

# **International Behavioral Neuroscience Society**



## *Annual Meeting Program and Abstracts*

*Whistler, British Columbia, Canada  
May 23-28, 2006*

**Abstracts of the International Behavioral Neuroscience  
Society, Volume 15, June 2006**

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## *IBNS CENTRAL OFFICE*

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Marianne Van Wagner, Executive Coordinator

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## *PRESIDENTIAL WELCOME*

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Dear Colleagues,

It my great pleasure, as President of the International Behavioral Neuroscience Society (IBNS) to welcome all of you to the 15<sup>th</sup> Annual meeting. This is a memorable occasion for me. Memorable because as the first Canadian president of the IBNS I have been afforded the honor of welcoming our international community of neuroscientists to our first Canadian meeting. The venue was chosen carefully to showcase some of the wonders of this vast country and its astonishingly pristine natural beauty. There is much to distract you here, and I sincerely hope you take the time to enjoy the many opportunities for outdoor activities provided by Whistler and the Fairmont, Chateau Whistler.

We are here, of course for other than reasons of tourism. Thanks to your gratifying interest, and to our program committee and its Chair, Dr. Andrew Holmes, we have a very strong, and varied scientific program. There are several firsts associated with the program worth mentioning. For the first time we have eight symposia. In addition there is record number of travel awards for our student members, which should make for a varied and rewarding student travel award blitz. We can look forward to addresses from three outstanding behavioral neuroscientists – our Canadian Keynote speaker, Dr. Michael Meaney; our American Keynote speaker, Dr. James McGaugh, and our American Wayner/NOXXe award winner, Dr. William Greenough. There are two oral sessions and 137 poster presentations. In all there will be a total of 205 presentations.

The success of this meeting depends on the efforts of many. Foremost it is you, the participants. However the work of making this meeting happen requires the energies of many IBNS members. The advice and efforts of the awards committee and its Chair, our past president, Dr. Sue Carter were invaluable and are gratefully acknowledged. Many thanks are due to our organizing committee members, Drs. Stefan Brudzynski, Robert Gerlai and Lisa Kalynchuk. Finally, the work of developing a venue is an important and difficult task. As chair of the venue committee, I have learned first hand what such a task entails. It could not have been done without the effort and considerable expertise of our Executive Coordinator, Marianne Van Wagner. I offer a special thanks to Marianne for her invaluable help in this endeavor.

I am looking forward, as I am sure are you, to a very successful meeting. So to one and all, welcome to the 15<sup>th</sup> Annual Meeting of the IBNS in beautiful British Columbia, Canada.

Best wishes,

*Bob*

*Robert Adamec*  
*IBNS President*

## **OFFICERS**

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<i>President</i> .....	Robert Adamec
<i>President-Elect</i> .....	Joseph Huston
<i>Immediate Past-Pres.</i> .....	C. Sue Carter
<i>Past-President</i> .....	Robert J. Blanchard
<i>Secretary</i> .....	Lisa Kalynchuk
<i>Treasurer</i> .....	Sonya Sobrian

### *Past Presidents*

Mark A. Geyer .....	2002
John P. Bruno .....	2001
Jacqueline N. Crawley .....	2000
László Lénárd .....	1999
Robert L. Isaacson .....	1998
Michael L. Woodruff .....	1997
Gerard P. Smith .....	1996
Linda P. Spear .....	1995
Robert D. Myers .....	1994
Paul R. Sanberg .....	1993

### *Founding President*

Matthew J. Wayner .....	1992
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## **COUNCIL MEMBERS**

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Australasia .....	Iain McGregor
Canada .....	Stefan Brudzynski
Europe .....	Anders Agmo
.....	Giovanni Laviola
Japan .....	Yoichi Ueta
Latin America .....	Magda Giordano
Student .....	Melanie Paquette
USA .....	Robert Gerlai
.....	Kelly Lambert
.....	Paul Rushing

## ***STUDENT TRAVEL AWARDS***

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We are pleased to announce the recipients of the IBNS Travel Awards for the 2006 meeting in Whistler, Canada. These awards will be presented at the Conference Banquet on Saturday evening. Award winners will receive a cash award, certificate, and waiver of registration and banquet fees. Congratulations to all.

### **TRAVEL AWARDS**

*(listed by category and alphabetically)*

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

#### ***Postdoctoral***

**Melissa Glenn**, *Duke University, USA*

**Todd Gould**, *NIMH/NIH, USA*

**Florence Roulet**, *The Brain Body Institute and McMaster University, Canada*

**Maria Toledo-Rodriguez**, *Swiss Federal Institute of Technology (EPFL),  
Switzerland*

**Ajai Vyas**, *Stanford University, USA*

#### ***Graduate***

**Karen Alsene**, *University of Wisconsin-Madison, USA*

**Nurith Amitai**, *University of California, San Diego, USA*

**David Ballok**, *McMaster University, Canada*

**Lisa Briand**, *University of Michigan, USA*

**Neil Fournier**, *University of Saskatchewan, Canada*

**Sarah A. Johnson**, *University of Toronto, Canada*

**Amanda C. Kentner**, *University of Ottawa, Canada*

**Stephen Mahler**, *University of Michigan, USA*

**Melissa Perreault**, *McMaster University, Canada*

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

## *SPONSORS*

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The IBNS would like to express our gratitude to the following organization who has given financial support to the 15th 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**

## *CORPORATE SPONSORS*

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

**Elsevier Science, Inc.**  
**TestDiet<sup>®</sup>** div. of Land O'Lakes Purina Feed, LLC  
**Stoelting Co.**  
**TSE Systems, Inc.**

## *EXHIBITORS*

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The IBNS would like to express our appreciation to the following exhibitors and publishers that are attending the meeting as booth exhibitors or have materials in an unmanned booth.

Clever Sys. Inc.  
MED Associates, Inc.  
Noldus Information Technology  
San Diego Instruments, Inc.  
Viewpoint Life Sciences Inc.  
Oxford University Press

## **ACKNOWLEDGMENTS**

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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 (Chairperson); Marcus Brandao; Jacqueline Crawley; Gary Coover; Scott Hall; Sarah A. Johnson (student representative); Juan Carlos Jorge; Gerlinde Metz; Emmanuel Onaivi; Klaus-Peter Ossenkopp; Paul Rushing; Holger Russig.

### ***EDUCATION AND TRAINING COMMITTEE:***

Vickie Risbrough (Chairperson); Pascual Gargiulo; Robert Gerlai; Susan Powell; Martin Sarter; *For the mentoring initiative:* Christine Hohmann; Nancy Ostrowski.

### ***LOCAL ORGANIZING COMMITTEE:***

Robert Adamec (Chairperson); Stefan Brudzynski; Robert Gerlai; Lisa Kalynchuk.

## **SCIENTIFIC PROGRAM**

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### ***KEYNOTE SPEAKERS***

- **James L. McGaugh**, Ph.D., University of California, Irvine, California, USA  
*Emotional Arousal and Amygdala Activation: The Making of Lasting Memory*
- **Michael J. Meaney**, Ph.D., Douglas Hospital Research Center, Montreal, Canada  
*Maternal Effects in Mammals as a Model for Environmentally-Driven Chromatin Plasticity*

### ***PRESIDENTIAL ADDRESS***

- **Robert Adamec**, Ph.D., Memorial University, St. John's, Newfoundland, Canada  
*Neural Pathways of Lasting Emotional Change -- A Tale of Two Hemispheres*

## **MATTHEW J. WAYNER-NNOXe PHARMACEUTICALS AWARD**

- **William T. Greenough, Ph.D.**, University of Illinois at Urbana-Champaign, IL, USA.  
*Plastic brain mechanisms in Fragile X Syndrome*

## **SPECIAL SYMPOSIA**

- ***Vocalization as an emotional indicator.***  
Chairs: Stefan M. Brudzynski and Uwe Juergens
- ***Sex, steroids and environment affect recovery from brain injury.***  
Chair: Joseph Nuñez
- ***Relation of dominant-submissive behavior to mania and depression; parallels between animal behavior and human disease.***  
Chair: Ewa Malatynska
- ***Behavioural Neuroscience - Quo Vadis.***  
Chair: Joram Feldon
- ***The underappreciated importance of the aversive properties of drugs of abuse.***  
Chair: F. Scott Hall
- ***Explorations of the parental brain***  
Chair: Kelly G. Lambert
- ***Genes Meet Behavior: a joint symposium between the International Behavioral Neuroscience Society and International Behavioural and Neural Genetics Society.***  
Chair: Andrew Holmes
- ***The pharmacological and neural modulation of defensive behavior.***  
Chairs: R.J. Blanchard and A.P. Carobres

## **WORKSHOPS**

- ***Student Workshop: Strategies for Successful Writing***

This workshop has been designed to address two major challenges facing students and post-docs: writing academic manuscripts, and writing funding applications. Dr. Lisa Kalynchuk (University of Saskatoon) and Dr. Deb Saucier (University of Saskatoon) will discuss strategies for developing your academic and grant writing abilities, and will then be joined by Dr. Caroline Blanchard (University of Hawaii) and Dr. Sue Carter (University of Illinois, Chicago) for a panel discussion and question-and-answer period. Workshop attendees will benefit from the expertise of panel members, who have a collective wealth of experience as textbook authors, editorial board members to neuroscience journals, and grant review committee members to federal funding agencies.



- ***Grant Workshop***

"NIH 101", Paul A. Rushing, National Institute of Diabetes and Digestive and Kidney Diseases. In these times of leaner budgets, it is especially important to be familiar with the grant process. This brief "NIH 101" workshop will provide information on aspects from submission to funding. Current issues including electronic submission and multiple PIs will also be discussed. In addition, the presentation will be followed by a question and answer period.



## ***IBNS 2007 - CALL FOR SATELLITE/SYMPOSIUM PROPOSALS***

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The Program Committee is now accepting proposals for symposia and satellites for the 2007 annual meeting. These may be submitted directly to the IBNS Central Office by email at [ibns@ibnshomepage.org](mailto:ibns@ibnshomepage.org) with a copy to the 2007 Program Chairperson, Andrew Holmes, at [holmesan@mail.nih.gov](mailto:holmesan@mail.nih.gov). Proposals should include the title of the satellite/symposium, list of speakers, titles of the speakers' presentations and the chairperson(s).

**NOTE:** Registration will be held in the foyer outside the Frontenac Ballroom. Oral presentations on Wednesday will be held in the Frontenac Ballroom, Sections A&B. From Thursday through Saturday the oral presentations will be held in the MacDonald Ballroom, Sections D,E,F. All exhibits, registration and food breaks will be held in Frontenac Ballroom, Section C on Wednesday and in the MacDonald Ballroom, Sections A,B,C for the remainder of the meeting. The opening reception will be held in the Mallard Lounge. Both poster sessions will be held in the MacDonald Ballroom, Sections A,B,C. Presenting authors are indicated by **bold** type. † Indicates Travel Award recipient.

## ***Tuesday, May 23, 2006***

- 16:00-18:00 Premeeting Student Social – Guest Room 494.
- 19:00-22:00 Registration - Foyer of the Frontenac Ballroom. For late arrivals only, the registration desk will be open during the **complimentary** continental breakfast each morning of the conference between 7:45-8:45. All breakfasts and breaks will be served in the same room as the Exhibitors, please see daily schedule.

## ***Wednesday, May 24, 2006***

- 08:15-08:45 **President's Welcome**. Frontenac Ballroom AB.
- 08:45-10:45 ***Symposium 1: The underappreciated importance of the aversive properties of drugs of abuse.*** Frontenac Ballroom AB. Chair: F. Scott Hall
- 08:45-09:15 EVIDENCE FOR CONCURRENT POSITIVE AND NEGATIVE ACTIONS OF COCAINE IN AN ANIMAL MODEL OF DRUG-SEEKING BEHAVIOR. **Ettenberg, A.**
- 09:15-09:45 ANIMAL MODELS OF DRUGS OF ABUSE: CONDITIONED TASTE AVERSION LEARNING. **Riley, A.;** Busse, G.
- 09:45-10:15 ULTRASONIC VOCALIZATIONS AS AN INDEX OF NEGATIVE AFFECTIVE STATES IN RATS. **Burgdorf, J.;** Panksepp, J.
- 10:15-10:45 GENE KNOCKOUT STUDIES OF THE AVERSIVE AND REWARDING PROPERTIES OF ADDICTIVE DRUGS. **Hall, F.S.;** Randall-Thompson J.; Jones, J.D.; Riley, A.L.; Uhl, G.R.
- 10:45-11:00 Break/**Exhibitors' Display**. Frontenac Ballroom C.
- 11:00-12:00 ***Presidential Lecture:*** Robert Adamec, Memorial University, St. John's, Newfoundland, Canada. *Neural Pathways of Lasting Emotional Change -- A Tale of Two Hemispheres.* Frontenac Ballroom AB.

- 12:15-14:15 **Council Meeting.** Montebello Room.
- 14:30-16:30 **Oral Session 1:** Stress, fear and emotion. Chair: Marcus Brandao Frontenac Ballroom AB.
- 14:30-14:45 REACTIONS TO NOVELTY IN COPULATING VERSUS NON-COPULATING MALE RATS. **Agmo, A.**; Spiteri, T.; Le Pape, G.
- 14:45-15:00 STRESS AND PAIRING STATUS AFFECT CORTISOL AND VASOPRESSIN, BUT NOT OXYTOCIN, IN TITI MONKEYS (CALLICEBUS CUPREUS). **Bales, K.L.**; Hostetler, C.M.; Mendoza, S.P.
- 15:00-15:15 DIFFERENTIAL NEURAL RESPONSES TO EMOTIONAL FACE EXPRESSIONS IN THE MONKEY PULVINAR. **Maior, R.S.**; Hori, E.; Tomaz, C; Ono, T.; Nishijo, H.
- 15:15-15:30 DEFENSE-LIKE BEHAVIORS INDUCED BY ULTRASOUND IN LISTER HOODED RATS: SENSITIVITY TO ANXIOLYTICS ACTING VIA DIFFERENT MECHANISMS. **Prinssen, E.P.**; Klein, S.; Nicolas, L.B.
- 15:30-15:45 FATTY-ACID AMIDE HYDROLASE: A NOVEL TARGET FOR ANTIDEPRESSANT THERAPY. **Bortolato, M.**; Mangieri, R.A.; Campolongo, P.; Trezza, V.; Arguello, O.; Cuomo, V.; Piomelli, D.
- 15:45-16:00 KINDLED RATS' FEAR BEHAVIOR IS REFLECTED BY A DISTINCT AND RELIABLE PATTERN OF ACTIVITY IN A NOVEL OPEN FIELD. **Wintink, A.J.**; Kalynchuk, L.E.
- 16:00-16:15 NEUROENDOCRINE CONTROL OF THE DEVELOPMENT OF AGONISTIC BEHAVIOR. **Delville, Y.**; Cervantes, M.C.; Taravosh-Lahn, K.; Wommack, J.C.
- 16:15-16:30 EXPOSURE TO A LITHIUM-PAIRED CONTEXT ELICITS GAPING IN RATS: A MODEL OF ANTICIPATORY NAUSEA. Limebeer, C.L.; Hall, G.; **Parker, L.A.**
- 16:30-16:45 Break/**Exhibitors' Display.** Frontenac Ballroom C.
- 16:45-18:45 **Symposium 2: Genes Meet Behavior: a joint symposium between the International Behavioral Neuroscience Society and International Behavioural and Neural Genetics Society.** Frontenac Ballroom AB. Chair: Andrew Holmes
- 16:45-17:15 HOW SMART IS MY MOUSE? THE GENETIC DISSECTION OF MEMORY SYSTEMS IN THE MOUSE **Crusio, W.E.**; Schwegler, H.
- 17:15-17:45 ZEBRA FISH AT THE DOOR STEPS OF BEHAVIORAL NEUROSCIENCE AND BEHAVIORAL GENETICS. **Gerlai, R.**

- 17:45-18:15 GENETIC ANIMAL MODELS OF ALCOHOL ABUSE: WHAT ARE WE  
LOOKING FOR, ANYWAY? **Crabbe, J.**
- 18:15-18:45 SYSTEMS GENETICS OF THE HIPPOCAMPUS: GENES, TRANSCRIPTS,  
CELLS, CIRCUITS, BEHAVIORS. **Williams, R.**; Peirce, J.; Lu, L.
- 19:00-20:00 **Reception.** Mallard Lounge. Refreshments and cash bar. Pianist.
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## ***Thursday, May 25, 2006***

- 08:45-10:45 ***Symposium 3: Vocalization as an emotional indicator.*** MacDonald Ballroom DEF. Chairs: Stefan M. Brudzynski and Uwe Juergens
- 08:45-09:10 50-KHZ ULTRASONIC VOCALIZATIONS AS AN INDEX OF POSITIVE AFFECTIVE STATES IN RATS. **Panksepp, J.**; Burgdorf, J.
- 09:10-09:35 DISTINCT BRAIN MECHANISMS FOR THE PROCESSING OF LAUGHTER AND SPEECH. **Alter, K.**; Szameitat, D.; Meyer, M.
- 09:35-10:00 COMMON ACOUSTIC FEATURES IN THE VOCAL EXPRESSION OF EMOTIONS IN MONKEYS AND MAN. **Juergens, U.**
- 10:00-10:25 A TELEMETRIC SINGLE-UNIT RECORDING STUDY ON VOCALIZATION-CORRELATED ACTIVITY IN THE BRAINSTEM OF THE SQUIRREL MONKEY. **Hage, S.**
- 10:25-10:45 BRAIN MECHANISMS AND ACOUSTIC CODING OF ULTRASONIC SIGNALS IN THE RAT'S VOCAL EXPRESSION OF EMOTIONAL STATES. **Brudzynski, S.M.**
- 10:45-11:00 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.
- 11:00-12:00 ***Keynote Speaker: Michael J. Meaney, Ph.D.,*** Douglas Hospital Research Center, Montreal, Canada. MATERNAL EFFECTS IN MAMMALS AS A MODEL FOR ENVIRONMENTALLY-DRIVEN CHROMATIN PLASTICITY. MacDonald Ballroom DEF.
- 14:00-16:00 ***Symposium 4: Relation of dominant-submissive behavior to mania and depression; parallels between animal behavior and human disease.*** MacDonald Ballroom DEF. Chair: Ewa Malatynska
- 14:00-14:30 DEVELOPMENT OF PROTOCOL TO MEASURE HUMAN DOMINANT-SUBMISSIVE SOCIAL BEHAVIOUR. **Tse, W.S.**; Bond, A.J.
- 14:30-15:00 THE IMPACT OF THE INTERACTION BETWEEN PERSONALITY AND DOMINANCE-SUBMISSIVE BEHAVIOR ON PHYSIOLOGICAL PARAMETERS. **Drent, P.**; Van Oers, C.
- 15:00-15:30 ETHOLOGICAL ANALYSIS OF RODENT BEHAVIOUR: ELUCIDATION OF THE BEHAVIOURAL EFFECTS OF ANTIDEPRESSANT DRUGS. **Mitchell, P.**; Redfern, P.
- 15:30-16:00 DOMINANT - SUBMISSIVE RELATIONSHIPS IN PAIRED ANIMALS AS MODELS FOR ANTIMANIC AND ANTIDEPRESSANT DRUG TESTING. **Malatynska, E.**

- 16:00-16:15 Break/**Exhibitors' Display**. MacDonald Ballroom ABC.
- 16:15-17:45 **Student Travel Award Slide Blitz**. MacDonald Ballroom DEF. **Chair:** Emmanuel Onaivi
- 16:15-16:21 CHRONIC ANTI-INFLAMMATORY TREATMENT FAILS TO PREVENT BRAIN PATHOLOGY IN A MODEL OF NEUROPSYCHIATRIC LUPUS. † **Ballok, D.A.**; Sakic, B.
- 16:21-16:27 SUPPLEMENTAL CHOLINE IN THE MATERNAL DIET OF RATS MODULATES HIPPOCAMPAL NEUROGENESIS AND EXPLORATORY BEHAVIOR IN OFFSPRING. † **Glenn, M.J.**; Kirby, E.D.; Wong-Goodrich, S.J.E.; Williams, C.L.
- 16:27-16:33 MOUSE STRAIN DIFFERENCES IN LITHIUM ATTENUATION OF D-AMPHETAMINE HYPERLOCOMOTION. † **Gould, T.D.**; O'Donnell, K.C.; Picchini, A.M.; Manji, H.K.
- 16:33-16:39 STIMULATION OF CENTRAL BETA NORADRENERGIC RECEPTORS DISRUPTS PPI. † **Alsene, K.M.**; Bakshi, V.P.
- 16:39-16:45 COGNITIVE-DISRUPTIVE EFFECTS OF THE PSYCHOTOMIMETIC PHENCYCLIDINE AND ATTENUATION BY ATYPICAL ANTIPSYCHOTICS. † **Amitai, N.**; Semenova, S.; Markou, A
- 16:45-16:51 EFFECTS OF KAPPA OPIOID RECEPTOR STIMULATION IN AN ANIMAL MODEL OF OBSESSIVE-COMPULSIVE DISORDER. † **Perreault, M.L.**; Seeman, P.; Szechtman H.
- 16:51-16:57 LATENT TOXOPLASMA INFECTION IN RODENTS CONVERTS AVOIDANCE OF CAT PHEROMONES INTO AN ATTRACTION. † **Vyas, A.**; Kim, S.K.; Giacomini, N.; Boothroyd, J.; Sapolsky, R.M.
- 16:57-17:03 LONG ACCESS COCAINE SELF-ADMINISTRATION LEADS TO PERSISTANT IMPAIRMENTS IN COGNITIVE PERFORMANCE. † **Briand, L.**; Sarter, M.; Robinson, T.E.
- 17:03-17:09 EXPERIMENTAL MANIPULATION OF BASAL RATE OF NEUROGENESIS INFLUENCES THE DEVELOPMENT OF AMYGDALOID KINDLING IN RATS. † **Fournier, N.M.**; Corcoran, M.E.; Kalynchuk, L.E.
- 17:09-17:15 CHRONIC STRESS AND LITHIUM TREATMENT MODULATE EXPRESSION OF PHOSPHORYLATED CYCLIC AMP RESPONSE ELEMENT BINDING PROTEIN IN THE RODENT AMYGDALA. † **Johnson, S.A.**; Wang, J.-F.; McEwen, B.S.; Young, L.T.

- 17:15-17:21 INTRA-AMYGDALA MU OPIOID RECEPTOR STIMULATION INCREASES CONDITIONED APPETITIVE BEHAVIOR IN RATS. † **Mahler, S.**; Berridge, K.
- 17:21-17:27 MATERNAL TREATMENT WITH VPA DURING PREGNANCY LEADS TO EARLY PHYSICAL AND SOCIAL DEFICITS IN MOUSE PUPS. † **Roulet, F.**; Hall, G. ; deCatanzaro, D.; Foster, J.
- 17:27-17:33 PRE-PUBERTAL STRESS: DIFFERENTIAL IMPACT ON MALES AND FEMALES. † **Toledo-Rodriguez, M.**; Lecroq, B.; Sandi, C.
- 17:33-17:39 REWARD EXPERIENCE MODERATES IMMUNE RESPONSE TO CYTOKINE CHALLENGE. † **Kentner, A.C.**; James, J.; Miguez, M.; Bielajew, C.
- 18:00-19:45 *Poster Session 1. Exhibitors' Display.* MacDonald Ballroom ABC.

*Prenatal, neonatal and parental factors*

1. SEPARATION-INDUCED ULTRASONIC CALLING IN RAT PUPS IS RELATED TO MATERNAL LICKING AND RETRIEVAL IN OPPOSITE WAYS. **Wöhr, M.**; Schwarting, R.K.W.
2. MATERNAL SEPARATION AND EFFECTS OF POST-WEANING HANDLING IN RATS. **Eklund, M.B.**; Arborelius, L.
3. NEONATAL EXPOSURE TO LIPOPOLYSACCHARIDE INCREASES ANXIETY-RELATED NEOPHOBIA TO SUCROSE IN ADULT MALE BUT NOT ADULT FEMALE RATS. **Tenk, C.M.**; Kavaliers, M.; Ossenkopp, K.-P.
4. INTRAHIPPOCAMPAL HIV-1 PROTEIN INJECTIONS: DIFFERENTIAL NEUROBEHAVIORAL EFFECTS IN NEONATAL RATS. **Fitting, S.**; Booze, R.M.; Mactutus, C.F.
5. MATERNAL TREATMENT WITH VPA DURING PREGNANCY LEADS TO EARLY PHYSICAL AND SOCIAL DEFICITS IN MOUSE PUPS. † **Roulet, F.**; Hall, G.; deCatanzaro, D.; Foster, J.
6. NEONATAL EXPOSURE TO FLUOXETINE MODULATES SOCIAL BEHAVIORS AFTER A DIAZEPAM CHALLENGE DURING ADULTHOOD. **Jiménez, J.**; Mattei, G.; Lathroum, L.; Jorge, J.
7. SUPPLEMENTAL CHOLINE IN THE MATERNAL DIET OF RATS MODULATES HIPPOCAMPAL NEUROGENESIS AND EXPLORATORY BEHAVIOR IN OFFSPRING. † **Glenn, M.J.**; Kirby, E.D.; Wong-Goodrich, S.J.E.; Williams, C.L.

8. NEONATAL EXPOSURE TO METHAMPHETAMINE INCREASES BDNF, BUT NOT NGF IN HIPPOCAMPUS AND STRIATUM. **Grace, C.E.**; Herring, N.R.; Schaefer, T.L.; Skelton, M.R.; Williams, M.T.; Vorhees, C.V.
9. MATERNAL CARE ALTERS ANXIOUS BEHAVIOR IN MALE, BUT NOT FEMALE, OFFSPRING. **Pawluski, J.L.**; Barha, C.; Galea, L.A.M.
10. NEONATAL STRESS ALTERS AGGRESSION IN STRESSED AND LITTER MATE CONTROL MICE. **Hodges, A.B.**; Anderson, M. E.; Beard, N.A; Hohmann, C.F
11. REPEATED EARLY LIFE MANIPULATION AFFECTS JUVENILE PARENTAL BEHAVIOR AND PUP-DIRECTED AGGRESSION IN VOLES. **Boone, E.**
12. PRELIMINARY EFFECTS OF IN UTERO COCAINE EXPOSURE ON INFANT RAT ULTRASONIC VOCALIZATIONS. **McMurray, M.S.**; Zeskind, P.S.; Moy, C., Jarrett, T.M.; Johns, J.M.
13. PRE-PUBERTAL STRESS: DIFFERENTIAL IMPACT ON MALES AND FEMALES. † **Toledo-Rodriguez, M.**; Lecroq, B.; Sandi, C.
14. 1-BROMOPROPANE PRENATAL EXPOSURE IMPARES SEXUAL DIFFERENTIATION OF EMOTIONAL AND SEXUAL BEHAVIOR IN RATS. **Narikiyo, K.**; Aou, S.; Fujimoto, T.; Ichihara, Y.; Ishidao, T.; Hori, H.; Fueta, Y.
15. PLASTICITY OF PATERNAL RESPONSIVENESS IN TWO PEROMYSCUS SPECIES. Everette, A. ; Tu,K.; Contino, R.; Rima, B.; Major, J.; Conway, A.F.; Kinsley, C.H.; **Lambert, K.G.**
16. PRE- AND POSTNATAL EXPOSURE TO BISPHENOL A ACCELERATES BEHAVIORAL AND NEURONAL RESPONSES TO STRESS CONDITIONS IN RATS. **Fujimoto, T.**; Aou, S.; Kubo, K.
17. NEONATAL HANDLING INCREASES CARDIOVASCULAR REACTIVITY AND FREEZING BEHAVIOR TO FEAR CONDITIONING IN BORDERLINE HYPERTENSIVE RATS (BHR). **Sanders, B.J.**; Knoepfler, J.D.
18. QUANTIFICATION OF MATERNAL CARE BEHAVIOR IN NEONATALLY STRESSED AND LITTERMATE CONTROL MICE. **Fowler, J.A.**; Hodges, A.B.; Hohmann, C.F.
19. VARIATIONS IN MATERNAL CARE ALTER CORTICOSTERONE RESPONSE TO STRESS IN MALE, BUT NOT FEMALE, OFFSPRING. **Barha, C.**; Pawluski, J.L.; Galea, L.A.M.



20. LATE GESTATIONAL STRESS EFFECTS IN MALE OFFSPRING. **Baker, S.L.**; Chebli, M.; Le Marec, N.; Rees, S.; Bielajew, C.
21. BEHAVIOURAL TERATOGENIC EFFECTS OF PRENATAL NICOTINE EXPOSURE IN MICE OFFSPRING. **Mesembe, O.**; Igiri, A.

*Stress, fear and anxiety*

22. CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE PERIAQUEDUCTAL GRAY ARE DIFFERENTIALLY SENSITIVE TO INJECTIONS OF FLUOXETINE INTO AMYGDALOID NUCLEI. **Martínez, R.C.R.**; Oliveira, A.R.; Macedo, C.E.A., Brandão, M.L.
23. DISTINCT FOS DISTRIBUTION FOLLOWING FREEZING BEHAVIOR INDUCED BY NMDA INJECTIONS INTO EITHER DORSAL OR VENTRAL INFERIOR COLLICULUS. Borelli, K.G.; Ferreira-Netto, C.; **Brandão, M.L.**
24. SOCIAL BEHAVIORS ASSOCIATED WITH PANIC SUSCEPTIBILITY IN RATS. **de Paula, H.M.G.**; Campos, K.M.R.; Hoshino, K.
25. CHRONIC STRESS AND LITHIUM TREATMENT MODULATE EXPRESSION OF PHOSPHORYLATED CYCLIC AMP RESPONSE ELEMENT BINDING PROTEIN IN THE RODENT AMYGDALA. † **Johnson, S.A.**; Wang, J.-F.; McEwen, B.S.; Young, L.T.
26. ULTRASONIC VOCALIZATIONS IN C57BL/6J AND BTBR T+ tf/J MICE. **McFarlane, H.G.**; Crawley, J.N.
27. LATENT TOXOPLASMA INFECTION IN RODENTS CONVERTS AVOIDANCE OF CAT PHEROMONES INTO AN ATTRACTION. † **Vyas, A.**; Kim, S.K.; Giacomini, N.; Boothroyd, J.; Sapolsky, R.M.
28. ANXIOLYTIC PROFILE OF THE ANANDAMIDE TRANSPORT INHIBITOR AM404. Campolongo, P.; **Bortolato, M.**; Mangieri, R.A.; Trezza, V.; Arguello, O.; Cuomo, V.; Piomelli, D.
29. CHRONIC ANTI-INFLAMMATORY TREATMENT FAILS TO PREVENT BRAIN PATHOLOGY IN A MODEL OF NEUROPSYCHIATRIC LUPUS. † **Ballok, D.A.**; Sakic, B.
30. ETHOPHARMACOLOGICAL ANALYSES OF VIGILANCE AS A BEHAVIORAL INDICATOR OF FEAR/ANXIETY IN MARMOSET MONKEYS. **Tomaz, C.**; Vilas Boas, N.; Souto, A.A.V.; Barros, M.

31. MEMORY REACTIVATION TREATMENT REINSTATES TEMPORALLY SPECIFIC FEAR BEHAVIOR FOLLOWING EXTINCTION TREATMENT. **Barnet, R.**
32. EXPERIMENTAL MANIPULATION OF BASAL RATE OF NEUROGENESIS INFLUENCES THE DEVELOPMENT OF AMYGDALOID KINDLING IN RATS. † **Fournier, N.M.**; Corcoran, M.E.; Kalynchuk, L.E.
33. CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE INFERIOR COLLICULUS ARE DIFFERENTIALLY SENSITIVE TO INJECTIONS OF MUSCIMOL INTO THE BASOLATERAL NUCLEUS OF THE AMYGDALA. **Macedo, C.E.**; Martinez, R.C.R.; Brandão, M.L.
34. NEUROPSYCHOLOGICAL ASSESSMENT IN VETERANS WITH POSTTRAUMATIC STRESS DISORDER. **Geuze, E.**; Vermetten, E.; de Kloet, C.S.; Hijman, R.; Westenberg, H.G.M.
35. TESTING FOR APPROACH-AVOIDANCE BEHAVIOUR IN THE HOME CAGE. **De Visser, L.**; Schenke, M.; Van den Bos, R.; Spruijt, B.M.
36. ANXIETY INDUCED BY DIAZEPAM WITHDRAWAL AND FOS IMMUNOREACTIVITY IN THE BRAINSTEM STRUCTURES. Fontanesi, L.; Carvalho, M.C.; Cabral, A.; Castilho, V.M.; Brandão, M.L.; **Nobre, M.J.**
37. IMMOBILIZATION STRESS INDUCES CHANGES IN NORADRENALINE IN THE STRIATUM. García-Saldívar, N. L.; González-López, M.R.A.; Gómez-Romero, J.G.; Rodríguez-Serrano, L.M.; Domínguez, R.; **Cruz-Morales, S.E.**
38. CHRONIC CANNABINOID TREATMENT PRODUCES AN ANTIDEPRESSANT-LIKE RESPONSE IN THE FORCED SWIM TEST: POSSIBLE ROLE OF NOREPINEPHRINE. **Morrish, A.**; Hill, M.; Froese, L.; Gorzalka, B.
39. ASSESSMENT OF EMOTION-RELATED BEHAVIORS IN NPY Y1 AND Y2 RECEPTOR KNOCK-OUT MICE. **Karlsson, R-M.**; Heilig, M.; Crawley, J.; Holmes, A.
40. REPEATED EXPOSURE TO CORTICOSTERONE INCREASES DEPRESSION-LIKE BEHAVIOR IN TWO DIFFERENT VERSIONS OF THE FORCED SWIM TEST INDEPENDENTLY OF ALTERATIONS IN NONSPECIFIC MOTORIC BEHAVIOR. **Kalynchuk, L.E.**; Marks, W.; Fournier, N.M.
41. “ANTIDEPRESSANT-LIKE” EFFECTS OF DAT OR NET, BUT NOT SERT, GENE KNOCKOUT IN THE FORCED SWIM TEST. Perona, M.T.; Waters, S.; **Hall, F.S.**; Sora, I.; Lesch, K.P.; Murphy, D.L.; Caron, M.; Uhl, G.R.

42. INTRA-SEPTAL INFUSIONS OF MUSCIMOL DIFFERENTIALLY AFFECT RATS' DEFENSIVE RESPONSES IN THE PLUS-MAZE AND CAT-ODOR TESTS. **Menard, J.L.**; Patel, R.
43. ANTINOCICEPTIVE AND ANXIOLYTIC TOLERANCE TO NITROUS OXIDE AND CROSS-TOLERANCE TO CHLORDIAZEPOXIDE IN THE ABDOMINAL CONSTRICTION TEST AND LIGHT/DARK EXPLORATION TEST. **Heckert, RW**; Quock DG; Quock RM
44. DO INTERLEUKIN-1 AND LIPOPOLYSACCHARIDE INDUCE ANXIETY? **Dunn, A.J.**; Swiergiel, A.H.
45. INTERLEUKIN-1 AND LIPOPOLYSACCHARIDE INDUCE CYCLOOXYGENASE-2 (COX2) IN BRAIN ENDOTHELIA PARALLELLING THE INDUCED HYPOPHAGIA. **Dunn, A.J.**; Swiergiel, A.H.; Zhang,H; Quan, N.
46. CORTICOTROPIN-RELEASING FACTOR IN THE DORSAL RAPHE INCREASES PREFRONTAL CORTICAL SEROTONIN VIA CRF-2 RECEPTORS AND MEDIAN RAPHE ACTIVITY. **Burke, A**; Mouw, N; Pringle, R; Watt, M; Barr, J; Lukkes, J; Summers, C; Renner, K; Forster, G
47. IDENTIFYING GENETIC FACTORS UNDERLYING AMYGDALA VOLUME AND EMOTION-RELATED PHENOTYPES IN RECOMBINANT INBRED MICE. **Yang, R.J.**; Mozhui, K.; Lu, L.; Williams, R.W.; Holmes, A.

*Sexual, endocrine and hormonal factors*

48. SEXUAL INTERACTION PRIOR TO ACUTE PREDATOR ODOR STRESS CAUSES INCREASED HIPPOCAMPAL CELL PROLIFERATION AND AFFECTS DEFENSIVE BEHAVIOR AMONG MALE RATS. **Spritzer, M.D.**; Weinberg, A.; Viau, V.; Galea, L.A.M.
49. EFFECTS OF GONADECTOMY ON SOCIAL INTERACTIONS IN MICE (MUS MUSCULUS). **Clipperton, A.E.**; Cragg, C.L.; Wood, A.J.; Choleris, E.
50. FUNCTIONAL IMAGING OF SOCIAL BONDING IN TITI MONKEYS (CALLICEBUS CUPREUS). **Bales, K.L.**; Mason, W.A.; Cherry, S.R.; Catana, C.; Mendoza, S.P.
51. EXPRESSION OF THE GALANIN-LIKE PEPTIDE GENE IN THE POSTERIOR PITUITARY GLAND BY OSMOTIC CHALLENGE AND ACUTE INFLAMMATORY STRESS. **Ueta, Y.**; Kawasaki, M.; Isa, K.; Kise, Y.; Saito, J.; Fujihara, H.

52. SOCIAL ISOLATION AFFECTS CORTICOTROPIN-RELEASING FACTOR-MEDIATED SEROTONIN RELEASE IN THE NUCLEUS ACCUMBENS. **Lukkes, J**; Forster, G; Watt, M; Renner, K; Summers, C
53. MALE URINARY STEROID LEVELS APPROACH VALUES SUFFICIENT TO ACCOUNT FOR THE BRUCE EFFECT IN MICE. **deCatanzaro, D.**; Beaton, E.; Khan, A.; Vella, E.
54. ADRENALECTOMY-INDUCED HIPPOCAMPAL GRANULE CELL DEATH AND MEMORY DEFICITS: EFFECTS OF CHRONIC CORTICOSTERONE REPLACEMENT THERAPY AND STIMULATION OF NEUROGENESIS. **S.C. Spanswick**, J Epp, J.R. Keith,R.J. Sutherland
55. BULLYING DURING PUBERTY AFFECTS PHYSIOLOGICAL MARKERS OF STRESS IN YOUNG ADULTS. **Hamilton, L.D.**; Newman, M.L.; Delville, Y.
56. SEXUALLY DIMORPHIC EFFECTS OF DOPAMINE RECEPTOR SUBTYPES ON ALLOPARENTAL BEHAVIOR IN THE PRAIRIE VOLE. **Hostetler, C.M.**; Bales, K.L.
57. GENDER-RELATED HEMISPHERIC LATERALIZATION OF EVENT RELATED POTENTIALS EVOKED BY EMOTIONAL CONTENT. Gasbarri, A.; Arnone, B.; Pompili, A.; Marchetti, A.; Delphino, P.; Pacitti, C.; Tavares, M.C.; **Tomaz, C.**
58. ANXIOLYTIC EFFECTS OF MUSIC DEPEND ON OVARIAN STEROID IN FEMALE MICE. **Chikahisa S.**; Sei H.; Sano A.; Kitaoka K.; Morita Y.
59. BEHAVIORAL AND CELLULAR MODULATION OF AAS IN REPRODUCTIVE-RELATED BEHAVIORS AND REWARD IN ADULT MICE. **Parrilla, J.**; Rundle, V.; Arriaga, D.; Jorge, J.C.; Barreto-Estrada, J.L.
60. ASSOCIATIONS BETWEEN OFFENSIVE AGGRESSION AND IMPULSIVITY IN ADULT MALE GOLDEN HAMSTERS. **Cervantes, C.**
61. MODULATION OF RISK ASSESMENT BEHAVIORS THROUGH GROUP I METABOTROPIC GLUTAMATE RECEPTORS IN THE BASOLATERAL AMYGDALA IN ESTROGEN-TREATED RATS. De Jesús-Burgos M.I.; **Vázquez-Fuentes B.M.**; Torres-Llenza V.; Ríos-Pilier J.; Rodríguez S.; Quiñones K.; and Pérez-Acevedo N.L.
62. EFFECT OF DIFFERENT TREATMENT SCHEDULE AND TEST ARENAS (TRADITIONAL AND MULTIPLE PARTNER CHOICE TEST) IN THE EXPRESSION OF PACING BEHAVIOR OF FEMALE RATS. **Ferreira-Nuño, A.**; Morales-Otal, A.; Martínez-Flores, K., González-González, C.; Fernández-Soto, C.; Olayo-Lortia, J.; Velázquez-Moctezuma, J.

