMPACTA (DMC) OF DORSOMEDIAL HYPOTHALAMIC NUCLEUS OF THE RAT. Alves, A.C.A.; Pezzin, F.D.N.; **Schenberg, L.C.**

106. PROGESTERONE EFFECTS ON DORSAL PERIAQUEDUCTAL GRAY (DPAG)-EVOKED DEFENSIVE BEHAVIORS OF OVARIECTOMIZED FEMALE RATS. Tiengo, A.N.P.; Vasconcellos, A.P.; Rosalém, G.F.; **Schenberg, L.C.**; Tufik, S.; Bittencourt, A.S.

107. ACUTE TREATMENT WITH DIAZEPAM BUT NOT CHRONIC TREATMENT WITH FLUOXETINE AND IMIPRAMINE REVERSED THE ANXIOGENIC PROFILE OF SHORT-TERM ISOLATION IN RATS TESTED IN THE ELEVATED PLUS-MAZE MODEL OF ANXIETY. Curio, M.; Jacone, H.; Perrut, J.; **Silva, R.C.B.**

108. EFFECTS OF MALNUTRITION ON MEMORY AND ANXIETY IN RATS. **Silveira, A.**; Dias, G.; Bevilaqua, M.; Moraes, M.; Cardenas, F.; Landeira-Fernandez, J.; Rocha, M.; Gardino, P.F.; Hokoç, J.N.

109. D2 AGONIST QUINPIROLE ELICITS 50 kHz ULTRASONIC VOCALIZATIONS FROM THE NUCLEUS ACCUMBENS IN RATS. **St. Pierre, J.**; Brudzynski, S.M.

110. THE ACUTE BEHAVIORAL AND PHYSIOLOGICAL RESPONSE IN RATS TO A PREDATOR-SCENTED STIMULUS: HOME CAGE VS. OPEN FIELD EXPOSURE TO THE STIMULUS. **Suarez, M.**; Walter, G.C.; Platt, D.W.; Thompson, A.C.; DiPirro, J.M.

111. ANXIOLYTIC EFFECT OF SWEET ORANGE AROMA IN WISTAR RATS. Faturi, C.B.; Leite, J.R.; Canton, A.C.; **Teixeira-Silva, F.**

112. BEHAVIORAL ACTIONS OF INTRANASAL APPLICATION OF DOPAMINE: EFFECTS ON FORCED SWIMMING, ELEVATED PLUS-MAZE AND OPEN FIELD PARAMETERS. **Topic, B.**; Buddenberg, T.; de Souza Silva, M.A.; Huston, J.P.; Mattern C.

113. ANTIPANIC-LIKE EFFECT OF CHRONIC TREATMENT WITH FLUOXETINE ON FEAR-INDUCED RESPONSES ELICITED BY PREYS IN CONFRONT WITH RATTLESNAKES. **Ubiali, W.A.**; Rocha, M.J.; Coimbra, N.C.

114. CORTISOL AND CARDIOVASCULAR RESPONSES TO PSYCHOLOGICAL STRESS: VULNERABILITY, RESILIENCE AND INDIVIDUAL DIFFERENCES. Souza, G.G.L.; Mendonça-de-Souza, A.C.F.; Vieira, A.; Barros, E.M.; Fischer, N.L.; Coutinho, E.F.S.; Oliveira, L.; Rumjanek, V.M.; Mendlowicz, M.V.; Figueira, I.; **Volchan, E.**

115. IMPACT OF SOLENACE EXTRACTS AND THE NITRIC OXIDE SYNTHASE INHIBITOR L-NAME ON ANXIETY AND PAIN RELATED BEHAVIOR IN RAT AS MEASURED IN THE STAIRCASE MODEL. **Wiertelak, E.P.**; Kaplan, R.

116. THE ROLE OF AMYGDALAR MU OPIOID RECEPTORS IN ANXIETY RESPONSES. **Wilson, M.A.**; Junor, L.; Ford, K.; Wilson, S.P.

117. ANTAGONISM OF NMDA RECEPTORS IN THE DORSOLATERAL PERIAQUEDUCTAL GREY INDUCES DIFFERENT PATTERNS OF CELLULAR ACTIVATION AFTER PREDATOR EXPOSURE. **Aguiar, D.C.**; Guimaraes, F.S.

118. INCREASES IN PLASMA CORTICOSTERONE AND STRETCHED-ATTEND POSTURES IN RATS NAIVE AND PREVIOUSLY EXPOSED TO THE ELEVATED PLUS-MAZE ARE SENSITIVE TO THE ANXIOLYTIC-LIKE EFFECTS OF MIDAZOLAM. **Albrechet-Souza, L.**; Franci, C.R.; Brandão, M.L.

119. SWIM-TEST AS A FUNCTION OF CATALEPSY INDUCED BY HALOPERIDOL IN MICE: AN ANIMAL MODEL FOR THE EVALUATION OF ADENOSINE A2A RECEPTOR ANTAGONISTS AS ANTI-PARKINSONIAN AGENTS. **Azam, F.**; Khokhra, S.L.; Prakash, O.

120. PERSISTENT DEFENSIVE BEHAVIOR AND RESPONSE PATTERN TO DIAZEPAM IN MARMOSETS FOLLOWING A RECENT PREDATORY STRESS CONDITION. **Barros, M.**; Giorgetti, M.; Souto, A.A.V.; Vilela, G.; Santos, K.; Vilas Boas, N.; Tomaz, C.

121. EFFECTS OF OVINE-CRF MICROINJECTIONS INTO THE DORSAL PERIAQUEDUCTAL GRAY ON DEFENSIVE BEHAVIOR IN RATS. **Borelli, K.G.**; Brandão, M.L.

122. ANXIOGENIC EFFECTS OF ACTIVATION OF NK-1 RECEPTORS OF THE DORSAL PERIAQUEDUCTAL GRAY AS ASSESSED BY THE ELEVATED PLUS-MAZE, ULTRASOUND VOCALIZATIONS AND TAIL-FLICK TESTS. Bassi, G.S.; Nobre, M.J.; **Brandão, M.L.**

123. 5-HT2-RECEPTOR MECHANISMS OF THE DORSAL PERIAQUEDUCTAL GRAY IN THE CONDITIONED AND UNCONDITIONED FEAR. Oliveira, L.C.; Macedo, C.E.; Landeira-Fernandez, J.; **Brandão, M.L.**

124. INVOLVEMENT OF THE DOPAMINERGIC D2 RECEPTORS OF THE VENTRAL TEGMENTAL AREA IN THE EXPRESSION OF CONDITIONED FEAR. Oliveira, A.R.; Reimer, A.E.; **Brandão, M.L.**

125. ANXIOLYTIC-LIKE EFFECTS OF CANNABIDIOL INJECTED INTO THE DORSOLATERAL PERIAQUEDUCTAL GREY. **Campos, A.C.**; Guimarães, F.S.

126. INFUSIONS OF MIDAZOLAM AND FLUMAZENIL INTO THE AMYGDALA PRODUCE ANXIOLYTIC-LIKE EFFECT IN MAZE-EXPERIENCED MICE. Barbalho, C.A.; **Canto-de-Souza, A.**

127. LOCAL INJECTION OF SUBSTANCE P INTO THE VENTRAL HIPPOCAMPUS INCREASES THE EXTRACELLULAR CONCENTRATION OF SEROTONIN. **Carvalho, M.C.**; Masson, S.; Brandão, M.L.; De Souza Silva, M.A.

128. EVALUATION OF BEHAVIORAL AND NOCICEPTIVE RESPONSES IN MICE CONFRONTED BY DIFFERENT STRAINS OF PREDATOR. **Carvalho-Netto, E.F.**; Toledo, A.V.; Amaral, V.C.S. ; Nunes-de-Souza, R.L.

129. RESTRICTION STRESS INDUCES AMNESIA AND DECREMENT IN SEROTONERGIC ACTIVITY IN PREFRONTAL CORTEX. García-Saldívar, N.L.; González-López, M.R.A.; Castillo-Roberto, G.; Domínguez, R.; **Cruz-Morales, S.E.**

130. ROLE OF 5-HT2C RECEPTOR WITHIN THE VENTRAL HIPPOCAMPUS ON ANXIETY INDUCED BY THE ELEVATED PLUS-MAZE. **Gomes, V.C.**; Scarpelli, G.; Alves, S.H.; Landeira-Fernandez, J.; Cruz, A.P.M.

131. METABOTROPIC GLUTAMATE RECEPTOR AGONIST DECREASES RISK ASSESMENT BEHAVIORS THROUGH THE BASOLATERAL AMYGDALA. **De Jesus-Burgos, M.I.**; Rodríguez-Aguiar, G.L.; Quiñones-Laracuente, K.; Pérez-Acevedo, N.L.

132. RELATIONSHIPS BETWEEN SOCIAL HIERARCHY, CORTICOSTERONE LEVELS AND THYMIC ALTERATIONS IN THE MICE RESIDENT-INTRUDER PARADIGM. Guazzelli, A.S.; **de Paula, H.M.G.**; Arruda, M.S.P.

133. THE ROLE OF GLUTAMATE-NMDA RECEPTORS IN THE DORSAL PREMAMMILLARY NUCLEUS ON THE DEFENSIVE BEHAVIOR TOWARD CAT ODOR OR CUED OLFACTORY CONDITIONED FEAR. **Do-Monte, F.H.M.**; Kroon, J.A.V.; Pavesi, E.; Canteras, N.S.; Carobrez, A.P.

134. EFFECTS OF CORTICOTROPIN-RELEASING FACTOR IN TESTS FOR DEPRESSION IN RATS AND MICE. **Dunn, A.J.**; Leskov, I.L.; Swiergiel, A.H.

135. ANXIOLYTIC-LIKE EFFECT OF INTRA-AMYGDALA NEUROPEPTIDE Y INFUSION IN ANIMAL MODELS OF CONDITIONED FEAR: AN NPY Y1 RECEPTOR INDEPENDENT EFFECT? **Fendt, M.**; Bürki, H.; Huber, C.; Imobersteg, S.; Jeker, A.; Mayer, R.; Portet, C.; Chaperon, F.; Lingenhöhl, K.; McAllister, K.H.; Orain, D.; Pryce, C.R.; Uzunov, D.P.

136. UNCONDITIONED AND CONDITIONED EFFECTS OF TRIMETHYLTHIAZOLINE, A COMPONENT OF FOX-ODOR, ON RAT BEHAVIOR. **Endres, T.**; Fendt, M.

137. EFFECTS OF INTRA-VENTRAL HIPPOCAMPUS INFUSION OF A 5-HT2C-RECEPTOR ANTAGONIST ON CONVETIONAL AND ETHOLOGICAL ANXIETY MEASURES IN THE ELEVATED PLUS-MAZE. **Ferreira, G.F.S.**; Salviano, M.F.; Landeira, J.F.; Cruz, A.P.M.

138. EFFECTS OF IPSAPIRONE ON HIGH/LOW ANXIETY-LIKE TRAIT RATS. **Salviano, M.F.**; Ferreira, G.F.S.; Vilela, G.; Paz, A.; Landeira, J.F.; Barros, M.; Cruz, A.P.M.

139. RESILIENCY IN RATS: AN INVESTIGATION OF THE EFFECTS OF COPING STRATEGIES ON NEUROBIOLOGICAL RESPONSIVENESS. **Fleming, D.F.**; Everette, A.M.; Higgins, T.J.; Tu, K.M.; Bardi, M.; Kinsley, C.H.; Lambert, K.G.

140. EFFECTS OF ANXIETY ON THE ESCAPE BEHAVIOR INDUCED BY THE MICROINJECTION OF NMDA IN THE DORSAL PERIAQUEDUCTAL GRAY. **Galvão, B.O.**; Larrubia, B.C.; Cardenas, F.P.; Landeira-Fernandez, J.

141. AMPA AND DOPAMINE RECEPTOR TRAFFICKING IN THE NUCLEUS ACCUMBENS DURING THE INCUBATION OF COCAINE CRAVING. †**Conrad, K.L.**, Marinelli, M., Wolf, M.E.

142. UNBALANCED EMOTIONS WITH VESTIBULAR DYSFUNCTION. **Goddard, M.**; Zheng, Y.; Darlington, C.; Smith, P.

143. BILATERAL LESIONS OF THE DORSAL PORTION OF THE MIDBRAIN PERIAQUEDUCTAL GRAY (PAG) REDUCE ANXIETY IN MICE EXPOSED TO THE ELEVATED PLUS MAZE (EPM). **Mendes-Gomes, J.**; Nunes-de-Souza, R.L.

144. ROLE OF THE 5HT2A RECEPTORS LOCATED WITHIN THE MIDBRAIN PERIAQUEDUCTAL GRAY ON THE ONE-TRIAL TOLERANCE PHENOMENON IN MICE. **Gomes, K.S.**; Nunes-de-Souza, R.L.

145. MODULATION OF DEFENSIVE RESPONSES BY GROUP I METABOTROPIC GLUTAMATE RECEPTORS LOCATED IN THE DORSOLATERAL PERIAQUEDUCTAL GRAY. **Guimaraes, F.S.**; Lima, V.C.F.; Molchanov, M.L.

146. ROLE OF VENTRAL AND DORSAL HIPPOCAMPUS NMDA-RECEPTOR ON RATS`DEFENSIVE BEHAVIORS TOWARDS CAT ODOR STIMULI. **Häckl, L.P.N**; Carobrez, A.P.

147. ACTIVITY OF BRAINSTEM CHOLINERGIC NEURONS DURING EMISSION OF 22 kHz ALARM CALLS INITIATED BY DIFFERENT METHODS. **Iku, A.**; Brudzynski, S.M.

148. TWO TYPES OF SOCIAL BUFFERING DIFFERENTIALLY ATTENUATE CONDITIONED FEAR RESPONSES IN MALE RATS. **Kiyokawa, Y.**; Kikusui, T.; Takeuchi, Y.; Mori, Y.

149. ANXIOLYTIC-LIKE EFFECT OF ANANDAMIDE INJECTED INTO THE RAT DORSOLATERAL PERIAQUEDUCTAL GRAY IN THE VOGEL TEST. **Lisboa, S.F.S.**; Aguiar, D.C.; Resstel, L.B.M; Guimarães, F.S.

150. SOCIAL ISOLATION ALTERS CORTICOTROPIN-RELEASING FACTOR RESPONSES IN ADULT RATS. **Lukkes, J.**; Renner, K.; Watt, M.; Summers, C.; Keifer, J.; Forster, G.

151. CROSS-BREEDING STUDIES ON THE NAPLES RAT LINES REVEAL STRONG HERITABILITY OF BEHAVIORAL SELECTION TRAIT. Gironi Carnevale, U.A.; Vitullo, E.; Varriale, B.; Viggiano, D.; Ruocco, L.A.; **Sadile, A.G.**

152. PRENATAL TETRAHYDROCANNABINOL (THC) EXPOSURE DISRUPTS SOCIAL AND OPEN FIELD BEHAVIOR IN MALE LONG EVANS RATS. **Newsom, R.J.**; Kelly, S.J.

153. EFFECTS OF MATERNAL SEPARATION AND SEX ON RISK-TAKING, ORIENTING AND GENERAL ACTIVITY OF ADOLESCENT HOLTZMAN RATS. Spivey, J.; **Padilla, E.**; Barrett D.; Gonzalez-Lima F.

154. BEHAVIORAL ALTERATIONS AND MEMORY IMPAIRMENTS IN RATS PRENATALLY EXPOSED TO GASTRIN-RELEASING RECEPTOR BLOCKADE. **Presti-Torres, J.**; de Lima, M.N.; Scalco, F.S.; Garcia, V.A.; Guimarães, M.R.; Schwartsmann, G.; Roesler, R.; Schröder, N.

155. ROLE OF ESTRADIOL ON THE REGULATION OF ELECTRICAL ACTIVITY OF CORTICO-AMYGDALOID-HIPPOCAMPAL CIRCUIT IN PRENATAL MALNOURISHED FEMALE RATS. **Pretelin-Ricardez, J.**; Cintra. L.; Duran, P.

156. RELATIONSHIP BETWEEN SLEEP PARAMETERS AND INHIBITORY AVOIDANCE PERFORMANCE IN SLEEP DEPRIVED RATS. **Moreira, K.M.**; Hipolide, D.C.; Tiba, P.A.; Tufik, S.; Oliveira, M.G.M.

157. GENDER DIFFERENCES IN REM SLEEP OF RATS SUBMITTED TO LONG AND BRIEF MATERNAL SEPARATION. **Tiba P.A.**; Tufik S.; Suchecki D.

158. EFFECTS OF DORSAL STRIATUM AND AMYGDALOSTRIATAL PATHWAY LESIONS ON FEAR CONDITIONING RETRIEVAL. **Ferreira, T.**; Moreira, K., Fornari, R.; Soares, J.; Tiba, P.; Oliveira, M.G.

159. EARLY HANDLING ENRICHMENT RENDERS MOUSE PUPS UNRESPONSIVE TO ANXIOLYTIC DRUGS AND INCREASES NGF LEVELS IN THE HIPPOCAMPUS. Capone, F.; Bonsignore, L.T.; Aloe, L.; Alleva, E.; **Cirulli, F.**

160. STRESS REACTIVITY IN MATERNALLY SEPARATED ADOLESCENT MICE. **Cornwell, C.A.**; Thomas, N.R.; Leister, K.

161. LONG-LASTING EFFECTS OF MATERNAL SEPARATION UPON DISTINCT MEMORY TASKS AND DEFENSIVE BEHAVIOR IN RATS. **Diehl, L.A.**; de Oliveira Alvares, L.; Andreazza, A.C.; Carobrez, A.P.; Gonçalves, C.A.; Quillfeldt, J.A.; Dalmaz, C.

162. PATERNAL EXPERIENCE ENHANCES BEHAVIORAL AND NEUROBIOLOGICAL RESPONSIVITY ASSOCIATED WITH AFFILIATIVE AND NURTURING RESPONSES. **Everette, A**; Fleming, D; Higgins, T.; Tu, K.; Bardi, M.; Kinsley, C.H.; Lambert, K.G.

163. 24H MATERNAL DEPRIVATION INDUCES ANXIETY AND DEPRESSIVE-LIKE BEHAVIOR IN ADULT WISTAR RATS. **FATURI, C.B.**; SUCHECKI, D.

164. ENDOCRINE ASPECTS OF THE OPIOIDERGIC STIMULATION IN PREGNANT RATS. **Felicio, L.F.**; Sukikara, M.H.; Felippe, E.C.G.; Anselmo-Franci, J.; Oliveira, C.A.

165. MATERNAL EXPERIENCE ENHANCES NEUROBIOLOGICAL AND BEHAVIORAL RESPONSES IN AN ATTENTION SET-SHIFTING PARADIGM. **Higgins, T.**; Everette, A.; Fleming, D.; Christon, L.; Kinsley, C.H.; Lambert, K.G.

166. NEONATAL STRESS AND MATERNAL CARE INTERACT IN CHANGING IN SELECTIVE GLUCOCORTICOID RECEPTOR mRNA CHANGES IN BALB/CBYJ MICE. **Hodges, A.B.**; Brown, L.D.; Nealy, C.J.; Fowler, J.A.; Hohmann, C.F.

167. TEMPORAL CHARACTERISTICS OF SHOALING BEHAVIOUR OF ZEBRA FISH: LARGE SCALE DEVELOPMENTAL AND FINE RESOLUTION CHANGES. **Buske, C.**; Gerlai, R.

Friday, June 15, 2007

Matthew J Wayner-NNOXe Pharmaceuticals Award Lectures

8:15-9:15 **William T. Greenough**, University of Illinois at Urbana-Champaign, USA. Plastic brain mechanisms in Fragile X Syndrome. Introduction: Wim Crusio.

9:15-10:15 **Donald Stein**, Emory University, Atlanta, USA, The trials and tribulations of progesterone in the treatment of brain injury: Was the game worth the candle? Introduction: Robert Gerlai.

10:15-10:30 Break & Exhibit Viewing

10:30-12:30 ***Symposium 5*:** The role of genetics and genomics in understanding fear- and anxiety-like behaviors. Chair: Abraham Palmer, University of Chicago

10:30 GENETIC REFERENCE POPULATIONS AND BEYOND. **Palmer, A.A.**

11:00 EMOTIONALITY-RELATED BEHAVIORS: WHAT GENOTYPES CAN TELL US ABOUT PHENOTYPES. **Ramos, A.**

11:30 INTERACTION OF GENOTYPE WITH THE EFFECTS OF CHRONIC ANTIDEPRESSANTS ON ANXIETY- AND DEPRESSION-RELATED BEHAVIORS. **Dulawa, S.C.**; Nitzke, A.M.

12:00 USING GENETICS AND GENOMICS TO UNDERSTAND RELATIONSHIPS AMONG ANXIETY-LIKE BEHAVIORS AND OTHER TRAITS. **Chesler, E.J.**; Li, Z.; Zhang, Y.; Philip, V.; Kirova, R.; Baker , E.J.; Langston, M.A.

12:30-6:15 FREE AFTERNOON

6:15-7:00 IBNS Business Meeting

7:15- Awards Banquet – Entertainment by the Brasil Jazz Band

Saturday, June 16, 2007

8:15-9:45 ***Symposium 6:*** Contributing factors to normal and pathological variation in social behaviors. Chair: Sandra J. Kelly, University of South Carolina

8:15 NEURAL AND BEHAVIORAL BASES OF ALCOHOL';S TERATOGENIC EFFECTS ON PLAY IN THE RAT. **Lawrence, R.C.**; Newsom, R.; Bonner, C.; Kelly, S.J.

8:45 MATERNAL CARE AND THE OFFSPRING REPRODUCTIVE BEHAVIOR IN THE RAT. **Cameron, N.;** Meaney, M.

9:15 IMPLICATIONS OF THE IMPACT OF ALCOHOL EXPOSURE DURING DEVELOPMENT ON SOCIAL RECOGNITION MEMORY. **Kelly, S.J.**; Leggett, D.C.

9:45-10:45 **Keynote Lecture, Ivan Izquierdo, PUCRS, Brazil** Different molecular mechanisms in different brain sites underlie memory consolidation. Introduction: Joseph Huston.

10:45-11:00 Break

11:00-12:30 **Student Workshop -** Preparing an Effective CV. Organizers: Susan Powell and Vickie Risbrough

12:30-2:00 **Grant Workshop –** NIH 101-From submission to funding. Organizer: Paul Rushing

ADJOURN

Wednesday, June 13, 2007

8:45-10:45 Symposium 1: Social and emotional behaviors: Focus on serotonin and vasopressin receptors.

SEROTONIN CELLS AND ESCALATED AGGRESSIVE BEHAVIOR: INTEGRATION OF SOMATODENDRITIC AUTORECEPTORS, PRE- AND POST-SYNAPTIC RECEPTORS AND TRANSPORTERS. Miczek, Klaus A. Tufts University, Medford, Massachusetts 02155, USA. 1. Quantitative ethological analysis identifies different types of aggressive behavior that ranges from adaptive patterns of dominance to territorial aggression. Offensive and defensive aggressive behaviors occur in bursts with each act and posture following a species-typical sequence. In contrast, escalated types of aggressive behavior have impulsive and violent characteristics, often under the influence of alcohol. 2. The long-established role of serotonin in impulsive and escalated forms of aggressive behavior is seen in (1) the dynamic state changes in corticolimbic serotonergic neurons during the termination of an aggressive bout and (2) in the deficient serotonergic trait in violence-prone individuals. Decreases in cortical serotonin are detected at the anticipated end of the fight. 3. Modulation of 5-HT by enkephalin and by CRF characterize defensive aggression and submission. 4. At the level of the serotonergic soma in the raphe, activation of autoreceptors by 5-HT1A agonists may mediate the antiaggressive effects. Neurotoxic lesions of the DRN point to the postsynaptic receptor pool as a further site of this action. 5. In the anterior hypothalamus, vasopressin facilitates offensive aggression in hamsters via action at V1A receptors. The co-localization of vasopressin and serotonin is the most likely mechanism for the antiaggressive effects of SSRIs. 6. Activation of 5-HT1B receptors, chiefly in the prefrontal cortex, transiently increases extracellular serotonin and reduces aggression with behavioral specificity. 7. Serotonergic influences on escalated aggressive behavior are seen (1) in individuals with predispositions to engage in aggressive behavior (trait), (2) in anticipation and in reaction to aggressive bouts (state), (3) in modulation by enkephalin, vasopressin and oxytocin that promote social bonding and nest defense, (4) in individuals treated with compounds targeting the 1B receptor subtype.

5-HT1B RECEPTOR AND ESCALATED AGGRESSION IN MALE AND FEMALE RODENTS. De Almeida, RMM. Psychology, Laboratorio de Neurociencias, UNISINOS, Sao Leopoldo, RS, Brazil. The current data focus on the prefrontal cortex (PFC), more specifically the ventro orbital area (VO), because of its important role in the inhibitory control of behavior. From a clinical perspective, it is important to study animal aggression that is escalated above the species-typical level. Activation of 5-HT1B receptors by CP-94,253, anpirtoline and zolmitriptan reduces several types of aggressive behavior in male when injected intraperitoneally under conditions that engender heightened aggression. The most selective 5-HT1B receptor agonist is CP-93,129. There is a few reports about the role of 5-HT receptor agonists on female aggression. After microinjections it is important to note that just the offensive components of female aggression are reduced by CP-93,129, while the defensive responses in the maternal aggression are not affected. It can be hypothesized that the VO PFC is an area that probably stimulates offensive relative to defensive components of behavior in female rats. Microinjections of 5-HT1B receptor agonists into the VO PFC of male mice and female rats decreased aggression which highlights the role of this brain area as an important site for the species-typical aggressive behavior in rodents.

VASOPRESSIN AND THE REGULATION OF AGONISTIC BEHAVIOR. Albers, H.E. Center for Behavioral Neuroscience, Dept. of Biology. Georgia State University, Atlanta, GA 30303 USA. There is substantial evidence that peptides in the arginine-vasopressin (AVP) family are involved in controlling social behavior in a wide range of species. In mammals, AVP is found in a number of limbic system circuits that are involved in the regulation of social behavior and emotion and the effects of AVP appear to be mediated by the AVP V1a receptor. In hamsters, injection of AVP into specific hypothalamic sites stimulates aggression and communicative behaviors while injection of selective V1a antagonists into these same regions inhibits these behaviors. We have investigated the hypothesis that the factors that influence the expression of aggression and communication (e.g., social experience) do so by altering the number of V1a receptors in these hypothalamic sites. In a series of experiments we have found that the number of V1a receptors within CNS circuits controlling social behavior differs dramatically depending on the social and hormonal factors experienced by that individual. These data support the hypothesis that individual differences in social behavior may be mediated at least in part by the effects of social and hormonal factors on the number of V1a receptors in key CNS sites.

SOCIAL ISOLATION AND GENE EXPRESSION OF SEROTONIN RECEPTORS. Chiavegatto, S. Institute of Psychiatry and InCor, University of Sao Paulo Medical School, SP, Brazil. Early life events influence brain neurodevelopment and originate long-lasting behavioral consequences. Postweaning social isolation in rodents induces emotional and neurochemical alterations similar as seen in some psychopathologies. The involvement of central serotonergic neurotransmission in the observed adjustments is known, but not the genomic impact of social deprivation upon this system. We have been investigating the effects of prolonged early social isolation on emotion-related behaviors and 5-HT-related gene transcription in mice. After weaning, male C57Bl/6J mice were reared singly or in groups of four during six weeks. Single-housed mice were hyperactive in a novel environment and exhibited signs of aggressive behavior. Interestingly, social isolation induced robust reduction in gene expression of 5-HT1A, 5-HT1B, 5-HT2A, 5-HT2C, 5-HT3A, 5-HT6 and 5-HT7 receptors in the prefrontal cortex determined by quantitative real-time PCR. At midbrain level, the transcription of 5-HT1B receptor gene was reduced, but not the 5-HT1A. There was no alteration in 5-HT transporter or synthetic enzyme (tph2) gene expression. These results indicate that early social isolation in mice induces marked disturbance in postsynaptic 5-HT-related gene transcription associated with motor hyperactivity and aggression. The overall decreased gene expression in the prefrontal cortex highlights its high vulnerability to environment and involves novel candidates that may have critical implications for underlying molecular mechanisms. Acknowledgement: FAPESP - Brazil

TARGETING GENE EXPRESSION IN SUBREGIONS OF DORSAL RAPHE ALTERS STRESS AND ANXIETY BEHAVIORS. Neumaier, J.F.; McDevitt, R; Hiroi, S. The dorsal raphe (DRN) serotonergic system is organized somatotopically with discrete subregions projecting to different areas of forebrain. Since 5-HT has complex effects on emotional behavior, we have been investigating whether subregions of rat DRN affect different behaviors. Stress exposure or hormonal challenges differentially regulate 5-HT1B autoreceptor and tryptophan hydroxylase-2 (TpH2) expression throughout the rostral-caudal extent of the DRN. For example, chronic estrogen was anxiolytic and produced the most pronounced effects on 5-HT1B and TpH2 mRNA expression in the mid-ventromedial DRN. Estrogen reduced 5-HT1B and increased TpH2 mRNA, and these changes correlated with reduced anxiety-like behavior in the open field. Contrarily, TpH2 expression in rostral dorsomedial DRN was inversely correlated with anxiety. We have further tested these observations using regionally precise viral mediated gene transfer (to increase gene expression) or a novel antisense oligonucleotide knockdown strategy. Increased 5-HT1B expression in rostral DRN reduces anxiety and fear conditioning in unstressed animals. Thus, there is a substantial interaction between stress context, gene expression, and the subregion within raphe being considered that summates to affect anxiety-related behaviors. We are presently investigating the effects of regional knockdown of TpH2 expression on behavior and will report these results as well. Together, we are using these regionally specific strategies to alter 5-HT1B and TpH2 expression to test our hypothesis that distinct subregions of DRN regulate emotional behaviors in very discrete manners.

11:00-12:00 Presidential lecture: Joseph Huston

BEHAVIORAL DESPAIR ICURRED BY WITHHOLDING REINFORCEMENT: EXTINCTION-INDUCED DEPRESSION? Huston, J.P. Institute of Physiological Psychology, University of Düsseldorf, Universitätsstr. 1, 40225 Düsseldorf, Germany. Extinction by withholding of a positive or negative reinforcer is well known to have negative emotional consequences for the organism. This procedure is a source of stress and is accompanied by behavioral changes, including escape, aggression, "displacement" activities, agitation, and so called "frustration". We hypothesised, that extinction may induce "despair" and behavioral and neurobiological indices of depression. Since extinction of conventional operant tasks does not provide obvious behavioral markers of "despair", we examined extinction of escape (a negative reinforcer) from the Morris water maze. We found that 1. Over the course of extinction trials, behavioral IMMOBILITY increased as a function of resistance to extinction (RTE), with aged rats showing more immobility than adults. 2. The antidepressant, desipramine, decreased immobility and increased RTE. 3. The expression of immobility was related to indices of fear in the aged. 4. In the aged, amount of ACh and DA in ventral striatum correlated positively with amount of immobility; NE correlated negatively in adults. 5. High immobility rats expressed a higher MR-/GR- receptor mRNA ratio in CA1 of hippocampus. 6. High immobility aged rats expressed less steroid-receptor co-activator mRNA in hippocampus than low immobility aged. 8. In the aged, NGF in frontal cortex correlated with immobility and with RTE. 9. In adults, BDNF in frontal cortex correlated with immobility over extinction trials, and with RTE. The concept of extinction-induced "despair" is held

to be a model of depression which develops as a consequence of stress incurred due to loss of reinforcers. It is presumed to be an especially useful analog of depression in the aged, who tend to experience parallel losses of reinforcers as a result of loss of health, family, employment, and other sources of well being.

Abstracts for the Student Travel Awardees are in the poster section in which they will be presenting.

3:45-5:45 Symposium 2: 5-HT and emotion: An appreciation of the contributions of Fred Graeff.

NEUROBIOLOGY OF PANIC DISORDER. Graeff, F.G.; Del-Ben, C.M. Psychiatry Division, Medical School, USP. 14049-900 Ribeirão Preto, SP, Brazil. Evidence from animal models of anxiety led to the hypothesis that serotonin (5-HT) enhances inhibitory avoidance (anxiety) in the forebrain, whereas inhibits one-way escape (panic) in the midbrain periaqueductal gray matter (PAG). Antidepressant drug treatment would prevent panic attacks by enhancing 5-HT inhibition in the PAG. The results of hormonal preclinical and clinical studies indicate that the hypothalamic-pituitary-adrenal axis is activated by anticipatory anxiety, but not by either PAG stimulation or the panic attack, stressing the difference between these emotional states. Reported functional neuroimaging results have shown activation of the insula and upper brain stem (including the PAG), as well as deactivation of the anterior cingulate area during experimental panic attacks. In addition, voxel-based morphometric analyses of brain magnetic resonance images have shown an increase of grey matter volume in the insula and upper brain stem, and a decrease in the anterior cingulate area of panic patients as compared to healthy controls. Since the insula and the anterior cingulate translate interoceptive stimulation into feeling, and that panic patients seem to overestimate bodily signals, it is suggested that these brain areas are a likely neural substrate of interoceptive supersensitivity, and a possible site of action of both drug and behavior therapy. Financial support: CNPq, FAEPA and FAPESP.

THE DEAKIN/GRAEFF HYPOTHESIS: UNFOLDING THE MODEL. Schenberg, L.C.; Vargas, L.C.; Lugon, A.B. Dept. of Physiological Sciences, UFES, 29043-125, Vitória, Brazil. About 15 years ago, Deakin and Graeff proposed that whereas the generalized anxiety is related to the hyperactivity of 5-HT excitatory projections to forebrain structures (prefrontal cortex and amygdala), panic disorder concerns to the malfunctioning of 5HT inhibitory projections from dorsal raphe to dorsal periaqueductal gray (DPAG). Main competitor hypotheses implicate panic attacks with either the locus coeruleus (LC) or the amygdala. Because the DPAG projects to the LC and receives inputs from anterior cingulate cortex (AC), evidences supporting the panic attack mediation by the DPAG-LC-AC circuit are reviewed. Early results showed that whereas the DPAG-evoked galloping was attenuated or almost abolished by 21-day administrations of serotonin selective reuptake inhibitors, DPAG-evoked immobility was selectively attenuated by maprotiline, a noradrenaline selective reuptake inhibitor ineffective in panic attacks. Whereas acute injections of antidepressants and anxiolytics, or 10-day injections of buspirone, were ineffective, immobility was attenuated by a sedative dose of midazolam. In contrast, the panicogenic drug pentylenetetrazole facilitated galloping. These data suggested that while immobility is a noradrenaline-mediated state of enhanced attentiveness, galloping is the panic attack best candidate response. Nevertheless, DPAG-evoked behaviors were markedly attenuated following i.c.v. injections of maprotiline and DSP-4, a drug that promotes the selective depletion of coeruleo-cortical noradrenergic projections. Overall, these data implicate the DPAG-LC-AC circuit in anticipatory anxiety and in drug and behavioral therapy of panic attacks.

IMPAIRED STRESS-COPING AND FEAR EXTINCTION AND ABNORMAL CORTICOLIMBIC MORPHOLOGY IN SEROTONIN TRANSPORTER KNOCK-OUT MICE. Holmes, A.; Izquierdo, A.; Wellman, C.L. Section on Behavioral Science and Genetic, National Institute on alcohol Abuse and Alcoholism, NIH, Rockville, MD 20852 USA. A lesser-expressing form of the human 5-HT transporter (5-HTT) gene has been associated with increased fear and anxiety and vulnerability to the effects of stress. These phenotypic abnormalities are linked to functional and anatomical disturbances in a neural pathway connecting the prefrontal cortex (PFC) and amygdala. Likewise, rodent and nonhuman primate studies indicate a major role for PFC and amygdala in the mediation of fear- and stress-related behaviors. We used a 5-HTT knock-out (KO) mouse to examine the effects of genetically driven loss of 5-HTT function for the following: (1) depression-related behavior in response to repeated stress, and pavlovian fear conditioning, extinction, and extinction recall; and (2) dendritic morphology and spine density of Golgi-stained pyramidal neurons in the infralimbic cortex (IL) and the basolateral amygdala (BLA). 5-

HTT KO mice exhibited increased depressive-like immobility after repeated exposure to forced swim stress, compared with wild-type (WT) controls. Whereas fear conditioning and fear extinction was normal, 5-HTT KO mice exhibited a significant deficit in extinction recall. The apical dendritic branches of IL pyramidal neurons in 5-HTT KO mice were significantly increased in length relative to WT mice. Pyramidal neurons in BLA had normal dendritic morphology but significantly greater spine density in 5-HT KO mice compared with WT mice. Together, the present findings demonstrate a specific phenotypic profile of fear- and stress-related deficits in 5-HTT KO mice, accompanied by morphological abnormalities in two key neural loci. These data provide insight into the behavioral sequelae of loss of 5-HTT gene function and identify potential neural substrates underlying these phenotypes. Research supported by National Institute on Alcohol Abuse and Alcoholism Intramural Research Program.

TESTS OF THE DEAKIN-GRAEFF THEORY IN HUMANS USING PHARMACO-MRI. Deakin, J.F.W.; Anderson, I.M.; Lythe, K.J.; Palm, M.E.; Elliott, R. Neuroscience and Psychiatry Unit, University of Manchester, M13 9PT. Deakin and Graeff suggested that different 5HT subsystems are engaged by aversive events with two principal functions – a) dorsal raphe nucleus (DRN) - 5HT2c projections to amygdala and basal ganglia serve to prevent the occurrence of future aversive events by motivating and directing avoidance behaviour and b)median raphe (MRN)- 5HT1A projections to hippocampus minimise the impact of current and past aversive events, by uncoupling acute stress reponses and preventing rumination. We have used pharmacoMRI in volunteers and in antisocial and anxious individuals to test some of these ideas. Intravenous administration of the 5HT2c agonist mCPP evokes subjective anxiety and MRI responses in amygdala and caudate that are blocked by oral pre-treatment with mirtazepine, a 5HT2c antagonist. Tryptophan depletion reduces central 5HT neurotransmission and selectively reduced the detection of fear in face emotion processing. Increased 5HT release induced by citalopram has the opposite effect. These findings are predicted by the DRN-5HT2c fear hypothesis. However, amygdala fMRI responses evoked by fearful faces were attenuated rather than enhanced by iv citalopram pre-treatment. 5HT modulation of MRI activations evoked by go/no-go, reward, worry and social tasks in volunteers and experiments in the clinical groups will be presented. Deakin JFW & Graeff FG (1991) 5HT and mechanisms of defence. J Psychpopharmacol 5, 305-315. Deakin JFW (1996) 5HT, antidepressant drugs and the psychosocial origins of depression. Journal of Psychopharmacology 10, 31-38. Lowry CA et al (2005) Modulation of anxiety circuits by serotonergic systems. Stress 8: 233-46

6:00-8:00 Poster Session 1

Nociception

PERIPHERAL ADMINISTRATION OF OFQ ALONE, BUT NOT IN COMBINATION WITH A PGC NANOCARRIER, PRODUCES ANALGESIA IN THE PREWEANING RAT. B.L. VANDERLINDEN[1], K.A. LEDBETTER[1], E. BOLOTIN2, G. CASTILLO2, AND E.RUIZ LIMÓN1. 1Department of Psychology, Seattle University, Seattle, WA 98122 and 2PharmaIn, Seattle, WA 98112. Pain is a serious clinical problem for human neonates and painful procedures can cause localized inflammation. Peripheral opioid injection can produce analgesia during development, but use of opiate drugs to provide safe and effective analgesia for infants remains problematic due to their differing effects in infant and adult patients. The opioid-like NOP ("novel opioid peptide") receptor and its endogenous ligand orphanin FQ (OFQ) may address this issue, since they are co-localized with peripheral opioid expression and involved in the mediation of nociception in the central nervous system of the infant rat in a manner that may involve non-opioid mechanisms. However, no data exists demonstrating the role of NOP/OFQ on nociception modulation during development when administered peripherally. To evaluate this, we administered OFQ to infant rats alone and in combination with a protected graft copolymer (PGC) nanocarrier. 21-day-old rats were administered OFQ alone (0.1, 1, or 10.0 nmol), or in combination with the nanocarrier (0.1, 1, or 10 nmol) via intraplantar (i.pl.) injection into the left hindpaw. Un-injected and saline-treated animals were used as controls. Five minutes later, rats received formalin (2%, 10 µl) in the same hindpaw. Immediately afterwards, behaviors were recorded every minute for one hour. OFQ alone produced analgesia at the highest dose (10 nmol); however, in combination with the PGC nanocarrier, the produced analgesia did not differ from the saline control at any dose. Overall, our results indicate that OFQ may be a viable means to address inflammation-induced nociception, but that this may not be enhanced by the particular nanocarrier method utilized.

EFFECT OF THE DENDRIMER-NALOXONAZINE COMPLEX IN THE μ1-OPIOID-RECEPTOR-MEDIATED POST-ICTAL ANALGESIA. [1]Felippotti. T.T.; [2]Do Carmo, D.R.; [2]Paim, L.L.; [1]Parada, C.A.; [2]Bicalho, U.O. & [1]Coimbra, N.C. [1]Dept. of Pharmacology, School of Medicine of Ribeirão Preto of the University of São Paulo. Ribeirão Preto, SP, Brazil. [2]Dept. of Physics and Chemistry of the UNESP, Ilha Solteira, SP, Brazil. In humans, many kinds of occipital epilepsy are followed by hypernociception. Interestingly, temporal-lobe epilepsy is followed by analgesia. Considering these reports, the post-ictal antinociception has been studied in animal models. The purpose of this work is to obtain preliminary information about the capacity of the dendrimer DAB-Am-16 (host) to be used as a drug carrier to reduce the time of action of the encapsulated (guest) naloxonaxine on the m_1-opioid receptor. The involvement of dendrimer-naloxonazine complex (DNC) was studied in the antinociception induced by convulsions elicited by peripheral administration of pentilenotetrazole (PTZ, 64 mg/kg). The analgesia was measured by the tail-flick test. Convulsions were followed by increase of the tail-flick latencies. The peripheral acute pre-treatment with DNC, but not with naloxonazine alone (30 mg/kg), antagonized the post-ictal analgesia in comparison with the control [$F(3,32) = 4.33$; p0.05] and, by the latencies and duration of the tonic-clonic seizures [$F(3,29) = 0.18$; $p > 0.05$], which not showed significant statistical effect in comparison with the control. These results indicate that the chemical interaction between dendrimers and naloxonazine decreases the time of the specific long-lasting pharmacological effect of this m_1-opioid antagonist.

IS THE PLUS MAZE-INDUCED ANTINOCICEPTION OPIOID MEDIATED? Cornélio, A.M.1; Nunes-de-Souza, R.L.2. 1Program of Physiological Sciences, Center of Health and Biological Sciences, Federal University of São Carlos. 2Lab. Pharmacology, School of Pharmaceutical Sciences, São Paulo State University, Brazil. E-mail:alianda@iris.ufscar.br. It has been demonstrated that mice exposed to the open elevated plus maze (oEPM: four open arms) exhibit naloxone-insensitive antinociception. This study investigated whether this type of antinociception shows cross-tolerance with morphine in rats. Rats were rendered tolerant to morphine (morphine 5 mg/kg, i.p., daily for 5-6 days. Control group received distilled water. Tolerance was assessed by tail-flick test) and then received intraplantar injection of 2.5% formalin in the right hind paw. Twenty-five minutes later they were exposed to the oEPM (aversive situation) or enclosed EPM (eEPM: 4 enclosed arms; control situation) for 10 min when the time (in seconds) spent licking the injected paw was recorded. Results confirmed oEPM-induced antinociception (Distilled water: eEPM: 96.17 ± 17.90; oEPM: 2.7 ± 1.87; $p<0.05$), an effect that was not altered in morphine tolerant animals (Morphine: eEPM: 93 ± 27.25; oEPM: 32 ± 7.70; $p<0.05$). However, tolerance significantly increased licking time when compared to control group in oEPM exposed rats only ($p<0.05$), suggesting an involvement of both opioid and non-opioid mechanisms in oEPM-induced antinociception. Financial Support: CNPq, FAPESP, PADC/FCFar-UNESP

CHRONIC TREATMENT WITH FLUOXETINE DO NOT REVERT THE HYPERALGESIA INDUCED BY REM SLEEP DEPRIVATION. Damasceno, F; Skinner, G; de Almeida, O. Dep Farmacologia e Psicobiologia, Universidade do Estado do Rio de Janeiro, RJ, Brazil Antidepressants can be used as analgesics in patients with chronic pain and no concomitant depression, indicating that the analgesic and antidepressant effects occur independently. The REM sleep deprivation (REMSD) alter several behavioral traits, including pain sensibility. This work has as objective to evaluate if the chronic treatment with fluoxetine is able to revert the hyperalgesia induced by REM sleep deprivation. Male Wistar rats (200 – 240 g) were randomly separated in 4 groups: Control Vehicle (n = 7), REMSD Vehicle (n = 7), Control Fluoxetine (n = 7), REMSD Fluoxetine (n = 7). Fluoxetine (5 mg/Kg/dia) or vehicle (water) were administered i.p. during 11 days. In the last 4 days of treatment the animals were submitted to REM sleep deprivation conditions or remained in home cages, being subsequently evaluated their thermal sensitivity on a hot plate test 1 hour after the last drug administration. The REMSD Vehicle animals showed a decrease in both hind paw withdrawal latency (-43%, p0,05; +1%, p>0,05) nor Control Fluoxetine groups (-8%, p>0,05; -7%, p>0,05), when compared to their respective vehicle groups. It is concluded that pain hypersensitivity induced by paradoxical sleep deprivation did not return to former condition after fluoxetine, as observed in other models of inductive pain. Future studies on neurotransmission systems related to sleep and pain regulation, as GABAergic neurotransmission in ventrolateral periaqueductal gray, can elucidate the mechanisms involved in this REMSD effect.

BEHAVIORAL ASSAYS OF PAIN SENSITIVITY: AN ALTERNATIVE MODEL FOR ASSESSING THE IMPACT OF NON-STEROIDAL ANTIINFLAMMATORY DRUGS IN THE RODENT HOT PLATE TEST. Koch, K.; Wiertelak, E.P.; Department of Psychology and Cognitive and Neuroscience Studies Program. Macalester College, Saint Paul MN 55105 USA The current paradigm for the rodent hot plate test pain assay is problematic in several ways. First, it uses very limited behavioral criteria to define pain, as typically the hot plate pain test measures

rats' latencies to performing a specified behavior (hind paw mouthing or jumping) when placed on a warm surface. Secondly, the hot plate test yields significant results for only certain analgesics: non-steroidal antiinflammatory drugs (NSAIDs), which have an analgesic effect in humans do not, however, affect hot plate latencies in rats, unlike opioid analgesics, such as morphine. The current study was intended to develop a new paradigm to enable use of the hot plate to determine the effectiveness of a larger range of analgesics. This study had two main components; first, development of an inventory of morphine and saline treated rats' behavior on the hot plate. Videotaped sessions of rat behavior following placement on the hot plate were used to quantify and operationally define several behaviors not commonly employed in hot plate analysis. Then, the frequencies of these behaviors were determined from the tapes and used to develop a paradigm intended to yield results sensitive to NSAID effects on pain. In the second component of this study, rats treated with ibuprofen, an NSAID, were subjected to the new paradigm. These rats displayed certain behaviors at a significantly different frequency than control rats, suggesting that there are in fact behavioral changes on the hot plate in response to NSAIDs, and they are detectable with the new paradigm. Supported by grant NIH (NCCAM) 1R15AT002705-01 to EPW.

PLACENTA INGESTION BY RATS ENHANCES CENTRAL d_1-, BUT NOT CENTRAL d_2-OPIOID-MEDIATED ANTINOCICEPTION Anne Neumann[1], Ksenia V. Kastanenka[1], Alexis C. Thompson[2], Reema T. Cheema[1], Jean M. DiPirro[3], Mark B. Kristal[1]. [1]Department of Psychology, University at Buffalo, Buffalo, NY, 14260, [2]Research Institute on Addictions, [3]University at Buffalo, Buffalo, NY, 14203, Department of Psychology, Buffalo State College, Buffalo, NY 14222. Our previous work has shown that ingestion of placenta and amniotic fluid (both containing what we presume to be Placental Opioid-Enhancing Factor [POEF]) enhances central d-opioid antinociception, induced by ICV administration of DPDPE, in rats. New information suggests, however, that there are multiple subtypes of the d-opioid receptor and that DPDPE may be selective to only the d_1-opioid-receptor subtype. The present study investigated the role of d_1-and d_2-opioid receptors in the enhancing effect of placenta ingestion on d-opioid-mediated antinociception. Female Long-Evans (hooded) rats ingested 1.0g rat placenta or 1.0g ground beef (as a control substance) and received an ICV injection of a d_1-opioid-receptor agonist (DPDPE; 0, 57 to 72 nmol in saline) or a d_2-opioid receptor agonist (deltorphin-II; 0, 15 – 32 nmol, in 10% DMSO). Antinociception was determined using the hotplate test, with the hotplate set at 52°C. Ingestion of placenta enhanced DPDPE-induced antinociception by as much as 90% (at DPDPE dose 57 nmol), whereas the ingestion of ground beef had no effect on DPDPE-induced antinociception. Ingestion of placenta did not enhance deltorphin-II-induced antinociception significantly. These findings support our previous work showing that placenta ingestion contains a substance, POEF, that when ingested, increases d-opioid-receptor-mediated analgesia and adds to the finding by showing that POEF enhancement of d-opioid antinociception is specific to the d_1-opioid-receptor subtype. SUPPORTED IN PART BY NSF GRANT IOB-0445679 AWARDED TO M.B.K.