63. CHRONIC ESTRADIOL AFFECTS DIFFERENT ASPECTS OF ADULT HIPPOCAMPAL NEUROGENESIS IN FEMALE, BUT NOT MALE, RATS. **Barker, J.**; Galea, L.A.M.
  64. ACTIVATION OF GROUP I METABOTROPIC GLUTAMATE RECEPTORS IN THE BASOLATERAL AMYGDALA PRODUCES ANXIOTIC-LIKE BEHAVIOR IN A PUNISHED DRINKING TEST ACCORDING TO SEX. **Torres-Llenza V**; De Jesús-Burgos MI; Ríos-Pilier J; Vázquez-Fuentes BM; Comenencia EJ; Ramos L; Angleró Y; Rodríguez G; and Pérez-Acevedo NL.
  65. THE EFFECTS OF ANDROSTANEDIOL AND 17 $\alpha$ -METHYLTESTOSTERONE IN SYSTOLIC BLOOD PRESSURE AND ANXIETY THROUGH THE DORSOMEDIAL HYPOTHALAMUS. **Velázquez, K.T.**; Jorge, J.C.
  66. WHEN DOES ESTRADIOL ENHANCE APPETITE? **Reid L. D.**; Reid L.D.; Boswell K.J.; Reid M.L.
  67. ANDROGENIC EFFECTS ON THE REWARDING COMPONENTS OF FEMALE SEXUAL BEHAVIOR THROUGH THE NUCLEUS ACCUMBENS SHELL. **Sanchez-Montoya, E.**; Hernandez, L.; Palacios, H.; Ortiz, A.; Valle, Y.; Jorge, J.C.
  68. PREOPTIC AREA INFLUENCES ON HYPOTHALAMIC SEROTONIN AND FEMALE SEX BEHAVIOR. **Watt, M.J.**; Feng, N.; Hoglund, E.; Mo, B.; Forster, G.L.; Renner, K.J.
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## ***Friday, May 26, 2006***

- 08:45-10:45 ***Symposium 5: Behavioural Neuroscience - Quo Vadis.*** MacDonald Ballroom DEF. Chair: Joram Feldon
- 08:45-09:15 THERE IS MORE TO REWARD THAN THE “PLEASURE PRINCIPLE”.  
**Phillips, A.**
- 09:15-09:45 DEVELOPING AND VALIDATING NEW BEHAVIOURAL TESTS FOR MICE. **Rawlins, J.N.P.** ; Bannerman, D.M.; Deacon R.M.J.
- 09:45-10:15 BEHAVIORAL NEUROSCIENCE IS THE BASIC SCIENCE DISCIPLINE FOR PSYCHIATRY. **Szechtman, H.**; Eilam, D.
- 10:15-10:45 BEHAVIOR IN THE GENOMIC ERA: THE HIGH THROUGHPUT IDOL  
**Weiner, I.**
- 10:45-11:00 Break/**Exhibitors’ Display.** MacDonald Ballroom ABC.
- 11:00-12:00 ***The Matthew J. Wayner/NNOXe Pharmaceuticals Award: William T. Greenough, Ph.D.,*** University of Illinois at Urbana-Champaign, IL, USA. *Two meanings of "translation:" Plastic Brain Mechanisms in Fragile X Disorder.* MacDonald Ballroom DEF.
- 14:30-15:30 ***Grant Workshop*** (organized by Paul Rushing). MacDonald Ballroom DEF.
- 15:30-15:45 Break/**Exhibitors’ Display.** MacDonald Ballroom ABC.
- 15:45-17:45 ***Symposium 6: The pharmacological and neural modulation of defensive behavior.*** MacDonald Ballroom DEF. Chairs: RJ Blanchard and AP Carobres
- 15:45-16:15 MODULATION OF DEFENSIVE BEHAVIOR BY CRF. **Blanchard, R.J.**; Yang, M.; Litvin, Y.; Borna Farrokhi, C.; Blanchard, D.C.
- 16:15-16:45 NEUROPHARMACOLOGY OF DEFENSIVE BEHAVIOR: ROLE OF NORADRENALINE TRANSMISSION. **Carobrez, A.P.**; Do-Monte, F.H.M.
- 16:45-17:15 NEUROPHARMACOLOGY OF DEFENSIVE BEHAVIOR: ROLE OF ATYPICAL NEUROTRANSMITTERS. **Guimarães, F.**; Moreira, F.; Bejjamini, V.; Aguiar, D., Braga, A.; de Oliveira R; Del Bel, E.
- 17:15-17:45 A ROLE FOR THE PERIAQUEDUCTAL GRAY IN SWITCHING ADAPTIVE BEHAVIORAL RESPONSES. **Canteras, N.S.**; Sukikara, M.H.; Mota-Ortiz, S.R.; Baldo, M.V.; Felício, L.F.

18:00-19:45 *Poster Session 2. Exhibitors' Display.* MacDonald Ballroom ABC.

*Reward and drugs of abuse*

69. THE EFFECTS OF THE SELECTIVE 5HT1B RECEPTOR AGONIST, CP94253, ON COCAINE SEEKING AND ANXIETY. **Acosta, J.I.**; Gaudet, L.; Browning, J.R.; Neisewander, J.L.
70. COMPARING THE EFFECTS OF SENSORY STIMULATION AND COCAINE ON SEROTONIN AND DOPAMINE ACTIVITY IN THE OCCIPITAL AND TEMPORAL CORTEX. Müller, C.P.; De Souza Silva, M.A.; **Huston, J.P.**
71. ASSOCIATION OF CANNABINOID RECEPTOR CB2 GENE WITH ALCOHOLISM AND DEVELOPMENT OF ALCOHOL PREFERENCE. Ishiguro, H.; Iwasaki, S.; Teasentfitz, L.; Higuchi, S3.; Arinami, T and **Onaivi, E.S.**
72. BEHAVIORAL EFFECTS OF CB2 CANNABINOID RECEPTOR LIGANDS. Teasentfitz, L.; Mora, Z.; Akinshola, B.E.; **Onaivi, E.S.**
73. TREATMENT WITH MDMA FROM P11-20 DISRUPTS SPATIAL LEARNING AND PATH INTEGRATION LEARNING IN ADOLESCENT RATS AND SPATIAL LEARNING IN OLDER RATS. **Skelton, M.**; Williams, M.; Vorhees C.
74. LONG ACCESS COCAINE SELF-ADMINISTRATION LEADS TO PERSISTANT IMPAIRMENTS IN COGNITIVE PERFORMANCE. † **Briand, L.**; Sarter, M.; Robinson, T.E.
75. INTRA-AMYGDALA MU OPIOID RECEPTOR STIMULATION INCREASES CONDITIONED APPETITIVE BEHAVIOR IN RATS. † **Mahler, S.**; Berridge, K.
76. ADULT METHAMPHETAMINE EXPOSURE RESULTS IN PATH INTEGRATION AND NOVEL OBJECT LEARNING DEFICITS IN RATS. **Herring, N.**; Schaefer, T.; Vorhees, C.; Williams, M.
77. CHRONIC COCAINE AND/OR STRESS EXPOSURE IN ADOLESCENT AND ADULT RATS DIFFERENTIALLY ALTERS THE LONG-TERM CONSEQUENCES OF COCAINE-INDUCED REWARD AND PSYCHOMOTOR STIMULATION. Sobrian, S.K.; Adams, N.S.; Wright, J.; Kuhn, D.; Gerald, S.; Arguinzoni, J.K.
78. REWARD EXPERIENCE MODERATES IMMUNE RESPONSE TO CYTOKINE CHALLENGE. † **Kentner, A.C.**; James, J; Miguez, M; Bielajew, C.
79. EFFECTS OF PRENATAL COCAINE EXPOSURE AND REARING CONDITION ON SOCIAL/AGGRESSIVE BEHAVIOR AND OXYTOCIN LEVELS IN YOUNG ADULT MALE RATS ON A WATER COMPETITION TASK. **Jarrett, T.M.**; McMurray, M.S.; Walker, C.H.; Johns, J.M.

80. CHANGES IN CORTICOSTERONE AND LIMBIC MONOAMINES DUE TO SENSITIZATION OR HABITUATION TO AMPHETAMINE. **Scholl, J.**; Phillips, M.; Feng, N.; Pringle, R.; Lukkes, J.; Watt, M.; Renner, K.; Forster, G.
81. DIFFERENTIAL HORMONAL EFFECTS OF ACUTE SYSTEMIC COCAINE ADMINISTRATION IN A NEOTROPICAL PRIMATE. **Barros, M.**; Lima, D.; Spíndola, D.B.; Dias, L.O.; Bessa, N.O.D.; Costa, S.S.S.; Vaz, J.A.R.; Abdalla, L.F.; Tomaz, C.
82. THE ROLE OF THE NK-3 RECEPTOR IN COCAINE-INDUCED BEHAVIOR IN MARMOSSET MONKEYS. **Barros, M.**; Mello Jr., E.L.; Müller, C.P.; Jocham G.; Maior, R.S.; Huston, J.P.; Tomaz, C.; de Souza Silva, M.A.
83. DEFICIT IN BRAIN REWARD FUNCTION ASSOCIATED WITH FENTANYL WITHDRAWAL IN RATS. **Bruijnzeel, A.**; Lewis, B.; Bajpai, L.; Dennis, D.; Morey, T.; Gold, M.
84. THE AGED FBN(F1) RAT - A MODEL OF AGE RELATED DEFICITS FOR DRUG DISCOVERY? **Curzon, P.**; Cronin, E.A.; Browman, K.E.; Fox G.B.
85. CHRONIC AMPHETAMINE ALTERS CORTICOTROPIN-RELEASING FACTOR-ELICITED SEROTONIN RELEASE IN THE PREFRONTAL CORTEX. **Barr, J.**; Pringle, R.; Watt, M.; Burke, A.; Mouw, N.; Renner, K.; Forster, G.
86. PRENATAL COCAINE EXPOSURE ALTERS RESPONSE TO NOVELTY AND ADRENERGIC SYSTEMS IN ADOLESCENT RATS. **Silvers, J.**; Ferris, M.; Harrod, S.; Mactutus, C.; Booze, R.
87. DATA GERMANE TO THE ALCOHOL DEPRIVATION EFFECT. **Reid L.D.**; Boswell K.J.; Prado-Alcala R.A.
88. INCREASED SENSITIVITY TO THE STIMULANT AND ANXIOLYTIC-LIKE EFFECTS OF ETHANOL IN PRE-ADOLESCENT MICE. **Hefner, K.**; Kash, T.; Winder, D.G.; Holmes, A.
89. QUANTITATIVE GENETIC ANALYSIS OF BRAIN COPPER AND ZINC IN BXD RECOMBINANT INBRED MICE. **Jones, L.**; McCarthy, K; Beard, J; Keen C; Jones, B.

*Learning, memory, cognition*

90. THE EFFECTS OF ETHANOL ON SHORT- AND LONG-TERM MEMORY IN C. ELEGANS. **Butterfield, M.P.**; Rankin, C.H.
91. LONG-TERM MEMORY IN C. ELEGANS IS SUBJECT TO RECONSOLIDATION. **Timbers, T.A.**; Rose, J.K.; Rankin, C.H.



92. THE GENERAL THEORY OF PSYCHOLOGICAL RELATIVITY AND COGNITIVE EVOLUTION. **Bailey, C.**
93. INTEGRATION OF CHINESE CHARACTERS AND SPATIAL LOCATIONS IN WORKING MEMORY: AN ERP STUDY. **Wang, Y.W.**; Lu, Z.H.; Zhou, X.L.; Lin, C.D.
94. FRONTAL LOBE INVOLVED IN UPDATING OF EXECUTIVE FUNCTION REVEALED BY EVENT-RELATED POTENTIALS. **Wang, Y.W.**; Lin, C.D.; Lu, Z.H.; Zhou, X.L.
95. EGCG, FROM GREEN TEA, REDUCES CEREBRAL AMYLOIDOSIS AND IMPROVES COGNITIVE FUNCTION IN ALZHEIMER TRANSGENIC MICE. **Shytle, R.D.**; Rezaei-Zadeh, K.; Sun, N.; Ehrhart, J.; Zeng, J.; Arendash, G.; Tan, J.
96. INSULAR CORTEX AND AMYGDALA KINDLING REINFORCES THE MEMORY-RETRIEVAL SYSTEM IN CONDITIONED TASTE AVERSION. **López-Velázquez, L.M.**; Camacho, F.J.; Paredes, R.G.
97. ACQUISITION OF OLFACTORY LEARNING SET FOR SEQUENCES OF CONSTANTLY CHANGING ODORS BY MICE. Cai, C.X.; Katz, E.; Rothschild, O.; **Bauchwitz, R.P.**
98. BEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDIES OF CHRONIC ORAL ADMINISTRATION OF L-TYPE CALCIUM CHANNEL BLOCKER VERAPAMIL ON LEARNING AND MEMORY IN RATS. **Lashgari, R.**; Motamedi, F.; Zahedi, S.
99. MEMORY SYSTEMS COMPETITION: THE HIPPOCAMPUS OVERSHADOWS OTHER NEURAL SYSTEMS FOR CONTEXT MEMORY. **Lehmann, H.**; Sparks, F.T.; Hadikin, C.; Sutherland, R.J.
100. ACUTE ADMINISTRATION OF INTERLEUKIN-1 $\beta$  DISRUPTS NON-HIPPOCAMPAL LEARNING. Hartle, K.D.; Ivanco, T.L.; **Larson, S.J.**
101. THE DEVELOPMENT OF THE P300 EVENT RELATED POTENTIAL IN RATS DURING THE INITIAL STAGES OF SHAPING LEVER PRESSING. **Klipec, W.D.**; Blomgren, K.; Rozek, E.; Verlautz, S.; Grinstead, K.
102. MUP-75 SAPORIN OLD AND NEW: EFFECTS ON BRAIN AND BEHAVIOUR. **Brown, R.E.**; Hoffman, N.; Currie, L.; Stamp, J.; Semba, K.
103. ORBITOFRONTAL NEURONS CATEGORIZE FOOD AND SEX IN THE RHESUS MONKEY. **Aou, S.**; Inoue, T.; Lukats, B.; Sakai, K.; Mizuno, M.

104. TIME-DEPENDANT EFFECTS OF SYSTEMIC MUSCIMOL ON EXTINCTION (EXT) OF A CONDITIONED TASTE AVERSION (CTA). **Mickley, G.A.**; Hoxha, Z.; Bacik, S.
105. INFLUENCE OF SEX AND AGE ON AN AMYGDALA-DEPENDENT MEMORY TASK. **Rubinow, M.J.**; Hagerbaumer, D.A.; Juraska, J.M.
106. EFFECTS OF MODAFINIL ON RADIAL ARM MAZE PERFORMANCE AFTER TWELVE HOURS OF REM SLEEP DISRUPTION. Mery, L.; McQuade, J.A.; **Wayner, M.J.**
107. DIFFERENTIAL EFFECTS OF MEMANTINE AND MK-801. **David, H.N.**; Ansseau, M.; Abraini, J.H.
108. GUT BACTERIA ALTERS THE STRESS SYSTEM: IMPACT ON LEARNING. **Neufeld, K.**; Bienenstock, J.; Foster, J.

*Models of schizophrenia, mania and OCD*

109. TOPIRAMATE REVERSES APOMORPHINE-MEDIATED DISRUPTION OF PREPULSE INHIBITION. **Bortolato, M.**; Frau, R.; Orru, M.; Casti, A.; Manunta, M.; Gessa, G.L.
110. ANTIPSYCHOTIC-LIKE PROFILE OF 5-ALPHA REDUCTASE INHIBITORS. **Bortolato, M.**; Frau, R.; Orru, M.; Casti, A.; Manunta, M.; Bourov, Y.; Gessa, G.L.
111. ROLE OF DOPAMINE D1 AND D2 RECEPTORS IN CRF-INDUCED ALTERATIONS IN STARTLE PLASTICITY. **Risbrough, V.**; Vinkers, C.; Geyer, M.; Caldwell, S.; Low, M.; Hauger, R.
112. LOSS OF OUABAIN BINDING IN THE  $\alpha 2$  ISOFORM OF NA, K-ATPASE AFFECTS LOCOMOTOR AND STARTLE BEHAVIOR. **Schaefer, T.**; Moseley, A.; Lingrel, J.; Vorhees, C.; Williams, M.
113. MODELING CHOLINERGIC-RELATED COGNITIVE IMPAIRMENTS IN SCHIZOPHRENIA: DISRUPTION OF LATENT INHIBITION BY SCOPOLAMINE AND ITS RESTORATION BY ANTIPSYCHOTIC DRUGS AND AN ACETYLCHOLINESTERASE INHIBITOR. **Barak, S.** Weiner, I.
114. STIMULATION OF CENTRAL BETA NORADRENERGIC RECEPTORS DISRUPTS PPI. † **Alsene, K.M.**; Bakshi, V.P.
115. NEONATAL NITRIC OXIDE SYNTHASE INHIBITION IN RATS: A NOVEL NEURODEVELOPMENTAL MODEL OF NEGATIVE SYMPTOMS IN SCHIZOPHRENIA. De Levie, A.; Zuckerman, L.; **Weiner, I.**

116. A SELECTIVE INTRACELLULAR SIGNALING PATHWAY IN THE ANTERIOR CINGULATE CORTEX REGULATES MANIA-RELATED BEHAVIOR. Creson, T.; Hao, Y.; Engel, S.; Yuan, P.; Manji, H.; Chen, G.
117. MOUSE STRAIN DIFFERENCES IN LITHIUM ATTENUATION OF D-AMPHETAMINE HYPERLOCOMOTION. † **Gould, T.D.**; O'Donnell, K.C.; Picchini, A.M.; Manji, H.K.
118. EFFECTS OF KAPPA OPIOID RECEPTOR STIMULATION IN AN ANIMAL MODEL OF OBSESSIVE-COMPULSIVE DISORDER. † **Perreault, M.L.**; Seeman, P.; Szechtman H.
119. COGNITIVE-DISRUPTIVE EFFECTS OF THE PSYCHOTOMIMETIC PHENCYCLIDINE AND ATTENUATION BY ATYPICAL ANTIPSYCHOTICS. † **Amitai, N.**; Semenova, S.; Markou, A

*Motor behaviors, exercise, and circadian rhythms*

120. EXPERIENTIAL THERAPY IMPROVES SKILLED MOTOR FUNCTION IN 6-OHDA DOPAMINE-DEPLETED RATS. **Jadavji, N.**; Kolb, B.; Metz, G.
121. EXERCISE, ETHOLOGY, AND MONOAMINERGIC ACTIVITY IN MICE SELECTED FOR INCREASED VOLUNTARY WHEEL-RUNNING. **Pringle, R.**; Forster, G.; Renner, K.; Waters, R.; Garland, T.; Malisch, J.; Swallow, J.
122. CONDITIONED LOCOMOTOR ACTIVITY FOLLOWING REPEATED INTERMITTENT ACTIVATION OF NEUROTENSIN RECEPTORS: COMPARISON BETWEEN FISCHER 344, LEWIS, AND LONG EVANS RATS. **Rompré, P.-P.**; Bauco, P.
123. DOPAMINERGIC RECEPTORS DIFFERENTIALLY REGULATE THE HYPERACTIVITY OBSERVED IN AN EXCITOTOXIC MODEL OF HUNTINGTON'S DISEASE. **Vázquez, I.**; Mendoza-Trejo, M.; Giordano, M.
124. MOTOR SKILL LEARNING MEDIATED BY D1 DOPAMINE RECEPTORS IN THE STRIATUM: FACILITATION BY COCAINE. **Willuhn, I.**; Steiner, H.
125. BIDIRECTIONAL SELECTION FOR ENDURANCE CAPACITY INFLUENCES GENERALIZED ANXIETY LEVEL AND STRESS COPING MECHANISMS IN NIH RATS. **Waters, R.P.**; Scholl, J.L.; Pringle, R.B.; Seiler, B.; Summers, C.H.; Watt, M.J.; Forster, G.L.; Renner, K.J.; Koch, L.G.; Britton, S.L.; Swallow, J.G.
126. GLUTAMATERGIC AND NICOTINIC MECHANISMS OF L-DOPA-INDUCED DYSKINESIAS IN THE HEMIPARKINSON RAT. **Paquette, M.A.**; Brudney, E.G.; Putterman, D.B.; Anderson, A.; Johnson, S.W.; Berger, S.P.

127. EXPOSURE TO CHRONIC STRESS LIMITS MOTOR RECOVERY AFTER FOCAL ISCHEMIC STROKE IN THE RAT MOTOR CORTEX. **Kirkland, S.**; Coma, A.; Metz, G.
128. NEUROBEHAVIORAL CHANGES IN A RAT MODEL OF MAMMARY ADENOCARCINOMA: EFFECTS OF MELATONIN INGESTION. **Wilson M.A.**; Meekins C.; Ford K.; Junor L.; Crapse T.
129. FOS EXPRESSION IN THE STRIATUM AFTER MODAFINIL ADMINISTRATION IN KAINIC ACID LESIONED ANIMALS. **Mendoza-Trejo, M.S.**; Mena-Segovia, J.; Giordano, M.
130. CHRONIC STRESS AND GLUCOCORTICOID TREATMENT SUPPORT RECOVERY OF MOTOR FUNCTION IN A RAT MODEL OF FOCAL CEREBRAL ISCHEMIA. **Smith, L.K.**; Kirkland, S.W.; Metz, G.A.
131. STRESS AND GLUCOCORTICIDS EXAGGERATE MOTOR IMPAIRMENTS IN A RAT MODEL OF PARKINSON'S DISEASE. **Smith, L.K.**; Jadavji, N.M.; Colwell, K.L.; Perehudoff, S.K.; Metz, G.A.
132. THE USEFULNESS OF THE SUNFLOWER SEED TEST IN EVALUATING FORELIMB MOTOR DYSFUNCTION AFTER BRAIN ISCHEMIA IN MICE. **Gomez, C.**; Santiago-Mejia, J.; Ventura-Martinez, R.; Rodriguez, R.
133. HIPPOCAMPUS NOREPINEPHRINE (NE) LEVEL AND EXERCISE BEHAVIOR IN SPORTS RATS. **Morishima, M.**; Harada, N.; Hara, S.; Takahashi, A.; Nakaya, N.
134. DIFFERENTIAL ROLE OF HIPPOCAMPAL GLUTAMATERGIC AFFERENTS IN ACCUMBAL DOPAMINERGIC LOCOMOTOR RESPONSES IN RATS. **Rouillon, C.**; David, H.N.; and Abraini, J.H.
135. ELECTROPORATION OF THE WILD-TYPE CASEIN KINASE 1-EPSILON GENE INTO THE SUPRACHIASMATIC NUCLEUS OF TAU MUTANT HAMSTERS LENGTHENS CIRCADIAN PERIOD. **Wang, H.**; Ko, C.H.; Ralph, M.R.; Yeomans, J.S.
136. EFFECTS OF THE D2 ANTAGONIST RACLOPRIDE ON SUCROSE FEEDING, LOCOMOTOR ACTIVITY, AND BEHAVIORAL SENSITIZATION TO THE D2/D3 AGONIST QUINPIROLE. **Foley, K.A.**; Kavaliers, M.; Ossenkopp, K.-P.

## ***Saturday, May 27, 2006***

- 08:45-10:45 ***Symposium 7: Explorations of the parental brain.*** MacDonald Ballroom DEF.  
Chair: Kelly G. Lambert
- 08:45-09:10 THE ADAPTIVE NATURE OF PARENTAL RESPONSIVENESS: LESSONS FROM THE RAT RACES, WILD-CAUGHT RATS, AND DEADBEAT DADS. **Lambert, K.**
- 09:10-09:35 PARITY AND MOTHERING AFFECT WORKING/REFERENCE MEMORY AND HIPPOCAMPAL NEUROGENESIS. **Galea, L.A.M.;** Pawluski, J.L.
- 09:35-10:00 WHEN THINGS GO WRONG; COCAINE'S DISRUPTION OF MATERNAL/SOCIAL BEHAVIOR IN RAT DAMS AND THEIR OFFSPRING: THE OXYTOCIN CONNECTION. **Johns, J.M.;** McMurray, M.S.; Jarrett, T.M.
- 10:00-10:25 THE EMOTIONS OF MOTHERHOOD: HOW REPRODUCTIVE EXPERIENCE REGULATES ANXIETY-LIKE RESPONSES IN RATS. **Byrnes, E.;** Scanlan, V.S.; Bridges, R.S.
- 10:25-10:45 THE INDUCTION, MAINTENANCE, & MEANING OF MATERNAL NEUROPLASTICITY. **Kinsley, C.H.**
- 10:45-11:00 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.
- 11:00-12:00 **Keynote Speaker: James L. McGaugh, Ph.D.,** University of California, Irvine, California, USA. *Emotional Arousal and Amygdala Activation: The Making of Lasting.* MacDonald Ballroom DEF.
- 12:00-13:45 **Student Workshop** (organized by Sarah Johnson). MacDonald Ballroom DEF.
- 14:15-16:15 ***Symposium 8: Sex, steroids and environment affect recovery from brain injury.*** MacDonald Ballroom DEF. Chair: Joseph Nuñez
- 14:15-14:45 EFFECTS OF AGE, SEX, AND EXPERIENCE ON RECOVERY CEREBRAL INJURY. **Kolb, B.**
- 14:45-15:15 SEX AND ESTRADIOL IN EARLY BRAIN INJURY: A TALE OF TWO FACTORS. **Nunez, J.**
- 15:15-15:45 NEUROSTEROIDS IN THE TREATMENT OF TRAUMATIC BRAIN INJURY AND STROKE. **Stein, D.**
- 15:45-16:15 NEUROPROTECTION BY ESTRADIOL IN A MODEL OF NEONATAL BRAIN INJURY. **Hilton, G.**

- 16:15-16:30 Break/**Exhibitors' Display**. MacDonald Ballroom ABC.
- 16:30-18:30 **Oral Session 2: Learning, reward and drug abuse**. MacDonald Ballroom DEF.  
Chair: Klaus-Peter Ossenkopp
- 16:30-16:45 ETHANOL AND MDMA: THE COMBINED EFFECT IS MORE THAN MDMA PLUS ETHANOL. **Jones, B.**; Ben-Hamida, S.; Plute, E.; Riegert, C.; Kelche, C; Cassel, J-C.
- 16:45-17:00 MIDBRAIN PATHWAYS FOR PREPULSE INHIBITION OF THE STARTLE REFLEX. **Yeomans, J.S.**
- 17:00-17:15 THE GENERAL THEORY OF PSYCHOLOGICAL RELATIVITY AND COGNITIVE EVOLUTION. **Bailey, C.**
- 17:15-17:30 BRAIN REGION-DEPENDENT EFFECTS OF GLUCOSE ON MEMORY. **Parent, M.B.**; Krebs, D.L.
- 17:30-17:45 DISCOVERY AND FUNCTIONAL EXPRESSION OF BRAIN CANNABINOID CB2 RECEPTORS INVOLVED IN DEPRESSION AND DRUG ABUSE. **Onaivi, E. S.**
- 17:45-18:00 THE FLUCTUATION OF LATENT INHIBITION ALONG THE ESTROUS CYCLE: DIFFERENT SENSITIVITY TO TYPICAL AND ATYPICAL NEUROLEPTICS IN INTACT AND OVARIECTOMIZED FEMALE RATS. **Arad M.**; Weiner I.
- 18:00:18:15 ROLE OF CRF IN THE NEGATIVE AFFECTIVE ASPECTS OF NICOTINE WITHDRAWAL. **Bruijnzeel, A.**; Zislis, G.; Wilson, C.; Gold, M.
- 18:15-18:30 DEVELOPMENTAL EXPOSURE TO MDMA RESULTS IN LONG-TERM DEFICITS IN SPATIAL VS. PATH INTEGRATION LEARNING AS A FUNCTION OF DOSE DISTRIBUTION. **Vorhees, C.V.**; Schaefer, T.L.; Williams, M.T.
- 18:30-19:00 **Business Meeting**. This meeting is for ALL IBNS members. MacDonald Ballroom DEF.
- 19:15- **Banquet and Presentation of Awards**. Frontenac Ballroom ABC.

## ***ABSTRACTS (in order of presentations)***

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**Wednesday, May 24, 2006**

**8:45-10:45 Symposium 1: *The underappreciated importance of the aversive properties of drugs of abuse.***

**EVIDENCE FOR CONCURRENT POSITIVE AND NEGATIVE ACTIONS OF COCAINE IN AN ANIMAL MODEL OF DRUG-SEEKING BEHAVIOR.** Ettenberg, A. Neuroscience & Behavior Program, Dept. of Psychology, University of California, Santa Barbara, CA 93106-9660 USA. Over the past 15 years, our laboratory has examined the concurrent positive and negative consequences of self-administered cocaine using a runway model of drug-seeking behavior in rats. Animals learn to traverse a straight-arm runway once each day to obtain an IV injection of cocaine upon entry into the goal box. The time required to traverse the runway and enter the goal box (Run Time) can therefore be used as an index of the undrugged subjects' motivation to return to a location where on previous trials cocaine reinforcement has been available. With this procedure, cocaine-seeking animals develop over trials a unique behavioral profile in the form of a highly distinct approach-avoidance conflict about re-entering the goal box. Our work suggests that this behavioral ambivalence stems from concurrent rewarding and anxiogenic properties of the drug – both of which come to be associated with the goal box. These “opponent-process” actions of cocaine were more directly observed in subsequent conditioned place preference studies where the initial immediate effects of IV cocaine were shown to reinforcing, while the state present 15 min post-injection was found to be aversive. In more recent work, we have shown that co-administration of alcohol or heroin can reduce the negative/anxiogenic properties of cocaine and may thereby account for the frequent co-abuse of these compounds with cocaine. Current studies are examining the motivating properties of centrally-applied cocaine with the goal of dissociating the brain regions responsible for the drug's positive and negative actions. In our view, a clear understanding of the neurobiological basis of cocaine abuse will require an assessment of both the positive and negative reinforcing properties of the drug that undoubtedly stem from its dual behavioral actions.

**ANIMAL MODELS OF DRUGS OF ABUSE: CONDITIONED TASTE AVERSION LEARNING.** Riley, A.L.; Busse, G.D. Psychopharmacology Laboratory, Department of Psychology, American University, Washington, DC 20016. The factors mediating drug use and abuse are multifaceted and dynamic, ranging from positive and negative reinforcement to sensitization and tolerance. Although the initiation of drug use and the subsequent progression to drug abuse are generally discussed in terms of a drug's rewarding effects, more recent work has shown that other affective properties of drugs may impact the likelihood of use and abuse. One such factor is the drug's aversive effects. The present talk discusses these effects in the context of a protective factor impacting the likelihood to initiate drug use, to progress from use to abuse and to maintain high levels of drug taking. Using the conditioned taste aversion preparation to assay the aversive effects of drugs, it is possible to evaluate the impact of aversions on drug vulnerability within the context of drug history, sex and strain differences, drug interactions and epigenetic factors. Differences in the sensitivity to the aversive effects of drugs or changes in these effects with drug history or experience may be important to the overall perceived affective state induced by the drug. Further, understanding the drug's aversive effects (and how they are influenced by the abovementioned factors) may provide insight into the mechanisms that alters one's susceptibility to drug use and abuse. It will be suggested that the balance of the drug's rewarding and aversive effects contribute to this behavioral vulnerability and that the aversive effects of drugs should be examined in this context. Research on which the abstract is based was supported in part by a grant from the Mellon Foundation to ALR.

**ULTRASONIC VOCALIZATIONS AS AN INDEX OF NEGATIVE AFFECTIVE STATES IN RATS.** Burgdorf, J.; Panksepp, J. Adolescent and adult rats exhibit two distinct ultrasonic vocalizations (USVs) that have been shown to reflect their affective states. 20-kHz USVs index a negative affective state akin to anxiety / depression, and are exhibited in response to social defeat and inescapable foot shock. Drug that are aversive to rats such as lithium chloride and naloxone have been shown to elevate levels of 20-kHz USVs. We have also found that levels of a variety of peptides associated with negative affective states (i.e., cholecystokinin, corticotropin-releasing factor, neuropeptide Y, substance P, and interleukin's) are positively related to 20-kHz calls in various brain regions. Whereas 50-kHz USVs have been found to be related to positive affective states akin to joy, and are exhibited during mating-rough-and tumble play and in response to drugs of abuse. A wide range of negative affective stimuli

including aversive drugs (i.e. lithium chloride and naloxone) have been shown to decrease levels of 50-kHz USVs. The strengths and weakness of using these vocalizations to index the aversive effects of drugs will be discussed.

**GENE KNOCKOUT STUDIES OF THE AVERSIVE AND REWARDING PROPERTIES OF ADDICTIVE DRUGS.** Hall, F.S. (1); Randall-Thompson, J. (1,2); Jones, J.D. (1,2); Riley, A.L. (2); Uhl, G.R. (1) (1) Molecular Neurobiology Branch, NIDA -IRP/NIH/DHHS, Baltimore, MD; (2) American University, Washington, DC Single gene knockout (KO) of the monoamine transporters for dopamine (DAT), serotonin (SERT) or norepinephrine (NET) do not eliminate cocaine reward. To the contrary, cocaine conditioned place preference (CPP) is increased in both NET KO and SERT KO mice. One possible hypothesis to explain these results is that SERT and NET gene deletions eliminate aversive properties of cocaine. We have begun to test this hypothesis using conditioned taste aversion (CTA) and combined CPP/CTA procedures. In the combined procedure, on Day 1 a preconditioning place preference is measured. On Day 2, after 1 h access to a novel saccharin solution, subjects receive cocaine (20 mg/kg) or saline injections and placed on the non-preferred side of the CPP apparatus. On day 3 after 1 h access to water, subjects receive saline and are placed on the opposite side of the CPP chamber. This procedure is repeated and followed post-conditioning by a preference test and an aversion test. Studies using the combined CPP/CTA procedure found that some mouse strains, contrary to previous findings in rats, exhibited a pronounced CPP to saccharin alone (as well as a CTA). Thus, in some cases, measures of place preference confounded the effects of cocaine and saccharin. Nonetheless, in those studies a significant cocaine CTA was not observed in DAT KO or combined DAT/SERT KO mice. Therefore, the effects of DAT KO were examined in the standard CTA procedure: access to a novel saccharin solution was followed by injection with saline or cocaine (18, 32 or 50 mg/kg s.c.); this procedure repeated every fourth day with intervening recovery days in which all mice had access to water. In this case DAT KO was found to be without effect. Further studies are underway to examine the effects of SERT and NET KO using this procedure.

***11:00-12:00 Presidential Lecture: Robert Adamec***

**NEURAL PATHS TO LASTING CHANGE IN AFFECT – A TALE OF TWO HEMISPHERES.** Adamec, R. Dept. of Psychology, Memorial University, Newfoundland, Canada, A1B 3X9. Several manipulations (kindling, pharmacological stress, or brief behavioral stress) in two species (cats and rats) produce long lasting changes in anxiety like behavior. Studies relating behavioral change to changes in transmission over amygdala pathways implicated in modulation of fearful behavior suggest a dynamic shifting over time of neural control of behavioral change. Involvement of both hemispheres appears early in the behavioral change, but there is a shift to the right hemisphere over longer time intervals (ranging from days to months). In rats and cats long term potentiation (LTP) like changes in monosynaptic pathways from amygdala to lateral column of the periaqueductal gray (PAG) in the right hemisphere appear important for lasting changes in fearfulness. The most direct tests of the degree of dependence of behavioral changes on right amygdala-PAG LTP have been done in the cat. Selective reversal of right amygdala-PAG LTP in the cat selectively reverses increases in fearfulness. In the rat, progress has been made in identifying several candidate neural circuit changes controlling some of the behavior changes by using multivariate correlation methods (including multiple regression and structural equation modeling) to relate electrophysiological measures of limbic neural transmission to behavior. This approach has led to two interesting findings. The first is that neural circuit changes mediating long lasting changes in anxiety like behavior appear to be lateralized to the right hemisphere. The second is that different functional modes of information transfer (parallel and serial processing) through these circuits may mediate particular behavioral changes. In both cats and rats, the effect of brief severe stress on fearfulness appears to depend on activation of NMDA receptors. In the rat, very recent evidence suggests a role for glutamate activation of gene regulation processes in initiation of lasting behavioral changes. Such processes may oversee neuroplastic changes which involve protein synthesis for initial consolidation, but not reconsolidation of lasting behavioral changes.

***14:30-16:30 Oral Session 1: Stress, fear and emotion***

**REACTIONS TO NOVELTY IN COPULATING VERSUS NON-COPULATING MALE RATS.** \*Agmo, A.; \*Spiteri, T.; +Le Pape, G.; \*Department of Psychology, University of Tromsø, 9037 Tromsø, Norway, and +Laboratoire d'Ethologie et de Psychophysiologie, Université de Tours, 37200 Tours, France. Some male rats will not display any sexual behavior when given access to a sexually receptive female (non-copulators). Most males, however, will initiate copulation within a few minutes (copulators). The causes for the lack of copulatory behavior in some males are presently unknown. One possible explanation is that non-copulators react to novelty in a way



different from that of copulators. At the first sex behavior test, the receptive female is, obviously, a new stimulus. Another explanation is that the female is not correctly identified as an object with which sexual interaction is possible. In the present experiment, rats were introduced into a circular arena and were then left alone for 10 min. Then, a porcelain coffee-cup turned upside down was put in the middle of the arena and left for 10 min. The cup was then removed, and a sexually receptive female was introduced and left for 30 min. This procedure was repeated until we had obtained 9 rats that did not show any copulatory behavior at all during the 30 min exposure to the female (non-copulators). Another 9 rats were randomly selected from the animals that achieved at least one ejaculation (copulators). The videotaped sessions were analyzed with regard to exploratory behaviors and behaviors directed towards the new object. Behaviors directed towards the female were also analyzed. The frequencies of several exploratory and self-centered behaviors were then subjected to a correspondence analysis. Results show that the behavior of the non-copulators differs from that of the copulators in a novel environment as well as when exposed to a novel object.

**STRESS AND PAIRING STATUS AFFECT CORTISOL AND VASOPRESSIN, BUT NOT OXYTOCIN, IN TITI MONKEYS (CALLICEBUS CUPREUS).** Bales, K.L.; Hostetler, C.M.; Mendoza, S.P. Dept of Psychology and California National Primate Research Center, University of California, Davis, 95616. The effects of stress on hormones, including cortisol (CORT), arginine vasopressin (AVP), and oxytocin (OT) are often context-, stressor-, and species-specific. In this study we investigated the effects of a mild stressor on plasma levels of CORT, AVP, and OT in the titi monkey, a monogamous New World primate species. Subjects included 6 females and 12 males that were in pair-bonds, as well as 4 males that were housed alone. Each animal underwent 4 test conditions on 4 different days. A baseline blood sample was drawn, then the animal was left quietly in a transport cage for 15, 30, 45, or 60 minutes, at which time a second sample was drawn. After the second sample, the animal was returned to its cage. The latency to contact with its mate, and the initiator of the contact, was recorded. Stress resulted in a significant ( $p < 0.05$ ) rise in CORT at all 4 time points; however, lone males had a significantly higher CORT rise than the other three groups at baseline and all stress time points. Stress also resulted in a significant rise in AVP at all 4 time points; however, lone males were higher only at the 30 minute time point. OT did not change after stress nor differ by pairing status. Higher levels of OT were associated with a higher likelihood of initiating contact with a mate. Supported by a pilot grant from the California National Primate Research Center.

**DIFFERENTIAL NEURAL RESPONSES TO EMOTIONAL FACE EXPRESSIONS IN THE MONKEY PULVINAR.** Maior, R.S.; Hori, E.; Tomaz, C.; Ono, T.; Nishijo, H. System Emotional Science, Graduate School of Medicine, University of Toyama, Sugitani 2630, Toyama 930-0194, Japan; CREST JST, 4-1-8 Honcho Kawaguchi 332-0012, Japan. There are extensive data relating the amygdala to the recognition of emotion, particularly of fear. The pulvinar nucleus of the thalamus has been shown to receive visual inputs from the superior colliculus and to project to the amygdala. To investigate whether this circuit codes emotion recognition, one adult *Macaca fuscata* monkey was painlessly restrained in a stereotaxic apparatus by a previously prepared, surgically fixed head holder. The monkey was to perform a delayed non-matching-to-sample (DNMS) task with a set of front-view human faces depicting emotions (sad, angry, happy, surprised and neutral) and another of simple pattern control figures. The human facial stimuli are comprised of the facial photos taken from 3 adult females and 4 adult males. Each pair of sample and target stimuli was selected from the same set of the visual stimuli. Neuronal activity was recorded from the medial and lateral parts of the right pulvinar. The results indicated that the pulvinar neurons differentially responded to the distinct emotional expressions of the human faces. These preliminary results suggest a role of the pulvinar nucleus in emotion recognition.

**DEFENSE-LIKE BEHAVIORS INDUCED BY ULTRASOUND IN LISTER HOODED RATS: SENSITIVITY TO ANXIOLYTICS ACTING VIA DIFFERENT MECHANISMS.** Prinssen, E.P.; Klein, S.; Nicolas, L.B. Behavioral pharmacology, F. Hoffmann-La Roche, CH-4070, Basel, Switzerland. In man, electrical stimulation of dorsal periaqueductal gray matter (dPAG) causes acute and intense distress with autonomic responses similar to those occurring during panic attacks. In rats, dPAG stimulation elicits wild running that is thought to be closely related to intense fear and panic. A non-invasive technique – exposure to ultrasound – has been reported to also stimulate the dPAG (Beckett et al., 1997) and to induce wild running followed by freezing in Lister Hooded rats. Reported findings showing that diazepam and yohimbine modulate ultrasound-induced wild running suggest predictive validity for anxiety/panic. Here, we studied the effects of anxiolytics acting via different mechanisms. Results showed that the low-potency benzodiazepine receptor agonists diazepam and chlordiazepoxide selectively reduced wild running (i.e., at doses lower than those that decreased spontaneous locomotion), whereas the high-potency agonist alprazolam did not show such a separation. The voltage-dependent calcium channel inhibitors

pregabalin and gabapentin and the putative anxiolytic and mGlu5 antagonist MTEP selectively reduced wild running. The putative anxiolytic and nociceptin OFQ peptide receptor agonist Ro 64-6198 did not affect wild running, but reduced freezing, a measure that was not affected by any of the other compounds. As expected, haloperidol did not show any selective effects. Our finding that anxiolytics independently modulate wild running or freezing, suggests that these behaviors reflect different aspects of panic and/or anxiety.

**FATTY-ACID AMIDE HYDROLASE: A NOVEL TARGET FOR ANTIDEPRESSANT THERAPY.** Bortolato, M; Mangieri RA; Campolongo P; Trezza, V; Arguello, O; Cuomo, V; Piomelli, D. Dept of Pharmacology, Univ. of California, Irvine, CA, USA; Dept of Human Physiology and Pharmacology, Univ. of Rome, Rome, Italy In previous work, our group showed that inhibition of fatty acid amide hydrolase - the enzyme responsible for intracellular hydrolysis of anandamide - elicits anxiolytic properties in rodents. To verify whether such properties are accompanied by a broader ability to regulate mood functions, we tested the effects of URB597, a potent inhibitor of FAAH, in three animal models of depression: the Forced Swimming Test (FST), the Tail Suspension Test (TST) and the chronic mild stress (CMS). Acute (0.1 - 0.3 mg/kg i.p.) or subchronic (4 days, 0.1 mg/kg i.p., once daily) administrations of URB597 reduced floating and increased swimming duration in the FST. Consistently, mice treated with URB597 either acutely (0.1-0.3 mg/kg i.p.) or subchronically (4 days, 0.1 mg/kg i.p., once daily) exhibited a significant reduction in stillness time in the TST, in comparison with controls. Both effects were prevented by the CB1 cannabinoid receptor antagonist rimonabant, suggesting that they were mediated by anandamide via CB1 receptor activation. CMS procedure induced significant reductions in sucrose intake in rats in comparison with controls. Such reductions were subsequently reversed by a 5-week-long treatment with URB597 (0.1 - 0.3 mg/kg i.p., once daily) in a dose-dependent fashion. To assess whether the antidepressant actions of URB597 were accompanied by hedonic properties, we tested the FAAH inhibitor in the conditioned place preference test (0.03-0.3 mg/kg i.p.). URB597 did not produce place preference. These results suggest that URB597 exerts potent antidepressant-like effects, which are not accompanied by overt abuse potential, pointing to FAAH inhibition as an innovative approach to anti-depressant treatment.

**KINDLED RATS' FEAR BEHAVIOR IS REFLECTED BY A DISTINCT AND RELIABLE PATTERN OF ACTIVITY IN A NOVEL OPEN FIELD.** Amanda J. Wintink <sup>1</sup> & Lisa E. Kalynchuk <sup>2</sup> <sup>1</sup>Department of Pharmacology, Laboratory of Molecular Neurobiology, Dalhousie University, Halifax, NS, Canada. <sup>2</sup>Department of Psychology, University of Saskatchewan, Saskatoon, SK, Canada. Long-term amygdala kindled rats exhibit extreme levels of fear behavior (Kalynchuk et al., 1997, Wintink et al., 2003) that is difficult to capture using conventional measures. Kindled-fear behavior is generally measured by placing rats in a novel open field and measuring their resistance to being picked up by a novel experimenter. Under such circumstances, kindled rats typically launch jump attacks at the experimenter's hand and attempt to bite the hand whereas control rats display little, if any, resistance. Open-field activity has also been used as a measure of fearfulness in kindled rats; however, these measures have proven more difficult because kindled rats freeze more in the first 30s of exposure yet also display hyperactivity when the entire exposure is taken into account (Kalynchuk et al., 2001). To address this discrepancy, open-field activity was examined during each minute of the 5-minute open-field exposure. The results indicate that kindled rats show an initial decrease in open-field activity during the first minute of open-field exposure relative to controls; however, kindled rats subsequently show a dramatic increase in activity above that of controls around the second or third minute and this hyperactivity remains elevated for the remainder of the open-field exposure. This pattern differs from control rats that show little change across the 5 minutes. Collectively, the behavior of kindled rats appears to represent an initial passive fear response followed by an active panic-like response that culminates in high resistance to being picked up by the experimenter. These findings contribute to the characterization of kindled fear as a unique demonstration of fear behavior.

**NEUROENDOCRINE CONTROL OF THE DEVELOPMENT OF AGONISTIC BEHAVIOR.** Delville, Y.; Cervantes, M.C.; Taravosh-Lahn, K.; Wommack, J.C. Psychology Dept. and Neuroscience Program, University of Texas, Austin, TX 78712, USA. We have studied the development of the offensive component of agonistic behavior during puberty in hamsters. Offensive responses can be studied as a frequencies summarized over a period of time and as sequences of events during a test. In addition, the behaviors can also be described as different display patterns. As such, the development of offensive responding during puberty has shown a peak of attack frequency and repetitions of attacks during bouts of contact early in puberty. This early peak was followed by a gradual decline into adulthood. In addition, the body parts targeted during these attacks (attack types) also changed gradually from the face and cheeks (play fighting) in early puberty to the rump and lower belly (aggression) in adulthood. These changes during puberty are correlated with increasing release of corticosteroids. The role of

corticosteroids was tested as exposure to stress in early puberty accelerates the development of attack types. This acceleration was replicated by treatment with cortisol and corticosteroid receptor type 2 agonists. The effects of cortisol were inhibited by treatment with corticosteroid receptor type 2 antagonists. While it took several days of treatment with cortisol to show a significant effect, a single injection of fluoxetine in early puberty was sufficient to accelerate the development of attack types. Moreover, treatment with fluoxetine early in puberty also had differential effects on attack frequency and repetition. These data show that corticosteroid hormones control the maturation of offensive responding during puberty, possibly through a modulation of serotonin systems.

EXPOSURE TO A LITHIUM-PAIRED CONTEXT ELICITS GAPING IN RATS: A MODEL OF ANTICIPATORY NAUSEA. <sup>1</sup>Limebeer, C.L., <sup>2</sup>Hall, G., Parker, L.A. <sup>1</sup>Department of Psychology, Wilfrid Laurier University, Waterloo, ON N2L 3C5 Canada; <sup>2</sup>Dept. of Psychology, University of York, York YO10 5DD, UK. Chemotherapy patients report anticipatory nausea and vomiting upon re-exposure to the cues previously associated with the treatment. Although rats do not vomit, they display a distinctive gaping reaction when exposed to a toxin-paired flavored solution. Here we report that rats also display gaping reactions during exposure to a context previously paired with the illness-inducing effects of lithium chloride (Experiment 1). This gaping reaction is suppressed by pretreatment with the antiemetic agent,  $\Delta^9$ -tetrahydrocannabinol, but not ondansetron (Experiment 2). The finding that gaping is elicited by an illness-paired context confirms the proposal that an illness-paired context can evoke a conditioned state of nausea and supports the case of context-aversion as a rat model for anticipatory nausea.

#### ***16:45-18:45 Symposium 2: Genes meet behavior***

HOW SMART IS MY MOUSE? THE GENETIC DISSECTION OF MEMORY SYSTEMS IN THE MOUSE. Crusio, W.E.; Schwegler, H. Laboratoire de Neurosciences Cognitives, CNRS UMR 5106, Talence, France and Institut für Anatomie, Universität Magdeburg, Germany. Male mice from several inbred mouse strains were tested in a number of different spatial and non-spatial radial maze tasks that assessed working (WM) and/or reference memory (RM). Large strain differences were obtained that were task-dependent. Other animals from the same strains were processed histologically to estimate the strain-specific extents of the hippocampal intra- and infrapyramidal mossy fibre projections (IIPMF). We estimated genetic correlations between the different behavioural and anatomical variables. The results of these experiments show that seemingly minor changes of procedure, such as turning the maze by 45 degrees between trials, can have dramatic effects on learning performance in some strains. A factor analysis rendered three factors: two representing non-spatial learning (factors I and III), one representing spatial learning (factor II). WM and RM did not differentiate on different factors. The IIPMF strongly loaded on the spatial learning factor only. We conclude that in radial maze tasks: (1) spatial learning, in contrast to non-spatial learning, is a unitary process, (2) WM and RM are probably not related to different neuronal mechanisms in mice, and (3) variations in the extent of the hippocampal IIPMF projection underlie individual differences in spatial learning abilities in the radial maze.

ZEBRA FISH AT THE DOOR STEPS OF BEHAVIORAL NEUROSCIENCE AND BEHAVIORAL GENET. Gerlai, R. Zebra fish has been a favorite of geneticists and developmental biologists but unlike classical laboratory rodents, it has been rarely used in behavioral or brain research. Nevertheless, the past few years saw a dramatic increase of interest in this species as the number of behavioral studies has exponentially grown. Zebra fish turns out to be an excellent system for the analysis of social behaviors, learning and memory, sleep, aggression, anxiety, consumption of alcohol and other types of drug of abuse, and the list goes on. The pioneering studies suggest that many of these complex behaviors may be amenable to high throughput mutagenesis screening. The current paper reviews this fast developing field and presents some novel data particularly on alcohol effects, social behavior, and alarm responses of zebra fish

GENETIC ANIMAL MODELS OF ALCOHOL ABUSE: WHAT ARE WE LOOKING FOR, ANYWAY? Crabbe, John. Portland Alcohol Research Center, Department of Behavioral Neuroscience, Oregon Health & Science University, and VA Medical Center, Portland, Oregon 97239 USA. Many animal models have targeted alcohol abuse and dependence. In the rodent, the majority of such models have sought to increase alcohol self-administration using genetic or environmental manipulations, or their combination. Strictly genetic manipulations (e.g. comparison of inbred strains or targeted mutants, selective breeding) have not yielded rat or mouse genotypes that will voluntarily self-administer to the point of intoxication. While some behavioral manipulations (e.g., scheduling and or limiting access to alcohol) will induce mice or rats to self-administer alcohol to intoxication, these

typically require significant food or water restriction and/or a long time to develop. Susceptible (i.e., relatively high-intake) genotypes do not appear to be preferentially susceptible to these effective behavioral manipulations. Some human alcoholics repeatedly drink to intoxication, even in the face of substantial physical and social feedback opposing this behavior. It would be useful to have a mouse genetic animal model that self-administers sufficient alcohol to become intoxicated. This talk will review progress toward that goal. In one set of experiments, we are selectively breeding High Drinking in the Dark mice to ingest 20% alcohol until they reach blood alcohol levels (BALs) exceeding 100 mg%. After three generations of selection, more than 25% of the population exceeds these BALs. These mice should be useful for mechanistic studies, and for pharmacological experiments designed to limit alcohol self-administration. Supported by the Integrative Neuroscience Initiative on Alcoholism, the NIAAA, and the Department of Veterans Affairs (AA13519, AA10760).

SYSTEMS GENETICS OF THE HIPPOCAMPUS: GENES, TRANSCRIPTS, CELLS, CIRCUITS, BEHAVIORS. Williams, R.; Peirce, J.; Lu, L. Reductionist approaches to understand the genetic modulation of behavior can now be complemented by more synthetic approaches that exploit natural variation at all levels of organization; from SNPs through to behavior. We summarize data on variation in gene expression in hippocampus generated across a genetic reference population consisting of approximately 100 well characterized strains of mice, including the BXD and CXB sets of recombinant inbred strains and 15 widely used standard inbred strains, such as C57BL/6J, DBA/2J, BALB/cJ, 129, and A/J. We demonstrate how expression data can be matched up with neuroanatomical and behavioral data for many of these same strains to generate models that attempt to account for relations between gene variants and complex behaviors. Predictive models can be generated efficiently, and can also be tested simply by acquiring stock of any of these 100 strains. We will provide specific examples of how this approach has yielded insights into the genetic basis of adult neurogenesis and relations with gene expression and possible behavioral variants.

*Thursday, May 25, 2006*

**8:45-10:45 Symposium 3: Vocalization as an emotional indicator**

50-KHZ ULTRASONIC VOCALIZATIONS AS AN INDEX OF POSITIVE AFFECTIVE STATES IN RATS. Panksepp, J.; Burgdorf, J. Falk Center for Molecular Therapeutics, Northwestern University, Evanston, IL 60208 USA. The nature of affective processes in the brain is rapidly becoming a key topic in behavioral neuroscience as well as cognitive neuroscience. One current view is that there are many varieties of affect (emotional, homeostatic, and sensory), and one view is that emotional affects are elaborated by the same brain operating systems that generate emotional-instinctual behaviors. We will summarize the evidence that this principle holds for 50 kHz ultrasonic vocalizations (USVs) that are especially evident during social-interactions and appetitive states. Converging evidence from ethological, pharmacological, and brain stimulation studies indicate that certain rat 50 kHz USVs reflect positive affective states. Indeed, 50 kHz ultrasonic vocalizations may be a rat homolog of human laughter, since they are especially evident during rough-and-tumble social play, and can be maximized by heterospecific hand play (i.e., "tickling"). They may reflect a positive affective state akin to human joy. These vocalizations are also seen during other positive social interactions, especially sexuality, and sometimes before intermale fighting. Euphoric / addictive drugs as well as rewarding brain stimulation also elevate 50-kHz calls. Rates of 50-kHz calls have been found to be consistently positively correlated to social reward across multiple studies. On the other hand, all aversive stimuli, including foot shock, bright light, predatory odor as well as aversive drugs have been shown to decrease levels of 50-kHz calls. Recently, detailed sonographical analysis of 50-kHz USVs have revealed multiple call subtypes, and of these only the frequency modulated variety are clearly related to reward. Fifty kHz USVs are modulated by brain dopamine systems that have also implicated in human positive affective. In sum, positive affective-appetitive processes in laboratory rats may be monitored through their 50 kHz emotional vocalizations.

DISTINCT BRAIN MECHANISMS FOR THE PROCESSING OF LAUGHTER AND SPEECH. (1) Alter, K.; (2) Szameitat, D.; (3) Meyer, M. (1) Newcastle University, Institute of Neuroscience, School of Neurology, Neurobiology and Psychiatry, Newcastle Auditory Group. (2) Max-Planck Institute of Human Cognitive and Brain Sciences, (3) University of Zurich, Research Group 'Neuroplasticity of the Auditory System', Department of Neuropsychology, Institute for Psychology. In this study, we used event-related fMRI to examine the neural responses to speech, vocal (human laughter), and non-vocal sounds. We aimed to delineate distinct peri-auditory regions which preferentially respond to speech, laughter, and sounds. Results show that (i) left inferior frontal as

well as left and right superior temporal regions subserve the comprehension of spoken utterances, (ii) in particular left anterior and posterior lateral temporal regions can be associated with the processing of speech, (iii) bilateral areas in the medial portion of Heschl's gyrus and at the medial wall of the posterior Sylvian fissure (planum parietale and parietal operculum) mediate the processing of non-vocal sounds with the right hemisphere being more strongly recruited. (iv) listening to human laughter more strongly involves secondary auditory and somatosensory fields also in the right rather than the left hemisphere, but (v) perceiving human laughter does not evoke responses in brain regions usually associated with emotions. However, in a recent study on the processing of laughter and crying (Sander & Scheich 2005), activations in the amygdala have been reported. The studies will be compared in this presentation with regard to design, method, and materials. The data of our study indicates that the perception of laughter does not activate regions which are associated with emotions but activates brain regions which control motor (larynx) functions. The latter observation speaks to the issue of a dense intertwining of expressive and receptive mechanisms functions in the auditory domain. Generally, the present study evidences a functional segregation of the temporo-parietal lobes and lends support to the notion of at least two separate pathways mediating speech and non-speech stimuli.

**COMMON ACOUSTIC FEATURES IN THE VOCAL EXPRESSION OF EMOTIONS IN MONKEYS AND MAN.** Juergens, U. Dept. of Neurobiology, German Primate Center, 37077 Goettingen, Germany. In order to find out to which extent monkey calls can be used as models to study the neurobiological basis of human emotional prosody, we have carried out a comparative acoustic analysis of squirrel monkey calls and human emotional intonations, looking for similarities in the vocal expression of specific emotional states. For this purpose, squirrel monkeys were tested in self-stimulation experiments with intracerebrally elicited vocalizations for the aversiveness of the emotional states accompanying specific call types. In humans, data were acquired by asking students of dramatic art to pronounce one and the same word in an aversive (rage, despair, disgust) or non-aversive (joyful surprise, voluptuous enjoyment, affection) mood. It turned out that in squirrel monkeys as well as humans, an increase in the aversiveness of the emotional state was accompanied by an increase in peak frequency (frequency of highest energy in the power spectrum), an increase in frequency range (difference between maximum and minimum frequency at a specific time) and an increase in the amount of non-harmonic time segments in relation to harmonic ones. These similarities suggest common phylogenetic roots in the vocal expression of emotion in monkeys and man, supporting the usefulness of monkey calls as models in studies on human emotional prosody.

**A TELEMETRIC SINGLE-UNIT RECORDING STUDY ON VOCALIZATION-CORRELATED ACTIVITY IN THE BRAINSTEM OF THE SQUIRREL MONKEY.** Hage, SR. Dept. of Neurobiology, German Primate Center, 37077 Goettingen, Germany. The ventrolateral pontine brainstem seems to play a crucial role in motor control of mammalian vocalization: Connections to all motoneuron pools involved in phonation do exist; its stimulation leads to vocalization and blocking of its excitatory neurotransmission eliminates specific vocalizations elicitable from the periaqueductal gray. Though very little is known about its specific role in vocal-motor control on the level of single neurons. We used a telemetric single-unit recording technique to explore the ventrolateral pontine brainstem for vocalization-correlated activity in freely behaving squirrel monkeys during vocal communication. We found a discrete area in the reticular formation just above the superior olivary complex showing vocalization-correlated activity. These neurons showed an increase in neuronal activity exclusively just before and during vocalization; none of them were active during mastication, swallowing or quiet respiration. Furthermore, the neuronal activity of these neurons reflected acoustic features, such as call duration or syllable structure of frequency-modulated vocalization, directly. Based on these findings and previously reported anatomical data, we propose that this area serves as a vocal pattern generator for frequency-modulated call types.

**BRAIN MECHANISMS AND ACOUSTIC CODING OF ULTRASONIC SIGNALS IN THE RAT'S VOCAL EXPRESSION OF EMOTIONAL STATES.** Brudzynski, S.M. Dept. of Psychology and Centre for Neuroscience, Brock University, St. Catharines Ontario, L2S 3A1, Canada. Emission of two main patterns of ultrasonic calls in adult rats, the 22 kHz and 50 kHz calls, is dependent on the activity of two different neurotransmitter systems, the tegmento-forebrain cholinergic system and the tegmento-accumbens dopaminergic system, respectively. Both these systems form ascending mesolimbic projections, which innervate extensive regions of the limbic brain. Activation of the mesolimbic dopaminergic or cholinergic systems has been consistently associated with a significant arousal and characteristic behavioral symptoms. These systems differ as well not only neurochemically, but also in the main projection targets, in the physiological states they control, and in the resulting behaviors, all of which are consistent with mutually exclusive appetitive or aversive behavioral states. Results are presented that the dopamine-dependent 50 kHz calls and the acetylcholine-dependent 22 kHz calls are acoustically different and also usually appear in a

mutually exclusive way. In a three dimensional analysis of duration-frequency-bandwidth dimensions, the 50 kHz and 22 kHz calls occupy non-overlapping spaces which cannot be acoustically confused by the recipients. This finding strongly supports the conclusion that rats can unequivocally distinguish the two call types from each other. Fifty kHz and 22 kHz calls are therefore specific for the state they are associated with and may reliably serve as an intraspecific and heterospecific signal of a general physiological and affective state of the animal. Supported by grant from NSERC of Canada.

**11:00-12:00 Keynote Speaker: Michael J. Meaney**

MATERNAL EFFECTS IN MAMMALS AS A MODEL FOR ENVIRONMENTALLY-DRIVEN CHROMATIN PLASTICITY. Michael J Meaney, McGill Program for the Study of Behaviour, Genes and Environment, Douglas Hospital Research Centre, McGill University, Montreal, Canada. Maternal care alters the development of adaptive behavioral and endocrine responses to stress in the rat; an example of maternally-regulated, phenotypic plasticity. The mechanisms for these 'maternal effects' involve stable changes in the expression of genes in brain regions that mediate stress reactivity as well as regions involved in the processing of information related to the stressor. Notable are the effects on systems that regulate central corticotrophin-releasing factor (CRF) synthesis and release from the hypothalamus and amygdala. The adult offspring of mothers that exhibit increased pup licking/grooming (LG) show increased glucocorticoid receptor mRNA throughout the hippocampus. The differences in glucocorticoid receptor expression are associated with effects at the level of both negative feedback inhibition and HPA responses to stress; the offspring of High LG dams show increased hippocampal glucocorticoid receptor expression, enhanced negative feedback regulation and more modest HPA responses to stress. These findings suggest that maternal care acts to 'program' HPA responses in the offspring through effects on systems that regulate CRF activity. Adoption studies reveal direct effects of maternal care. Recent studies focus on the mechanisms for these effects by examining DNA methylation within a brain-specific glucocorticoid receptor gene promoter. These studies reveal sustained effects of maternal behavior on the cytosine methylation of the consensus binding sequences for specific transcription factors that regulate glucocorticoid receptor gene expression. Pharmacological manipulations that reverse the maternal effect on cytosine methylation of the glucocorticoid receptor promoter eliminate the effect at the level of both glucocorticoid receptor expression and HPA responses to stress. These findings suggest that differential methylation mediates the sustained effects of maternal care on glucocorticoid receptor gene expression. The maternal effect on DNA methylation appears to involve an active demethylation process at specific CpG dinucleotides that is targeted by intracellular processes sensitive to the tactile stimulation associated with pup licking. Such a process may reveal experience-dependent plasticity in the chemistry of the DNA and chromatin structure.

**14:00-16:00 Symposium 4: Relation of dominant-submissive behavior to mania and depression; parallels between animal behavior and human disease.**

DEVELOPMENT OF A PROTOCOL TO MEASURE HUMAN DOMINANT-SUBMISSIVE SOCIAL BEHAVIOUR. Wai S. Tse.<sup>a</sup> & Alyson J. Bond<sup>b</sup>, <sup>a</sup>Department of Applied Social Studies, City University of Hong Kong, Tat Chee Ave. Hong Kong, <sup>b</sup>Division of Psychological Medicine, Institute of Psychiatry, King's College London, UK. The social behaviour of untreated depressed patients is characterized by paucity of speech, lack of energy and decreased eye contact. These social behaviours have been found to lead to rejection by others. Manic social behaviours can be described as talking non-stop and without regard to others' wishes to communicate. Much less work has examined the consequences of manic behaviour on social integration. Therefore, depression can be viewed as passive or submissive and hypomania can be viewed as active or dominant. A standard behavioural measurement protocol was constructed based on the description of depression and hypomania in DSMIV. It measured 4 styles of interpersonal behaviour. Two of the roles portrayed abnormal social behaviour, active non-participant 'manic' and passive non-participant 'sad', and two portrayed normal social behaviour, active participant 'warm' and passive participant 'shy'. The interaction of subjects with a confederate acting these 4 roles and their subsequent behaviour on a dyadic game was recorded. Subjects were more likely to reject confederates in the manic or sad roles. This was shown by both non-verbal behaviour and verbal report. They also behaved more punitively on the dyadic game. Thus displaying depressed or manic behaviour not only results in social rejection but also in the reduction of social reinforcement. In a healthy volunteer study, 2 weeks of antidepressant treatment significantly altered eye gaze behaviour, indicating a change in dominant-submissive behaviour. This observation provided further evidence that the protocol is a valid method to evaluate human dominant-submissive behaviour, which is sensitive to pharmacological agents.

THE IMPACT OF THE INTERACTION BETWEEN PERSONALITY AND DOMINANCE-SUBMISSIVE BEHAVIOR ON PHYSIOLOGICAL PARAMETERS. Pieter, J. Drent & Kees van Oers, Neth. Inst. of Ecology, Heteren, 6666 ZG, The Netherlands. Like many vertebrates, including humans, birds frequently cope with challenges in a changing environment. The best evolutionary solution would be if individuals were flexible and optimal in their reaction to separate challenges. However, in most species neuro-endocrine and developmental constraints have probably resulted in genetically based variation in reactions towards mild challenges like e.g. exploration and aggressiveness. Thereby, as a consequence of structural pleiotropy many behavioral reactions are correlated and show carry-over effects over contexts. So evolutionary, selection on one trait will have consequences for the selection on another one. Therefore, reaction norms are not determined by for each of the challenges independently, but by selection on different optimal behavioral compromises. Such variations in packages of behavioral reactions with relatively low plasticity are referred to as variation in coping strategy, behavioral syndrome or personality. The great tit is the only wild animal for which laboratory- and field work is combined, thereby integrating genetic, mechanistic and evolutionary aspects of (animal) personalities. Hand-reared birds of lines selected for different personalities and similarly characterized wild birds were used in an array of experiments on social behavior and its consequences in terms of relative benefits and (physiological) risks. Here we will argue that the knowledge on personality is essential to be able to interpret results and risks for mania and depression.

ETHOLOGICAL ANALYSIS OF RODENT BEHAVIOUR: ELUCIDATION OF THE BEHAVIOURAL EFFECTS OF ANTIDEPRESSANT DRUGS. Mitchell, P.J.; Redfern, P.H. Dept. of Pharmacy and Pharmacology, University of Bath, Bath. UK. BA2 7AY. A wide diversity of animal models has been used to examine psychotropic drug activity. In recent years antidepressant drug research has focused on the search for new therapies with a rapid onset of action. It follows that, to be relevant, animal models must have the ability to measure the time course of drug-induced changes in behaviour. Two 'ethologically-relevant' animal models, the resident-intruder and social hierarchy paradigms, have been especially useful in elucidating the behavioural effects of antidepressant drugs. In the social hierarchy model male Wistar rats are housed in triads. All group members are routinely involved in intense levels of social and agonistic behaviour at the onset of the dark phase of the light:dark cycle. Ethological analysis of such behaviour (where the 'winner' and 'loser' of each social encounter is identified) reveals the relative social position of each group member (the most successful group member during these encounters indicates the dominant animal). In the resident-intruder paradigm, male Wistar resident rats are housed in isolation for a minimum of 3 days before being exposed to an unfamiliar conspecific intruder. During the ensuing social encounter, control resident rats exhibit a wide range of non-social, social and conflict-related (i.e. agonistic) behaviours which are quantified during subsequent ethological analysis. Together these models of rodent social and agonistic behaviour have demonstrated that chronic treatment with antidepressant drugs (irrespective of their acute pharmacological activity) increases rodent aggressive behaviour which, in turn, results in increased hierarchical status in closed social groups. Furthermore, the increased rodent aggression is most likely a behavioural manifestation of increased assertive behaviour and arguably reflects similar changes in human behaviour (including the externalization of emotions) expressed during the recovery from depressive illness.

DOMINANT - SUBMISSIVE RELATIONSHIPS IN PAIRED ANIMALS FOR ANTIMANIC AND ANTIDEPRESSANT DRUG TESTING. Malatynska, E., Johnson Pharmaceutical Research & Development, L.L.C, Spring House, PA 19477. This presentation discusses dominant-submissive relationships (DSR) formed between paired mice and rats in a food competition test. We are using dominant behavior for antimanic and submissive behavior for antidepressant drug testing in the reduction of dominant behavior model (RDBM) or the reduction of submissive behavior model (RSBM), respectively. In our experiments, Sprague Dawley rats or C57Bl/J6 mice were food-restricted, randomly paired and placed in an apparatus allowing them to compete for a food reward. A fraction of rats and mice population tested developed dominant-submissive relationships over a two-week period, which was stable for at least three weeks. The experimental conditions have to be adjusted for mice as compared to rats. Sprague Dawley rat dominant behavior is sensitive to antimanic drugs. Submissive mice, similar to rats, are sensitive to antidepressants of different classes. However, the selectivity profile for drugs that are not used in the clinic as antidepressants appears to be slightly different in mice than rats. In summary, the major focus of this presentation is on the predictive validity of DSR based tests. However, some aspects of construct validity that correlates between animal dominant or submissive behavior and human mania or depression will be also discussed.

*16:15-17:45 Student Travel Award Slide Blitz*

**CHRONIC ANTI-INFLAMMATORY TREATMENT FAILS TO PREVENT BRAIN PATHOLOGY IN A MODEL OF NEUROPSYCHIATRIC LUPUS.** Ballok, D.A.; Sakic, B. Dept. of Psychiatry and Behavioral Neurosciences. McMaster University, Hamilton, ON, CANADA. Neurologic deficits and psychiatric problems are severe complications of systemic lupus erythematosus. As commonly seen in patients, spontaneous development of lupus-like disease in MRL/MpJ-Faslpr (MRL-lpr) mice is accompanied by brain atrophy and behavioral dysfunction. We presently examine inflammatory and ultrastructural aspects of the CNS involvement using a non-selective COX-2 inhibitor and measuring effects on behavior, microglial activation, and neuronal morphology. Ibuprofen (IBU) was provided in a rodent chow (375 ppm) from 519 weeks of age. Exploration of a novel environment and performance in the forced swim test assessed effects on behavior. Immunohistochemistry, Fluoro Jade B (FJB) staining, and flow cytometry were employed in neuropathological analysis. Transmission electron microscopy examined ultrastructural morphology of cortical, hippocampal, hypothalamic, and cerebellar cells. Chronic IBU treatment failed to normalize immune status, behavior, and brain mass in lupus-prone MRL-lpr mice. It also did not reduce density of CD3+ lymphocytes in the choroid plexus, or FJB+ neurons in the hypothalamus. Activated F4/80+ microglia increased with age, but IBU treatment was not effective in reducing their numbers. Although numerous dark cells were seen in functionally critical brain regions (e.g. the PVN and the subgranular zone), ultrastructural morphologies of classical apoptosis or necrosis were not detected. The COX-dependent pathway does not seem to be critical in the etiology of CNS disease in this model of neuropsychiatric lupus. Reduced brain mass, increased microglial activation, and condensation of cytoplasm point to a metabolic perturbation (e.g. excitotoxic damage) which compromises function and survival of central neurons during lupus-like disease.

**SUPPLEMENTAL CHOLINE IN THE MATERNAL DIET OF RATS MODULATES HIPPOCAMPAL NEUROGENESIS AND EXPLORATORY BEHAVIOR IN OFFSPRING.** Glenn, M.J.; Kirby, E.D.; Wong-Goodrich, S.J.E.; Williams, C.L. Prenatal choline supplementation has a profound and lasting effect on cognitive function, leading to improved memory capacity and precision that resists normal, age-induced decline. In the current study we tested the hypothesis that supplemental choline in the maternal diet may exert its effects on cognition across the lifespan of offspring by enhancing neuronal proliferation in adult hippocampus. We were also interested in exploring whether supplemental choline alters how rats interact with and respond to novel objects and environments. On embryonic days 12-17, pregnant rats received a control diet containing 1.1 g/kg choline chloride (CON), or a diet supplemented with 5 g/kg choline chloride (SUP). We observed the CON and SUP offspring exploring a novel environment with and without objects. In addition, CON and SUP rats were given 10 injections of the cell division marker, BrdU (100 mg/kg), one per day for 10 consecutive days, and killed either 1 or 28 days after the last injection. Our results indicated that SUP rats showed more object investigation in an open field than CON rats. SUP rats also displayed significantly more BrdU-labeled cells than CON rats and when we used doublecortin to assess numbers of new neurons, SUP rats had more cells exhibiting this marker. These results suggest that prenatal choline supplementation alters rat's responses to novel environments and increases hippocampal plasticity and these effects may contribute to the life-long changes in cognition that are seen with this early diet manipulation.

**MOUSE STRAIN DIFFERENCES IN LITHIUM ATTENUATION OF D-AMPHETAMINE HYPERLOCOMOTION.** Gould, T.D.; O'Donnell, K.C.; Picchini, A.M.; Manji, HK. Laboratory of Molecular Pathophysiology, NIMH, Bethesda, MD, 20892-3711, USA. Recent advances in neurobehavioral genetics have increased our awareness of the behavioral patterns of different mouse strains, and have characterized essential neural processes that are influenced by strain-dependent inheritable traits. Lithium attenuation of stimulant-induced hyperlocomotion represents a rodent model for the mechanism of the therapeutic action of lithium, and for the development of novel lithium-mimetic compounds; this hyperlocomotion also models a putative clinical endophenotype (mania in response to a dopamine agonist). We studied 12 (3 outbred) mouse strains (129S6/SvEv, A/J, C3H/HeJ, C57BL/6J, C57BL/6NTac, CBA/J, DBA/2J, FVB/NJ, SWR/J, Black Swiss, CD-1, NIH Swiss). Mice received either 1) no drugs, 2) lithium only, 3) d-amphetamine only, or 4) d-amphetamine and lithium. Lithium chloride (100mg/kg) was administered 15 minutes prior to d-amphetamine (2mg/kg). There was a large degree of strain variation in the effects of lithium in this model. For example, d-amphetamine hyperlocomotion was attenuated by lithium chloride in C57/BL6J, C57BL/6Tac, Black Swiss, and CBA/J mice, while CD-1, FVB/NJ, SWR/J and NIH Swiss mice, which were responsive to amphetamine, showed no significant effect of lithium. D-amphetamine hyperlocomotion in the C3H/HeJ strain was enhanced by pretreatment with lithium. Four weeks of lithium administration prior to d-amphetamine produced locomotion effects identical to acute administration in C57/BL6J



(decrease), C3H/HeJ (increase) and FVB/NJ (no change) strains. The results are not explained by brain lithium levels, suggesting that the behavioral differences are under the control of inherent genetic or other biological mechanisms specific to the effects of lithium on brain function.

**STIMULATION OF CENTRAL BETA NORADRENERGIC RECEPTORS DISRUPTS PPI.** Alsene, K.M; Bakshi, V.P. University of Wisconsin-Madison, Dept. of Psychiatry and Neuroscience Training Program, Madison, WI 53719 USA. Prepulse inhibition (PPI) refers to the ability of a weak stimulus (the prepulse) to inhibit the magnitude of the startle response to a subsequent, intense stimulus (the pulse). PPI is deficient in a number of psychiatric illnesses including schizophrenia. There is evidence that the norepinephrine (NE) system may be important in regulating PPI. The NE system has traditionally been divided into  $\alpha_1$ ,  $\alpha_2$  and  $\beta$  receptor subtypes and recent studies have found that PPI is disrupted by either stimulation of central postsynaptic  $\alpha_1$  NE receptors or blockade of pre-synaptic  $\alpha_2$  receptors. The role of  $\beta$  receptors in regulating PPI however, remains largely unexplored. This study examined the effects of intracerebroventricular (ICV) administration of the mixed  $\beta$  receptor agonist, isoproterenol (ISO), on PPI. Male Sprague-Dawley rats (N=9) were surgically prepared with cannulae aimed at the lateral ventricle. Following recovery from surgery rats were given ICV infusions of ISO (0, 3, 10, or 30  $\mu\text{g}/5\mu\text{L}$ ) and immediately thereafter tested in startle chambers for assessment of PPI and baseline startle reactivity. ISO significantly and dose-dependently disrupted PPI. Importantly, this disruption in PPI was independent from changes in baseline startle responses as ISO did not alter baseline startle at any of the doses tested. The results therefore indicate that stimulation of central  $\beta$  receptors disrupts PPI. This finding supports the general hypothesis that stimulation of postsynaptic NE receptors can disrupt PPI. Studies examining the ability of  $\beta_1$  and  $\beta_2$  receptor antagonists to block the ISO-induced deficits in PPI are underway.

**COGNITIVE-DISRUPTIVE EFFECTS OF THE PSYCHOTOMIMETIC PHENCYCLIDINE AND ATTENUATION BY ATYPICAL ANTIPSYCHOTICS.** Amitai, N.1,2; Semenova, S.1; Markou, A1,2. 1Molecular and Integrative Neurosciences Dept., The Scripps Research Institute, and 2Graduate Program in Neurosciences, University of California at San Diego, La Jolla, CA 92037 USA. Cognitive deficits in schizophrenia are pervasive and respond poorly to current antipsychotic treatments. The development and validation of animal models of cognitive schizophrenia symptoms is crucial for the study of these deficits and the discovery of better treatments. We investigated disruptive effects of phencyclidine (PCP), a non-competitive N-methyl-D-aspartate receptor antagonist, on cognitive performance in a test of attention, as well as the potential attenuation of this disruption with atypical antipsychotics. Rats were trained on the 5-choice serial reaction time task (5-CSRTT). The effects of PCP (2 mg/kg s.c.) injected either acutely or subchronically on task performance were assessed. Further, the effects of the atypical antipsychotics clozapine, risperidone, quetiapine, and olanzapine and the typical antipsychotic haloperidol in the 5-CSRTT under baseline conditions were investigated. We then explored the effects of acute clozapine or risperidone, as well as chronic clozapine, on PCP-induced attentional disruption. Acute PCP had nonspecific response-depressing effects in the 5-CSRTT. Subchronic PCP administration caused selective performance disruption, characterized by decreased accuracy and increased impulsivity. Under baseline conditions, atypical antipsychotics did not affect attentional accuracy except at high doses, and dose-dependently reduced impulsivity. The response depression induced by acute PCP was exacerbated by acute clozapine or risperidone, and was unaffected by chronic clozapine. Importantly, chronic clozapine significantly attenuated the performance disruption caused by subchronic PCP. In conclusion, the effects of subchronic PCP in the 5-CSRTT may constitute a useful animal model for cognitive symptoms of schizophrenia that is sensitive to reversal by atypical antipsychotics and may aid discovery of novel targets for medications ameliorating attentional deficits in schizophrenia.