Ingestion-Related Behaviors

EFFECTS OF 5-HT1A, 5-HT1B and 5-HT 2C RECEPTOR AGONISTS ON BEHAVIORAL SATIETY SEQUENCE IN RATS. Mancilla-Díaz, J.M.; López-Alonso, V.E.; Ecartín-Pérez, R.E. Psychobiology of the Eating Laboratory, FES-Iztacala, UNAM, Mexico. Sponsored by PAPIIT IN303103 and IN304406. Previous studies have shown that feeding behavior is affected by serotonergic neurotransmission, mainly in the hypothalamus. The serotonergic system plays a significant role in the control of feeding behavior mainly controlling carbohydrate intake. Furthermore, it has been reported that 5-HT1 and 5-HT2 serotonin receptors are required for regulating serotonin activity in the control of food intake. However, the effect of this regulatory activity on particular behavioral mechanisms remains unclear. The aim of the present study was to evaluate the effects of 8-OH-DPAT (5-HT1A receptor agonist), CP93129 (5-HT1B receptor agonist) and Ro-60-0175 (5-HT2C receptor agonist), injected into the paraventricular nucleus (PVN) on the behavioral satiety sequence (BSS) in rats. Rats were individually housed in clear Perspex cages with free access to individual sources of protein, carbohydrate, fat and water. The experimental room was maintained on a reversed 12:12-h light:dark cycle (lights on at 21:00 h). The behavioral test consisted in the analysis of the duration of three mutually exclusive behavioral categories within 60 min (feeding, resting, and activity) at the beginning of the dark phase; food intake was measured in the same observation period. Our results show that the serotonin-induced hypophagic effect was enhanced by the administration of all agonists. Nevertheless, the behavioral analysis indicated that the administration of 8-OH-DPAT interrupted the natural BSS with an increase in non-feeding behavior, whereas administration of CP93129 or Ro-60-0175 promoted early development of the natural BSS. In conclusion, specific 5-HT receptor activation affected serotonergic modulation of feeding behavior in a functionally selective way.

EFFECTS OF CHRONIC ADMINISTRATION OF CAFFEINE AND STRESS ON FEEDING BEHAVIOR AND ABDOMINAL FAT OF MALE RATS. Pettenuzzo, L.F.; Noschang, C.; Toigo, E.v.P.; Vendite, D.; Dalmaz, C. Dep Bioquímica, ICBS, UFRGS. Anorectic effects of caffeine are controversial in the literature. In addition, stress and obesity are growing problems in our society. Considering that many stressed people are coffee drinkers, the objective of the present study was to evaluate the effect of stress and chronic administration of caffeine on feeding behavior, body weight and abdominal fat content in male rats. 64 Wistar male rats were divided in 3 groups: control (water), caffeine 0.3 g/L and caffeine 1.0 g/L (in the drinking water). These groups were subdivided in control and stressed (repeated restraint stress during 40 days). During all treatment, chow consumption was monitored and rats were weight weekly. Afterwards, feeding behavior was evaluated during 3 min trials with food-deprivation and non-food-deprivation, and also in 8 trial exposures using palatable food (Froot Loops® and Cheetos®). After the behavioral procedures, we evaluate abdominal fat. The chronic administration of caffeine diminishes the consumption of Cheetos® (1,0 g/L) in the animals food-deprived and Froot Loops® (0,3 and 1,0 g/L) in fed rats. In the 8-trial tests, stress diminishes the Cheetos® consumption in the last exposures (5-8) and caffeine diminishes the Froot Loops® consumption in the early exposures (1-4). Neither caffeine nor stress altered body weight, but caffeine 0,3 and 1,0g/L diminishes abdominal fat content. These observations suggest that chronic caffeine consumption can diminishes palatable food ingestion and may be useful to help in obesity treatments. (Financial Support: CNPq)

CLONIDINE INJECTED SUBCUTANEOUSLY REDUCES WATER AND NACL INTAKE INDUCED BY GABAERGIC ACTIVATION OF THE LATERAL PARABRACHIAL NUCLEUS. Roncari, C.F.; Oliveira, L.B.; Barbosa, S.P.; De Luca Jr., L.A.; Colombari, D.S.A.; De Paula, P.M.; Menani, J.V. Department of Physiology and Pathology, Dentistry School, UNESP, Araraquara, SP, Brazil. While bilateral injections of muscimol ($GABA_a$ agonist) into the lateral parabrachial nucleus (LPBN) induce water and NaCl intake in satiated and normovolemic rats, injections of clonidine (a2-adrenergic/imidazoline agonist) into the forebrain or peripherally inhibit angiotensin II-induced water and NaCl intake. Therefore, in the present study we investigated the effects of subcutaneous (sc) clonidine on water and 1.8% NaCl intake induced by muscimol injected into the LPBN in satiated and normovolemic rats. Male Holtzman rats (280-320 g, n = 7) with bilateral stainless steel guide-cannulas implanted into the LPBN were used. Water and 1.8% NaCl intake was recorded for 4 h starting immediately after injections of muscimol (0.5 nmol/0.2 µl) or saline (sal) bilaterally into the LPBN. Clonidine (80 µg/kg b. w.) was injected sc 1 h after LPBN injections. We found that muscimol into LPBN induced 1.8% NaCl (20.4 ± 10.9 ml/4 h, vs. sal: 0.8 ± 0.4 ml/4 h) and water intake (9.1 ± 3.1 ml/4 h, vs. sal: 2.3 ± 1.1 ml/4 h, $p < 0.05$). Clonidine sc abolished 1.8% NaCl (0.9 ± 0.8 ml/4 h) and water intake (1.7 ± 0.7 ml/4 h, $p < 0.05$) induced by bilateral injections of muscimol into the LPBN. The results suggest that mechanisms activated by muscimol into the LPBN to induce water and NaCl intake are inhibited by the activation of a2-adrenergic/imidazoline receptors probably located in the forebrain. Supported by: FAPESP, CNPq.

LESIONS OF COMMISSURAL NUCLEUS OF THE SOLITARY TRACT ENHANCE WATER INTAKE INDUCED BY PERIPHERAL OSMORECEPTOR ACTIVATION. Blanch[1] G. T.; Freiria-Oliveira[1] A. H.; Vendramini[1] R. C.; de Paula1 P. M.; Menani[1] J. V.; Colombari[1,2] E.; Colombari[1] D. S. A.; [1] Dept. of Physiology and Pathology, School of Dentistry - UNESP, [2] Dept. of Physiology, UNIFESP/EPM, São Paulo. The commissural subnucleus of the nucleus of the solitary tract (commNTS) receives information from peripheral osmoreceptors. A previous study demonstrated that commNTS lesions enhanced water intake induced by intragastric (ig) 2 M NaCl, which activates peripheral and central osmoreceptors. Differently from 2 M NaCl, ig 0.6 M NaCl induces water intake due to activation of peripheral (hepatoportal), not central, osmo receptors (Am. J. Physiol., 269: R 1085, 1995). Therefore, in the present study, we investigated the effects of commNTS lesions on water intake and renal excretion in rats treated with ig 0.6 M NaCl. Male Holtzman rats (300-340 g, N = 6-8) with acute (2 days) sham or commNTS electrolytic lesions (1mA, 10 s) were used. Water intake and renal excretion were recorded for 120 min immediately after the ig 0.6 M NaCl (2 ml). Water intake induced by 0.6 M NaCl ig was enhanced in commNTS lesioned rats (2.1±0.2 vs. sham 1.3±0.2 ml/100 g body wt./120 min, $p<0.05$). During water intake test, urinary volume was reduced in commNTS lesioned rats (0.2 ± 0.05 vs. sham 0.6±0.1 ml/100 g body wt./120 min, $p< 0.05$). Acute commNTS lesions also reduced sodium excretion (21±7 vs. sham 110±25 and µEq/100 g body wt./120 min, $p<0.05$) and potassium excretion (15±5 and vs. sham 60±10 µEq/100 g body wt./120 min, $p<0.05$). These data suggest that commNTS is part of the brain circuitry that inhibits water intake and facilitates the increase in renal excretion induced by peripheral osmoreceptor activation. Financial Support: CNPq, FAPESP.

THE EFFECTS OF GLOBAL UNDERNUTRITION DURING FETAL DEVELOPMENT ON LEARNING IN ADULT LIFE. Krägeloh, C.U.[1,2]; Davison, M.[1,3]; Landon, J.[1,3]; Miles, J.L.[1,3]; Thompson, N.M.[1,3]; Breier, B.H.[1,3] [1]National Research Centre for Growth and Development, [2]Auckland University of Technology, [3]The University of Auckland, New Zealand. Intrauterine growth restriction can lead to significant long-term health consequences in later life, such as metabolic dysregulation and cardiovascular disorders, but less is known about its effects on behaviour and cognitive function. The present study investigated the effects of prenatal undernutrition on learning in adulthood. Virgin Wistar rats were time mated and randomly assigned to receive either ad-libitum access to a standard laboratory diet to generate control offspring or 30% of that level during pregnancy to generate growth-restricted offspring. At 60 days of age, six female offspring from each group were trained to respond for food reinforcers on a two-lever concurrent-schedule procedure in which the relative reinforcer rates changed frequently and unpredictably within sessions. Offspring from mothers that were undernourished during pregnancy learned less, as shown by lower values in sensitivity to reinforcement. This parameter from the generalised matching law measures the extent to which subjects' response allocation to the two levers tracks changes in relative reinforcer rates. We replicated this finding in male rats that were slightly older and from a different breeding cohort. In summary, the results provide direct experimental evidence for a link between prenatal environmental conditions and reduced learning in later life. The operant procedure that we used is novel and provides detailed, quantitative and theory-based measures of learning that can capture the effects of both shorter- and longer-term events.

EFFECT OF ADULT-ONSET CALORIE RESTRICTION ON ANXIETY, SOCIAL AND SEXUAL BEHAVIOR AND NEUROENDOCRINE MEASURES. Levay, E. A.; Govic, A.; Penman, J.; Paolini, A. G.; Kent, S. School of Psychological Science. La Trobe University Victoria, 3086 Australia. Despite an abundance of research on calorie restriction (CR) and health, the consequences of CR on anxiety, sexual, and social behavior remain to be examined. Rats were subjected to 1 of 4 dietary regimens: ad libitum controls, CR25%, CR50%, and Acute CR50% and administered 2 tests of anxiety: the open field (OF) test, and the elevated plus maze (EPM). In addition, social interaction (SI), social recognition memory, sexual behavior, and partner preference (PP) were investigated. In the OF, both chronic CR groups made more central zone entries and spent more time there than controls. In addition, the Acute group exhibited longer latencies to leave the central zone at the onset of the test. In the EPM, the Acute group made fewer open arm entries than all other groups. Both the CR25% and CR50% group spent more time in SI than the other treatment conditions; only the CR25% group did not display memory for the juvenile conspecific during the re-exposure session of the social recognition test. In the PP test, females spent more time with and engaged in greater investigation of the control group compared to the CR50% group. Sexual performance was also affected by CR; the CR50% group exhibited fewer mounts, intromissions, and a longer latency to intromission compared to controls. Serum testosterone was reduced in both CR groups compared to controls. Serum leptin was only reduced in the CR50% group; and adrenocorticotropic hormone and corticosterone were unaffected by CR. Our results indicate that CR initiated in adulthood leads to an altered behavioral and neuroendocrine phenotype.

Reward and Addiction

CHARACTERIZATION OF THE ALCOHOL ESCALATION EFFECT IN C57BL/6J MICE. Melendez, R.I. Medical University of South Carolina, Charleston, SC. Relapse-like drinking has been recently studied in C57BL/6J (B6) mice expressing the alcohol escalation effect (AEE), also known as a progressive increase in ethanol preference and consumption following repeated abstinence periods (Melendez et al., 2006). Our data indicates that 6 weeks of continuous access to ethanol followed by repeated 6-day deprivation periods (i.e., weekly access to ethanol) induce a robust AEE in adult male B6 mice. The expression of the AEE was observed following 6 consecutive weekly re-exposure periods. Thereafter, the AEE reached a plateau for 3 consecutive weekly re-exposure sessions. Interestingly, the persistence of excessive ethanol consumption returned to basaline-control levels following 10 days of continuous daily exposure to ethanol, a condition that does not produce the AEE. Indeed, no significant differences in ethanol intake and preference were observed in non-deprived B6 mice, which further indicates a remarkably stable pattern of daily ethanol consumption. Together, these findings suggest that when access time to a continuous schedule of ethanol intake is restricted (i.e., deprivation period), B6 mice tend to loose the capacity to limit intake to a certain level over time. Considering that the transition to drug addiction has been hypothesized to result from loss of capacity to limit consumption (Koob and Lemoal, 1997), studying this capacity may be important for the science of addiction. The present study extends our previous results in two fundamental ways. First, the study was designed to test the hypothesis that the expression of the AEE in B6 mice is dependent on the initial length of daily access to ethanol (i.e., 2, 4 vs. 6 weeks). Second, in two separate experiments, we previously reported (paradoxically) that increasing the deprivation length to a period of 14 days (versus 6 days) reduces the onset and

magnitude of the AEE in B6 mice. Thus, the present study will also determine the optimal deprivation length yielding a reliable expression of the AEE in B6 mice. Finally, considering that changes in glutamate homeostasis have been suggested to account as a neural substrate of alcohol addiction, alterations in neuronal glutamate transport will also be evaluated in B6 mice expressing the AEE. Further work on the neural mechanisms of the AEE in B6 mice may ultimately lead to advances in effective molecular treatments for preventing relapse of alcohol drinking in humans. [Funded by AA 015953]

REWARDING AND AVERSIVE PROPERTIES OF THE CANNABINOID AGONIST WIN 55,212-2: INFLUENCE OF THE AGE AND RAT STRAIN. Pandolfo, P.1; Vendruscolo, L.F.1; Pamplona, F.A.1; Prediger, R.D.1; Takahashi, R.N. 1 1Departamento de Farmacologia, Universidade Federal de Santa Catarina – UFSC, SC, Florianópolis, Brasil. Converging evidence points to adolescence as a critical period for the onset of a wide range of neuropsychiatric disorders, including drug addiction. Moreover, attention deficit hyperactivity disorder (ADHD) has also been considered as a risk factor for substance use disorders. The Spontaneously Hypertensive Rats (SHR), which are considered a suitable genetic model for the study of ADHD for showing hyperactivity, impulsivity and impaired attention, are more sensitive to cocaine and amphetamine than other rat strains, but little is known about their sensitivity to cannabinoids. Moreover, despite the high prevalence of ADHD among adolescents, studies using SHR have mainly been carried out with adult subjects. The aim of the present study was to compare the behavioral effects of WIN 55,212-2 (WIN, 0.125-2.5 mg/kg; i.p.), a cannabinoid receptor agonist, in SHR and Wistar rats (representing a "normal" genetically heterogeneous population) tested in open field and conditioned place preference tests. Adolescent (27-38 days old) and adult (80-110 days old) rats were used. WIN (0.25 and 1.25 mg/kg) promoted locomotor stimulation in adolescent SHR, but not in adult SHR or Wistar rats (regardless of age), in the open field test. Moreover, WIN (0.25, 1.25 and 2.5 mg/kg) clearly produced conditioned place aversion in adult Wistar rats, while no effects were detected in adolescent Wistar rats. On the other hand, WIN induced rewarding effects in both adolescent (2.5 mg/kg) and adult (0.25 mg/kg) SHR. The behavioral effects of WIN were fully antagonized by pretreatment with a CB1 cannabinoid receptor antagonist, AM 251 (0.25 mg/kg). The present results suggest that the SHR strain provides a useful tool for the study of the behavioral and molecular mechanisms underlying the relationship between ADHD and drug addiction and confirm clinical observations that adolescence and ADHD might represent risk factors for the abuse of cannabinoids.

CORTICAL AND LIMBIC MODULATION OF LOCOMOTOR ACTIVITY PRODUCED BY ACTIVATION OF DOPAMINERGIC POSTSYNAPTIC RECEPTORS IN THE NUCLEUS ACCUMBENS Rouillon, C.; Abraini, J.H. and David, H.N. Centre CYCERON, CNRS UMR 6185, University of Caen, 14074 Caen, FRANCE. The nucleus accumbens, which is part of the ventral striatum, modulate and regulate motivational and motor behaviors. The nucleus accumbens is described as a limbic-motor interface and receives glutamatergic projections from the prefrontal cortex (PFC), hippocampus, and amygdala (BLA), and a dense dopaminergic input from the ventral tegmental area. Numerous studies showed that functional interactions between dopaminergic neurotransmission and glutamatergic neurotransmission in the rat nucleus accumbens are involved in the development of environmentally adapted behaviors. Here, we characterized the role of the PFC and the BLA in the locomotor responses induced by activation of D1-like receptors or co-activation of both D1-like and D2-like receptors, a pharmacological condition required for the full expression of the postsynaptic effects of D2-like receptor agonists. Infusion of lidocaine into the BLA or the PFC showed no effect on basal locomotor activity. Administration of the selective D1-like receptor agonist SKF 38393 or co-administration of SKF 38393 and of the selective D2-like receptor agonist quinpirole in the nucleus accumbens induced an increase in locomotor activity. Infusion of lidocaine in the BLA, but not in the PFC, decreased locomotor activity induced by SKF 38393, while administration of lidocaine in the PFC, but not in the BLA, amplified the locomotor response induced by co-infusion of SKF 38393 + quinpirole. Our results suggest that striatal output neurons that express D1-like receptors would be positively controlled by the BLA, while striatal projection neurons that express D2-like receptors would be negatively controlled by the PFC. They further support that limbic and prefronto-cortical inputs to the NAcc selectively and respectively involve D1-like receptors and D2-like receptors.

ETHANOL SELF-ADMINISTRATION IN ß-ENDORPHIN DEFICIENT TRANSGENIC MICE. Williams, S.; Hollaway, A.; Allen, S.A.; Grisel, J.E. Dept. of Psychology. Furman University, Greenville, SC 29613 USA. Evidence shows that EtOH modifies the production and/or release of endogenous opioid peptides, specifically ß-endorphin (Gianoulakis, 2004; Przewlocka et al., 1994; Schulz et al., 1980). Opioids subsequently influence the reinforcing properties of EtOH and the development of alcoholism (Terenius, 1996; Van Ree, 1996). In this study, beta-endorphin deficient mutant mice were used to examine the effects of a specific opioid peptide on EtOH

consumption. Mice were obtained from The Jackson Laboratory, Bar Harbor, ME, USA. Male and female, adult naïve mice were single housed in Plexiglas cages with corn cob bedding and ad lib access to food (mouse chow) and water. A two-bottle free choice EtOH oral self-administration paradigm was administered to homozygous mutant mice (void of all beta-endorphin), heterozygous mice (50% beta-endorphin expression), and sibling wildtype mice (C57BL/6J). Subjects received increasing concentrations of EtOH (0%, 3%, 6%, 12%, and 15%) each given over an eight day span, and were evaluated for preference and consumption each day. Bottles were switched every other day to avoid the development of a side preference. Overall, homozygous mutant mice (KO) showed decreased preference for EtOH at all concentrations, but did not self-administer significantly less than heterozygous mice (HT) and wildtype mice (C57). This effect is sex dependent with male KO mice displaying the lowest preference (never lower than 50%). Females did not differ according to genotype. In fact, there was a strong tendency ($p = .06$) for KO males to consume less EtOH across all doses, but not genotypically different in females. These data support the hypothesis that beta-endorphin influences the reinforcing effects of EtOH in a sex-dependent manner.

ANTAGONISM OF NK3-RECEPTOR DOES NOT ALTER HORMONAL EFFECTS OF ACUTE SYSTEMIC COCAINE ADMINISTRATION IN MARMOSET MONKEYS. Barros, M.[1]; Lima, D.[1]; Spíndola, D.B.[1]; Dias, L.O.[1]; de Souza Silva, M.A.[2]; Huston, J.P.[2]; Tomaz, C.[3] [1]Dept. of Pharmaceutical Sciences, University of Brasilia, 70910-900, Brazil. [2]Institute of Physiological Psychology I, University of Dusseldorf, 40225, Germany. [3]Primate Center, University of Brasília, Brazil. Neuropeptides of the tachykinin family are known to mediate reinforcement processes and affective behavior. In fact, the neurokinin3-receptor (NK3) was recently shown to modulate the rewarding, hyperlocomotor and hypervigilance effects of cocaine in rats and marmoset monkeys. This psychostimulant, however, also induces specific neuroendocrine effects. Thus, in the present study, NK3-receptor antagonism upon acute systemic cocaine-induced changes in circulating ACTH, cortisol and prolactin levels were investigated in eleven adult marmoset monkeys (Callithrix penicillata). Each subject was initially pre-treated with SR142801 (0, 0.2 mg/kg; ip), followed 20-min later by a cocaine (10 mg/kg; ip) or saline (ip) treatment. A blood sample was obtained 20-min after the last treatment and plasma/serum ACTH, cortisol and prolactin concentrations were determined by quimioluminescence. Cocaine alone did not significantly alter marmoset ACTH and cortisol concentrations. Prolactin levels, however, decreased significantly following cocaine administration; such change was not significantly reversed by SR142801 pre-treatment. In addition, this NK3-receptor antagonist and vehicle/saline administration did not have an effect on their own. Taken together, the present findings suggest that NK3-receptor antagonism may not block the typical neuroendocrine effects observed following acute systemic cocaine administration in marmosets, although this same dose significantly reversed the behavioral response. This result – particularly for ACTH and cortisol – may be related to the glucocorticoid resistance commonly observed among neotropical primates, as well as to the time-course normally observed for each hormonal response following cocaine administration.

CONTEXT-SPECIFIC SENSITIZATION OF LOCOMOTOR BEHAVIOUR PRODUCED BY A SINGLE ADMINISTRATION OF APOMORPHINE. aBloise, E.; bCarey, R.J.; aCarrera, M.P. aLaboratory of Animal Health, State University of North Fluminense, Campos dos Goytacazes, RJ 28013-600 Brazil bResearch and Development (151), VA Medical Center and SUNY Upstate Medical University, Syracuse, NY 13210, USA. The present study examined the minimal number of exposures to the D1/D2 agonist apomorphine capable of producing behavioral sensitization. Rats received one (experiment 1) or two administrations on two successive days (experiment 2) of apomorphine (0.5 and 2.0 mg/kg) paired or unpaired to an open-field environment. After 2 days of drug withdrawal, the rats received a challenge injection with the same dose of apomorphine (sensitization test) and locomotion, rearing and sniffing were measured. The results of the first experiment showed that locomotor sensitization occurred after a single acute exposure to apomorphine and that 0.5 and 2.0 mg/kg treatments were equally effective. This sensitization effect was context-specific and was limited to locomotion. The second experiment revealed a differential dose effect on the sensitization test. Two treatments with 2.0 mg/kg potentiated locomotor sensitization as compared with a single treatment but two treatments with 0.5 mg/kg did not increase the sensitization effect more than the single 0.5 mg/kg treatment. This result indicates an interaction between drug dose and frequency of drug treatment for the induction of apomorphine locomotor sensitization. In that the sensitization effects are considered to be a core contributor to psychostimulant addiction, the present findings are of importance to understanding addiction because they indicate that sensitization processes can be initiated with a single drug experience and amplified with exposure to higher drug dosage levels.

A NEW MODEL TO EVALUATE AFFECTIVE STATES ASSOCIATED WITH REWARD-PREDICTING CUES IN MICE. Cagniard, B., Murphy, N.P. Neuronal Circuit Mechanisms Research Group, RIKEN Brain Science Institute, Wako-shi, Japan. Environmental cues, repeatedly present during reward consumption, serve as a reminder and motivator to seek rewards. The main obstacle to the treatment of addiction is relapse, i.e. restoration of reward intake, even after a long period of abstinence. Relapse can be precipitated by environmental cues previously associated with reward. Although the psychological processes underlying relapse are not yet known, changes in affective states (emotions) induced by environmental cues associated with reward could be an important factor. However, very little research has been performed on the affective states that result from presentation of cues predicting reward and even less research has been done on the role of cue-induced changes in affective states in creating and maintaining addiction. In order to identify changes in affective states induced by reward-associated cues, I first adapted to mice the taste reactivity paradigm; a procedure to measure affective states. I also developed a procedure to induce anticipation of reward in mice. I am in the process of coupling these two separate behavioral paradigms to create an entirely new paradigm to evaluate if cues predicting rewards induce changes in affective states. This model should greatly help us understand the neurobiology underlying addiction behavior.

EEG MAPPING IN ALCOHOL DEPENDENCE OFFENDERS. Calzada A; Alvarez A. Legal Medicine Institute. Havana, Cuba. INTRODUCCION: A deficiency in information processing capacity of central nervous system constitutes one of possible mechanisms related to increase the likelihood of criminal act in alcohol dependence offender.Objectives: The aim of the investigation is to contribute to electrophysiological characterization of the offender with alcohol dependence. Methods: The resting electroencephalogram was recorded in 10 alcohol dependence offenders, with antisocial personality disorders evaluated for forensic psychiatrics (Experimental Group). They were compared with 9 offenders without psychiatrics disorders (Control Group). The features at visual inspection of the Electroencephalogram and the use of frequency domain quantitative analysis techniques (Broad Band and Narrow Band Spectral Measures) are described. Results: 60% of alcohol dependence offenders with antisocial personality disorder subjects had electroencephalographic abnormalities. The most frequent were organizational alterations, low amplitude electrogenesis, an attenuated alpha rhythm. Delta-theta slow activity in the temporal, parietal and occipital lobes. The quantitative analysis showed differences between the frequency spectrums and between the broad band spectral measures from both groups and between experimental groups and the Cuban norms. The delta-theta frequencies and beta activity in anterior regions predominate in the alcohol dependence offenders. Conclusion: A high incidence of electroencephalographic abnormalities was found in the alcohol dependence offender. The most frequents were: electrogenesis alterations, attenuated alpha rhythm and delta-theta slow activity in the posterior region and excess of beta activity in lobe. In the quantitative analysis confirmed the results of time analysis.

EFFECTS OF MORPHINE WITHDRAWAL ON THE DEFENSIVE RESPONSES INDUCED BY ELECTRICAL STIMULATION OF THE MIDBRAIN TECTUM. Castilho, V.M.; Ávila, M.A.V., Ruggiero, R.N., Nobre, M.J. Laboratório de Psicobiologia, FFCLRP, Universidade de São Paulo, Ribeirão Preto, SP, Brasil. Anxiety is one of the affective symptoms of opiate withdrawal. The dorsal periaqueductal gray matter (dPAG) and the inferior colliculus (IC) are the main midbrain tectum (MT) structures involved in the elaboration of defensive behavior. The aim of this study was to investigate whether these MT structures are sensitized during the morphine withdrawal. Rats submitted to a chronic treatment with saline or morphine (10 days; 10 mg/kg; sc) were implanted with an electrode glued to a guide-cannula in the dPAG or IC. Gradual increases in the intensity of the electrical stimulation of these structures was used to determine the freezing and escape thresholds 24 and 48 hours after the last injection of morphine or saline. The results showed that the morphine withdrawal promoted significant reductions in the freezing and escape thresholds determined by the electrical stimulation of the IC, without changing the aversive responses to the stimulation of the dPAG. These findings suggest that morphine withdrawal recruits the neural substrates of aversion of the IC, whereas the dPAG does not appear to be involved in this process. Financial support: FAPESP (04/02859-0).

ALCOHOL-HEIGHTENED AGGRESSION IN MICE IS ASSOCIATED WITH mRNA LEVELS OF SEROTONIN RECEPTORS IN THE PREFRONTAL CORTEX. CHIAVEGATTO S[12], QUADROS IMH[3], TRINDADE A[3], AMBAR G[1], MICZEK KA[3]. Inst. of Psychiatry[1] and InCor[2], Univ. of Sao Paulo Medical School, SP, Brazil and Tufts University[3], Medford, MA, USA. Some primates and rodents engage in heightened levels of aggression after consuming moderate doses of ethanol (EtOH). Serotonin (5-HT) receptors are key modulators of escalated aggressive behavior, and preventing this escalation may be possible by targeting receptors that are preferentially involved in aggressive behavior. 5-HT1B agonists administered systemic or microinjected into the

infralimbic region of the prefrontal cortex reduce alcohol-heightened aggression (AHA) in mice. Here we investigate if mice that show AHA differ from those that do not (ANA), in terms of expression levels of different serotonin receptors subtypes transcripts in the prefrontal cortex. Male CFW mice self-administered EtOH (6%) by being reinforced for an operant response. Each mouse was repeatedly tested for aggression towards a male intruder after consumption of either 1.0 g/kg EtOH or water, and was characterized as AHA or ANA, based on these confrontations (n=5-8/group). One week later, animals were decapitated, prefrontal cortices were dissected, and expression levels of mRNA for 5-HT receptor subtypes: 1A, 1B, 2A, 2C, 3A, 6 and 7 were determined by quantitative real-time PCR. Mice that displayed AHA showed significantly lower levels of all but 5HT3A receptor transcript (the only ligand-gated ion channel) relative to ANA mice. Reductions in expression of the different 5HT receptors ranged from 49% (5HT6) to 76% (5HT7) in AHA mice. Decreased cortical G-protein coupled 5-HT receptors expression may contribute to an overall decreased cortical serotonergic tone, which may contribute to the phenomenon of escalated aggression.

PERSISTENT INCREASES IN COCAINE SEEKING BEHAVIOR AND IN DOPAMINE NEURON ACTIVITY AFTER ACUTE EXPOSURE TO COLD SWIM STRESS. Conrad KL, Beales M, Rudick CN, Unal CT, Cotterly LM, and Marinelli M. Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA Stressful events have been shown to exacerbate a number of psychiatric disorders, including drug-taking and drug-seeking. Animal models show that these effects occur during, or immediately after the exposure to the stressor. However, the possible long-term effects of acute stress on drug-seeking behavior and its neuronal substrates have not been examined.We tested the hypothesis that exposure to a brief stressor can have persistent effects on drug-seeking behavior. We also studied concurrent changes in the activity of dopamine neurons, which are important modulators of addiction-associated behaviors.Rats were trained to self-administer cocaine (0.5 mg/kg/infusion, 2h/day, for 8 days). Then, animals underwent extinction training, during which responding was not reinforced with cocaine. After reaching an extinction criterion, animals were submitted to a brief (5-min) cold swim stress and, 16-24 h later, tested for seeking behavior (non-reinforced responding). In a separate group of rats, we monitored dopamine neuron activity, using in vivo extracellular recordings in anesthetized animals.Cold swim stress reinstated drug-seeking behavior, an effect that lasted for 16-48 hrs after the end of the stressor. Cold swim stress also increased dopamine neuron activity, with a time-course similar to the behavioral effects. Thus, neuronal activity was increased 16h, 24, and 48h after the end of the stressor, but returned to baseline-values 72h following the stressor. The stressor also modified the firing pattern of these cells. It increased non-bursting activity and the amount of bursting, without influencing the characteristics of the bursts. These studies indicate that stress can have long-term effects on drug-seeking behavior and dopamine neuron activity.

NEUROKININ3-RECEPTORS MODULATE THE NEUROCHEMICAL AND BEHAVIORAL EFFECTS OF COCAINE IN RATS AND NON-HUMAN PRIMATES. De Souza Silva, M.A.[1]; Jocham, G. [1], Müller, C.P. [1]; Barros, M.[2]; Tomaz, C.[2]; Huston, J.P. [1]. [1]Institute of Physiological Psychology, University of Düsseldorf, Germany; [2]Institute of Biology and Department of Pharmaceutical Sciences, University of Brasilia, Brazil Most of the research on cocaine's mechanism of action has focussed on monoaminergic systems. Little is known about its interactions with neuropeptidergic systems. Several lines of evidence point to a role of neurokinin3 (NK3) receptors in reinforcement mechanisms and in the modulation of the mesolimbic dopamine (DA) system. In in vivo microdialysis experiments, the agonist senktide potentiated DA overflow induced by cocaine (10 mg/kg) in both subregions of the nucleus accumbens (Nac) and simultaneously potentiated cocaine-induced hyperlocomotion. The antagonist SR142801 potentiated the DA response to cocaine selectively in the core of the Nac. In conditioned place preference (CPP) experiments, no influence of either agonist or antagonist on cocaine-induced CPP could be found. However, SR142801 suppressed, while senktide potentiated the acute hyperlocomotor effects of cocaine. Comparative studies in non-human primates (Callithrix penicillata) revealed that, interestingly, both the agonist and the antagonist inhibited the acute hyperlocomotor effects of cocaine. Taken together, these results provide evidence that NK3 receptors contribute to the dopaminergic and hyperlocomotor effects of cocaine. An involvement of NK3 receptors in the rewarding effects of cocaine could not be demonstrated. These data also show that the hyperlocomotor and Nac DA response to cocaine can be modulated without affecting the rewarding properties of the drug. The results obtained with the NK3 receptor antagonist in primates revealed species differences that might be due to the differential expression pattern of NK3 receptors in rats and primates.

DIFFERENCIAL EFFECT OF LIDOCAINE IN THE DORSAL AND VENTRAL HIPPOCAMPUS ON THE EXPRESSION OF BEHAVIORAL SENSITIZATION TO AMPHETAMINE. Degoulet M.; Abraini J.H. Centre CYCERON, CNRS UMR 6185, University of Caen, 14074 Caen, FRANCE. The nucleus accumbens (NAcc) is well known to be involved in drug addiction to amphetamine. It receives dopaminergic afferents from the ventral tegmental area and glutamatergic inputs from the ventral hippocampus (VH) and the dorsal hippocampus (DH). Here, we examined the role of the VH and the DH on (i) spontaneous locomotion, (ii) acute systemic amphetamine-induced hyperactivity and (iii) the expression of behavioral motor sensitization to chronic systemic amphetamine in rats very well habituated to their experimental environment. To answer these questions rats were given injection of lidocaine in the VH or the DH through pre-implanted cannulae. Our results show that reversible inhibition of the VH or the DH by lidocaine does not influence spontaneous locomotion, but increases hyperactivity induced by acute amphetamine. In addition, administration of lidocaine in the DH, but not in the VH, blocks the expression of behavioral motor sensitization to amphetamine. Taken together these data indicate that both the DH and the VH play a role in the acute amphetamine-induced hyperlocomotion. This indicates that the VH and the DH would exert, under lidocaine-free condition, a tonic inhibitory modulation on the brain structures involved in the production of locomotor activity in response to acute amphetamine. In addition, our results further suggest that the DH, but not the VH, would play a crucial role in the expression of behavioral sensitization to amphetamine. Given that the DH is well known to be involved in spatial learning and memory, our results suggest that behavioral sensitization to amphetamine in rats well habituated to their experimental environment and protocol may involve important contextual and environmental conditioning processes.

'PROPHYLACTIC' NPY TREATMENT DECREASES OPERANT ETHANOL RESPONDING BY DEPENDENT AND NON-DEPENDENT RATS. N.W. Gilpin; G.F. Koob. Committee on Neurobiology of Addictive Disorders, The Scripps Research Institute, La Jolla, CA 92037. Neuropeptide Y (NPY) infused into the lateral ventricles selectively suppresses operant alcohol responding by alcohol-dependent rats when infusions occur directly prior to post-dependence testing. It is thought that brain NPY systems are recruited during the transition to alcohol dependence. The purpose of this investigation was to determine if dependence-induced elevations in operant alcohol responding are blocked by 'prophylactic' treatment with intracerebroventricular NPY infusions during the transition to dependence. Wistar rats (n=14) were trained to respond for 10% (w/v) alcohol in an operant situation and then divided into four groups based on g/kg alcohol intake: dependent rats repeatedly infused with either NPY or aCSF, and non-dependent rats repeatedly infused with either NPY or aCSF. Rats were implanted with a single cannula in the lateral ventricle, and dependent rats were then exposed to alcohol vapor for 15 days, while non-dependent rats were exposed to air vapor for 15 days. According to group designations, rats were infused with either 10.0Î¼g NPY or vehicle on days 2, 4, 6, 8, 10, 12, and 14 of vapor exposure. Rats were tested for operant alcohol responding on days 3, 7, 11, and 15 of vapor exposure. All infusions and operant tests occurred 6 hours into withdrawal. On days 11 and 15 of alcohol vapor exposure, rats chronically treated with NPY responded significantly less for alcohol than rats chronically treated with aCSF. These results are partly consistent with past findings and may be explained by downstream interactions of NPY with CREB and its target genes. Supported by NIH grants AA08459 and AA06420.

COCAINE MICROINJECTIONS INTO THE NUCLEUS ACCUMBENS SHELL, BUT NOT MEDIAL PREFRONTAL CORTEX, PRODUCE APPROACH AVOIDANCE BEHAVIOR IN A RUNWAY MODEL OF SELF-ADMINISTRATION. Guzman, D. and Ettenberg, A. Behavioral Pharmacology Laboratory, Dept. of Psychology, University of California, Santa Barbara, Ca 93106. Rats traversing an alley for reinforcing stimuli typically show a decrease in run times as trials proceed. In previous work from our laboratory, animals running for either intravenous (IV) or intracerebroventricular (ICV) injections of cocaine develop a unique approach-avoidance behavior about entering the goal box resulting in an increase in run times over trials. This conflict behavior (retreats) has been hypothesized to be the result of cocaine's well documented reinforcing (positive) and anxiogenic (negative) properties. The present studies aimed to assess the involvement of the specific brain regions previously associated with cocaine reward in the development of these retreat behaviors. Male Sprague-Dawley rats were surgically implanted with a bilateral cannula aimed at the NA shell or the mPFC and trained to run an alley for a single daily infusion of cocaine (12.5 µg - 50µg / 0.5 µl per side). Control animals received an infusion of cerebrospinal fluid (0.5µl per side) upon goalbox entry. Cocaine infusions administered into the NA shell resulted in increased levels of retreats compared to controls, while intra-mPFC cocaine failed to produce retreat behaviors over trials. Furthermore, animals running for mPFC cocaine showed a reliable decrease in run times across trials compared to controls. These results support the idea that the NA shell region is involved in mediating both the reinforcing and the anxiogenic

properties of cocaine, while the mPFC region is involved primarily in the reinforcing properties of cocaine. Supported by NIDA grant DA05041 awarded to AE.

EXAGGERATED EMOTIONAL RESPONSES FOLLOWING WITHDRAWAL FROM HYPNOTIC-SEDATIVE DRUGS OR STRESS ARE ASSOCIATED WITH THE LACK OF FEED-BACK INHIBITION ON RAT BASOLATERAL AMYGDALA. Isoardi, N.A.[1]; Rodríguez Manzanares, P.A.[1]; Bertotto, M.E.1, Martijena, I.D.[1]; Carrer, H.F.[2] and Molina, V.A[1]. [1]Departamento de Farmacología, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba.[2]Instituto de Investigación Médica M. y M. Ferreyra, INIMEC-CONICET. Córdoba, ARGENTINA. In this report we demonstrated that discontinuation from chronic ethanol (ETOH) and from diazepam (DZM) administration or previous exposure to an uncontrollable stressor facilitated the formation of a new fear memory. The infusion of bicuculline into the basolateral amygdala complex (BLA) induced the same behavioral effect. Using extracelullar recording methods, we demostrated that withdrawn or stressed animals show increased neuronal excitability and facilitated LTP in the BLA. Pretreatment with midazolam prevented both the facilitating influence of stress on fear memory and synaptic excitability in the BLA. Inhibitory postsynaptic potentials (IPSPs), were studied in pyramidal neurons from BLA, using whole cell patch-clamp. In control animals, a small picrotoxin-sensitive IPSP was evoked by sub threshold stimulation of EC. When an action potential (AP) was evoked by supra threshold stimuli, the IPSPs were considerably larger. On the other hand, in DZM or ETOH withdrawn and in stressed rats IPSPs were significantly reduced. Firing of an AP by a depolarizing pulse applied through the patch pipette consistently evoked a glutamatergic antagonists-sensitive inhibitory postsynaptic current (IPSCs) of control animals. In contrast, in slices from BDZ or ETOH withdrawn or stressed animals, IPSCs were greatly decreased. It is concluded that a history of severe stress or withdrawal to hypnotic-sedative drugs results in the suppression of feed-back inhibition in BLA projection neurons, which represents an essential mechanism underlying the emergence of a negative emotional state, including exaggerated fear and anxiety.

ESCALATION OF MORPHINE SELF-ADMINISTRATION IS ATTENUATED IN PERIADOLESCENT MALE RATS Doherty JM, Ogbonmwan Y, Li C, Waldron N, Moffett AE, Williams BF, Frantz KJ. Department of Biology, and the Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA, 30302. Despite steady levels of opiate drug abuse among human adolescents, few laboratory experiments address adolescent vulnerability to opiate drugs using animal models. To help understand the transition from recreational or controlled drug use to compulsive or escalated drug abuse during adolescence, we used the escalation paradigm to compare intravenous morphine self-administration in short (1 hr) vs. long (8 hr) daily access conditions in both periadolescent (PND 35-63) and adult (PND 91-119) male Sprague-Dawley rats. Subjects were allowed to acquire lever-pressing maintained by morphine infusions (0.6 mg/kg/infusion) on a fixed ratio 1 (FR1) schedule of reinforcement during daily 1 hr sessions over six days. Subjects were then assigned to either short- or long-access conditions for 18 days of escalation testing. Periadolescent rats took less morphine than adults in the first six days and throughout the short-access conditions, confirming previous results from this laboratory. Under long-access conditions, periadolescent rats displayed attenuated escalation of morphine intake compared to adults. These results suggest that adolescent male rats are less vulnerable to escalation of morphine intake, or they develop less tolerance to morphine. Follow-up analyses of extinction and reinstatement of drug-seeking behavior are in progress.

EXPLORING THE INFLUENCE OF REWARD ON SICKNESS AND IMMUNITY IN THE FEMALE RAT. Kentner, A.C.; Takeuchi, A.; Miki, T.; James, J.; Seino, S.; Bielajew, C. School of Psychology. University of Ottawa, Ottawa Canada and Graduate School of Medicine. Kobe University, Kobe Japan. Brain stimulation reward has been employed as a tool for tracking hedonic status in animals. It has been shown to elevate peripheral natural killer cell activity in rats receiving either lateral hypothalamus or ventral tegmental stimulation. Discerning the mechanisms underlying this relationship has great implications for understanding the relationship between reward and immune activation. In this study, we examined whether the severity of endotoxin-induced sickness behaviours was tied to reward condition (ventral tegmental area stimulation versus environmental enrichment, or control conditions) in female Sprague-Dawley rats. Animals remained in their respective conditions for two weeks, at which point each rat was challenged with a 150 ul/kg i.p. injection of lipopolysaccharide. Tail blood was collected for PCR analysis and sickness behaviours (piloerection, ptosis, lethargy, sleep) were observed. Animals were then returned to their respective conditions for an additional two weeks at which point the above procedures were repeated. Using the real-time RT-PCR technique, we determined the peripheral mRNA expression of several cytokines and their receptors in order to distinguish how these levels change within animals over time, as a consequence of reward, as well as contribute to overall sickness severity. Brain stimulation reward and environmental enrichment appeared to have modulating effects on immunity as determined by the diminished sickness behaviours observed in these rats

compared to the control group. In addition, the cytokine profile observed showed considerable between-group variation at the second blood collection time point, particularly in environmentally enriched animals, whereas the receptors remained relatively stable between groups. Together, these data indicate that the experience of reward influences immune activity.

THE EFFECTS OF SINGLE AND MULTIPLE MONOAMINE TRANSPORTER GENE DELETION ON COCAINE-INDUCED CONDITIONED TASTE AVERSION J.D. Jones[1´2], F.S. Hall[2] G.R. Uhl[2] and A.L. Riley[1], American University[1], Washington DC 20016 USA. National Institute on Drug Abuse/IRP, NIH/DHHS[2], Baltimore, MD, 21224 USA Cocaine nonselectively prevents the reuptake of monoamine (MA) neurotransmitters through blockade of their neuronal plasma membrane transporters. It is commonly accepted that dopamine transporter inhibition is the property of cocaine most associated with reward/reinforcement; and while studies have shown that cocaine has both rewarding and aversive effects, the molecular basis of these aversive effects remains poorly understood. Neither norepinephrine nor serotonin selective transporter inhibitors have been found to engender reinforcing value, and knockout (KO) subjects lacking either of these transporters display enhanced cocaine place preference. These studies suggest that cocaine's actions at these transporters may be aversive and, therefore, antagonistic to its reward value. Using the conditioned taste aversion preparation, the present study attempted to characterize the effects of lifelong single and multiple monoamine transporter deletions on cocaine-induced conditioned taste aversions (CTA). Initially, DAT, SERT and NET KO mice were given access to saccharin and then injected with one of four doses of cocaine (0, 18, 32 or 50 mg/kg). The elimination of any single monoamine transporter did not significantly disrupt cocaine CTA, although a slight attenuation was found in single NET KO subjects. Mice with multiple transporter deletions, particularly the DAT/SERT and NET/SERT double KOs, displayed a more significant attenuation. These findings suggest that cocaine's actions at multiple transporters may underlie its aversive effects or in response to lifelong elimination of a single transporter, significant neuroadaption occurs allowing for the maintenance of cocaine CTA via mechanism's involving other transporters than normally mediate its aversive effects.

Learning and Memory

NEUROGENESIS IN THE MEDIAL PREOPTIC AREA (MPOA), AFTER THE ADMINISTRATION OF AN AROMATASE INHIBITOR OR AN ANDROGEN RECEPTOR ANTAGONIST.Medina JP; Dominguez Salazar E; Paredes R.Dept.de Nurobiologia Conductual y Cognitiva. INB-UNAM, Mexico. During a critical perinatal period, androgens and their estrogenic methabolites act on the central nervous system by permanently altering its structure and function. During this period, the neuronal pathways for sexual behavior, partner and olfactory preferences, are established. In the present study, we meassured the neurogenesis of the Medial Preoptic Area (MPOA) in normal conditions, and by modifying the hormonal patal envoirment, using flutamide (an androgen receptor blocker) or ATD (an aromatase inhibitor, blocks conversion of testosterone to estradiol). The flutamide tratment was administrated by a subcutaneus injection to a pregnant rat with proenilglicol:ethanol (9:1) twice a day (9:00-10:00 and 20:00-21:00 hrs) in a 10mg/kg dosis, and ATD was administrated by a subcutaneus implant of a silastic capsule. Both treatments were administrated from embrionic day (E) 12 to the birth of the animals.The pregnant rats were subcutaneus inyected with BrdU (25 mg BrdU body weight in 1ml of NaCl 9%) from E12 to E14. After 3 months of birth, the rats were intracardially perfused, and 10 brains from each treatment (5 males and 5 females from each litter) were cut at the level of preoptic area (POA) in coronal sections (35 ¦Ìm thick). The tissue was treated with standarised inmunohistochimestry for BrdU to identify newly generated cells in the MPOA. Labeled sections were analized by a image-analysis softwere Image-Pro Plus 5.1. In normal conditions, female rats had a statisaclly grater amount of positive BrdU labeled neurons in comparison with males. Both treatments (flutamide and ATD) significantly modified the number of positive BrdU labeled cells, but only male rats treated with flutamide show a cell number which is statistically equal to control females, sugesting a significant feminzation in the males MPOA.

LEVELS OF NORADRENALINE IN THE INSULAR CORTEX DURING NOVEL AND AVERSIVE TASTE MEMORY FORMATION. Miranda M.I.; Romero M.; Reyes-López J. Instituto de Neurobiología, Universidad Nacional Autónoma de México,Querétaro 76230, México. Insular cortex (IC) plays an important role during taste memory formation, such as conditioned taste aversion (CTA). The IC contains adrenergic neuronal terminals and adrenoreceptors through which noradrenaline (NA) might affect the strength of the associations between the taste and the circumstances in which it was found. The aim of this work was to elucidate whether NA release in the IC is involved during CTA formation and its retrieval; and also evaluate if NA release is involved during novel and

familiar non-aversive taste memory recognition. Free-moving microdialysis (MD) was conducted in rats implanted with a MD cannula directed to the right IC. Rats were habituated to drink water in the MD chamber for six days. During the MD sampling day, flow dialysates were collected every 15 min and then analysis by HPLC; eight samples were collected before the taste consumption through sample 9, and after 2 hours (eight more samples) they received i.p. injections based on groups: a) water and i.p. NaCl isotonic injections, b) novel saccharine, c) novel saccharine and LiCl injections, d) familiar non-aversive saccharin and e) familiar aversive saccharine. We found an increase in NA release during novel saccharin consumption and also after LiCl injections, but no significant changes during water and saline injections. Interestingly, aversive saccharin induced a significant NA release 30 min after consumption. Taken together, these results indicate that NA activity in the IC is induced during novel and familiar taste recognition, but there is a different timing release, depending on the aversive degree of the taste stimulus. Support by: IN219605-03 and CONACyT 46161M and 46754Q.

ENVIRONMENTAL ENRICHMENT PREVENTS OBJECT RECOGNITION MEMORY DEFICIT CAUSED BY HYPOXIA ISCHEMIA. Nabinger, PM[1,2]; Orlandi Pereira, L[1]; Strapasson, ACP[1]; Netto, CA[1]. [1] Departamento de Bioquímica, UFRGS; [2] FFFCMPA; Brazil. Previous studies from our laboratory indicate that the environmental enrichment (EE) prevents the memory deficit caused by neonatal hypoxia ischemia (HI) as measured in adult rats, without affecting hippocampal atrophy. The purpose of the present work is to evaluate whether EE effects also occur in adolescent HI rats, by the use of object recognition test and the measurement of striatal area. Male and female Wistar rats were used divided in four experimental groups: Control, standard environmental (CTSE, n=20); CTEE (n=21); HISE (n=17) and HIEE (n=19). The neonates were submitted, at postnatal day 7, to permanent occlusion of the right common carotid artery (ischemia); after, they were exposed to hypoxic atmosphere (90 min; 8%-O_2; 92%-N_2). From 8^{th} to 30^{th} postnatal days, litters were maintained in the enriched environment. The HI caused recognition memory impairment, as HISE exhibited smaller time of new object exploration in comparison with CTSE group; conversely HIEE performance was better than that of HISE and equal to both CTSE and CTEE groups. HI also caused striatal atrophy (as measured by structure area at level 1.00 mm from bregma in the Paxinos and Watson Atlas) which was not recovered by the EE. We conclude that environmental enrichment exerted a protective cognitive effect against hypoxia ischemia memory impairment, without affecting striatum damage. (CNPq)

SPATIAL MEMORY IMPAIRMENTS CONSEQUENT TO NEONATAL HYPOXIA-ISCHEMIA ARE PREVENTED BY ENVIRONMENTAL ENRICHMENT HOUSING. 1Orlandi Pereira, L; 1,2Nabinger, PM; 1Strapasson, ACP; 1Netto, CA. 1 Departamento de Bioquímica, UFRGS; 2 FFFCM de Porto Alegre; Brazil. Environmental enrichment (EE) has been investigated as one experimental strategy to recover from cognitive deficits consequent to ischemic events; our previous results indicate that male rats submitted to hypoxia-ischemia (HI) were protected against spatial memory deficits, although with maintained hippocampal (HC) atrophy, after 9 weeks of daily EE. The aim of present study was to evaluate the consequences of early EE housing in female HI rats in the adolescence and adult period, both on spatial memory and HC damage. Groups were: CTSE, controls maintained in standard environment; CTEE; HISE and HIEE. Wistar female rats, at the 7th PND, received neonatal HI (permanent occlusion of the right common carotid artery and a 90min period of hypoxia; 8%O2–92%N2). As from the next day, animals were housed in the EE until 30th PND. Water maze protocols (reference and working memory) were started two days after and at 90th PND. HI adolescent rats had greater latencies to find the platform than CT rats and the EE effect was verified only in the CTEE group; in the working memory test, HI had also greater latencies than CT groups and the HIEE had smaller latencies than HISE group. Experiments in the adults demonstrated similar results. HC volume was measured after the behavioral study; HI groups presented right HC atrophy and EE showed no effect on this variable. Concluding, enriched housing conditions results in improved spatial memory in adult and adolescent rats previously submitted to neonatal HI, with no effect upon HC atrophy. (CNPq)

INTERACTION OF ANGIOTENSINERGIC,SEROTONERGIC SYSTEM AND K-ATP CHANNEL ON WATER INTAKE BEHAVIOR IN ADULT MALE WISTAR RATS. Oryan,S;Alemi,S;Ebrahimi,A.Dept. of Biology,Tarbiat Moalem University.Tehran.Iran. Angiotensin II is highly effective as dipsogenic stimuli in rats.In this study,the interaction of icv injection of 5HT,K-ATP ch. and AngII systems in water intake was investigated.Fluxetine,5HT2 rec.,Agonist (10µg/rat),Glibenclamide,K-ATP ch.blocker(0.5,1µg/rat), increased,while LOsartan,AngII antagonist(45µg/rat),Risperidone,5HT2 rec. antagonist(4,8µg/rat),Diazoxide,K-ATP ch. opener(5µg/rat),decreased water intake in isolated and water deprived rats.Stimulation of water intake by Fluxetine and Glibenclamide attenuate the inhibitory effect of Losartan,while treatment with Risperidone and Diazoxide decreased the inhibitorial response of Losartane.Therefore,AngII,5HT systems and K-ATP channels have a close interaction in water intake

mechanisms.

HIPPOCAMPUS, NEURONAL NITRIC OXIDE SYNTHASE AND SPATIAL LEARNING IN PIGEONS. Ferrari, EAM1; Silva, M.I.1; Canova, F. 1; Langone, F. 1; Toledo, CAB2. 1Departamento de Fisiologia e Biofísica, IB, UNICAMP, Campinas 13083-970, SP, Brasil; 2Laboratório de Neurociências, UNICID, São Paulo, SP, Brasil. The nitric oxide (NO) is a molecule that acts as neural messenger regulating neuronal plasticity in the hippocampus, amygdala and cerebellum. NO is synthesized by activation of different isoforms of nitric oxide synthases (NOS). The neuronal nitric oxide synthase (nNOS) has been implicated in synaptic plasticity and learning in rats although changes of nNOS-positive neurons after learning are not yet clear. Additionally, NOS immunoreactivity (IR) has been scarcely described in the avian brain. The present study examined the nNOS-IR in cells of the hippocampus of pigeons trained in a food location task. Training was conducted in one (EXP1) or five (EXP5) sessions or one (CONT1) or five sessions (CONT5) of exposure to the arena. Daily sessions with six trials were conducted in one circular arena containing 4 food cups, one of which had food. Latency and accuracy of choice were recorded. After behavioral tests, nNOS immunoreactivity in hippocampal cells was analyzed. EXP5 birds showed reduction in latency of choice ($F_{4,28}=23.74$; $p<0.001$) and increases in correct choice ($F_{4,35}=8.66$; $p<0,001$) as function of the training. The expression of nNOS- positive cells was significantly higher in the dorsal hippocampus of EXP5 group as compared both with the ventral hippocampus ($F_{4,22}=104.79$; $p<0.001$)and the other groups ($F_{4,22}=10.17$; $p<0.001$). The data indicate that increases of nNOS- immunorreactive neurons in the hippocampus of pigeons were induced by learning. The dorsal hippocampus may have a key role as the site for nNOS mediated mechanisms of spatial choice in pigeons. Financial support: CAPES, CNPq, FAPESP

FOS-LIKE IMMUNOREACTIVITY IN THE RAT BRAIN ASSOCIATED WITH PLACE CONDITIONED AVERSION INDUCED BY INHIBITION OF GLUTAMIC ACID DECARBOXYLASE IN THE DORSAL PERIAQUEDUCTAL GRAY. Zanoveli, J.M.; Ferreira-Netto, C.; Brandao, M.L. Laboratorio de Psicobiologia, FFCLRP-Universidade de São Paulo, Ribeirao Preto-SP. Previous studies have described Fos distribution in the rat brain following freezing and escape responses induced by chemical stimulation of the dorsal periaqueductal gray (dPAG). However, little is known about the neural substrate activated in conditioned fear responses induced by dPAG stimulation. To investigate further this issue, rats were submitted to a place conditioned aversion (PCA) test. The behavioral testing apparatus was a circular open field consisting of four uniform quadrants that were equally preferred by the rats prior to drug treatments. For conditioning, rats were placed into a given quadrant and were chemically stimulated in the dPAG with semicarbazide (SCB, 5 µg/0.2 µL) – a glutamic acid decarboxylase inhibitor - on two consecutive days. On the test day, animals were placed again in the open field and the time spent in each quadrant was recorded. After 2 h, the brains were processed for detection of Fos-protein in fear/ anxiety-related brain regions. Our results showed that SCB injections into the dPAG produced PCA effects, with reduced time spent in the drug-paired quadrant on the testing day. The PCA was associated with an increase in Fos-labeling in the laterodorsal nucleus of the thalamus (LD), dorsomedial PAG, dorsolateral PAG and in the basolateral nucleus of the amygdale (BLA). Our results suggest that dPAG neurons participate of the mediation of fear conditioned response. The present data also suggest that PCA, elicited with the involvement of the dPAG stimulation as unconditioned stimulus, activates structures that are involved in the sensory processing of aversive information, such as LD and BLA. Financial Support: FAPESP.

EFFECT OF EMOTIONAL CONTENT ON EXPLICIT MEMORY: A STUDY CONDUCTED ON MIGRAINE HEADACHE PATIENTS Gasbarri, A.1; Arnone, B.1; Pompili, A.1; Pacitti, C.1; Di Fabrizio, P.1; Marini, C.2; Tavares,M.C.3, Tomaz, C.3. 1Dept. of Sciences and Biomedical Technologies, University of L'Aquila, Italy 2Dept. of Internal Medicine, University of L'Aquila, Italy 3Lab. of Neurosciences and Behavior, University of Brasilia, CEP 70910-900 Brasilia, DF, Brazil Many studies suggest that emotional arousal improves memory storage. The aim of this study was to evaluate the effects of emotional content on explicit memory in cephalalgic patients. We utilized an adaptation of two versions of the same story, with different arousing properties (neutral or emotional), which have been already employed in experiments involving the enhancing effects of emotions on memory retention. Subjects of the present study were healthy subjects and cephalalgic patients, suffering from migraine headache, which included untreated migraineurs and migraineurs treated with the antidepressant amitriptyline. The findings of our experiments suggest that chronic migraine is related to memory impairment. Taking into account that migraine is associated with major depression, in the present research the effect of the antidepressant amitriptyline was also evaluated. Our results showed that amitriptyline has an impairment effect on memory. Infact, the untreated migraineurs recalled the most emotional phase of the arousal story significantly better compared to migraineurs treated with amitriptyline. Then, our data suggest that amitriptyline prevents the enhancing effects of emotional

content on memory processes. Moreover, in agreement with our previous data, this study suggests the existence of gender differences in the processing of emotional stimuli and underscores the view that the gender influences should be considered in future studies on neural correlates of emotion, and on the relation of emotion to memory.

EFFECTS OF ANISOMYCIN INFUSIONS INTO INSULAR CORTEX ON MEMORY CONSOLIDATION OF INHIBITORY AVOIDANCE. Huchín-Ramírez, T.C.; Quirarte, G.L.; Medina, A.C.; Prado–Alcalá, R.A. Instituto de Neurobiología, Universidad Nacional Autónoma de México, Querétaro, Qro., México, 76230. The insular cortex (IC) participates in memory of gustatory and olfactory stimuli, and some data suggest that it is also engaged in other types of learning. The aim of this work was to determine the effects of protein synthesis inhibition within IC on memory consolidation of avoidance learning. Male Wistar rats were trained in a one-trial step-through inhibitory avoidance task and received a bilateral microinjection of anisomycin (15, 30 or 60 µg/0.5 µl) or its vehicle into IC, immediately after training; retention of the task was measured 48 h later. Anisomycin produced an amnesic effect which was inversely related to the dose of this drug. These results indicate that IC is sensitive to protein synthesis inhibition and support the hypothesis that this cerebral region participates in memory consolidation of inhibitory avoidance learning. We thank Ángel Méndez, Norma Serafín, Omar González and MVZ Martín García for their excellent technical assistance. Supported by PAPIIT-UNAM (IN208803) and CONACYT (46754Q).

PHYSOSTIGMINE MITIGATES SPATIAL MEMORY LOSS DURING HYPOBARIC HYPOXIA THROUGH CHOLINERGIC SYSTEM S.Muthuraju, Shashi B.Singh, P. Maiti, Alpesh , Amitabh, G.Ilavazhagan , P.K.Baneerjee. Defence Institute of Physiology and Allied Sciences, Delhi, INDIA. ABSTRACT: Hypobaric hypoxia is known to cause memory dysfunctions. The present study was aimed at investigating the neuroprotective effects of physostigmine, a potent acetylcholinestrase inhibitor, against the hypobaric hypoxia induced cognitive and memory dysfunctions. Rats were trained in Morris Water Maze for 8 days after which they were exposed to hypobaric hypoxia (6100m) for 7 days. The performance in MWM (escape latency and path length) was recorded after exposure to evaluate the memory dysfunction. The rats were then decapitated and the cortex and hippocampus were isolated for biochemical estimation of Ach and AChE activity. The expression for AChE, ChAT, á7nAChR and M1mAChR in cortex and hippocampus was studied by Immunohistochemistry, PCR and Western blotting. When compared with control group, rats exposed to hypobaric hypoxia displayed severe spatial memory deficits accompanied with significant reduction in ACh levels and increased AChE levels in cortex and hippocampus. The rats exposed to hypobaric hypoxia exhibited transcriptional and translational upregulation for AChE in cortex and hippocampus when compared to control rats. There was significant transcriptional and translational downregulation of cholinergic markers in cortex and hippocampus in rats exposed to hypobaric hypoxia as compared to control. Physostigmine treatment (0.5mg/kgBW) resulted in significant improvement in ACh levels and reduction in AChE level leading to spatial memory improvement along with increase in the expression of ChAT, á7nAChR and M1mAChR at both transcriptional and translational levels. Thus chronic hypobaric hypoxia induced loss of cholinergic markers was associated with cognitive deficits and physostigmine treatment ameliorated these effects by augmenting the cholinergic transmission in the brain. Physostigmine therefore exhibits therapeutic potential for the treatment of memory loss occurring in hypobaric hypoxia.

EMOTIONAL AROUSAL ENHANCES DECLARATIVE MEMORY IN ALZHEIMER'S DISEASE. Satler, C.[1]; Martinez Garrido, L.[3]; Prada Sarmiento, E.[3]; Leme, S.[1]; Conde, C.[2]; Tomaz, C.[1] 1. Laboratory of Neurosciences and Behavior, University of Brasília, CEP Brasília DF 70910-900, Brazil. 2. Grupo de Neurociencias y Comportamiento UIS-UPB, Universidad Industrial de Santander. A.A. 678, Bucaramanga, Colombia. 3. Grupo de Neurociencias y Comportamiento UIS-UPB, Universidad Pontificia Bolivariana, A.A. 2932, Bucaramanga, Colombia. Emotional arousal and valence of stimuli enhance declarative memory storage. This study aimed to verify whether the long-term retention of an emotionally arousing story is stronger than the retention of a neutral story, and the enhancing effects of emotional arousal on declarative memory in Alzheimer's disease patients. Subjects and Methods: Twenty subjects, ten with Alzheimer's disease and ten normal elderly controls, matched for age and educational level, attended to a slide presentation with neutral content. Subjective arousal levels were registered and the declarative memory was assessed by a multiple-choice questionnaire about the stories. Two weeks later, they watched the same slides with an emotional arousing narrative, repeating the same procedure. Results: Subjects when watched the emotionally arousing story assigned a score of emotionality higher than in the neutral version ($p = 0.023$). In addition, the participants remembered more details of the arousing story, and had a higher score in the questionnaire ($p < 0.001$). Conclusion: These results show that an emotionally arousing content enhances long term declarative memory in Alzheimer's disease. Furthermore, present finding supports the use of this instrument for clinical and research purposes. Financial Support: a Fellowship from Universidade de Brasília CAPES/PROF to the first author.

EFFECTS OF GABAERGIC TRNSMISSION IN THE DENTATE GYRUS ON ACQUISITION, CONSOLIDATION AND RETRIEVAL OF PASSIVE AVOIDANCE LEARNING AND MEMORY TASK IN RAT. Shahidi S.; Komaki A.; Nourbakhshnia M.; Akbari Mani M.; Shooshtari R. Department of Physiology, Hamedan University of Medical Sciences, Hamedan, Iran. The hippocampal GABAergic interneurons are responsible for controlling the output and efficacy of synaptic input of large principal cell populations and, thereby, determine the oscillatory discharge patterns and synaptic plasticity in the hippocampus. Oscillations within and across neuronal systems serve various complex functions, such as perception, cognition, plasticity and memory. The aim of this study is to define the physiology of GABAergic synaptic transmission in the dentate gyrus of hippocampus on the different stages of passive avoidance learning and memory in rat. Rats carrying chronically implanted cannulae aimed above the hippocampal dentate gyrus (DG). Then, they were trained on a step-through passive avoidance (PA) task and received intra- DG injection of Picrotoxin or saline before training, after training or before retrieval test. The results show that post training injection of picrotoxin impaired the PA. On the other hands, pre training and pre retrieval injection of picrotoxin had no significant effects on PA activity. Therefore it seems that dentate gyrus inhibitory interneurons are active in the consolidation step of PAL and may control the output to the principal cells. It is possible they are not active in the acquisition and retention steps of PAL.

AMNESIC ACTION OF UROCORTIN 3 IN PASSIVE AVOIDANCE LEARNING IN MICE. INVOLVEMENT OF NEURO-TRANSMITTERS.Telegdy G.; Adamik A. Dept. Pathophysiology, University of Szeged Szeged, Hungary The action of urocortin 3 on one-way passive avoidance learning was studied in male mice. The possible involvement of various neurotransmitters in mediating the action of urocortin 3 on consolidation of memory was followed by pretreating the animals with different receptor antagonists. The urocortin 3 was administered into the lateral brain ventricle and the latency of the passive avoidance response was measured 24 h later. The urocortin 3 attenuated the consolidation of passive avoidance response. Thus elicited an amnesic action. The following receptor antagonists blocked the action of urocortin 3 on consolidation: Astressin 2B (by blocking the CRF2 receptor) atropine, haloperidol, phenoxybenzamine, propranolol. Bicuculline attenuated but didnot fully block the action of urocortin 3, while antalarmin, a CRF1 receptor antagonist, was ineffective. The results obtained demonstrate that urocostin 3 attenuates the consolidation in a passive avoidance learning in mice. Muscarinic cholinergic, D2, alfa- and beta-adrenergic, CRF2 and patly GABA-B receptors are involved in the attenuation of the consolidation of the passive avoidance response. The involvement of CRF1 receptor can be excluded.

THE SONGSYSTEM OF SONGBIRDS: STRICTLY FOR THE SONG? Tokarev, K.I. (1); Tiunova, A.A. (2); Scharff, C. (1); and Anokhin, K.V. (2) (1) Free University Berlin, Department of Animal Behaviour, Faculty of Biology, Chemistry and Pharmacy, Takustr. 6, 14195 Berlin, Germany (2) P.K.Anokhin Research Institute of Normal Physiology, Mokhovaya 11/4, 125009 Moscow, Russia Certain structures in the forebrain of songbirds are highly specialized on learning, production and perception of conspecific songs. They are considered to be analogous to the regions of human brain specialized on speech, since both share rare trait for vocal learning which leads to formation of species-specific vocalization. Although these structures should have evolved from unspecialized brain regions of the ancestors, it remains unknown whether they may have other functions, i.e. whether their neurons can be involved in other behaviors. Passive avoidance, a one-trial learning model with aversive reinforcement, was chosen as a non-vocal model. We used expression of two immediateearly genes (IEG), ZENK and c-Fos, to determine brain regions involved in the studied behaviors. These genes are immediately induced in the adult brain in situations of novelty and learning. Perception of a novel conspecific song by adult male zebra finches results in the robust increase of ZENK expression in the auditory area NCM; it also encourages them to sing by themselves which in turn results in the enhancement of expression of both IEGs in two motor song nuclei, HVC and RA, and in area X, when the song is undirected. Colocalization of neurons with expression of these two IEGs for the first time is studied in our work. We also observed enhancement of c-Fos expression in song motor nuclei after one trial learning to avoid novel food of bitter taste. According to the expression of IEGs, the structures of the song system may be divided into three groups: 1) LMAN and area X, which probably are not active in non-vocal learning; 2) NCM, where the induction of transcriptional activity was rather due to acoustic stimulation even in the passive avoidance group; 3) HVC and RA, in which transcriptional activity is as well induced by non vocal learning, but in the different way than by singing.

AUTONOMIC AND BEHAVIORAL RESPONSES DURING ENCODING AND REMEMBERING OF EMOTIONALLY AROUSAL AUDIOVISUAL STIMULI. Uribe, C.[1,2]; Conde, C.[2]; Botelho, S.[3]; Tomaz, C.[1] 1. Laboratory of Neurosciences and Behavior, University of Brasília, 70910-900, Brazil. 2. Grupo de Neurociencias y Comportamiento UIS-UPB, Universidad Industrial de Santander. A.A. 678, Colombia. 3. Grupo de Neurociencias y Comportamiento UIS-UPB, Universidad Pontificia Bolivariana Bucaramanga, A.A. 2932, Colombia. Emotional arousal and valence of stimuli enhance declarative memory storage. In the present study their interactions with gender and their impact over behavioral and physiological measures during encoding, early consolidation and retrieval phases of audiovisual information were assessed. Subjects and Methods: Twenty-nine healthy volunteers attended to a slide presentation with either emotional arousing or neutral content. Subjective arousal levels and physiological responses were registered. Declarative memory was assessed by recognition questionnaire. Results: Emotional material induced higher levels of arousal, surprise, sadness and fear. Sadness was higher in women than men. The emotional content was better remembered than the neutral one. Emotional content induced higher heart rate (HR) and higher skin conductance level (SCL) during emotional value evaluation phase compared to encoding phase, and higher HR compared to its neutral content counterpart. Retrieval of emotional content produced higher HR and SCL compared to neutral content retrieval. Conclusion: These results show that early consolidation and retrieval of emotional information are accompanied by physiological responses that participate decisively in the memory enhancement phenomenon. Financial Support: COLCIENCIAS (1210-04-13002) - Universidad Industrial de Santander - Universidad Pontificia Bolivariana, and by a fellowship from Universidade de Brasília CAPES/PROF to the first author.

EVALUATION OF ATTENTION, LANGUAGE AND EMOTIONAL MEMORY IN LOBECTOMIZED PATIENTS. Botelho, S.; Acevedo, L.M.P.; Conde, C.; Franky, J.F.;Tomaz, C. Neuroscience and Behavior Laboratory. Universidad Pontificia Bolivariana, Santander, Colombia. Several studies have demonstrated that long-term declarative memory is enhanced by emotional arousal contents. Different works have evaluated the role of the temporal lobe on memory associated to emotional stimuli with an Audio-Visual Emotional Memory Test. Considering the emotional content in this test include verbally complex narrative, which demands participation and activation of temporo-mesial brain structures, the objective of the present study was to investigate performance in a special test for verbal comprehension - The Token Test -, in patients with unilateral temporal lobectomy. For this purpose, we evaluated a sample of 48 adult subjects (23 females and 25 males), divided in an experimental (n=16; unilateral lobectomized patients) and a control group (n=32-halthy volunteers). Each group was randomized to be tested under neutral or arousal version of Audio-Visual test. Results indicate that in contrast to control subjects, patients with temporal lobectomy did not show the mnemonic enhancement effect induced by arousal. Additionally, in spite of low performance, the majority of lobectomized patients, did not show any correlation between performance in the Token and the Audio- Visual Test. Taken together, the results highlight the importance of the medial temporal lobe integrity for the long-term enhancement of declarative memory associated with emotional content independently of talking and comprehension language.

WORKING MEMORY AND VARIABILITY OF REACTION TIME EVALUATED IN UNIVERSITY STUDENTS UNDER DIFERENTS STIMULI'S TIME EXPOSITION USING "MEMONUM" SOFTWARE. Albarracin A.P. and Conde C. Grupo de Neurociencias y Comportamiento UIS-UPB. Universidad Industrial de Santander, Bucaramanga, Colombia. Working memory has been widely studied by digits retention tests used in memory and intelligence scales 1,2,3,4,5. In diverse studies, young people can retain between 5 to 10 units of information (digits)2, when the protocol include around 1 second as stimuli's time exposition. Nevertheless, is considered that greater intervals of exposition can be strongly involve with processes like the maintenance of attention and modify the probability of reverberation of the information during the acquisition, with consequent changes in mnemonic performance6. The present work assessed the influence of stimuli's time exposition (1, 8 and 16 seconds) with or without visual interference, on mnemonic performance and on variability of reaction time responses. The "Memonum" was applied to 28 students from the "Universidad Industrial de Santander", each one, randomly, was exposed to all times of exposure, with and without visual interferences in 3 different days. In all cases, were measured the number of digits retained (ND) and more than 30 variables in the time dominium analysis from the time reaction to response each digitations. The results showed an increment of ND with time exposition of 8 and 16 seconds, compared with 1 second, but no difference were found between versions (with and without visual interference). The variability of time reaction shows differences between the experimental protocols, specially, the pNN0 (proportion of differences between consecutive intervals longer or shorter than zero). These variables were sensitive to the visual interference and to exposure time. Taking all, these results suggest that "Memonum" with the

variability analysis of the reaction time are a good tool to elaborate new inferences about the information processing associated to the working memory task.

TEMPORARY INACTIVATION REVEALS AN ESSENTIAL ROLE OF THE DORSAL HIPPOCAMPUS IN CONSOLIDATION OF OBJECT RECOGNITION MEMORY. de Lima, M.N.M.[1]; Luft, T.[2]; Roesler, R.[2,3]; Schröder, N[1]. - [1]Neurobiology and Developmental Biology Laboratory, Faculty of Biosciences, Pontifical Catholic University; [2]Department of Biochemistry, Institute for Basic Health Sciences, Federal University of Rio Grande do Sul; [3]Department of Pharmacology, Institute for Basic Health Sciences, Federal University of Rio Grande do Sul - Porto Alegre, RS, Brazil. Recognition memory is one of the most impaired types of memory in Alzheimer's disease, as well as in normal aging. It is well established that the dorsal hippocampus is a brain region crucially involved in formation of spatial and contextual memories. However, the role of the hippocampus in recognition memory remains controversial. The aim of the present study was to evaluate the effect of temporary inactivation of area CA1 of the hippocampus on consolidation of object recognition memory. Male Wistar rats were trained in a novel object recognition task. At different postraining delays (0, 3, or 6 h) animals received a bilateral infusion of vehicle or muscimol (5µg/µl) into the CA1 hippocampal area. Muscimol inactivation of the dorsal hippocampus immediately or 3 h, but not 6 h posttraining impaired 24 h retention of recognition memory. These results strongly indicate that the dorsal hippocampus is required for early and delayed consolidation of novel object recognition memory.

DISSOCIATION BETWEEN CORTICAL ACTIVATION AND COGNITIVE PERFORMANCE FOLLOWING PHARMACOLOGICAL BLOOD PRESSURE ELEVATION IN CHRONIC HYPOTENSION. Duschek, S.; Hadjamu, M.; Schandry, R. Dept. of Psychology. University of Munich, 80802 Munich, Germany. The present study explored the impact of pharmacological blood pressure elevation on cortical activation and reaction time in chronic hypotension. Effects of the sympathomimetic etilefrine were investigated in 50 hypotensive persons based on a randomized, placebo-controlled double blind design. As an indicator of cortical excitability, the contingent negative variation (CNV), induced by a constant foreperiod reaction time task, was assessed at frontal (F3, Fz, F4) and central (C3, Cz, C4) scalp sites. Etilefrine provoked a decrease in the frontal and central CNV. In contrast, shorter reaction times were observed following drug administration. The degree of pharmacologically induced blood pressure elevation was correlated to CNV attrition as well as to performance enhancement. Inhibitory effects of baroreceptor activation on cortical excitability and enhanced cerebral blood flow are considered to be involved in mediating the effects of blood pressure elevation on cerebral functioning. Implications for the treatment of chronic hypotension are discussed.

ENHANCEMENT OF DECLARATIVE MEMORY ASSOCIATED WITH EMOTIONAL CONTENT IN MAJOR DEPRESSION PATIENTS. Garcia RG.1,2; Zarruk JG.1; Arenas W.1; Reyes L.1; Ruiz S.1; López-Jaramillo P.1; Tomaz C.2. 1. Autonomic Physiology Laboratory, Fundación Cardiovascular de Colombia, Bucaramanga, Colombia. 2. Laboratory of Neurosciences and Behavior, University of Brasilia, Brasilia, DF, Brazil. A great body of evidence has indicated that subjects with major depression (MD) have a pronounced bias to recall depression-related memories. The aim of this study was to evaluate the effect of negative emotional content on declarative memory of MD patients. Major Depression was diagnosed by a Structured Clinical Interview for DSM-IV criteria. We used a paradigm previously validated in Colombian population to evaluate the influence of emotion on long-term retention. A sample of 32 patients with MD watched a slide presentation of stories. A randomly assigned group watched a story with a negative-valenced content and another group watched a neutral-valenced story. The stories were matched for structure and comprehensibility and the set and order of the 11 slides were the same in both conditions. According to previous findings, the arousing story was divided into 3 phases, being the second phase (slides 5-8) the most emotional of the story. After the slide presentation, the MD patients were asked to rate the emotionality of the narrative. The negative-valenced story was rated as being more emotional than the neutral one ($p=0.0002$). Three days later, it was applied a multiple-choice questionnaire of recognition memory. The patients who watched the negative-valenced story had higher scores in the questions related with the second phase of the story ($p=0.003$). Our results confirm that a negative-valenced content enhances long-term declarative memory in MD patients and provides an explanation for the maintenance of mood disturbances in these subjects. Financial Support: CNPq, COLCIENCIAS (project N. 6566-04-16494)

CARDIOVASCULAR AUTONOMIC FUNCTION IN RESPONSE TO PSYCHOLOGICAL STRESS TESTS IN MAJOR DEPRESSION PATIENTS. García, R.G.1,2;Zarruk,J.G.1;Barrera,C.2; Trillos,E.2;Quintero,D.2;Lopez-Jaramillo,P.1;Tomáz, C.3. 1.Autonomic Physiology Laboratory – Fundación Cardiovascular de Colombia. 2.Mental Health Department – Universidad Industrial de Santander, Bucaramanga, Colombia. 3.Laboratory of Neurosciences and Behavior – University of Brasilia, Brasilia DF, Brazil. An association between an impaired Cardiovascular Autonomic Function (CAF) and depressive mood has been suggested in subjects with cardiovascular disease; however, the results of different studies in healthy depressive patients are contradictory. The aim of this study was to evaluate the CAF of patients with Major Depression (MD) and Healthy Controls (HC) in response to psychological stress tests. Major Depression was diagnosed by a Structured Clinical Interview for DSM-IV diagnostic criteria. Patients with cardiovascular risk factors, and anxiety diagnosis or a mood disorder different from MD were excluded. Speech and Stroop tests were applied, and the CAF function was evaluated during these tests. Continuous Blood Pressure (BP) and DII ECG signal were registered using a Finometer (Finapress Medical System, The Netherlands). Data were digitized and stored using a signal acquisition system DATAQ 720-WINDAQ PRO (DataQ Instruments, Akron, OH, USA) and winCPRS (Absolutely Aliens, Finland) for all data analysis. 34 MD and 34 HC subjects paired by age, sex and scholar level were recruited. General characteristics were comparable between the groups. No significant differences were observed in the time-domain (RMSSD, pNN50) and frequency-domain (HF, LF, and HF/LF) analyses of the heart rate and blood pressure variability. This study didn't show significant differences in the CAF between MD patients and HC in response to psychological stress tests. Results of previous studies showing an impaired CAF in depressive patients could be related with the manifestations of cardiovascular diseases in the MD patients evaluated. Financial Support: CNPq, COLCIENCIAS (project N. 6566-04-16494)

DIFFERING EFFECTS OF ECS ON CONSOLIDATION OF TRACE VS. DELAY FEAR CONDITIONING. Glover, E.M.; Paschall, G.Y.; & Davis, M. Dept. of Psychology and Neuroscience Program. Emory University, Atlanta, GA 30329 USA. Post-training electroconvulsive shock treatment (ECS) blocks the consolidation of inhibitory avoidance learning (i.e., McGaugh & Dawson, 1971). However, some literature suggests that this effect of ECS is not wholly amnesic. When latency to enter a shock compartment is measured, a retention deficit is apparent. However, under the same conditions, animals show signs of retention when such responses as heart-rate suppression, urination, and defecation are measured (see Bueno et al., 1993; Chorover & Schiller, 1966; Hine & Paolino, 1970). We hypothesize that ECS disrupts hippocampal-dependent explicit fear memory, but not hippocampal-independent implicit fear memory. We tested the effect of post-training ECS treatment on two Pavlovian fear conditioning tasks that differ in hippocampal involvement. Rats (N=24) were presented with a single odor-shock pairing which either overlapped and co-terminated in time (delay fear conditioning – hippocampal independent) or was separated by a 15 s trace interval (trace fear conditioning – hippocampal dependent). Within 30 s after the shock, each rat was given a 0.5 s, 40 mA ECS. When tested 24 hrs later, trace conditioned rats showed significantly less startle to the odor CS than delay conditioned rats ($p < 0.05$). These findings suggest that ECS selectively disrupts hippocampal-dependent fear memories, but leaves hippocampal-independent fear memories intact.

BLOCKADE OF NMDA RECEPTORS IN ROSTRAL AND CAUDAL DORSOLATERAL PERIAQUEDUCTAL GRAY REVEAL DIFFERENT CONTRIBUTIONS TO THE INNATE AND TO THE CONTEXTUAL FEAR CONDITIONING. Souza, R.R.; Cavalli, J.; Carobrez, A.P.. Dept. Farmacologia, Universidade Federal de Santa Catarina, Florianopolis, SC, Brazil. Laboratory rats exposed to a cat odor stimulus show a strong increase in defensive behaviors. These responses may depend on brain structures related to emotional reaction as the midbrain periaqueductal gray (PAG). The PAG is organized in columnar groups that modulate different behavior and neurovegetative responses. The dorsolateral PAG (dlPAG) is frequently related to defensive responses and it seems to present anatomical and functional differences along its rostro-caudal axis. In the present study, we examined the participation of glutamatergic NMDA receptors in the rostral and the caudal dlPAG in the modulation of defensive behavior towards a cat odor stimulus and to the context, 24 h later. The administration of AP5 (6 nmol) only within the rostral dlPAG 10 minutes before the cat odor exposure, reduced the defensive behaviors and impaired the acquisition of a contextual increased avoidance. On the other hand, the contextual fear response was reduced by administration of AP5 (6 nmol) only within the caudal dlPAG 10 minutes before the context session. The results showed a distinct rostral and caudal dlPAG modulation of defensive reactions regarding innate and contextual fear, reinforcing the role of this structure in the modulation of the defensive behavior. Financial Support: CNPq, CAPES, FAPESP, FAPESC, PRONEX.

DORSAL PERIAQUEDUCTAL GRAY GLUTAMATERGIC MEDIATION OF THE DEFENSIVE BEHAVIOR OF RATS EVALUATED IN THE ELEVATED PLUS MAZE. Kincheski, G.C., Moraes, C.L.K., Carobrez, A.P. Dept. Farmacologia, CCB, Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil.The elevated plus-maze (EPM) has been frequently used as a tool to evaluate anxiety-related behavior. Maze-experienced rodents show pharmaco-resistance to anxiolytics and an increased open arm avoidance in a retest session. The dorsal periaqueductal gray matter (dPAG) is known to be involved in the modulation of defensive behavior in the EPM. The present study was outlined to study the role played by the dPAG in the performance of rats during the test and the retest in the EPM. For this purpose, male Wistar rats received microinjections (0.3 ¦Ìl) of PBS, NMDA and AP5 (NMDA-antagonist) at the caudal dPAG 10 min, prior to the test in the EPM. The results showed that during test session, an anxiogenic-like effect was obtained only with the low dose (25pmol) of NMDA used whereas an anxiolytic effect was detected with both AP5 doses (3 and 6 nmol). On the other hand during the retest session, rats pre-treated with the higher dose of NMDA (100 pmol), exhibited an impaired avoidance learning response in the EPM. In addition, subjects previously treated with PBS and receiving AP5 before the retest showed an anxiolytic-like effect in the EPM. These results suggest that dPAG activity under the influence of NMDA-receptors might underlie the acquisition and the expression of the defensive behavior in the test as well as interfere with the expression of avoidance learning displayed during the retest in the EPM. Financial Support: CNPq, CAPES, FAPESP, FAPESC, PRONEX

BRAIN LEVELS OF CELLULAR PRION PROTEIN AFFECT LEARNED AVERSION IN MICE. Lobão-Soares, B.1; ; 3 Calvo, F. 1; Martins, V.3, Bianchin MM 4; Walz, R.1,5 Coimbra N.C.1 1FMRP-USP; 3Ludwig Institute for Cancer Research; 4UFRGS; 5UFSC. Genetically modified mice were confronted with false-coral snakes (Oxyrophus guibei) in a quadrangular arena, and the defensive responses were recorded in the presence of the snakes and 24h after the prey/predator interaction, in the same apparatus without the predator. Strains of animals lacking the PrPc (KO), wild type animals (WT) and the transgenic (Tg-20) with 6 times greater PrPc levels in the brain than WT were studied (n= 10): first day snake-exposed groups (SE) and first day exposed to the context (AE), and control groups All data were submitted to ANOVA/Tukey´s tests ($p<0.05$). The intra-strain arena-exposed and snake-exposed mice comparisons revealed that WT snake-confronted group disclosed increased number of alertness and freezing, as well as an increased number ($p<0.01$) and duration of grooming behavior episodes compared to non- previously confronted WTs, indicating efficiency of this model. In turn, snake-confronted mice Tg-20 presented an increased duration of grooming behavior ($p<0.001$) when compared to controls ($p<0.05$). Snake-confronted knockout mice presented increase in the duration of freezing ($p<0.05$). The inter-strain comparisons among snake-confronted WT, PrnP 0/0 and Tg-20 groups also revealed significant differences related to aversive learning behaviours. Tg-20 mice disclosed a decrease in number of alertness and freezing, as well as in grooming duration ($p<0.001$, in all cases) compared to WT and in duration of grooming compared to Prnp0/0 ($p<0.05$). Prnp0/0 animals showed decrease in the frequency of defensive attention compared to WT mice ($p<0.05$). These findings suggest that alterations in brain levels of PrPC affect learned aversion in adult life. Support: FAPESP; FAPESC; CNPQ; CAPES.

OPERANT CONDITIONING IN ZEBRAFISH. Miller, N.Y.; Gerlai, R.G. Department of Psychology. University of Toronto, Toronto, Ontario, M5S 3G3, Canada. Research on conditioning in fish has lagged behind other species due to a lack of testing methods. According to our preliminary data zebrafish is capable of solving complex learning tasks and thus this species, a frequently utilized model organism in developmental biology and genetics, may be an excellent subject for the analysis of the mechanisms of vertebrate learning and memory as well. We present a novel computerized system (hardware and software) for testing both Pavlovian and operant conditioning in zebrafish. The apparatus is functionally similar to traditional operant boxes. It can be used to display any number of arbitrary stimuli in a variety of locations, and can deliver either food or a social stimulus as reinforcement. We also present an example, in which zebrafish were trained to discriminate between two different samples or locations (Matching-to-Sample). The apparatus and paradigm are highly amenable to automation and thus allow scaling up and high throughput screening. The development of a fully automated system will allow us to conduct conditioning in a large number of fish and then screen hundreds of mutagenized fish, ultimately leading to the identification of novel genes involved in associative learning.

Sensorimotor-Gating, Neurodegeneration and Dopamine-Related Behaviors

THE EFFICACY OF HALOPERIDOL IN RESTORING LATENT INHIBITON IN FEMALE RATS IS ESTROGEN DEPENDENT Arad M.; Weiner I. Dept. of Psychology. Tel-Aviv University, Israel. Elevated relapse rates and symptoms remission in schizophrenic women tend to correlate with low and high estrogen levels, respectively. Consequently, the estrogen hypothesis of schizophrenia postulates that estrogen is a neuroprotective factor delaying the onset of schizophrenia and reducing its severity in women. Latent inhibition (LI), the capacity to ignore stimuli that received nonreinforced preexposure prior to conditioning, is disrupted in acute schizophrenia patients and in rats and humans treated with the psychosis inducing drug amphetamine. Disruption of LI is reversible by typical and atypical antipsychotic drugs (APDs). Last year we reported that LI was disrupted in ovariectomized (OVX) rats and could be restored by 17-ß estradiol (150 µg/kg) and the atypical APD clozapine (5 mg/kg), but was resistant to the typical APD haloperidol (0.1, 0.2, 0.3 mg/kg). Here we show that haloperidol is able to restore LI only when administered with 17-ß estradiol (50 µg/kg). Furthermore, under conditions that yield LI in both OVX and sham female rats, amphetamine disrupts LI in all rats, but restoration of LI by haloperidol in amphetamine-treated rats is observed only in sham rats. While resistance of disrupted LI to haloperidol in the absence of estrogen is in line with reduced efficacy of haloperidol in menopausal women, our results suggest that pro-psychotic action of dopamine (DA) releaser apparently does not require estrogen. This differential sensitivity of OVX rats to DA stimulation and DA blockade may have important implications for the clinical development of schizophrenia and APD treatment in women because it suggests that naturally occurring reduction in hormonal levels may increase the danger of relapse/ severity of symptoms while concomitantly reducing the efficacy of conventional treatment.

VISUAL SENSORY-MOTOR GATING BY SEROTONIN ACTIVATION IN THE MEDIAL PREFRONTAL CORTEX, BUT NOT IN THE RHINAL CORTICES Müller, C.P.; Pum, M.E.; Huston, J.P. Inst Physiol Psychol, Univ Düsseldorf, 40225 Düsseldorf, Germany. The behavioral response to sensory stimulation is a function of many variables. Sensory-motor gating, however, appears to be disrupted in various psychiatric disorders. In a behavioral study in well habituated rats we characterized the behavioral response elicited by a simple visual stimulus (white light, 0, 8, 22, 82, 155 or 440 lux) presented 10 times continuously for 30 s randomly distributed over a 20 min interval. Visual stimulation induced a significant dose-dependent and temporally restricted behavioral activation, most evident in rearing behavior and locomotion. In an in-vivo microdialysis study in freely moving rats we investigated potential neurochemical mechanisms by measuring extracellular serotonin (5-HT) and dopamine (DA) activity in the medial prefrontal cortex (mPFC), entorhinal cortex (EC) and perirhinal cortex (PRC), areas associated with the processing of highly elaborated visual information. Visual stimulation (0, 22 and 82 lux) caused a dose-dependent behavioral activation and selectively elevated the 5-HT, but not DA activity in the mPFC. An auditory control stimulus (white noise, 82 dB, 10 x for 30 s) did not affected behavior nor neurochemical activity in the mPFC. Neither stimulation affected 5-HT or DA in the EC or PRC. These data suggest that visual stimulation activates 5-HT activity in the mPFC, which might facilitate exploratory behavioral activity. However, if the selective 5-HT increase is cause or consequence of the behavioral activity needs to be clarified in further experiments (supported by grant HU 306/ 23-5 from the Deutsche Forschungsgemeinschaft).

HALOPERIDOL-INDUCED CATALEPSY CAN BE REVERSED BY MK-801 MICROINJECTED INTO THE INFERIOR COLLICULUS IN RATS. Melo, L..L. 1; Ferrari, E.A.M.2; Santos, P.1; Maisonette, S.S. 1 1Laboratório de Neuropsicofarmacologia, Universidade São Francisco, Av. São Francisco de Assis, 218, Jardim São José, Bragança Paulista – SP; 12916-900. 2Laboratório de Sistemas Neurais e Comportamento, DFB-IB, UNICAMP. The inferior colliculus (IC) is primarily involved in conveying auditory information to higher cortical structures. It has been shown that this structure may also be part of a brain system commanding defensive behavior. Much evidence suggests that the neural substrates responsible for defensive behavior in the IC can also be regulated by excitatory amino acids since microinjections of NMDA into this structure induce defensive behaviors, characterized by running, rearing, and jumping. It has been shown that stimulation of the neural substrates of fear in the IC causes a significant increase in the extracelular levels of dopamine (DA) in other structures such as frontal cortex. Linking these two pieces of information, this work examined whether the microinjection of the non-competitive NMDA receptor-channel blocker MK-801 into the IC is able to influence the catalepsy induced by systemic injections of the neuroleptic haloperidol. Each rat had a cannula implanted in the IC. The rats were injected with MK-801 (5 micrograms/0.5 microliter) or saline into the IC prior to systemic administration of haloperidol (1 mg/kg). Immediately after that they were placed in an open-field where three catalepsy evaluations were conducted during 10 minutes. Additionally the following behavioral items were recorded: crossing, running, rearing and jump. The

results showed that IC microinjection of MK-801 significantly reversed the catalepsy elicited by systemic injections of haloperidol. Based on these findings, it is suggested that mechanisms mediated by excitatory amino acids of the IC may play a role in the haloperidol-induced catalepsy.

ROLE OF SIGMA RECEPTORS IN L-DOPA-INDUCED DYSKINESIAS. Paquette, M.A.; Brudney, E.G.; Putterman, D.B.; Johnson, S.W.; & Berger, S.P. Laboratory of Translational Behavioral Neuroscience, Oregon Health & Science University and the VAMC, Portland, OR 97239. The NMDA antagonist dextromethorphan (DM) reduces L-dihydroxyphenylalanine (L-DOPA)-induced dyskinesias in animal models of Parkinson's Disease, as well as clinically. However, DM also has sigma binding activity. To investigate the roles of NMDA and sigma receptors in L-DOPA-induced dyskinesias, hemiparkinson rats received L-DOPA (7.5 mg/kg) daily until dyskinesias developed, then twice weekly to maintain their expression. The effects of DM (45 mg/kg), the NMDA antagonist MK-801 (0.1 mg/kg), the sigma agonist DHEA (25 mg/kg), or the sigma antagonist BMY-14802 (15 mg/kg) as adjuncts to L-DOPA were assessed using the Abnormal Involuntary Movement Scale (AIMS) and the vibrissae-stimulated forelimb placing test. As expected, DM reduced dyskinesia severity. However, MK-801 failed to affect dyskinesias. DHEA also had no effect, but BMY-14802 reduced dyskinesias even more effectively than DM. Furthermore, antagonism of NMDA, but not sigma sites, caused impairment in the vibrissae-stimulated forelimb placing task. These data suggest that sigma, rather than NMDA receptors, may mediate LIDs and could serve as therapeutic targets. Furthermore, our data suggest that NMDA antagonists may be contra-indicated, as they may reduce L-DOPA-mediated improvement of function. Supported by the VA Merit Grant #07-1003.

THE EFFECTS OF THE 5-HT2A AGONIST DOI AND THE 5-HT2A INVERSE AGONIST AC90179 ON PREPULSE INHIBITION AND LOCOMOTOR ACTIVITY IN C57 MICE. Ruderman, M.A.; Powell, S.B.; Geyer, M.A. University of California, San Diego, La Jolla, CA. The link between naturally occurring and drug-induced hallucinations has led to the hypothesis that there may be a direct link between serotonin (5-HT) function and schizophrenia. The central role of 5-HT2A receptors in this link has been made because of the strong correlation between the hallucinogenic effects of drugs and their activation of 5-HT2A receptors. In addition, the relative 5-HT2A/D2 binding affinity of newer generation "atypical" antipsychotic drugs suggests that a primary mechanism of action for the therapeutic efficacy of these agents may be blockade of 5-HT2A receptors. As such, there has been an increased interest in the role of 5-HT2A receptors in the pathophysiology of schizophrenia and as targets for antipsychotic drugs. To further examine the role of 5-HT2A receptors in animal models related to schizophrenia, we conducted dose responses of DOI and AC90179 in C57BL/6 mice in two behavioral paradigms, prepulse inhibition (PPI) of startle and locomotor activity. DOI disrupted PPI in C57 mice, which was reversed by AC90179. AC90179 increased PPI on its own at lower doses, an effect which has been reported with several antipsychotics in mice. DOI increased locomotor activity and produced an interesting profile on investigatory behavior. DOI decreased rearing and produce an inverted U-shaped dose response function on holepoking behavior. AC90179 decreased locomotor activity at the highest dose tested and dose-dependently decreased holepokes. These studies in mice corroborate our findings in rats in which AC90179 reversed DOI-induced PPI deficits and allow us to assess the effects of DOI and AC90179 in 5-HT2A knockout mice on a C57BL/6 background.

NITRIC OXIDE MODULATION OF BASOLATERAL AMYGDALA DOPAMINERGIC-DISRUPTION OF PREPULSE INHIBITION. Salum, C.[1]; Issy, A.C.[1]; Brandão, M.L.[2]; Guimarães, F.S.[3]; Del Bel, E.A.[1] [1]Dept. Physiology-MEF-FORP; [2] Psychobiology-FFCLRP [3]Dept. Pharmacology-FMRP, University of São Paulo.We have shown that systemic injection of the nitric oxide (NO) inhibitor (L-NOARG) prevented the disruptive effect of amphetamine (Amph) on prepulse inhibition (PPI), a model used to assess deficits in sensorimotor gating. PPI refers to the attenuated amplitude of startle response (ASR) when the startling sound (pulse) is immediately preceded by a weaker acoustic stimulus (prepulse). Dopamine (DA) projection to the basolateral amygdala (BLA) is involved in brain processes that control different forms of information processing. Our aim was to investigate the nitrergic modulation of the disruptive effect of intra-BLA dopaminergic agonists in PPI. Bilateral intra-BLA (0,2 µl/min/side) infusion of Amph (30 µg), apomorphine (Apo, 10 µg) or quinpirole (3 µg) strongly disrupted PPI. The bilateral intra-BLA infusion of 50 nmol of L-NOARG did not affect PPI, but prevented the disruptive effect of Apo, when microinjected 5 min before Apo. None of these treatments significantly affected the ASR to pulse alone or to prepulse+pulse, although significant differences between these responses were found within the treatments with saline-saline, L-NOARG-saline and L-NOARG-Apo. These results suggest that NO may modulate the dopaminergic involvement of BLA in PPI. However, the mechanisms underlying the interactions between DA and NO still need elucidation.