**EFFECTS OF KAPPA OPIOID RECEPTOR STIMULATION IN AN ANIMAL MODEL OF OBSESSIVE-COMPULSIVE DISORDER.** Perreault, M.L.; Seeman, P.; Szechtman, H. Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON L8N 3Z5 Canada. Dept. Pharmacology, University of Toronto, Toronto, ON M5S 1A8 Canada. In small activity chambers activation of the kappa-opioid system by U69593 enhances locomotor sensitization to the D2/D3 dopamine agonist quinpirole (QNP). However, in addition to locomotor sensitization QNP induces compulsive checking when rats are tested in a large open field, a phenomenon that may constitute an animal model of obsessive-compulsive disorder (OCD). Therefore, the present study examined how U69593 may affect QNP-induced compulsive checking, and whether changes in drug-induced behaviour are related to alterations in dopamine receptors. A 2x2 design with two fully crossed factors was employed, chronic dose of QNP (0 vs 0.5 mg/kg) and chronic dose of U69593 (0 vs 0.3 mg/kg). Rats were administered fourteen biweekly injections and behavioural activity monitored after each treatment. Results showed that U69593 co-treatment enhanced locomotor sensitization to QNP, altered the topography of motion through

space, and accelerated the development of compulsive checking compared to rats treated with QNP alone; U69593 alone had no effect on compulsive checking. Despite the differences in behaviour, similar increases in the levels of D2High in the striatum and nucleus accumbens (NAC) were observed in rats treated with either U69593 or QNP or the two drugs together. Moreover, although there were elevations in D1High and D3High in the NAC, these changes also did not discriminate among the drug groups. These results suggest that the opioid system may accelerate development of OCD-like behaviours but this effect does not simply reflect an increase in dopamine receptor activity.

**LATENT TOXOPLASMA INFECTION IN RODENTS CONVERTS AVOIDANCE OF CAT PHEROMONES INTO AN ATTRACTION.** Ajai Vyas<sup>1</sup>, Seon-Kyeong Kim<sup>2</sup>, Nicholas Giacomo<sup>1</sup>, John Boothroyd<sup>2</sup>, and Robert M Sapolsky<sup>1,3</sup>. <sup>1</sup> Department of Biological Sciences; <sup>2</sup> Department of Microbiology and Immunology; <sup>3</sup> Departments of Neurology and Neurological Sciences, and of Neurosurgery, Stanford University, Stanford, CA 94305, USA. The Protozoan parasite *Toxoplasma gondii* blocks the innate aversion of rats for bobcat urine, which should increase the likelihood of a cat preying on a rat. This is thought to reflect adaptive behavioral manipulation by *Toxoplasma*, in that the parasite, while capable of infecting rats, reproduces sexually only in the guts of cats. The ‘behavioral manipulation’ hypothesis postulates that a parasite will manipulate only those host behaviors essential for enhancing its own transmission. In contrast, the neural circuits implicated in innate fear, anxiety and learned fear all overlap considerably, suggesting that *Toxoplasma* should disrupt all of these non-specifically. We investigated these conflicting predictions. In mice and rats, latent *Toxoplasma* infection converts the aversion to feline odors into attraction. Such loss of fear is remarkably specific, as infection does not diminish learned fear, anxiety-like behavior, olfaction or non-aversive learning. These effects on both aversion and attraction are commensurate with our finding of broad and uniform distribution of *Toxoplasma* throughout the brain. These effects are not part of a generalized response to the infection, thus supporting the behavioral manipulation hypothesis. Additionally, *Toxoplasma* provides a unique model for studying the neurobiology of innate fear and attraction.

**LONG ACCESS COCAINE SELF-ADMINISTRATION LEADS TO PERSISTENT IMPAIRMENTS IN COGNITIVE PERFORMANCE.** Briand, L.A, Sarter, M., Robinson, T.E. Department of Psychology and Neuroscience. The University of Michigan, Ann Arbor, MI 48109 USA. Long-term drug abusers exhibit cognitive deficits that persist long after the cessation of drug use, and these deficits may contribute to relapse. Surprisingly, however, preclinical studies have found little evidence for these persistent cognitive deficits. This may be due to the utilization of limited access self-administration procedures. Thus, the present study was aimed at utilizing an extended access cocaine self-administration protocol, which has been found to induce escalation of drug intake and symptoms associated with drug dependence, to examine the persistent effects of drug abuse on cognitive function. In the first experiment, rats were trained on a sustained attention task until reaching stable performance at criterion level. Animals were divided into drug naïve, short (ShA) and long (LgA) access groups and underwent four weeks of cocaine self-administration. Attentional performance was reexamined 24 hours following the final self-administration session. Fourteen days later, performance was again assessed and daily testing resumed thereafter until animals reached asymptotic performance levels. At both time points tested, the performance of LgA animals was significantly impaired relative to the ShA or drug naïve groups; this impairment improved following daily testing, but never reached the level of performance seen in the other two groups. The nature of the impairment suggested a fundamental disruption of the animals’ ability to generate correct responses evoked by either the presence or absence of the attentional cue. In the second experiment, animals were trained identically to experiment one and following the final self-administration session, animals were withdrawn for 24 hours, 14 days or 1 month and attentional performance was reexamined. At all three time points tested, animals in the LgA group performed worse than animals in the two other groups. These results indicate that extended access to cocaine leads to a persistent deficit in cognitive performance. Given the potential involvement of drug-induced cognitive deficits to relapse, characterizing this phenomena and elucidating the neurobiological underpinnings of the cognitive deficits may be important for developing better treatments for drug addiction.

**EXPERIMENTAL MANIPULATION OF BASAL RATE OF NEUROGENESIS INFLUENCES THE DEVELOPMENT OF AMYGDALOID KINDLING IN RATS.** Fournier, N.M; Corcoran, M.E.; Kalynchuk, L.E. *Dept. of Psychology, University of Saskatchewan, Saskatoon, SK S7N 5A5 Canada.* The suggestion that hippocampal neurogenesis might play a role in the development of temporal lobe epilepsy is a topic of extensive debate. Generally, seizure-induced neurogenesis is thought to participate in the formation of epileptogenic networks that encourage the spread of epileptic activity. The possibility that seizure-induced neurogenesis is part of a beneficial or reparative process has been curiously overlooked. To characterize the role of neurogenesis during the

development of epilepsy, we administered compounds known to either decrease or increase neurogenesis in the adult brain before the commencement of amygdaloid kindling. When administered for 14 days, the selective serotonin reuptake inhibitor fluoxetine (Prozac, 5 mg/kg, s.c.) increased the number of newly born (BrdU labeled) cells in the dentate gyrus. In turn, the DNA-methylating agent methylazoxymethanol acetate (MAM, 7 mg/kg, s.c.) reduced the number BrdU cells in the dentate gyrus. Twenty-four hours after treatment with MAM acetate, there was no influence on the minimal threshold to induce an epileptic afterdischarge in the amygdala; however, the number of stimulations required to elicit the first motor convulsion was substantially lower after MAM treatment. Alternatively, 14 day pretreatment with fluoxetine raised the afterdischarge threshold, but produced inconsistent convulsive responses during amygdaloid kindling. These results indicate that fluoxetine pretreatment might exert partial antiepileptic effects on amygdala kindling. Our findings suggest the possibility that the newly generated cells in the adult hippocampus exert seizure suppressive effects during the development of epilepsy but as seizures are continually evoked the normal homeostatic influence from these cells dissipates resulting in the progressive intensification of limbic seizures.

**CHRONIC STRESS AND LITHIUM TREATMENT MODULATE EXPRESSION OF PHOSPHORYLATED CYCLIC AMP RESPONSE ELEMENT BINDING PROTEIN IN THE RODENT AMYGDALA.** Johnson, S.A.; Wang, J.-F.; McEwen, B.S.; Young, L.T. Centre for Addiction and Mental Health, Institute of Medical Science, University of Toronto, Toronto, ON, Canada. Chronic restraint stress (CRS) leads to distinct patterns of dendritic remodeling in the rodent amygdala; however, the molecular mechanisms underlying this stress-induced plasticity, and the accompanying enhancement of fear and anxiety behaviour, remain unclear. As a regulator of many plasticity-related genes, the transcription factor cyclic AMP response element binding protein (CREB) is optimally positioned to mediate these morphological and behavioural changes. Furthermore, recent evidence suggests that the mood-stabilizing drug lithium prevents dendritic remodeling in the hippocampus after chronic stress, and may do so via a CREB-dependent pathway. Accordingly, the present experiment characterized amygdalar expression of phosphorylated CREB (pCREB) after CRS exposure, and determined whether lithium has similar protective effects in the amygdala. Male rats were exposed to CRS (21d, 6h/day), with or without concurrent lithium treatment. Coronal brain sections spanning the basolateral, central, and lateral amygdalar nuclei were subjected to immunohistochemistry, and the total number of pCREB-positive nuclei was estimated in these regions by non-biased stereological methods. Rats exposed to CRS without concurrent lithium treatment showed a reduction in the number of pCREB-positive nuclei in the lateral amygdala, while lithium treatment during CRS reversed this effect. Intriguingly, lithium treatment alone also reduced the number of pCREB-positive nuclei in the lateral amygdala, suggesting divergent mechanisms of action of this mood-stabilizing agent in the face of chronic stress. Our results indicate that detailed characterization of lithium action in pathological models, rather than cell culture and naïve animals, could provide novel insight into its neuroprotective properties.

**INTRA-AMYGDALA MU OPIOID RECEPTOR STIMULATION INCREASES CONDITIONED APPETITIVE BEHAVIOR IN RATS.** Mahler, S.; Berridge, K. The amygdala is involved in appetitive emotion and learning, in addition to learning about negative emotion. Mu opioids in many brain areas, including the amygdala, mediate reward-related behaviors. In the present experiment, we tested whether intra-amygdala infusion of the mu opioid agonist DAMGO would increase the motivational magnet, or incentive properties that attract behavior toward reward CS+s. We used an autoshaping paradigm, in which rats learn that Pavlovian cues predict sucrose rewards, and then spontaneously begin to approach those cues. Rats received daily DAMGO (0.1µg/0.5 µl) or vehicle control microinjections before the first six days of autoshaping training to assess effects on acquisition of conditioned incentive approach. During training, rats learned to associate an 8 second compound lever and tone cue presentation (CS+) with sucrose rewards. DAMGO increased CS+ cue lever interactions in rats that learned to approach the cue lever during the CS+ (i.e., rats that autoshaped). DAMGO also increased approach to a control lever (CS-) in these rats, but only when the CS+ was not present. In other rats that merely learned to approach the sucrose dish during the CS+ (i.e. conditioned anticipatory approach to UCS source), DAMGO increased sucrose dish entries, but not interactions with either the CS+ or CS- levers. These results suggest that intra-amygdala mu opioid agonist administration can alter attributions of incentive properties to reward CS+s. Furthermore, DAMGO's effects on cue-appetitive behavior differed based on individual differences in the cue-directed behavior that was initially learned (lever vs. sucrose dish approach). These findings may have implications for understanding the role of amygdala opioid receptors in appetitive disorders like addiction and obesity.  
Support Contributed By: NIH MH63649 and NIH DA015188

**MATERNAL TREATMENT WITH VPA DURING PREGNANCY LEADS TO EARLY PHYSICAL AND SOCIAL DEFICITS IN MOUSE PUPS.** Rouillet, F.II.3; Hall, G.B.1,3, deCatanzaro, D.2; Foster, J.A.1,3 Dept. of Psych. & Behav. Neurosci.1 and Dept. of Psychology.2, McMaster University and the Brain and Body Institute3, St. Joseph's Hospital. Hamilton, ON Canada. Autism is an early developmental illness, and because the onset of autism takes place before 3 years old, it appears crucial to examine the early lifetime period in order to determine potential predictors of the disease. Epidemiological studies reveal that valproic acid (VPA) exposure during the first trimester in humans induces higher incidence of autism in the offspring. Moreover, several studies have reported striking neuroanatomical and behavioural similarities between autism and rats exposed to VPA in utero. In our experiments, we examined the impact of the VPA administration in pregnant dams on pup development. To date animal experiments have been performed only in rats. The advantage to moving this model into mice is the availability of genetic mice for future studies. Our results show that prenatal exposure to VPA leads to alterations in postnatal growth and maturation, revealed by a delay in eye opening and reduced weight in VPA compared to control pups. Behavioural deficits were also detected. Specifically, VPA pups showed an increased latency to reach home bedding in a nest-seeking task. Using a 3-chamber social behaviour apparatus, control mice showed a significantly higher sociability score for interactions with the stranger versus empty side. In contrast, VPA mice showed no significant difference in their sociability score between stranger and empty sides. Taken together, these alterations in postnatal growth, maturation, and behaviour are consistent with those reported for rats and support the validity of using prenatal VPA exposure in mice as a model to study the development of autistic-like behaviours.

**PRE-PUBERTAL STRESS: DIFFERENTIAL IMPACT ON MALES AND FEMALES** Toledo-Rodriguez, M.; Lecroq, B.; Sandi, C. Brain Mind Institute, Swiss Federal Institute of Technology (EPFL), Lausanne, CH-1015 Switzerland. Adolescence is a period when major physical, hormonal and psychological changes take place. In humans, adolescence is a developmental phase characterized by a significant increase in a) depressive behavior and/or eating disorders (especially among girls); b) impulsive behavior and aggressiveness (mainly in boys) and/or c) addictive use of drugs of abuse. Stress is an important risk factor for a wide variety of psychopathological alterations. In particular, adverse experiences during childhood and adolescence have been associated to the development of psychiatric disorders. Despite the severity and high cost to society of these pathologies, information on the nature of the behavioral alterations resulting from stress experiences during peri-adolescence is scarce, particularly for females. In this study, we aimed to evaluate the impact of stress during early puberty on emotional behavioral responses displayed by male and female rats during early adulthood. While both genders were submitted to the same stressors and at the same age, male and female rats developed a differential pattern of anxiety-like behaviors in adulthood, which significantly differed from their respective non-stressed controls. Males showed higher latency to explore new territories and objects than controls, while stressed females were significantly more hyperactive in adulthood when exposed to stress or to a novel environment. These results indicate that peri-pubertal stress affects the coping responses displayed by rats in adulthood to both novel and stressful situations in a sex dependent manner.

**REWARD EXPERIENCE MODERATES IMMUNE RESPONSE TO CYTOKINE CHALLENGE.** Kentner, A.C; James, J; Miguelez, M; Bielajew, C. School of Psychology. University of Ottawa, Ottawa Ontario CANADA. Interferon-alpha (IFN-alpha) is a cytokine used as a treatment for cancer and Hepatitis C. The benefits however are frequently accompanied by adverse side-effects such as flu-like symptoms and in some individuals, depression. We have been exploring an animal model of cytokine challenge. In this study, we investigated the short- and long-term effects of a single systemic injection of vehicle, 10, or 1000 units of IFN-alpha. The measures included temperature, body weight, food intake, sickness behaviours, locomotor activity, and brain stimulation reward (BSR) thresholds elicited from the ventral tegmental area in female Long Evans rats. Brain stimulation reward, long employed for studying motivational processes, has been exploited as a tool for tracking hedonic status in animal models of depression. Thresholds in the present study did not reveal an anhedonic effect. As expected, locomotor activity was shown to be decreased in animals receiving both doses of the IFN-alpha compared to the vehicle group. Sickness behaviors were measured in all animals three times daily for two days, and included ptosis (droopy eyelids), piloerection, lethargy, and sleep measures. Each behavior was scored on a three point scale (none = 0, mild = 1, or severe = 2), except for sleep which was scored on a two point scale as either 0 (absent) or 1 (present). Non-parametric analyses unveiled a significant increase in piloerection in all sham operated animals that received an IFN-alpha injection at each time point measured while the BSR animal scores remained relatively unchanged between pre- and post-injection days. This pattern was also evident in the total sickness scores. Temperature, recorded at the same times as sickness behavior collection showed increases only in the group not receiving BSR. Taken together, these data suggest that the behavioral disruptions elicited by a single cytokine challenge are

significantly diminished in animals receiving rewarding brain stimulation, indicating that the experience of reward influences immune activity.

**18:00-19:45 Poster Session 1**

***Prenatal, neonatal and parental factors***

1. SEPARATION-INDUCED ULTRASONIC CALLING IN RAT PUPS IS RELATED TO MATERNAL LICKING AND RETRIEVAL IN OPPOSITE WAYS. Wöhr, M.; Schwarting, R.K.W. Experimental and Physiological Psychology, University of Marburg, Germany. Rat pups emit ultrasonic vocalizations (USV) in response to aversive situations, like separation from the nest, or drops in ambient temperature. USV appear to be a valid index of pup anxiety, since USV can be attenuated by anxiolytics. Furthermore, USV play an important role in pup survival, since they elicit maternal retrieval. However, it is not clear whether USV are related to other maternal behaviors, like licking. In the rat, variations in maternal care, particularly licking, can affect emotional development. Adult rats, which were licked more often during infancy (HL), show less anxiety-related behavior in response to aversive situations than rarely licked rats (LL). Here, we asked whether variations in maternal behavior are associated with individual differences in emotionality already during early life. Licking and retrieval behavior of Wistar dams towards their pups were observed within the first days of life. On postnatal day 11, pups were removed from the nest and isolated shortly under room temperature. Their emotional response was measured using USV and overt behavior. USV was related to licking and retrieval in opposite ways, and retrieval was positively associated with USV. Additionally, playback of USV induced stimulus-directed search behavior in the dams. By contrast, licking was negatively associated with USV, since LL emitted more USV than HL. Further differences were obtained in call amplitude, frequency modulation, and bout size. Interestingly, apart from grooming no differences were detectable in overt behavioral parameters. The findings are consistent with differences in anxiety-related behavior of adult HL and LL rats.
2. MATERNAL SEPARATION AND EFFECTS OF POST-WEANING HANDLING IN RATS. Eklund, M.B.; Arborelius, L. Maternal separation (MS) is used as an animal model for depression as it increases anxiety-like behaviour and produces dysregulation of the hypothalamic-pituitary adrenal axis. However, results are not consistent. Environmental enrichment (EE) after weaning has been suggested to induce compensatory mechanisms for some of the behavioural and neuroendocrine effects of MS. We investigated whether brief weekly handling after weaning (post-weaning handling, PWH) like EE can normalise both some behavioural and neuroendocrine effects of MS. Wistar rat pups of both sexes were subjected to one of the following postnatal manipulations: separation from the dams for either 4 h (MS) or 15 min on 8 random days during the first two weeks after birth, or not at all. As adults they were tested for anxiety-like behaviour in the defensive withdrawal test, spontaneous motor activity, and stress response (plasma corticosterone levels). An effect of MS on behaviour was observed in males only, and this was abolished by PWH. In females, PWH resulted in increased activity and decreased anxiety-like behaviour regardless of rearing condition. This suggests that PWH has an anxiolytic effect in females but not males. Gender differences were also observed in plasma corticosterone levels where interactions between postnatal manipulation and stress response, and handling and stress response were found in females only. These results suggest that brief, repeated handling after weaning may affect some behavioural and neuroendocrine effects of MS. Hence, differences in the amount of handling of the rats after weaning may explain some of the discrepancy between laboratories regarding effects of MS.
3. NEONATAL EXPOSURE TO LIPOPOLYSACCHARIDE INCREASES ANXIETY-RELATED NEOPHOBIA TO SUCROSE IN ADULT MALE BUT NOT ADULT FEMALE RATS. Tenk, C.M.; Kavaliers, M.; Ossenkopp, K.-P. Psychology Department & Graduate Program in Neuroscience. University of Western Ontario. London, ON. CANADA. Previous research has shown that neonatal exposure to the bacterial cell wall component, lipopolysaccharide (LPS) alters anxiety-like behaviour in the adult rat, increasing anxiety on some tests, but decreasing anxiety on others. However, despite sex differences in untreated adult rats and hormonal evidence of sex differences in the acute effects of neonatal LPS, few studies have examined sex differences in the long-term effects of neonatal LPS. We sought to explore possible sex differences in the long-term effects of neonatal LPS on anxiety-like behaviour in adult rats. Male and female Long-Evans rats were treated (i.p.) with either LPS (50µg/kg) or 0.9% NaCl on postnatal

days 3 & 5. Anxiety-like behaviour was then assessed in adulthood (day 90) using the neophobia to sucrose test where a higher degree of neophobia reflects higher levels of anxiety. Following a water restriction schedule, rats received 30 minutes access to distilled water in an automated lickometer apparatus for 5 consecutive baseline days. Subsequently, animals were given 30 minutes access to 0.3M sucrose for two consecutive days. The volume of sucrose consumed during the first exposure was used as the measure of neophobia. Males treated neonatally with LPS consumed significantly less sucrose during the first exposure than saline-treated males. This difference was not observed in females. These results provide evidence of sex differences in the long-term effects of neonatal LPS on anxiety-like behaviour and suggest that early bacterial exposure may have more pronounced long-term effects in males than females.

4. **INTRAHIPPOCAMPAL HIV-1 PROTEIN INJECTIONS: DIFFERENTIAL NEUROBEHAVIORAL EFFECTS IN NEONATAL RATS.** Fitting, S.; Booze, R.M.; Mactutus, C.F. Dept. of Psychology, Behavioral Neuroscience Program. University of South Carolina, Columbia, SC 29208 USA. Developmental impairments of cognitive and motor systems are common among children infected with HIV. The neuropathology of AIDS in the brain is believed to be mediated indirectly through the HIV proteins Tat and gp120. The present study was designed to determine the potential role of Tat and gp120 and their interaction on neurobehavioral/developmental milestones in neonatal rats. On postnatal day (P)1, one male and one female pup of 14 Sprague-Dawley litters were bilaterally injected with vehicle (0.5 µl saline), 25 µg Tat, 150ng gp120 or Tat+gp120 (25 µg/150ng). Animals were tested (< P30) for weight, eye opening, righting reflex, negative geotaxis, prepulse inhibition (PPI) of the auditory startle response (ASR), and locomotor activity. Preliminary behavioral analyses focused on the effects of the individual viral proteins. Body weight was not influenced by protein treatments and was comparable between groups, whereas all behavioral tests revealed an acute effect of Tat. In contrast, the only behavioral effect of gp120 was a significant attenuation of negative geotaxis. Results suggest that the effects of Tat-derived toxic fragments were less specific than those of gp120. Additional long-term effects of these viral proteins and their potential for synergistic effects are presently under analysis. It is critical for future studies to determine the potential contribution of the viral proteins, Tat and gp120, to the neurological and neuropsychiatric impairment consequent to HIV-1 infection. (Supported by DA13137, DA014401, HD043680).
5. **MATERNAL TREATMENT WITH VPA DURING PREGNANCY LEADS TO EARLY PHYSICAL AND SOCIAL DEFICITS IN MOUSE PUPS.** Roulet, F.I.1,3; Hall, G.B.1,3, deCatanzaro, D.2; Foster, J.A.1,3 Dept. of Psych. & Behav. Neurosci.1 and Dept. of Psychology.2, McMaster University and the Brain and Body Institute3, St. Joseph's Hospital. Hamilton, ON Canada. Autism is an early developmental illness, and because the onset of autism takes place before 3 years old, it appears crucial to examine the early lifetime period in order to determine potential predictors of the disease. Epidemiological studies reveal that valproic acid (VPA) exposure during the first trimester in humans induces higher incidence of autism in the offspring. Moreover, several studies have reported striking neuroanatomical and behavioural similarities between autism and rats exposed to VPA in utero. In our experiments, we examined the impact of the VPA administration in pregnant dams on pup development. To date animal experiments have been performed only in rats. The advantage to moving this model into mice is the availability of genetic mice for future studies. Our results show that prenatal exposure to VPA leads to alterations in postnatal growth and maturation, revealed by a delay in eye opening and reduced weight in VPA compared to control pups. Behavioural deficits were also detected. Specifically, VPA pups showed an increased latency to reach home bedding in a nest-seeking task. Using a 3-chamber social behaviour apparatus, control mice showed a significantly higher sociability score for interactions with the stranger versus empty side. In contrast, VPA mice showed no significant difference in their sociability score between stranger and empty sides. Taken together, these alterations in postnatal growth, maturation, and behaviour are consistent with those reported for rats and support the validity of using prenatal VPA exposure in mice as a model to study the development of autistic-like behaviours.
6. **NEONATAL EXPOSURE TO FLUOXETINE MODULATES SOCIAL BEHAVIORS AFTER A DIAZEPAM CHALLENGE DURING ADULTHOOD.** Jiménez, J.1; Mattei, G.1; Lathroum, L.2; Jorge, J.3; 1. Department of Biology, 2. Department of Chemistry, Rio Piedras Campus, University of Puerto Rico, 3. Department of Anatomy, Medical Science Campus, University of Puerto Rico- San Juan, Puerto Rico 00931 Fluoxetine (FOX) is a selective serotonin receptor inhibitor (SSRI) which is used to treat affective

disorders. The aim of the present study was to investigate the long-term behavioral effects of FOX (1, 10, 15 mg/Kg) in postnatal Sprague Dawley rats (PN) day 1 to 14. Adult behavioral responses to diazepam (DZ) after neonatal exposure to FOX were examined with the social interaction test (SIT). FOX exposed females with diazepam displayed more social interaction than males. There were significant differences in the following discrete social behaviors: following, body contact, anogenital investigation. We found that pre-exposure to FOX altered the behavioral sensitivity to DZ in adulthood for body contact ( $P=0.02$ ) and anogenital investigation ( $P=0.04$ ). These data suggest that neonatal exposure to SSRI has permanent behavioral consequences on the sensitivity to benzodiazepines later in life. Supported by NIH-COBRE (RR15565) and the RCMI Program at MSC-UPR (G1RR3051) to JCJ.

7. SUPPLEMENTAL CHOLINE IN THE MATERNAL DIET OF RATS MODULATES HIPPOCAMPAL NEUROGENESIS AND EXPLORATORY BEHAVIOR IN OFFSPRING. Glenn, M.J.; Kirby, E.D.; Wong-Goodrich, S.J.E.; Williams, C.L. Prenatal choline supplementation has a profound and lasting effect on cognitive function, leading to improved memory capacity and precision that resists normal, age-induced decline. In the current study we tested the hypothesis that supplemental choline in the maternal diet may exert its effects on cognition across the lifespan of offspring by enhancing neuronal proliferation in adult hippocampus. We were also interested in exploring whether supplemental choline alters how rats interact with and respond to novel objects and environments. On embryonic days 12-17, pregnant rats received a control diet containing 1.1 g/kg choline chloride (CON), or a diet supplemented with 5 g/kg choline chloride (SUP). We observed the CON and SUP offspring exploring a novel environment with and without objects. In addition, CON and SUP rats were given 10 injections of the cell division marker, BrdU (100 mg/kg), one per day for 10 consecutive days, and killed either 1 or 28 days after the last injection. Our results indicated that SUP rats showed more object investigation in an open field than CON rats. SUP rats also displayed significantly more BrdU-labeled cells than CON rats and when we used doublecortin to assess numbers of new neurons, SUP rats had more cells exhibiting this marker. These results suggest that prenatal choline supplementation alters rat's responses to novel environments and increases hippocampal plasticity and these effects may contribute to the life-long changes in cognition that are seen with this early diet manipulation.
8. NEONATAL EXPOSURE TO METHAMPHETAMINE INCREASES BDNF, BUT NOT NGF IN HIPPOCAMPUS AND STRIATUM. C.E. Grace, N.R. Herring, T.L. Schaefer, M.R. Skelton, M.T. Williams, C.V. Vorhees, Div. of Neurology, Cincinnati Children's Res Found, Univ. Cincinnati Col Med. Cincinnati, OH, USA. Corticosterone (CORT), brain derived neurotrophic factor (BDNF), and nerve growth factor (NGF) are important in the maintenance of neurons during development. The stress hyporesponsive period (SHRP) is a period of adrenal quiescence that is believed to protect neurons during development. CORT levels are increased in developing animals exposed to d-methamphetamine (MA) during the SHRP following a 4-dose regimen. Here we determined if multiple applications of MA or a stressor induces changes in neurotrophins and/or CORT. Rats were administered either MA, saline (SAL) or were forced to swim for 15 min (FS) or placed in isolation for 15 min (ISO), either once on P11, four times on P11, or four times daily from P11-14 and/or once or four times on P15. CORT levels were elevated in MA administered animals compared to other groups. Although CORT was increased in FS and ISO animals, it was lower than that of MA administered animals. BDNF and NGF were measured by ELISA in the hippocampus and striatum. Generally, BDNF in the hippocampus was increased in MA administered animals on P15 relative to all other treatments, although no comparable changes were observed in NGF among groups. In the striatum, BDNF was also increased after the first dose of MA on P15 compared to other treatments, while no changes were observed in NGF levels among groups. These data suggest that CORT and BDNF may be important in MA-induced effects, however NGF likely is not. Furthermore, multiple stressors did not alter the neurotrophins or increase CORT to the levels observed in MA-treated animals.
9. MATERNAL CARE ALTERS ANXIOUS BEHAVIOR IN MALE, BUT NOT FEMALE, OFFSPRING. Pawluski, J.L.; Barha, C.; Galea, L.A.M. Department of Psychology, Program in Neuroscience and the Brain Research Centre, University of British Columbia, Vancouver, BC. Naturally occurring variations in maternal care during the early postnatal period has been shown to alter male offspring behavior later in life. However, less is known about the effects of maternal care on behavior of adult female offspring. The present study investigated the role of maternal care, either high or low levels of licking, on measures of

anxiety in adult male and female offspring. Offspring from either 'high' or 'low' licking dams were tested on the elevated plus maze and the open field test in adulthood. Preliminary results suggest that there is a slight difference in anxious behavior of male offspring of high and low licking dams, but not in female offspring. Males of low licking dams appear to make more entries into the open arm of the elevated plus maze, and more open and peripheral crossings on the open field test than males of high licking dams. Interestingly variations in maternal care seem to have greater effects on the behavior of adult male and not female offspring. Future research aims to determine the neural correlates of this behavior.

10. NEONATAL STRESS ALTERS AGGRESSION IN STRESSED AND LITTER MATE CONTROL MICE. Hodges, A.B., Anderson, M. E., Beard, N.A. and Hohmann, C.F., Morgan State University, Baltimore, MD. Environmental factors feature in the etiology of many mental health disorders, thus a better understanding of the neurobiology/neuropathology that connects early stress and later onset of behavioral alterations is needed. Using a split litter design, our lab found that neonatal maternal separation/temperature stress caused increased exploration and impaired spatial memory in stressed mice (STR), while littermate controls (LMC) were hyper-reactive to spatial change and novelty in the Open Field Object Recognition [OFOR] task compared to age matched controls (AMC). Early isolation stress in rodents can result in increased aggressive biting and boxing in adulthood (Wongwitdecha and Marsden, 1996, Matsumoto et al., 2005). Therefore, the present study investigated the effects of neonatal stress on aggressive behavior displays. Mice were either tested on both the OFOR task immediately followed by a modified resident-intruder task, or just the modified resident-intruder task. Our data show that, compared to the AMC, both the STR and LMC display increased nipping in the aggression task when it follows the OFOR task. Preliminary data suggests that male STR displayed more nipping than male LMCs when tested on both the OFOR and aggression tasks. However, when only tested on the aggression task, the male LMCs display more nipping than the STR males. Thus, our results suggest that the STR mice are cognitively impaired and more aggressive, while LMC are hyper-reactive to novelty and more aggressive compared to the AMC. LMC are not performing like normal mice, indicating that they may be exhibiting stress effects, albeit different from STR mice. We hypothesize that LMC's stress effects may be caused by differences in maternal care. Supported by: SO6 GM051971 and R25 GM058904.
11. REPEATED EARLY LIFE MANIPULATION AFFECTS JUVENILE PARENTAL BEHAVIOR AND PUP-DIRECTED AGGRESSION IN VOLES. Boone, EM; Sanzenbacher LL; Carter CS; Bales KL. In mammals, the neonatal period is a time of significant social interaction. This early life period, and experiences received during this time, can have very important consequences for shaping development and expression of emotional and social behavior. It can also be important for the acquisition and exhibition of parenting behavior later in life. In this study, we used the socially-monogamous prairie vole (*Microtus ochrogaster*) to examine the effects of repeated neonatal manipulation (MAN) on spontaneous parental behavior. Prairie voles were subjected to brief neonatal manipulation (being picked up) one time on postnatal day 1 (MAN1), three times on postnatal day one (mMAN1) or no handling (MAN0). Animals were subsequently tested for juvenile parental behaviors at approximately 21-24 days of age. On day of testing, animals received a 10-min parental care test and infant-directed behavior was scored. Preliminary results suggest that the amount of early postnatal handling significantly affects future demonstration and quality of parental care. In general, MAN1 animals spent more time engaged in parental behaviors (e.g., huddling, retrieval, licking/grooming) with pups. mMAN1 males, relative to mMAN1 females and all other groups, spent significantly less time engaged in pup-directed behaviors and less time in close proximity to pups. mMAN1 males were also significantly more likely to attack pups than all other groups. This study demonstrates sex differences in the exhibition of parental and aggression-like behavior. Results also support the hypothesis that even mild changes in the neonatal experience, possibly mediated by parental stimulation, can lead to long-term developmental consequences for behavior. This research was supported by National Alliance for Autism Research and NIH PO1 HD 38490 to CSC, NRSA F32 HD 08702 and NSF #0437523 to KLB, MH 073022 to CSC and KLB and American Psychological Association/DPN to EMB.
12. PRELIMINARY EFFECTS OF IN UTERO COCAINE EXPOSURE ON INFANT RAT ULTRASONIC VOCALIZATIONS. McMurray, M.S.; Zeskind, P.S.; Moy, C., Jarrett, T.M.; Johns, J.M. Departments of Psychology, Psychiatry, and Pediatrics. University of North Carolina, Chapel Hill, NC 27599 USA. Clinical studies with human infants have shown that the cries of babies exposed to cocaine in utero are



perceived as more aversive than the cries of normal babies. Furthermore, reported deficits in maternal care of cocaine-exposed rat pups suggest that pup-elicited cues may play a role in these deficits. In our preliminary study, ultrasonic vocalizations (USVs) were recorded from cocaine exposed and untreated litters on postnatal days (PND) 1 and 5. Pups were tested in two different environments (warm and cold) and USVs were analyzed for a variety of descriptive characteristics and waveform patterns. Results indicate that cocaine-exposed pups cry more frequently in the cold environment, have longer cry latencies, demonstrate fewer complex cries, and cry at a lower fundamental frequency on PND 1 and a higher frequency on PND 5 compared to controls. This general pattern of results is similar to the pattern of effects found in the cries of human infants with prenatal alcohol exposure and prenatal selective serotonergic reuptake inhibitor-exposure. Of particular interest, cocaine-exposed pups also had higher rates of dysphonation, paralleling those reported in human alcohol-exposed infants. Whether these patterns can be tied to altered maternal care of cocaine-exposed pups has yet to be addressed. This project was supported by NIH DA R01-13283.

13. **PRE-PUBERTAL STRESS: DIFFERENTIAL IMPACT ON MALES AND FEMALES** Toledo-Rodriguez, M.; Lecroq, B.; Sandi, C. Brain Mind Institute, Swiss Federal Institute of Technology (EPFL), Lausanne, CH-1015 Switzerland. Adolescence is a period when major physical, hormonal and psychological changes take place. In humans, adolescence is a developmental phase characterized by a significant increase in a) depressive behavior and/or eating disorders (especially among girls); b) impulsive behavior and aggressiveness (mainly in boys) and/or c) addictive use of drugs of abuse. Stress is an important risk factor for a wide variety of psychopathological alterations. In particular, adverse experiences during childhood and adolescence have been associated to the development of psychiatric disorders. Despite the severity and high cost to society of these pathologies, information on the nature of the behavioral alterations resulting from stress experiences during peri-adolescence is scarce, particularly for females. In this study, we aimed to evaluate the impact of stress during early puberty on emotional behavioral responses displayed by male and female rats during early adulthood. While both genders were submitted to the same stressors and at the same age, male and female rats developed a differential pattern of anxiety-like behaviors in adulthood, which significantly differed from their respective non-stressed controls. Males showed higher latency to explore new territories and objects than controls, while stressed females were significantly more hyperactive in adulthood when exposed to stress or to a novel environment. These results indicate that peri-pubertal stress affects the coping responses displayed by rats in adulthood to both novel and stressful situations in a sex dependent manner.
14. **1-BROMOPROPANE PRENATAL EXPOSURE IMPAIRES SEXUAL DIFFERENTIATION OF EMOTIONAL AND SEXUAL BEHAVIOR IN RATS.** Narikiyo, K.<sup>1</sup>; Aou, S.<sup>1</sup>; Fujimoto, T.<sup>1</sup>; Ichihara, Y.<sup>1</sup>; Ishida, T.<sup>2</sup>; Hori, H.<sup>2</sup>; Fueta, Y.<sup>2</sup> Dept. of Brain Sci. and Eng., Kyushu Inst. of Technol.<sup>1</sup>; Dept. of Environm. Manage., Sch. Health Sci., Univ. Occup. Environm. Health<sup>2</sup> 1-Bromopropane (1-BP) is an ozone-depleting substance replacement which has neurotoxicity and reproductive toxicity in adult animals. In this study, we investigated the effects of prenatal exposure to 1-BP on sexual differentiation of emotional and reproductive behavior. Pregnant rats were exposed to 700 ppm of 1-BP during gestational day 1 to 20 (6 hours per day). Behavioral properties of exposed rats were examined by open-field test, elevated plus maze test, passive avoidance test and forced swimming test. In the open-field test, the number of entries into the center area and the locomotor activity were significantly reduced in 1-BP exposed female rats but not in males. In the forced swimming test, the duration of immobility was significantly reduced in 1-BP exposed male rat but not in females. In the elevated plus maze test and the passive avoidance test, 1-BP exposed rats did not show significant difference in comparison with control rats. In female sexual behavior, the number of ear wiggles, an index of female proceptive behavior, was decreased and the rejection score (rejection to male mounting) was increased by 1-BP exposure. These results suggest that prenatal exposure of 1-BP impairs differentiation of emotional behavior and female sexual behavior. 1-BP is the potential candidate of endocrine disruptors which affect sexual differentiation of brain.
15. **PLASTICITY OF PATERNAL RESPONSIVENESS IN TWO PEROMYSCUS SPECIES** Everette, A.<sup>1</sup>; Tu, K.<sup>1</sup>; Contino, R.<sup>2</sup>; Rima, B.<sup>2</sup>; Major, J.<sup>2</sup>; Conway, A.F.<sup>1</sup>; Kinsley, C.H.<sup>2</sup>; Lambert, K.G.<sup>1</sup>; Randolph-Macon College, Ashland VA 23005 USA.<sup>1</sup>; University of Richmond, VA 23173, USA.<sup>2</sup> Prior research has established that maternal experience enhances behavioral responsiveness in foraging and exploratory tasks. In the current study, we explored the effect of parenting experience on the paternal brain by utilizing two

species of the genus *Peromyscus*: *P. californicus*, a bi-parental model, and *P. maniculatus*, a uni-parental model. In Experiment 1, virgin males of both species were exposed to four days of 10 minute pup exposure or the same time in a pup-free environment. Additionally, pup-sensitized males were exposed to primiparous female odors daily. In a subsequent paternal test with an alien pup, regardless of pup-sensitization, *P. californicus* males exhibited more nurturing responses toward the pups than the *maniculatus* males. Focusing on their brains, pup-sensitized males exhibited increased fos-immunoreactivity in the medial preoptic area; additionally, significant main effects were observed for both species and pup-sensitization factors in vasopressin-immunoreactivity in the paraventricular nucleus of the hypothalamus; specifically, increased immunoreactivity was found in *californicus*, as well as in pup-sensitized males (across both species). No effects in oxytocinergic-immunoreactivity were observed; however, plasma OT concentrations were higher in pup-sensitized males. In Experiment 2, *maniculatus* males that were either fathers or virgins were exposed to an alien pup restrained in a wire-mesh tent (i.e., a pup-tent). The *maniculatus* fathers approached the isolated pups faster and spent more time exploring the tents than their virgin counterparts, suggesting the possibility of plasticity in paternal responsiveness in the nonpaternal *maniculatus* males. In sum, these results suggest that the *Peromyscus* genus is a valuable model to explore the neurobiological effects of paternal experience.