ENHANCING CENTRAL NOREPINEPHRINE TRANSMISSION DISRUPTS PREPULSE INHIBITION: RESPECTIVE CONTRIBUTIONS OF THE LOCUS COERULEUS, MEDIAL PREFRONTAL CORTEX, AND NUCLEUS ACCUMBENS. Karen M. Alsene, Marcia J. Ramaker, Vaishali P. Bakshi Dept. of Psychiatry & Neuroscience Training Program, UW-Madison, Madison, WI USA. Prepulse inhibition (PPI) is the process in which a weak stimulus inhibits the magnitude of the startle response to a subsequent intense stimulus. PPI is a measure of sensorimotor gating, or the ability to filter information from the internal and external environment, and is deficient in several psychiatric illnesses, including schizophrenia. There is emerging evidence indicating that increasing central norepinephrine (NE) transmission disrupts PPI. Our lab recently found that stimulation of central á1 NE receptors disrupts PPI. In the present study, the roles of three different brain nuclei in NE-mediated disruptions in PPI were examined to determine the neuroanatomical circuitry mediating this effect. First, pharmacological stimulation of the locus coeruleus (LC), which is the primary source of NE to the forebrain, was found to decrease PPI; this effect was blocked by systemic administration of an á1 NE receptor antagonist. Second, microinfusion of NE receptor agonists into one of two different LC terminal regions, the medial prefrontal cortex and the nucleus accumbens, revealed that the nucleus accumbens shell, but not the medial prefrontal cortex, may mediate NE-induced PPI deficits. Taken together, these data strongly support an important role for the NE system in regulating sensorimotor gating and begins to identify the neural circuitry underlying this modulation. These finding may have important implications for psychiatric illnesses with sensorimotor gating deficits that are thought to involve dysfunction of the NE system.

NEUROPROTECTIVE EFFECTS OF PYRUVATE AND PIROXICAM IN ANIMALS TREATED WITH MPTP. Soliman, YI; Soliman KFA. College of Pharmacy and Pharmaceutical Sciences, Florida A&M University, Tallahassee, FL 32307 USA MPTP (1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine) is a prototypical toxin used to induce Parkinsonism in experimental animal models and is known to involve mitochondrial complex I inhibition, oxidative stress and robust gliosis with inflammation. In this study, neuroblastoma N2A cell line was used to investigate the neuroprotective effects of pyruvate and piroxicam. The results demonstrate that pyruvate is both an effective antioxidant and ergogenic fuel capable of sparing neuronal cell damage induced by reactive oxygen species, 6-hydroxydopamine MPP+. In addition, piroxicam (COX inhibitor) spared the loss of neuronal cell death induced by MPP+ without restoring mitochondrial oxidative function, where other selective COX inhibitors such as salicylic acid were without effect. In another study to examine the extent to which each of these compounds may prevent the loss of SN dopaminergic neurons induced by administration of MPTP in C57/b6 mice. The administration of pyruvate 150-mg/kg and piroxicam 20 mg/kg I.P, 3 days pre and post MPTP administration, were effective in reducing the loss of locomotive function, SN tyrosine hydroxylase concentration and attenuating the loss of dopamine. These data suggest that pyruvate which is a non-toxic food derived carboxylic acid may have therapeutic value in the treatment of PD. The data also support previous studies reporting COX inhibitors to attenuate MPTP toxicity in animal models. It was concluded from these study that pyruvate as well as piroxicam may be used in PD prevention and therapy. (Supported by NIH Grant RR03020)

QUALITATIVE CHANGES IN ULTRASONIC VOCALIZATIONS (USVS) OF THE RAT PARKINSON'S DISEASE MODEL AFTER UNILATERAL LEASION OR HALOPERIDOL. Ma, S.T.; Ciucci M; Fox C.; Kane J.R.; Ramig L.O.; Schallert T. Institute for Neuroscience. The University of Texas at Austin, Austin, TX, 78712 USA. The sensorimotor speech/voice deficits associated with Parkinson's Disease have been well-documented in humans. As described in clinical studies (Fox 2002), PD patients not only suffer deficits in limb motor function, the gradual loss of speech also impairs their ability to communicate. These symptoms include decreased vocal loudness, decreased frequency variability, hoarse voice quality, and imprecise articulation. They are largely resistant to pharmacological treatment. The mechanisms underlying this phenomenon are not well understood. We turned to the rat as a model. In rats, 50 kHz calls are elicited during positive affective situations, like courtship interaction with opposite sex, playing with cage mates, etc.(Burgdorf 2006). To gain insight into the postulated role of dopamine in human speech/voice, 50 kHz calls were selected for their wide frequency modulation features to help investigate qualitative changes as a model for sensorimotor phonatory control. We've analyzed changes in rat ultrasonic vocalization (USV) associated with unilateral infusion of the dopamine neurotoxin 6-OHDA and low doses of the dopamine antagonist haloperidol. Results have shown significant changes in bandwidth of the 50 kHz calls for both treatment groups.

SLEEP DEPRIVATION DISRUPTS SENSORIMOTOR GATING IN RATS IN AN ANTIPSYCHOTIC-SENSITIVE FASHION. Frau R.; Orrù M.; Mereu G.; Gessa G.L.; Marrosu F.; Bortolato M. Dept. of Cardiovascular and Neurological Science. University of Cagliari, Cagliari, Italy. Schizophrenic and manic patients exhibit a number of typical alterations in sleep continuity and architecture, such as severe insomnia and reductions in rapid eye movement (REM) latency and duration. Notably, clinical reports have documented that the degree of intensity of sleep alterations is highly correlated to the severity of psychotic symptoms, suggesting that sleep deprivation (SD) may precipitate the neurobiological dysfunctions underlying the cognitive and behavioral alterations in schizophrenia and bipolar disorder. Based on the hypothesis that both disorders are accompanied by remarkable alterations in sensorimotor gating, the present study was aimed at the assessment of the impact of SD on the behavioral model of prepulse inhibition of the startle (PPI), a reliable paradigm for the study of informational filtering. SD (for 24, 48 and 72 h) induced PPI deficits in a time-dependent fashion. Gating functions, however, were completely restored 24 h after the termination of SD. Interestingly, PPI disruption was completely reversed by the antipsychotic drugs haloperidol (0.1 mg/kg, i.p.) and clozapine (5 mg/kg, i.p.). Furthermore, nicotine (0.1-0.2 mg/kg, i.p.) dose-dependently attenuated PPI disruption. Notably, neither the anxiolytic diazepam (5 mg/kg, i.p.) nor the antidepressant citalopram (10 mg/kg, i.p.) produced significant effects on the PPI disruption mediated by SD. Our data suggest that SD might be a robust paradigm to model psychotic-like phenomena in animals, with high face, construct and predictive validity. Further studies are warranted to evaluate the impact of SD on the neurochemical and neuroendocrine substrates of PPI and gating functions.

TRYPTOPHANE-FREE DIET SENSITIZES RATS TO THE EFFECTS OF D-AMPHETAMINE IN RAT MODELS OF SCHIZOPHRENIA. Bortolato M.; Carta M.; Frau R.; Orrù M.; Mereu G.; Fadda F.; Stancampiano R. The serotonergic system plays a key role in the modulation of dopamine transmission, yet the pathophysiological significance of such role in schizophrenia is mostly elusive. Evidence shows that reductions in serotonergic signaling induced by pharmacological, surgical or neurotoxic manipulations, enhance the dopaminergic responses in animal models of psychosis. However, the invasiveness of these experimental approaches limit their ability to investigate the neurobiological relationships of dopamine and serotonin systems within a naturalistic framework, more likely to closely reproduce neuropathologic alterations. An intriguing alternative to reduce serotonin brain content is offered by the dietary restriction to its precursor, L-tryptophane (TRP). Thus, in the present study, we investigated the impact of a TRP-deficient diet in two rat models of schizophrenia, such as the hyperlocomotion and the reduction in prepulse inhibition of the startle (PPI) induced by d-amphetamine. After fourteen days of TRP-deficient diet, rats displayed a significant decrease in striatal levels of serotonin, but not dopamine. Furthermore, animals did not display significant spontaneous changes in either locomotor activity or PPI. However, TRP-deficient animals exhibited a significant sensitization to the effects of d-amphetamine (1.25-5 mg/kg, s.c.) in both paradigms. Such changes were completely prevented by pre-treatment with landmark typical and atypical antipsychotics, such as haloperidol (0.1 mg/kg, i.p.) and clozapine (5 mg/kg, i.p.), which are both known to elicit their therapeutic action through blockade of dopamine D2 receptors. The present results confirm and extend previous findings on the impact of serotonergic signaling in the modulation of dopamine transmission in schizophrenia and point to the tryptophane deprivation as a potential model of environmental manipulation that may produce a sensitization to psychotic symptoms.

MONOAMINE OXIDASE A/B KNOCK-OUT MICE ARE HYPERSENSITIVE TO THE PSYCHOTOMIMETIC ACTIONS OF NMDA RECEPTOR ANTAGONISTS. Bortolato M.1; Frau R.1; Orrù M.1; Mereu G.1; Chen K.2; Shih J.C.2 1Dept. of Cardiovascular and Neurological Science, School of Medicine, University of Cagliari, Cagliari, Italy; 2 Dept. of. Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Southern California, Los Angeles (CA), U.S.A. Brain monoamines play a critical role in the pathophysiology of psychotic phenomena. In particular, activation of dopamine (DA) and serotonin receptors induces psychotic-like symptoms in humans. An interesting experimental tool to explore the impact of monoaminergic activation in schizophrenia may be offered by animals displaying genetic deletions of monoamino oxidases (MAOs), the main enzymes involved in the catabolism of these neurotransmitters. Thus, in the present study we evaluated the behavioral responses of MAO A, MAO B and MAO A/B knockout (KO) mice in the model of the prepulse inhibition (PPI) of the startle reflex, one of the best-validated behavioral paradigms to study psychotic-like behaviors in animals. Interestingly, no group displayed significant changes in PPI values in comparison to wild type mice, both spontaneously and after administration of the DA receptor agonists apomorphine (2-10 mg/kg, i.p.) and d-amphetamine (5 mg/kg, i.p.). All the groups exhibited a significant reduction of PPI values following treatment with dizocilpine (0.3 mg/kg, i.p.), the glutamate N-methyl-d-aspartate (NMDA) receptor antagonist used to model psychotic effects resistent to neuroleptic treatment. However, low doses of the same compound (0.1 mg/kg, i.p.) induced dramatic PPI

decrements only in MAO A/B KO mice, but not in the other groups. Such reductions were not affected by either the D2 DA receptor antagonist blocker haloperidol (1 mg/kg, i.p.) or the atypical antipsychotic clozapine (5 mg/kg, i.p.), but were attenuated by the DA D1 receptor antagonist SCH 23390 (1 mg/kg, i.p.). The present results highlight a possible contribution of DA and other monoamines in the pathophysiology of treatment-resistent psychotic phenomena and point to MAO A/B mice as an interesting murine model to study psychotic-like behaviors induced by NMDA receptor antagonists.

GABA(B) RECEPTOR SIGNALING DYSREGULATIONS UNDERPIN GATING DEFICITS AND SEIZURE IN DBA/2J MICE. Bortolato, M.; Frau R.; Orrù M.; Piras A.P.; Castelli M.P.; Mereu G.; Marrosu F. Dept. of Cardiovascular and Neurological Science. University of Cagliari, Cagliari, Italy. Gamma-amino-butyric acid (GABA)B receptors play a key role in the pathophysiology of psychotic disorders and epileptic phenomena. We previously reported that baclofen, the prototypical GABAB agonist, elicits antipsychotic-like effects in the rat paradigm of prepulse inhibition (PPI) of the startle, a highly validated animal model of schizophrenia. Thus, in the present study we studied the role of GABAB receptors in the spontaneous PPI deficits displayed by DBA/2J mice, a seizure-susceptible strain. Baclofen (1.25-5 mg/kg, i.p.) dose-dependently restored PPI deficit in DBA/2J mice, in a fashion similar to the antipsychotic clozapine (5 mg/kg, i.p.), and induced a simultaneous precipitation of spontaneous seizures. Pre-treatment with the GABAB antagonist SCH50211 (50 mg/kg, i.p.) reversed both effects. In contrast, baclofen did not affect either PPI or EEG activity in C57BL/6J mice. Finally, quantitative autoradiographic analyses assessed a lower GABAB receptor expression in DBA/2J mice in comparison to C57BL/6J controls in prefrontal cortex and hippocampus, but not in other brain regions. Our data highlight GABAB receptors as an important substrate for sensorimotor gating control and epileptogenesis in DBA/2J mice, and encourage further investigations on the role of GABAB receptors in sensorimotor gating, as well as in the reciprocal interplays between psychotic disturbances and epileptic phenomena.

SPECTRAL ANALYSIS OF EEG IN PERSONALITY DISORDER SUBJECTS. Calzada A; Alvarez A. Legal Medicine Institute, Havana, Cuba. INTRODUCCION: Functional alterations of the Central Nervous System constitute one of the neurobiological related factors to personality disorders.Objectives: The aim of the investigation is to contribute to electrophysiological characterization of the subjects with personality disorders.Methods: The resting electroencephalogram was recorded in 18 subjects, with personality disorders evaluated for forensic psychiatrics (Experimental Group). They were compared with 10 subjects without personality disorders (Control Group). The features at visual inspection of the Electroencephalogram and the use of frequency domain quantitative analysis techniques (Broad Band and Narrow Band Spectral Measures) are described. Results: 53,6% of personality disorder subjects had electroencephalographic abnormalities. The most frequent were the background activity organizational alterations, low amplitude electrogenesis, an attenuated alpha rhythm and sometimes barely incipient. Delta-theta slow activity in the frontal lobe. The quantitative analysis showed differences between the frequency spectrums and between the broad band spectral measures from both groups and between experimental groups and the Cuban norms. The Delta-theta frequencies predominate in the personality disorders whereas the alpha activity did it in the Control Group.Conclusion: A high incidence of electroencephalographics abnormalities were found in the personality disorder subjects. The most frequents were: electrogenesis alterations, attenuated alpha rhythm and delta-theta slow activity in the frontal lobe. In the quantitative analysis the delta-theta frequencies predominate in the personality disorders and the alpha activity did it in the Control Group.

THE MPTP RAT MODEL OF THE EARLY STAGE OF PARKINSON'S DISEASE. 1Da Cunha, C. 1Wietzikoski E.C., 1Kouzmine I., 1Gregorio M.L., 1Ferro M.M., 1Vital M.A.B.F., 2Canteras N.S. 1Laboratório de Fisiologia e Farmacologia do Sistema Nervoso Central, Departamentos de Farmacologia e Bioquímica, UFPR, Curitiba, Brazil, E-mail: dacunha@ufpr.br; 2Departamento de Anatomia, Instituto de Ciências Biomédicas-3, USP, São Paulo, Brazil. The screening of drugs for the treatment of Parkinson's disease (PD) has improved notably after the advent of the 6-hydroxydopamine (6-OHDA) rat model, which resembles the end stage of the disease. Injected into the medial forebrain bundle, this neurotoxin causes an almost total loss of mesencephalic dopamine neurons, upregulation of D2-like dopamine receptors in the striatum, and contralateral turning behavior when unilaterally lesioned rats are challenged with dopamine receptor agonists. The purpose of the present study was to validate another rat model that resembles the early stage of PD characterized by partial loss of dopamine neurons. Male Wistar rats received an infusion of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) into the substantia nigra pars compacta (SNc). The partial loss of tyrosine hydroxylase-immunoreactive neurons mainly restricted to the SNc and the partial depletion of striatal dopamine levels in the dorsal striatum showed that this model was successful in mimicking the early stage of PD. These MPTP rats presented dose-dependent ipsilateral turning behavior when

challenged either with the dopamine receptor agonist, apomorphine, or with the indirect dopamine receptor agonist, amphetamine. This behavior also qualitatively differed from that observed in 6OHDA rats, which presented contralateral turns when challenged with apomorphine and ipsilateral turns when challenged with amphetamine. The present results validate the ipsilateral turning behavior of MPTP rats as a simple and quantitative model with predictive value for the screening of drugs potentially effective to improve the motor impairments observed in the early stage of PD.

Animal Models of Behavior and Neural Function

INTRINSIC FACTORS ASSOCIATED WITH WILD-RUNNING SUSCEPTIBILITY IN THE COMMON WISTAR RAT. de Paula, H.M.G.; Aquino, S.; Miwa, M.K.; Matsunaga, Jr. M.M. UNESP – Bauru, Sao Paulo, Brazil. Extrinsic factors, like treatment with excitatory drugs, predispose the common Wistar rat for reacting to a high-intense acoustic stimulation with the wild running (WR) behavior. However, some rats are susceptible to WR without external agents, and they appear independently in different rat colonies. The objective of this work was investigate intrinsic factors, like parental inheritance, gender, and behaviors exhibited during the stimulation, that could be associated with the WR susceptibility. For that, adult female (n=66) and male (n=63) Wistar rats were all tested for the WR susceptibility by stimulating the subjects with a ringing bell (120 dB) during 60s. Positive results for WR were only observed among the rats bred from WR-sensitive parents (16.9%) and such deviation in distribution is statistically significant ($X2=9.76$; $df=1$; $p<0.01$). The proportion of males (9.1%) and females (11.1%) susceptible to WR did not differ, and previous exposition to the stimulus failed to interfere in WR susceptibility. During the tests, exploratory activity most frequently preceded the WR fits ($p=0.01$), and low latencies of WR were associated with multiple WR episodes ($p<0.01$). Such findings are suggestive that environmental factors may weakly influence the WR susceptibility. According to our previous work, genetic propensity to anxiety seems to strongly contribute to the WR susceptibility.

EFFECTS OF A NEURONAL NITRIC OXIDE SYNTHASE INHIBITOR ON HIPPOCAMPAL GENE EXPRESSION PROFILE. Ferreira, F.R; Joca, S.R.; Santos, A.R; Silva, Jr. W.A; Guimarães, F.S. Dept. Pharmacology, Ribeirão Preto Medical School, University of São Paulo (FMRP-USP). E-mail: ferreirafr@usp.br<p>The hippocampus is a limbic structure that contains a high density of glucocorticoid receptors. It has been linked to behavioral responses to stress. Systemic or intra-hippocampal administration of 7-nitroindazole (7-NI), a preferential inhibitor of the neuronal nitric oxide (NO) synthase enzyme, decreases immobility time in rodents submitted to the forced swimming test (FST), an animal model predictive of antidepressant activity. Therefore, the aim of this study was to evaluate the effect of chronic treatment with 7-NI on gene expression pattern in the hippocampus of rats submitted to FST using Serial Analyses of Gene Expression (SAGE). Male rats were treated with 7-NI (60mg/kg/daily) or vehicle (DMSO:saline, 1:1) for 14 days. One h after the last injection they were submitted to the FST and two hours later total hippocampal mRNA was extracted for SAGE analyses. 7-NI treatment significantly decreased the immobility time (7-NI: 111.80±60.08, n=5, vehicle: 222.12±17.96s, n=8, $p<0.05$). With 6,736 gene tags expressed in the hippocampus of animals treated with 7-NI and 11,137 gene tags of animals treated with vehicle, both submitted to the FST, there were 276 gene tags (15.44%) differentially expressed (up to fivefold). These genes belong to a variety of functional classes, including basic metabolism, transcription regulation, synaptic plasticity and genes of unknown identity of function. Our data confirm that the systemic inhibition of NO synthesis induces antidepressant-like effects and indicate that this effect may be related to the modulation of gene expression associated with stress adaptation.<p>Financial support: FAPESP, CNPq, FAEPA.

THE MULTIPLE PARTNER CHOICE ARENA: AN ANIMAL MODEL TO EVALUATE THE PREMATURE EJACULATION IN RATS. Ferreira-Nuño, A.; Morales-Otal, A.; Fernández-Soto, C.; Olayo-Lortia, J.; Velázquez-Moctezuma, J. Depto. Biología de la Reproducción. Universidad Autónoma Metropolitana-Iztapalapa. México. D. F. 09340. fena@xanum.uam.mx. Premature ejaculation is one of the most common ejaculatory dysfunction in men. However, there are only few proposals of animal models to evaluate this problem. Recently we developed a Multiple Partner Choice Test (MPT) in which a female can freely choose a male to mate with. We have reported that in the conditions of the test, the female rat choose only one of the four possible males to mate, remaining most of the time with him and having only ocassional contacts with the other males. In these circumstances, the non preferred males are able to ejaculate after 3 or 4 intromissions. This study was done to assess if the MPT could be a useful model to analyze the premature ejaculation in the rat. Adult sexually experienced male rats were used. Their sexual activity was recorded both in standard conditions as well as when they were submitted to the MPT conditions. The number

of intromissions needed to reach the first ejaculation after mating in standard conditions was compared against those obtained when submitted to the MPT conditions. Males needed a significant lower number of intromissions (4.74 ± 1.8) to reach ejaculation in the MPT conditions compared to the number of intromissions needed in under standard conditions (7.7± 3). It is possible that the condition in the MPT generates, in the non preferred males, an state of anxiety similar to that observed in many men suffering from premature ejaculation. Therefore, the MPT could be a good model to evaluate premature ejaculation in the rat.

BIOCHEMICAL AND BEHAVIORAL EFFECT OF GLUTATHIONE DEPLETION IN RAT BRAIN. Gonzalez Fraguela ME.Neurochemistry Department. International Center for Neurological Restoration. CIREN. email: rmunoz@infomed.sld.cu Our purpose was to test the effects of depleting tissue glutathione (GSH) by buthionine sulfoximine (BSO, 10mM, intracerebroventricular (icv)) on brain oxidative metabolism and cognitive performance in rats. The experimental groups were: icv BSO–treated at 24h and 48h, icv saline-treated at 24h and 48h and untreated groups. 24h after BSO treatment, GSH levels in hippocampus dropped down to 55% as compared to untreated animals, 48h later the hippocampal GSH values showed a slight increase, in contrast, had been significantly restored in striatum and frontal cortex. GSH depletion modified superoxide dismutase, catalase, glutathione peroxidase activities, malondialdehide, tumor necrosis factor a and interleukine IL1 content and DNA damaged markedly in the BSO-treated group as compared to untreated animals in 24h and 48h and saline-treated group followed 48h, however the way in which it occurs is different for each indicator. Glutathione depletion did not influence the performance of animals in the step-through passive avoidance test in the BSO treatment, but impairs the acquisition in the Morris water maze when given before training, and affect the retention at the following day. BSO-treated group at 48h was significantly better than the performance of the same group at 24h. Our results support that glutathione status is a key piece acting in the regulation of brain function.

FREQUENCY DISTRIBUTION OF THE MAO-A PROMOTER ALLELIC VARIANTS IN A MALE POPULATION SAMPLE Oliveira, L.L. ; Lage, C.A.C. ; Melgaço, M.C.P. ; Urmenyi, T.P. ; Rondinelli, E. ; Moura-Neto, R. ; Silva, R. Instituto de Biofísica Carlos Chagas F., UFRJ, RJ; Programa DNA, Defensoria Pública, RJ; Faculdade de Medicina, UFRJ; Departamento de Genética, IB, UFRJ; Instituto de Pesquisa e Perícia em Genética Forense, PCERJ, Rio de Janeiro, Brazil Functional allelic variation in the transcriptional control region of monoamine oxidase A (MAO-A) known as MAOA-uVNTR (for the upstream variable-number tandem repeat region) has been associated with anxiety- and aggression-related behavior in humans. The MAO-A gene is localized in the X chromosome, and the promoter functional polymorphism is characterized by nucleotide repetitions in tandem. The gene transcription is affected according to the number of these repetitions. Alleles with 3.5 or 4 copies of the repeat sequence are transcribed 2 to 10 times more efficiently than those with 3 or 5 copies of the repeat. The lower activity of MAO-A, due to the transcription of variant alleles, was associated with the development of aggressive behavior in maltreated male children in a large birth cohort study. The objective of this work is to evaluate the distribution of alleles frequencies of MAO-A promoter polymorphisms in a male population sample from São Paulo and Rio de Janeiro, which belongs to different ethnic groups. The ethnic classification is being achieved by the analysis of mitochondrial DNA and Y chromosome haplotypes, which are determined through the paternal and maternal lineages. Preliminary results showed the following allelic distribution: 5 repetitions, 0,275; 4, 0,400; 3,5, 0,175 and 3, 0,100. Considering the paternal lineage, 29,4% was related to West Europe; 5,9% to West Asia and 64,70% was not found in the Y-Chromosome haplotype reference database. The mitochondrial DNA analysis shows that most of the white males are related to Africans and Europeans. Forthcoming, this correlation will be an important tool to evaluate the role of genotypes on the human aggression. Acknowledgements: FAPERJ, CNPQ

VENDOR EFFECTS IN BEHAVIOR: KNOWING YOUR MOUSE FROM YOUR MOUSE. Buell, M.R.; Young, J.W.; Geyer, M.A. Psychiatry Dept.; Univ. of Calif. San Diego; 9500 Gilman Dr.; La Jolla, CA 92093-0804. Since the creation of transgenic technology, the mouse has become an extremely valuable research tool. For example, given that schizophrenia patients exhibit deficiencies in sensorimotor gating and that sensorimotor gating can be reliably assessed across species by measuring prepulse inhibition (PPI) of startle, PPI in genetically modified mice has been used to complement psychopharmacology studies of psychosis. Commonly, inbred strains of mice are used to reduce genetic and potentially phenotypic variability. The C57BL/6 inbred strain of mice is often used for backcrossing to produce congenic lines and reduce variability between studies. However, the source of the C57BL/6 mice used often varies, based on the assumption that no differences exist between mice from different vendors. To investigate the validity of this assumption, we compared the behavior of C57BL/6 mice from four different vendors. C57BL/6 mice from Harlan (n=23), Charles River (n=24), Jackson (n=24) and Hilltop (n=24) were tested in both the

startle/PPI and locomotor paradigms under control conditions and with standard pharmacological manipulations. The animals were tested with 5 mg/kg apomorphine in PPI and 3 mg/kg amphetamine in locomotor activity. Our results showed that even in the same inbred strain of mice (C57BL/6), the vendor of origin significantly affected the results. The present studies demonstrate that vendor can be yet another source of variability in studies of both PPI and locomotor activity, suggesting that caution be exercised when selecting the source of mice used to generate congenic lines.

NORMALIZING CHOLINERGIC TONE TO AMELIORATE THE MANIFESTATION OF CLINICAL SYMPTOMS IN NEUROLOGICAL PATHOLOGIES. Paskvan, C.D.; Edmonds B.W.; Schulte, M.K. Department of Biochemistry and Molecular Biology, University of Alaska Fairbanks, Fairbanks, AK 99775, USA. Department of Natural Sciences, University of Alaska Southeast, Juneau, AK 99801, USA & IDeA Network of Biomedical Research Excellence (INBRE), University of Alaska Fairbanks, Fairbanks, AK 99775, USA. Neuronal nicotinic acetylcholine receptors (nAChRs) are ligand-gated ion channels (LGICs) that mediate cholinergic tone in the central nervous system (CNS). In the mammalian brain, heterogeneous populations of nAChRs maintain the normal properties of neuronal circuits. Disruptions in cholinergic signaling induce cognitive deficits evident in numerous neurological pathologies including, but not limited to, autism, nicotine addiction and corresponding smoking cessation strategies, schizophrenia, and Alzheimer's disease. In this work, we review the pharmacological relevance of competitive and non-competitive ligands (NCLs) of nAChRs for palliative care. Specifically, we illuminate the therapeutic potential of subtype-specific allosteric modulators of nAChRs to restore cholinergic tone and thus decrease the severity of symptoms while increasing the overall quality of life.

IDENTIFICATION AND BEHAVIORAL CORRELATES OF THE UROCORTINERGIC SYSTEM IN PIGEONS. R.P. Cunha1; J.A. Cavani1, A. Reiner2, and C. A.B. Toledo1. 1Lab. of Neuroscience, Universidade Cidade de São Paulo, 03071-000, SP, Brazil; 2Dept. of Anatomy & Neurobiology, The University of Tennessee, 38163, Memphis, TN, USA. Urocortin-1 (Ucn1) belongs to the corticotropin releasing hormone (CRH) family, all of which show affinity for corticotropin receptors (CRs). The major Ucn1-containing neurons in rats are located below the midbrain central gray, and they give rise to projections to the thalamus and hypothalamus, as well as to medullary and spinal cord sites. The specific projection targets of the Ucn1 neurons are consistent with their demonstrated involvement in anxiogenic and stress responses. Since such responses are found in birds as well, we submitted pigeons to restraint stress and determined by proto-oncogene immunolabeling if the Ucn1 neurons below the midbrain central gray in this representative avian species showed activation. We also verified the descending projections of this cell group in pigeon with neuro-tracers. Our data showed that the main Ucn1-positive population in pigeons consists of paired cell columns, positioned in the diencephalic-mesencephalic transition zone, along the ventral aspect of the central gray. Tracer injections revealed that these Ucn1-neurons project to the medulla, as they do in mammals as well. Restraint stress caused an increase in EGR-1 expression in the majority of the Ucn1 neurons below the central gray. Territories that in mammals are rich in CRH receptors, such as the amygdala, septum, periventricular hypothalamus, and the supraoptic and paraventricular nuclei, did not significantly express EGR-1 in pigeons during stress. These results indicate that the connectivity and role during stress of the subgriseal Ucn1 neurons of pigeons (and likely birds in general) closely resemble that in mammals. This circuit may, thus, be an ancient one responsible for mediating stress reactions in the amniote brain. Supported by FAPESP (04/11039-6 to C.T.) and NIH (EY-05298 to A.R.).

ASSOCIATIONS BETWEEN OFFENSIVE AGGRESSION AND IMPULSIVITY IN ADULT MALE GOLDEN HAMSTERS. Cervantes, M.C.; Delville, Y. Institute for Neuroscience and Psychology Department, The University of Texas at Austin, 78712 USA. There are strong differences in the definitions and subtypes of aggression between humans and animals. For example, impulsive aggression is well characterized in humans, but not in animals. The purpose of this study is to identify differences in aggression and associated impulsive characteristics. Adult male hamsters were repeatedly tested for offensive responses and divided into High-Aggression or Low-Aggression groups. They were then trained and tested under a delay-discounting paradigm used as an index for impulsivity. Our data showed that H-Agg animals consistently attacked and bit more frequently and faster, but showed decreased efficiency of behavior, indicated by a lower percentage of attacks followed by bites. They also showed highly repetitive behavior, indicated by increased attacks per contact bout. During impulsivity testing, H-Agg animals preferred immediate smaller rewards over delayed larger rewards. Furthermore, serotonin and vasopressin immunoreactivity was compared between the groups. As compared to the L-Agg group, H-Agg animals showed increased serotonin varicosities in several key brain areas involved in aggressive and/or impulsive behavior and decreased vasopressin fibers in the anterior hypothalamus. Together, these data show associations between offensive

aggression and impulsivity. These behavioral observations provide an animal model to aggression-related personality disorders and may also be applicable to personality profiling. The data also confirm the importance of serotonin and vasopressin availability in the modulation of aggressive and impulsive behaviors.

FEMALES EXPOSED TO AN ANABOLIC STEROID DISPLAYED AN INCREASE IN SEXUAL MOTIVATION WITHOUT ALTERING SOCIAL DOMINANCE [1]Parrilla, J; [2]Jorge, JC; [2]Barreto-Estrada, JL. [1]Department of Sciences and Technology, Universidad del Este, Carolina, P.R. 2School of Medicine, Department of Anatomy, University of Puerto Rico-Medical Sciences Campus. Androgens may play an important modulatory role in libido and sexual performance among females. We aimed to establish the effect of the AAS 17 alpha-methyltestorene in female sexual behavior paired with control males or control females under continuous systematic expousure (7.5 mg/kg) to this androgen. The frequency of mounts, attempts and latency to the first mount were studied. In addition, anogenital investigation, fights, escapes, rejection, pelvic thrusts and lordotic response were scored. We found that males displayed a significant decrease in the frequency of mounts to AAS-exposed females, when compared to mating encounters with control females. Moreover, the lordosis quotient was affected. Females under androgen exposure attempt to mount control females, but not males, and their behavior was accompanied by a significant increase in the number of fights, escapes, and rejections to the males. There were no differences between AAS-exposed females and males when the frequency of mount and pelvic thrust towards control females were compared. In fact, the lordotic response of control females was similar for either partner. Aside from showing a male-like pattern, AAS exposed females displayed a higher frequency of anogenital investigation toward control females than males, and the latency to the first mount was similar to males. None of these changes were associated with social dominance. We conclude that the sex partner greatly influence the sexual response of AAS-exposed female mice. Supported by MBRS-RISE (GM61838), (1R25-GM066250-01A3), NIH-COBRE (RR15565), RCMI (G12RR03051), NIH-MRISP (MH048190) and NIH-NCRR (P20RR016470).

BEHAVIOURAL EFFECTS OF HIPPOCAMPAL OVEREXPRESSION OF BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) IN RATS. Pietropaolo, S.2; Paterna J.C.2; Büeler, H.1; Yee, B.K.2; Feldon, J.2 1 Institute of Molecular Biology, University of Zurich, 8057 Zurich, Switzerland; 2 Laboratory of Behavioural Neurobiology, ETH, 8603 Schwerzenbach, Switzerland. Converging lines of evidence suggest that aberration or interference with BDNF-related functions are implicated in the pathogenesis of schizophrenia and depression. The aim of the present study was to analyse the behavioural effects of overexpressed BDNF in the dorsal hippocampus of adult male Wistar rats. Recombinant adenovirus-associated virus (rAAV) vectors encoding C-terminal myc-tagged rat BDNF or enhanced green fluorescent protein (EGFP) were stereotaxically delivered bilaterally into the dorsal hippocampus. Two months postinjection, the two groups underwent a battery of behavioural tests. Surprisingly, BDNF rats did not perform differently from the EGFP group in a spatial memory test (water maze), but BDNF rats could unambiguously be segregated into two behaviourally distinct subgroups: Among the ten BDNF rats, four good learners were identified by their shorter latency to reach the hidden platform, while six bad learners evidently performed significantly worse relative to the EGFP group. This distinction was also detectable in anxiety-related behaviour (elevated plus maze) and in another cognitive test (two-way active avoidance). All BDNF rats showed significant hyperactivity in anxiogenic testing conditions (elevated plus maze, conditioned freezing, and active avoidance). Quantification of rat BDNF levels in the dorsal hippocampus (ELISA) revealed no significant differences between untreated and EGFP expressing animals, whereas all BDNF animals demonstrated exceptionally elevated BDNF levels. Furthermore, the behavioural difference between the two BDNF subgroups was reflected by the BDNF levels measured: the good learners showed a lower relative BDNF increase in comparison with the bad learners. Our data suggest that increasing BDNF hippocampal levels affects several behavioural traits including the cognitive abilities and the direction of the change appears to depend on and correlates with the BDNF expression level.

Thursday, June 14, 2007

8:15-10:15 Symposium 3. Early-life stress to model the interactions between genes and the environment: From the clinic to animal models.

GENE X ENVIRONMENT INTERACTIONS: EXAMPLES IN DEPRESSION AND AGGRESSION. Reif, A.; Lesch, K.-P. Dept. of Psychiatry, University of Wuerzburg, Fuechsleinstr. 15, 97080 Wuerzburg, Germany. Depression is an etiologically heterogeneous group of brain disorders with complex genetics. Definition of clinical phenotypes are not rooted in their neurobiology and animal models of behavioral dispair have considerable limitations. Likewise, aggressive behaviors are complex traits with equally diverse underlying neurobiological underpinnings not readily explained by simplistic models. Although research on the neurobiology of those behaviors is still in its infancy, several milestones have already been reached: Variation in gene expression were confirmed to play a predominant role in individual differences in complex traits including personality and behavior; gene x environment interaction were established in humans and the nonhuman primate model; gene-phenotype correlations were substantiated by functional neuroimaging; as well as the notion that both genes and environmental factor impact on brain development and thus set the stage for the susceptibility to depression is increasingly appreciated. Investigation of subtle alterations in the expression of genes of the serotonergic pathway, such as the serotonin transporter (5HTT), of correlations between 5HTT genotype and brain activity, and of environmental variables interacting with 5HTT variants currently strengthen research on the genetics of depression. A similar line of evidence, linking rodent behavior, genetic variation in humans, environmental factors, and neuroimaging data, is emerging for a functional MAO-A polymorphism and impulsive-aggressive behavior. Given the etiological and psychobiological complexity of depression and aggression, it is not surprising that the identification of vulnerability genes and elucidation of their interaction with environmental stressors is extremely difficult and continues to be among the last challenges of genomics, behavioral neurosciences, and psychiatry.

EARLY RISK FACTORS FOR NEUROPSYCHIATRIC DISEASES: COMPARATIVE APPROACHES TO INVESTIGATE INTERACTIONS BETWEEN GENES AND ENVIRONMENT. Cirulli, F. (a); Francia, N. (a); Capone, F. (a); Aloe, L. (b); Suomi, SJ (c); Alleva, E. (a). (a) Section of Behavioural Neuroscience, Department of Cell Biology and Neuroscience, Istituto Superiore di Sanità, Rome, Italy; (b) Institute of Neurobiology and Molecular Medicine, CNR, European Brain Research Institute (EBRI), Rome, Italy; (c) Laboratory of Comparative Ethology, National Institute of Child Health and Human Development (NICHD), Poolesville, MD, USA. In humans, both genetic and experiential factors can shape individual vulnerability to psychiatric illness. However, the quality and quantity of experience predisposing an individual towards psychopathology and the specific neural substrates affected are still open questions. We have used a comparative approach using both rodents and primates (rhesus macaques) to test the hypothesis that changes in the levels of neurotrophic factors (NGF and BDNF) during critical periods of brain development, as a result of different rearing experiences, might affect the ability to cope with stress and lead to behavioural changes at adulthood. Neurotrophic factors are good candidates for mediating long-term effects of experience on brain function since they are involved in synaptic plasticity. In addition, they are involved in the response to psychosocial stress in animal models and in psychiatric disorders in humans. We have shown that, in rodents, neurotrophins are sensitive to manipulations of the mother-infant relationship and, more in general, of the rearing environment. In particular, our data indicate that NGF levels increase in an age- and time-dependent fashion following maternal separation, while a prolonged maternal deprivation can lead to a long-term reduction in BDNF levels in the prefrontal cortical areas of rats. We have recently established a methodological protocol to measure levels of neurotrophins (NGF and BDNF) in rhesus macaques exposed to early stress (reared in the presence of peers, rather than by the mother) both in the cerebrospinal fluid and in the peripheral circulation. Data gathered in these studies show that changes in plasma levels of neurotrophins might function as peripheral markers of early adversity in primates, being differentially affected by changes in the rearing environment.

DEVELOPING AN EARLY LIFE STRESS MODEL THAT RELIABLY ALTERS ADULT NEUROENDOCRINE AND BEHAVIORAL STRESS-REACTIVITY IN C57BL/6 MICE: NEONATAL HANDLING VS. MATERNAL SEPARATION. David B. Parfitt, Department of Psychiatry, Rochester Center for Mind-Body Research, University of Rochester Medical Center, Rochester, NY 14642 USA. Understanding environmental effects on mouse brain development would allow us to take advantage of powerful genetic tools to determine the interaction between genetic and epigenetic factors governing brain development. This talk will describe ongoing experiments designed to optimize parameters of an early life stress model that exerts permanent long-term effects on hormone secretion and behavior in adult male C57BL/6 mice. One experiment examined

whether time of day for neonatal manipulations affects adult stress-induced hormone secretion. Three rearing groups were examined: early handled (EH; dam removed 10 min/day); maternal separated (MS; dam removed 180 min/day), and an animal facility raised (AFR) control. Separations occurred during either the first or last 3 hours of the light phase for the first 10 days of life. Male offspring were allowed to grow to adulthood when corticosterone (CORT) secretion in response to 100 dB white noise was assessed. Only EH males handled during the last three hours of the light phase exhibited blunted stress-induced CORT compared to all other groups. A second experiment kept time of day of neonatal manipulations constant (last 3 hours of the light phase) but varied time of behavior testing. In addition to the three groups described above, a fourth group was also added: maternal isolated (MI; separated from dam and littermates 180 min/day). Adult male behavior was assessed in three different tests during the light or dark phase. Only EH males tested in the elevated zero maze during the light phase exhibited diminished anxiety-like behavior compared to the other groups. We conclude from these studies that the EH protocol utilized is marginally effective in blunting stress-induced CORT secretion and anxiety-like behavior in C57BL/6 mice, and these early handling effects are influenced by time of day. We also conclude from these data that the three hour repeated maternal separation protocol (either MS or MI) is not effective in consistently exacerbating future adult stress-induced CORT secretion or anxiety-like behavior in C57BL/6 mice. Ongoing work is focused on developing a different early life stress model with more robust effects on brain development in order to study gene X environment interactions in this species.

MATERNAL SEPARATION AS A MODEL OF GENE-ENVIRONMENT INTERACTIONS IN THE MOUSE, IS MORE THAN ONE GENERATION AFFECTED? Russig, H.; Franklin, T.B.; Mansuy, I.M. Brain Research Institute. University Zürich / Swiss Federal Institute of Technology Zürich, Switzerland. Traumatic psychosocial and physical experiences during early life constitute risk factors for the development of behavioral and emotional disorders. The impact of adverse events on behavior is generally durable and repeatedly reported to be transmitted to the offspring. Here, we describe a novel mouse model of early trauma in which disruption of normal rearing conditions by unpredictable maternal separation combined with maternal stress impairs behavioral control in the progeny when adult. The induced loss of behavioral control is manifested by reduced risk assessment during exploration of novel environments and behavioral abnormalities associated with symptoms of depression in human. Neurobiological alterations in serotonergic neurotransmission and stress hormone pathways may underlie these behavioral alterations. Further, the behavioral impairments not only persist throughout life but are also transmitted to the progeny by both females and males. These findings suggest the intervention of epigenetic mechanisms in the impact of early stress on behavior.

10:30-11:30 Elsevier Keynote Lecture: John Aggleton

BUILDING BRAIN SYSTEMS FOR MEMORY. Aggleton, J.P. School of Psychology, Cardiff University, Cardiff, Wales, UK. Understanding anterograde amnesia remains a critical stepping-stone in the quest to understand the neural basis of episodic memory. Using complementary tract tracing and neuropsychological techniques I have explored the anatomical and functional relationships between the anterograde amnesic syndromes associated with damage to the medial temporal lobe and damage to the medial diencephalon. The key question was whether these syndromes should be seen as different aspects of the same underlying deficit or whether they reflect disruptions to two, separate memory systems. Detailed descriptions of the consequences of fornix damage in humans, along with analyses of the fibre pathways that use this tract, strongly support the view that diencephalic and temporal lobe amnesias are closely inter-related. Disconnection studies with animals add further support and so highlight the mutual importance of the hippocampus and anterior thalamic nuclei. These studies also reveal the disproportionate importance of the hippocampus and the fornix for the recollection, rather than the recognition, of recent events. This particular finding helps to explain why it had previously been supposed that fornix damage was not sufficient to induce amnesia. By combining these data details of a system vital for recollective memory emerges. At the heart of the system are reciprocally linked structures in the medial temporal lobe and medial diencephalon.

DORSAL HIPPOCAMPAL CA3 LESIONS IMPAIR EPISODIC-LIKE MEMORY IN RATS. Li, J.S.; Chao, Y.S. Department of Psychology, National Chung Cheng University, Chia-Yi, Taiwan, R.O.C. The episodic memory is the ability to recollect one's past experiences occurring in an unique spatial and temporal context. During the search for its neural substrates, the hippocampus has attracted a lot of attentions. Yet, researchers trying to study this topic in animals were confronted with two challenges. First, the notion that non-human animals are capable of processing the episodic memory is controversial. Second, hippocampus is involved in many memory systems, especially in the spatial leaning and memory. Since the episodic memory is defined by the integration of spatial and temporal elements in the memory associated with certain events, it is difficult to selectively manipulate the memory system alone, without impairing the spatial component itself. Recently, two groups have successfully developed behavioural paradigms to observe episodic-like memory in rodents. It is expressed in animals' ability to combine "what", "where" and "when" factors to form an integrated memory system. Here we applied one of them to investigate the effects of bilateral electrolytic lesions of dorsal CA3 regions in the episodic memory system of rats. In their spontaneous exploratory preferences, lesioned rats showed no interaction between the temporal and spatial elements in their memory associated with the objects, thus, evidencing deficits in the episodic-like memory. Furthermore, we successfully demonstrated that the same animals still expressed abilities to process spatial, temporal, and object recognition memory in subsequent tasks carried out separately.

REVERSION OF RECOGNITION MEMORY IMPAIRMENT ASSOCIATED WITH AGING OR BRAIN IRON ACCUMULATION BY THE TYPE 4 PHOSPHODIESTERASE INHIBITOR ROLIPRAM. de Lima, M.N.M.[1]; Torres, J.P.[1]; Garcia, V.A.[1]; Roesler, R.[2]; Schröder, N.[1] - [1]Neurobiology and Developmental Biology Laboratory, Faculty of Biosciences, Pontifical Catholic University; [2]Department of Pharmacology, Institute for Basic Health Sciences, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil. Increasing evidence indicates that iron accumulation in selective brain regions may lead to cytotoxic free radical formation, thereby possessing implications for the etiology of neurodegenerative disorders. Studies have also demonstrated that iron accumulates in the brain during the normal aging process. We have previously reported that neonatal administration of iron induces severe recognition memory deficits in adulthood comparable to memory impairment observed in aged rats. The aim of the present study was to evaluate the effect of the type 4 phosphodiesterase inhibitor, rolipram, on iron-induced and aging-associated recognition memory deficits. In Experiment I, rats received vehicle or Fe+2 at 10.0 mg/kg orally at postnatal days 12 to 14. When they reached the age of 3 months both groups were further divided in four experimental groups receiving rolipram (0.0, 0.01, 0.03 or 0.1 mg/kg i.p.) immediately after the training trial of the novel object recognition task. Iron-treated rats that received rolipram (0.03 and 0.1 mg/kg) showed normal recognition memory. In Experiment II, aged rats (24 months old) received rolipram (0.0 or 0.1 mg/kg i.p.) immediately after the training trial of the novel object recognition task. Rolipram-treated rats showed normal recognition memory. The present results show that rolipram reverses neonatal iron- and aging-induced recognition memory deficits, providing support for the use of phosphodieterase inhibitors as a potential therapy for cognitive decline associated with aging and neurodegenerative disorders.

INFUSIONS OF NALOXONE INTO THE MEDIAL PREOPTIC AREA AND VENTROMEDIAL NUCLEUS OF THE HYPOTHALAMUS BLOCK CONDITIONED PLACE PREFERENCE INDUCED BY PACED MATING BEHAVIOR IN FEMALE RATS. Sonia P. Garcia-Horsman, Anders Ågmo and Raúl G. Paredes, Instituto de Neurobiología UNAM, Querétaro, México. Several lines of evidence indicate that opioids are released during sexual behavior and are involved in the rewarding aspects of copulation. Systemic administration of the opioid antagonist naloxone, blocks conditioned place preference (CPP) induced by paced mating in female rats. The same treatment as well as the infusion of this antagonist into the medial preoptic area (MPOA) blocks CPP induced by ejaculation in males. The present experiment was designed to investigate if infusion of naloxone into the MPOA and ventro medial nucleus of the hypothalamus (VMH) can block CPP induced by paced mating in female rats. Female Wistar rats were bilaterally implanted with a cannula aimed at the MPOA and VMH. Then they were ovariectomized and treated with estradiol benzoate and progesterone to induce receptivity. Females were infused with naloxone methiodide (5µg/cannula) before mating. After 10 to 15 intromissions, females were placed in the non-preferred (reinforced) compartment. Three reinforced sessions associating naloxone with paced mating were alternated with three non-reinforced sessions where the animals only received a saline injection before they were placed in the preferred (non-reinforced) compartment with no sexual contact. Naloxone did not affect sexual behavior. The groups infused with naloxone before sexual test did not change their preference when compared with saline treated animals. These results suggest that infusions of naloxone into MPOA and VMH block the rewarding aspects of

paced mating in female rats. It appears that these structures are important structures involved in sexual reward in female rats.Supported by Conacyt 140286M, DGAPA IN204206.

AMYGDALA OPIOID STIMULATION ENHANCES 'WANTING' BUT NOT 'LIKING' OF SUCROSE REWARD. Mahler, S; Berridge, K. University of Michigan, Ann Arbor, MI. The amygdala is perhaps best known for its role in aversive learning and memory, though it is also necessary for appetitive learning and reward. Here we investigated the role of μ opioids in the central nucleus of the amygdala (CeA) in reward 'wanting' and 'liking.' Specifically, we asked if infusion of the μ agonist DAMGO in the CeA (which increases feeding behavior) would increase measures of 'wanting' such as the motivational magnet effect of a CS in autoshaping, and cue-triggered 'wanting' in Pavlovian to Instrumental Transfer. We also asked if DAMGO in the CeA affected 'liking' for food reward, as measured by positive 'liking' taste reactivity patterns elicited by sucrose, and 'disliking' reactions elicited by quinine. We determined that CeA DAMGO markedly increased measures of 'wanting' for sucrose rewards, with little effect on measures of 'liking' of intraoral sucrose solutions. These findings indicate that increasing μ opioid neurotransmission in the CeA amplifies the incentive salience of a CS for food reward without amplifying hedonic 'liking' of the same reward.

2:00-4:00 Symposium 4: Gene-environment Interactions: animal models for mental health research.

EARLY ENRICHMENT SHAPES ADULT MOUSE SOCIAL PATTERNS: A COOPERATIVE ROLE FOR NEUTROPHINES. Branchi, I; Alleva, E. Istituto Superiore di Sanità, Rome, Italy. During early postnatal development, important processes that shape the mammalian brain are taking place. This highly plastic period offers the possibility to epigenetic factors to affect brain structure and function. Indeed, the early social environment is crucial for brain and behavior development, as shown by the disrupting effects of its impoverishment or deterioration. Children who experience severe perturbations in care are at higher risk for the emergence of behavioral problems or psychiatric disorders later in life. In order to study the effects of the early experiences on adult brain function and behavior, we exposed mouse pups to an early social enrichment: Communal Nesting (CN). CN, which consists in a single nest where three mothers keep their pups together and share care-giving behavior from birth to weaning, mimics the natural ecological niche of the mouse species. At adulthood, mice reared in CN display higher propensity to interact socially and better social skills when compared to mice reared in standard laboratory conditions. Furthermore, mice reared in CN show higher NGF and BDNF levels in selected brain areas, including hippocampus and hypothalamus, and increased rate of newly generated brain cells. With regard to emotional behavior, we found that the ability to exploit social cues in facing challenging situations at adulthood changes according to the early social experiences. Overall, these findings confirm the crucial role played by early social experiences in shaping adult social and emotional behavior and suggest a role for neurotrophins as factors mediating the long-term effects of experiences on brain function.

DIETARY SUPPLEMENTATION AND HOUSING ENVIRONMENT ALTERS BEHAVIOR AND NEUROANATOMY IN A MOUSE MODEL OF RETT SYNDROME. Nag N[1].; Ward B[2]. Berger-Sweeney J[2]. Dept. Biology[1] and Neuroscience Program[2]. Wellesley College. Wellesley MA 02481. USA. Environmental factors, e.g. housing and nutrition, can interact with genetic backgrounds in neurological disorders. Here we examine the effect of choline supplementation and environmental enrichment on behavior and neuroanatomy in a mouse model of Rett Syndrome (RTT). RTT is associated with mutations in the X-linked gene encoding MeCP2, a transcriptional repressor that binds methylated DNA. We have shown previously that $Mecp2^{1lox}$ null mice display motoric, cognitive and anxiety-related behavioral abnormalities, and show reduced brain volumes—characteristic of RTT. RTT individuals show decreased cholinergic markers. In rodents, choline supplementation during critical periods of brain development can enhance cholinergic neurotransmission; alter neuronal size and distribution; and facilitate performance of a variety of memory and motoric tasks. We show here that supplementing the drinking water of $Mecp2^{1lox}$ lactating dams with choline, thereby altering the postnatal environment of the offspring, can attenuate some behavioral symptoms in the mutant offspring. Using T2-weighted magnetic resonance images, we observe significant increases in the brain size of $Mecp2^{1lox}$ heterozygous mice after choline supplementation. Perinatal dietary environment can interact with this genetic disorder in interesting, and not always predictable, ways. We are currently investigating whether housing environment (environmental enrichment) may also affect behavior and anatomy in *Mecp*[2] mice, further exploring a role of gene-environment interactions in the treatment of neurological disorders.

INTERACTIONS OF NEONATAL STRESS AND MATERNAL CARE BEHAVIOR: DEVELOPMENT OF THE CORTICOSTERONE RESPONSE SYSTEM AND POSSIBLE MODULATION VIA SEROTONIN. Christine F. Hohmann and Amber Hodges, Department of Biology, Morgan State University, Baltimore MD. Early life experience is implicated as a trigger in mental health disorders, particularly, schizophrenia. In animal models, the effects of early stress and maternal care on behavioral and stress response profiles, in maturity, have been well established. However, little is known about the impact such early exposures might have on brain morphogenesis and plasticity. We have developed a paradigm where 1/2 of a Balb/CByJ litter is removed from the dam and exposed to 1 hour/day of maternal separation/temperature stress [STR] between PND 2 and PND7 while littermates remain with the dam [LMC]. We have observed that both STR and LMC display, in adulthood, altered affective and cognitive behavior, albeit to a different degree. Both STR and LMC males, compared to age matched controls [AMC], also displayed increased cortical width when reared in a regular laboratory environment but decreased cortical width when exposed to behavioral training/testing in young adulthood. Subsequent experiments have suggested that maternal licking and grooming is decreased for LMC but increased for STR pups compared to AMC. These findings indicate, in conjunction with recent studies on corticosterone receptor expression (see poster Hodges et al. this meeting), that neonatal LMC mice are "stressed" due to diminished maternal care. Furthermore, the data suggest an altered plasticity response in stressed mice following an "enrichment" stimulus such as behavioral training/testing. We will discuss these findings within the context of monoaminergic regulation of cortical development and plasticity and their possible implications for the etiology of mental health disorders. Supported by SO6 GM051971 and R25 GM058904

INTERACTION OF PRENATAL INFECTIONS WITH A GENETIC RISK FACTOR FOR SCHIZOPHRENIA: MOUSE MODEL. Pletnikov, M. Johns Hopkins Univ. Sch. of Medicine, Baltimore, MD. The etiology of schizophrenia is likely to involve subtle neurodevelopmental abnormalities with both genetic and environmental contributions. Studying the mechanisms of gene-environment interactions in mental health has been difficult due to the lack of experimental models where clear mutations in candidate genes interact with identified infectious agents. Recent studies have implicated Disrupted-in-Schizophrenia 1 (DISC1) in neurodevelopment and suggested that a predicted mutant DISC1 could produce a loss of function of wild-type DISC1 via dominant-negative mechanisms. Among environmental factors, influenza virus, Herpes Simplex Virus-1 (HSV-1) and Toxoplasma gondii have been implicated in the pathogenesis of schizophrenia and represent promising infectious agents for experimental studies. In this symposium presentation, we will introduce our novel transgenic mouse model of inducible expression of DISC1 as a promising experimental system for future studies of gene-environment interactions in the pathogenesis of schizophrenia. Characterization of neurobehavioral alterations in DISC1 transgenic mice exposed during pregnancy to infectious factors is under way, and the results will be presented and discussed. We believe that the proposed approach will facilitate mechanistic studies of gene-environment interactions in psychiatric disorders.

EFFECTS OF NEONATAL HANDLING ON MATERNAL ODOR PREFERENCE IN RAT PUPS: ROLE OF NORADRENALINE/CREB PATHWAY. 1Lucion AB; 1Raineki C; 1Lutz ML; 1Vasconcellos LFT; 2Szawka RE; 2Anselmo-Franci JA; 1Sanvitto GL; 3Bevilaqua LRM; 4Izquierdo I; 3,4Cammarota M. 1Physiology, UFRGS, Porto Alegre; 2Physiology, USP, Ribeirão Preto, 3Biochemistry, UFRGS, Porto Alegre; 4IPB, PUCRS, Porto Alegre, Brazil The disruption of the mother-pup relationship may induce profound long-lasting behavioral and neuroendocrine changes. The early odor learning in rats is associated with increased noradrenaline (NA) and cAMP response element-binding protein (CREB) phosphorylation in the olfactory bulb (OB). Present study aimed to analyze the effects of neonatal handling on the maternal odor preference test and the NA/CREB pathway in female rat pups. Pups were daily handled for 1 min during the first 7 days (repeated handling) or just once on day 7 after delivery (acute handling). A nonhandled group, litter and dam were left undisturbed, was used as control. The behavior in the odor preference test was evaluated on day 7 (15 min after handling) and 8 (24 h after handling). Levels of CREB, pCREB, NA and MHPG in the OB were analyzed. Repeated handled pups showed increased latency to reach the nest bedding compared to nonhandled. The time spent on the nest bedding area of repeated handled (day 7 and 8) was not different than the time spent on the fresh bedding area, while nonhandled pups spent more time on the nest bedding area. Acute handling induced no change on the odor preference test. Acute handling increased pCREB levels in the OB compared to nonhandling group, while repeated handling did not significantly change pCREB. MHPG increased in the repeated and acute handling. Neonatal handling decreases maternal odor preference and increases activity of NA/CREB system in the OB of rat pups. FAPESP, CNPq, CAPES

4:15-5:45 Oral Session 2: Animal Models of Behavior and Disease

TURNING ORDER INTO CHAOS THROUGH REPETITION AND ADDITION OF ELEMENTARY ACTS IN OBSESSIVE-COMPULSIVE DISORDER (OCD). [1]Zor, R. ; [2]Hermesh, H.; [3]Szechtman, H.; [1]Eilam, D. Dept of Zoology[1] and Psychiatry[2], Tel-Aviv University, Israel, and [3]Dept. of Psychiatry and Behavioural Neurosciences, McMaster University, Canada. A concept and methodology derived from an animal model was applied in studying rituals in Obsessive Compulsive Disorder (OCD) patients, to reveal objective and observable criteria for compulsive rituals and to identify a common structure underlying OCD rituals, pointing to a shared psychopathology. Eleven OCD rituals, each performed at the patient's home environment, were videotaped and compared with the behavior of healthy individuals instructed to perform the same rituals. The videotaped rituals were deconstructed into visits to specific locations or objects (ritual space), and to the acts performed at each location/object (ritual basic components). Quantitative analyses revealed that compulsiveness emanate from the expansion of repeats for some acts and visits, and from the addition of superfluous act types. Best discrimination between OCD and control rituals (90.9% success) was provided by the parameter 'maximum of act repeats in a ritual' (R2=0.77). Diverse compulsive rituals were based on the expansion of particular act repeats and visits, and incorporation of unnecessary acts. These attributes may elucidate the mechanism whereby ritual behavior shifts attention from a normal focus on structured actions to a pathological attraction on processing of basic acts that overtaxes memory, as recently hypothesized. These mechanisms may prove useful in objective assessment of psychiatric disorders, behavioral therapy, and OCD nosology.

ANTIDEPRESSIVE-LIKE EFFECTS OF RAPAMYCIN IN ANIMAL MODELS. Einat, H1; Linde, J1; Hiscock, K1; Cleary, C1; Belmaker, RH2; Agam, G2. 1College of Pharmacy, Duluth, University of Minnesota, Duluth, MN,2Faculty of Health Sciences, Ben-Gurion University, Beersheba, Israel. Lithium was recently demonstrated to enhance autophagy in cells. Recent hypotheses regarding the source of therapeutic effects of lithium as well as antidepressant drugs suggest that they may be related to increased neuroprotection and cellular ability to withstand a variety of insults. Hence it is a possibility that the action of lithium to enhance autophagy may be involved in its therapeutic action. A well documented mechanism to induce autophagy is by inhibition of mTOR and rapamycin is a commonly used inhibitor of mTOR. Accordingly, the present study was designed to evaluate the effects of rapamycin in animal models of antidepressant activity. The forced swim test in mice was used to explore doses and schedules of administration and was followed by additional experiments with mice and rats in the large open field, activity monitors, forced swim test and tail suspension test. Sub-chronic, but not acute administration of rapamycin doses of 10 mg/kg and above resulted in an antidepressant-like effect in mice and rats but had no affects on the amount or distribution of spontaneous activity. The results suggest an antidepressant effect of rapamycin. It is tempting to conclude that this effect is related mTOR inhibition but it is also possible that it is the consequence of effects on other intracellular pathways. Additional studies are now planned to further explore the behavioral range of rapamycin's effects in models of affective and anxiety disorders as well as further understanding the underlying biological mechanisms of these effects.

ASCENDING PROJECTIONS FROM THE ROSTRAL LATERAL PERIAQUEDUCTAL GRAY (rlPAG): A CRITICAL SITE FOR CONTOLLING FORANGING BEHAVIOR. Mota-Ortiz, S.R.; Bittencourt, J.C.; Elias, C.F.; Canteras, N.S. Dept Anatomy, Inst Biomed Sci, Sao Paulo 05508-900, BRAZIL. Previous studies suggested a role for the rlPAG in controlling foranging and insect hunting behavior. Both conditions are known to up-regulate c-fos expression in this particular PAG region, located in the outer half of the lateral column at the level of the oculomotor nucleus. In a recent study, we have shown that NMDA lesions of the rlPAG, in rats, drastically reduce the motivational drive to chase the prey during insect hunting. To understand how the rlPAG would be able to influence foranging activity, we first examined the ascending projections of the rlPAG using the Phaseolus vulgaris-leucoagglutinin (PHA-L) method. Ascending fibers from the rlPAG provide a substantial input to the lateral hypothalamic area, and also, to a lesser extent, to several intralaminar thalamic nuclei. In the lateral hypothalamus, these fibers were mostly distributed dorsolaterally to the fornix, in the region containing melanin concentrating hormone (MCH) and hypocretin/orexin (H/O) neurons. By immunostaining these peptides, we were able to confirm that the rlPAG anterogradely labeled fibers largely overlap with MCH and H/O neurons, where we could find a number of PHA-L labeled boutons in close proximity with these cells, perhaps establishing functional synapses. In conclusion, our results suggest that the rlPAG projects to the lateral hypothalamic area, and may provide direct inputs to MCH and H/O cells. This pathway certainly represents a likely candidate for the rlPAG to control foraging activity. Financial Support: FAPESP Grant 04/13849-5 and 04/14312-5

EFFECTS OF INTRAAMYGDALOID MICROINJECTIONS OF ACYLATED-GHRELIN ON FOOD INTAKE AND LEARNING. Lénárd, L.; Tóth, K.; László, K.; Lukács, E.; and Bagi, É. Institute of Physiol. and Neurophysiol. Res. Group of the Hungarian Academy of Sciences, Pécs University Medical School, Pécs, Hungary. Peripheral or hypothalamic injections of acylated-ghrelin (AGhr) increase food intake and influence learning processes. AGhr acts on growth hormone secretagouge receptor-(GHSR)-1a. I.c.v. applied AGhr caused c-Fos overexpression in the amygdala (AMY) and projections of ghrelinergic neurons to the basolateral nucleus of the AMY (BLA) were identified. In the experiments liquid food intake (MilkQuick, Nutricia; 136.45 kJ/100ml) was studied and open field, two-compartment passive avoidance (PAV) and elevated plus maze (EPM) paradigms were used after bilateral AGhr microinjections into the BLA of male wistar rats. Vehicle (0.15 M NaCl, 0.4 µl), AGhr (Sigma, G8903; 25, 50, 100 or 250 ng) or selective GHSR antagonist D-Lys3-GHRP-6 (ANT, Tocris, 1922; 30 ng) were applied and the ANT was also used 15 min prior AGhr applications. The 50 and 100 ng AGhr treatments caused significant decrease in food intake. In PAV 50 ng AGhr significantly increased latency time even after 1 week of conditioning. In the experiments ANT alone was ineffective. AGhr effects were eliminated by ANT pretreatments. There were no any alterations in the parameters of open field or EPM in AGhr treated rats. Results show that AGhr in the AMY decreases food intake and in aversive situations enhances learning and memory. These effects are specific because they can be eliminated by ANT pretreatment. AGhr effects can not be explained by any changes of general motor activity or by anxiety. Further experiments with specific antagonists of GHSR subgroups and investigations in other learning paradigms are necessary to cast light on detailed AGhr mechanisms of the AMY, however. Supported by ETT 317/2006, RET-0008 MEDIPOLIS and the HAS.

HYPERSENSITIVITY OF DOPAMINE TRANSPORTER KNOCKDOWN MICE TO THE EFFECTS OF THE DOPAMINE TRANSPORTER ANTAGONIST GBR 12909 Young, JW., Goey, AKL1., and Geyer, MA. Department of Psychiatry, UCSD, Gilman Drive, La Jolla, CA, 92093, U.S.A.. 1Utrecht University, Sorbonnelaan 16, 3584 CA, Utrecht, The Netherlands. Dopamine transporter (DAT) abnormalities have been linked to Bipolar Disorder (BD) mania and Attention Deficit Hyperactivity Disorder (ADHD). Genetic models of DAT abnormalities, such as DAT knockdown (KD) mice, have been proposed as a model of BD/ADHD. Their habituation to test conditions however, limits their use in assessing putative mania/hyperactivity alleviating agents. Combining a low dose of the DAT antagonist GBR 12909 may reassert the phenotype of DAT KD mice without altering normal WT behavior. To assess this hypothesis, male DAT KD and WT mice habituated to the mouse Behavioral Pattern Monitor were administered vehicle or 9 mg/kg GBR 12909 (n=8-9) immediately prior to spontaneous locomotor and exploratory behavior assessment. Over 60 min, significant interactions between gene and drug were observed for transitions ($F(1,29) = 5.03$, $p < 0.05$), whilst significant main effects of gene ($F(1,29) = 7.47$, $p < 0.05$) and drug ($F(1,29) = 5.59$, $p < 0.05$) were observed for nose-poking behavior. Post hoc analyses revealed that DAT KD mice administered GBR 12909 were significantly more active with greater exploratory behavior than both WT mice administered GBR 12909 and KD mice administered vehicle ($p < 0.05$). Additionally, WT mice administered vehicle did not differ significantly in any measure from those given GBR 12909, or from KD mice administered vehicle ($p > 0.05$). The results provide information on real time in vivo pharmacology in the context of habituation to testing in a novel environment. Moreover, this combined pharmacological and genetic manipulation provides a more compelling model with which to assess putative treatments for manic/hyperactive behavior.

CREB IS NECESSARY FOR LONG-TERM MEMORY FOR HABITUATION AND FOR MEMORY ASSOCIATED CHANGES IN GLUTAMATE RECEPTOR SUBUNIT EXPRESSION IN *CAENORHABDITIS ELEGANS*. Timbers, T.A.; Rankin, C.H. Dept. of Psychology and Brain Research Centre. University of British Columbia, Vancouver, BC V6T 2B5 Canada. Through behavioral mutant analysis we have shown that the transcription factor CREB (cAMP response element binding protein) is necessary for long-term of mechanosensory habituation in the nematode, *Caenorhabditis elegans*. *crh-1* (homologous to the mammalian CREB protein) mutant worms were not significantly different from wild-type worms when tested for short-term habituation, but when tested for long-term memory of habituation, *crh-1* mutant worms showed no evidence of long-term memory 24 hours after training. Through confocal imaging of GLR-1 (a non-NMDA-type ionotropic glutamate receptor subunit) subunits tagged with GFP our lab has shown that consolidation of memory for habituation in *C. elegans* is associated with a decrease in the average area of GLR-1 synaptic clusters 24 hours after long-term memory training. This is not observed in naïve worms (Rose et al., 2003 J. Neurosci., 23:9595-9600). Here we report that *crh-1* mutant worms expressing the GLR-1::GFP transgene do not show a decrease in the average area of GLR-1 synaptic clusters 24 hours after long-term memory training. This suggests that the decrease observed in wild-type worms expressing the transgene is caused by an as yet unknown CREB-dependent mechanism. We are currently using

mutant analysis to identify kinases that are responsible for CREB activation during long-term memory training, as well as using a CRE (cAMP response element) reporter gene assay to identify which neurons undergo changes in CREB-mediated synaptic plasticity. This work was supported by operating grants from NSERC to CHR and by Graduate Fellowships from MSFHR and CIHR to TAT.

6:00-8:00 Poster Session 2

Fear, Anxiety and Defense

OVEREXPRESSION OF CHIMERIC ESTRADIOL-GLUCOCORTICOID RECEPTOR (ERGR) IN BASOLATERAL AMYGDALA REDUCES ANXIETY AND INCREASES FEAR CONDITIONING IN NORMAL AND STRESSED RATS. Mitra R, Sapolsky RM. Department of Biological Sciences, Stanford University, Stanford CA-94305. Stress and glucocorticoid treatment is known to enhance anxiety. In fact, a single session of acute stress or glucocorticoid treatment can have enduring effect on amygdaloid neurons and amygdala-dependent behavior. On the other hand estradiol treatment and modulation of glucocorticoid receptors in amygdala is known to influence anxiety. To enhance the beneficial effects of estradiol and block the deleterious effects of glucocorticoid we overexpressed a chimeric receptor ERGR, with C-terminal glucocorticoid binding domain of GR (glucocorticoid receptor) and N-terminal DNA-binding domain of ER (estradiol receptor) in the basolateral amygdala (BLA) of adult rats via a herpes simplex viral vector gene therapy. This chimeric receptor can potentially transduce an adverse glucocorticoid signal to a protective estrogenic one. Following overexpression rats were either exposed to a single acute stress session or a single acute injection of high physiological glucocorticoid concentrations. Long-term effects of ERGR overexpression in stress and glucocorticoid treated animals on anxiety and fear conditioning were examined after 10 days of acute treatment. ERGR infusion in BLA reduced anxiety in all group of animals, independent of any treatment. This effect was specific to anxiety as general locomotion in all the treatment groups remained unaffected. Interestingly, fear conditioning was enhanced in all ERGR-treated animals. Thus, we show that overexpression of ERGR can reduce amygdala-dependent anxiety and facilitate fear memory in both normal and stressed animals.

CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE PERIAQUEDUCTAL GRAY ARE DIFFERENTIALLY REGULATED BY SEROTONERGIC MECHANISMS IN THE BASOLATERAL AMYGDALA. Martinez, R.C.R.; Oliveira, A.R.; Brandão, M.L. Universidade de São Paulo, FFCLRP, Brazil. Amygdala is an important filter for unconditioned and conditioned aversive information. The amygdala synthesizes the stimuli input from the environment and then signals the degree of threat that they represent to the dorsal periaqueductal gray (dPAG), which would be in charge of selecting, organizing and executing the appropriate defense reaction. We examined the influence of fluoxetine microinjections (1.75 and 3.5 nmol/0.2 mL) into the lateral (LaA) and basolateral (BLA) amigdaloid nuclei on the freezing and escape responses induced by electrical stimulation of the dPAG. Freezing behavior was also measured after the interruption of the electrical stimulation of the dPAG. On the following day, these rats were also submitted to a contextual fear paradigm to examine whether these microinjections would affect the conditioned freezing to contextual cues previously associated with foot shocks. Fluoxetine injections into both amygdaloid nuclei did not change the freezing and escape thresholds, but disrupted the dPAG-post-stimulation freezing. Moreover, the conditioned freezing was enhanced by fluoxetine. Whereas 5-HT mechanisms in the amygdala facilitate the acquisition of conditioned fear they inhibit the dPAG-post-stimulation freezing. However, the unconditioned fear triggered by activation of the dPAG is produced downstream of the amygdala.

ANXIETY-LIKE BEHAVIORS AND ANTINOCICEPTION INDUCED BY CORTICOTROPIN RELEASING FACTOR INJECTION INTO THE MOUSE PERIAQUEDUCTAL GRAY. Miguel, T. T.1; Nunes-de-Souza, R. L.2. 1PPG-CF UFSCar/UNESP, Sao Carlos, SP; 2Lab. Pharmacology, FCFAr/UNESP, Araraquara, SP, Brazil. It has been demonstrated that activation of the midbrain periaqueductal gray (PAG) elicits anxiety and antinociception. The neuropeptide corticotropin releasing factor (CRF) seems to be a candidate in the mediation of both reactions. This study investigated the effect of CRF (0-150 pmol/0.2 µl) injections into the mouse PAG on anxiety and nociception. Anxiety was assessed by recording % open arm entries and % open arm time in the elevated plus-maze (EPM) during 5 minutes. Nociception was assessed during 10 minutes through the formalin test (injection of 50 microliters of formalin 2.5% into the dorsal surface of the right hind paw). Intra-PAG infusion of CRF (150 pmol)

decreased % open arm entries (saline: 32.16 ± 3.04, CRF 75 pmol: 31.53 ± 2.92 and CRF 150 pmol: 18.54 ± 3.62; $p<0.05$, n = 9-15) and % open arms time (saline: 19.26 ± 2.09, CRF 75 pmol: 15.07 ± 1.59 and CRF 150 pmol: 9.27 ± 1.47; $p<0.05$). This anxiogenic effect was not related to any change in closed arm entries ($p > 0.05$). CRF (150 pmol) also decreased time (sec) spent licking the injected paw (saline: 168.01 ± 23.98, CRF 75 pmol: 152.55 ± 16.52 and CRF 150 pmol: 58.25 ± 17.99; $p<0.05$, n = 8-13). These results indicate an involvement of CRF mediation on anxiety and antinociception within the PAG in mice. It remains to be investigated whether the antinociceptive effect of CRF depends on its anxiogenic action. Financial support: Fapesp and CNPq.

FICTION OR TRUTH? DIFFERENTIAL PROCESSING OF AVERSIVE SCENES: AN ERP STUDY. Mocaiber, I.*; Erthal, F.S.*; Cagy, M.**; Figueira, I.*; Pereira, M.G.**; Machado-Pinheiro, W.**; Volchan, E.*; Oliveira, L.** *Federal University of Rio de Janeiro; **Federal Fluminense University. Brasil. Previous studies showed that task irrelevant aversive stimuli slowed the reaction time during the performance of the main task. Here we studied the effects of attenuating their affective content on both the behavioral task and the P300 component. Participants (N=30) had to judge the orientation of two peripheral bars (0.3º x 3.0º) presented bilaterally with a simultaneous central picture (9º x 12º) for 200ms. They had to ignore the central picture and attend to the peripheral bars, pressing one of two keys as quickly as possible as to whether the bars were in the same or different orientation. The pictures could display either injured or non-injured people. Participants performed the task in two contexts. In the "Fictitious" one, instructions read were that the injuries resulted from cinema make-up; while in the "Real" one, they were taken from real scenes. The EEG was recorded from Fz, Cz, Pz and the P300 component was extracted from a 200-500 ms window after stimuli onset. Results showed that the interference of the aversive pictures prolonging the reaction times during the "Real" context was abolished during the "Fictitious" one, aimed to attenuate their emotional content. Larger P300 waves for aversive pictures in the "Real" context were not present in the "Fictitious" one, suggesting a cognitive modulation of eletrocortical responses. Financial Support: CAPES, PRONEX-FAPERJ, MCT-CNPq, CNPq-Projeto Milênio.

CORRELATION BETWEEN C-FOS EXPRESSION AND BEHAVIOR OF RATS TESTED IN THE ELEVATED PLUS-MAZE IN THE PRESENCE AND ABSENCE OF LIGHT. Rico, J.L.; Morato, S. Dept. of Psychology and Education. University of São Paulo, Ribeirão Preto, SP 14040-901 Brazil. The elevated plus-maze is sensitive to environmental illumination and rats exhibit increases in the exploration of the open arms when tested in the dark. We investigated the activation of brain areas related to fear/anxiety after testing rats in the elevated plus-maze in the presence and absence of light. Male rats were divided into two groups and exposed either to an elevated plus-maze or a control cage similar to the home cage. Each group was divided into two subgroups, which were tested for 5 min either in the presence or absence of light. Two h later, their brains were removed and processed for c-Fos immunohistochemistry. Rats exposed to the elevated plus-maze in the dark exhibited significant increases in the exploration of the open arms, as well as significant increases in c-Fos expression in the lateral, basolateral, medial and central amygdala and dorsomedial hypothalamic nuclei when compared to rats tested in this model under illumination and to rats that remained in the control cage in the dark. Spearman correlations proved to be significant between c-Fos expression and exploratory behavior in the open arms, mainly in the dark condition involving the following areas: piriform cortex, central and basolateral amygdala, dorsomedial hypothalamus and deep layers of the superior colliculus. The exploration of the closed arms was also correlated with c-Fos expression in the median raphe nucleus. These results suggest a possible role for the piriform cortex, amygdala and hypothalamus in the modulation of rat exploratory behavior (involving anxiety or not) in the elevated plus-maze in the dark.

MODULATION AGGRESSION LEVELS IN THE RESIDENT - INTRUDER PARADIGM. Motta,S.C.; Gouveia,F.V.; Canteras,N.S. Departamento de Anatomia – ICB – USP – Brazil. The resident-intruder paradigm has been widely studied in the investigation of the aggressive behavior. In the present study we investigated the influence of the female's odors on the level of aggressiveness. During the three-week adaptation period, the resident was left with a female. Previous to the test, the female was removed, and during the test, an unfamiliar intruder was exposed to the resident. The female had been always removed one day before the test. In one group, we kept the wood shavings with the female scent, and compared to another group where the resident's cage was cleaned. More attack episodes and longer attacking periods were observed in males left with female scent. An examination of Fos expression in these residents revealed that increased aggression levels is apparently correlated with a weaker mobilization of elements of the sexual dimorphic hypothalamic system. The present study provides a reliable model to modulate the level of aggressiveness, a fact that can be really useful to understand its mechanisms. Financial Support: FAPESP n. 05/54511-0 and 05/59286-4.

IN VIVO LEVELS OF GASTRIN-RELEASING PEPTIDE AT THE BASOLATERAL AMYGDALA PREDICT FREEZING TO A FEAR-INDUCING EVENT Mountney, C.L., Kent, P., & Merali, Z. School of Psychology and Institute of Mental Health Research, University of Ottawa, Ontario, Canada. K1N 6N5. Gastrin-releasing peptide (GRP) has been shown to modulate conditioned fear. Research in our laboratory has demonstrated that GRP administered either intraventricularly (i.c.v.), or locally into the central or basolateral nucleus (BLA) of the amygdala or medial prefrontal cortex (mPFC), attenuated expression of fear in a conditioned fear paradigm. Receptor blockade and knockout studies have yielded mixed results. For instance, i.c.v. administration of a GRP receptor antagonist or the deletion of GRP receptor enhanced freezing in a fear conditioning paradigm, while antagonist administration directly into the BLA or infralimbic cortex decreased freezing. Given the modulatory effect of GRP on conditioned fear, the present study sought to measure the fear-induced release of GRP at the mPFC or BLA (in the same conditioned fear paradigm) using in vivo microdialysis. Rats were divided into 2 conditions; one group received 6 trials of a 20s (75kHz) tone paired with a 1s, 1 mA footshock (given during the final second of the tone), while the second group received the tone alone. The following day, in vivo dialysates were collected from animals (in their home cages) 1 h after probe insertion. After a baseline collection for 2 h, animals were tested for fear by scoring freezing behavior in response to the tone alone in cages different from the cages they were trained in the day before (different context). Freezing was scored for 10 min, after which the animals were returned to their home cages. The collection of dialysates was not interrupted during this testing period and was continued for an additional 3 h. Analyses of dialysates revealed that GRP release at the BLA increased in response to the tone and that this increase was significantly higher in animals that had previously received tone-shock pairings. Moreover, the increased GRP release was significantly correlated with freezing behavior such that levels of freezing (an indication of fear in the rat), accounted for a significant portion or the variability in release of GRP in the BLA. Similar peptidergic changes were not observed at the mPFC. These data indicate that at the BLA, GRP release is significantly correlated with levels of fear, suggesting that GRP may be an indicator/mediator of fear or that this peptide may play a role ascribing emotional salience of an aversive event.

ANXIETY INDUCED BY DIAZEPAM WITHDRAWAL REDUCES 22-kHz ULTRASOUND VOCALIZATIONS AND ENHANCES STARTLE REFLEX. De Ross, J.B., Castilho, V.M., Nobre, M.J. Laboratório de Psicobiologia, FFCLRP, Universidade de São Paulo, Ribeirão Preto, SP, Brasil. The interruption of a prolonged treatment with diazepam (DZP) leads to a withdrawal syndrome. In animals these signs oscillate from irritability to extreme anxiety-like behaviors. The expression of 22-kHz ultrasonic vocalization (USV) and the enhancement of startle reflex (SR) to a loud noise have been considered to be reliable measures of fear in rats. In this study we examined the effects of the DZP withdrawal on the expression of defensive reaction elicited by novelty or a loud noise. Wistar rats were submitted to 18-day oral treatment with sucrose (5%) or diazepam (10 mg/kg added to 2 ml of control solution). After 30 min (baseline) or 48 h (withdrawal) from the last drug administration the animals were tested on the USV and later to the SR procedures to evaluate changes in their reactivity to novelty or loud noise (40 trials of 110 dB stimulus). The results showed that control animals readily emitted 22-kHz calls during exposure to a novel environment and enhanced the SR. However, in spite of cause a significant increase in the SR amplitude DZP withdrawal reduced the 22-kHz USV induced by a new environment. We suggest that the high fear states promoted by DZP withdrawal reduces the ability of the animals to vocalize in the presence of proximal danger. Financial support: FAPESP (04/02859-0).

CHARACTERIZATION OF BETA-CATENIN KNOCK-OUT MICE IN BEHAVIORAL MODELS OF MOOD DISORDERS. O'Donnell, K.; Picchini, A.; Manji, H.; Gould T. National Institute of Mental Health, NIH, Bethesda MD. Lithium, a commonly prescribed mood stabilizer, has several direct targets, one of which is the enzyme glycogen synthase kinase-3 (GSK-3). We have been particularly interested in the role of GSK-3 in the canonical Wnt pathway, where its inactivation increases levels of the transcription factor beta-catenin. To explore the role of this pathway both in the central nervous system and in the therapeutic mechanism of lithium, we created conditional beta-catenin knockout mice. In situ hybridization revealed a progressive knockout of beta-catenin that began between 2 and 4 weeks of age, and resulted in minimal beta-catenin expression in many areas of the forebrain by 12 weeks. Behavioral characterization of the mice revealed relatively circumscribed behavioral alterations. Knockout mice did not differ from their wild-type littermates in the open field test, the black-white box, the active avoidance test, amphetamine-induced hyperlocomotion and sensitization, the hot plate test of pain sensitivity, or the forced swim test. In the tail suspension test, however, knockout mice spent significantly less time struggling (a depression-like phenotype). We are following up on these findings with additional behavioral tests relevant to bipolar disorder

and depression, such as sucrose preference and learned helplessness, as well as testing the response of these mice to antidepressant and mood stabilizing medications in the tail suspension test.

PERITRAUMATIC TONIC IMMOBILITY PREDICTS A POOR RESPONSE TO PHARMACOLOGICAL TREATMENT IN VICTIMS OF URBAN VIOLENCE WITH PTSD.Fiszman A[1]; Rego-Rocha V[1]; Mendlowicz, MV[2]; Marques-Portella C[1]; Coutinho EFS[3]; Souza WF[3]; Lima AA[1]; Volchan E[1]; Oliveira L[2]; Figueira I[1];[1]Federal University of Rio de Janeiro;[2]Federal Fluminense University;[3]Oswaldo Cruz Foundation. Tonic immobility is the last defense against predation in animals and is characterized by paralysis/rigidity and analgesia. In humans, it has only been reported in women victims of sexual abuse;This study evaluated the prevalence of peritraumatic tonic immobility (PTI) in patients with PTSD and investigated its association with response to treatment. Victims of urban violence with PTSD diagnosed through the SCID-IV (n=23) underwent a naturalistic pharmacological treatment according to the recommended guidelines for PTSD. The Post-Traumatic Stress Disorder Checklist - Civilian Version (PCL-C) and the Clinical Global Impressions (CGI) Severity scores were applied at baseline and endpoint. PTI was assessed using the Tonic Immobility Scale. Patients with PTI responded significantly poorly to treatment than those without it, either considering the PCL-C ($p<.05$) or the CGI ($p<.001$) scores. We have expanded the scope of the two previous investigations on PTI by showing its occurrence also in men and during non-sexual violence. In addition, the finding of a significant relationship between PTI and poor response to treatment of PTSD.

AFFECTIVE CHRONOMETRY OF SECURITY MOTIVATION. Hinds, A.; Szechtman, H. Dept. Psychiatry & Behav Neurosc, McMaster Univ, Hamilton, ON and Woody, E. Dept. Psychol., Univ Waterloo, Waterloo, ON, Canada. A recent theory (Szechtman & Woody, Psychol Review, 111:111-127, 2004) posits a Security Motivation System (SMS) activated by potential, rather than by imminent, threat to the individual. SMS coordinates species-typical motor activity that probes the environment for danger and includes behaviors such as checking (eg, for the presence of predators) and cleaning (for potential threats from germs, etc). Activation of SMS induces also an affective phenomenological cue of potential danger that is experienced as anxiety. We investigated whether a physiological correlate of an activated SMS would show the expected properties: activation by a relevant stimulus and persistence of activity until performance of the appropriate behavior. We report here on a paradigm that produces the expected results, a paradigm that can be employed in future studies to investigate the disturbance in SMS proposed to characterize obsessive-compulsive disorder. Participants were instructed to contact a high contamination-threat stimulus (diapers appearing soiled). Physiological measures of anxiety—heart rate variability and facial EMG activity—were taken prior to, during, and after exposure. Separate groups were either permitted to engage in the appropriate behavior (washing) or engaged in an irrelevant task. Measures of anxiety were significantly higher after exposure to the diapers as compared to baseline resting recordings. These measures remained significantly elevated in participants not given an opportunity to wash as compared to those permitted to wash. After hand washing, measures of anxiety returned to baseline. Supported by CIHR MOP134450.

CONDITIONED AND UNCONDITIONED FEAR ARE REGULATED BY GABAERGIC MECHANISMS IN THE DORSAL PERIAQUEDUCTAL GRAY. Reimer, A.E.; Oliveira, A.R.; Brandão, M.L. Laboratório de Psicobiologia, FFCLRP-USP, Ribeirão Preto, São Paulo. GABAergic neurons exert a tonic control on the neural substrates of the dorsal periaqueductal gray (dPAG) involved in the expression of defensive behavior. Microinjections of gabaergic agonists and antagonists into the dPAG reduce and promote defensive reactions, respectively. This work was aimed at investigating the effects of local injections of muscimol (1 and 2 nmol), a GABAA agonist, and semicarbazide (5 µg), an inhibitor of the GABA synthesis, into the dPAG on the expression of conditioned and unconditioned fear. To this end, Wistar rats chronically implanted with a chemitrode in dPAG were submitted to the fear potentiated startle test and dPAG electrical stimulation procedure for determination of freezing and escape thresholds. The dPAG post-stimulation freezing was also evaluated. Muscimol reduced the fear-potentiated startle, the aversiveness of the dPAG electrical stimulation (freezing and escape threshold) and dPAG post-stimulation freezing. In general, semicarbazide caused opposite effects. These data extend to the conditioned fear previous evidences that GABA exerts a control on the fear generated at the dPAG level.

POSTERIOR CINGULATE CORTEX HYPOMETABOLISM IMPAIRS SPATIAL MEMORY IN A FOOD SEARCH TASK. Riha, P.D.; Rojas, J.C., Gonzalez-Lima, F. Depts. Psychology and Neuroscience. University of Texas, Austin, TX 78712 USA. Posterior cingulate cortex (PCC) is the earliest to be metabolically affected by Alzheimer's disease (AD). Cytochrome oxidase (CO) activity is lowered within the PCC in AD. CO inhibition and resulting memory impairments was modeled in rats by injecting sodium azide into the PCC. Rats were trained in a baited holeboard task, subjected to either azide or sham surgery, and tested in an unbaited probe trial. Brains were

analyzed for CO activity. The effect of CO inhibition on lipid peroxidation, a measure of oxidative stress, was studied in vitro using brain homogenates exposed to different azide concentrations and quantified using the thiobarbituric acid reactive substances assay. Only azide-treated rats showed impaired memory for the baited pattern in the probe trial as compared to their training scores before treatment. This was not due to differences in general activity. CO histochemistry revealed significant decreases in the PCC in azide-treated rats as compared to controls. Interregional covariance analysis of CO activity revealed significant correlations between the PCC and other brain regions in the control group that were absent in the azide-treated group. Compared to controls, a seven-fold increase in lipid peroxidation was produced by the azide concentration used in the in vivo experiment. Thus, CO inhibition in the PCC resulting in reduced interregional correlations in brain activity and an increase in oxidative stress caused memory impairment in a holeboard task. This animal model presenting a metabolic inhibition similar to that in early stage AD could advance the understanding and treatment of AD. Supported by NIH grant MN65728.

DIFFERENT CONDITIONS OF CHRONIC SOCIAL ISOLATION INDUCES SIMILAR ANXIETY-LIKE BEHAVIOR IN RATS. Faggioni, F; Fabíola; Rosa, MLNM. Department of Biochemistry, Faculty of Medicine-FPA. Catanduva-SP, Brazil. Social isolation is considered to be a chronic source of stress and its effects have been related to alcoholism, pathologic depression, anxiety, and schizophrenia. The aims of the present study were to examine the exploratory activity and the levels of fear and anxiety in rats submitted to two different conditions of chronic social isolation, isolation-reared rats from weaning or isolated adult rats. Four groups of male wistar rats (n=12/each) were used. They were housed in a temperature-controlled room (23ºC), on a 12:12-h light:dark cycle, with free access to food and water. In two groups the pups remained with their mothers (6 pups per mother) until weaning (21 days) when they were allocated randomly to one of two conditions: 1) grouped, housed 4 per cage and handled 3 times a week; 2) isolated, housed individually and handled once a week. In the other two groups, the rats (130g) were allocated in the same conditions. Behavioral tests began after ten weeks of isolation. Exploratory activity was tested in a circular open arena (75 cm diameter) with the floor divided in 12 sections (same area). The animals were put into the middle of the arena and the behavioral responses scored every minute for 5 minutes: Number of crossings (horizontal exploration) and number of rearings (vertical exploration). The levels of fear and anxiety were tested in an elevated plus-maze (EPM) with two open and two closed arms. The animals were put on the middle of the arms and the behavioral responses scored for 5 minutes: Number of entries and time on the open arms, and number of entries and time on the closed arms. Groups were compared by Student t-tests and the level of significance was $p<0.05$. No change was found on horizontal exploratory activity following any condition of isolation stress. However, a statistically significant reduction (40-43%, $p<0.001$) was found on vertical exploratory activity in both isolated groups during the first minutes in the arena. Isolation-reared rats but not isolated adult rats showed significant reduction in the number of entries in both open (73%) and closed (47%) arms. However, the two isolation conditions induced an increase in the time spent on closed arms (28-33%). In addition, the time in the open arms were only 1,0% and 1,6% of the total time in isolation-reared rats and isolated adult rats, respectively. The results show that chronic isolation of adult rats or from weaning has no effect in the locomotor activity in a novel environment. However, the reduction in vertical exploratory activity induced by any isolation condition may be correlated with the anxiety-like effects observed in the EPM. Financial support: FAPESP (Processo: 2005/01501-7).

FMRI IN MICE REVEALS THAT EARLY LIFE STRESS IMPAIRS SEROTONERGIC NEUROTRANSMISSION IN THE PREFRONTAL CORTEX. Russig, H. (a); Razoux, F. (b,c); Mueggler, T. (b,c); Franklin, T.B. (a); Rudin, M. (b,c); Mansuy, I.M. (a). (a) Brain Research Institute, (b) Institute for Biomedical Engineering, University & ETH Zurich, (c) Institute of Pharmacology & Toxicology, University Zurich, Switzerland. Early life stress is a risk factor for the development of psychological and psychiatric disorders, such as depression in human. Although the underlying mechanism for this is not fully understood, the involvement of changes in serotonergic neurotransmission has been suggested. We are investigating these mechanisms in a mouse model of early life stress using C57Bl6 mice subjected to unpredictable maternal separation (daily 3h between post-natal days 1-14) combined with unpredictable maternal stress (MSUS). We observed that adult MSUS mice exhibit a depression-like phenotype in the Porsolt swim task and anhedonia in a sucrose consumption test. Since the 5-HT1A receptor has been implicated in the pathophysiology of depression and the action of antidepressant drugs, we examined whether serotonergic neurotransmission is altered in our mouse model using functional magnetic resonance imaging (fMRI, Bruker Pharmascan 47/16). During image acquisition MSUS and normally reared control (CON) animals were injected with the 5-HT1A receptor agonist 8-hydroxy-N-(di-n-propyl)-aminotetralin (8-OH-DPAT, 0.1mg/kg). A dose-dependent decrease in cerebral blood volume (CBV) was detected in brain regions expressing the 5-HT1A receptor in both CON and MSUS animals. However in the prefrontal cortex, this decrease was significantly diminished in MSUS compared to CON mice. These data therefore show that functional

investigation of the 5-HT1A receptor by fMRI is possible in adult mice using the 5-HT1A receptor agonist 8-OH-DPAT, and that this in vivo approach allowed us to demonstrate that early stress impairs serotonergic neurotransmission in the prefrontal cortex.

INVOLVEMENT OF DORSOMEDIAL AND VENTROMEDIAL HYPOTHALAMIC NUCLEI IN CONDITIONED FEAR AS ASSESSED BY FREEZING BEHAVIOR AND FEAR-POTENTIATED STARTLE. Santos, J.M.; Brandão, M.L. Dept. of Psychology and Education, University of São Paulo, Ribeirão Preto, Brazil. It is well established that GABAA receptor-mediated mechanisms regulate the defensive reaction organized in the medial hypothalamus (MH). However, there are few studies that investigated the involvement of the MH in conditioned fear. The aim of this work is to examine the involvement of gabaergic mechanisms of the dorsomedial hypothalamic nucleus (DMH) and ventromedial hypothalamic nucleus, dorsomedial part (VMHDM) in the expression of conditioned fear using the fear-potentiated startle (FPS) paradigm. In this test, the increase in startle reflex in the presence of a light that has been previously paired to a footshock is taken as an index of fear. To evaluate the role of GABA mechanisms of the DMH and VMHDM in conditioned fear, the GABAA agonist, muscimol (1 nmol) and the glutamic acid decarboxylase blocker, semicarbazide (6 mg) were microinjected into these nuclei before the testing session of the FPS. The local injection of muscimol into DMH and VMHDM decreased the time of freezing and counteracted the potentiation of the startle reflex to the light-CS when compared to saline. On the other hand, semicarbazide promoted an increase in both freezing and FPS when microinjected into these nuclei. Our results indicate that gabaergic mechanisms modulate conditioned fear responses in the DMH and VMHDM in a similar manner as they do with unconditioned fear. Thus, it is suggested that gabaergic mechanisms also exert an inhibitory control on the conditioned fear generated at these hypothalamic nuclei.

USE OF A PLATFORM IN AN AUTOMATED OPEN-FIELD TO ENHANCE ASSESSMENT OF ANXIETY-LIKE BEHAVIORS IN MICE. Pogorelov, V.M.; Lanthorn, T.H.; Savelieva, K.V. Lexicon Genetics, Inc., Department of Neuroscience, The Woodlands, TX, USA. The present report describes a new setup for simultaneously measuring anxiety-like behaviors and locomotor activity in mice. Animals are placed in a brightly-lit, standard automated open-field (OF) in which a rectangular ceramic platform 8 cm high covers one quadrant of the floor. Mice preferred to stay under the platform, avoiding the area with bright illumination. Activities under and outside the platform were measured for 5 min. Chlordiazepoxide and buspirone dose-dependently increased time spent outside platform (L-Time) and the light distance to total OF distance ratio (L:T-TD) in both genders without changing total OF distance. By contrast, amphetamine decreased L-Time and L:T-TD in males, thus displaying an anxiogenic effect. Imipramine was without effect on L-Time or L:T-TD, but decreased total OF distance at the highest dose indicative of a sedative effect. Drug effects were also evaluated in the OF without platform using conventional anxiety measures. Introduction of the platform into the OF apparatus strongly enhanced the sensitivity to anxiolytics. Comparison of strains differing in activity or anxiety levels showed that L-Time and L:T-TD can be used as measures of anxiety-like behavior independent of locomotor activity. Changes in motor activity are reflected in the total distance traveled under and outside the platform. Therefore the platform test is fully automated, sensitive to both anxiolytic and anxiogenic effects of drugs and genetic phenotypes with little evidence of gender-specific responses, and can be utilized by most laboratories measuring behavior. This work was published in J Neurosci Methods: 2007 Jan 26

BEHAVIORS OF WISTAR, WILD (Rattus norvegicus sp) AND HYBRID RATS IN THE RESIDENT-INTRUDER MODEL. Póvoa, R.M.F., Schenberg, L.C., Dept. of Physiological Sciences, UFES, 29043-125, Vitória, ES, Brazil. Here we examined the behaviors of Wistar (WIS), wild (WLD) or hybrid (HBR) rats (n=15/group) in the resident-intruder territory aggression. Male 'resident' rats were placed alone in a 100x40x40 cm wooden box with glass in top and front walls. Seven days after that, an intruder rat of any strain was introduced in the box and behaviors were recorded throughout 2 min with inside and outside cameras. Behavior frequencies were subjected to ANOVA and FACTOR analyses. Whereas the WLD resident rats showed high frequencies of lateral threat, jumping attack, approach and pursuing (offense), intruder responses were most often submission, supine attack, galloping and trotting (defense). These repertoires were mutually exclusive. In contrast, shrieking, hissing, boxing and biting were presented by rats both resident and intruder. Hybridization resulted in a loss of most territory aggression responses. The 3 principal factors of the whole rat population accounted for 100% of behavior variance (F-I, 60%; F-II, 24%; Factor-III, 21%). F-I loaded positively for most offensive items, but negatively for the defensive ones. However, trotting, boxing and shrieking correlated positively with F-I (offense), whereas galloping and biting did it negatively (defense). Thus, trotting and boxing seems to be the resident defensive items against the intruder defensive aggression.