16. PRE- AND POSTNATAL EXPOSURE TO BISPHENOL A ACCELERATES BEHAVIORAL AND NEURONAL RESPONSES TO STRESS CONDITIONS IN RATS. 1 Fujimoto, T; 1 Aou, S; 2 Kubo, K. 1 Dept. of Brain Sci. and Eng., Kyushu Inst. of Technol., Kitakyushu, 808-0196, Japan. 2 Dept. of Otorhinolaryngol., Chidori-bashi Hospital, Fukuoka, 812-8633, Japan Perinatal six weeks exposure to Bisphenol A (BPA, 0.1 and 1.0 ppm) impairs the sexual differentiation of brain and behaviors [Kubo et al. 2003]. Recently we found that one week exposure to BPA (0.1 ppm, 15 micro g/kg/day) during the final week of prenatal period impairs the sexual differentiation of exploratory behavior and enhances depressive behavior [Fujimoto et al. 2006]. In the present study, we investigated the effects of prenatal exposure to BPA (0.1 ppm) on behavioral responses to predator odor and olfactory responses of medial amygdala neurons. In addition, we examined the effects of postnatal one week exposure to BPA (0.1 ppm, 24 micro g/kg/day) on open-field behavior and depressive behavior. In the odor avoidance test, the smell of fox predominantly suppressed locomotor activity and enhanced avoidance response in the BPA-treated rats. In the electrophysiological study, sex difference of the ratio of excitatory responses (male > female) in the medial amygdala was abolished by prenatal BPA treatment. Male medial amygdala neurons showed selective excitatory responses to predator odors. This type of neurons did not respond to plant odors. In contrast, female amygdala neurons did not show such selectivity. The postnatal exposure to BPA was less effective on the open-field behavior, but more effective on depressive behavior than the case of prenatal exposure. These findings suggest that BPA impairs sexual differentiation of medial amygdala neurons which affect emotional responses to the olfactory cues. In addition, pre- and postnatal exposure to BPA differently affect sexual differentiation of behavioral responses.
17. NEONATAL HANDLING INCREASES CARDIOVASCULAR REACTIVITY AND FREEZING BEHAVIOR TO FEAR CONDITIONING IN BORDERLINE HYPERTENSIVE RATS (BHR). Sanders, B.J.; Knoepfler, J.D. Dept. of Psychology and the Neuroscience Program, Drake University, Des Moines, IA 50311 USA. The purpose of this experiment was to determine the effects of an early environmental manipulation, handling (H), on cardiovascular (CV) reactivity, freezing behavior and corticosterone (CORT) responses to fear conditioning in the BHR, which is genetically susceptible to environmental stressors. H subjects were separated from the nest for 15 mins/day on post-natal days 1-14, while non-handled (NH) controls remained in the home cage. Adult BHR from each group were implanted with a femoral arterial catheter for mean arterial pressure (MAP) recording and blood sampling. Two days later, subjects were exposed to the fear conditioning procedure. This consisted of allowing the subject to explore the chamber for 30 sec before receiving a 2 sec, 1.5 mA footshock. Subjects remained in the chamber for an additional 30 sec before being transported back to the home cage. Subjects were returned to the chamber the next day for 10 min during which time freezing behavior, CV responses and CORT measurements were taken. H subjects displayed significantly more freezing behavior compared to NH (92%±2.2 vs 80.7%±5.7,  $p < .05$ ). Although resting MAP did not differ between groups, H subjects had increased MAP reactivity when returned to the fear conditioning chamber ( $p < .01$ ). Finally, H subjects had significantly lower CORT levels at the end of the 10 min test period (173±8 ng/ml vs 217.7±22.2 ng/ml,  $p < .05$ ). These results indicate that neonatal H produces enhanced biobehavioral responses to fear

conditioning in BHR and may suggest a useful model with which to study the interaction of genetics, emotionality, and heart disease. Supported by NIH grant HL073894.

18. **QUANTIFICATION OF MATERNAL CARE BEHAVIOR IN NEONATALLY STRESSED AND LITTERMATE CONTROL MICE.** Fowler, J. A., Hodges, A.B. and Hohmann, C.F., Morgan State University, Baltimore, MD. Previous work in our lab has shown that using a split litter design, neonatal stress causes changes in cerebral cortical development and alters cognitive performance in both stressed mice (STR) and their littermates (LMC) compared to age matched controls (AMC). Moreover, when tested during postnatal days (PND) 1 and 7, ultrasonic vocalizations (USV) in LMC and STR was substantially altered compared to AMC. Maternal care during early development in rodents powerfully influences cognitive performance in adulthood (Bredy, et al., 2004). Therefore, we hypothesize that USVs emitted from STR and LMC pups contribute to altered maternal care and subsequent behavioral performance compared to AMC. We have developed a method to quantify the maternal care of dams as well as ultrasonic vocalizations during the first week of life. During PND 2-7, half of the litter received maternal separation/temperature stress, while LMCs remained with the dam. On PND 1, USVs emitted from all the pups were quantified using a U30 bat detector, and baseline maternal care behavior was assessed. On PND 2-7, USVs and maternal interaction with the pups (at one minute increments) were recorded for 30 minutes directly before removal of the stressed pups, during removal, and directly after removal of stressed pups. Licking/grooming, nesting, nursing, resting, sniffing, and digging were quantified using the CleverSys Topscan/Topview 1.0 system. We measured an increase in the amount of licking/grooming received by the STR compared to the LMC suggesting that decreased licking/grooming received by LMCs may be responsible for altered cognitive performance in adulthood. Supported by SO6 GM051971 and R25 GM058904.
19. **VARIATIONS IN MATERNAL CARE ALTER CORTICOSTERONE RESPONSE TO STRESS IN MALE, BUT NOT FEMALE, OFFSPRING.** Barha, C.; Pawluski, J.L.; Galea, L.A.M. Department of Psychology, Program in Neuroscience and the Brain Research Centre, University of British Columbia, Vancouver, BC V6T 1Z4 Canada. Naturally occurring variations in maternal care during the early postnatal period results in altered functioning of the hypothalamic-pituitary-adrenal (HPA) axis and altered hippocampal-dependent learning and memory in adult male offspring. However, much less is known about the effects of variations in maternal care on HPA functioning and learning and memory in female offspring. The present study investigated the role of restraint stress on hippocampus-dependent learning and memory performance in adult male and female offspring exposed to differing levels of maternal licking/grooming. Rats were trained and tested on the spatial working/reference memory version of the radial arm maze for 12 consecutive days, and subjected to 2 h of restraint on testing day 9. Corticosterone levels were assessed at 0, 30, 60, and 120 minutes after the onset of restraint. Preliminary results suggest restraint stress enhanced performance in adult offspring regardless of differences in maternal care and sex. In addition, offspring of high licking dams tended to make more errors on this task than offspring of low licking dams. With regards to corticosterone response to restraint, females, regardless of level of maternal care, had higher elevations in the corticosterone response to restraint compared to male offspring. Interestingly, 50% of male offspring from low licking dams did not show a normal elevation in corticosterone in response to restraint stress. Our results show that variation in maternal care altered the CORT response to stress in male, but not female, offspring of low licking dams. Future work aims to determine whether how differences in maternal care (ie. licking/grooming) alter corticosterone levels in response to stress in male offspring.
20. **LATE GESTATIONAL STRESS EFFECTS IN MALE OFFSPRING.** Baker, S.L.; Chebli, M.; Le Marec, N.; Rees, S.; Bielajew, C. School of Psychology. University of Ottawa, Ottawa, ON; Hopital Sacre-Coeur, Université de Montréal, Montreal, QC, Canada. Physical restraint is commonly employed to induce stress in pregnant rats and has been shown to induce various deficiencies in pups that persist throughout life. This method is attractive because stress severity is easily manipulated by varying the length of restraint exposure. However, it is unclear if the effects are due to the stress itself or stress-induced changes in postnatal maternal behaviour. In the present study, restraint was applied three times on each of gestational days 10 to 19, for a total of 75 minutes/day. Included was a control group of pregnant rats that received no manipulation. Results demonstrated that there was a global impact of stress- litter composition, weight, and sex ratio were adversely affected by prenatal stress. Behavioural measures employed to assess cognitive ability and anxiety levels in male offspring suggest that gestational stress had a negative impact.

Juvenile rats from stressed mothers displayed poorer performance in the T-maze and increased anxiety in the elevated plus maze compared to their control counterparts. Specifically, the stressed group showed no significant difference among the three choices available in the T-maze (correct, incorrect, and none) while control rats made more correct choices and fewer no-choice selections. In the elevated plus maze task, control rats spent significantly more time exploring the open arm at 10 minutes and made more open arm entries early in the 15 minute session than stressed rats that were more active later. Preliminary analyses suggest the effects of gestational stress persist at least into young adulthood and may be related to postnatal maternal behaviour of the prenatally -stress dams.

21. BEHAVIOURAL TERATOGENIC EFFECTS OF PRENATAL NICOTINE EXPOSURE IN MICE OFFSPRING Mesembe, O. E., Igiri, A. O. Department of Anatomy, Faculty of Basic Medical Sciences, University of Calabar, Calabar, Nigeria. The behavioural teratogenic effects of prenatal nicotine exposure on 5 parameters in male albino mice were assessed. Twenty virgin female albino mice weighing between 30g to 38g were used for this study. The animals were divided into 2 groups of 10 mice each (A and B). Each group was kept in a separate plastic cage. The rats were fed with commercial mice feed and tap water ad libitum throughout the experimental period. The females were caged overnight with sexually mature male mice of the same strain. The presence of sperm (tailed structures) in the vaginal smears obtained the following morning confirmed coitus and the sperm positive day was designated as day zero of pregnancy. Dams in group A were injected intraperitoneally with 0.5 mg/kg/day of nicotine dispersed in distilled water on gestation days 9 - 12. Dams in group B served as control received only the vehicle on corresponding days. The dams were allowed to deliver spontaneously. At 4 days after birth, litters were culled randomly to group of 10 fetuses; at 21 days, they were weaned, separated by sex and housed 6 per cage. Before weaning the offspring were examined to test their surface righting reflex (5 days of age), cliff avoidance response (6 days), negative geotaxis response (7 days) and swimming development (8, 10, and 12 days). After weaning, the males were examined using the open field maze (7 weeks), and the shuttle- box-avoidance learning test. The results showed that the avoidance learning of the mice in the treatment group A was significantly poorer than that of the control group B. In swimming development, offspring of group A had significantly less successful and slower response times. There were also significant differences between group A and B offspring for the surface righting and negative geotaxis responses. The findings suggest that prenatal exposure to nicotine may retard early response development; impair learning ability, development of motor coordination and developmental pattern of behaviour of offspring of albino mice exposed to nicotine during pregnancy.

### *Stress, fear and anxiety*

22. CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE PERIAQUEDUCTAL GRAY ARE DIFFERENTIALLY SENSITIVE TO INJECTIONS OF FLUOXETINE INTO AMYGDALOID NUCLEI. Martinez, R.C.R.; Oliveira, A.R.; Macedo, C.E.A., Brandão, M.L. Department of Psychology and Education. Faculty of Philosophy, Science and Letter of Ribeirão Preto. University of São Paulo, Brazil. The lateral (LaA) and basolateral (BLA) nuclei of amygdala are mainly involved in the filtering of aversive stimuli, while the central (CeA) nucleus constitutes the output for the autonomic and somatic components of the fear reaction through major projections to the hypothalamus and brain stem regions (see Davis et al, 1994; LeDoux, 1994; LeDoux et al, 1988). It has been shown that the dorsal periaqueductal gray (dPAG) is activated by threatening stimulus and has important functional links with the amygdala. We studied the effects of fluoxetine (3.5 nmol/0.2 µl) microinjected in the LaA, BLA and CeA on the contextual fear paradigm evaluated by conditioned freezing and unconditioned fear determined by the measurements of the threshold for freezing and escape induced by dPAG electrical stimulation. Injections of fluoxetine into the three amygdaloid nuclei did not change the aversive thresholds but disrupted the dPAG post-stimulation freezing and the contextual freezing. The data obtained showed that amygdala regulates contextual conditioned freezing and some aspects of unconditioned fear generated in the neural circuits of fear. Supported by CNPq, FAPESP.
23. DISTINCT FOS DISTRIBUTION FOLLOWING FREEZING BEHAVIOR INDUCED BY NMDA INJECTIONS INTO EITHER DORSAL OR VENTRAL INFERIOR COLLICULUS. Borelli, K.G.; Ferreira-Netto, C.; Brandão, M.L. Laboratory of Neuropsychopharmacology, Dept. of Psychology, FFCLRP, University of São Paulo, Ribeirão Preto, SP, 14049-901 Brazil. The inferior colliculus (IC) is an

important relay center for auditory information in its ascending way to medial geniculate nucleus (MGN) and temporal cortex. It has been reported that the central (CIC) and dorsal (DIC) nuclei of IC are involved with the generation and expression of defensive reactions and audiogenic seizures, respectively. As freezing is the first response that appears when each one of these IC nuclei is gradually stimulated with increasing doses of excitatory amino acids (EAA) the question arises as to the extent of the independence of fear and audiogenic seizures at the IC level. To examine this issue we analyzed the Fos distribution in selected limbic structures following injections of N-Methyl-D-Aspartate (NMDA) into the CIC and DIC at freezing (7 nmol)- and escape (20 nmol)-producing doses. Freezing behavior followed by NMDA injections into the DIC caused increased Fos expression in the MGN, dorsomedial periaqueductal gray and laterodorsal nucleus of the thalamus while freezing induced by NMDA stimulation of CIC caused a significant Fos immunolabeling in the ventrolateral PAG, basolateral nucleus of amygdala and cingulate cortex. Escape behavior induced by NMDA injections (20 nmol) into both nuclei caused a widespread increase in Fos expression in the brain. These results suggest that distinct circuits underlie the freezing behavior generated at the level of ventral or dorsal regions of the IC. Moreover, while processing of sensory information preceding audiogenic seizures in the DIC recruits structures related to the processing and output of acoustic information, those activated by stimulation of CIC are more related to the neural substrates of fear.

24. SOCIAL BEHAVIORS ASSOCIATED WITH PANIC SUSCEPTIBILITY IN RATS. de Paula, H.M.G.; Campos, K.M.R.; Hoshino, K. Dept. of Biological Sciences/ FC/ UNESP-Bauru, 17033-360, Brazil. Around 20% of rats present the wild running behavior (WR) in response to acoustic stimulation, which may be interpreted as a panic susceptibility. The WR-sensitive rats also show elevated anxiety levels in etho-experimental tests. Aiming to investigate the effects of such anxiety/panic susceptibility upon social behavior of rats, WR-sensitive rats were then compared with WR-resistant ones regarding their social hierarchical rank and behaviors emitted in the male intruder paradigm and in a reproductive-competition test. Methods: Adult male Wistar rats were tested in an acoustic stimulation trial (120 dB, 60s) for determination of WR susceptibility. Intruder test was conducted by behavioral recordings in six-rats colonies randomly composed either by WR-sensitive (n=8) and WR-resistant (n=18) subjects when a male rat was introduced for 60 min. Social hierarchy was analyzed in mixed-composed colonies of three and six animals. Introduction of a sexually receptive female in 6 cages containing two males (one WR-sensitive and one WR-resistant rat) served for evaluation of female access and copulatory behaviors. Results: WR-sensitive rats presented increased aggressiveness and freezing in response to the intruder. WR-sensitive rats showed a trend to occupy the lowest hierarchical rank in colonies with six, but not with three animals. The access to the female and copulatory behaviors did not differ between WR-resistant and -sensitive rats. Conclusion: Susceptibility to anxiety/panic in male rats may be associated with low hierarchical ranks in large groups and with elevated defensiveness towards an intruder, but not with altered reproductive behaviors. Financial support: FUNDUNESP.
25. CHRONIC STRESS AND LITHIUM TREATMENT MODULATE EXPRESSION OF PHOSPHORYLATED CYCLIC AMP RESPONSE ELEMENT BINDING PROTEIN IN THE RODENT AMYGDALA. Johnson, S.A.; Wang, J.-F.; McEwen, B.S.; Young, L.T. Centre for Addiction and Mental Health, Institute of Medical Science, University of Toronto, Toronto, ON, Canada. Chronic restraint stress (CRS) leads to distinct patterns of dendritic remodeling in the rodent amygdala; however, the molecular mechanisms underlying this stress-induced plasticity, and the accompanying enhancement of fear and anxiety behaviour, remain unclear. As a regulator of many plasticity-related genes, the transcription factor cyclic AMP response element binding protein (CREB) is optimally positioned to mediate these morphological and behavioural changes. Furthermore, recent evidence suggests that the mood-stabilizing drug lithium prevents dendritic remodeling in the hippocampus after chronic stress, and may do so via a CREB-dependent pathway. Accordingly, the present experiment characterized amygdalar expression of phosphorylated CREB (pCREB) after CRS exposure, and determined whether lithium has similar protective effects in the amygdala. Male rats were exposed to CRS (21d, 6h/day), with or without concurrent lithium treatment. Coronal brain sections spanning the basolateral, central, and lateral amygdalar nuclei were subjected to immunohistochemistry, and the total number of pCREB-positive nuclei was estimated in these regions by non-biased stereological methods. Rats exposed to CRS without concurrent lithium treatment showed a reduction in the number of pCREB-positive nuclei in the lateral amygdala, while lithium treatment during CRS reversed this effect. Intriguingly, lithium treatment alone

also reduced the number of pCREB-positive nuclei in the lateral amygdala, suggesting divergent mechanisms of action of this mood-stabilizing agent in the face of chronic stress. Our results indicate that detailed characterization of lithium action in pathological models, rather than cell culture and naïve animals, could provide novel insight into its neuroprotective properties.

26. ULTRASONIC VOCALIZATIONS IN C57BL/6J AND BTBR T<sup>+</sup> tf/J MICE. McFarlane, H.G.<sup>\*©®</sup> and Crawley, J.N.<sup>\*</sup>. Laboratory of Behavioral Neuroscience, National Institute of Mental Health, Bethesda MD, USA<sup>©®</sup>. Department of Psychology, Kenyon College, Gambier OH USA<sup>\*©®</sup>. Abnormal communications and social interactions are among the main features of autism spectrum disorders (ASDs) and finding or developing a genetic strain of mice that model these features would be beneficial to ASD research. Ultrasonic vocalizations (USVs) by infant mice have been reported to facilitate maternal behavior and pup retrieval, suggesting that these calls may play an important role as a means of social communication between mother and infant. Previous research has suggested that the BTBR T<sup>+</sup> tf/J mice show less social approach in our new three-chambered social task and so may function as an ASD model of diminished social interaction. In order to assess whether this strain also demonstrates abnormal communication, we measured the ultrasonic vocalizations in the 40 kHz to 90 kHz range of infant BTBR T<sup>+</sup> tf/J and C57BL/6J mice. 2, 4, 6, 8, 10, and 13 day old infant male mice were removed from the home cage and placed in a small Plexiglas container and their USVs recorded for five minutes in one-minute blocks at an ambient temperature of approximately 23°C. We also compared these two strains on the three chambered social approach task. Preliminary results suggest that at all ages tested, both the calling rate (calls per minute) and duration of calls of the BTBR T<sup>+</sup> tf/J mice were significantly greater than those of the C57BL/6J mice, although similar to that of other strains. Further, BTBR T<sup>+</sup> tf/J mice showed significantly lower social approach in the three chambered task than C57BL/6J mice, replicating previous findings (Moy et al., submitted). These results highlight the difficulty of finding multiple features of ASDs in a single animal model and support the idea that individual features of ASDs may be modeled in different strains of mice. *This research was supported by the NIMH Intramural Program.*
27. LATENT TOXOPLASMA INFECTION IN RODENTS CONVERTS AVOIDANCE OF CAT PHEROMONES INTO AN ATTRACTION. Ajai Vyas<sup>1</sup>, Seon-Kyeong Kim<sup>2</sup>, Nicholas Giacomini<sup>1</sup>, John Boothroyd<sup>2</sup>, and Robert M Sapolsky<sup>1,3</sup>. <sup>1</sup> Department of Biological Sciences; <sup>2</sup> Department of Microbiology and Immunology; <sup>3</sup> Departments of Neurology and Neurological Sciences, and of Neurosurgery, Stanford University, Stanford, CA 94305, USA. The Protozoan parasite *Toxoplasma gondii* blocks the innate aversion of rats for bobcat urine, which should increase the likelihood of a cat preying a rat. This is thought to reflect adaptive behavioral manipulation by *Toxoplasma*, in that the parasite, while capable of infecting rats, reproduces sexually only in the guts of cats. The “behavioral manipulation” hypothesis postulates that a parasite will manipulate only those host behaviors essential for enhancing its own transmission. In contrast, the neural circuits implicated in innate fear, anxiety and learned fear all overlap considerably, suggesting that *Toxoplasma* should disrupt all of these non-specifically. We investigated these conflicting predictions. In mice and rats, latent *Toxoplasma* infection converts the aversion to feline odors into attraction. Such loss of fear is remarkably specific, as infection does not diminish learned fear, anxiety-like behavior, olfaction or non-aversive learning. These effects on both aversion and attraction are commensurate with our finding of broad and uniform distribution of *Toxoplasma* throughout the brain. These effects are not part of a generalized response to the infection, thus supporting the behavioral manipulation hypothesis. Additionally, *Toxoplasma* provides a unique model for studying the neurobiology of innate fear and attraction.
28. ANXIOLYTIC PROFILE OF THE ANANDAMIDE TRANSPORT INHIBITOR AM404. Campolongo, P; Bortolato, M; Mangieri RA; Trezza V; Arguello O; Cuomo V; Piomelli D Anandamide deactivation may be a promising target for the management of mood disorders, yet evidence on its possible role in modulating these functions is still inconclusive. The present study investigated the effects of AM404, a prototypical anandamide transport inhibitor, in rat models of anxiety-related behaviors. To evaluate the effects of AM404 on anxiety-related behaviors, the drug was tested in three models of anxiety in rodents: the elevated plus maze, the ultrasonic vocalization models and the defensive withdrawal in an open field. AM404 evoked anxiolytic-like responses at doses that did not alter locomotor activity. Rats treated with AM404 (1-5 mg/kg, i.p.) spent a longer time in the open arms of the elevated plus maze than did vehicle-treated controls. This effect was likely dependent on endocannabinoid-mediated activation of CB1

receptors, because it was prevented by the CB1 antagonist/inverse agonist rimonabant (1 mg/kg, ip.), administered 30 min before AM404. Accordingly, AM404 (1-5 mg/kg, i.p.) dose-dependently decreased the latency to leave the start box and increased the time spent outside the box in a defensive withdrawal apparatus. This effect was significantly reduced by rimonabant (1 mg/kg, i.p.). Finally, AM404 (1-2 mg/kg) reduced the rate of ultrasonic emissions in rat pups in a rimonabant-sensitive manner. To assess the ability of AM404 to blunt reactivity to environmental stimuli, we tested the ability of this compound to modify startle responses. Unlike diazepam, AM404 (1-10 mg/kg, i.p.) did not alter magnitude and latency of startle reflex, suggesting a limited impact of this drug on reflex functions. Collectively, our results highlight anandamide reuptake inhibitors as a novel, promising category of anxiolytic agents.

29. CHRONIC ANTI-INFLAMMATORY TREATMENT FAILS TO PREVENT BRAIN PATHOLOGY IN A MODEL OF NEUROPSYCHIATRIC LUPUS. Ballok, D.A.; Sakic, B. Dept. of Psychiatry and Behavioral Neurosciences. McMaster University, Hamilton, ON, CANADA. Neurologic deficits and psychiatric problems are severe complications of systemic lupus erythematosus. As commonly seen in patients, spontaneous development of lupus-like disease in MRL/MpJ-Faslpr (MRL-lpr) mice is accompanied by brain atrophy and behavioral dysfunction. We presently examine inflammatory and ultrastructural aspects of the CNS involvement using a non-selective COX-2 inhibitor and measuring effects on behavior, microglial activation, and neuronal morphology. Ibuprofen (IBU) was provided in a rodent chow (375 ppm) from 5-19 weeks of age. Exploration of a novel environment and performance in the forced swim test assessed effects on behavior. Immunohistochemistry, Fluoro Jade B (FJB) staining, and flow cytometry were employed in neuropathological analysis. Transmission electron microscopy examined ultrastructural morphology of cortical, hippocampal, hypothalamic, and cerebellar cells. Chronic IBU treatment failed to normalize immune status, behavior, and brain mass in lupus-prone MRL-lpr mice. It also did not reduce density of CD3+ lymphocytes in the choroid plexus, or FJB+ neurons in the hypothalamus. Activated F4/80+ microglia increased with age, but IBU treatment was not effective in reducing their numbers. Although numerous dark cells were seen in functionally critical brain regions (e.g. the PVN and the subgranular zone), ultrastructural morphologies of classical apoptosis or necrosis were not detected. The COX-dependent pathway does not seem to be critical in the etiology of CNS disease in this model of neuropsychiatric lupus. Reduced brain mass, increased microglial activation, and condensation of cytoplasm point to a metabolic perturbation (e.g. excitotoxic damage) which compromises function and survival of central neurons during lupus-like disease.
30. ETHOPHARMACOLOGICAL ANALYSES OF VIGILANCE AS A BEHAVIORAL INDICATOR OF FEAR/ANXIETY IN MARMOSET MONKEYS. Tomaz, C.; Vilas Boas, N.; Souto, A.A.V.; Barros, M. Primate Center, Institute of Biology, University of Brasília, 70910-900, Brazil. Vigilance-associated behaviors, although frequently analyzed in rodents, have not been used in similar tests with non-human primates. Therefore, we investigated vigilance behaviors (aerial/terrestrial scan and glance) in marmoset monkeys (*Callithrix penicillata*) using the Predator Confrontation Test of fear/anxiety. This procedure analyzes the behavioral repertoire induced by exposure to a taxidermized predator (wild oncilla cat; *Felis tigrina*) while in a maze environment. Thirteen marmosets were initially submitted to four 30-min maze-habituation trials (HTs), in 48-h intervals, and in the absence of the 'predator'. Each subject was then submitted to five 30-min randomly assigned treatment trials, held 72-h apart, and in the presence of the 'predator': three drug administrations (1, 2 and 3 mg/kg of diazepam or 0.1, 0.5 and 1.0 mg/kg of buspirone), a saline injection and a sham trial. High scan and glance rates were observed, remaining constant during the course of the HTs. Locomotion, however, significantly decreased during these trials. Subsequent confrontations with the wild-cat stimulus altered neither the marmosets' vigilance response itself (i.e. saline), compared to the last maze-habituation trial, nor after diazepam or buspirone treatments, relative to saline trial. The results indicate that, similar to feral monkeys, high constant basal levels of vigilance are observed in marmosets exposed to this procedure. However, this response also remained constant during the wild-cat confrontations, precluding analysis of the pharmacological manipulations held. This effect may be due to characteristics of the test (e.g. novel environment, brief isolation), than to a lack of responsiveness to the stimulus or drug treatments, indicating the need for further studies on marmosets' vigilance behavior under different conditions. Financial support: CNPq (no. 412542/2003), FINATEC.

31. MEMORY REACTIVATION TREATMENT REINSTATES TEMPORALLY SPECIFIC FEAR BEHAVIOR FOLLOWING EXTINCTION TREATMENT. Barnet, R. Department of Psychology. The College of William and Mary, Williamsburg, VA 23187 USA. Timing specificity of fear behavior implies that the neural systems which underlie fear are not static but are themselves modulated in a temporally dynamic fashion. Two experiments with rats using the fear-potentiated startle paradigm (FPS) examined timing specificity of FPS. During initial fear training, a 30-s light CS was paired with a shock US, in order to produce learning of a light-shock association. Shock always occurred at the end of the 30-s light (Light→shock). Level of learned fear elicited by early versus late portions of the light was assessed using the FPS paradigm. The magnitude of FPS was found to be maximal during late as opposed to early portions of the 30-s CS, suggesting rats had learned to time shock delivery and that level of fear varied with the expected time of shock delivery (cf. Davis, Schlesinger, & Sorenson, 1989). Experiment 1 revealed that this temporal specificity effect could be extinguished by nonreinforced exposure to the light CS after fear training and that the loss of this temporal specificity effect due to extinction could be recovered by a memory reactivation or “reminder” treatment. In Experiment 2, temporally specific fear behavior was lost when testing followed fear training by a long (i.e., 28 day) retention interval. Outcomes suggest temporal memory can be preserved after extinction but that rats can retrieve the central light-shock representation learned in earlier fear training without retrieving timing information. Behavioral dissociation of fear memory from temporal memory implies a functional independence of neural systems responsible for the temporally specific expression of acquired fear.
32. EXPERIMENTAL MANIPULATION OF BASAL RATE OF NEUROGENESIS INFLUENCES THE DEVELOPMENT OF AMYGDALOID KINDLING IN RATS. Fournier, N.M.; Corcoran, M.E.; Kalynchuk, L.E. *Dept. of Psychology, University of Saskatchewan, Saskatoon, SK S7N 5A5 Canada*. The suggestion that hippocampal neurogenesis might play a role in the development of temporal lobe epilepsy is a topic of extensive debate. Generally, seizure-induced neurogenesis is thought to participate in the formation of epileptogenic networks that encourage the spread of epileptic activity. The possibility that seizure-induced neurogenesis is part of a beneficial or reparative process has been curiously overlooked. To characterize the role of neurogenesis during the development of epilepsy, we administered compounds known to either decrease or increase neurogenesis in the adult brain before the commencement of amygdaloid kindling. When administered for 14 days, the selective serotonin reuptake inhibitor fluoxetine (Prozac, 5 mg/kg, s.c.) increased the number of newly born (BrdU labeled) cells in the dentate gyrus. In turn, the DNA-methylating agent methylazoxymethanol acetate (MAM, 7 mg/kg, s.c.) reduced the number BrdU cells in the dentate gyrus. Twenty-four hours after treatment with MAM acetate, there was no influence on the minimal threshold to induce an epileptic afterdischarge in the amygdala; however, the number of stimulations required to elicit the first motor convulsion was substantially lower after MAM treatment. Alternatively, 14 day pretreatment with fluoxetine raised the afterdischarge threshold, but produced inconsistent convulsive responses during amygdaloid kindling. These results indicate that fluoxetine pretreatment might exert partial antiepileptic effects on amygdala kindling. Our findings suggest the possibility that the newly generated cells in the adult hippocampus exert seizure suppressive effects during the development of epilepsy but as seizures are continually evoked the normal homeostatic influence from these cells dissipates resulting in the progressive intensification of limbic seizures.
33. CONDITIONED AND UNCONDITIONED FEAR ORGANIZED IN THE INFERIOR COLLICULUS ARE DIFFERENTIALLY SENSITIVE TO INJECTIONS OF MUSCIMOL INTO THE BASOLATERAL NUCLEUS OF THE AMYGDALA. Macedo, C.E.; Martinez, R.C.R.; Brandão, M.L. Department of Psychology and Education. University of São Paulo, Ribeirão Preto, SP, 14040901 Brazil. Chemical stimulation of the inferior colliculus (IC) with semicarbazide – an inhibitor of the GABA synthesizing enzyme – functions as unconditioned stimulus in the conditioned place aversion test (CPA) and electrolytic lesions of the basolateral amygdala (BLA) enhance the aversiveness of the IC stimulation. This study examined the effects of inactivation of BLA with muscimol on the conditioned and unconditioned fear using semicarbazide injections into the IC of rats subjected to conditioned (CPA) or unconditioned (open field) fear tests. In both tests the animals were injected with semicarbazide or saline into the IC and muscimol or saline into the BLA. Muscimol decreased the CPA and increased the unconditioned fear elicited by IC injections of semicarbazide. These findings indicate that distinct modulatory mechanisms in the BLA are recruited during the conditioned and unconditioned fear triggered by IC activation.



34. **NEUROPSYCHOLOGICAL ASSESSMENT IN VETERANS WITH POSTTRAUMATIC STRESS DISORDER.** Geuze, E.; Vermetten, E.; de Kloet, C.S.; Hijman, R.; Westenberg, H.G.M. Dept. of Military Psychiatry, Central Military Hospital, Utrecht, The Netherlands and Dept. of Psychiatry, Rudolf Magnus Institute of Neuroscience, Utrecht, The Netherlands. Background: Several studies have shown that posttraumatic stress disorder (PTSD) is associated with memory and concentration deficits. Deficits in both immediate and delayed recall of verbal memory have been displayed in patients with PTSD related to both civilian and combat related trauma. However most of these studies had several methodological disadvantages related to medication use, the use of healthy controls, and usually examined just one neuropsychological test. Methods: Fifty Dutch veterans of UN peacekeeping missions (25 with PTSD and 25 without PTSD matched for age, year, and country of deployment) were assessed with a comprehensive neuropsychological testbattery consisting of four subtests of the WAIS III (Picture Arrangement, Block Patterns, Similarities, and Vocabulary), WMS-R Figural Memory, WMS-R Logical Memory, the California Verbal Learning Test (CVLT), and the Rey Auditory Verbal Learning Test (AVLT). Patients with PTSD were free of medication and substance abuse. Multivariate analyses of variance were used to assess group differences of memory performance and cognition. Results: Patients with PTSD had similar verbal, performance, and total IQ scores compared to control veterans without PTSD, but displayed deficits of figural and logical memory. Patients with PTSD also performed significantly lower on measures of immediate and delayed recall. Conclusions: Deficits of memory performance were displayed in a sample of medication and substance abuse free veterans with PTSD when compared to matched control veterans without PTSD. Deficits in memory performance were not related to IQ or trauma providing evidence for a structural memory performance deficit in PTSD.
35. **TESTING FOR APPROACH-AVOIDANCE BEHAVIOUR IN THE HOME CAGE** De Visser, L.; Schenke, M.; Van den Bos, R.; Spruijt, B.M. Dept. of Animals, Science and Society, Utrecht University and Rudolf Magnus Institute of Neuroscience, UMC, The Netherlands. C57BL/6 mice are reported to be less anxious than DBA/2 mice in several tests, such as elevated plus maze and modified hole board. These tests have in common that they are short lasting and the observed behaviour is always affected by novelty and pre-experimental factors such as handling and transport. To tackle these problems, we developed a system that allows for continuous registration of mouse locomotor behaviour in a home cage environment. Apart from detailed analysis of baseline activity and circadian rhythmicity, this set-up could be used to study approach-avoidance behaviour in a familiar environment. Therefore, avoidance of an aversive stimulus was measured in male C57BL/6 and DBA/2 mice. Mice were allowed to habituate to the novel home cage for four days before they were presented with a bright white light spot (1000 lux) directed on the feeding station for three hours at the onset of the dark phase. This induced an approach-avoidance conflict. Surprisingly, C57BL/6 showed a much stronger avoidance of the illuminated zone than DBA/2 mice. Furthermore, a strong rebound effect was seen in both strains when the light spot was turned off. This was reflected by a sharp increase in time spent at the feeding station. Administration of an anxiolytic compound (diazepam, 1.0 mg/kg) increased time spent in the light spot zone in a separate group of C57BL/6 mice. These findings suggest that avoidance behaviour in inbred mice may be dependent on familiarity with the environment. Testing in a home cage environment yields new information on how mice deal with an aversive stimulus and how this interacts with other motivational systems such as feeding behaviour and baseline activity.
36. **ANXIETY INDUCED BY DIAZEPAM WITHDRAWAL AND FOS IMMUNOREACTIVITY IN THE BRAINSTEM STRUCTURES.** Fontanesi, L.; Carvalho, M.C.; Cabral, A.; Castilho, V.M.; Brandão, M.L.; Nobre, M.J. Benzodiazepines are prescribed for the treatment of anxiety and sleep disorders. The interruption of its prolonged treatment leads to the appearance of a withdrawal syndrome characterized mainly by the appearance of high levels of “anxiety”. This “anxiety” state also appears in animals submitted to dangerous situations or after chemical or electrical stimulation of some mesencephalic structures which suggest that they may share similar neurobiological mechanisms. C-fos immunolabeling technique has been used as a marker for neural activation, which occurs even in response to mild stress. Therefore, based on the behavioral similarity observed during abstinence and that induced in animals exposed to stressful situations, in this work, we investigated the effects of diazepam withdrawal in rats tested in the elevated plus-maze using a new method of oral drug ingestion, avoiding the unpleasant effects of the gavage or i.p. administration), and the consequent C-fos neural expression on brainstem structures. Our results showed that diazepam withdrawal increases both “anxiety” levels and number of Fos

immunoreactivity labeled cells in structures responsible for the generation of fear and “anxiety”-like behaviors. These results suggest that the rebound anxiety elicited by diazepam withdrawal, differently from drugs acting on the dopaminergic system, could be the result of the activation of early mechanisms in brainstem structures mainly those belonging to the so-called brain aversion system.

37. **IMMOBILIZATION STRESS INDUCES CHANGES IN NORADRENALINE IN THE STRIATUM.** García-Saldívar, N. L.; González-López, M.R.A.; Gómez-Romero, J.G.; Rodríguez-Serrano, L.M.; <sup>1</sup>Domínguez, R.; Cruz-Morales, S.E. FES-Iztacala and <sup>1</sup>FES-Zaragoza, UNAM, Mexico. There is evidence that the noradrenergic system plays an important role in the regulation of stress response. Exposition to stress increases the concentration of noradrenaline (NA) in several cerebral structures (hippocampus, locus coeruleus, prefrontal cortex). A regional distribution of acetylcholine, dopamine and GABA in the striatum has been described, but few reports deal with the noradrenergic system. This experiment was designed to evaluate the activity of NA in dorsal (DS) and ventral striatum (VS) in subjects submitted to stress by immobilization (IMO). Male Wistar rats (250-270 g), were assigned to four independent groups (N=7): an untouched group (control), and three groups exposed to IMO during 60 min and killed 5 min, 24 or 48 h after IMO. The animals were decapitated, the VS and DS dissected and NA and MHPG levels were measured by HPLC. Because no significant differences were observed in NA and MHPG levels between VS and DS the data were computed together. In comparison with control, the NA levels were significantly higher in those animals submitted to IMO and sacrificed 5 min ( $F_{3,52} = 8.40$ ,  $p < 0.0001$ ), while the noradrenergic activity was lower in all groups of animals submitted to IMO ( $F_{3,52} = 22.86$ ,  $p < 0.0001$ ). Present results suggest that the striatal noradrenergic system plays a significant role in the response to stress induced by IMO. Supported by PAPIIT IN301102, DGAPA, UNAM.
38. **CHRONIC CANNABINOID TREATMENT PRODUCES AN ANTIDEPRESSANT-LIKE RESPONSE IN THE FORCED SWIM TEST: POSSIBLE ROLE OF NOREPINEPHRINE.** Anna C. Morrish, Matthew N. Hill, Larissa M. Froese, Boris B. Gorzalka. Department of Psychology, University of British Columbia. Vancouver, B.C. Canada. A recent surge of evidence has indicated that pharmacological activation of the cannabinoid system elicits antidepressant-like responses in preclinical paradigms. However, there is an increasing body of clinical evidence suggesting that protracted cannabinoid exposure may be associated with the onset of mood disorders. This research aimed at determining if chronic cannabinoid treatment altered behavioral responses in the forced swim test. To this aim, we administered the potent CB1 receptor agonist HU-210 (0.1 mg/kg) for 12 days and then subdivided into three groups: vehicle, 10 mg/kg imipramine or 10 mg/kg desipramine. Animals that had received chronic HU-210 exhibited significantly less immobility than vehicle treated animals, which in turn was matched by a selective increase in struggling behavior. In this study, desipramine, but not imipramine, produced an antidepressant response in vehicle treated animals. More interestingly though, in HU-210 treated animals desipramine resulted in a robust suppression of immobility while imipramine treated animals behaved identically to those treated with imipramine in the vehicle treated group. Collectively, these data demonstrate that chronic cannabinoid treatment can reduce immobility in the forced swim test possibly through a noradrenergic mechanism. In support of this hypothesis, animals treated with desipramine (a norepinephrine reuptake inhibitor) exhibited robust immobility in HU-210 treated animals, while the response to imipramine (a non-selective 5-HT reuptake inhibitor) was not affected by HU-210 treatment.
39. **ASSESSMENT OF EMOTION-RELATED BEHAVIORS IN NPY Y1 AND Y2 RECEPTOR KNOCK-OUT MICE.** Rose-Marie Karlsson<sup>1,2</sup>, Markus Heilig<sup>1</sup>, Jacqueline Crawley<sup>3</sup> and Andrew Holmes<sup>2</sup> Laboratory of Clinical and Translational Science, National Institute of Alcoholism and Alcohol Abuse, National Institute of Health, Bethesda, Maryland. Section on Behavioral Science and Genetics, Laboratory for Integrative Neuroscience, National Institute of Alcoholism and Alcohol Abuse, National Institute of Health, Rockville, Maryland, Laboratory of Behavioral Neuroscience, National Institute of Mental Health, National Institute of Health, Bethesda, Maryland. Neuropeptide Y (NPY) is densely localized in brain regions implicated in the mediation of emotion and targeting this system may offer opportunities for the development of novel treatments for affective illness. Previous studies have shown that intracerebral administration of NPY produces anxiolytic- and antidepressant-like behaviors in rodents. However, which of the 5 NPY receptor subtypes (Y1-Y5) mediate these effects remains to be fully determined. Administration of compounds with selectivity for either Y1R or Y2R, as well as gene deletion of Y1R and Y2R in ‘knockout’ (KO) mice, produces alterations in emotion-related behaviors under certain conditions.

The aim of the present study was to confirm and extended these data. Y1R KO and Y2R KO on a congenic C57BL/6 background were compared to their wild-type littermates (WT) on tests for anxiety-like behavior (novel open field, elevated plus-maze, light/dark exploration test), depression-related behavior (forced swim test), and emotional memory (Pavlovian fear conditioning). Results showed that Y1R KO mice have late-onset obesity and exhibited evidence of a modest increase on some tests for anxiety- and depression-related behavior as compared to WT. Y2R KO mice did not show significant changes in emotion-related behaviors. These data are consistent with recent reports that emotion-related behaviors in Y1R KO and Y2R KO mice may be more modest than indicated in earlier reports. Y1R KO and Y2R KO mice remain a valuable tool for delineating the receptor subtypes mediating the anxiolytic- and antidepressant-like effects of NPY administration.

40. REPEATED EXPOSURE TO CORTICOSTERONE INCREASES DEPRESSION-LIKE BEHAVIOR IN TWO DIFFERENT VERSIONS OF THE FORCED SWIM TEST INDEPENDENTLY OF ALTERATIONS IN NONSPECIFIC MOTORIC BEHAVIOR. Kalynchuk, L.E.; Marks, W.; Fournier, N.M. Dept. of Psychology, University of Saskatchewan, Saskatoon, SK S7V1C9 Canada. Repeated exposure to stress is a known risk factor for the onset of depression. However, the specific relationship between stress, glucocorticoids, and depression is not well understood, partly because many animal models of repeated stress produce inconsistent behavioral changes. We have recently shown that repeated high dose injections of corticosterone (CORT) reliably increase depression-like behavior on a modified, one-day version of the forced swim test. The purpose of this experiment was to compare the effect of these CORT injections on our modified forced swim test and the traditional two-day version of the forced swim test, and to determine whether altered behavior in the forced swim test could be due to nonspecific motoric effects. Separate groups of rats received either a high dose CORT injection (40mg/kg) or a vehicle injection every day for 21 consecutive days. Then, half the rats from each group were exposed to the traditional two-day forced swim test and the other half were exposed to our modified one-day forced swim test. After the forced swim testing, all the rats were tested in a novel open field and in a grip strength test. The CORT injections significantly increased immobility and decreased the latency to immobility in both versions of the forced swim test. However, they had no significant effect on grip strength or overall open field exploration. These results show that repeated CORT injections increase depression-like behavior regardless of the specific parameters of forced swim testing, and that these behavioral changes are independent of nonspecific motoric effects.
41. "ANTIDEPRESSANT-LIKE" EFFECTS OF DAT OR NET, BUT NOT SERT, GENE KNOCKOUT IN THE FORCED SWIM TEST. Perona, M.T.(1); Waters, S.(1); Hall, F.S.(1); Sora, I.(2); Lesch, K.P.(3); Murphy, D.L.(4); Caron, M.(5); Uhl, G.R.(1) (1)Molec. Neurobiol. Branch, NIDA-IRP/NIH/DHHS, Baltimore, MD; (2)Dept. Neurosci., Tohoku Univ. Grad. Sch. Med. Sendai, Japan; (3)Dept. Psychiatry, Univ. Wuerzburg, Germany; (4)Lab. Clin. Sci., NIMH-IRP/NIH/DHHS, Bethesda, MD; (5)Depts. Cell Biol. and Med., Duke Univ., Durham NC. Antidepressant drugs produce therapeutic actions and many of their side effects via blockade of the plasma membrane transporters for serotonin (SERT), norepinephrine (NET) and dopamine (DAT). Many antidepressants block several of these transporters; some are more selective. Mice with knockouts of the genes that encode these transporters provide interesting models for effects of chronic antidepressant treatments. To examine the role of these monoamine transporters in depressive behavior forced swim test behavior was examined in DAT, NET and SERT knockout mice and wildtype littermates. DAT gene knockout had the greatest antidepressant-like effects on forced swim test behavior, virtually eliminating immobility. In confirmation of previous findings, NET knockout (KO) mice exhibited reduced immobility but SERT KO mice did not. Effects of DAT deletion were not simply due to hyperactivity. Decreased immobility was observed in heterozygous DAT KO mice that display modest alterations in locomotion as well as in homozygous DAT KO mice that display marked changes in locomotion. Struggling (e.g. escape attempts) were increased, while swimming was almost eliminated in DAT -/- mice. Reduced struggling in combination with increased immobility has been observed in the FST in animal models of depression. Reduced expression of DAT thus produces effects complementary to models of depression that are larger than those produced by reduced expression of NET or SERT. These data support re-evaluation of the role of differences in DAT expression in the etiology of depression and the efficacy of direct blockade of DAT in treatment of depression. In particular these data raise the possibility that DAT gene variants, or reduced DAT expression, may complement other gene variants that increase predisposition to depression.

42. INTRA-SEPTAL INFUSIONS OF MUSCIMOL DIFFERENTIALLY AFFECT RATS' DEFENSIVE RESPONSES IN THE PLUS-MAZE AND CAT-ODOR TESTS. Menard, J.L.; Patel, R. Queen's University, Kingston, ON, CANADA.K7L 3N6. Previous studies showed that intra-septal infusions of the benzodiazepine receptor agonist, midazolam suppress rats' burying behavior in the shock-probe test and their open-arm avoidance in the elevated plus-maze. We currently explored whether inhibiting septal activity similarly reduces rats' defensive responses towards a predator cue in the cat odor test. Anesthetized rats were chronically implanted with guide cannulae aimed at the septum. Following recovery, the rats were infused with either saline or the GABA-A receptor agonist, muscimol and then were tested in the plus-maze. One week later, rats received a 2nd infusion and were tested in the cat odor test. Intra-septal infusions of muscimol suppressed open-arm avoidance in the plus-maze. In contrast, this same treatment failed to alter rats' defensive reactions towards a piece of cat collar that had been previously worn by a cat (i.e., a soiled collar). This was not secondary to low baseline levels of defensive behavior. Rats exposed to a soiled cat collar displayed significantly more defensive behavior (e.g., hide-box entries and risk-assessment behaviors) than did rats exposed to clean control collars. Interestingly, intra-septal muscimol selectively reduced the number of times rats hid in the hide-box, as well the number head-pokes they made from the hide-box entrance. However, the magnitude of this effect was the same for both soiled collar and control collar rats. Together, these findings suggest that although the septum regulates rats' behavioral defense profiles in threatening environments, it does not seem to regulate defensive responses that are specific to a predator odor cue.
43. ANTINOCICEPTIVE AND ANXIOLYTIC TOLERANCE TO NITROUS OXIDE AND CROSS-TOLERANCE TO CHLORDIAZEPOXIDE IN THE ABDOMINAL CONSTRICTION TEST AND LIGHT/DARK EXPLORATION TEST. Rick W. Heckert, Daniel G. Quock, and Raymond M. Quock Graduate Program in Pharmacology/Toxicology and Department of Pharmaceutical Sciences, College of Pharmacy, Washington State University, Pullman, WA 99164-6534 USA. We have had a long interest in the pharmacology of the anesthetic gas nitrous oxide (N<sub>2</sub>O), notably the mechanism of its antinociceptive and anxiolytic effects. The development of tolerance to N<sub>2</sub>O-induced antinociception has been reported (Berkowitz et al., *Anesthesiology* 51:309, 1979), but possible tolerance to N<sub>2</sub>O-induced anxiolysis has not been investigated. Male NIH Swiss mice were exposed to compressed air (CA) or 70% N<sub>2</sub>O/30% O<sub>2</sub> for 0-24 hr, removed from the exposure chamber for 30 min, and then assessed for responsiveness to 70% N<sub>2</sub>O in the abdominal constriction test or light/dark exploration test. Compared to CA controls, animals exposed to 90 min of 70% N<sub>2</sub>O had a significantly reduced responsiveness to the antinociceptive effect of a subsequent exposure to N<sub>2</sub>O. Compared to CA controls, prior exposure to no less than 9 hr of 70% N<sub>2</sub>O caused tolerance to the anxiolytic-like effect of a subsequent exposure to N<sub>2</sub>O. Mice that were exposed to at least 9 hr of 70% N<sub>2</sub>O also demonstrated a cross-tolerance to chlordiazepoxide-induced anxiolytic-like effects. These results offer preliminary evidence for the development of tolerance to the anxiolytic effects of N<sub>2</sub>O and cross-tolerance with chlordiazepoxide. (This investigation was supported in part by funds provided for medical and biological research by the State of Washington Initiative Measure No. 171.)
44. DO INTERLEUKIN-1 AND LIPOPOLYSACCHARIDE INDUCE ANXIETY? Dunn, A.J.; Swiergiel, A.H. Dept. Pharmacology, Toxicology and Neuroscience, Louisiana State University Health Sciences Center, Shreveport, LA 71130 USA. Interleukin-1 (IL-1) has been reported to be anxiogenic because it induces anxiety-like changes in the elevated plus-maze (EPM), and in the open field (OF). Male CD-1 mice were injected ip with mouse IL-1 $\beta$  (100, 300 or 1000 ng) or lipopolysaccharide (LPS: 0.5, 1 or 5  $\mu$ g) and were subsequently tested in the OF and the EPM. 300 ng and 1  $\mu$ g mL-1 $\beta$  or 1 or 5  $\mu$ g LPS injected 1 hour previously dose-dependently decreased open arm entries and the time spent on the open arms in the EPM, effects normally considered to reflect anxiety. However, the number of entries to closed arms, and all arms, was also reduced, indicating an overall decrease in locomotor activity. The same doses of IL-1 and LPS decreased activity in the central area of the OF. However, line-crossings in the peripheral areas were also reduced, once again indicating a general decrease in locomotor activity. These results indicate that both IL-1 $\beta$  and LPS can induce anxiety-like effects in the EPM and the OF. However, the doses necessary to induce these changes reduced feeding and activity in an open field and in the EPM. Thus the effects observed in the EPM and OF could be attributed to a general reduction in locomotor activity. Therefore, these results do not provide significant support for an IL-1 hypothesis of anxiety

45. INTERLEUKIN-1 AND LIPOPOLYSACCHARIDE INDUCE CYCLOOXYGENASE-2 (COX2) IN BRAIN ENDOTHELIA PARALLELLING THE INDUCED HYPOPHAGIA. Dunn, A.J.; Swiergiel, A.H.; Zhang, H.; Quan, N. Dept. of Pharmacology, Toxicology and Neuroscience, Louisiana State University Health Sciences Center, Shreveport, LA 71130 USA. Interleukin-1 (IL-1) and LPS injection induces hypophagia in mice. This response to IL-1 is rapid and dissipates within an hour, whereas that to LPS is slower and more prolonged. These effects of IL-1 and LPS are sensitive to cyclooxygenase (COX) inhibitors. Previous studies showed that COX1 is involved in the early response, while COX2 is important later. We studied induction of COX2 in the brains of mice treated with IL-1 $\beta$  or LPS ip. COX2-ir was sparse in the brains of controls, but IL-1 and LPS both increased expression of COX2 in the brain. The COX2 induction was not regionally specific, but appeared to be confined to blood vessels. COX2 in the parenchyma did not change significantly following IL-1 $\beta$  or LPS. This is consistent with the presence of receptors for IL-1 and LPS on brain endothelial cells, and with results showing that IL-1-induced changes in feeding to selective COX2 inhibitors appears around 1-2 h after IL-1 or LPS, and these responses are diminished in COX2-ko mice. The time courses of the IL-1- and LPS-induced increases in plasma corticosterone resembled those in feeding, but, the changes in body temperature (a delayed fever) were not obviously related. Thus endothelial COX2 may also be involved in the HPA axis activation. The results suggest that the hypophagia induced by IL-1 $\beta$  and LPS is mediated by binding to endothelial cells in the brain and subsequent induction of COX2 resulting in the production of prostanoids that induce the hypophagic response.
46. CORTICOTROPIN-RELEASING FACTOR IN THE DORSAL RAPHE INCREASES PREFRONTAL CORTICAL SEROTONIN VIA CRF-2 RECEPTORS AND MEDIAN RAPHE ACTIVITY. A.R. Burke<sup>1</sup>, N.J. Mouw<sup>1,2</sup>, R.B. Pringle<sup>1</sup>, M.J. Watt<sup>1,2</sup>, J.L. Barr<sup>1</sup>, J.L. Lukkes<sup>1</sup>, C.H. Summers<sup>1,2</sup>, K.J. Renner<sup>1,2</sup> & G.L. Forster<sup>1</sup>. <sup>1</sup> Basic Biomedical Sciences, <sup>2</sup> Biology Dept., University of South Dakota, Vermillion, SD, USA. Serotonin (5HT) and corticotropin-releasing factor (CRF) are thought to play an important role in fear and anxiety behaviors. We have previously demonstrated that CRF applied to the dorsal raphe nucleus (dRN) increases 5HT release in the medial prefrontal cortex (mPFC) of rats, which appears to suppress fear behavior. We determined which CRF receptor type in the dRN mediates mPFC 5HT activity and tested the role of median raphe nucleus (mRN) in these 5HT responses. Pre-infusion of the CRF-2 receptor antagonist, ASV, into the dRN of urethane-anesthetized rats abolished the excitatory effects of CRF on mPFC 5HT release, as measured with *in vivo* microdialysis. In contrast, pre-treatment of the dRN with the CRF-1 receptor antagonist, antalarmin, had no effect on CRF-mediated effects. Pharmacological inactivation of the mRN prior to CRF infusion into the dRN also blocked increased mPFC 5HT release. These results imply that CRF acts upon CRF-2 receptors in the dRN to influence mPFC 5HT activity and that interplay between the dRN and mRN contribute to this CRF-induced release of 5HT in the mPFC. Supported by NIH grants P20 RR15567, R03 MH068303 & R01 DA019921.
47. IDENTIFYING GENETIC FACTORS UNDERLYING AMYGDALA VOLUME AND EMOTION-RELATED PHENOTYPES IN RECOMBINANT INBRED MICE. Yang, R.J.<sup>1</sup>; Mozhui, K.<sup>2</sup>; Lu, L.<sup>2</sup>; Williams, R.W.<sup>2</sup>; Holmes, A.<sup>1</sup> <sup>1</sup>Section on Behavioral Science and Genetics, Laboratory for Integrative Sciences, NIAAA, Rockville, MD; <sup>2</sup>Department of Anatomy and Neurobiology and Department of Pediatrics, University of Tennessee Health Science Center, Memphis, TN. The amygdala is a key neural locus region regulating emotional processes in animals and man. Patients with anxiety disorders exhibit abnormalities in amygdala volume and altered functional connectivity with other brain regions such as the prefrontal cortex. However, it remains uncertain whether these disturbances are a consequence of mental illness or precede and predispose individuals to anxiety disorders, perhaps due to genetic factors. One approach to identifying genetic determinants of amygdala function and 'emotion-related' behaviors is via QTL analysis of recombinant inbred (BXD RI) strains of mice. BXD strains were generated by sibling-mating of the progeny of C57BL/6J x DBA/2J, with each RI inheriting a unique pattern of chromosome segments from the two parents. QTL analysis provides a measure of the strength of an association between markers of inheritance and phenotypic measures of emotion/amygdala function. In the present study, we combined stereological data on volume and cell number of the basolateral complex of the amygdala (BLA) in 15 BXD RI and both parental strains with extensive behavioral data. The strains were compared on tests for fear-, anxiety-, depression- and stress-related behaviors (elevated plus-maze, light/dark exploration test, novel open field test, forced swim test, Pavlovian fear conditioning, stress-induced plasma corticosterone). Results showed that BLA volume differed markedly across strains. Behaviorally, there were significant

strain differences on all tasks, with particular strains showing consistently high or low 'emotion-related' behaviors, relative to the other strains. Detailed analyses are being performed to identify covariation between BLA volume and emotion-related behavior, and QTL associated with these phenotypes. Present data could have implications for elucidating genetic factors contributing to the pathophysiology of affective disease.

### ***Sexual, endocrine and hormonal factors***

48. SEXUAL INTERACTION PRIOR TO ACUTE PREDATOR ODOR STRESS CAUSES INCREASED HIPPOCAMPAL CELL PROLIFERATION AND AFFECTS DEFENSIVE BEHAVIOR AMONG MALE RATS. Spritzer, M.D.<sup>1</sup>; Weinberg, A.<sup>1</sup>; Viau, V.<sup>2</sup>; Galea, L.A.M.<sup>1</sup>; Dept. of Psychology,<sup>1</sup>, Dept. of Cellular and Physiological Sciences<sup>2</sup>, The University of British Columbia, Vancouver, Canada. Acute exposure to the predator odor trimethyl thiazoline (TMT) has been found to increase defensive behaviors and decrease cell proliferation within the dentate gyrus of the hippocampus among adult male rats. Sexual interactions lead to multiple hormonal changes among male rats, and hormone levels have been shown to influence hippocampal cell proliferation. Furthermore, sexual interactions have anxiolytic effects among male rats. Therefore, prior sexual interactions could influence cell proliferation and the behavioral response to acute stress among male rats. Sexually competent adult male rats were assigned to four treatment groups: sex/TMT, sex/water, no-sex/TMT, no-sex/water. The "sex" groups were exposed to an estrous female for 30 min on five consecutive days, while the "no-sex" groups were exposed to an empty sex-testing chamber. On the fifth day, rats were transferred from the sex-testing chambers to Plexiglas boxes containing a vial of either TMT or water. All rats were injected with the DNA-synthesis marker bromodeoxyuridine (BrdU; 200 mg/kg) during TMT or water exposure and were perfused 24 h later. The sex/TMT group had higher cell proliferation within the dentate gyrus than did any other group. The no-sex/TMT group displayed more stretching behavior toward the vial than did the no-sex/water group, whereas there was no difference in stretching between the sex/TMT group and the sex/water group. Within the sex/TMT group, males experiencing more ejaculations showed more defensive burying. Hence, sexual interactions prior to TMT exposure altered the behavioral and neurological response to TMT. These results suggest that the effects of an acute stressor can be modified by past social experiences.
49. EFFECTS OF GONADECTOMY ON SOCIAL INTERACTIONS IN MICE (*MUS MUSCULUS*). Clipperton, A.E.; Cragg, C.L.; Wood, A.J.; Choleris, E. Dept of Psychology, Dept of Biomedical Science, Dept of Zoology, University of Guelph, Guelph, Ontario, Canada. Hormones are known to play important roles in social behaviour. Testosterone, for example, has been shown to mediate aggressive behaviours in males, and as testosterone is converted to estradiol in the male brain, these effects could result from the action of estradiol on its receptors. The present study investigates the effect of gonadectomy on social interactions in mice. Intact and gonadectomized male and female mice were individually housed for a week in order to establish a territory, and were then exposed to a same-sex, gonadectomized intruder mouse in their home cage for 15 minutes. The interactions were videotaped and analyzed for 21 behaviours, which fell into four categories: social aggressive, social investigative, nonsocial active, and nonsocial inactive. The test was divided into three five-minute intervals to assess the time course of the behaviours over the duration of the test. Preliminary results show that the gonadally intact females engaged in more nonsocial inactive behaviour and social aggressive behaviour, while the ovariectomized (Ovx) females performed more social investigation. Additionally, the Ovx females' performance of nonsocial active behaviours (e.g., rearing, exploration) peaked during the middle segment of the test, while the intact females increased their nonsocial active behaviour throughout the duration. These results suggest that the female gonadal hormones mediate both aggressive and investigative social behaviour, as well as nonsocial active behaviours such as exploration. Ongoing studies with males may show a similar effect of castration on social behaviour.
50. FUNCTIONAL IMAGING OF SOCIAL BONDING IN TITI MONKEYS (*CALLICEBUS CUPREUS*). Bales, K.L.<sup>1</sup>; Mason, W.A.<sup>1</sup>; Cherry, S.R.<sup>2</sup>; Catana, C.<sup>2</sup>; Mendoza, S.P.<sup>1</sup> 1. Dept of Psychology and California National Primate Research Center, University of California, Davis, 95616. 2. Center for Molecular and Genomic Imaging, UC-Davis. The numerous differences in rodent and primate neurobiology make a non-human primate model of the neuroendocrine basis of social bonding desirable. Titi monkeys (*Callicebus cupreus*) form strong pair-bonds, characterized by preference for a familiar

partner and activation of the hypothalamic-pituitary-adrenal axis upon separation. We used functional neuroimaging in order to investigate baseline differences in brain metabolism of pair-bonded and non-bonded monkeys. Positron emission tomography (PET) technology using fluorodeoxyglucose (FDG) measures glucose metabolism, which reflects changes in functional synaptic activity. 16 conscious adult titi monkey males (4 that were housed alone, 12 that were pair-bonded) were used in this study. Males were injected with 1 mCi/kg of FDG, then returned to their cage; pair-bonded males were returned to their mates. Approximately 40 min later, the males were placed under anesthesia and scanned for 1 hour on a microPET P4 primate scanner. 3 of the 4 lone males were then introduced to a female and rescanned 48 hours later. Brain regions showing significant ( $p < 0.05$ ) differences between males in pair-bonds and lone males included the nucleus accumbens, ventral pallidum, medial preoptic area, supraoptic nucleus of the hypothalamus, and hippocampus. In contrast, the caudate-putamen, insular cortex, mediodorsal thalamus and periaqueductal gray did not vary significantly in metabolic activity based on social status of the male. Supported by a pilot grant from the California National Primate Research Center.

51. EXPRESSION OF THE GALANIN-LIKE PEPTIDE GENE IN THE POSTERIOR PITUITARY GLAND BY OSMOTIC CHALLENGE AND ACUTE INFLAMMATORY STRESS. Ueta, Y.; Kawasaki, M.; Isa, K.; Kise, Y.; Saito, J.; Fujihara, H. Dept. of Physiology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu 807-8555, Japan Galanin-like peptide (GALP) has been newly isolated from the porcine hypothalamus as endogenous ligand for galanin receptor subtype 2. In the rat pituitocytes in the posterior pituitary gland (PP) GALP mRNA was markedly increased after dehydration, chronic salt loading and intraperitoneal (i.p.) injection of bacterial endotoxin lipopolysaccharide (LPS). Pretreatment with indomethacin attenuated LPS-induced increase of GALP mRNA levels in the PP significantly but not completely. There is possibility that inflammatory signals such as cytokines except synthesis of prostaglandins (PGs). We examined the effects of intravenous (i.v.) administration of proinflammatory cytokines such as interleukin  $1\beta$  (IL-1  $\beta$ ), IL-6 and tumor necrosis factor  $\alpha$  (TNF  $\alpha$ ) on the expression of the GALP gene in the PP, using *in situ* hybridization histochemistry. Six hours after i.v. administration of IL-1  $\beta$ , IL-6 and TNF  $\alpha$  in conscious rats GALP mRNA levels were increased in the PP. This result suggests that not only PGs but also proinflammatory cytokines such as IL-1  $\beta$ , IL-6 and TNF  $\alpha$  may cause an increase of the GALP gene expression in the PP after i.p. administration of LPS.
52. SOCIAL ISOLATION AFFECTS CORTICOTROPIN-RELEASING FACTOR-MEDIATED SEROTONIN RELEASE IN THE NUCLEUS ACCUMBENS. Lukkes, J<sup>1</sup>; Forster, G<sup>1</sup>; Watt, M<sup>1,2</sup>; Renner, K<sup>1,2</sup>; Summers, C<sup>1,2</sup>. <sup>1</sup>Basic Biomedical Sciences, <sup>2</sup>Biology & Neuroscience, University of South Dakota, Vermillion, SD. Early life isolation from social contact is a stressful experience that leads to long-lasting alterations in behavior and monoaminergic activity. Corticotropin-releasing factor (CRF) is a neurohormone that mediates stress, anxiety, and monoaminergic activity. Neuroactive CRF plays an important role in regulating serotonergic systems in response to stress-related stimuli, with potential long-term behavioral consequences. This study investigated the effects of social isolation on CRF-mediated serotonin (5HT) release in a key limbic structure, the nucleus accumbens (NAc). On postnatal day 21, male rats were housed either individually, or in groups of 2-3, for a 3-week period during a critical phase of development when pre-adolescents are particularly vulnerable to stress. After 3 weeks of isolation, rats were group-housed according to treatment for a further 2 weeks. After the 5-week isolation/re-socialization procedure, male rats were implanted with microdialysis probes into the NAc, and CRF or vehicle was infused into the dorsal raphe (dRN). A significant decrease in NAc 5HT release was observed in group-housed animals infused with CRF (100 ng/0.5  $\mu$ l) in the dRN, but this effect was completely absent in isolation-housed animals. In contrast, infusion of 500 ng (0.5  $\mu$ l) CRF into the dRN resulted in a significant acute increase in NAc 5HT release in group-housed animals, but isolated animals resulted in an extended increase in NAc 5HT. This study suggests that isolation during the early part of development causes alterations in CRF-mediated 5HT limbic systems underlying stress and anxiety responses.
53. MALE URINARY STEROID LEVELS APPROACH VALUES SUFFICIENT TO ACCOUNT FOR THE BRUCE EFFECT IN MICE. deCatanzaro D.; Beaton, E.; Khan, A.; Vella, E. Dept. of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, Ontario, L8S 4K1, Canada. Early pregnancy in mammals can be disrupted by novel males and their urine, a phenomenon known as the Bruce effect. Treatment with minute doses of exogenous estrogens can also completely terminate intrauterine implantation of fertilized ova. We established minimal doses of estradiol necessary to disrupt pregnancy,

quantified levels of androgens and estrogens in male urine, and examined behaviour that males use to deliver their excretions to previously inseminated females. Daily dosages of less than 0.15 µg of 17β-estradiol during days 1-5 of pregnancy reliably disrupt pregnancy in inseminated female mice, both when administered subcutaneously and when applied to the external nasal area of the female. Enzyme immunoassays applied to male excretions indicate that substantial quantities of unconjugated estradiol and testosterone are reliably present in both feces and urine. A small but significant increment in the amount of urinary estradiol was observed in males housed nearby previously inseminated females as opposed to those housed in isolation. This influence was absent in the sire and absent in novel males when the sire was also present. Novel males actively deliver their steroid-laden urine to nearby inseminated females through nasal-genital and other forms of contact. The quantity of active steroids in novel male urine approaches the level sufficient to account for disruption of intrauterine implantation in nearby inseminated females.

54. ADRENALECTOMY-INDUCED HIPPOCAMPAL GRANULE CELL DEATH AND MEMORY DEFICITS: EFFECTS OF CHRONIC CORTICOSTERONE REPLACEMENT THERAPY AND STIMULATION OF NEUROGENESIS. Simon C. Spanswick\*1, Jon R. Epp\*2, Julian R. Keith3, and Robert J. Sutherland1 \*these authors contributed equally. 1.Canadian Centre for Behavioural Neuroscience, University of Lethbridge 2.Department of Psychology, University of British Columbia 3.Department of Psychology, University of North Carolina Long-term bilateral adrenalectomy (ADX) produces a selective loss of the granule cell layer in the dentate gyrus of the hippocampus in rats. This loss of cells is associated with learning and memory deficits in a variety of behavioural tasks. Here we report on an experiment designed to determine if treatment with corticosterone (CORT) alone or treatment with a combination of CORT and fluoxetine, a neurogenic compound, can alleviate the behavioural deficits associated with ADX. Both ADX and control rats were trained on a moving, hidden version of the Morris water task (MWT) prior to chronic administration of CORT or a combination of CORT and fluoxetine, or CORT and vehicle. After six weeks of treatment, all rats were retested in the MWT. Brains were then labeled for both the endogenous proliferative marker Ki67 and the migratory marker doublecortin (DCX). Prior to treatment with CORT or fluoxetine, ADX rats were behaviourally impaired. Neither chronic treatment with CORT nor chronic treatment with CORT and fluoxetine normalized the behaviour of ADX animals in the MWT. Both Ki67 and DCX expression did not differ between ADX-fluoxetine, ADX-vehicle or controls, suggesting that neurogenesis continues in the ADX rat at a normal level. Interestingly, ADX-fluoxetine rats displayed a tendency for thicker granule cell layers than ADX-vehicle rats perhaps as a result of a transient increase in the neurogenic process. Thus, we find that chronic ADX is associated with deficits in the MWT that are not alleviated by treatment with CORT or a combination of CORT and fluoxetine. Supported by AHFMR, CIHR, and NIH.
55. BULLYING DURING PUBERTY AFFECTS PHYSIOLOGICAL MARKERS OF STRESS IN YOUNG ADULTS. \*Hamilton, L.D., +Newman, M.L., & \*Delville, Y. \*Department of Psychology, The University of Texas at Austin, Austin, TX, 78712, USA. +Department of Psychology, Bard College, Annandale, NY, 12504, USA. Bullying during puberty is undoubtedly a stressful experience for victims, and this stress may be manifested in a variety of ways, from exhibiting learned helplessness to extreme violent revenge. Stress has also been linked to numerous health problems, particularly cardiovascular disease. However, the association between bullying during adolescence and cardiovascular responses has never been tested. In the present study we examined physiological responses to a stressful laboratory situation among participants pre-selected for the absence or existence of a history of bullying. Blood pressure, heart rate, and cortisol levels were measured before the introduction of the stressor (Time 1), during the stressful situation (Time 2), and after the stressor had been removed (Time 3). Participants who had a history of frequent bullying showed higher cortisol levels at Time 3. Women who had been frequently bullied also showed a 10% higher heart rate at all three time points compared to women who had never been bullied. Elevated cortisol levels in the bullied participants showed longer stress responses and suggest differences in coping responses. In addition, the data also suggest that experience with bullying during puberty is a risk factor for cardiovascular disease later in adulthood. Supported by IOB0516272 from the NSF to YD.
56. SEXUALLY DIMORPHIC EFFECTS OF DOPAMINE RECEPTOR SUBTYPES ON ALLOPARENTAL BEHAVIOR IN THE PRAIRIE VOLE. Hostetler, C.M. and Bales, K.L. Department of Psychology, University of California, Davis, CA 95616. The mesolimbocortical pathway is directly implicated in maternal behavior, and is associated with motivational processes of reward. This pathway is characterized



by two dopamine receptor subtype groups, D1-like and D2-like, with distinct physiological properties, distribution, and behavioral functions. The evolution of paternal behavior in biparental species appears to at least partially involve sexually dimorphic neuroendocrine regulation. Alloparental response to a pup is sexually dimorphic in sexually naïve prairie voles: whereas males tend to be highly parental, females are often infanticidal upon contact with a pup. This study examines the role of dopamine receptor subtypes on the alloparental behavior of sexually naïve prairie voles (*Microtus ochrogaster*). Male and female voles were given one of the following treatments (n=10/treatment): saline (vehicle control), SKF38393 (D1 agonist), quinpirole (D2 agonist), SCH23390 (D1 antagonist), and eticlopride (D2 antagonist). After a habituation and treatment uptake period of one hour, an unrelated vole pup was then placed in the testing chamber with the vole and behavior was videotaped for 20 minutes. The following pup-directed behaviors will be scored: latency to approach pup, sniffing, licking or grooming, huddling, non-huddling physical contact, retrievals, and attacks. We hypothesize that treatments will have receptor subtype specific and sexually dimorphic effects on these behaviors, allowing us to further characterize dopaminergic function in the social behavior of this species.

57. GENDER-RELATED HEMISPHERIC LATERALIZATION OF EVENT RELATED POTENTIALS EVOKED BY EMOTIONAL CONTENT. Gasbarri, A.(1); Arnone, B.(1); Pompili, A.(1); Marchetti, A.(1); Delphino, P.(2); Pacitti, C.(1); Tavares, M.C.(2); Tomaz, C.(2). Dept. of Sci.& Biomed. Technol., Univ. of L'Aquila, Italy (1) Dept. of Physiol. Sci., Lab. of Neurosci.& Behavior, Univ. Brasília, Brazil (2) Many researches suggest that emotional arousal can promote memory storage. The aim of this study was to evaluate the effects of emotional content on declarative memory, utilizing 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. We used event related potentials to evaluate whether there is a sex-related hemispheric lateralization of electrical potentials elicited by the emotional content of a story. We compared left and right hemisphere P300 waves, recorded in P3 and P4 electrode sites, in response to emotional or neutral stimuli in men and women. In the left hemisphere, emotional stimuli elicited a stronger P300 in women, compared to men, as indexed by both amplitude and latency measures; moreover, the emotional content of the story elicited a stronger P300 in the right hemisphere in men than in women. The better memory for the arousal material may be related to the differential P300 at encoding. These data indicate that both sex and cerebral hemisphere constitute important, interacting influences on emotion, and emotional memory.
58. ANXIOLYTIC EFFECTS OF MUSIC DEPEND ON OVARIAN STEROID IN FEMALE MICE. Chikahisa S.; Sei H.; Sano A.; Kitaoka K.; Morita Y. Dept. Integrative Physiology, The University of Tokushima Graduate School, Tokushima 770-8503, Japan Music is known to be able to elicit emotional changes including anxiolytic effect. The previous studies have revealed gender differences in music processing in human. The gonadal steroid hormone estrogen (E2) has been associated with anxiety levels. In the present study, we examine whether the effect of music on anxiety is related with ovarian steroid in female mice. Behavioral paradigms measuring anxiety (open field, elevated plus maze, dark-light transition and marble burying test) were tested in gonadally intact (sham-operated) and ovariectomized (OVX) female mice treated with placebo (OVX + placebo) or chronic estradiol (OVX + E2) replacement. In three behavioral tests except for open field, sham-operated mice exposed to music showed less anxiety than those exposed to white-noise and silence, while OVX + placebo mice did not show these effects at all. OVX + E2 mice showed the anxiolytic effect of music only in the marble burying test. These results suggest that exposure to music reduce anxiety levels, and ovarian steroids may be, at least partially, involved in the anxiolytic effects of music observed in female mice.
59. BEHAVIORAL AND CELLULAR MODULATION OF AAS IN REPRODUCTIVE-RELATED BEHAVIORS AND REWARD IN ADULT MICE. Parrilla, J1; Rundle, V2; Arriaga, D1; Jorge, JC3; Barreto-Estrada, JL3. Department of Sciences, Mathematics and Technology-Universidad del Este, Carolina, P.R.,1 University of Puerto Rico-Río Piedras,2 University of Puerto Rico-MSU, Department of Anatomy3. Previous studies using IHC have shown modulation of GABA-IR cells after anabolic androgenic steroid (AAS) exposure in a region-specific manner in the brain. The percent of GABA-IR cells in the mPOA and the VMN were significantly modulated in female mice, while in the males, the VTA was affected. In this study we have investigated the effect of AAS in sexual behaviors in females and voluntary ethanol consumption in males. The non-aromatizable AAS, 17alpha-methyltestosterone or saline were

chronically administered through an osmotic pump. For female sexual behavior, frequency of mounts, pelvic thrusts, lordosis, fights and escapes were measured. We have found that AAS-treated females (F/AAS) showed a low number of mounts when paired with an intact male. This behavior was accompanied with aggressive episodes. However, F/AAS showed a strong significant tendency to mount a female control (F/C) in a male-like pattern. When compared mounts and pelvic thrust to F/C, there was no difference between a male and F/AAS. Finally, lordosis strength (LS) was greater when a male and F/C were paired. In males, we observed a significant increase in the preference score for ethanol consumption during the second week of AAS withdrawal. The results presented in this study suggest that androgen exposure regulates reproductive-related behaviors as well as some aspects of reward activity through the GABAergic mechanism of the brain. Supported by MBRS-RISE (GM61838), (1R25-GM066250-01A1), NIH-COBRE (RR15565), RCMi (G12RR03051), and NIH-MRISP (MH048190).