DEFENSIVE BEHAVIORS PRODUCED BY STIMULATION OF DORSAL PERIAQUEDUCTAL GRAY MATTER (DPAG) OF WISTAR, WILD AND DERIVED RAT STRAINS. Póvoa, R.M.F.; Schenberg, L.C., Dept. of Physiological Sciences, UFES, 29043-125, Vitória, ES, Brazil. Stimulation of DPAG of rats produces exophthalmus (EXO), immobility (IMO), micturition (MIC), defecation (DEF), trotting (TRT), galloping (GLP) and jumping (JUM). Here we appraised the genetic determinants of DPAG-evoked defense reaction. Male rats (n=20) of Wistar (WIS), wild (WLD, Rattus norvegicus sp.), hybrid (HBR, WISxWLD), hypertensive (SHR) and Wistar-Kyoto (WKY) strains were implanted with electrodes in the DPAG and stimulated with stepwise-increasing sine-wave pulses (0-70 µA, 60 Hz). Median intensities (I50) and maximum responsiveness (R50, slope at I50) were estimated through the logistic threshold analysis and compared by likelihood ratio c2 tests. WIS rats presented the lowest I50 for most defensive responses, but not DEF and MIC which thresholds were the highest second to SHR (these responses virtually lacked in SHR). In contrast, WLD rats presented the highest I50 for IMO, EXO and JUM, being the second to SHR for TRT and GLP. Yet, WLD (and WKY) rats presented the highest R50 for most defensive behaviors, whereas the lowest ones were those of WIS and SHR. Thus, the lower thresholds of WLD rats to predators (higher reactivity) should be ascribed to differences in brain areas other than the DPAG. However, once the threat is detected, the response readiness of this species is likely to be due to the higher responsiveness of DPAG.

EFFECTS OF CORTICOSTEROID CENTRAL INJECTIONS (ICV) ON DEFENSIVE BEHAVIORS PRODUCED BY STIMULATION OF DORSAL PERIAQUEDUCTAL GRAY MATTER (DPAG) OF THE RAT. Rangel, T.C.; Schenberg, L.C. Dept. of Physiological Sciences, UFES, 29043-125, Vitória, ES, Brazil. Previous results showed that peripheral injections of dexamethasone (DEXA) caused a marked reduction in the thresholds of DPAG-evoked immobility. In contrast, micturition thresholds were significantly increased. Because DEXA is supposed to suppress the hypothalamus-pituitary-adrenal (HPA) axis peripherally, we evaluated the effects of ICV injections of corticosterone (CORT) and DEXA on these behaviors. Wistar male rats bearing an electrode in the DPAG and a cannula in the lateral ventricle were submitted to 4 stimulation sessions with sine-wave increasing intensities (0-90 µA, 60 Hz, a.c.) in 3 consecutive days: Day 1 - control, Day 2 - 15 min and 3 h after the central injection of either CORT (40 µg /15 µL, n=20) or DEXA (0.8 µg /15 µL, n=20), Day 3 – washout. Threshold logistic curves were compared through likelihood ratio tests. Whereas the DEXA central injections facilitated jumping, they attenuated galloping and defecation. CORT had similar effects on jumping and galloping, but facilitated defecation and micturition. Thus, DEXA previous effects should be ascribed to the peripheral suppression of HPA axis and ensuing reduction in CORT plasma levels. Financial support: CNPq, CAPES.

HYPOTHALAMUS-PITUITARY-THYROID (HPT) FUNCTION IN PERIAQUEDUCTAL GRAY (PAG)-EVOKED DEFENSIVE BEHAVIORS. Siqueira, C.C., Tiengo, A.N.C.P., Schenberg, L.C., Dept. of Physiological Sciences, UFES, 29043-125, Vitória, ES, Brazil. Because thyroid diseases had been long related to psychiatric disorders, we examined the influence of HPT axis function in the PAG-evoked defense reaction and in the elevated-plus-maze (EPM), models of spontaneous panic attacks and generalized anxiety disorder, respectively. The acute treatment with TRH (1 mg/kg, i.p.) produced significant increases (? =39-50%, $P<0.05$) in the thresholds of PAG-evoked immobility, trotting, galloping, jumping and exophthalmus. Saline had no effects. Moreover, the 10-day treatment with the antithyroid drug methymazol (MTZ, 0.6 mg/kg/day/10 days) produced significant increases (?=51-108%, $P<0.05$) in the thresholds of exophthalmus, immobility, trotting, galloping, jumping, defecation and micturition. Particularly, galloping threshold increases outlasted the hypothyroidism in almost 20 days. MTZ increased the EPM open-arm exploration in the 5th treatment day and in the 10th washout day but not in the 10th treatment day in which we found the highest level of thyrotrophin. These data suggest that whereas the TRH inhibits the PAG-evoked defensive behaviors, it has no effects on EPM anxiety-like behaviors. The present study corroborates the clinical evidences suggesting that panic attacks are inhibited in hypothyroidism and facilitated in hyperthyroidism. Support: CNPq.

DEFENSIVE BEHAVIORS INDUCED BY INTENSITY- OR FREQUENCY-VARYING STIMULATION OF PARS DIFUSA (DMD) AND PARS COMPACTA (DMC) OF DORSOMEDIAL HYPOTHALAMIC NUCLEUS OF THE RAT. Alves, A.C.A.; Pezzin, F.D.N., Schenberg, L.C., Dept. of Physiological Sciences, UFES, 29043-125, Vitoria, Brazil. The dorsomedial hypothalamic nucleus has been proposed as a crucial structure in the organization of defensive behaviors in rats and anxiety disorders in humans. Nevertheless, its role in rat defensive behaviors remains uncertain. Here we examined the behavioral repertoire induced by sine-wave pulses of increasing intensities (0-75 µA, 60 Hz), or square-wave pulses of increasing frequencies (30 µA, 1 ms, 0-130 Hz), applied either to the DMD or DMC. Response curves were fitted by logistic threshold analysis and compared by likelihood ratio c2 tests

(5% Bonferroni's criterion). As previously described for the dorsal periaqueductal gray matter (DPAG), sine-wave stimulation of both divisions produced immobility, exophthalmus, defecation, micturition, trotting, galloping and jumping. In contrast, frequency-varying high-resolution stimulation failed in producing the last 3 responses and was only effective in the DMC. Moreover, apart from trotting and jumping, responses were less vigorous and presented higher thresholds than those of DPAG. These data implicate the DMC in the organization of exophthalmus, defecation, micturition and, perhaps, immobility, but not the remaining defensive responses that were most probably due to the stimulus spreading to nearby structures.Support: CAPES, CNPq.

PROGESTERONE EFFECTS ON DORSAL PERIAQUEDUCTAL GRAY (DPAG)-EVOKED DEFENSIVE BEHAVIORS OF OVARIECTOMIZED FEMALE RATS. Tiengo, A.N.P.[1]; Vasconcellos, A.P.[3]; Rosalém, G.F.[1]; Schenberg, L.C.[1]; Tufik, S.[4]; Bittencourt, A.S.[2]; Depts. of [1]Physiological Sciences and [2]Morphology, Federal University of Espírito Santo, 29043-125, Vitória, ES; [3]Salesiano School of Vitória, 29017-950, Vitória, ES, [4]Dept. of Psychobiology, Federal University of São Paulo, 04023-900, São Paulo, SP, Brazil. Because progesterone (PROG) and its metabolite, allopregnanolone, have conspicuous anxiolytic actions, plasma level fluctuations of these hormones have been implicated with female emotional changes and premenstrual syndrome (PMS). Here we examined whether the suspension of the chronic administration of PROG, a model of PMS, has any effect on PAG-evoked defensive behaviors, a model of panic attack. Ovariectomized female Wistar rats bearing electrodes in the DPAG were chronically treated with either saline or PROG (4 mg/kg/day/10 days, sc). Thresholds of defensive behaviors were recorded before, in the 10th treatment day and throughout a 20-day washout. Response curves were fitted by threshold logistic analysis. Compared to saline group, micturition thresholds were significantly increased following PROG suspension. Trotting and galloping thresholds were increased in both PROG and saline groups. Thresholds of exophthalmus, immobility, jumping and defecation did not change. Thus, the present data suggest that estradiol but not PROG exerts an inhibitory modulation of these behaviors. Support: CNPq, AFIP.

ACUTE TREATMENT WITH DIAZEPAM BUT NOT CHRONIC TREATMENT WITH FLUOXETINE AND IMIPRAMINE REVERSED THE ANXIOGENIC PROFILE OF SHORT-TERM ISOLATION IN RATS TESTED IN THE ELEVATED PLUS-MAZE MODEL OF ANXIETY. 1CURIO, M;1JACONE, H;1PERRUT, J;1SILVA, RCB; 2BRANDÃO,ML. 1 Dep. of Psychology Univ. Estacio de Sá; 2 Lab. de Neuropsicofarmacologia Univ. de São Paulo, Brasil. Isolated rats display anxiogenic profile on the elevated plus-maze (EPM) compared to grouped controls. The EPM is one of the most widely used animals models in contemporary preclinical research on anxiety. The present study investigated if the treatment with diazepam, fluoxetine and imipramine, drugs with distinct pharmacological mechanisms of action, would reverse the anxiogenic profile of short-term isolation in rats tested in the EPM. Male Wistar rats were isolated for a period of 12 or 24 h and their behavior on the EPM was studied. Acute treatment with diazepam (5 mg/kg; IP) produced an anxiolytic profile in rats isolated for both 12 and 24 h. This effect was observed by the increase in the percentage of open-arms entries and percentage of time spent in the open arms. Chronic treatment (21 days) with fluoxetine and imipramine (10 mg/kg, IP) decreased the percentage of open arms entries and percentage of time spent in the open arms in rats isolated for 24 h . No effect was observed in rats isolated for 12 h. The anxiolytic effect of diazepam observed in this study corroborate with the effect of this treatment in the clinic. The lack of anxiolytic effects of chronic fluoxetine and imipramine also conforms with the poor efficacy of this drug in anxiety. Although diazepam has been used to treat anxiety, fluoxetine and imipramine is a mainstay in the treatment of depression.

EFFECTS OF MALNUTRITION ON MEMORY AND ANXIETY IN RATS. Silveira, A.C.D.1; Dias, G.P.1; Bevilaqua, M.C.N.1; Moraes, M.C.S.2; Cardenas, F.P.3; Landeira-Fernandez, J.4; Rocha, M.S. 2; Gardino, P.F.1; Hokoç, J.N.1.1-Lab. Neurobiologia da Retina, IBCCF/UFRJ; 2- Lab. Farmacologia da Neuroplasticidade – Depto Farmacologia Básica e Clínica – UFRJ 3- Lab.Neurociência e Comportamento – Universidad de los Andes, Colombia; 4– Lab.Neurociência e Comportamento – PUC-RJ e Universidade Estácio de Sá. Malnutrition is one of the major causes of mortality. This study aimed to investigate the effects of Regional Basic Diet, a Brazilian malnutrition model on hippocampal neurons as well as on memory and anxiety-like behavior in adult rats. Animals were tested in the elevated plus-maze (EPM), the Morris water maze (MWM) and the inhibitory avoidance test (IAT). Animal brains were sectioned (40µm) and stained trough Nissl and BrdU methods. Statistical analysis was made using the t test or two way ANOVA test. Malnourished rats have significantly less hippocampal Nissl stained cells (CA1: 24.69±0.48/100µm²;.CA3:.24.50±0.59/100µm²; DG: 25.69±0.94/100µm²) when compared to control (CA1: 31.54±0.59/100µm²; CA3: 29.54±0.84/100µm²; DG: 34.76±0.61/100µm²). Significantly less proliferating cells (BrdU+) were observed in the malnourished group (154.7±26.40/mm³; control: 300.0±35.13/mm³). EPM: Malnourished rats presented an increase in percentage of open arm entries. MWM: Latency in malnourished rats

(82.2±11.2s) did not decrease as observed in control animals (11.6±3.9s). The experimental group showed difference from the 2nd testing day. IAT: No significant difference was observed in the average latency time between groups (control: 118.7s; malnourished: 120.0s). These preliminary data show that malnutrition alters the number of cells and proliferating cells in the hippocampus. These changes could be deleterious for spatial memory and learning (MWM). The emotional system also seems to be impaired, as revealed by the tendency of malnourished rats to explore even aversive environments (EPM). Interestingly, malnourished rats did not present alterations concerning aversive stimuli learning (IAT).

D2 AGONIST QUINPIROLE ELICITS 50 kHz ULTRASONIC VOCALIZATIONS FROM THE NUCLEUS ACCUMBENS IN RATS. St. Pierre, J.; Brudzynski, S.M. Dept. of Psychology, Brock University, St. Catharines, ON, L2S 3A1 Canada. In rat vocal communication, 50-kHz ultrasonic vocalizations are an important element of social behaviour, including sexual behaviour, play, and food reward, and can signal an appetitive state in the rat. These calls can be pharmacologically elicited, primarily by activation of the dopaminergic system terminating in the nucleus accumbens shell. The purpose of this study was to determine whether a D2 receptor agonist (quinpirole) apllied directly to the nucleus accumbens shell is capable of eliciting 50 kHz vocalizations. A selective D2 agonist, quinpirole was able to elicit significantly higher numbers of 50-kHz calls than saline ($p < .04$) in a group of 15 animals. This response was copmparable to that induced by intraccumbens d-amphetamine injections ($p < .02$) in the same animals. The pharmacologically induced vocalizations were acoustically indistinguishable from naturally ocurring calls in sound frequnecy, single call duration, and bandwidth. The response to quinpirole was dose-dependent from 3 ìg to 20 ìg, with a maximal response at 6 ìg. When the site of injection was pretreated with raclopride, a selective D2 antagonist, the number of calls was decreased to control levels, however this effect did not reach statistical significance due to a small number of repetitions. This study indicates that the direct activation of the D2 receptor in the nucleus accumbens shell is capable of eliciting 50 kHz calls in Wistar rats. Supported by a grant from NSERC of Canada.

THE ACUTE BEHAVIORAL AND PHYSIOLOGICAL RESPONSE IN RATS TO A PREDATOR-SCENTED STIMULUS: HOME CAGE VS. OPEN FIELD EXPOSURE TO THE STIMULUS. [1]Suarez, M., [2]Walter, G.C., [2]Platt, D.W., [3]Thompson, A.C., & [2]DiPirro, J.M. [1]Dept. of Psychology, University at Buffalo, [2]Dept. of Psychology, Buffalo State College, [3]Research Institute on Addictions, University at Buffalo, Buffalo, NY, USA. Exposing a rat to a cat-scented cloth induces long term changes in behavior that model Posttraumatic Stress Disorder (PTSD). It is generally believed that PTSD is initiated by the acute biological response to a traumatic event and that the probability of developing PTSD is related to the intensity of that response. Our lab has been developing a predator exposure model with which to study PTSD that exposes a rat to the scent of a cat. The current study was designed to determine if the magnitude of the stress response to a cat-scented stimulus varied as a result of the environment in which the rat was exposed to the stimulus: the rat's home cage vs. an open field apparatus. Changes in defensive behavior, pain sensitivity and plasma glucose levels were used to evaluate the stress response. Adult male Long Evans rats were exposed for 15 minutes to a cat-scented cloth, an unscented cloth, or no cloth in either their home cage or an open field; pain sensitivity was assessed by hotplate assay at the end of the test in some rats while other rats were immediately killed to collect trunk blood and brain tissue. Rats exposed to the cat-scented cloth showed significantly more avoidance behavior and significantly higher glucose levels than rats in the other groups. Behavioral differences, but not glucose levels, were more pronounced among rats tested in their home cage. These results support the idea that cat-scent induces a stress response, and that the environment in which the rat is exposed to the cat-scent modifies the intensity of the response.

ANXIOLYTIC EFFECT OF SWEET ORANGE AROMA IN WISTAR RATS. Faturi, C.B.[1]; Leite, J.R.[1]; Canton, A.C.[2]; Teixeira-Silva, F.[2] [1]Department of Psychobiology, Universidade Federal de São Paulo, Brazil. [2]Department of Physiology, Universidade Federal de Sergipe, Brazil. Aromatherapy is the use of essential oils as an alternative treatment for medical purposes. Despite the lack of sufficient scientific proof, it is considered a holistic complementary therapy employed to enhance comfort and decrease distress. Citrus fragrances have been particularly used by aromatherapists for the treatment of anxiety symptoms. Based on this claim, the present study investigated the effects of Citrus sinensis (sweet orange) essential oil on rats evaluated in the elevated plus-maze followed by the light/dark paradigm. The animals were exposed to the orange aroma (100, 200 or 400 µl) for five minutes while in a Plexiglas chamber and were then immediately submitted to the behavioral tests. At all doses, Citrus sinenis oil demonstrated anxiolytic activity in at least one of the tests and, at the highest dose it presented significant effects in both animal models, as indicated by increased exploration of the open arms (elevated plus-maze) and of the lit

chamber (light/dark paradigm). These results suggest an acute anxiolytic activity of sweet orange essence, giving some scientific support to its use as a tranquilizer by aromatherapists.

BEHAVIORAL ACTIONS OF INTRANASAL APPLICATION OF DOPAMINE: EFFECTS ON FORCED SWIMMING, ELEVATED PLUS-MAZE AND OPEN FIELD PARAMETERS. Bianca Topic[1], Tim Buddenberg[1], Maria A. de Souza Silva[1], Joseph P. Huston[1], Claudia Mattern[2] [1]Institute of Physiological Psychology, University of Düsseldorf, Universitätsstr. 1, 40225 Düsseldorf, Germany [2]Mattern Pharmaceuticals AG, Stans, Switzerland . Recently, we found evidence that dopamine (DA), dissolved in a special galenic formulation (DopaMat) and administered intra-nasally in the rat, can enter the brain, leading to an immediate pronounced increase in extracellular DA levels in striatal subregions. This offers a potential alternative approach to treat Parkinsons's Disease (PD), since systemically administered dopamine by conventional routes cannot cross the blood brain barrier. In the present study, we aimed to examine whether the neurochemical effects of intra-nasally applied DA finds a parallel on behavioral activity when applied via this route. Male Wistar rats (3-4 months old) were tested for potential behavioral effects of intra-nasally applied dopamine in a behavioral screening paradigm for antidepressive-like activity (forced swimming test, FST), as well as a test for anxiety (elevated plus-maze), and on general motor activity in a novel and familiar open field. We found that intra-nasally administered dopamine in a dose of 0.3 mg/kg exerted antidepressant-like activity in the FST, but had neither anxiolytic- nor anxiogenic-like effects in the elevated plus-maze. Furthermore, intranasal dopamine (0.3 mg/kg) stimulated locomotor activity in a familiar, but not novel, open field. Thus, these results provide support for the view that intra-nasally applied DA might act on the central nervous system by entering the brain via the nose-brain pathway, making this kind of application procedure a promising alternative for targeting the brain, and, thus, treating disorders involving dopaminergic deficiencies, such as PD.

ANTIPANIC-LIKE EFFECT OF CHRONIC TREATMENT WITH FLUOXETINE ON FEAR-INDUCED RESPONSES ELICITED BY PREYS IN CONFRONT WITH RATTLESNAKES Ubiali, WA; Rocha, MJ; Coimbra, NC. Department of Pharmacology, FMRP-USP, Brazil - The aim of the present study was to investigate the effect of the peripheral and chronic treatment with fluoxetine, a selective serotonin reuptake inhibitor on the defensive behavior evoked by rodents confronted with wild venomous snakes in a prey/predator paradigm. The defensive behavior was recorded as follows: interruption of movements with attentive response toward the snake was considered alertness; defensive immobility followed by exophthalmus, piloerection and/or defecation/urination were considered freezing response; jumps, running were considered escape responses. Flat back approaching (risk assessment) with startle, and interaction with the serpent were also recorded as defensive responses. The fear-induced behavior of rodents and the motor/aggressive behavior of snakes were recorded from 1-1min during 15-min inside a quadrangular arena with transparent walls, recovered with insulfilm and illuminated with a 20W fluorescent lamp. Data were submitted to Kruskal-Wallis One-Way analysis of variance (ANOVA), followed by Mann-Whitney post hoc test. The present results suggest that the chronic serotonin reuptake inhibition with fluoxetine caused antipanic-like effect in animals in critical survival conditions, and reinforce the defensive immobility (freezing) response as an efficient experimental model for panic syndrome disorder studies, using prey/predator agonistic behavioral procedures. This work was supported by FAPESP, CNPq and FAEPA.

CORTISOL AND CARDIOVASCULAR RESPONSES TO PSYCHOLOGICAL STRESS: VULNERABILITY, RESILIENCE AND INDIVIDUAL DIFFERENCES. Souza GGL[1]; Mendonça-de-Souza ACF[1]; Vieira, A[1]; Barros, EM[1]; Fischer NL[1]; Coutinho EFS[2]; Oliveira,L[3]; Rumjanek VM[1]; Mendlowicz MV[3]; Figueira I[1]; Volchan E[1]. [1]Federal University of Rio de Janeiro; [2]Oswaldo Cruz Foundation; [3]Federal Fluminense University. Previous studies showed that glucocorticoids play a central role in stress responses. Cardiovascular activation is also part of the acute stress response but there is uncertainty about the relationship between cortisol release and cardiovascular stress responses. We investigated if individual predispositions and emotional priming influence the reactivity to and the recovery from a psychological stress. Psychometric scales and resting cardiac vagal tone were used to measure individual traits. Heart period and salivary cortisol were recorded throughout the experiment as dependent variables. After adaptation, participants viewed either a sequence of pleasant or unpleasant pictures as emotional primers. Then, they had to prepare and deliver a speech in front of a camera. Stress induced tachycardia irrespective to mood induction or individual traits. However, cortisol response to acute stress was only present for those that viewed unpleasant pictures and scored above the average in the negative affect scale. In the recovery phase, participants presenting higher resting vagal tone and those presenting higher resilience significantly turned down the heart acceleration. Furthermore, these traits interacted synergistically in the promotion of the recovery of heart period. Pleasant priming also improved recovery for participants with lower negative affect. In conclusion, participants presenting high

negative affect were more vulnerable to unpleasant priming prior to an acute stressor and were the ones that showed significant cortisol release. The heart period recovery was modulated by "healthier" affective predisposition and pleasant emotional priming.

IMPACT OF SOLENACE EXTRACTS AND THE NITRIC OXIDE SYNTHASE INHIBITOR L-NAME ON ANXIETY AND PAIN RELATED BEHAVIOR IN RAT AS MEASURED IN THE STAIRCASE MODEL. Wiertelak, E.P.; Kaplan, R.; Department of Psychology and Cognitive and Neuroscience Studies Program. Macalester College, Saint Paul MN 55105 USA. While therapeutic intervention in anxiety has been traditionally comprised of the use of such prototypic anxiolytics as benzodiazepines, the study of an endogenous neurotransmitter associated with anxiety like nitric oxide (NO) allows a clearer picture on neural mechanisms underlying anxiety. Such mechanisms may also have strong overlap with circuitry underlying the reported pain relief provided by a variety of natural remedies that are currently not confirmed by findings in standard pain assays such as the tailflick or hotplate tests. The present studies were aimed at examining the range of behaviors produced in the rat staircase model of anxiety for the purpose of exploring these possibilities. In rats given a NO synthase inhibitor, L-NAME, we found that L-NAME significantly reduced apprehensive behaviors associated with anxiety. This data adds to the converging evidence that NO plays a significant role in the regulation of anxiety. The impact of extracts of plants from the solenace family, used in many folk medicines for pain relief will also be examined. The initial data also supports the contention that use of the staircase apparatus may provide a relatively simple procedure for assessing the behavioral impact of a variety of substances. Supported by grant NIH (NCCAM) 1R15AT002705-01 to EPW.

THE ROLE OF AMYGDALAR MU OPIOID RECEPTORS IN ANXIETY RESPONSES. Marlene A. Wilson, Lorain Junor, Kris A. Ford, And Steven P. Wilson, Dept. Pharmacology, Physiology & Neuroscience, Univ. South Carolina School of Medicine, Columbia SC. Our recent work suggests that the anxiolytic effects of the benzodiazepine agonist diazepam involve opioid systems in the central nucleus of the amygdala. These studies investigated the role of mu opioid receptors (MOR) in the central amygdala on anxiety-related behaviors and the anxiolytic actions of diazepam in two animal models of anxiety behavior, the elevated plus maze and the defensive burying task. Male rats were outfitted with indwelling cannulas aimed at the central amygdala one week before testing. Animals were injected with a MOR agonist (DAMGO), a MOR antagonist (CTAP), or vehicle (saline) into amygdala prior to receiving a systemic injection of vehicle or diazepam (1 mg/kg, i.p.). Thirty minutes later animals were tested in the plus maze or defensive burying test. Since opioid peptides in the amygdala modulate nociception, a ferret-scented towel was used in the defensive burying test. DAMGO significantly decreased open arm time in the plus maze compared to control levels, while CTAP had an anxiolytic-type effect ($P<0.05$). In contrast, DAMGO significantly decreased burying behavior (an anxiolytic-like effect) in the defensive burying test, although this may have been due to a shift toward escape behaviors in DAMGO-treated animals (rather than burying). DAMGO or CTAP injections into the amygdala did not influence the anxiolytic actions of diazepam in either test. The results suggest that opioid peptides acting via MOR may influence distinct circuits in amygdala to influence anxiety-like behaviors in these two tasks. We are currently using virus-mediated gene transfer to modify MOR expression in this area to further elucidate the role of amygdalar MOR receptors in controlling anxiety responses. Supported by NIH RO1 MH063344.

ANTAGONISM OF NMDA RECEPTORS IN THE DORSOLATERAL PERIAQUEDUCTAL GREY INDUCES DIFFERENT PATTERNS OF CELLULAR ACTIVATION AFTER PREDATOR EXPOSURE. Aguiar DC, Guimarães FS- Department of Pharmacology, FMRP-USP, Brazil Nitric oxide (NO) is closely associated with glutamate-mediated neurotransmission in the central nervous system. NOS containing neurons are located in brain areas related to defensive reactions, including the dorsolateral periaqueductal gray (dlPAG). Glutamate antagonists and NOS inhibitors injected into this structure induce anxiolytic responses whereas glutamate agonists and NO donors promote flight reactions. Exposure to an innate fear induces defensive reactions, cFos expression and activation of NO producing neurons in areas related to defensive behavior. The aim of the present study was to test the hypothesis that a glutamate NMDA-receptor antagonist, AP7, injected into the dlPAG would attenuate defensive reactions and cellular activation in regions related to defensive reactions following exposure to a live predator. Methods: Male Wistar rats (n=5-7) with cannulas aimed at the dlPAG received injections of AP7 (2 nmol/0.2 microL) or saline and were exposed to a toy (control) or live cat for 10 min in a Plexiglas box. After cat exposure the brains were removed and processed for cFos and NOS immunochemistry. Double-stained cells (DS) were represented as percentage of NOS positive neurons. Results: Exposition to the predator induces defensive reactions which were prevented by AP7 pretreatment. Cat exposure induced an increase in Fos positive cells and % of DS in the dlPAG, paraventricular nucleus and premammillary dorsal nucleus (PMd). AP7 pretreatment reduced this effect

only in the dlPAG, but enhanced cellular activation in the PMd. Conclusions: These results suggest that activation of glutamatergic neurotransmission in the dlPAG is essential for the behavioral responses to predator exposure. Blocking of this neurotransmission attenuates these responses but enhances activation of rostral areas involved in fear responses. Financial Support: FAPESP

INCREASES IN PLASMA CORTICOSTERONE AND STRETCHED-ATTEND POSTURES IN RATS NAIVE AND PREVIOUSLY EXPOSED TO THE ELEVATED PLUS-MAZE ARE SENSITIVE TO THE ANXIOLYTIC-LIKE EFFECTS OF MIDAZOLAM. Laboratório de Psicobiologia, FFCLRP, Universidade de São Paulo - Ribeirão Preto, SP, Brazil. Albrechet-Souza, L; Franci, CR and Brandão, ML. A single exposure to the elevated plus-maze (EPM) test reduces the anxiolytic effects of benzodiazepines on a second trial. This phenomenon is known as one-trial tolerance. Activation of the hypothalamo-pituitary-adrenal (HPA) axis is a usual response to stressful conditions. The present study looked at the functioning of the HPA axis underlying one-trial tolerance through the examination of midazolam effects on the behavior and plasma corticosterone of rats exposed to single or repeated sessions in the EPM. The results obtained confirmed that the approach/avoidance conflict on the first trial of the EPM is sensitive to the anxiolytic effects of midazolam. Moreover, stressful stimuli present upon initial exposure render the standard measures of the EPM resistant to these effects on re-exposure. The increases in plasma corticosterone and risk-assessment behavior observed in rats submitted to single or repeated sessions in the EPM were reversed by pretreatment with midazolam. As the stress activation of the HPA axis occurs in both the conflict of the test and the anxiolytic-insensitive fear state of the retest, it is suggested that while the conflict is suppressed upon re-exposure to the EPM the fear of the open arms remains unchanged across the sessions.

SWIM-TEST AS A FUNCTION OF CATALEPSY INDUCED BY HALOPERIDOL IN MICE: AN ANIMAL MODEL FOR THE EVALUATION OF ADENOSINE A2A RECEPTOR ANTAGONISTS AS ANTI-PARKINSONIAN AGENTS. Azam, F.1,2; Khokhra, S.L.1; Prakash, O.1 1.Department of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, Haryana 136119, India; 2.Faculty of Pharmacy, Seventh of October University, PO Box 2909, Misurata, Libya. Catalepsy is induced by the dopamine D2 receptor block of haloperidol (HP) and characterized by the rigid state of a part or all of the muscle representing an animal model for Parkinson's disease or for neuroleptic-induced Parkinsonism in humans. In the present study we investigated the fact that swim-test which reveals an overall motor ability of the animal is a reliable method to study catalepsy induced by the HP. Chronic treatment of HP induces oxidative stress due to increased turnover of dopamine, and is thought to be responsible for its extrapyramidal side effects. The oxidative stress and extrapyramidal side effects attenuate on increasing doses of HP as evidenced by the decrease in brain glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD) content as well as increased lipid peroxidation (LPO) rendering the animals unable to swim. The experimental groups were: group 1-control mice (saline); group 2-HP; group 3-caffeine and group 4-SCH 58261. The brain levels of GSH, CAT and SOD decreased by 68% in group 2 animals while LPO increased by 43% as compared to the control animals. An improvement in the motor disability as a function of swimming ability and oxidative stress caused by HP was noted in groups treated with caffeine and SCH 58261, known adenosine A2A receptor antagonists. The results indicate that swim-test could be one of the most convenient methods for monitoring the overall motor deficit in rodent models of Parkinsonism.

PERSISTENT DEFENSIVE BEHAVIOR AND RESPONSE PATTERN TO DIAZEPAM IN MARMOSETS FOLLOWING A RECENT PREDATORY STRESS CONDITION. Barros, M.[1]; Giorgetti, M.[2]; Souto, A.A.V.[1]; Vilela, G.[1]; Santos, K.[1]; Vilas Boas, N.[1]; Tomaz, C.[3] [1]Dept. of Pharmaceutical Sciences, University of Brasilia, 70910-900, Brazil. [2]Amgen Pharmaceuticals, 1120 Veterans Blvd., South San Francisco, CA 94080, USA. [3]Primate Center, Institute of Biology, University of Brasília, Brazil. Initial investigations have indicated the use of the Marmoset Predator Confrontation Test (MPCT) as an experimental procedure to measure fear/anxiety-related behaviors in non-human primates. However, possible long-term habituation effects and re-use of experimental subjects need to be verified. This study, therefore, compared the behavioral response of experienced versus naïve adult black tufted-ear marmosets (Callithrix penicillata) in the MPCT, with/without diazepam administrations. Subjects were tested in the figure-eight maze and confronted with a taxidermized wild-cat predator stimulus. After four initial 20-min maze habituation sessions, each subject was submitted to two randomly-assigned 20-min predator confrontation sessions: vehicle and 2 mg/kg of diazepam. Confrontation with the predator induced significant behavioral changes; i.e., proximic avoidance and tsik-tsik alarm call. Diazepam administration, concomitant to predator exposure, reversed the behavioral changes observed. In both the experienced and naïve marmosets a similar behavioral profile and response pattern to diazepam was detected, corroborating the important selective pressure that felines seem to have on marmoset behavioral ecology. Therefore, during more naturalistic-like regimen – i.e.,

recurring intermittent predator encounters – the general response pattern remains highly consistent, regardless of prior experience. One may thus consider the re-use of marmoset subjects in the MPCT, particularly under these specific conditions (i.e. repeated 20-min confrontations, 72-h apart).

EFFECTS OF OVINE-CRF MICROINJECTIONS INTO THE DORSAL PERIAQUEDUCTAL GRAY ON DEFENSIVE BEHAVIOR IN RATS. Labotatório de Psicobiologia - FFCLRP, Universidade de São Paulo, Ribeirão Preto - SP. Borelli, KG and Brandão, ML. Corticotropin-releasing factor (CRF) and its receptor subtypes have been implicated in the regulating of endocrine, behavioral and autonomic responses to stress, fear and anxiety. Ovine CRF (oCRF) is a nonspecific CRF receptor agonist that produces anxiogenic-like effects in some animal models of anxiety. Besides, there is an increasing interest in the participation of CRF mechanisms of the dorsal periaqueductal gray (PAG) in the organization of defense reactions. The present study investigated the effects of oCRF (0.25; 0.5 and 1 µg/0.2 µL) injected into the dorsomedial (dm), dorsolateral (dl) and lateral (l) columns of PAG of rats submitted to the elevated plus-maze (EPM) test. The results showed that microinjections of oCRF intra-dmPAG reduced entries and time spent in the open arms and decreased end-arm exploration and head-dipping. In contrast, oCRF intra-dlPAG or lPAG did not affect the behavioral responses analyzed in the EPM. The proaversive effects in the dmPAG gain further relevance when combined with previous immunohistochemical study showing CRF-immunoreactive fibers from periventricular system arch dorsomedially to PAG via medial forebrain bundle. These findings indicate a columnar specificity of CRF mechanisms in modulation of aversive states in the PAG.

ANXIOGENIC EFFECTS OF ACTIVATION OF NK-1 RECEPTORS OF THE DORSAL PERIAQUEDUCTAL GRAY AS ASSESSED BY THE ELEVATED PLUS-MAZE, ULTRASOUND VOCALIZATIONS AND TAIL-FLICK TESTS. Bassi G.S.; Nobre M.J.; Brandão M.L. Laboratorio de Neuropsicofarmacologia, Dep Psicologia, FFCLRP-USP, Av Bandeirantes, 3900, Campus USP, Ribeirão Preto, São Paulo. Ultrasound vocalizations (USVs) known as 22 kHz are usual components of the defensive responses of rats exposed to threatening conditions. The amount of emission of 22 kHz USVs depends on the intensity of the aversive stimuli. While moderate fear causes an anxiolytic-sensitive enhancement of the defensive responses, high fear tended to reduce the defensive performance of the animals to aversive stimuli. The dorsal periaqueductal gray (dPAG) is an important vocal center and a crucial structure for the expression of defensive responses. Substance P (SP) is involved in the modulation of the defensive response at this midbrain level, but the type of neurokinin receptors involved in this action is not understood yet. In this study we examined whether local injections of the selective NK-1 agonist SAR-MET-SP (10-100 pmol/0.2 µL) into the dPAG i) cause anxiogenic effects in the elevated plus-maze (EPM) (Exp. I), ii) influence the novelty-induced 22 kHz USVs recorded within the frequency range of 20-26 kHz (Exp. II) and iii) change the nociceptive reactivity to heat applied to the tail (Exp III). The data obtained showed that SAR-MET-SP elicited significant "anxiety-like" behaviors, as revealed by the decrease in the number of entries into and time spent onto the open arms of the EPM. These anxiogenic effects were accompanied with antinociception and disrupted the novelty-induced increase in the number and duration of 22 kHz USVs. These findings are in agreement with the notion that NK1 receptors of the dPAG may be an important neurochemical target for new selective drugs aimed at the control pathological anxiety states.

5-HT2-RECEPTOR MECHANISMS OF THE DORSAL PERIAQUEDUCTAL GRAY IN THE CONDITIONED AND UNCONDITIONED FEAR. L.C. Oliveira; C.E. Macedo; J. Landeira-Fernandez; M.L. Brandão. Laboratorio de Neuropsicofarmacologia, Dep Psicologia, FFCLRP-USP, Av Bandeirantes, 3900, Campus USP, Ribeirão Preto, São Paulo. It has been shown that intense contextual fear conditioning (CFC) may activate brainstem regions such as the dorsal periaqueductal gray (dPAG). Several studies have been carried out to disclose how 5-HT2 mechanisms modulate the aversive stimulation of the dPAG. One prominent function of 5-HT2 receptors is to phasically regulate the aversive states induced by activation of the dPAG. However, in spite of the notion that past stressful experiences play a crucial role in certain types of anxiety only studies with stimulation of the dPAG of rats without previous aversive experience have been conducted so far. In this study, we investigated the 5-HT2 -mediated mechanisms of the dPAG of rats submitted to the electrical stimulation of this structure at the freezing and escape thresholds during testing sessions of CFC, in which animals were placed in a context previously paired to footshocks. Time of freezing after the interruption of the dPAG stimulation was recorded as an additional measure of innate fear. Drug effects on conditioned fear were also evaluated through the fear-potentiated startle paradigm (FPS). The 5-HT2 function of the dPAG in this condition was evaluated by local injections of a-methyl-5-HT and ketanserin, selective agonist and antagonist of 5-HT2 receptors, respectively. In keeping with previous studies, dPAG injection of ketanserin did not produce any significant effects and a-methyl-5-HT increased the aversive thresholds determined by stimulation of the dPAG in naive rats. On the other hand, ketanserin enhanced the freezing response induced by the dPAG

electrical stimulation while a-methyl-5-HT continued to show antiaversive effects in these animals. Also, whereas dPAG-post-stimulation freezing was not altered the FPS was significantly reduced by a-methyl-5-HT. These results suggest that reduction of the 5HT2-mediated mechanisms sensitizes the dPAG to the aversive effects of its electrical stimulation in rats under conditioned fear.

INVOLVEMENT OF THE DOPAMINERGIC D2 RECEPTORS OF THE VENTRAL TEGMENTAL AREA IN THE EXPRESSION OF CONDITIONED FEAR. Oliveira, A.R.; Reimer, A.E.; Brandão, M.L. Laboratório de Psicobiologia, FFCLRP-USP, Ribeirão Preto, São Paulo. The increase in startle reflex in the presence of a stimulus that has been previously paired to footshock has been named fear potentiated startle (FPS) and, together with freezing behavior, considered an index of anxiety. A growing body of evidence has suggested that dopaminergic mechanisms are implicated in different aspects of anxiety. However, studies that have examined which dopaminergic mechanisms influence fear have yielded contradictory results. This work is aimed at examining the involvement of dopaminergic D2 receptors of the ventral tegmental area (VTA) in the acquisition and expression of conditioned fear to light-CS. To this end, we evaluated the effects of bilateral intra-VTA administration of the D2 agonist, quinpirole (1.0 µg/0.2 µL), before conditioning and/or testing sessions of the FPS test. Freezing behavior was also assessed during the testing session. Rotarod test was used to detect eventual motor deficit. Quinpirole injected before testing, but not before conditioning session, reduced the FPS, but not freezing or motor activity of the animals. Our findings indicate that dopaminergic mechanisms mediated by presynaptic D2 receptors of the VTA are involved in the expression, but not in the acquisition, of conditioned fear using light-CS.

ANXIOLYTIC-LIKE EFFECTS OF CANNABIDIOL INJECTED INTO THE DORSOLATERAL PERIAQUEDUCTAL GREY. Campos, AC ; Guimarães, FS. Dept. Pharmacology, School of Medicine of Ribeirão Preto, Campus USP, 14049-900, Ribeirão Preto, SP, Brazil Introduction: Cannabidiol (CBD) is a nonpsychotomimetic constituent of Cannabis sativa plant that produces anxiolytic-like effects after systemic administration. The brain mechanisms of these effects, however, are unknown. The dorsolateral periaqueductal grey (dlPAG) has been associated with anxiety-like behaviors and express a significant number of cannabinoid receptors. Objective: To investigate the effects of CBD injected into the dlPAG of rats submitted to two models of anxiety, the elevated plus maze (EPM) and the Vogel conflict test. Methods: Male Wistar rats (220-230g, n=5-11) with cannulas aimed at the dlPAG received microinjections of CBD (15-60 nmol) or vehicle (V, 0.2uL) and, 10 min later, were submitted to the EPM or the Vogel tests. Also, in the EPM test rats received intra-dlPAG injections of V or AM251 (100 pmol, a CB1 antagonist) followed by V or CBD (30 nmol). Animals receiving the active doses of CBD outside the dlPAG were joined in an OUT group. Results: In the EPM CBD (30 nmol) significantly increased the % of entries and time spent in the open arms (% of entries, V: 13.1±3.6; CBD: 30.2±5.1, OUT: 9.1±3.6; % of time, V: 4.1±1.4; CBD: 12.3±2.7; OUT: 3.7±1.65). The drug, however, produced an inverted bell-shaped dose response curve, with the doses of 15 and 60 nmol being ineffective. CBD effects were not prevented by AM251. In the Vogel test CBD (30 nmol) increased the number of punished licks (number of punished licks, V: 116.4±21.9; CBD: 269.9±53.3; OUT: 95.3±16.8). Conclusions: The dlPAG could be involved in the anxiolytic-like effects of CBD observed after systemic injection. These effects are probably not being mediated by CB1 receptors. Financial support: FAPESP, CNPq

INFUSIONS OF MIDAZOLAM AND FLUMAZENIL INTO THE AMYGDALA PRODUCE ANXIOLYTIC-LIKE EFFECT IN MAZE-EXPERIENCED MICE. 1Barbalho, C.A.; 2Canto-de-Souza, A. 1Program of Physiological Sciences-CCBS, 1,2Psychobiology Group. Federal University of São Carlos-UFSCar, Sao Paulo, Brazil. Objective: We have demonstrated that microinjections of midazolam (MDZ) into the amygdala (AMY) produce anxiolytic effects in the elevated plus-maze (EPM) in mice (Psychopharmacol., v.150, n.3, p.300-310, 2000). This study investigated the effects of intra-AMY injections of MDZ and flumazenil (FLU), respectively, benzodiazepine receptor agonist and antagonist, on anxiety in maze experienced-mice. Five days after bilateral cannulae implantation in the amygdala, male Swiss albino mice (n=8-14) were exposed to the EPM for 5 minutes (without drug). Twenty-four hours later each mouse received intra-AMY injection of MDZ (0, 2.26 and 30 nmol/0.1ìl) or FLU (0, 16 nmol/0.1ìl), and was individually re-exposed to the EPM. The following behaviors were recorded: anxiety indices [% open arm entries (%OE) and % open arm time (%OT)] and the locomotor activity [closed arm entries (CE)]. While intra-Amy infusions of MDZ (both doses) attenuated both anxiety indices [%OE (*saline*: 38.2±5.1; *MDZ 2.26*: 62.8±6.2; *MDZ 30*: 69.6±6.8); $F(2,37)=8.38$, *Psaline*: 16.5±5.1; *MDZ 2.26*: 63.9±7.4; *MDZ 30*: 49.6±8.1; $F(2,37)=11.73$, *Pvehicle*:41.1±5.1; *FLU*: 58.4±6.6; $t(14)=2.07$, *Pvehicle*: 28.1±5.1; *FLU*: 36.3± 7.8); $t(14)=0.88$, NS)]. Neither MDZ [*saline*: 5.3±0.6; *MDZ 2.26*: 4.6±0.8; *MDZ 30*: 4.1±0.6; $F(2,37)=0.76$, NS] nor FLU [*vehicle*: 4.9±0.6; *FLU*: 4.7±0.3; $t(14)=0.18$, NS] changed CE. Interestingly, both benzodiazepine receptor

agonist and antagonist, MDZ and FLU, respectively, produced selective anxiolytic-like effects when injected into the amygdala in maze-experienced mice. These results suggest that the emotional state induced by plus-maze test someway releases endogenous benzodiazepine receptor inverse agonist within the amygdala. Further studies are required to investigate this hypothesis. Financial Support: FAPESP, CAPES, Dept. Psychology/UFSCar.

LOCAL INJECTION OF SUBSTANCE P INTO THE VENTRAL HIPPOCAMPUS INCREASES THE EXTRACELLULAR CONCENTRATION OF SEROTONIN. Carvalho, M.C.; Masson, S.; Brandão, M.L.; De Souza Silva, M.A.* Laboratory of Psychobiology, FFCLRP-USP, São Paulo, Brazil; *Institute of Physiological Psychology, University of Düsseldorf, Düsseldorf, Germany. Substance P (SP) is found in brain regions associated with fear/anxiety reactions such as the amygdala, hypothalamus, periaqueductal gray and hippocampus. The ventral hippocampus (VH) has been related with cognitive and emotional processes. Considering that the hippocampus also receives serotoninergic terminals, and both SP/ serotonin (5-HT) mechanisms have been implicated in the expression of fear/anxiety-like processes, the aim of the present study was to investigate the effects of administration of SP (10,100,1000 ng/ 0.5µL) on the serotoninergic activity of the VH through microdialysis technique. Besides, it was investigated the role of SP-VH on exploratory behavior of rats submitted to the elevated plus maze (EPM). The results showed that only SP-100 ng increased the extracellular level of serotonin in the VH. SP did not cause significant effects on the exploratory behavior of rats in the EPM. Therefore, it appears that the observed interaction of SP and 5-HT mechanisms in the VH is not implicated in the expression of fear responses to the height and openness of the EPM. A research for the involvement of this neurochemical interaction in conditioned fear paradigm is under way in this laboratory.

EVALUATION OF BEHAVIORAL AND NOCICEPTIVE RESPONSES IN MICE CONFRONTED BY DIFFERENT STRAINS OF PREDATOR. Carvalho-Netto, E.F.1,2; Toledo, A.V.2; Amaral, V.C. de S.2,3,4. Nunes-de-Souza, R.L.2; 1Psychobiology-USP/RP; 2Pharmacology-FCF/UNESP, 3UnUCET-UEG, 4PPGCF/UFSCar, Brazil. Predator-prey confronts induce physiological and behavioral changes that are usually followed by antinociception in the prey. This study investigated both behavioral and nociceptive responses in mice exposed to a predator (the rat exposure test - RET). The RET provides a home chamber connected via tunnel to a surface area in which a wire mesh prevents the rat from approaching or contacting the mouse. Twenty-five minutes after formalin injection (50 µl, 2.5% formalin) into the hind paw (nociceptive stimulus), male Swiss mice were placed in the RET with a toy rat (TR), Holtzman rat (HR) or Long Evans rat (LER) for recording time spent licking the injected paw for a 10-min period. Defensive behaviors were also assessed in mice that had not received formalin injection. Compared to TR- and HR-exposed mice, exposure to LER increased significantly percent risk assessment (stretch attend posture) in the chamber (TR: 1.1 ± 0.6, HR: 2.1 ± 0.5, LER: 5.9 ± 0.9) and tunnel (TR: 5.9 ± 1.7, HR: 33.1 ± 4.3, LER: 44.3 ± 4.6), as well as inhibitory avoidance [time (in sec.) in the home chamber] (TR: 123.1 ± 13.8, HR: 291.3 ± 43.1, LER: 394.2 ± 41.2), while reducing contact time with wire mesh (TR: 206.4 ± 17.8, HR: 44.6 ± 10.9, LER: 18.6 ± 6.1). Moreover, LER- and HR-exposed mice spent less time licking the injected paw than HR-exposed mice (TR: 115.4 ± 14.3, HR: 74.5 ± 13.7, LER: 47.8 ± 12.9), indicating an antinociception effect. Present results suggest that the LER is more aversive than the HR, since LER-exposed mice exhibited higher level of defensive behavior. In addition, this study indicates that the RET is a suitable animal model to study the underlying mechanisms of fear-induced antinociception. Financial Support: CAPES, CNPq, FAPESP

RESTRICTION STRESS INDUCES AMNESIA AND DECREMENT IN SEROTONERGIC ACTIVITY IN PREFRONTAL CORTEX. García-Saldívar, N. L.; González-López, M.R.A.; Castillo-Roberto,G.; 1Domínguez, R.; Cruz-Morales, S.E. FES-Iztacala,UNAM, Tlalnepantla, Mexica. Acute stress modifies serotonergic activity in several cerebral structures. The dorsolateral region of prefrontal cortex (PFC) receives serotonergic innervations from the raphe nuclei and it has been related with explicit memory formation in situations associated with emotional states. At present, little is known about the effects of acute stress on memory and its relation with serotonergic system. This experiment was designed to evaluate the activity of serotonin (5-HT) in PFC in subjects submitted to stress by restriction (R) for 60 min and trained in the elevated T maze (ETM). Male Wistar rats (250-270 g) were assigned to five independent groups (N=7): an intact group (I), a group exposed to the ETM and three groups exposed to R and trained in the ETM. Five min, 24 or 48 h after testing in the ETM the animals were decapitated, the PFC dissected and 5-HT and its metabolite levels were measured by HPLC. In comparison with the intact group, the rats submitted to R showed lower retention latencies and a decrease in 5-HT activity, however significant differences were detected only in the group trained after 24 h after R. Present results suggest that the serotonergic system in the PFC is involved in the modulation of memory affected by restriction stress. Supported by PAPIIT IN300806, DGAPA, UNAM.