60. ASSOCIATIONS BETWEEN OFFENSIVE AGGRESSION AND IMPULSIVITY IN ADULT MALE GOLDEN HAMSTERS. Catalina Cervantes, Juan Salinas, and Yvon Delville. Psychology Department and Institute for Neuroscience, University of Texas, Austin, TX 78712. There are strong differences in definitions and subtypes of aggression between humans and animals. For example, impulsive aggression is well characterized in humans, but not in animals. This study attempts to provide a model of impulsive aggression in golden hamsters and identify differences in aggression levels and associated impulsive characteristics. Adult male hamsters were tested for offensive responses for 10 consecutive days under a resident-intruder paradigm. Animals were screened for level of aggression (High-Aggression vs. Low-Aggression). Animals were then trained under a fixed-ratio schedule (FR-1) to obtain food pellets, and then tested under a choice paradigm as an index for impulsivity. The choice paradigm involved an IR-lever, which dispensed one pellet immediately, and a DR-lever, which dispensed 5-6 pellets after a 30-second wait. Our data showed significant differences between HAgg and LAgg animals. H-Agg consistently attacked and bit more frequently and faster than L-Agg. Also, there was a decreased efficiency of behavior in the H-Agg group, as indicated by the lower percentage of attacks that were followed by bites. Data from impulsivity testing showed that H-Agg had a higher number of both total lever presses and immediate lever presses than the L-Agg. Also, H-Agg had a preference for the IR-lever, while L-Agg preferred the DR-lever. Furthermore, reward ratios were calculated as the ratio of pellets received to number of lever presses made. H-Agg had significantly lower reward ratios on the DR-lever than the L-Agg. These data show an association between aggression and impulsivity and provide the possibility of using these traits to test for impulsive aggression, behavioral predictors and personality profiling. Funded by NSF IOB 0516272
61. MODULATION OF RISK ASSESMENT BEHAVIORS THROUGH GROUP I METABOTROPIC GLUTAMATE RECEPTORS IN THE BASOLATERAL AMYGDALA IN ESTROGEN-TREATED RATS. <sup>1</sup>De Jesús-Burgos MI, <sup>1</sup>Vázquez-Fuentes B.M.; <sup>2</sup>Torres-Llenza V.; <sup>2</sup>Ríos-Pilier J.; <sup>2</sup>Rodríguez S.; <sup>2</sup>Quiñones K.; and <sup>3</sup>Pérez-Acevedo N.L. <sup>1</sup>Dept of Biology, UPR- Bayamón Campus; <sup>2</sup>Dept of Biology, UPR- Río Piedras Campus; and <sup>3</sup>Dept of Anatomy, UPR-MSc Campus. Glutamate is an excitatory neurotransmitter that its function is mediated through ionotropic (iGluRs) and metabotropic glutamate receptors (mGluRs). mGluRs are widely expressed throughout the CNS including the basolateral nucleus (BLA) of the amygdala complex. A role for mGluRs has been implicated in the regulation of anxiety. Since females are more susceptible to develop anxiety-related behaviors, we hypothesize that these differences might be due to variations in the hormonal cycle. Comparisons of ovariectomized female rats that received either empty implants (OVX) or implants containing estradiol (OVX-EB) were tested. Adult ovariectomized Sprague Dawley rats were tested in the elevated plus-maze (EPM) to measure anxiety-related behaviors. In addition, risk assessment behaviors (RABs) were recorded during the EPM. RABs included: stretch attended postures, head dippings, flat attended behaviors, rearing, closed arm return, sniffing and grooming. The vehicle or 1 $\mu$ M DHPG, a group I mGluR agonist, were bilateral infused (0.5 $\mu$ L/side) 5 minutes prior to the EPM. Results show significant differences in head dipping, freezing and stretch attended postures within the OVX-EB group. These differences suggest that estrogen can have a modulatory effect in risk-assessment through mGluRs via BLA. De Jesús-Burgos MI and Ríos-Pilier J was supported and, Vázquez-Fuentes BM, and Torres-Llenza V are supported by MBRS-RISE Program (Rise GM61838). Ríos-Pilier J was supported by Alliance for Minority Participation (PR-LSAMP). Supported by RCMi Program (G12RR03051), NIH-COBRE (RR15565) and NIH-MRISP (MH048190).

62. EFFECT OF DIFFERENT TREATMENT SCHEDULE AND TEST ARENAS (TRADITIONAL AND MULTIPLE PARTNER CHOICE TEST) IN THE EXPRESSION OF PACING BEHAVIOR OF FEMALE RATS. Ferreira-Nuño, A; Morales-Otal, A.; Martínez-Flores, K., González-González, C; Fernández-Soto, C.; Olayo-Lortia, J.; Velázquez-Moctezuma, J. *Biól. Reprod.*, Universidad Autónoma Metropolitana-Iztapalapa. México. Pacing Behaviour (PB) could it be induced in ovariectomized (OVX) rats after the administration of estradiol benzoate (EB, 5 µg/rat) alone for 6 days or after 10 µg/rat of EB and progesterone (P, 1 mg/rat) 48 h and 4 h respectively, prior to be tested under the traditional arena used for PB (TA = 2 compartment chamber equally divided by a wall with a small hole through which only the female can enter or exit through the wall). Recently we study PB in a Multiple Partner Choice Test Arena (MPT), made with 4 acrylic cylinders disposed in a cross fashion, each with a sexually active male. The female placed in the central compartment, could choose the male she wants to mate, crossing the smaller hole that each cylinder has in the bottom. In this condition OVX female rats treated with two daily injections of EB (5 µg/rat) and P (1 mg/rat), remains the entire test with the preferred male in the MPT, without showing PB. To evaluate if the treatment schedule or the testing arena could influence the expression of PB, six OVX female rats received first 10 µg/rat of EB and 1 mg/rat of P respectively, 48 h and 4 h prior to be tested in the TA during 15 min (TA10 condition) and immediately after they were tested in the MPT arena with 4 males for 15 min (MPT10 condition). Two weeks later the same experiment was done but the females received two daily injections of 5 µg/rat of EB and 1 mg/rat of P 44 h after the first injection (TA5+5 and MPT5+5 conditions). The percentage of females that displays PB (enter and exit the male's compartment) in the four conditions were TA10: 66 %, MPT10: 83 %, TA5+5: 33 % and MPT5+5: 100%. Then the testing arena and schedule treatment could influence the expression of PB.
63. CHRONIC ESTRADIOL AFFECTS DIFFERENT ASPECTS OF ADULT HIPPOCAMPAL NEUROGENESIS IN FEMALE, BUT NOT MALE, RATS. Barker, J.M.; Galea, L.A.M. Dept. Psychology and Graduate Program in Neuroscience. University of British Columbia, Vancouver, BC, Canada. Short-term estradiol administration enhances the survival of young neurons in the adult hippocampus of male rats. To test the effects of chronic estradiol adult male and female Sprague-Dawley rats were gonadectomized and given one i.p. injection of BrdU followed by daily s.c. injections for 15 days of either estradiol benzoate (EB; 15mg for males and 10mg for females) or oil (vehicle). On Day 16, rats were perfused and the dentate gyrus examined for neurogenesis including cell proliferation (cells expressing Ki-67, present in cycling cells) and cell survival (BrdU+ cells), and for cell death (pyknotic cells or cells containing active caspase-3 (ActC3), present in apoptotic cells). Chronic estradiol in females increased the density of Ki-67+ cells, indicating an increase in cell proliferation, and decreased the density of pyknotic and ActC3+ cells, indicating a decrease in cell death. Interestingly, chronic estradiol in females also decreased the density of BrdU+ cells, indicating a suppression of survival of young cells. However, a strikingly different pattern was seen in males. In males chronic estradiol had no significant effect on cell proliferation, death, or survival. Thus the effects of estradiol on young cells are dependent on the timing and duration of administration, and are sex-specific.
64. ACTIVATION OF GROUP I METABOTROPIC GLUTAMATE RECEPTORS IN THE BASOLATERAL AMYGDALA PRODUCES ANXIOGENIC-LIKE BEHAVIOR IN A PUNISHED DRINKING TEST ACCORDING TO SEX. <sup>1</sup>Torres-Llenza V; <sup>2</sup>De Jesús-Burgos MI; <sup>1</sup>Ríos-Pilier J; <sup>2</sup>Vázquez-Fuentes BM; <sup>3</sup>Comenencia EJ; <sup>1</sup>Ramos L; <sup>1</sup>Angleró Y; <sup>1</sup>Rodríguez G; and <sup>4</sup>Pérez-Acevedo NL. <sup>1</sup>Dept of Biology, UPR-Río Piedras Campus; <sup>2</sup> Dept of Biology, UPR-Bayamón; Campus; <sup>3</sup> Dept of Biology, UPR-Cayey Campus; and <sup>4</sup>Dept of Anatomy, UPR-MSU Campus. Metabotropic glutamate receptors (mGluRs) regulate a variety of nervous system functions. It has been suggested that mGluRs are involved in mechanisms associated to anxiety-related behaviors. Human data suggests that females are twice susceptible to develop anxiety-related disorders than males. We investigated whether activation of group I mGluR within the basolateral amygdala (BLA) modulate anxiety in a sex specific manner. Adult gonadally-intact Sprague Dawley male rats were compared to ovariectomized female rats. Our data shows that bilateral infusion of 1µM DHPG, a group I mGluR agonist, reduces the number of licks in males but not in females when tested in the Vogel's drinking conflict test (sex x DHPG interaction;  $F(1, 47) = 6.23$ ,  $p=0.016$ ). In addition, there is a significant difference between vehicle-treated male and vehicle-treated OVX female when compared the number of licks ( $p < 0.05$ ). These results suggest a sexually dimorphic response for VCT behavior under BLA control. Ríos-Pilier J and De Jesús-Burgos MI was supported and, Torres-Llenza V and Vázquez-Fuentes BM are supported by MBRS-RISE Program (Rise GM61838).

Comenencia-Ortiz E and Ríos-Pilier J was supported by Alliance for Minority Participation (PR-LSAMP). Supported by RCMI Program (G12RR03051), NIH-COBRE (RR15565) and NIH-MRISP (MH048190).

65. THE EFFECTS OF ANDROSTANEDIOL AND 17  $\alpha$ -METHYLTESTOSTERONE IN SYSTOLIC BLOOD PRESSURE AND ANXIETY THROUGH THE DORSOMEDIAL HYPOTHALAMUS. Kandy T Velázquez<sup>1</sup> and Juan Carlos Jorge<sup>2</sup> Department of Physiology 1 and Department of Anatomy 2, Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico USA 00936. The use of anabolic androgenic steroid (AAS) produce disruption of affective components of behavior including anxiety. The dorsomedial hypothalamus (DMH) plays a key role in the cardiovascular changes associated with the emotional or exteroceptive stress, as well as short-term regulation of blood pressure. Blood pressure measures the physiological changes resembling those seen in acute experimental anxiety and stress. Consequently, we wanted to know whether acute infusion of androstane diol, a naturally-occurring androgen, or 17  $\alpha$ -methyltestosterone, a synthetic androgen, produces changes in systolic blood pressure (SBP) as a physiological correlate of anxiety-related responses through the DMH. We found that infusion of androstane diol significantly increased SBP ( $p < 0.001$ ) whereas 17  $\alpha$ -methyltestosterone significantly decreased SBP ( $p < 0.001$ ). Changes observed in SBP by 17  $\alpha$ -meT were mimicked by muscimol infusion. Changes in SBP induces by 17  $\alpha$ -meT does not correlate with behavior changes in the elevated plus maze, Vogel conflict test and social interaction. We conclude that androgen changes in SBP in male rats through the DMH may be structure-dependent. Support provided by the MBRS-RISE Program at MSC-UPR (GM61838) to KTV. Study funded by the NIH-COBRE (RR15565) to JCJ.
66. WHEN DOES ESTRADIOL ENHANCE APPETITE? Reid L.D.; Reid L.D.; Boswell K.J.; Reid M.L. Laboratory for Psychopharmacology Rensselaer Polytechnic Institute and Siena College. Estrogenic agents, when used as drugs, reduce intake of food. That is the reasonable conclusion to be drawn from hundreds of studies applying estradiol and other estrogenic drugs to female rats. Yet, at recent meetings of the IBNS, we have presented data indicating that estradiol valerate (EV), when injected into female rats, can enhance the intake of chocolate cake mix batter, a mixture of fat and sugar, a saccharin solution and sweetened alcoholic beverages. Under what circumstances (what procedures) do you see reductions in appetite and under what circumstances do you see enhanced appetite? Across our experiments, we have used slightly different procedures and, recently, a variety of doses of EV. From those experiments, we have derived some information about the circumstances in which estradiol is apt to reduce or enhance appetite. We discuss those circumstances here. We present new data on the effects of 0.09 mg/kg doses of EV on intake of chocolate cake mix batter to illustrate some of the issues.
67. ANDROGENIC EFFECTS ON THE REWARDING COMPONENTS OF FEMALE SEXUAL BEHAVIOR THROUGH THE NUCLEUS ACCUMBENS SHELL. E. Sanchez-Montoya, L. Hernandez, H. Palacios, A. Ortiz, Y. Valle, JC Jorge, Department of Anatomy, Medical Sciences Campus, University of Puerto Rico-San Juan, Puerto Rico 00936. Within the mesolimbic circuitry of reward that is activated by drugs of abuse, the nucleus accumbens shell has a major role in the reinforcing properties of psychostimulants. Does this circuitry play a similar role in sexual motivated behavior? It has been established that an endogenous androgenic neurosteroid, 3 $\alpha$ -Diol, has hedonic effects through the nucleus accumbens (NA) in male rats. We have recently shown that 3 $\alpha$ -Diol is self-administered by ovariectomized female rats. We now investigate the impact of 3 $\alpha$ -Diol as a natural reinforcer by modulating sexual motivation in hormone-primed ovariectomized female rats. Rats with bilateral cannulae in the nucleus accumbens shell and primed with two different doses of estradiol (E) plus progesterone (P) were tested on paced-mating behavior. At a priming dose of 10  $\mu$ g of E and 500  $\mu$ g of P (s.c.) we found that either 1  $\mu$ M of 3 $\alpha$ -Diol or the GABA-A agonist muscimol microinjected into the NA shell increases the lordosis rating by 25% ( $p \leq 0.05$ ) and doubles the duration and frequency of proceptive behaviors such as ear wiggling and hopping/darting ( $p \leq 0.05$ ) when compared to vehicle. At a lower priming dose (E= 7.5  $\mu$ g and P = 375  $\mu$ g, s.c.) infusion of 1  $\mu$ M of 3 $\alpha$ -Diol increased lordosis rating ( $p \leq 0.05$ ) but had no effect in proceptive behaviors. 3 $\alpha$ -Diol failed to modulate lordosis rating and proceptive behavior when administered subcutaneously after E+P priming at the highest dose. We conclude that 3 $\alpha$ -Diol can modulate sexual motivation through a fast-acting mechanism via the mesolimbic circuitry of reward. Supported by NIH-COBRE (RR15565) and the RCMI Program at MSC-UPR (G1RR3051) to JCJ.

68. PREOPTIC AREA INFLUENCES ON HYPOTHALAMIC SEROTONIN AND FEMALE SEX BEHAVIOR. MJ Watt<sup>1,2</sup>, N Feng<sup>1</sup>, E Höglund<sup>1</sup>, B Mo<sup>1</sup>, GL Forster<sup>2</sup>, and KJ Renner<sup>1</sup>. 1.Biology Dept, 2.Basic Biomed. Sci., Uni. South Dakota, Vermillion, SD, 57069. Expression of sexual receptivity in female rats is attenuated upon increased serotonin (5-HT) release in the ventromedial hypothalamus (VMN). Previous work demonstrated that sex behavior is also influenced by the medial preoptic area (mPOA), with expression declining after mPOA pharmacological inactivation. In this study, we used *in vivo* microdialysis to examine the possible effects of mPOA inactivation on VMN 5HT release and concurrent sex behavior. Bilateral infusion of muscimol (18.5ng/0.5µl) into the mPOA of ovariectomized hormone-primed female rats increased VMN extracellular 5-HT levels and decreased lordosis expression, with females also producing defensive behaviors such as kicks and rolls. In contrast, controls receiving vehicle exhibited no change in VMN 5-HT and maintained high sexual receptivity. These results suggest that mPOA influences on VMN 5-HT levels may regulate female sex behavior. Supported by NIH P20 RR15567.

*Friday, May 26, 2006*

**8:45-10:45 Symposium 5: Behavioural Neuroscience – Quo Vadis**

THERE IS MORE TO REWARD THAN THE 'PLEASURE PRINCIPLE'. Phillips, A. Dept. of Psychiatry, University of British Columbia, Vancouver, Canada. Is 'reward' a verb or a noun? As a verb, how is it related to the concept of reinforcement: As a noun, to the term 'hedonic stimulus' and the concept of 'pleasure'? Imprecise terminology has given rise to the assertion that dopamine is essential for reward, when all of the empirical evidence supports a role in 'incentive motivation' and memory modulation. This lecture will provide a historical perspective on these different definitions of 'reward', before reviewing the case for a broad definition of 'reward' as a synonym for 'incentive'. Resolution of these issues is of critical importance given the broad interest in the role of dopamine in several topics of central importance to understanding higher brain function including memory, stimulus value, decision making and addiction. Data obtained by *in vivo* sampling of dopamine efflux in terminal regions of the mesocorticolimbic DA system in the context of specific phases of preparatory and consummatory behavior, will be used to support the hypothesis that dopamine serves as an important neurochemical correlate of incentive motivation.

DEVELOPING AND VALIDATING NEW BEHAVIOURAL TESTS FOR MICE. Rawlins J.N.P.; Bannerman D.M.; Deacon R.M.J. Oxford University, Department of Experimental Psychology, South Parks Road, Oxford OX1 3UD, UK. Molecular biologists have developed increasingly sophisticated methods for selectively targeting genes and their products. These offer unprecedented analytic power to the study of neural events underlying specific psychological states, but their development in mammals is largely confined to mice, whereas a long tradition of behavioural task development has focussed on studies in rats. Tasks developed for rats are not always optimal for behavioural testing of mice (and vice versa), so we have developed and extensively validated mouse phenotyping tasks designed to assess different aspects of learning and memory, emotion and motivation, and sensorimotor function. Our primary goal has been to assess cognition and emotion in glutamate receptor knockout mice and progressive neurodegeneration models, while also evaluating the sensory, motor and motivational factors on which the tasks also depend. This approach has enabled us to dissociate two distinct components of hippocampus-dependent spatial memory, which differ in their dependence on the presence of the GluR-A subunit of the glutamate AMPA receptor (Reisel et al., *Nature Neuroscience*, 5: 868-73; Schmitt et al., *Nature Neuroscience*, 8: 270-272), as well as enabling us to detect the early signs and relate the progressive development of central nervous system prion infection to the underlying, developing neuropathology (Cunningham et al., *European Journal of Neuroscience* 17: 2147-55). Continued development of sophisticated behavioural phenotyping will allow the potential offered by advances in genetic analysis, genetic engineering, and newly developed mouse disease models to be realised.

BEHAVIORAL NEUROSCIENCE IS THE BASIC SCIENCE DISCIPLINE FOR PSYCHIATRY. <sup>1</sup>Szechtman, H; <sup>2</sup>Eilam, D. <sup>1</sup>Dept Psychiatry & Behavioural Neurosciences, McMaster Univ; <sup>2</sup>Dept Zoology, Tel-Aviv Univ. Animal models have always played an integral part in the advancement of medical research but their acceptance in psychiatry is both recent and instructive. The change in attitude from a past anathema to the present embracement of animal models reflects the profound shift of how today psychiatry views mental disorders and the successful efforts of basic science in showing the utility and the limits of animal studies of psychopathology. I will consider the conflicts associated with a rise of a biological psychiatry perspective on mental illness and suggest that the

current pre-eminence of this biological viewpoint has aligned clinical psychiatry with behavioral neuroscience for the source of much of its basic science knowledge. I will argue that the methods of behavioral neuroscience are just what is needed to investigate mechanisms of mental disorders of interest to psychiatry.

**BEHAVIOR IN THE GENOMIC ERA: THE HIGH THROUGHPUT IDOL.** Weiner, I. Department of Psychology, Tel-Aviv University, Tel-Aviv 69978, Israel. The revolution in mammalian genetics culminating in the elucidation of the human and mouse genome had for some time encouraged the belief that knowing the genes would suffice for the understanding of normal and abnormal brain function. As the number of genetically manipulated mice grew, it has become clear that molecular genetic technologies must be supplemented with behavioral analysis, launching an era of “genes searching for a function”. Unfortunately, advances in implementing and interpreting behavioral assays have not kept pace with the rapid advances in mouse genetics and genomics. The gap is typically attributed to “traditional” behavioral analysis being slow and labor intensive; accordingly, increased speed and quantity of behavioral assessment using high throughput systems is advocated as the solution. I will suggest that the gap between the two fields stems from the secondary role of “behavior” in the “gene-behavior” dyad, and that what is needed in order to maximize the extent to which the revolution in mammalian genetics may be effectively applied to neuroscience and psychiatric research, is increased sophistication of the experimental paradigms and behavioral analysis in both the conceptual and technological domains. This requires expert and hypothesis-driven application of the principles of learning and behavior coupled with creative instrumentation and advanced computer technology, to target specific questions on gene-function relationships. In order to attain this goal, it is imperative that behavior is granted the status of an equal partner to that of the genes searching for a function.

**11:00-12:00 The Matthew J. Wayner/NNOXe Pharmaceuticals Award: William T. Greenough**

**TWO MEANINGS OF “TRANSLATION:” PLASTIC BRAIN MECHANISMS IN FRAGILE X DISORDER.** Greenough, W. Swanlund Professor of Psychology, Psychiatry and Cell & Developmental Biology, University of Illinois at Urbana-Champaign. While I now spend much of my time investigating cellular mechanisms underlying the most common genetically inherited form of mental retardation, I did not set out to study Fragile X Disorder—in fact, I had barely heard of it. I was pursuing synaptically-associated protein synthesis, now widely regarded as a likely aspect of memory-associated plastic change at the synapse. In the course of determining what proteins were being made at synapse, my colleagues Ivan Jeanne Weiler and Jim Eberwine and I discovered that the protein that is absent in Fragile X Disorder, FMRP, was translated in response to synaptic activation in a purified neocortical synapse preparation. Subsequently we demonstrated its neocortical synthesis in response to enriched rearing. This has led to intense pursuit of the functions of FMRP, the causes of deficits in Fragile X Disorder and the possible roles of FMRP synthesis in memory.

**15:45-17:45 Symposium 6: The pharmacological and neural modulation of defensive behavior**

**MODULATION OF DEFENSIVE BEHAVIOR BY CRF.** Blanchard, R.J.1; Yang, M.1; Litvin, Y.1.; Borna Farrokhi, C.1; Blanchard, D.C. 2,3. 1. Department of Psychology. University of Hawaii, Honolulu, HI 96822 USA. 2. John A. Burns School of Medicine, University of Hawaii, Honolulu, HI 96813 USA. 3. Pacific Biomedical Research Center, University of Hawaii, Honolulu, HI.96822 USA. ICV infusion of Ovine CRF into CD1 mice that are immediately replaced in their home cages suppresses sleeping and produces prolonged episodes of freezing compared to vehicle controls. In the Mouse Defense Test Battery (MDTB) icv o-CRF potentiates risk assessment, flight, and freezing in mice that are confronted, approached, chased, and contacted by a predator (rat) in escapable or inescapable situations. In a Rat Exposure Test (RET), mice have access to an enclosed “home” area with homecage bedding, connected via a tunnel to a chamber containing a rat. Although the rat is separated from the mouse subject by wire mesh, it is consistently active due to a 5 mg/kg dose of amphetamine, making it an intense threat stimulus. In this situation, icv o-CRF increases mouse freezing, and avoidance of the rat. When o-CRF was infused into the dorsal periaqueductal gray (PAG), and the MDTB and RET were run in the same order, it also produced avoidance and freezing in the RET but was without effects in the MDTB, suggesting differential modulation of behaviors of the two tests by o-CRF in structures reached icv but not by dorsal PAG infusion.

**NEUROPHARMACOLOGY OF DEFENSIVE BEHAVIOR: ROLE OF NORADRENALINE TRANSMISSION.** Carobrez, A.P.; Do-Monte, F.H.M. Noradrenergic transmission has long been implicated in stress-related changes in behavior. Epinephrine released during stress is able to stimulate both peripheral and central beta-adrenoceptors which will in turn mediate the cardiovascular, as well as, the cognitive responses expressed in this particular event.

Results obtained from experiments involving the fear from a predator odor is a notable approach to study the neural substrates underlying defensive system related to potential danger. It has been shown that the potential danger produced by the cat-odor in rats is capable of induce c-Fos protein expression in various structures related to the defensive system. Of particular interest is a structure component of the medial hypothalamic defensive zone, called the dorsal premammillary nuclei (dPM). Pharmacological studies using systemic injections of beta-adrenoceptor blockers (BB) have shown that propranolol, a central and peripheral acting BB, is capable of reduce the defensive behavior toward a cloth impregnated with a blend of cat-fur odor, when compared to the one expressed by saline treated rats. No effects were detected in rats treated with Nadolol, a more peripheral acting BB. In a context session, 24h after, using a neutral-odor cloth, Propranolol pre-treated rats showed also a reduced contextual fear response, when compared to Saline or Nadolol pre-treated rats. When given only before the context propranolol was not capable of reduce the expression of the defensive response acquired in the cat-odor session 24h before. These results suggest a possible noradrenergic involvement in the acquisition but not in the expression of the defensive response of a rat to the cat odor. A group of rats with cannula implanted within the dPM was injected with atenolol a BB selective for receptors type 1. The results showed that the beta receptors blockade within the dPM elicited a reduced defensive response to the cat-odor and also to the context 24h after, when compared to the control rats. Taken together these results suggest also that the activation of noradrenergic system within the dPM might underlie part of the acquisition of defensive responses to a potential danger, as is the case of the predatory odor. Financial support: CNPq, Capes, FAPESC, FAPESP, UFSC

**NEUROPHARMACOLOGY OF DEFENSIVE BEHAVIOR: ROLE OF ATYPICAL NEUROTRANSMITTERS.** Guimaraes, F.S.; Moreira, F.A.; Beijamini, V.; Aguiar, D.C., Braga, A.; de Oliveira R.W.; Del Bel, E.A. Dept. Pharmacology, School of Medicine of Ribeirão Preto, USP, Ribeirão Preto, SP, 14049-900, Brazil. Nitric oxide (NO) formation in the brain is linked to the activation of NMDA receptors. NO is not stored in vesicles and can diffuse freely to act on nearby neurons. Therefore, it is considered an atypical neurotransmitter. NO synthase (NOS) containing neurons are located in brain areas controlling defensive behavior, such as the dorsolateral periaqueductal grey (dlPAG), inferior coliculus, paraventricular and dorsal premammillary nuclei of the hypothalamus and the medial amygdala. These neurons are activated in rats exposed to natural threats, and NOS expression in most of these areas is increased by restraint stress. NOS inhibition in the dlPAG attenuates defensive responses to a predator. Similar treatment in this region or in the medial amygdala produces anxiolytic-like effects in the elevated plus maze (EPM). On the contrary, NO donors injected into the dlPAG cause flight reactions that are completely prevented by local pretreatment with glutamate ionotropic receptor antagonists. Endocannabinoids, another class of atypical neurotransmitters, have also been proposed to modulate defensive reactions. Low doses of cannabinoid agonists are anxiolytic in animal models. We have recently found that intra-dlPAG injection of anandamide produces anxiolytic-like effects in the EPM. Therefore, in addition to glutamate, GABA and serotonin, atypical neurotransmitters can also play an important modulatory role in brain areas related to defensive reactions. Financial support: FAPESP, Capes, CNPq

**A ROLE FOR THE PERIAQUEDUCTAL GRAY IN SWITCHING ADAPTIVE BEHAVIORAL RESPONSES.** Canteras, NS1; Sukikara, MH2; Mota-Ortiz, SR1; Baldo, MV3; Felício, LF2. 1Dept. Anatomy, Institute of Biomedical Sciences, University of São Paulo; 2Dept. Pathology, School of Veterinary Medicine, University of São Paulo; 3Dept. Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo. Previous studies suggested a role for the rostral lateral PAG in the inhibition of maternal behavior induced by low doses of morphine in dams with previous morphine experience. In the present study, we first showed that unilateral NMDA lesions placed in this particular PAG region prevented the morphine-induced inhibition of maternal behavior in previously morphine-sensitized dams. As suggested by previous Fos data on the PAG, predatory hunting appears as a likely candidate to replace maternal behavior in the morphine-treated dams. By testing saline- and morphine-treated dams with live cockroaches only, we have presently shown that morphine challenge increased insect hunting. Moreover, morphine- and saline-treated dams were also observed in an environment containing pups and roaches. While most of the saline-treated animals displayed active nursing and only occasionally presented insect hunting, all the morphine-treated animals ignored the pups and avidly pursued and caught the roaches. We next questioned whether the rostral lateral PAG would be involved in this behavioral switch. Our results showed that unilateral lesions of the rostral lateral PAG, but not other parts of the PAG, partially impaired predatory hunting and restored part of maternal response. Moreover, bilateral lesions of the rostral lateral PAG produced even more dramatic effects in inhibiting insect hunting and restoring maternal behavior. The present findings indisputably show that the rostral lateral PAG influences switching from maternal to hunting behavior in morphine-treated dams, thus supporting a hitherto unsuspected role for the PAG in selecting adaptive behavioral responses.

*Reward and drugs of abuse*

69. THE EFFECTS OF THE SELECTIVE 5-HT<sub>1B</sub> RECEPTOR AGONIST, CP94253, ON COCAINE SEEKING AND ANXIETY. Acosta J.I.; Gaudet L.; Browning J.R.; Neisewander J.L.\* Dept of Psychology, Arizona State University, Tempe, AZ, USA. Exposure to cues associated with cocaine or cocaine itself can elicit incentive motivation that manifests as craving in humans and cocaine-seeking behavior in animals. We have previously reported that a 5-HT<sub>1B/1A</sub> receptor agonist attenuates cocaine-seeking behavior elicited by either cocaine cues or cocaine priming, and these effects are reversed by a 5-HT<sub>1B</sub> antagonist. However, we also casually observed that the nonselective agonist produced anxiety-like behavior on the test day. Therefore, this study examined the effects of the selective 5-HT<sub>1B</sub> agonist, CP94253, on cue and cocaine-primed reinstatement of extinguished cocaine-seeking behavior, as well as anxiety-like behavior using the elevated plus maze. Rats were trained to press a lever on a VR 5 schedule of cocaine (0.75 mg/kg, IV) reinforcement paired with light and tone cues. Rats then underwent extinction during which responses had no consequences and cocaine-seeking behavior, defined as lever presses in the absence of cocaine reinforcement, declined across daily sessions. Rats were then tested for cue and cocaine-primed (10 mg/kg, IP) reinstatement of cocaine-seeking behavior and exploration of an elevated plus maze following pretreatment with an assigned dose of CP94253 (0.0-10.0 mg/kg, SC). CP94253 dose-dependently attenuated cue and cocaine-primed reinstatement of cocaine-seeking behavior, as well as open arm entries on the elevated plus maze. These findings suggest that stimulation of 5-HT<sub>1B</sub> receptors may decrease motivation for cocaine, although it is not clear whether this effect is independent of, or secondary to, the drug's anxiogenic effects. Supported by DA11064 and the Ford Foundation, MEG
70. COMPARING THE EFFECTS OF SENSORY STIMULATION AND COCAINE ON SEROTONIN AND DOPAMINE ACTIVITY IN THE OCCIPITAL AND TEMPORAL CORTEX. Müller, C.P.; De Souza Silva, M.A.; Huston, J.P. Inst Physiol Psychol & Ctr. Biol Med Res, Univ Düsseldorf, 40225 Düsseldorf, Germany. It is generally agreed upon that classical and instrumental conditioning change the processing of visual information dramatically in cocaine addicts, in a way that formerly neutral stimuli gain predominant influence over behavior as a result of pairing with the drug effects. In two experiments using in-vivo microdialysis in freely moving rats we compared the effects of visual (white light; 82 lux) and auditory stimulation (white noise; 82 dB; both stimuli: 10 x for 30 sec.) with that of cocaine (0, 5, 10, 20 mg/kg; i.p.) on the extracellular serotonin (5-HT) and dopamine (DA) activity in the occipital and temporal cortices in relation to behavior. Visual stimulation increased 5-HT in the occipital, but not temporal cortex, parallel to an increase in locomotion. Auditory stimulation decreased 5-HT in the auditory, but not occipital cortex, thus, showing a double dissociated 5-HT response. DA levels were not affected by either stimulus, nor correlated with the 5-HT response. Cocaine dose-dependently increased 5-HT and DA in the occipital and temporal cortex and increased behavioral activity. Thereby, the 5-HT and the DA responses were correlated. These data suggest that during cocaine-exposure visual cues are not processed normally in the visual stimulation sensitive occipital cortex, but are amplified. These results suggest that concepts of how neutral visual cues become powerful energizers of addiction-related behaviors should consider not only an acute enhancement of reward processing mechanisms, but, in parallel, also an amplified processing of visual stimuli in the occipital cortex. (supported by grant HU 306/ 23-3 from the Deutsche Forschungsgemeinschaft).
71. ASSOCIATION OF CANNABINOID RECEPTOR CB2 GENE WITH ALCOHOLISM AND DEVELOPMENT OF ALCOHOL PREFERENCE. Ishiguro, H.; Iwasaki, S.; Teasenfiz, L.; Higuchi, S.; Arinami, T and Onaivi, E. S. Institute of Basic Medical Sciences, University of Tsukuba, Japan, and William Paterson University, Wayne NJ, USA, and Kurihama National Hospital, Japan. We tested the hypothesis that genetic variants of CB2 gene might be associated with alcoholism in human population and this was probed using the non-synonymous polymorphisms, R63Q and H316Y in the CB2 gene in Japanese alcoholic subjects. In mice CB2 gene expression was determined in brain regions after acute administration of ethanol, and development of alcohol preference. Ethanol consumption in mice subjected to chronic mild stress and the effect of chronic daily administration with CB2 agonist JWH015 on ethanol consumption in stressed and control animals were measured. High incidence of the Q63R but not the H316Y polymorphism was found in Japanese alcoholics. Mice that developed alcohol preference had reduced CB2 gene



expression and chronic treatment with JWH015 enhanced alcohol consumption in stressed but not in control mice. CB2 cannabinoid receptors are involved with the effects of alcohol along with epigenetic factors, such as stressors, and may be targeted with CB2 ligands in alcoholism. Supported by University of Tsukuba and WPUNJ center for research.

72. BEHAVIORAL EFFECTS OF CB2 CANNABINOID RECEPTOR LIGANDS. Teasenfiz, L.; Mora, Z.; Akinshola, B. E and Onaivi, E.S. William Paterson University, Wayne, NJ and Howard University, Washington DC, USA. We have identified the neuronal expression of the so called “peripheral” cannabinoid CB2 receptors and shown that direct CB2 antisense oligonucleotide administration into the brain modifies mouse behavior. We now describe the effects of the putative CB2 agonist, JWH015, the mixed CB1/CB2 agonist WIN55212-2 and CB2 antagonist SR144528 in mouse motor function tests and in the two compartment black and white box. Acute treatment with CB2 agonist (JWH015) altered mouse locomotor activities in a strain and gender dependent fashion. A general pattern of depression in locomotor activity was induced by JWH 015 in both males and females in the three mouse strains tested as the dose was increased. In the two compartment black and white box the acute effects of JWH015 at low doses (1-20 mg/kg) did not induce robust anxiolytic response rather this peripheral administration of JWH015 induced an anxiogenic profile of response in the black-white test box. In contrast chronic treatment of control mice with JWH015 induced an anxiolytic profile of response in comparison to the chronic mild stress animals. Using the DBA/2 strain the spontaneous locomotor activity and stereotype behavior was enhanced by acute administration of low doses of SR144528. SR144528 did not induce stereotype behavior in female mice at the doses used. In the two compartment black and white box test box treatment with SR144528 had little or no effect on the time mice spent in both chambers by male or female DBA/2 mice except a reduced time spent in the white chamber by the male mice at the highest dose used. The spontaneous locomotor activities in both chambers by both DBA/2 male and female treated with SR144528 were also not significantly different from vehicle treated control mice. These effects of CB2 cannabinoid receptor ligands in in vivo behavioral tests are provided as functional evidence of CB2 cannabinoid receptors in the brain that plays a role in motor function and emotionality tests.
73. TREATMENT WITH MDMA FROM P11-20 DISRUPTS SPATIAL LEARNING AND PATH INTEGRATION LEARNING IN ADOLESCENT RATS AND SPATIAL LEARNING IN OLDER RATS Matthew R. Skelton\*, Michael T. Williams, and Charles V. Vorhees. Div. of Neurology, Cincinnati Children’s Res. Foundation and Univ. of Cincinnati College of Medicine, Cincinnati, OH 45229 The popular club drug 3,4-methylenedioxymethamphetamine (MDMA) has been previously shown to impair spatial as well as path integration learning and memory in young adult rats (P60) that were exposed from postnatal days (P) 11-20. This exposure period corresponds to late third trimester human development. The purpose of this study was to further characterize the MDMA-induced learning deficits by testing adolescent (P30 & 40) and older (P180 & P360) rats. Litters were treated twice daily with MDMA (20 mg/kg) or saline vehicle from P11-20. In adolescent rats, MDMA administration caused increased latency and path length to reach the submerged platform during three distinct phases of the Morris water maze (MWM); as well as increasing the latency to completion and errors committed in the Cincinnati water maze (CWM; path integration). Older rats showed similar effects in the MWM, with MDMA-treated animals taking longer and traveling farther to find the platform. However, older animals treated with MDMA showed no deficits in CWM performance. The results suggest that developmental MDMA exposure causes spatial learning deficits that emerge early and persist; whereas path integration effects emerge early but may decrease at older ages.
74. LONG ACCESS COCAINE SELF-ADMINISTRATION LEADS TO PERSISTANT IMPAIRMENTS IN COGNITIVE PERFORMANCE. Briand, L.A, Sarter, M., Robinson, T.E. Department of Psychology and Neuroscience. The University of Michigan, Ann Arbor, MI 48109 USA. Long-term drug abusers exhibit cognitive deficits that persist long after the cessation of drug use, and these deficits may contribute to relapse. Surprisingly, however, preclinical studies have found little evidence for these persistent cognitive deficits. This may be due to the utilization of limited access self-administration procedures. Thus, the present study was aimed at utilizing an extended access cocaine self-administration protocol, which has been found to induce escalation of drug intake and symptoms associated with drug dependence, to examine the persistent effects of drug abuse on cognitive function. In the first experiment, rats were trained on a sustained attention task until reaching stable performance at criterion level. Animals were divided into drug

naïve, short (ShA) and long (LgA) access groups and underwent four weeks of cocaine self-administration. Attentional performance was reexamined 24 hours following the final self-administration session. Fourteen days later, performance was again assessed and daily testing resumed thereafter until animals reached asymptotic performance levels. At both time points tested, the performance of LgA animals was significantly impaired relative to the ShA or drug naïve groups; this impairment improved following daily testing, but never reached the level of performance seen in the other two groups. The nature of the impairment suggested a fundamental disruption of the animals' ability to generate correct responses evoked by either the presence or absence of the attentional cue. In the second experiment, animals were trained identically to experiment one and following the final self-administration session, animals were withdrawn for 24 hours, 14 days or 1 month and attentional performance was reexamined. At all three time points tested, animals in the LgA group performed worse than animals in the two other groups. These results indicate that extended access to cocaine leads to a persistent deficit in cognitive performance. Given the potential involvement of drug-induced cognitive deficits to relapse, characterizing this phenomena and elucidating the neurobiological underpinnings of the cognitive deficits may be important for developing better treatments for drug addiction.