ROLE OF 5-HT2C RECEPTOR WITHIN THE VENTRAL HIPPOCAMPUS ON ANXIETY INDUCED BY THE ELEVATED PLUS-MAZE. Gomes, V.C. (1); Scarpelli, G. (3); Alves. S.H. (3); Landeira-Fernandez, J. (1,2); Cruz, A.P.M.(3). (1)Pontifícia Universidade Católica do Rio de Janeiro, RJ, Brasil. (2) Universidade Estácio de Sá, RJ, Brasil (3) Universidade de Brasília, DF, Brasil. This study aim to investigate the behavioral effects in the rat elevated plus-maze (EPM) of infusing the selective serotonin2C (5-hydroxytryptamine, 5-HT2C) receptor-acting compounds into the ventral hippocampus (VH). In this experiment, naïve male Wistar rats were exposed to the EPM 10 min following VH infusions of either vehicle or the selective 5-HT2C-receptor agonist RO-60-0175 (0.3, 1.0, 3.0 and 10.0 µg). In addition to conventional parameters of open arm exploration (i.e. percentages of open arm entries and of time spent into these arms), risk assessment-related behaviors were recorded as anxiety-like measure in EPM scoring. RO-60-0175 selectively decreased open arm exploration at the dose of 1.0 µg, while inducing robust locomotor-suppressant effects at the highest doses. These results further corroborate our previous findings showing that VH 5-HT2C receptor activation is associated with anxiogenic-like and locomotor-suppressant effects.

METABOTROPIC GLUTAMATE RECEPTOR AGONIST DECREASES RISK ASSESMENT BEHAVIORS THROUGH THE BASOLATERAL AMYGDALA. 1De Jesus-Burgos, MI; 2Rodríguez-Aguiar, GL; 2Quiñones-Laracuente, K; 1Pérez-Acevedo, NL. 1Medical Sciences Campus Anatomy Department, 2UPR-Río Piedras Campus, General Sciences The present study wanted to determine whether metabotropic glutamate receptors (mGluRs) modulate the response to anxiolytic drugs in both sexes. Ovariectomized and estrogen replaced females (OVX and OVX-EB, respectively), and intact male rats were compared with regard to risk assessment behaviors. Adult Sprague Dawley rats were exposed to fur/skin cat odor stimuli during two consecutive 5 minutes trials. 3,5 dihydroxyphenylglycine (DHPG; 1µM/0.5µL/side) was centrally infused five minutes prior to the test into the basolateral amygdala. DHPG significantly reduced risk assessment behaviors (flat back approach and stretch attended posture) in male and OVX female rats (Two-Way ANOVA, $p<0.05$) while OVX-EB DHPG-treated rats were unaffected. Interestingly, estrogen by itself significantly decreased risk assessment behaviors. An increase in exploratory behavior (rearing) was observed in males treated with DHPG but not females. These results suggest that estrogen counteracts the anxiolytic effects of DHPG. This project was supported by RCMI Program (G12RR03051) and NIMH MRISP (MH48190) to NLPA and MBRS-RISE Program (RISE GM61838) to MIJB, GLRA and KQL.

RELATIONSHIPS BETWEEN SOCIAL HIERARCHY, CORTICOSTERONE LEVELS AND THYMIC ALTERATIONS IN THE MICE RESIDENT-INTRUDER PARADIGM. Guazzelli, A. S., de Paula, H. M. G., Arruda, M. S. P. Dept. of Biological Sciences, UNESP - Bauru / Brazil. The mice resident-intruder paradigm has been employed in the study of the thymic alterations derived from the psychosocial stress. This work investigated which physiological and behavioral aspects of the resident-intruder interaction are correlated with thymic alterations. Eight Swiss male mice were used, being four of them housed separately in 4 home-cages (the resident group) for six days. After that, each one of the four remaining mice (the intruder ones) was placed in the same cage of a resident animal, but the two animals were separated by a perforated partition that allowed sensory, but not physical contact. The partition was removed daily for a maximum period of 5 minutes, when the animals could freely interact. Such interactions were videotaped for 21 days. The mice were then sacrificed, blood corticosterone levels (CL) were measured and thymuses were weighed and submitted to cells viability evaluation. Aggressions, escapes and submission postures were considered as behavioral variables. Social hierarchies were established in the dyads, with the dominance being assumed regardless of intruder/resident condition. Aggression latency showed a negative correlation with the thymuses weight in subordinates mice ($r= -0.96$; $p=0.038$) and a positive correlation with the cells viability in dominants mice ($r=0.99$; $p=0.006$). CL was higher for the subordinates ($p<0.05$) and in such animals the thymuses weight correlated negatively with the CL ($r= -0.92$; $p=0.038$). The aggression latency and the CL showed to be associated with the thymuses alteration as a consequence of the social stress in the mice resident-intruder paradigm.

THE ROLE OF GLUTAMATE-NMDA RECEPTORS IN THE DORSAL PREMAMMILLARY NUCLEUS ON THE DEFENSIVE BEHAVIOR TOWARD CAT ODOR OR CUED OLFACTORY CONDITIONED FEAR.. Do-Monte, F.H.M.1; Kroon, J.A.V.1; Pavesi, E.1; Canteras, N.S.2. Carobrez, A.P.1 . 1- Dept. Farmacologia, CCB, Universidade Federal de Santa Catarina, Florianopolis, SC, Brazil; 2- Dept. Anatomia, ICB, Universidade de Sao Paulo, Sao Paulo, SP, Brazil. Fear is considered a defensive mechanism that protects animals or humans against potentially dangerous environmental threats. Olfaction is the primary sense of rodents and is critical to detect threatening stimulus. These olfactory signals may be innately recognized as in the predator-prey relationship, or learned as in the olfactory conditioned fear. Previous studies have shown that electrolytic and neurotoxic lesions in

the dorsal premammillary nucleus (PMd) reduced defensive responses to cat odor stimuli. In fact, immunohistochemical studies revealed an increased Fos activity in the PMd of rats exposed to the cat odor. In the present study, we first demonstrated that the intra-PMd microinjection of AP5 (6 nmol) – an antagonist of glutamate –NMDA receptors - reduced innate defensive behaviors in rats confronted with the cat odor. For this reason, cued olfactory fear conditioning was conducted in order to verify the presumable role of glutamate-NMDA receptors in the PMd of rats during the re-exposure of the olfactory cue in a new environment. Subjects were trained in a classical fear conditioning where a neutral stimulus (coffee odor) was paired with an aversive unconditioned stimulus (5 footshocks, 0,4mA; 2s duration; 40s intervals). During test, in a different context, defensive responses toward olfactory conditioned stimuli were decreased following intra-PMd AP5 administration. These findings suggest a role of glutamate-NMDA receptor in the PMd on the expression of defensive behavior response of rats challenged with an innate or a conditioned olfactory aversive stimulus. Financial support: CNPq, CAPES, FAPESP, FAPESC, PRONEX.

EFFECTS OF CORTICOTROPIN-RELEASING FACTOR IN TESTS FOR DEPRESSION IN RATS AND MICE. Dunn, A.J., Leskov, I.L. and Swiergiel, A.H. Dept. of Pharmacology, Toxicology and Neuroscience. Louisiana State University Health Sciences Center, Shreveport, LA 71103 USA. Corticotropin-releasing factor (CRF) has been implicated in behavioral responses in stress, and may be a factor in depressive illness. However, there is a paucity of evidence for effects of CRF in the behavioral tests commonly used for depression. Therefore we examined the effects of CRF injected intracerebroventricularly (icv) in both rats and mice in the Porsolt forced swim test (FST), and mice in the tail suspension test (TST). Adult male Harlan Sprague Dawley rats or CD-1 mice were implanted bilaterally with icv cannulae and infused with CRF 25 min before the TST and 30-35 min before the FST. In rats, icv CRF (100 and 300, but not 30 ng) consistently increased the duration of floating in the FST. By contrast, CRF administration to mice consistently decreased the duration of immobility in the FST, statistically significant at 100 ng. Similarly, icv CRF (30 and 100 ng) decreased the time spent immobile in the TST. Parallel tests in the open field (OF) indicated that the results tests were not obviously related to changes in locomotor activity. Line crossings in an open field were only slightly decreased by 300 ng CRF in rats, but in mice it was strongly depressed by 100 ng, whereas 30 ng increased activity. CRF caused both rats and mice to remain longer in the center of the field where they were placed at the start of the OF test. We conclude that in rats, CRF induced responses like those to stressors such as footshock, whereas in mice, CRF induced antidepressant-like effects. This interspecies difference is striking. The findings suggest that the results of tests commonly used for depression should be interpreted very carefully.

ANXIOLYTIC-LIKE EFFECT OF INTRA-AMYGDALA NEUROPEPTIDE Y INFUSION IN ANIMAL MODELS OF CONDITIONED FEAR: AN NPY Y1 RECEPTOR INDEPENDENT EFFECT? Fendt, M.; Bürki, H.; Huber, C.; Imobersteg, S.; Jeker, A.; Mayer, R.; Portet, C.; Chaperon, F.; Lingenhöhl, K.; McAllister, K.H.; Orain, D.; Pryce, C.R.; Uzunov, D.P. Novartis Institutes for BioMedical Research, Neuroscience DA, Preclinical Psychiatry, CH-4056 Basel, Switzerland. Neuropeptide Y (NPY) and its receptors are densely localized in brain regions involved in the mediation and modulation of fear, including the amygdala. The level of fear negatively correlates with the number of NPY-containing neurons within the amygdala and after infusions of NPY into the amygdala, retention on aversive memory is impaired. In the present study, we infused NPY, NPY Y1 (NPY1) receptor agonists, and/or a NPY1 receptor antagonist into the amygdala of mice, and tested the effect on the expression of conditioned fear, measured by conditioned freezing, fear-potentiated startle, and plasma hormone levels. Intra-amygdala NPY infusion had an anxiolytic-like effect on the behavioral expression of both conditioned freezing and fear-potentiated startle. This occurred despite the endocrine response to the CS, measured in terms of plasma levels of ACTH and corticosterone, being significantly increased in the NPY infused mice. Surprisingly, intra-amygdala infusion of the NPY1 receptor agonists Y-28 or Y-36 did not mimic the NPY effects, and co-infusion of the NPY1 receptor antagonist BIBO3304 did not block the NPY effects. Furthermore, we did not observe any effect of the infused compounds on extinction of conditioned freezing. Taken together, these data show an important role of the transmitter NPY within the amygdala for the expression of conditioned fear. NPY1 receptors do not appear to be involved, suggesting that the observed NPY effect is mediated via other NPY receptors (NPY2, NPY5).

UNCONDITIONED AND CONDITIONED EFFECTS OF TRIMETHYLTHIAZOLINE, A COMPONENT OF FOX-ODOR, ON RAT BEHAVIOR. Endres, T[1] and Fendt, M[1, 2] [1]Dept. of Animal Physiology, University of Tübingen, Germany. [2]Novartis Institutes for BioMedical Research, Neuroscience DA, Basel, Switzerland. In the last decade, an increasing number of studies have used Trimethylthiazoline (TMT), a synthetic derived component of fox feces, to induce fear behavior in rodents. Here, we present results of three different experiments (1)

comparing unconditioned effects of TMT with other synthetic odors, (2) testing conditioned behavioral responses to a TMT-paired context, and (3) comparing fear conditioning using TMT as well as other odors as a conditioned stimulus. Experiment 1: We exposed rats to different concentrations of TMT, butyric acid, limonene and ethyl acetate, and measured freezing behavior. Only TMT but not the other odors were able to induce freezing behavior. Experiment 2: We exposed two groups of rats to TMT in two different experimental setups and observed strong freezing behavior during TMT exposure. Thereafter, we tested whether these different experimental setups by themselves were able to induce conditioned fear behavior. Using a one-compartment setup, no conditioned fear behavior was observed. In contrast, conditioned fear behavior could be observed in a two-compartment setup. That is, the animals either avoided the TMT-paired compartment or showed risk assessment behavior towards this compartment. Experiment 3: We used a low TMT concentration which is not able to induce unconditioned fear behavior as well as other odors as a conditioned stimulus for one trial fear conditioning. We compared acquisition, expression, and extinction of conditioned fear to these odor stimuli. We observed no differences in conditioned freezing behavior to the different conditioned odor stimuli.

EFFECTS OF INTRA-VENTRAL HIPPOCAMPUS INFUSION OF A 5-HT2C-RECEPTOR ANTAGONIST ON CONVETIONAL AND ETHOLOGICAL ANXIETY MEASURES IN THE ELEVATED PLUS-MAZE. Ferreira, G.F.S.(1; 2); Salviano, M.F.(1); Landeira, J.F.(3); Cruz, A.P.M.(1). (1) Universidade de Brasília, DF, Brasil; (2) Instituto de Educação Superior de Brasília, DF, Brasil; (3) Pontifícia Universidade Católica do Rio de Janeiro, RJ, Brasil. The role of serotonin (5-HT) on anxiety mediation seems to be dependent on the brain area. For example, serotonin and several 5-HT agonists enhance anxiety-like measures in the amygdaloid complex, whereas attenuates panic-like reaction in periaqueductal gray matter (PAG). Amygdala and PAG receive important 5-HT projections from the dorsal raphe nucleus (DRN). The present study investigated the behavioral effects in rat elevated plus-maze (EPM) of infusing the selective 5-HT2C-receptor antagonist into the ventral hippocampus (VH), another important post-synaptic site that receives 5-HT projections from the DRN. Male Wistar rats were injected (0.2 µl) either with vehicle or the selective 5-HT2C-receptor antagonist RS 102221 (0.75; 1.25 or 2.5 µg). Fifteen min later, each animal was exposed for 5 min to the EPM. The percentages of open arm entries and of time spent into these arms were employed as conventional anxiety indexes, whereas the time spent in risk-assessment was used as an ethological parameter of anxiety. In addition to these conventional and ethological anxiety measures, the total number of entries (open + closed) was calculated as an indicative of locomotor activity. VH microinjection of the three RS 102221 doses increased open-arm exploration while reducing risk-assessment. This behavioral profile, indicative of anxiolytic-like effect in the EPM, was observed without locomotor-suppressant effects. Results are discussed in terms of an involvement of VH 5-HT 2C receptor in the modulation of anxiety states. Key-words: serotonin, anxiety, ventral hippocampus, elevated plus-maze.

EFFECTS OF IPSAPIRONE ON HIGH/LOW ANXIETY-LIKE TRAIT RATS. Salviano, M.F.[1]; Ferreira, G.F.S. [1]; Vilela, G. [2]; Paz, A. [1]; Landeira, J.F. [3]; Barros, M. [2]; Cruz, A.P.M. [1]; [1] Psychology Dept., [2] Pharmaceutical Sciences Dept., University of Brasília, Brazil; [3] Psychology Dept., PUC University, Rio de Janeiro, Brazil. Animal models have been extensively employed for studying the neuropsychological mechanisms underlying anxiety disorders, as well as the behavioral effects of putative/novel anxiolytics. However, little attention has been given to the use of animals with different anxiety-like traits. In the present study, male Wistar rats – selectively bred for either high or low anxiety-like traits – were submitted to either a 5-HT1A-receptor agonist ipsapirone (2,5mg/Kg; i.p.) or saline (i.p.) treatment and tested in the conditioned freezing procedure. Accordingly, each subject initially submitted to a training session, which consisted of placing the animal in an experimental chamber and applying three inescapable electric foot-shocks (0.5 mA). Following a 24-h interval, the animal was re-exposed to the same chamber without applying a foot-shock (test session). Saline or ipsapirone was injected 30-min before each training and test session. Conditioned freezing behavior was observed in all experimental groups; i.e. control, high and low anxiety-like trait groups. Ipsapirone administration significantly increased this behavioral parameter in the low anxiety-like trait group, remaining constant in the control and high anxiety-like trait animals. In addition, response to the drug treatment was found to be significantly influenced by the level of anxiety. Taken together, the present results indicate a possible differential effect of 5-HT1A-receptor activation in the conditioned freezing procedure, which may be related to the specific high/low anxiety-like trait in the rats tested. Furthermore, the use of selectively bred animals may provide a unique approach for screening novel anxiolytic/anxiogenic compounds. Financial support: CNPq.

RESILIENCY IN RATS: AN INVESTIGATION OF THE EFFECTS OF COPING STRATEGIES ON NEUROBIOLOGICAL RESPONSIVENESS [1]Fleming, D.F.; [1]Everette, A.M.; [1]Higgins, T.J.; [1]Tu, K.M.; [2]Bardi, M.; [2]Kinsley, C.H. & [1]Lambert, K.G. Dept of Psychology. Randolph-Macon College, Ashland, VA 23005 USA1; Dept of Psychology, University of Richmond, Richmond, VA 23173 USA2 Effective coping strategies are important for diminishing allostatic load during chronic stress. Extending on prior research in our lab showing heightened resilience in flexible coping rats, the current study investigated effects of the different coping strategies [passive (consistently passive), active (consistently active), or flexible (variable response) on various neurobiological responses. Twenty-four post-weaned male rats, categorized by their coping profiles determined by a back restraint test (Schouten et al., 1997), were exposed to a Chronic Unpredictable Stress (CUS) paradigm for approximately two weeks. Cardiovascular responsiveness was assessed via tail cuff sensors; additionally, fecal boli samples were collected to assess corticosterone and Dehydroepiandrosterone (DHEA). Upon sacrifice, Neuropeptide Y (NPY), a neurotransmitter known for its role in resilience, was quantified in the Bed Nucleus of the Stria Terminalis (BNST), amygdala, and the paraventricular nucleus of the hypothalamus (PVN). Flexible rats altered their behavioral responses more dramatically in repeated forced swim tests ($p = .016$); additionally, flexible rats had significantly more NPY in the amygdala and BNST ($p = .001$; .015, respectively). All animals' heart rates increased by approximately 30% during CUS, confirming that the paradigm was stressful for the animals. At the completion of the study, flexible copers had significantly lower systolic blood pressure than passive copers ($p = .04$). Corticosterone/DHEA ratios were lower in flexible copers at baseline ($p=.036$); interestingly, in this unpredictable stress paradigm, corticosterone levels were higher in flexibles than the other groups ($p=.006$), but not at baseline. The convergence of these data suggests that flexible coping strategies lead to enhanced resiliency (lower blood pressure, higher NPY, higher DHEA).

EFFECTS OF ANXIETY ON THE ESCAPE BEHAVIOR INDUCED BY THE MICROINJECTION OF NMDA IN THE DORSAL PERIAQUEDUCTAL GRAY. Galvão, B.O. (1); Larrubia, B.C. (1); Cardenas, F.P. (2); Landeira-Fernandez, J. (1,3);. (1) Pontifícia Universidade Católica do Rio de Janeiro, RJ, Brasil, (2) Universidad de Los Andes, Bogotá, Colômbia (3) Universidade Estácio de Sá, RJ, Brasil. The relationship between anxiety and panic is still unclear. Some authors sustain that anxiety increases the occurrence of panic episodes, while there are clinical reports showing an inverse correlation between anxiety and panic attacks. The present study investigated this issue in animal models of anxiety. The escape response induced by local NMDA microinjection in the dorsal periaqueductal grey (dPAG) was employed as an animal model of panic. Freezing to contextual cues previously associated with electric shocks was used as an animal model of anxiety. The relationship between anxiety and panic was studied in Wistar male rats (250g; 12hours light/dark). All the subjects were implanted with a 12,5mm cannula, aimed to dPAG (AP=2.3; DV=4.5; ML=1.7) under standard stereotaxic surgery (Tribromoethanol, 250mg/Kg). Six days later, the animals were randomly assigned to one of two groups: with or without contextual fear conditioning (1sec¡V1,0mA current). Six hours later, half of the rats in each group were microinjected with 0,5ƒÝl NMDA (15ug/ul) or saline solution (0,9%). Immediately after the injection, every rat was allowed to explore an open field (20 minutes). The frequency of jumping and running behavior was analyzed using a computer program. None of the animals trained in the contextual fear conditioning ran after the NMDA microinjection, while all the animals without the training ran ($F[1,20]=4,615$; $P=0,044$). Therefore, it was concluded that contextual fear conditioning had a ¡§protective¡¨ effect on the course of the escape behavior induced by NMDA injections into the dPAG. These results support the point of view of an inverse correlation between anxiety and panic attacks.

AMPA RECEPTOR TRAFFICKING IN THE NUCLEUS ACCUMBENS DURING THE INCUBATION OF COCAINE CRAVING. Conrad KL, Marinelli M, Wolf ME. Rosalind Franklin University. 3333 Green Bay road, North Chicago, IL 60064. Cocaine-seeking behavior increases progressively over the first three months of withdrawal from cocaine self-administration in rats (Grimm et al, 2001). This time-dependent increase in drug seeking is termed "incubation of cocaine craving." Based on the importance of AMPA receptor trafficking for regulating synaptic strength in neuronal plasticity, our objective was to determine if increased cell surface expression of AMPA receptors in the nucleus accumbens (NAc) accompanied intensification of craving during cocaine withdrawal. Rats self-administered saline or cocaine 6 hrs/day for 10 days. After 1 or 45 days of withdrawal, cell surface and intracellular AMPA receptor subunits were distinguished using a membrane-impermeant crosslinking agent that selectively modifies surface proteins, and quantified by Western blotting. As previously reported, cocaine-seeking behavior (non-reinforced nose-poking) was higher on day 45 compared with day 1 of withdrawal. Analysis of GluR1 in NAc tissue from these rats, as well as rats trained identically but killed without a test for drug-seeking, demonstrated a 2-3 fold increase in surface (S) and intracellular (I) GluR1 levels on day 45 compared to day 1 of withdrawal. Cocaine withdrawal-associated increases in GluR1 levels occurred in the absence

of an increase in GluR2; in fact, there was a small but significant decrease in the GluR2 S/I ratio in cocaine rats on day 45. This suggests a selective increase in homomeric GluR1 receptors on day 45 of withdrawal from cocaine self-administration. We provide initial evidence suggesting a role for metaplasticity, a switch from Calcium impermeable (GluR2-containing) to Calcium permeable (GluR2-lacking) AMPA receptors, during the incubation of cocaine craving.

UNBALANCED EMOTIONS WITH VESTIBULAR DYSFUNCTION. Goddard, M.J.; Zheng, Y.; Darlington, C.L.; Smith, P.F. Dept. of Pharmacology and Toxicology. University of Otago, Dunedin, New Zealand. The vestibular system detects linear and angular acceleration and is integrated with the nervous system to provide a sense of balance, for postural, homeostatic, and optic reflexes. The vestibular system is also reciprocally connected with the limbic system – which suggests that affective status may influence the sensation of balance, and vice versa. Psychiatric illnesses such as depression, anxiety and agoraphobia have previously been described in patients with chronic vestibular dysfunction. The aim of the present investigation was to characterize the development of changes in emotionally-indicated behavior in a rodent model of chronic bilateral vestibular failure, using the open field maze (OFM), elevated plus maze (EPM) and elevated T-maze (ETM). Male Wistar rats with complete bilateral surgical vestibular lesions (BVL, n=18) were compared against control rats' (n=17) behavior in potentially anxiogenic environments. In the OFM, BVL rats covered 40-50% more distance at 50-60% greater velocity compared to controls, while control rats engaged in wall-supported rearing more often than BVL rats. An analysis of movement paths revealed that BVL rats tended to explore the central - more exposed - areas of the maze, unlike control rats' wall-seeking behavior. BVL rats' proclivities in navigating exposed parts of their local environment, rapidly, with reduced awareness of their extra-maze environment suggests that their emotional reactivity was altered following the lesion. This suggestion was corroborated in two other classical anxiety models. In the EPM, BVL rats spent more time in the open arms of the maze compared to sham controls. In the ETM, while control rats learned inhibitory avoidance of the open arms, BVL rats did not. These results strongly suggest a change in emotional-reactivity to salient environmental parameters in rats with chronic vestibular failure.

BILATERAL LESIONS OF THE DORSAL PORTION OF THE MIDBRAIN PERIAQUEDUCTAL GRAY (PAG) REDUCE ANXIETY IN MICE EXPOSED TO THE ELEVATED PLUS MAZE (EPM). 1Mendes-Gomes, J.; 2Nunes-de-Souza, R.L.; 1Psychobiology/FFCLRP/USP, Ribeirão Preto; 2Lab. Pharmacology/FCFAr/UNESP, Araraquara, Brazil. We have recently demonstrated that unilateral lesion of the dorsal columns [dorsolateral (dl) and dorsomedial (dm)] of the midbrain periaqueductal gray (dPAG) does not alter anxiety in mice exposed to the EPM and submitted to the formalin test (nociceptive stimulation). The present study investigated the effect of bilateral lesion of the dPAG on anxiety in mice. dPAG lesion was produced through bilateral injections of 0.2 µl NMDA (N-metil-d-aspartic acid, 1 µg/0.1 µl). Five days after dPAG lesion, mice (n = 12-15) were exposed to the EPM to recording the anxiety indices [% open arm entries (%OE) and % open arm time (%OT)] and locomotor activity [closed arms entries (CE)]. dPAG lesion increased %OE (sham lesion: 29.5 ± 2.5; lesion: 45.7 ± 2.0; $t = -5.21$; $p < 0.01$) and the %OT (sham lesion: 21.8 ± 2.6; lesion 38.8 ± 2.8; $t = -4.41$; $p < 0.01$). dPAG lesion did not change closed arms entries ($t = 0,63$; $p = 0.53$). Present results (i) corroborate previous studies demonstrating that dPAG plays a role in defensive system and (ii) indicate that bilateral (rather than unilateral) dorsal columns are crucial for the anxiety modulation in mice. Financial support: FAPESP, CNPq, PADC-FCFAr/UNESP

ROLE OF THE 5HT2A RECEPTORS LOCATED WITHIN THE MIDBRAIN PERIAQUEDUCTAL GRAY ON THE ONE-TRIAL TOLERANCE PHENOMENON IN MICE. Gomes, K. S. (1) & Nunes-De-Souza, R. L. (1,2). (1) Psychobiology/FFCLRP/USP, Ribeirão Preto, Brazil; (2) Lab. Pharmacol./FCFar/UNESP, Araraquara, Brazil. Elevated plus-maze (EPM) experienced rodents no longer respond to systemic treatment with anxiolytic drugs on second trial (Trial 2) in this animal model of anxiety. A learned avoidance response hypothesis has been proposed to explain this 'one-trial-tolerance' (OTT) phenomenon in maze-experienced rats and mice. Previous results have demonstrated that the dorsal periaqueductal gray matter (dPAG) inactivation reinstates the anxiolytic-like effect of midazolam on trial 2, and activation of 5-HT2A receptors located within the dPAG modulates fear/anxiety states. The present study investigated the role of the 5-HT2A receptors located in this midbrain structure on the OTT phenomenon in mice. Mice (n=11-13/group) received intra-dPAG infusions of saline or DOI (8 nmol/0.1 microliter), a preferential 5HT2A receptor agonist, 5 min prior Trial 1 and Trial 2 in the EPM. Two-way ANOVA (drug x trial) showed a decrease in the open arm exploration on Trial 2 [percent of open entries (%OE: ($F_{1,45}=29.3$, $p<0.05$); percent of open time (%OT: $F_{1,45}=22.15$, $p<0.05$)] as well as an effect of drug x trial interaction [%OE: ($F_{3,45}=3.45$, $p<0.05$); %OT: ($F_{3,45}=3.06$, $p<0.05$)]. The F test for planned comparisons showed an increase in %OT during Trial 2 for DOI/DOI group when compared to sal/sal ($F_{1,45}=5.85$, $p<0.05$) and DOI/sal ($F_{1,45}=7.7$,

p<0.05) groups. These results (i) corroborate previous studies showing that maze-experienced mice explore less the open arms during Trial 2 and (ii) suggest an involvement of 5HT2A receptors located within the dPAG on the anxiety modulation in maze-experienced mice. The role of this serotonin receptor subtype on the OTT phenomenon needs to be confirmed through combined injections with selective 5HT2A receptor antagonists. Financial Support: FAPESP, CNPq, PADC/FCFar-UNESP

MODULATION OF DEFENSIVE RESPONSES BY GROUP I METABOTROPIC GLUTAMATE RECEPTORS LOCATED IN THE DORSOLATERAL PERIAQUEDUCTAL GRAY. Guimaraes, F.S.; Lima, V.C.F.; Molchanov, M.L. Departament of Pharmacology, School of Medicine of Ribeirão Preto, Campus USP, 14049-900, Ribeirao Preto, SP, Brazil. Glutamatergic neurotransmission in the dorsolateral periaqueductal grey (dlPAG) is related to defensive responses. However, the role of group I glutamate metabotropic receptors (mGluR) in these responses have been poorly investigated. The objective of the present study, therefore, was to test the hypothesis that interference with group I mGluR-mediated neurotransmission in dlPAG could modulate defensive responses. Male wistar rats with cannulae aimed at the dlPAG were submitted to the following experiments: 1. intra dlPAG injections of vehicle (veh, 0.2 uL) or (RS)1-aminoindan-1,5-dicarboxylic acid (AIDA, 30-100 nmol, a mGluR1 receptor competitive antagonist) followed, 5 min later, by veh or trans-(+)-1-amino-1,3-ciclopentanedicarboxylic acid (tACPD, a group I and II mGluR agonist, 30 nmol); 2. intra-dlPAG injections of veh, AIDA (30 nmol) or 2-methyl-6-(phenylethynyl)-pyridine (MPEP, a mGluR5 receptor non-competitive antagonist, 50 nmol) followed by trans-azetidine-2,4-dicarboxylic acid (tADA, a group I mGluR agonist, 10 nmol); 3. and 4. intra-dlPAG injections of vehicle, AIDA (10-30 nmol) or MPEP (10-50 nmol) before the elevated plus maze (EPM) test; 5. intra-dlPAG injections of vehicle, AIDA (30 nmol) or MPEP (50 nmol) before the Vogel punished licking test. tACPD induced defensive responses characterized by jumps and an increased number of crossings in the observation box that were attenuated by AIDA (30 nmol). tADA produced similar responses, although of lower intensity. tADA effects were prevented by AIDA and MPEP. These two drugs also produced anxiolytic-like effects in the EPM and Vogel tests when injected alone. The results suggest that group I metabotropic glutamate receptors facilitate defensive responses in the dlPAG. Financial support: FAPESP, CNPq

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ROLE OF VENTRAL AND DORSAL HIPPOCAMPUS NMDA-RECEPTORS ON RATS´ DEFENSIVE BEHAVIORS TOWARDS CAT ODOR STIMULI. Hackl, L.P.N.; Carobrez, A.P., Depto Farmacologia, CCB, UFSC, Florianópolis, SC, Brazil The glutamatergic transmission have been implicated in mechanisms related to defensive behaviors (DB) and some pharmacological studies have shown that systemic or intra-periaqueductal gray matter injections of NMDA receptor antagonists elicit an anti-aversive profile. Studies using lesion techniques have shown a differential involvement of the ventral (HIPv) and the dorsal (HIPd) hippocampus in the mediation of the DB of rats towards a cat odor, however, the identification of neurotransmission systems involved in these effects have not been evaluated. Based on these facts, the present work was outlined to study the role of NMDA receptors of HIPv and HIPd in the DB of rats confronted to a cat odor stimulus. Rats with bilateral cannulas at the HIPv or HIPd were submitted to a cat odor protocol of 3 consecutive days (habituation, cat odor exposure and context conditioning) during 10 min each session. The test box was divided into 2 compartments comprising an open (2/3 of the total area where a cloth impregnated with cat odor was placed) and an enclose area. The infusion into the HIPv of the NMDA receptor antagonist aminophosphonopentanoic acid (AP5) were able to reduce the DB of rats exposed to cat odor expressed through percentage approach time to and hide time from the odor source, when compared to the control group. However, when given only before the context conditioning, AP5 was not able to reduce the expression of the DB acquired previously. Furthermore, no effects were detected in rats treated with AP5 into the HIPd either during the exposure to the cat odor or to the context session. The present results indicate that NMDA receptors of the HIPv, but not the HIPd, are involved in mechanisms related the acquisition of DB during exposure to the cat odor stimuli, considered a potential threat. Financial support: CNPq, CAPES, FAPESC, FAPESP

ACTIVITY OF BRAINSTEM CHOLINERGIC NEURONS DURING EMISSION OF 22 kHz ALARM CALLS INITIATED BY DIFFERENT METHODS. Iku, A.; Brudzynski, S.M. Departments of Biological Sciences and Psychology, Brock University, St. Catharines, ON L2S3A1 Canada. The laterodorsal tegmental nucleus (LDT) contains largely cholinergic neurons, which have an ascending projection to mesencephalic and diencephalic structures involved in the production of ultrasonic calls. Adult rats emit 22 kHz alarm calls in aversive and dangerous situations. These calls can be induced in response to an airpuff and also initiated following an intracerebral injection of cholinergic agonists into the medial preoptic area (MPA). It was hypothesized that

activation of the LDT cholinergic neurons releases acetylcholine in the basal forebrain and initiates 22 kHz calls. The purpose of the study was to determine whether the activity of cholinergic LDT neurons is increased during emission of 22 kHz alarm calls induced by an airpuff or by an intracerebral injection of carbachol (Cch) into the MPA. Immunofluorescent staining of choline acetyltransferase was used to identify the cholinergic neurons of the LDT, whereas c-Fos immunostaining was used as an indication of cellular activity. Double-labelled neurons would indicate active cholinergic neurons. Results showed that the overall number of LDT c-Fos labelled neurons and the number of LDT double-labelled cells were significantly higher ($p<0.05$) in the Cch-injected vocalizing animals than in non-vocalizing and control animals. For the airpuff treatment, there were significantly more c-Fos labelled cells ($p<0.05$) in the vocalizing animals than in non-vocalizing and control animals. Further comparison revealed significantly more double-labelled cells ($p<0.05$) in the injected animals than the air-puffed vocalizing and control animals. Significantly higher number of cholinergic neurons in the LDT in vocalizing rats supports the hypothesis that these cells are involved in the initiation of 22 kHz alarm calls. Supported by NSERC of Canada.

TWO TYPES OF SOCIAL BUFFERING DIFFERENTIALLY ATTENUATE CONDITIONED FEAR RESPONSES IN MALE RATS. Kiyokawa, Y.; Kikusui, T.; Takeuchi, Y.; Mori, Y. Laboratory of Veterinary Ethology, The University of Tokyo, Tokyo, JAPAN. It is known in many species that the presence of conspecific animal attenuates stress responses, which is called 'social buffering'. In this study, the effects of two types of social buffering i.e., the social buffering during memory consolidation and that during fear expression, on the conditioned fear responses were examined in adult male Wistar rat. On the training day, the subject was solitary fear conditioned using tone as conditioned stimuli (CS) and foot shocks as unconditioned stimuli. After the training, the subject rat was housed for one day either solitary or with an unfamiliar male rat (Pair-housing). On the next day, the subject rat was placed in a different context and was exposed to the CS either solitary or with an unfamiliar male rat (Pair-exposing). Its autonomic and behavioral responses to the CS were observed for assessing the two types of social buffering effects on fear responses. The Pair-housing suppressed the rise in body temperature in response to the CS, whereas the Pair-exposing diminished the freezing behavior in subject rat. In addition, these two types of social buffering additively attenuated the fear responses. These results suggest that the autonomic and behavioral components of conditioned fear responses are differentially attenuated by social buffering effects of a conspecific depending on the timing of its accompaniment.

ANXIOLYTIC-LIKE EFFECT OF ANANDAMIDE INJECTED INTO THE RAT DORSOLATERAL PERIAQUEDUCTAL GRAY IN THE VOGEL TEST. Lisboa, S.F.S.; Aguiar, D.C.; Resstel, L.B.M; Guimarães, F.S. Department of Pharmacology, FMRP-USP, Brazil Contradictory results exist concerning the effects of systemic injections of cannabinoid agonists on anxiety-related behaviors. Direct drug administration into brain structures related to aversive responses can help to clarify the role of cannabinoids on these behaviors. One such structure is the midbrain dorsolateral periaqueductal gray (dlPAG). The activation of CB1 receptors by the administration of the endocannabinoid anandamide (AEA) into this structure induces anxiolitic-like effects in the elevated pus-maze. This model measures the conflict generated by the drive to explore a safe (closed arms) versus unsafe (open arms) place. The aim of this work was to verify if AEA microinjection into the dlPAG would also evoke anxiolitic-like effects in another conflict model that is not based on exploratory behaviour, the Vogel conflict test. Male Wistar rats (n=4-6) with cannulas aimed at the dlPAG were water deprived for 24 hours and pre-exposed to the apparatus where they were allowed to drink for 3 min. After another 24 hours of water deprivation, they received a microinjection of vehicle or AEA (5 pmol/ 200 nL) into the dlPAG and 10 min later were placed in the experimental box. In the box they received an electrical shock (0.5 mA, 2 s) in the spout of a drinking bottle at every twenty licks. AEA significantly increased the total number of punished licks (192.0 ± 42) when compared with control animals (61±14, $t=3.2$, $D.F.= 8$, $p<0.05$). These results confirm, in a different conflict model, that AEA evokes an anxiolitic-like effect when microinjected in the dlPAG. Financial support: FAPESP, CAPES

SOCIAL ISOLATION ALTERS CORTICOTROPIN-RELEASING FACTOR RESPONSES IN ADULT RATS. Lukkes J[1]; Renner K[1,2]; Watt M[1,2]; Summers C[1,2]; Keifer J[1]; Forster G[1]; [1]Basic Biomedical Sciences, [2]Biology, University of South Dakota, Vermillion, SD. Early life isolation leads to alterations in stress behavior and monoaminergic activity in adulthood. Corticotropin-releasing factor (CRF) is a neurotransmitter that mediates stress and monoaminergic activity. Therefore, we hypothesize that early life stress enhances responses to CRF in adulthood. We investigated the effects of social isolation on CRF-mediated serotonin (5HT) release in the nucleus accumbens (NAc), and on CRF receptor levels in the dorsal raphe (dRN). On postnatal day 21, male rats were housed either individually (IH), or in groups of 3 (GH), for a 3 week period and then group-housed according to treatment for a further 2 weeks until adulthood. After the 5 week treatment, adult rats were implanted with

microdialysis probes into NAc, and CRF was infused into dRN. A significant decrease in NAc 5HT release was observed in GH animals infused with 100 ng CRF in the dRN, but this effect was completely absent in IH rats. In contrast, infusion of 500 ng CRF into the dRN resulted in an acute increase in NAc 5HT release in GH animals, which was greater in IH rats. To determine whether these enhanced effects of CRF in isolates were due to changes in CRF receptor levels in the dRN, immunofluorescence staining of CRF receptors was performed in IH rats and compared to GH rats. An increase in CRF_2 receptor levels in the lateral dRN of IH animals was observed. This study suggests that isolation during the early part of development causes alterations in both CRF receptor levels and CRF-mediated 5HT activity, which may underlie the increased sensitivity to stress observed in isolates.*Supported by NIH P20 RR15567 & R03 MH068303.*

CROSS-BREEDING STUDIES ON THE NAPLES RAT LINES REVEAL STRONG HERITABILITY OF BEHAVIORAL SELECTION TRAIT. Gironi Carnevale, U.A.; Vitullo, E.; Varriale, B. ;Viggiano, D.; Ruocco, L.A.; and Sadile,A.G. Lab. Neurophysiol. Behav. & Neural Networks, Dept Exptl. Med., II University of Naples, Naples, Italy Model systems, such as the Naples rat lines, can be used to study the genetic control of behavioral traits. The Naples High (NHE) and Low Excitability (NLE) rats have been studied in classical mendelian crosses. Thus, from parental lines P1 (NHE) and P2 (NLE), F1 and F2 hybrids and related backcrosses B1 (F1 x P1) and B2 (F1 x P2) were obtained. In addition sex-linkage of the trait was tested adding parental gender. Young adult (60-80 days) hybrids of both gender were exposed to spatial novelty (Lát-maze) for two 10-min tests measuring horizontal (corner crossings: HA), vertical (rearings on hindlimbs: VA) or total activity (HVA) scores. The heritability of HVA trait was estimated on the first 5-min of the test across the 20 generations of selection and all mendelian cross hybrids. Quantitative genetic analysis on HVA trait and HA and VA components, was applied by the Lynch and Walsh joint-scaling test procedure. Moreover, correlation between experimental data and different estimated models were also computed. Data indicate i) activity scores of mendelian hybrids graded and intermediate between parental lines, ii) no sex-linkage of trait, iii) higher activity scores for female, iv) high heritability of HVA trait (h2 index=0.824), v) polygenic+epistatic model for HVA and HA genetic transmission but a simpler one with fewer genes and lower epistatic effect for VA. In conclusion the Naples lines reveal strong genetic determinants for behavioral traits associated with polygenic pattern. Moreover, HA and VA activity components with prevailing cognitive and non cognitive meaning respectively, show differential genetic control. (Supported by a cofin-MIUR grant)

PRENATAL TETRAHYDROCANNABINOL (THC) EXPOSURE DISRUPTS SOCIAL AND OPEN FIELD BEHAVIOR IN MALE LONG EVANS RATS. Newsom, R. J.; Kelly, S. J. Department of Psychology, University of South Carolina, Columbia, SC 29208. Marijuana is the most frequently used illegal drug among women of reproductive age, but little is known about the consequences of using marijuana during pregnancy. THC (delta-nine-tetrahydrocannabinol), one of the active chemicals in marijuana, has been shown to cross the placental barrier as well as to be present in breast milk. In this study, pregnant Long Evans rats were assigned to one of three treatment groups (THC-exposed, vehicle control, and non-treated control) on day 1 of gestation. Drug exposure consisted of 2mg/kg of natural THC, administered twice daily by subcutaneous injection, from gestational day 1 through the entire pregnancy. Pups continued to receive drug exposure through postnatal day 10, in order to mimic exposure during all three trimesters in humans. Male rats from each group were tested starting on postnatal day 90 in a battery of tests, which included open field activity, active social interaction, and forced-swim test. There were no significant differences in weight gained by dams or weight of offspring when compared to controls. THC-exposed rats showed decreased distance traveled in the inner part of the open field and an increase in investigation time in the test of social interaction compared to both control groups. THC-exposed rats did not differ from controls in the forced-swim test. Thus, delta-9-THC exposure during development can result in increased susceptibility to anxious behavior and may impair social functioning in adulthood, suggesting permanent socioemotional effects of this type of exposure. (Supported by NIAAA RO1 11566 to SJK and the University of South Carolina Honor's College.)

EFFECTS OF MATERNAL SEPARATION AND SEX ON RISK-TAKING, ORIENTING AND GENERAL ACTIVITY OF ADOLESCENT HOLTZMAN RATS. Spivey, J.; Padilla, E.; Barrett D.; Gonzalez-Lima F. University of Texas at Austin. Institute for Neuroscience. 1 University Station A8000, Austin, Texas 78712 USA. The objective of this study was to determine the effects of mother-infant separation on adolescent behavior of male and female rats. The use of different separation protocols and rat strains has led to discrepancies in the literature. One common feature, regardless of these differences, is that maternal separation (MS) is a stressful manipulation that results in immediate and long-term behavioral changes. Sixty Holtzman albino rat pups born to 6 timed-pregnant mothers were separated into 3 groups consisting of equal male-to-female ratios at postnatal day 2 (P2). The

MS group was separated 6 hours daily, early handled (EH) group 15 min daily and standard facility reared (SFR) group was not separated. Separations were performed during P2 through P6, and P9 through P13. Animals were tested for novel open-field activity (P28), followed by testing in the defensive withdrawal (DW) apparatus (P29) and familiar open field (P30). Behavioral measures were classified into general activity (ambulatory and stereotypic time), orienting (rearing time) and risk-taking (velocity and exposed zone time). Generally, the MS group showed less activity and risk-taking than the EH or SFR groups. The MS group showed more orienting behavior in the familiar open field, less risk-taking in the light-dark test (DW), and less ambulatory and stereotypic activity. Males showed more activity, impulsivity and risk-taking than females in novel open field. Previously, contradictory results have been found using different rat strains. Therefore, this methodology may represent a unique approach to the study of genetic and environmental interactions and could be useful in the development of selectively-bred animal models. (Supported by NIH grant T32MH065728).

BEHAVIORAL ALTERATIONS AND MEMORY IMPAIRMENTS IN RATS PRENATALLY EXPOSED TO GASTRIN-RELEASING RECEPTOR BLOCKADE.Presti-Torres, J.; de Lima, M.N.; Scalco, F.S.; Garcia, V.A.; Guimarães, M.R.; Schwartsmann, G.; Roesler, R.; Schröder, N. Laboratório de Biologia e Desenvolvimento do Sistema Nervoso, Programa de Pós Graduação em Biologia Celular e Molecular, Faculdade de Biociências, Pontifícia Universidade Católica do Rio Grande do Sul, Brasil. The gastrin-releasing peptide receptor (GRPR) has been implicated in central nervous system (CNS) diseases, including neurodevelopmental disorders associated with autism. In the present study we examined the effects of GRPR blockade during the neonatal period on behavioral measures relevant to animal models of neurodevelopmental disorders. Male Wistar rats were given an intraperioteneal (i.p) injection of either saline (SAL) or the GRPR antagonist [D-Tpi6, Leu13 psi(CH2NH)-Leu14] bombesin (6-14) (RC-3095; 1 or 10mg/kg) twice daily for 10 days from postnatal days (PN) 1 to 10. Animals treated with RC-3095 showed pronounced deficits in social interaction when tested at PN 30-35 and impaired 24-h retention of memory for both novel object recognition (NOR) and inhibitory avoidance tasks tested at PN 60-71. Neither short-term memory tested 1.5h posttraining nor open field behavior were affected by neonatal GRPR blockade. The implications of the findings for animal models of neurodevelopmental disorder are discussed.

ROLE OF ESTRADIOL ON THE REGULATION OF ELECTRICAL ACTIVITY OF CORTICO-AMYGDALOID-HIPPOCAMPAL CIRCUIT IN PRENATAL MALNOURISHED FEMALE RATS. J Pretelín, Cintra L, P Durán Neurobiología del desarrollo, INB, UNAM Campus Juriquilla, Queretaro, Mexico Increased probability to suffer emotional disorders has been linked to variation of estrogens. In women, hormonal replacement therapy seems to solve mood disorders associated to post menopause. It is not well known how estradiol acts to produce this regulation on emotional homeostasis. It is known some structures of the limbic system presents estradiol receptors and it is also possible that the hypothalamic-hypophysis-adrenal axis is involved on the regulation of female anxiety and other disorders. On the other hand, although a proper functioning of limbic system structures is important to keep an optimal emotional state, its known that prenatal protein malnutrition generates behavioral deficits related to stressful experiences. Previous studies in our lab had shown a refractory effect of stress in the dynamic oscillations of cortico-amygdaloid-hippocampal electrical activity on male malnourished rats. Assuming a role of oestradiol on the regulation of emotional status, the aim of the present study is to determine if the exogen administration of estradiol reestablish the electrical activity of cortico-amigdaloid-hipocampal circuit in female malnourished rats submitted to a restraint stress experience. Preliminary results shows a hemispheric asymmetry in the basal electrical brain activity of malnourished female rats and after stress estradiol seems to generate a dynamic coupling on electrical pattern similar to that observed in control rats. INB- UR 304 , DGAPA IN 201505 and CONACYT 40168-M

RELATIONSHIP BETWEEN SLEEP PARAMETERS AND INHIBITORY AVOIDANCE PERFORMANCE IN SLEEP DEPRIVED RATS Moreira K.M., Hipolide D.C., Tiba P.A., Tufik S. and Oliveira M.G.M. Psychobiology Department, Universidade Federal de Sao Paulo - BRAZIL. A relationship between sleep and memory has been proposed by a large body of literature. Accordingly, sleep deprivation (SD) produces deleterious effects on learning and memory processes. However, few studies have raised the question that SD induces a sleep rebound, which would hypothetically be positive to memory consolidation. The aim of the current work was to quantify the sleep disruption after a period of sleep loss in male Wistar rats submitted to the multiple trial inhibitory avoidance task. This task allows accessing both acquisition and retention phases of memory formation. Rats were trained on the task after 96h of SD or control condition. Retention test was performed 24h later. Sleep recording was conducted continuously between training and test sessions. Sleep deprived rats required more trials to reach the criteria than control during task acquisition. Test performance was still impaired, although the percentage and episode number of

REM and transition sleep (TS) were augmented. Correlative analyses between sleep variables and rats performance showed that SWS amount was directly correlated with training performance but not test. REM and TS parameters were inversely correlated with both training and test performances. These results suggest that sleep loss before training may be responsible for memory deficits during both task acquisition and retention and post training REM increasing does not revert impairment induced by SD. Moreover, acquisition and retention seem to be regulated by particular elements of sleep since SWS is related only with training performance. Supported by Fapesp, Capes, Afip.

GENDER DIFFERENCES IN REM SLEEP OF RATS SUBMITTED TO LONG AND BRIEF MATERNAL SEPARATION. Tiba P.A.; Tufik S.; Suchecki D. Psychobiology Department, Universidade Federal de Sao Paulo - BRAZIL. In humans, biopsychosocial factors, including early trauma and familiar problems may predispose to sleep disturbances. In view of the established correlation between HPA axis disturbances and sleep parameters, in addition to gender differences and influences, we sought to investigate the effects of brief (BMS) and long maternal separation (LMS) on baseline and cold stress-induced sleep of male and female rats. Whole litters were submitted to BMS or LMS (15 or 180 min /day away from the mother, from postnatal days 2-14) or kept undisturbed in their home cage (CTL). Baseline sleep was recorded for 22 h and again after 1h of exposure to cold stress. Additional subsets of animals were sacrificed before, 1 or 3h after the stressor for plasma corticosterone determination. We found an increase of baseline REM sleep in male Wistar rats submitted to LMS, compared to CTL and BMS rats; in response to cold stress, however, all three groups exhibit the same pattern of sleep rebound. In females, on the other hand, we did not observe major differences in the baseline sleep among the groups, but LMS led to a significant stress-induced REM sleep rebound during the nighttime period. All groups exhibited similar basal and stress-induced corticosterone levels. The present results indicate that manipulations applied during infancy modify the sleep pattern and the expression of sleep rebound. The augment in baseline REM sleep for males, and as a response to stress in LMS female rats suggest some sex-differences for the effects of early manipulations. Supported by FAPESP, CNPq, AFIP.

EFFECTS OF DORSAL STRIATUM AND AMYGDALOSTRIATAL PATHWAY LESIONS ON TONE FEAR CONDITIONING RETRIEVAL Ferreira, T.L.; Moreira, K.M.; Fornari. R.V.; Soares, J.C.K.; Tiba, P.A.; Oliveira, M.G.M. Department of Psychobiology, Federal University of Sao Paulo, Brazil. The central nucleus of the amygdala (CeA) - a critical structure in emotional memory - projects substantially to the substantia nigra pars compacta and retrorubral nucleus, both of which provide dopaminergic innervation of the dorsal striatum (DS). DS is involved in various forms of learning and memory such as procedural learning, habit learning, reward-association and emotional learning. Previous studies from our group showed that pre-training DS and asymmetrical contralateral (CeA-DS) lesions impaired tone fear conditioning task (TFC). The purpose of present study was to verify the role of: 1) DS on TFC evaluated by somatomotor response (freezing) and neuroendocrine response (ACTH levels), and 2) CeA-DS communication on retrieval of TFC. Male Wistar rats were lesioned in DS or CeA-DS (consisting of electrolytic lesion of CeA in one hemisphere combined with a dorsal striatum lesion in the contra-lateral hemisphere) 21 days after training of TFC task. Seven days after lesion, the animals were tested to TFC. Bilateral DS lesion impaired freezing time in TFC task. ACTH levels were not different between groups (DS and control) 20 min after TFC test. CeA-DS lesion did not impair the freezing response on TFC. These results suggest that the DS itself is not the locus for CS-US association and probably, is involved only with somatomotor response conditioned to tone. On the other hand, amygdalo-striatum pathway could be involved only with acquisition and consolidation of TFC, in accordance with previous results. Supported by: AFIP, CNPq, FAPESP, CAPES.

EARLY HANDLING ENRICHMENT RENDERS MOUSE PUPS UNRESPONSIVE TO ANXIOLYTIC DRUGS AND INCREASES NGF LEVELS IN THE HIPPOCAMPUS. [1]Capone, F.; [1]Bonsignore, L.T.; [2]Aloe, L.; [1]Alleva E.; [1]Cirulli F. [1]Section of Behavioural Neuroscience, Department of Cell Biology and Neurosciences, Istituto Superiore di Sanità, Viale Regina Elena 299, I-00161 Rome, Italy. [2]Institute of Neurobiology and Molecular Medicine, CNR, European Brain Research Institute (EBRI), Via Fosso di Fiorano 64/65, I-00143 Rome, Italy. Early life experiences, such as early handling, can influence neural development of rodents leading to changes in physiological and behavioural reactivity to stress. These effects are likely to be mediated by changes in maternal behaviour. This study analyzed the effects of different manipulations of the rearing environment on maternal behaviour and the behavioural and physiological response to mild challenges in CD-1 mouse pups early during development. Litters underwent either 15 min of neonatal handling (H) or were exposed briefly to an unfamiliar male intruder from postnatal (PND) days 2 to 14 (MI). Both groups were compared with litters which were not manipulated (NH). Compared to NH subjects, licking behaviour in the MI group was increased only on the first day of introduction of the male intruder, while the H group showed an increase in maternal behaviour on PND 10. On PND 8, pups

ultrasonic vocalizations were recorded upon treatment with an anxiolytic drug (chlordiazepoxide 0, 2, or 7.5 mg/kg). Results indicate that, although there were no differences among the groups when mice were injected with vehicle, handled subjects did not reduce their calling rate following drug administration, in contrast to the NH and MI groups. Following maternal separation and novelty exposure on PND 9, levels of hippocampal NGF increased significantly only in the H group. These data suggest that active pup manipulations in the form of handling favour behavioural and neural plasticity resulting in the maintenance of a high level of arousal and in increased neurotrophin levels in response to an acute manipulation. Changes in hippocampal levels of NGF might be involved in the appraisal of subtle changes in the early social environment.

STRESS REACTIVITY IN MATERNALLY SEPARATED ADOLESCENT MICE. Cornwell, C.A.; Thomas, N.R.; Leister, K. Dept. of Psychology. Syracuse University, Syracuse NY 13244 USA. The maternal separation (MS) procedure consists of removing infant rodents from their nest and mother for 3 hours daily during the first 2 weeks of life, to model the effects of rearing human infants in environments that prevent normal bonding with a caretaker, such as orphanages or successive foster homes. Heightened stress reactivity has been documented in adult MS rodents, but its developmental time course has not been examined. The present study evaluated adolescent MS and control mice, in the elevated plus maze – a measure of fear of heights, and the open field – a measure of response to novelty. On postnatal day 40-41, 1 male and 1 female from each of 9 MS and 9 control litters were tested on the open field, and another male and female were tested on the elevated plus maze. The open field was a Plexiglas box with a floor grid of 64 squares, 36 of which were central squares not adjacent to the wall. The elevated plus maze was supported 1 m above the floor and had 4 arms arranged as a cross, with an open platform connecting them at the center. Walls enclosed 2 opposing arms, and the other 2 arms were open. In the elevated plus maze, MS reduced male total time on the open arm, increased male total time on the closed arm, and reduced the percent of male arm time spent on the open arm. It also reduced the time males spent in the central squares of the open field apparatus. Maternal separation did not significantly influence any of these variables for females, implying that MS affects the development of underlying neuroendcrine substrates differently in males vs. females. Supported by the Center for Health and Behavior, Syracuse University.

LONG-LASTING EFFECTS OF MATERNAL SEPARATION UPON DISTINCT MEMORY TASKS AND DEFENSIVE BEHAVIOR IN RATS. Diehl, L.A.; de Oliveira Alvares, L.; Andreazza, A.C.; Carobrez, A.P.; Gonçalves, C.A.; Quillfeldt, J.A.; Dalmaz, C. Dep. Bioquímica e Biofísica e PPG Neurociências, UFRGS, and Dep. Farmacologia, UFSC. The first two weeks of life are a critical period for neural development in rats, and postnatal rearing conditions are known to influence this process. Prolonged periods of maternal separation (MS) usually increase stressor reactivity during adulthood, and enhance anxiety-like behavior. The purpose of the present study was to verify if repeated long-term MS would affect performance in different memory tasks when adults; we also verified DNA damage to the hippocampus. Male Wistar rats were subjected to repeated MS (3h/day) during post-natal days 1-10. At 70 days of age, the subjects were exposed to sequential (7 days apart) different tasks to evaluate memory. One month after the last behavioral evaluation, the animals were sacrificed and DNA damage to the hippocampus was assessed using the comet assay. In the object recognition test, MS animals showed a deficit in performance, with less exploration of the new object. No effects were observed in the Morris water maze. In the inhibitory avoidance task, MS animals presented a marginally significant difference, with higher latencies to step-down, especially when short-term memory was tested (90 min after training). An increased defensiveness towards the cat odor (conditioning session) was detected in MS rats, whereas no significant effect was detected 24h later, during the context session. A higher score of DNA damage was observed in hippocampus of MS rats. These results suggest that an early stress experience such as MS may increase damage to the hippocampus and also affect defensive behavior during adulthood, and that this effect is task-specific. Performance was affected mainly in tasks involving emotional aversive contents, which underlies the consolidation of the memory process. Supported by CAPES and CNPq.

PATERNAL EXPERIENCE ENHANCES BEHAVIORAL AND NEUROBIOLOGICAL RESPONSIVITY ASSOCIATED WITH AFFILIATIVE AND NURTURING RESPONSES [1]Everette, A.,[1]Fleming, D., [1]Higgins, T.,[1]Tu, K., [2]Bardi, M., [2]Kinsley, C.H., & [1]Lambert, K.G. Dept of Psychology, Randolph-Macon College, Ashland, VA 23005 USA1; Dept of Psychology, University of Richmond, VA 231732. To further investigate the degree of plasticity in the paternal/nurturing response, the goal of the current study was to investigate affiliative behavior in fathers, virgins, and pup-exposed virgins from both the nonpaternal *Peromyscus maniculatus* and paternal *Peromyscus californicus* species. In the pup affiliation assessment, each male was exposed to a conspecific alien pup constrained in a mesh enclosure (i.e., *pup tent*). Pup-exposed males and fathers of both species showed more interest

in the restrained pup (e.g., increased contact time) than virgin males (p=.03). Further, *californicus* males contacted the pup tent more than *maniculatus* males (p=.03). Brain analyses indicated that vasopressin-immunoreactive (ir) cell bodies and fibers were increased in the paraventricular nucleus (PVN) of the hypothalamus in fathers and pup-exposed males of both species compared to virgins (p=.00); additionally, *californicus* males exhibited more vasopressin-ir fibers and oxytocin-ir in the PVN than *maniculatus* (p=.00, .00, respectively). Furthermore, in response to the pup-exposure test, paternal and pup-exposed males had more *c-fos-ir* in CA1 of the hippocampus than virgins (p=.00)—perhaps indicating enhanced motivation or problem/solving to retrieve the pup from the enclosure. Additionally, pup-exposed males and fathers exhibited more *c-fos-ir* in the prefrontal cortex, also involved in cognitive functions (p=.00), than virgins. In sum, the current data suggest minimal exposure to conspecific pups enhances both social interest toward a novel pup and immunoreactivity in brain circuits associated with parental/nurturing and positive social responses. Future research with these species may serve as a valuable animal model for disorders such as autism, in which affiliative behaviors are compromised.

24H MATERNAL DEPRIVATION INDUCES ANXIETY AND DEPRESSIVE-LIKE BEHAVIOR IN ADULT WISTAR RATS FATURI, C.B.; SUCHECKI, D. Psychobiology Department – UNIFESP, Brazil. Adverse events in childhood have been related to development of psychopathologies, such as depression and anxiety disorders. In rats, stressful events during neonatal period, like 24h Maternal Deprivation (MD), may be an interesting tool to understand how stress during early life leads to changes in behavior and stress response in adulthood. According to some studies, MD on the 3rd day (MD 3-4) or 11th day (MD 11-12) of life results in opposite changes in Hypothalamus-Pituitary-Adrenal (HPA) axis functioning, i.e., hyper and hyporresponsiveness, respectively. Since in human beings anxiety and depression, are somehow related to changes in stress response, the aim of this work was to investigate whether MD leads to differential behavioral responses in adult rats submitted to MD 3-4 or MD 11-12. Non deprived animals formed the control group (CTL). In order to assess anxiety-like behavior adult male rats were tested in the Light/Dark Box (L/D) Test. ANOVA showed that the percentage of time spent in the lit compartment was different between groups (p=0.03), so that PM 11-12 group was lower than CTL (P=0.03). Anhedonia induced by the Chronic Mild Stress (CMS) Test was evaluated to investigate depressive-like behavior. Two-way ANOVA showed interaction between MD and CMS factors in the percentage of sucrose intake (p=0.03). Post hoc analysis showed no change of intake in non-CMS, whereas PM 3-4/CMS presented pronounced decrease in this parameter in comparison to CTR/CMS group (p=0.00). PM 11-12/CMS was not different from either group. These results corroborate our hypothesis and strength the possibility of using MD as an animal model of susceptibility to human psychopathologies. Work supported by AFIP and FAPESP, and fellowships from CAPES and CNPq.

ENDOCRINE ASPECTS OF THE OPIOIDERGIC STIMULATION IN PREGNANT RATS. Felicio, L.F.; Sukikara, M.H.; Felippe, E.C.G.; Anselmo-Franci, J.; Oliveira, C.A. University of Sao Paulo, Sao Paulo, Brazil. Opioid peptides play an important role in maternal behavior as well as in physiological and pathological phenomena involving motivation. Morphine low doses treatment during late pregnancy is able to change the expression of maternal behavior patterns. This study was designed to investigate the endocrine aspects of this animal model. Aiming this, corticosterone, progesterone, estradiol and prolactin serum concentrations were measured in morphine treated animals during late gestational period. Wistar rats 80-120 days old were mated and separated in two major groups: Saline and Morphine. Treatment was initiated in 17th gestation day, when morphine or saline injections started in daily doses of 3.5mg/kg, until day 21. Animals were decapitated 30 minutes after each saline/morphine injection and serum samples were colleted. Hormonal levels were measured by radioimmunoassay. Results: there were no significant alterations in corticosterone levels. This result suggests that the treatment was unable to promote more stressor effects than those caused by saline injections. Concerning to progesterone concentrations there were a significant differences between saline and morphine groups. The serum concentrations of this steroids were increase in all treatment days. This increase may be cause the behavioral changes induced by of this morphine treatment. Estradiol and prolactin serum concentrations did not show significant changes as compared just to saline group. Since this opioidergic stimulus altered progesterone concentrations, this suggests that morphine stimulates progesterone release during late gestational period with possible behavioral consequences. Supported by FAPESP # 2004/00571-9

MATERNAL EXPERIENCE ENHANCES NEUROBIOLOGICAL AND BEHAVIORAL RESPONSES IN AN ATTENTION SET-SHIFTING PARADIGM [1]Higgins, T., [1]Everette, A.,[1]Fleming, D., [2]Christon, L., [2]Kinsley, C.H., & [1]Lambert, K.G. Dept of Psychology, Randolph-Macon College, Ashland, VA 23005 USA1; Dept of Psychology, University of Richmond, VA 23273 USA2 Research suggests that maternal experience remodels the female rodent brain, resulting in adaptive responses (e.g., efficient foraging) for taking care of offspring (Kinsley & Lambert,

2006). The current study explored the effects of maternal experience on attentional processes in multiparous (two litters), primiparous (one litter), and virgin aged-matched Long-Evans rats (n=8, each group) in an attention set-shifting paradigm. Rats were exposed to various olfactory stimuli and bedding materials in simple and compound discrimination trials with intra- and extra-dimensional shifts. Although all groups performed similarly in the simple discrimination trials, maternal animals performed more efficiently in the remaining, more challenging tasks ($p<.05$ in all cases). Specifically, in the complex discrimination trial, multiparous animals found the froot loop reward faster than virgins; in the intra-dimensional shift task, both multiparous and primaparous animals retrieved the reward faster than virgins and virgins made more errors; and in the extra-dimensional shift trials, multiparous rats had shorter latencies than primiparous and virgins rats, and the multiparous animals had fewer errors than the other groups. Histological analyses suggested enhanced neuroplasticity in the maternal hippocampus following training; specifically, a trend for increased CA3 nestin-ir [an intermediate filament protein marker for progenitor cells in developing and adult nervous systems (Rao et al., 2004)] ($p=.07$) was observed in multiparous animals compared to virgins. Finally, following the final trial, which was made unsolvable to activate problem solving circuits in the animals, no differences in fos-ir were observed in the hippocampus or prefrontal cortical areas. In sum, maternal experience enhances attention toward salient cues in complex tasks; such effects may have adaptive significance for maternal rats competing for limited resources.

NEONATAL STRESS AND MATERNAL CARE INTERACT IN CHANGING IN SELECTIVE GLUCOCORTICOID RECEPTOR mRNA CHANGES IN BALB/CBYJ MICE. Hodges, A.B., Brown, L.D., Nealy, C.J. Fowler, J.A. and Hohmann, C.F. Morgan State University, Baltimore, MD. Modifications in neonatal stress and maternal care can permanently alter stress reactivity and cognitive behavior in rodents (Champagne & Meaney, 2001). Neonatal handling and increased maternal care decrease stress reactivity (Beane et al., 2002) and enhance cognitive performance (Bredy et al., 2004). Conversely, chronic stress and maternal deprivation increase stress reactivity (Levine S., 2005) and impair cognitive behavior (Zaharia et al., 1996). Using a split litter design, we found that neonatal temperature/maternal separation stress (STR) during PNDs 2-7 causes altered cortical morphology and impaired cognition in Balb/CbyJ mice. Unexpectedly, littermate controls (LMC) were hyper-reactive to spatial change and novelty, and showed subtle altered cortical morphology compared to age matched controls (AMC). We have shown that STR pups receive significantly more licking/grooming (L/G) compared to LMC and AMC pups. The current study correlates maternal care received by STR versus LMC with cortical and hippocampal glucocorticoid receptor (GCR) expression throughout development and adulthood. PCR methods quantified GCR expression in extracted tissues at PNDs 7, 30 and 120. Preliminary data indicate STR mice (PND 120) express significantly less cortical and hippocampal GCRs compared to AMC. LMC also show subtle decreases in GCR levels. GCR expression was undetectable at PND 7. PND 30 is being analyzed. Decreased GCR expression in STR mice is consistent with previous observations in brains of maternally deprived rodents (Holmes et al., 2005), suggesting that altered cortical morphogenesis and cognitive behavior results from altered corticosterone responsiveness. Furthermore, the trend for decreased GCR levels in LMC mice supports our hypothesis that decreased L/G induces a persistent stress response in LMC mice. Supported by: SO6 GM051971 and R25 GM058904.

TEMPORAL CHARACTERISTICS OF SHOALING BEHAVIOUR OF ZEBRA FISH: LARGE SCALE DEVELOPMENTAL AND FINE RESOLUTION CHANGES. Buske, C.; Gerlai, R. Depart. of Psychology, University of Toronto at Mississauga, Canada. Vertebrate social behaviour is complex and its mechanisms are not fully understood. Numerous human clinical conditions exist in which abnormal social behaviour is the core symptom. Zebra fish, a highly social species, may be an excellent model organism to further our understanding of the mechanisms of social behaviour. However, social behaviour of zebra fish has not been characterized in a detailed manner. The first aim of this study was to determine how shoaling, a form of social attachment in fish, changes during the ontogenesis of this species. Anecdotical evidence and our pilot studies suggested that small fry did not shoal. We quantified shoal density (group cohesion) by measuring the distance between every pair of fish in a freely swimming group of 9 subjects using a custom software application developed in the lab. Group cohesion was tested across seven age groups (4, 11, 18, 28, 42, 68 and 92 days of age) in arenas proportional to the body size of the subjects. We observed a quasi-linear significant increase of group cohesion with age, the first demonstration of this phenomenon which will allow us to characterize the genetic and environmental factors underlying shoaling. We have started the analysis of the effects of different environmental factors (including visual stimuli, food and drugs) on shoaling in the adult and discovered that ethanol and exposure to food following a 24-hour food deprivation period decreased shoal density. In our fine grained analyses we also discovered a dynamic change of shoal density that appears to be cyclical. We are in the process of mathematically describing the parameters of the cycle pattern.

We hope that these pilot studies will lead us to the development of novel behavioural tests and quantification methods with which we will study the biological and genetic mechanisms of vertebrate social behaviours.

Friday, June 15, 2007

8:15-9:15 Matthew J Wayner-NNOXe Pharmaceuticals Award Lecture: William T. Greenough

PLASTIC BRAIN MECHANISMS IN FRAGILE X DISORDER. Greenough, W.T. Dept. of Psychology and Psychiatry and Neuroscience Program. University of Illinois at Urbana-Champaign, Champaign, IL 61820 USA. The cell, neural and behavioral biology of Fragile X Disorder, the most common form of inherited mental retardation, will be reviewed. The fragile X protein (FMRP), which is missing in fragile X disorder (FX), may be a fundamental component of plastic synaptic mechanisms. FMRP appears to be involved in the transport of mRNA from the nucleus to cytoplasmic sites of translation including locations in dendrites near synapses. Proteins encoded in transported mRNA include members of signaling pathways, neuronal structural proteins and contributors to a wide array of cellular functions, and many of these appear to depend on FMRP to assure their transport and translation at appropriate locations. FMRP itself is translated at synapses and this appears to be elevated by demands such as learning and environmental enrichment. Symptoms of the absence of FMRP in affected people or animal models include disordered neuronal morphology, excess numbers of synapses autistic-like behaviors, social aversion, mild to severe mental retardation, broad spectrum developmental delay, sensory hypersensitivity and seizures. This wide range of symptoms may reflect the functions of the individual genes whose mRNA is transported and translated by FMRP. Recent data indicate that effective drug treatment reverses FX-dependent alterations in cellular signaling pathways. Support: NIMH and Fraxa Fndn.

9:15-10:15 Matthew J Wayner-NNOXe Pharmaceuticals Award Lecture: Donald Stein

THE TRIALS AND TRIBULATIONS OF PROGESTERONE IN THE TREATMENT OF BRAIN INJURY: WAS THE GAME WORTH THE CANDLE? Stein, DG. Emory University, Dept. Emergency Medicine, Atlanta, GA 30322 USA. I will discuss how my laboratory came to view progesterone and its precursors and metabolites as agents that could enhance functional and structural recovery in the damaged brain. Our studies to confirm the beneficial effects of these neurosteroids took over 17 years to complete. At first the work was met with incredulity--it seemed just too good to be true. Fortunately, the salutary effects we observed eventually began to be replicated in other laboratories and in other injury models, including stroke. Recently our team at Emory completed an NIH-sponsored, Phase II (a), single-center trial for safety and efficacy of progesterone in 100 traumatically brain-injured patients resulting in a decrease of mortality of more than 50%. This is the first successful trial for TBI treatment in over 40 years of clinical testing, and has led to the support of the National Institutes of Neurological Disorders and Stroke to plan a much larger, multi-center trial. The functional, physiological and genomic mechanisms underlying progesterone's beneficial effects are still being discovered. These more recent developments will be discussed, including some of the more novel receptor and non-receptor mechanisms and actions of progesterone and allopregnanolone in the injured brain and spinal cord. I will provide experimental and clinical evidence that progesterone and its metabolites play a substantial role in reducing the metabolic and functional deficits in stroke and TBI, and will discuss other evidence showing that the hormones may also be effective in the treatment of some types of neurodegenerative injuries.

10:30-12:30 Symposium 5: The role of genetics and genomics in understanding fear- and anxiety-like behaviors.

GENETIC RELATIONSHIP OF FEAR AND ANXIETY: LESSONS FROM GENETIC REFERENCE POPULATIONS AND BEYOND. Palmer, A.A. University of Chicago, Chicago, IL. We will review recent evidence that indicates that there is a genetic correlation between the capacity for fear learning and innate anxiety, which can be thought of as an example of unlearned fear. A similar positive correlation has been reported for fear learning in human anxiety disorder patients. By examining learned fear and innate anxiety behaviors in populations of mice that were selectively bred for differential fear learning we have identified correlated responses to selection

for two measures of innate anxiety. In addition, we have employed a consomic mouse panel (B6.A) that has allowed us to is olate specific chromosomes that harbor genes that pleiotropically influence both fear and anxiety. These data support the existence of a broad genetic construct that has previously been termed "emotionality". Results of efforts to identify the underlying polymorphisms that pleiotropically influence learned fear and innate anxiety and their potential significance for the broader understanding of clinical anxiety disorders will also be discussed.

EMOTIONALITY-RELATED BEHAVIORS: WHAT GENOTYPES CAN TELL US ABOUT PHENOTYPES. Ramos, A. Department of Cell Biology, Embryology and Genetics. Federal University of Santa Catarina, Florianopolis, SC, Brazil. For over 50 years, behavioral scientists have compared distinct genetic groups of rodents reared in the same environment in a variety of emotionality-related behavioral tests. The pioneer studies aimed basically to demonstrate that genetic factors could influence emotional behaviors, whereas more sophisticated intercrossing approaches could be used to investigate their genetic architecture. More recently, contrasting inbred strains started to be used as tools to map and identify yet unknown genes influencing fear-related traits, whereas mutant strains differing for specific manipulated genes started to be broadly characterized. This huge amount of data mostly focused on the effects that genes and gene products might have on emotionality. However, interpreting the psychological significance of a given "emotional behavior" obtained from a particular test is extremely difficult. In this presentation, I will change the aforementioned focus in order to demonstrate how the accumulated behavioral data obtained from animals with different genotypes can contribute to the psychological understanding of emotional phenotypes and their relationship with other traits which, a priori, do not reflect emotionality. A series of studies using specific rat strains, either selectively bred or not, will be used as examples to illustrate: i) the multidimensional view of emotionality; ii) the relationship between emotionality and other traits such as drug addiction; iii) the idea that the genetic correlation between two types of emotional reactions should be always partial and thus vary among different populations; iv) the fact that using the mean values of genotypic groups instead of using individual scores seems to be more appropriate to unveil genetic and biological correlations among emotional behaviors.

INTERACTION OF GENOTYPE WITH THE EFFECTS OF CHRONIC ANTIDEPRESSANTS ON ANXIETY- AND DEPRESSION-RELATED BEHAVIORS. Dulawa, S.C.; Nitzke, A.M. Dept. of Psychiatry, University of Chicago, Chicago, IL 60637, USA. The onset of the therapeutic response to antidepressant treatment exhibits a characteristic delay. Animal models in which behavioral responses to antidepressants emerge following chronic, but not subchronic, treatment have remained elusive. Such models are required to study the mechanisms underlying the therapeutic effects of antidepressant treatment. We have investigated the behavioral effects of chronic treatment with selective serotonin reuptake inhibitors (SSRIs) in a broad panel of inbred mouse strains. Mice were evaluated for anxiety- and depression-related behavior in the open field, forced swim, and tail suspension tests following three weeks of SSRI administration in the drinking water. We found that only certain inbred strains, including the Balb/cJ, showed reduced anxiety- and depression-related behavior in response to chronic, but not subchronic, SSRI treatment. Our findings show that certain inbred mouse strains can be utilized to study the therapeutic effects of chronic antidepressant treatment, without any stress-inducing procedures. Studies investigating the role of specific serotonin receptors in the response to chronic SSRI treatment are currently underway.

USING GENETICS AND GENOMICS TO UNDERSTAND RELATIONSHIPS AMONG ANXIETY-LIKE BEHAVIORS AND OTHER TRAITS. E.J. Chesler, Z. Li, Y. Zhang, V. Philip, R. Kirova, E.J. Baker and M.A. Langston. Biosciences Division, Oak Ridge National Laboratory, Oak Ridge TN. Computer Science Department, Baylor University, Waco TX. Computer Science Department, University of Tennessee, Knoxville, TN. Fundamental research challenges in understanding the biology of anxiety, stress and fear behavior are to interpret relationships among behaviors, and to identify behaviors that share a biological substrate. Because the attributes we study are typically defined using phenomenology, they do not always map onto natural biological systems, nor do behavioral classification systems necessarily map onto essential drivers of behavioral categories. Systems biological approaches, including the development of high-throughput molecular profiling, have lead to a tremendous wealth of data that can be exploited to understand the ontology of behavior. Genetic approaches, including genetic correlations of behavior in genetic reference populations, have been successfully deployed on a large scale in databases and web tools such as GeneNetwork.org and the Mouse Phenome Database. Genomic approaches, including gene-phenotype associations, can also be ascribed using genetic correlation. These associations can be driven purely by genetic architecture, and must be validated using orthogonal populations or alternative experimental methods. By mining gene-phenotype associations across behaviors and experiments, we can define behaviors that share a similar biological basis. In this way, anxiety, stress, and fear can be placed in the context of other neurobiological phenotypes, and behavioral assays applied in various model organisms can be compared. Our approach is

implemented as a web-based tool called "Ontological Discovery Environment." It incorporates in novel ways combinatorial algorithms and statistical associations of genes and phenotypes.

Saturday, June 16, 2007

8:15-9:45 Symposium 6: Contributing factors to normal and pathological variation in social behaviors.

NEURAL AND BEHAVIORAL BASES OF ALCOHOL'S TERATOGENIC EFFECTS ON PLAY IN THE RAT. R.C. Lawrence; R. Newsom; C.H. Bonner; S.J. Kelly. Dept. of Psychology, University of South Carolina, Columbia, SC29208. Alcohol exposure during development induces characteristic physiological and cognitive deficits in both humans and rats. Importantly, this exposure also negatively impacts social behaviors. Social play is critical for the development of species-typical adult social behaviors. Somatosensory cues, particularly on the nape of the neck, are a key component in initiating pinning, which is central to play behavior in rats. Importantly, the somatosensory system may be a target of alcohol's teratogenic effects during development. This study systematically degraded somatosensory processing using topical anesthetic in order to determine the role of alterations in somatosensory processing in alcohol's effect on play behavior. The three trimester model of Fetal Alcohol Spectrum Disorder was used; experimental rats received alcohol from gestational day (GD) 1 thru 22 and from postnatal day (PD) 2 thru 10. Controls consisted of non-treated and intubated rats. Testing was conducted from PD 35-39 with each rat receiving four subcutaneous (sc) injections with either vehicle (saline), 0.5, 1.0, 2.0, or 4.0% xylocaine around the nape of the neck 15 minutes prior to a 5 minute test session. The number of pins and dorsal contacts were recorded. Perinatal ethanol exposure did not affect the number of dorsal contacts across any xylocaine condition. However, pinning was increased in the ethanol-exposed group. This increase was strongly reduced by the xylocaine manipulation at the 2.0% dose, an effect not observed in controls. Thus, play behavior in ethanol-exposed rats are at least in part due to changes in somatosensory processing. Supported by NIAAA 11566 to S.J.K.

MATERNAL CARE AND THE OFFSPRING REPRODUCTIVE BEHAVIOR IN THE RAT. Cameron, N.; Meaney, M. Douglas Hospital, Verdun, QC, Canada. Maternal care influences the development of neuroendocrine system and sexual behaviors in rats. High and Low licking and grooming (LG) mothers and their female offspring differ in the expression of estrogen-receptor a (ER a). High females show increased ER a expression in the medial preoptic area and decreased expression in the ventral medial hypothalamus (VMH) than Low offspring. During development, Low female offspring have a shorter anogenital distance and reach puberty earlier than High female offspring. Estrogen acting in the VMH influences sexual behaviors. Low offspring showed significantly greater lordosis ratings and shorter inter-intermission-intervals (III) than High females during pace-mating. Interestingly, in ovariectomized steroid-primed females, difference in lordosis was abolished whereas it was increased in III, suggesting that these behaviors are under different gonadal hormones regulations. The endocrine system in the two groups of females differs greatly. Estrogen, progesterone and LH surges were greater in Low proestrus female offspring compared to Highs. Pregnancy rate was also greater in Lows. In a partner-preference study, High females spent more time with High male offspring than Low males. Although in this study, Low male offspring were more often the first to ejaculate and showed a lower frequency of mount-without intromission compared to High males. These results suggest that offspring of Low LG mothers may be more reproductively successful under laboratory conditions, and underscore the importance of maternal care on the reproductive function and behavior in the rat. Funded by NIMH (RO1 MH 60381-06) and CIHR.

IMPLICATIONS OF THE IMPACT OF ALCOHOL EXPOSURE DURING DEVELOPMENT ON SOCIAL RECOGNITION MEMORY. Kelly, S. J.; Leggett, D. C. Department of Psychology, University of South Carolina, Columbia, SC 29208. Alcohol exposure during development has a variety of effects on social behavior in humans and rats that are strikingly comparable. The mechanistic explanation for these changes in complex behavior can be broached on a behavioral and on a neural level. On a behavioral level, social recognition memory may be critically involved in many social processes, particularly those occurring over long periods of time. Social recognition memory of a same-sex juvenile rat was tested in a group of adult rats exposed to alcohol during development, a group receiving the administration procedures but no alcohol exposure, and a group given no treatment. The first period of exposure to the juvenile was varied in order to affect the amount of time that the adult rat could investigate the juvenile to form the memory. The duration of the delay to the second period of exposure to the juvenile was

varied in order to assess the duration of the social memory. Investigation time was measured in both periods. Among female rats, ethanol exposure only results in social recognition deficits when the first period of investigation is limited, suggesting an initial encoding deficit. Among male rats, ethanol exposure causes social recognition deficits across all initial investigation periods but only at the later delays, suggesting a deficit in the ability to maintain memory. These findings suggest a behavioral cascade of deficits accounting for changes in adult social behavior. The manner in which perturbations in fundamental processes give rise to changes in complex behaviors demands further investigation using a multidisciplinary approach. Supported by NIAAA 11566 to SJK.

9:45-10:45 Keynote Lecture: Ivan Izquierdo

DIFFERENT MOLECULAR MECHANISMS IN DIFFERENT BRAIN SITES UNDERLIE MEMORY CONSOLIDATION. Izquierdo, I. Memory Center. Pontifical Catholic University of Rio Grande do Sul. Porto Alegre, RS 90610-000, Brazil. Evidence accumulated through the past 15 years has shown that memory consolidation of one-trial avoidance learning relies on a sequence of molecular events in the CA1 region of the hippocampus that closely resemble that of long-term potentiation (LTP) in that area, and probably represent LTP. However, abundant evidence suggests that, in addition, other molecular events, partly involving the same steps but with different timing and in different sequence in the basolateral amygdala, entorhinal, parietal and cingulate cortex are as important as those of the hippocampus for memory consolidation. I will review the various mechanisms involved and the possible interconnections between all these processes. In addition, the putative participation of other molecular events in the same or other brain areas will be commented upon. Overall, the findings indicate that memory consolidation of even a task as deceivingly simple as one-trial avoidance does not rely solely on hippocampal LTP or LTP-like events, and requires the concomitant participation of other brain systems and molecular processes. Supported by FAPERGS and CNPq, Brazil.

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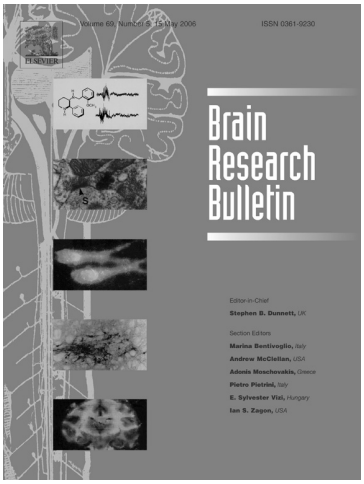

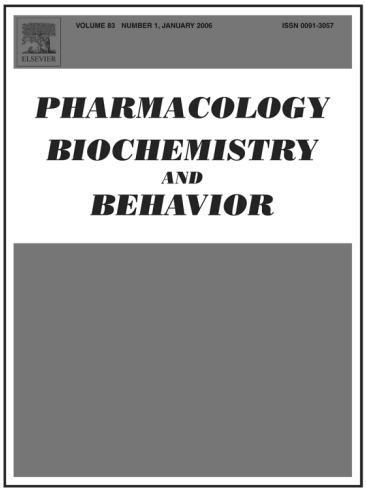

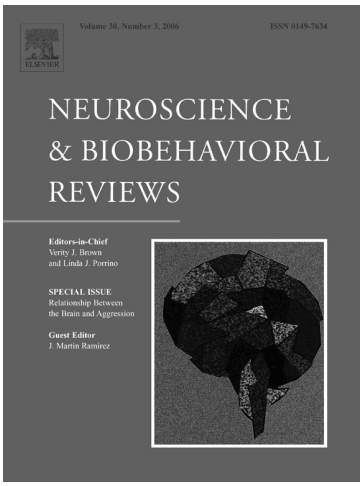

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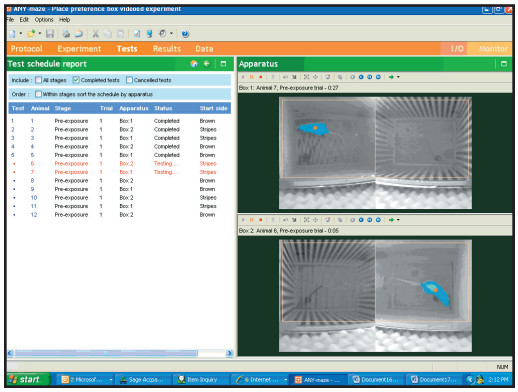

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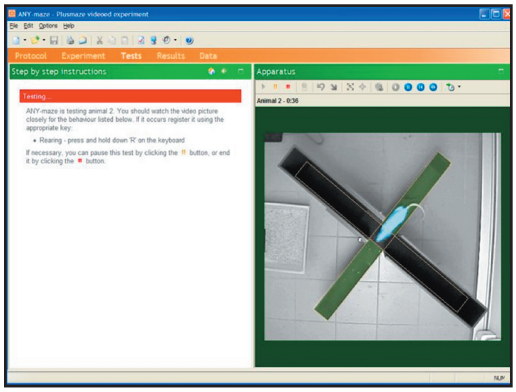

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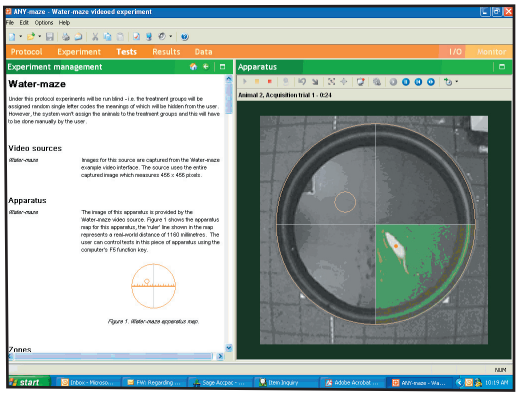

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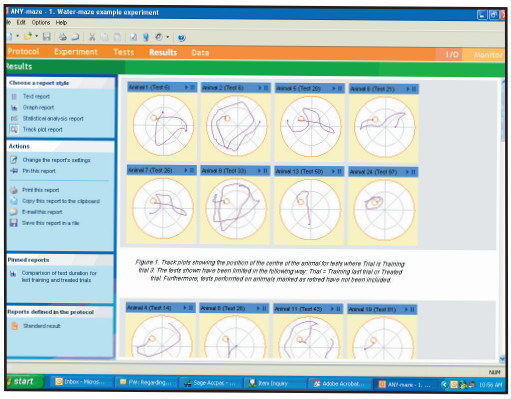

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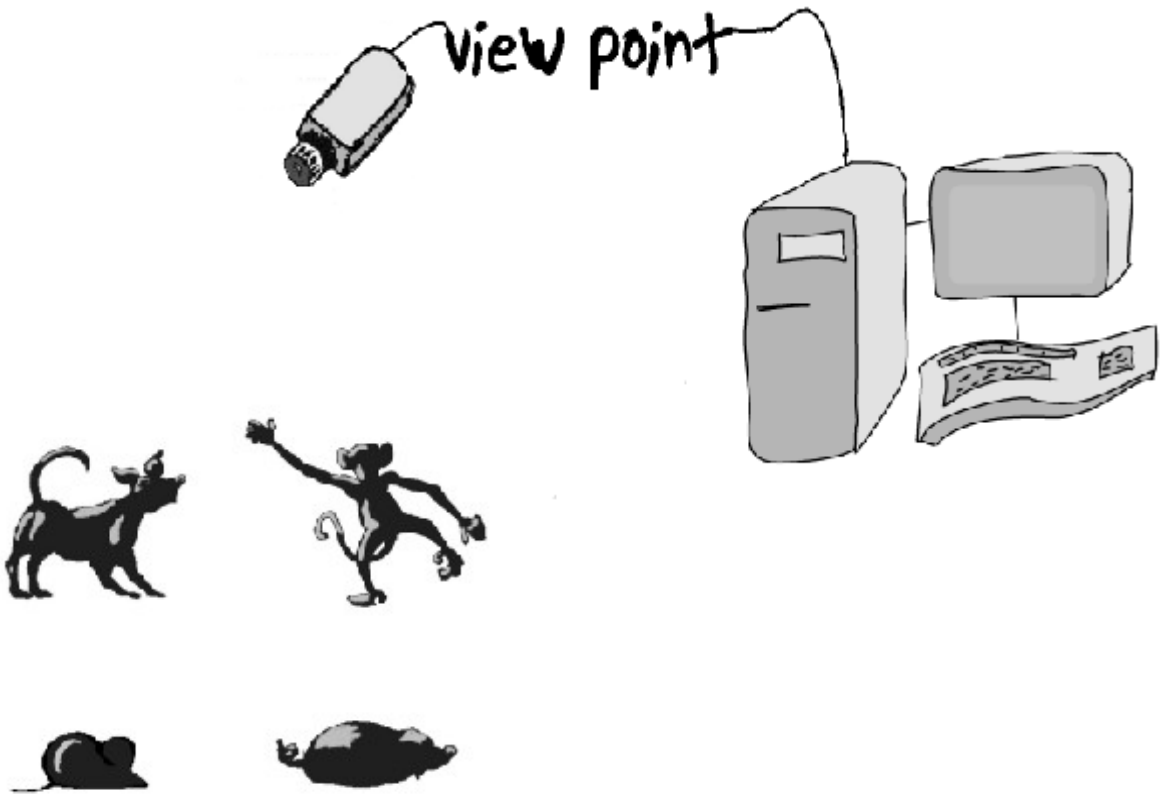

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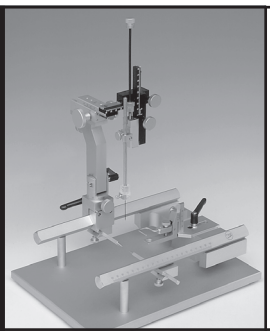

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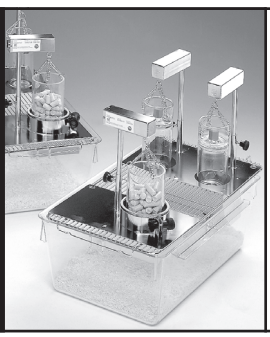

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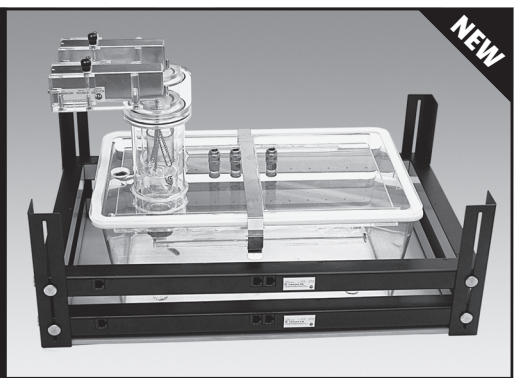
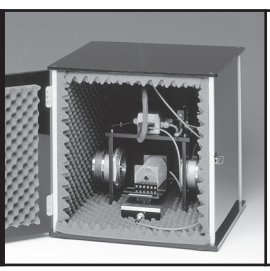


- Open circuit calorimetry system
- Quantifies energy expenditure & respiratory quotient RER
- Measures food & fluid intake
- Outputs total, ambulatory & fine movements as well as rearing

Passive Avoidance

- Step-through avoidance for rats & mice
- Variety of hardware components
- Optional rearing detection
- Comprehensive analysis
- Active or step-down avoidance option

Startle Response



- Acoustic, tactile & fear-potentiated startle
- User-defined trial sequences
- Complex PPI designs
- Outputs response latency & amplitude and more...

Please contact us for other products and details.

USA/Canada/Mexico:

TSE Systems, Inc.
784 S. Poseyville Road
Midland, Michigan 48640/USA
Phone: 1-989-698-3067
Fax: 1-989-698-3068
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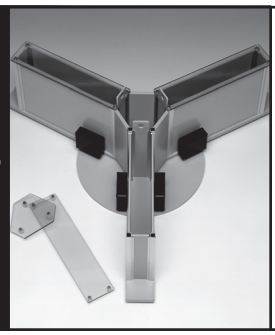
Internet: www.TSE-Systems.com

TSE systems

Sophisticated
Life Science Research
Instrumentation

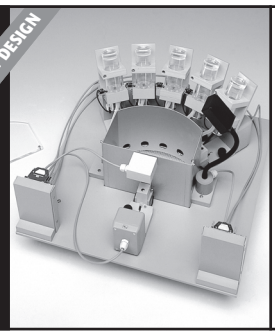
Maze Systems



- Y-maze, T-maze, radial maze or elevated plus maze
- Infra-red sensors monitor animal transfers
- Variety of hardware options e.g. shock grids, automatic feeders, sliding doors
- Easy-to-use software

5-Hole-Box

NEW DESIGN

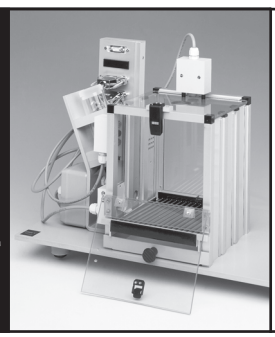


- Versatile attention testing system for rats & mice
- 5-choice serial reaction task
- Pellet feeder or liquid dispenser configuration
- Assess incorrect, correct & premature responses

VideoMot2 – Video Activity System

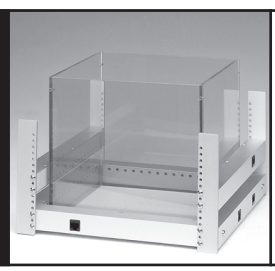
- For all arenas including open field, water maze, elevated plus maze, radial maze...
- Outputs distance travelled, time spent, latencies, entries, speed, rotation
- With key-board event recorder
- Optional 3D-rearing indicator

Operant Behavior



- Fully computerized modular Skinner boxes
- Suitable for intra-venous self-administration
- Incl. FR, VR, PR, FI, VI, DRH and DRL schedules
- Total flexibility due to the integrated schedule editor!

Motility Systems



- Study open field behavior or home-cage activity
- Variable box sizes and infra-red sensor densities
- Vertical movement detection
- Detailed spatial & temporal analysis of locomotion

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TSE systems

IBNS Program (short version)

All oral presentations will be held in the Itaipu Meeting Room.

Tuesday, June 12, 2007

2:00-4:00 Registration
4:00-6:00 Student Social - Location: Asian Corner Room.
7:00-8:00 Registration - Location: Foyer of the Itaipu Meeting Room
8:00-9:00 Welcome Reception - Location: Foyer of the Itaipu Meeting Room

Wednesday, June 13, 2007

8:30-8:45 President's Welcome
8:45-10:45 Symposium 1: Social and emotional behaviors: Focus on serotonin and vasopressin receptors.
10:45-11:00 Break & Exhibit Viewing
11:00-12:00 Presidential Lecture: Joseph Huston
12:00-2:00 Break /IBNS Council Meeting – Location: Mar Azul
2:00-3:30 Student Travel Award Slide Blitz
3:30-3:45 Break & Exhibit Viewing
3:45-5:45 Symposium 2: 5-HT and emotion: An appreciation of the contributions of Fred Graeff.
5:45-6:00 Break & Exhibit Viewing
6:00-8:00 Poster Session 1 – Location: Foyer of the Itaipu Meeting Room

Thursday, June 14, 2007

8:15-10:15 Symposium 3. Early-life stress to model the interactions between genes and the environment: From the clinic to animal models.
10:15-10:30 Break & Exhibit Viewing
10:30-11:30 Elsevier Keynote Lecture: John Aggleton
11:30-12:30 Oral session 1: Neural substrates of behavior.
12:30-2:00 Break
2:00-4:00 Symposium 4: Gene-environment Interactions: animal models for mental health research.
4:00-4:15 Break & Exhibit Viewing
4:15-5:45 Oral Session 2: Animal models of behavior and disease.
5:45 -6:00 Break & Exhibit Viewing
6:00-8:00 Poster Session 2 – Location: Foyer of the Itaipu Meeting Room

Friday, June 15, 2007

8:15-9:15 Matthew J Wayner-NNOXe Pharmaceuticals Award Lecture: William T. Greenough
9:15-10:15 Matthew J Wayner-NNOXe Pharmaceuticals Award Lecture: Donald Stein
10:15-10:30 Break & Exhibit Viewing
10:30-12:30 Symposium 5: The role of genetics and genomics in understanding fear- and anxiety-like behaviors.
12:30-6:15 FREE AFTERNOON
6:15-7:00 IBNS Business Meeting
7:15 Awards Banquet

Saturday, June 16, 2007

8:15-9:45 Symposium 6: Contributing factors to normal and pathological variation in social behaviors.
9:45-10:45 Keynote Lecture: Ivan Izquierdo
10:45-11:00 Break
11:00-12:30 Student Workshop
12:30-2:00 Grant Workshop
ADJOURN

Future IBNS Meetings:

June 17-22, 2008
Frenchman's Reef & Morning Star Marriott Beach Resort
St. Thomas, Virgin Islands

June 9-14, 2009
Wyndham Grand Bay - Isla Navidad Resort
Manzanillo, Mexico

2010 is still in negotiations
but will be outside North America.