75. INTRA-AMYGDALA MU OPIOID RECEPTOR STIMULATION INCREASES CONDITIONED APPETITIVE BEHAVIOR IN RATS. Mahler, S.; Berridge, K. The amygdala is involved in appetitive emotion and learning, in addition to learning about negative emotion. Mu opioids in many brain areas, including the amygdala, mediate reward-related behaviors. In the present experiment, we tested whether intra-amygdala infusion of the mu opioid agonist DAMGO would increase the motivational magnet, or incentive properties that attract behavior toward reward CS+s. We used an autoshaping paradigm, in which rats learn that Pavlovian cues predict sucrose rewards, and then spontaneously begin to approach those cues. Rats received daily DAMGO (0.1µg/0.5 µl) or vehicle control microinjections before the first six days of autoshaping training to assess effects on acquisition of conditioned incentive approach. During training, rats learned to associate an 8 second compound lever and tone cue presentation (CS+) with sucrose rewards. DAMGO increased CS+ cue lever interactions in rats that learned to approach the cue lever during the CS+ (i.e., rats that autoshaped). DAMGO also increased approach to a control lever (CS-) in these rats, but only when the CS+ was not present. In other rats that merely learned to approach the sucrose dish during the CS+ (i.e. conditioned anticipatory approach to UCS source), DAMGO increased sucrose dish entries, but not interactions with either the CS+ or CS- levers. These results suggest that intra-amygdala mu opioid agonist administration can alter attributions of incentive properties to reward CS+s. Furthermore, DAMGO s effects on cue-appetitive behavior differed based on individual differences in the cue-directed behavior that was initially learned (lever vs. sucrose dish approach). These findings may have implications for understanding the role of amygdala opioid receptors in appetitive disorders like addiction and obesity. Support Contributed By: NIH MH63649 and NIH DA015188
76. ADULT METHAMPHETAMINE EXPOSURE RESULTS IN PATH INTEGRATION AND NOVEL OBJECT LEARNING DEFICITS IN RATS. Nicole R. Herring\*, Tori L. Schaefer, Charles V. Vorhees, and Michael T. Williams, Div. of Neurology, Cincinnati Children's Research Foundation & Univ. Cincinnati College of Medicine, Cincinnati OH 45229 Studies examining the consequences of adult d-methamphetamine (MA) exposure on learning and memory have demonstrated few effects. The lack of findings may be due to the learning tasks employed or the dosing regimens used. The purpose of this study was to investigate multiple learning paradigms in adult rats administered MA every 15 minutes or every 2 hours. This was a 2 x 2 factorial design with Drug (MA v. SAL) and Regimen (4 v. 24 doses; same cumulative dose) as factors. MA (10 mg/kg) or SAL were administered 4 times with 2 h intervals between administrations, or MA (1.67 mg/kg) or SAL were administered 24 times with 15 min intervals between administrations. Regardless of dosing regimen, MA-treated groups demonstrated hypoactivity at 24 h; however at 48 h the 15 min MA-treated group displayed hyperactivity. In novel object recognition (NOR), MA-treated groups spent significantly less time with the novel object compared to SAL-treated groups. In the Cincinnati water maze, a test of path integration, MA-treated animals demonstrated longer latencies and committed more errors in locating the escape ladder. Finally, in the Morris water maze MA-treated groups performed similarly to SAL-treated groups overall on acquisition and probe. The results suggest that path integration and NOR learning are affected by MA treatment while spatial acquisition and memory are largely unaffected. There was little or no influence of dosing regimen on most of the behaviors in this study.

77. CHRONIC COCAINE AND/OR STRESS EXPOSURE IN ADOLESCENT AND ADULT RATS DIFFERENTIALLY ALTERS THE LONG-TERM CONSEQUENCES OF COCAINE-INDUCED REWARD AND PSYCHOMOTOR STIMULATION Sonya K. Sobrian, Nailah S. Adams, Jewel Wright, Daniela Kuhn, Sweelan Gerald and Jason K. Arguinonzi. Dept. of Pharmacology. Howard University College of Medicine, Washington, DC 20059 USA. Adolescence is potentially a critical period for the development of drug addiction. Moreover, stressful experiences appear to influence susceptibility to drug-taking behavior. To determine the pattern of behavioral sensitization to cocaine, male and female rats were subjected to 14 consecutive days of sound stress [SS: 30 minute exposure to an 85 dB, 2000- 4000 Hz fire alarm bell; 30 rings on a variable interval schedule], followed by a s.c. injection of 20 mg/kg of cocaine (C) or saline vehicle (V), starting at either PND 28 or PND 88. Non-stressed controls (NS) received drug injections after a 30 min confinement in the sound-attenuated room. Four weeks later, rats were challenged with saline, 1, 3, and 10 mg/kg of cocaine in a cumulative dosing regimen. Pre-treatment with cocaine and/or stress during adolescence did not alter baseline activity or the locomotor response to either of the three challenge doses of cocaine. The 2 lower doses decreased activity below baseline levels in all groups and for both sexes when tested at PND 70. In animals pre-treated as adults, baseline activity was lower in C rats. The 2 lower doses also reduce activity below baseline in all groups, a decrease that was enhanced by pre-treatment with cocaine alone or in combination with stress. At 10 mg/kg, activity was elevated above baseline in all but the C group. Thus, while cocaine sensitization was seen only following adult pre-treatment, a clear desensitization to the stimulant effects of cocaine was seen following pre-treatment at both ages. Both phenomena have been linked to changes in reward mechanisms. Supported by grant #S06GM 08016-36.
78. REWARD EXPERIENCE MODERATES IMMUNE RESPONSE TO CYTOKINE CHALLENGE. Kentner, A.C; James, J; Miguez, M; Bielajew, C. School of Psychology. University of Ottawa, Ottawa Ontario CANADA. Interferon-alpha (IFN-alpha) is a cytokine used as a treatment for cancer and Hepatitis C. The benefits however are frequently accompanied by adverse side-effects such as flu-like symptoms and in some individuals, depression. We have been exploring an animal model of cytokine challenge. In this study, we investigated the short- and long-term effects of a single systemic injection of vehicle, 10, or 1000 units of IFN-alpha. The measures included temperature, body weight, food intake, sickness behaviors, locomotor activity, and brain stimulation reward (BSR) thresholds elicited from the ventral tegmental area in female Long Evans rats. Brain stimulation reward, long employed for studying motivational processes, has been exploited as a tool for tracking hedonic status in animal models of depression. Thresholds in the present study did not reveal an anhedonic effect. As expected, locomotor activity was shown to be decreased in animals receiving both doses of the IFN-alpha compared to the vehicle group. Sickness behaviors were measured in all animals three times daily for two days, and included ptosis (droopy eyelids), piloerection, lethargy, and sleep measures. Each behavior was scored on a three point scale (none = 0, mild = 1, or severe = 2), except for sleep which was scored on a two point scale as either 0 (absent) or 1 (present). Non-parametric analyses unveiled a significant increase in piloerection in all sham operated animals that received an IFN-alpha injection at each time point measured while the BSR animal scores remained relatively unchanged between pre- and post-injection days. This pattern was also evident in the total sickness scores. Temperature, recorded at the same times as sickness behavior collection showed increases only in the group not receiving BSR. Taken together, these data suggest that the behavioral disruptions elicited by a single cytokine challenge are significantly diminished in animals receiving rewarding brain stimulation, indicating that the experience of reward influences immune activity.
79. EFFECTS OF PRENATAL COCAINE EXPOSURE AND REARING CONDITION ON SOCIAL/AGGRESSIVE BEHAVIOR AND OXYTOCIN LEVELS IN YOUNG ADULT MALE RATS ON A WATER COMPETITION TASK. Jarrett, T.M., McMurray, M.S., Walker, C.H., and Johns, J.M. Departments of Psychiatry and Psychology, University of North Carolina, Chapel Hill, N.C. 27599 USA. Many rodent models of prenatal cocaine exposure document dysregulation of adult male offspring social behavior concurrent with disruptions in various neurochemical pathways. No models, to date, have assessed whether prenatal exposure to cocaine and rearing environment (drug treated versus non-treated dam) interact to affect subsequent male offspring behavior and oxytocin system function. Since male offspring with a prenatal cocaine exposure or reared by a cocaine treated dam have been shown to have altered social behavior and oxytocin levels, then offspring with a prenatal cocaine exposure and reared by a

cocaine treated dam are likely to be more aggressive and less successful on a competition task coincident with an altered oxytocin system. Offspring from control or prenatal cocaine exposure conditions were cross-fostered at birth and reared by either control or cocaine treated dams until weaning. At 60 days of age male offspring were tested for unprovoked aggression and success in obtaining water in an adaptation of a previously used water competition task. Prenatal exposure to cocaine combined with rearing by cocaine treated dams, significantly increased aggressive behaviors such as threats and attacks and reduced success of attaining water. Males reared by cocaine treated dams regardless of their prenatal exposure condition, had reduced levels of amygdaloidal oxytocin following completion of the water competition task. These studies were supported by NIH R01 grants DA -13283 and DA-13362 awarded to Dr. Johns.

80. CHANGES IN CORTICOSTERONE AND LIMBIC MONOAMINES DUE TO SENSITIZATION OR HABITUATION TO AMPHETAMINE Jamie L. Scholl<sup>1</sup>, Michelle A. Phillips<sup>1</sup>, Na Feng<sup>1</sup>, Ron B. Pringle<sup>1,2</sup>, Jodi L. Lukkes<sup>2</sup>, Michael J. Watt<sup>1,2</sup>, Kenneth J. Renner<sup>1,2</sup>, and Gina L. Forster<sup>2</sup> <sup>1</sup>Dept. Biology, <sup>2</sup>Basic Biomedical Sciences, University of South Dakota, Vermillion, SD, USA. Repeated amphetamine (Amp) causes locomotor sensitization, which it thought to underlie addiction, in the majority of treated rats. Chronic Amp also increases corticosterone (B) responses to stress. We tested whether Amp sensitization is necessary for changes in basal B and limbic monoamines during Amp withdrawal. Male rats received injections of d-amphetamine (2.5 mg/kg, ip) or saline for 6 days. Amp-induced locomotion and anxiety behaviors were measured during the withdrawal period and brains and plasma were later collected for analysis. Monoamines were measured by HPLC, and plasma B was measured with immunoassay. Sixty-two percent of the rats treated with Amp sensitized to the locomotor effects of the drug. Anxiety behavior, as measured in an open-field, was increased in sensitized rats only. Basal plasma B levels were higher in sensitized rats; however, B levels in non-sensitized rats were not different from controls. Furthermore, rats that habituated (non-sensitized) to the locomotor effects of Amp also exhibited habituation to Amp-induced B responses, suggesting endocrine tolerance to Amp. Basal levels of dopamine and serotonin were altered in the medial prefrontal cortex, nucleus accumbens, and the hippocampus depending on sensitization or habituation to Amp. The results suggest that Amp-induced alterations to plasma B and limbic monoamines differ depending on ability to sensitize. These results may have implications for the neuroendocrine basis of individual propensity for addiction and relapse.
81. DIFFERENTIAL HORMONAL EFFECTS OF ACUTE SYSTEMIC COCAINE ADMINISTRATION IN A NEOTROPICAL PRIMATE. Barros, M.; Lima, D.; Spindola, D.B.; Dias, L.O.; Bessa, N.O.D.; Costa, S.S.S.; Vaz, J.A.R.; Abdalla, L.F.; Tomaz, C. Primate Center, Institute of Biology, University of Brasília, 70910-900, Brazil. Cocaine administration induces specific neuroendocrine effects, which may have a facilitatory role on the behavioral response to this psychostimulant and its neural mechanisms of addiction. However, the mechanisms by which cocaine induces hormonal responses are not fully understood. Therefore, the present study investigated the hormonal effects of acute systemic cocaine administration in nine adult marmoset monkeys (*Callithrix penicillata*) known to have high basal levels of circulating glucocorticoids. For each subject, a blood sample was obtained 30-min after cocaine (10 and 20 mg/kg) administration. After a 7-day interval, a second sample was obtained 60-min post-cocaine injection. Samples were also taken 0, 30 and 60-min after saline administration, in 7-day intervals. Plasma concentration of ACTH, cortisol and prolactin were determined via quimioluminescence. Cocaine altered ACTH levels, although high between-subject variations were observed. Furthermore, cocaine induced an increase in plasma cortisol, although significantly only after 60 min of the 20 mg/kg dose. Conversely, prolactin concentrations decreased significantly 30 and 60 min following both doses of cocaine. Saline administration (0, 30, and 60-min) did not significantly alter plasma concentration of the three hormones analyzed. Taken together, the results indicate that acute systemic cocaine administration alters plasma concentrations of different hormones. However, the response pattern seems to be hormone, dose and time-dependent, differing from results typically observed in rodents and humans, particularly for cortisol. This differentiated response, may be related to glucocorticoid resistance observed in neotropical primates. Therefore, the use of neotropical primates may provide a unique and complex model for the study cocaine-induced neuroendocrine effects. Financial support: CNPq (412542/2003), FINATEC, Laboratório Sabin de Brasília
82. THE ROLE OF THE NK-3 RECEPTOR IN COCAINE-INDUCED BEHAVIOR IN MARMOSSET MONKEYS. Barros, M.<sup>1</sup>; Mello Jr., E.L.<sup>1</sup>; Müller, C.P.<sup>2</sup>; Jocham G.<sup>2</sup>; Maior, R.S.<sup>1</sup>; Huston, J.P.<sup>2</sup>; Tomaz,

C.<sup>1</sup>; de Souza Silva, M.A.<sup>2</sup>. <sup>1</sup> Primate Center, Institute of Biology, University of Brasília, 70910-900, Brazil; <sup>2</sup> Institute of Physiological Psychology I, University of Dusseldorf, 40225, Germany. Neuropeptide transmitters of the tachykinin family are long known to mediate reinforcement processes and affective behavior. The neurokinin3-receptor (NK3), one of the three tachykinin receptors in the brain, was recently shown to modulate the rewarding and hyperlocomotor effects of cocaine in rats. In order to test if these findings can be generalized to primates, we investigated the role of the NK3-receptor in the acute behavioral effects of cocaine in marmoset monkeys (*Callithrix penicillata*). In two separate experiments animals were pre-treated with either the NK3-receptor antagonist SR142801 (0, 0.02, 0.2, 2.0 mg/kg, i.p.) or the NK3-receptor agonist senktide (0, 0.1, 0.2, 0.4 mg/kg, i.p.), followed by a treatment with cocaine (10 mg/kg, i.p) or saline (i.p.). Cocaine increased locomotor activity, but attenuated exploratory behavior and bodycare activities in both experiments. A decrease in scent marking and effects on aerial and terrestrial scanning and glance behaviors were only found in one study. Sensitivity analysis revealed for both studies that two responder types can be differentiated among these primates. SR142801 blocked the actions of cocaine on locomotion, aerial and terrestrial scanning and aerial glance dose-dependently for each responder type. Surprisingly, senktide also blocked the cocaine-induced hyperlocomotion, but enhanced the inhibitory effects on exploratory activity, aerial scanning frequency and terrestrial glance. Neither SR142801 nor senktide had an effect on behavior on its own. Taken together, the present findings suggest that the NK3-receptor contributes, in a complex way, to the acute behavioral responses of marmoset monkeys to cocaine.

83. DEFICIT IN BRAIN REWARD FUNCTION ASSOCIATED WITH FENTANYL WITHDRAWAL IN RATS. Bruijnzeel, A.W.1; Lewis, B.1; Bajpai, L.K.2; Dennis, D.M.2; Morey, T.E.2; Gold, M.S.1,2. Department of Psychiatry 1, Department of Anesthesiology 2, University of Florida, Gainesville, FL 32611 USA. Fentanyl is a mu -opioid receptor agonist that is used as analgesic for the treatment of severe chronic pain. During the last decade, there has been a strong increase in the use and abuse of fentanyl. Cessation of chronic administration of drugs may result in a withdrawal syndrome that is specific for the class of drug used. It is hypothesized here that antagonism of opioid receptors in fentanyl dependent rats or cessation of fentanyl administration results in somatic withdrawal signs and depressive-like behavior. An intracranial self-stimulation paradigm was used to provide a measure of brain reward function. Somatic signs were recorded from a checklist of opioid abstinence signs. Previous studies have shown that withdrawal from drugs of abuse results in an elevation of brain reward thresholds, which is indicative of a depressive-like state. We show here that injections of the opioid receptor antagonist naloxone resulted in a dose-dependent increase in somatic withdrawal signs and dose-dependently elevated brain reward thresholds in rats chronically treated with fentanyl (1.2 mg/kg/day fentanyl salt for 14 days via osmotic minipump) while having no effect in saline-treated controls. In addition, abrupt cessation of fentanyl administration, as induced by minipump removal, resulted in a time-dependent increase in somatic withdrawal signs and a time-dependent elevation of brain reward thresholds. These results indicate that withdrawal from fentanyl is associated with somatic and depressive-like signs that may provide motivation for the continuation of fentanyl use.
84. THE AGED FBN(F1) RAT - A MODEL OF AGE RELATED DEFICITS FOR DRUG DISCOVERY? Curzon, P.; Cronin, E.A.; Browman, K.E.; Fox G.B. Neuroscience Research, Abbott Laboratories, Abbott Park, IL 60064 USA. Impaired spatial working memory is frequently associated with aging. However, within-group variability has hampered progress and there are few studies showing clear drug reversal of age-related impairment. Here we established and tested a colony of aged FBN(F1) rats in a variety of water maze procedures. Two groups of rats were selected, mature (6 mo) and aged (27 mo). Rats were in the standard fixed position hidden platform 4-trials/day model of spatial reference memory for 5 days, followed by a 3-day reversal test. In a second paradigm, acquisition of proximal – distal cue discrimination learning was investigated using a 2-choice visible platform spatial task, followed by a 3-day reversal test. Finally in a third version, rats were trained and tested repeatedly in a paired trial working memory task, where the rat was required to remember the position of a hidden platform that was changed for each of 4 trials. In addition, task difficulty was progressively increased by increasing the delay between the sample run and test run. A fixed position water maze age-related impairment was observed on days 4 and 5 of training, whereas in the proximal distal cue training on days 2 and 3, there was no effect in the reversal test in either case. Age-related impairment was also seen in the working memory tests although variability limited usefulness in a drug discovery setting.

85. CHRONIC AMPHETAMINE ALTERS CORTICOTROPIN-RELEASING FACTOR-ELICITED SEROTONIN RELEASE IN THE PREFRONTAL CORTEX. JL Barr<sup>1</sup>, RB Pringle<sup>1</sup>, MJ Watt<sup>1,2</sup>, AR Burke<sup>1</sup>, NJ Mouw<sup>1,2</sup>, KJ Renner<sup>1,2</sup>, & GL Forster<sup>1</sup>, <sup>1</sup> Basic Biomedical Sciences, <sup>2</sup> Biology Dept., University of South Dakota, Vermillion, SD, USA. Serotonergic (5HT) neurons of the dorsal raphe nucleus (dRN) have been implicated in anxiety and fear behaviors and acute stress responses. During stress, the activity of this system is thought to be mediated by corticotrophin releasing factor (CRF). Administration of amphetamine activates neuroendocrine systems, increasing plasma levels of adrenocorticotrophic hormone and corticosterone through CRF. Withdrawal from chronic amphetamine affects vulnerability to stressful stimuli. To test the hypothesis that chronic amphetamine treatment (2.5 mg/kg,ip.) would alter 5HT release in the medial prefrontal cortex (mPFC) following CRF administration to the dRN, we treated adult male rats with either amphetamine or saline for two weeks. Using *in vivo* microdialysis immediately following treatment or after a two week withdrawal period, infusion of CRF (100 ng/0.5 µl) into the dRN of urethane-anaesthetized rats resulted in increased extracellular 5HT levels in the mPFC of saline treated rats. In contrast, amphetamine treated rats exhibited no CRF-elicited change in mPFC 5HT. This effect persisted throughout the withdrawal period. These results suggest that chronic amphetamine treatment may alter CRF-5HT pathways involved in stress and anxiety behavior. Support: NIH P20 RR15567 & R01 DA019921.
86. PRENATAL COCAINE EXPOSURE ALTERS RESPONSE TO NOVELTY AND ADRENERGIC SYSTEMS IN ADOLESCENT RATS. Silvers, J; Ferris, M; Harrod, S; Mactutus, C; Booze, R. Psychology, Physiology and Pharmacology, Program in Behavioral Neuroscience, Univ of South Carolina, Columbia, SC USA. In rodent models, behavioral alterations following prenatal cocaine have been demonstrated into adulthood (Foltz et al., 2004; Gendle et al., 2003); however little is known regarding behavioral alterations in during adolescence in regard to prenatal effects. The adolescent period has emerged as a time of unique vulnerability to drugs of abuse. The current studies were designed to explore differences in response to novelty in adolescent animals prenatally exposed to cocaine. Female Sprague-Dawley rats were surgically implanted with an intravenous access port (Mactutus et al., 1994) and subsequently bred. Beginning on GD8, animals received saline or 3.0 mg/kg IV cocaine either 1/day or 2/day until GD21, delivered as a bolus injection. On postnatal day 35-37, animals were trained and tested in a task requiring discrimination between a familiarized object and a novel object. Our results demonstrate lack of discrimination between novel and familiar objects in animals prenatally exposed to cocaine. Following behavioral testing, animals were sacrificed for autoradiography studies of receptors and norepinephrine transporter. Prenatal cocaine exposure was shown to alter alpha 2 adrenergic receptor density in hippocampus and norepinephrine transporter density in prefrontal cortex. Response to novelty is thought to be dependent on the medial prefrontal cortex and hippocampus, further suggesting that the adrenergic system may underlie the behavioral alterations following prenatal cocaine exposure. Supported by NIDA grants DA009160, DA013965, DA013137, DA013712, and DA014401.
87. DATA GERMANE TO THE ALCOHOL DEPRIVATION EFFECT. Reid L.D.; Boswell K.J.; Prado-Alcala R.A. Rensselaer Polytechnic Institute, Siena College and Institute for Neurobiology, UNAM. The alcohol deprivation effect (ADE) is a concept that emerged from research with rats and their intake of alcoholic beverages. After rats have developed the habit of drinking daily, and when a period of no opportunity to drink is imposed, supposedly a process is begun that enhances the appetite for alcohol, a deprivation effect. ADE is manifest as greater intake of alcohol when the opportunity to drink is re-instated. The ADE supposedly models the motivational processes associated with relapse to drinking prevalent among persons attempting to stop drinking permanently, but frequently relapse to drinking. Previously, we deprived rats of the opportunity to drink and then provided new opportunities and did not observe enhanced drinking with the re-instatement of opportunity. More recently, we collected data germane to the ADE and those data are presented here. Our data show that ADE-like effects occur with saccharin solution and occur only sometimes with alcoholic beverage (when intakes of alcohol are small). The data lead to questioning the utility of the procedures associated with ADE in modeling events germane to alcohol abuse and alcoholism.
88. INCREASED SENSITIVITY TO THE STIMULANT AND ANXIOLYTIC-LIKE EFFECTS OF ETHANOL IN PRE-ADOLESCENT MICE. Hefner, K.,<sup>1</sup> Kash, T.<sup>2</sup>, Winder, D.G.,<sup>2</sup> Holmes, A.<sup>1</sup> <sup>1</sup> Section on Behavioral Science and Genetics, Laboratory for Integrative Sciences, NIAAA, Rockville, MD;

2 Department Molecular Physiology & Biophysics, Vanderbilt University Medical Center, Nashville, TN. Adolescence is characterized by emotional lability, risk-taking, and impulsivity, and by rapid maturation of neural pathways implicated in the pathophysiology of alcohol abuse, including the corticolimbic glutamatergic system. Individuals who have experience with alcohol in adolescence are more likely to become alcoholic. Previous studies have shown that adolescent rats are less sensitive to the ataxic and sedative/hypnotic effects of ethanol (EtOH). However, while the mouse has considerable appeal as a model system to study alcoholism, little is currently known about possible changes in EtOH sensitivity across adolescence in mice. In the present study, pre-adolescent (4-weeks), peri-adolescent (6-week) and post-adolescent/adult (8-weeks) mice were assessed for neural and behavioral effects of EtOH. The effects of EtOH (1.5 g/kg) on locomotor activity and anxiety-like behavior were tested in the open field and elevated plus-maze. Ataxia-related effects of EtOH (2.0-2.5 g/kg) were evaluated using the accelerating rotarod test. Acute sensitivity and chronic functional tolerance to the sedative/hypnotic effects of EtOH (3.5-4.5 g/kg) were tested via loss sleep time/loss of righting. Results showed that pre-adolescent mice demonstrated significantly decreased sensitivity and tolerance to the ataxic and sedative/hypnotic effects of EtOH as compared to peri-adolescent and adult mice. In marked contrast, pre-adolescent mice exhibited significantly greater sensitivity to anxiolytic-like and locomotor-stimulant effects of EtOH than the older age groups. On the basis of these data, we assessed actions of EtOH on NMDA and GABAA receptor function in the bed nucleus of the stria terminalis; key targets of actions of EtOH in a brain region critically involved in mediating anxiety-related behaviors. Taken together, present findings suggest a relative bias away from negative (sedative, ataxic) to positive (anxiolytic, stimulant) behavioral effects of EtOH during pre-adolescent development. Elucidating the neural and genetic basis of these effects could have implications for understanding the effects EtOH on brain function and behavior.

89. QUANTITATIVE GENETIC ANALYSIS OF BRAIN COPPER AND ZINC IN BXD RECOMBINANT INBRED MICE. Jones, L.C., McCarthy, K.A., Beard, J.L., Keen, C.L., and Jones, B.C. Neuroscience Graduate Program. The Pennsylvania State University, State College, PA 16801 USA. Imbalances of copper or zinc are associated with a host of behavioral abnormalities and are implicated in the etiology of several neurological diseases. Therefore, in the brain, copper and zinc must be kept in a delicate homeostatic balance. The network of genes and environmental cues that maintain this balance are as yet unexplored. We recently conducted a quantitative trait loci (QTL) analysis to identify chromosomal regions in the mouse containing possible regulatory genes. The animals were 15 strains of the BXD/Ty recombinant inbred (RI) strain panel and the brain regions analyzed for copper and zinc content were frontal cortex, caudate-putamen, nucleus accumbens, and ventral midbrain. Genetic correlational analysis revealed associations between these metals and dopamine, cocaine and ethanol responses, saccharine preference, immune response, and seizure susceptibility. Several QTL were identified for copper and/or zinc, most notably on chromosomes 1, 8, 13 and 17. The QTL on chromosome 17 is common to copper, zinc, and iron, and is associated with seizure susceptibility. This chromosomal region contains the histocompatibility H2 complex. This work shows that brain copper and zinc concentrations are under polygenic influence and that their regulation is intimately related to CNS function. Future work will reveal genes underlying the QTL and how they interact with other genes and the environment. More importantly, revelation of the genetic underpinnings of copper and zinc brain homeostasis will aid our understanding of neurological diseases that are related to copper and zinc imbalance. Supported in part by USPHS grants USPHS grants NS 35088 and AG 21190 and by grants from the Restless Legs Foundation and from GlaxoSmithKline.

### *Learning, memory, cognition*

90. THE EFFECTS OF ETHANOL EXPOSURE ON SHORT- AND LONG-TERM MEMORY IN *C. ELEGANS*. Michael P. Butterfield and Catharine H. Rankin. Department of Psychology, Graduate Program in Neuroscience and Brain Research Centre, University of British Columbia, Vancouver, BC Canada. Ethanol has been shown to inhibit memory formation. Using a distributed training protocol our lab has demonstrated that the nematode worm, *C. elegans* is capable of long-term memory for habituation (>24 hours). We have investigated the effects of ethanol on long-term memory by exposing worms to various concentrations of ethanol (0.0M, 0.2M, and 0.4M; as originally described in Davies et al. 2003) during habituation training and testing retention 24 hours later in the absence of ethanol. Worms given habituation training 24 hours earlier without ethanol (0.0M) showed significantly smaller responses than

the control group that did not receive any habituation training ( $p < 0.0001$ ), indicating long-term memory. Worms trained on 0.2M ( $p = 0.1787$ ) and 0.4M ( $p = 0.7235$ ) ethanol showed no significant difference in responses between control and trained suggesting that ethanol exposure during training interferes with memory formation. Short-term memory has also been examined in our lab using a short-term habituation (STH) protocol consisting of a period of 30 tap stimuli followed by 3 tap stimuli to assess the recovery from the habituation training. To identify if ethanol affects STH, worms were placed on ethanol plates for one hour and then were administered the STH protocol. Preliminary results indicate that ethanol exposure decreases the rate of habituation as compared to controls ( $p = 0.0876$ ) at a 60 sec interstimulus interval (ISI) but ethanol appears to have little effect on the rate of habituation when administered at a 10 sec ISI. Currently we are examining the effects of ethanol on memory using different mutant strains that have been shown to have altered behavioral responses to ethanol exposure.

91. LONG-TERM MEMORY IN *C. ELEGANS* IS SUBJECT TO RECONSOLIDATION. Timbers, T.A.; Rose, J.K.; Rankin, C.H. Memory for habituation in *C. elegans* is subject to reconsolidation (the theory that retrieval of a previously consolidated memory renders it, at least partially, to a labile state (Nader et al., 2000)) and further, this reconsolidation shares some of the same molecular mechanisms necessary for consolidation. Results show that long-term memory (LTM) for habituation lasts upwards of 48 hours and is not disrupted by protein synthesis inhibition delivered 24 hours post training. However, if protein synthesis inhibition is given immediately after a reminder treatment (10 taps) this interferes with the memory; the animal responds to the tap stimulus at 48 hours as if it were a novel stimulus. From this it can be determined that reactivation of the memory prior to protein synthesis inhibition was required to interrupt memory reconsolidation. We are currently investigating the amount of reminder stimulation necessary to reactivate the previously consolidated memory for habituation in order for memory to be disrupted by reconsolidation blockade. Consolidation of LTM for habituation in *C. elegans* is dependent upon both the presence and activation of non-NMDA -type glutamate receptors. Results show that reconsolidation blockade shares a molecular mechanism with consolidation as it also requires non-NMDA-type glutamate receptors and a change in GLR-1 expression is noted following either phenomenon. We are currently testing a variety of genes including CREB and CRE responsive genes to further investigate whether more molecular mechanisms are also shared between consolidation and reconsolidation.
92. GENERAL THEORY OF PSYCHOLOGICAL RELATIVITY AND COGNITIVE EVOLUTION. Bailey, Charles E. M.D. General Psychiatrist and Medical Director at Accurate Clinical Trials Inc., Cognitive Neuroscientist, and Clinical Research Psycho-pharmacologist, in Orlando, Florida. There is no existing unifying theory of brain, behavior, and Psychology with an established reference point. This theory presents a unifying Psychological theory utilizing a reference point of cognitive accuracy and rational bias, including the tenets of Rational Emotive and Cognitive Behavioral Science and our current general knowledge of brain functioning. The theory ties together emotions, brain function, and cognition. Cognitive thought processes are delineated in relationship to cognitive accuracy; information accuracy, thought process accuracy, and time space continuum accuracy. The evolution of the human frontal lobes is compared to the evolution of our thought processes relative to cognitive accuracy. Generally our thinking is fraught by cultural belief systems that tend to utilizing rigid inaccurate irrational thinking. These irrational thought processes lag behind the evolution of our frontal lobe potential to utilize flexible accurate rational thinking. This irrationality in our thinking inhibits accurate executive functioning which in turn diminishes our rational thought and behaviors, along with decreased rational outcomes, and promotes further irrational thought and behavior in the future that are passed down as cultural belief systems from generation to generation. The theory offers a timely reference point for implementation of cognitive accuracy along with our current knowledge of general brain functioning in order to increase our rational thought and behavior along with improved adaptability, harmony, and survival.
93. INTEGRATION OF CHINESE CHARACTERS AND SPATIAL LOCATIONS IN WORKING MEMORY: AN ERP STUDY. Wang, Y.W.; Lu, Z.H.; Zhou, X.L.; Lin, C.D. Research Center for Learning Science, Southeast University, Nanjing 210096, China; Department of Psychology, Shandong Normal University, Jinan 250014, China; College of Psychology, Beijing Normal University, Beijing 100875, China. Working memory (WM) is a system involved in temporary maintenance and manipulation of information. For maintenance of different types of information, the integrative processes are needed. Integration of information has an important role in human cognitive activities. The prefrontal cortex



activated greater for maintaining integrated information rather than unintegrated information revealed by fMRI, whereas the posterior brain regions showed the opposite pattern. But the time-course of integrative process was not well understood. The present study explored spatiotemporal patterns of the brain activation during integration of Chinese characters and spatial locations using scalp and dipole source analysis of event-related potentials (ERPs). The delay-response paradigm consisted of bound and separate tasks. Fourteen healthy undergraduates or graduates in Beijing (eight female) with aged from 19 to 24 years (mean 20.8 years old) participated in the experiment as paid volunteers. In the present study, ERPs of maintaining bound or separate Chinese characters and spatial locations during delay interval was analyzed. The accuracy of separate task (Mean $\pm$ ASE: 88.4 $\pm$ 6.7%) was significantly higher than the accuracy of bound task (85.4 $\pm$ 7.2%). Mean reaction times (RTs) were 934 $\pm$ 79.2ms (Mean $\pm$ ASE) for separate task, 920 $\pm$ 68.0ms for bound task. The anterior P260, late positive component (LPC) and posterior N150, late negative component (LNC) were elicited by both bound and separate tasks. The amplitudes of N150 and P260 have not differences between separate task and bound task. The amplitude of the posterior LNC of separate task was significantly larger than that of bound task. The amplitude of the anterior LPC elicited during bound task was larger than that elicited during separate task. The maximal amplitude of difference wave obtained from bound minus separate task located on Fz site of the scalp. In separate task, WM maintains separated four Chinese characters and four spatial locations. In bound task, brain not only maintains the equal amounts of Chinese characters and spatial locations, but also integrates the different type of the materials. The difference wave of P400 was obtained by bound task subtracts separate task. The P400 possibly is a pure ERP component indicates the integration of information in WM. The inverse source analysis based on a four-shell spherical head model was performed on the grand-average difference wave in order to localize neural generators of P400. The cortical current density of the P400 was reconstructed at 400ms using minimal norm method. The reconstructed result showed that strong current density in the prefrontal lobe cortex. Using principal component analysis (PCA) a single dipole model that fitted within the time interval of 380-420ms was reconstructed. The dipole source analysis showed a generator located in the vicinity of anterior cingulate cortex (ACC). The present study provided some electrophysiological evidences of integrative processes of Chinese characters and spatial locations.

94. **FRONTAL LOBE INVOLVED IN UPDATING OF EXECUTIVE FUNCTION REVEALED BY EVENT-RELATED POTENTIALS.** Wang,Y.W.; Lin,C.D.; Lu,Z.H.; Zhou,X.L. Research Center for Learning Science,Southeast University,Nanjing 210096,China; Department of Psychology,Shandong Normal University,Jinan 250014, China; College of Psychology,Beijing Normal University, Beijing 100875,China. In order to explore the role of cerebral cortex in updating of executive function and load effect in 1/2/3-back tasks of Chinese characters, the 64 channels event-related potentials (ERPs) of 14 healthy adults were measured. The participants were volunteers from undergraduate and graduate students in Beijing, who were 6 males and 8 females and their average age was 20.7 years old (ages from 18 to 25 years old ). N360 was elicited by 1/2/3-back tasks at pre-frontal scalp. The duration of the N360 was from 250ms to 600ms after stimuli occurred. The peak-to-peak amplitude of the N360 increased with the working memory load enhancement and showed load effects. High cortical density current distributions and three dipoles located in the both hemispheres' frontal lobe and the posterior areas were found by source analysis to the N360 of 3back tasks. Results suggest that both hemispheres involved in the executive control of updating Chinese characters at different extents, but the left frontal lobe has a relative hemispherical dominance. Key words executive function, updating, frontal lobe, event-related potentials (ERPs)
95. **EGCG, FROM GREEN TEA, REDUCES CEREBRAL AMYLOIDOSIS AND IMPROVES COGNITIVE FUNCTION IN ALZHEIMER TRANSGENIC MICE.** R. Douglas Shytle; Kavon Rezai-Zadeh; Nan Sun; Jared Ehrhart; Jin Zeng; Gary Arendash; and Jun Tan. Center for Excellence in Aging and Brain Repair, Dept. of Neurosurgery; Child Development Center, Dept. of Psychiatry; Dept. of Pharmacology, Dept. of Biology and Neuroscience Program, University of South Florida College of Medicine, Tampa, FL. Alzheimer's disease (AD) is a progressive neurodegenerative disorder pathologically characterized by deposition of  $\beta$ -amyloid (A $\beta$ ) peptides as senile plaques in the brain. We report that (-)-epigallocatechin-3-gallate (EGCG), the main polyphenolic constituent of green tea, reduced A $\beta$  generation in both murine neuron-like cells (N2a) transfected with the human "Swedish" mutant amyloid precursor protein (APP) and in primary neurons derived from Swedish mutant APP-overexpressing mice (Tg APP<sup>sw</sup> line 2576). In concert with these observations, we found that EGCG markedly promoted cleavage of the a-C-terminal

fragment of APP and elevated the N-terminal APP cleavage product, soluble APP-a. These cleavage events were associated with elevated  $\alpha$ -secretase activity. In order to validate these findings in vivo, we treated Tg APPsw transgenic mice overproducing A $\beta$  with EGCG and found decreased A $\beta$  levels and plaques associated with promotion of the nonamyloidogenic  $\alpha$ -secretase proteolytic pathway. In addition, preliminary data suggests that EGCG improved cognitive performance in these mice as well. These data raise the possibility that EGCG dietary supplementation may provide effective prophylaxis for AD. This work was supported in part by the Alzheimer's Association (JT) and a Johnny B Byrd Sr. Alzheimer's Center & Research Institute Award (DS and JT).

96. INSULAR CORTEX AND AMYGDALA KINDLING REINFORCES THE MEMORY-RETRIEVAL SYSTEM IN CONDITIONED TASTE AVERSION. López-Velázquez, L.M.; Camacho, F.J. and Paredes, R.G. Instituto de Neurobiología, UNAM, Querétaro. Kindling is a model in which an initially electrical subconvulsive stimulation of certain brain areas eventually develops generalized seizures that produce behavioral and long term neuronal changes. We have previously shown that kindling strengthens the taste aversive response (conditioned taste aversion, CTA). In the present study we evaluated, if the increased in the aversive response induced by kindling is due to blockade of the extinction or whether kindling reinforces the memory-retrieval system in CTA. Male wistar rats were implanted with bipolar electrodes at the right amygdala (AMG), right insular cortex (IC) or right medial preoptic (MPOA). The animals were stimulated daily until kindling was fully established (3 stage 5 seizures). Subjects were divided in 2 groups: 1) Kindled Rats trained with low doses of LiCl (0.015 and 0.030M) that do not produce CTA. 2) Kindled Rats trained with a dose of LiCl (0.2M) that produce CTA. Once extinction occurred, this group was retrained for CTA with the low doses of LiCl. Group 1 did not develop taste aversion. Animals from group 2 implanted in IC and AMG develop a stronger aversion, the trace becomes much more resistant to extinction, than animals with kindling in the MPOA or Sham stimulated. The same animals showed taste aversion when retrained with low doses of LiCl. The IC and AMG kindled animals showed a higher aversion than the MPOA and sham kindling group. These results indicate that kindling reinforces the memory-retrieval system of CTA.
97. ACQUISITION OF OLFACTORY LEARNING SET FOR SEQUENCES OF CONSTANTLY CHANGING ODORS BY MICE. Cai, C.X.; Katz, E.; Rothschild, O.; and Bauchwitz, R.P. St. Luke's-Roosevelt Institute for Health Sciences, Columbia University, 432 W. 58th St., Room 411, New York, NY 10019, USA. Tests of higher order cognition include acquisition of learning sets, in which a rule or procedure is learned and applied to different problems of a common type. It has been previously reported that rodents can demonstrate a primate-like acquisition of learning sets when tested with odor cues. In this study, inbred and F1 hybrid strains of wildtype and Fragile X (FX) mice were assessed in a five-odor sequence learning and memory task employing buried food rewards as previously described for rats. It was discovered that mice were able to detect small pieces of buried cereal, indicating that scaling the apparatus for physical size does not account for relative olfactory ability between mice and rats. Furthermore, it was determined that criterion on such apparent five-odor sequence tasks could be achieved by recall of only the first two odors. A two-odor test of sequence-dependent working memory using a post choice, drop-in food reward and a novel decoy odor was developed. Odors were changed in each trial to test working memory, and to allow each trial to become a new problem with which to assess acquisition of learning set. Performance differences between inbred and F1 hybrid strains could be readily distinguished; however, the FX mutation did not produce an effect. After achievement of stable average plateau scores, a streak and slump pattern was observed. Even the best performing F1 hybrid mice did not appear to effortlessly acquire sequences of odors in this working memory paradigm, regardless of stringency. This argues against a special facility for memorization of sequences of odors by mice. Furthermore, the streak and slump performance pattern persisted over hundreds of trials, even as average performance continued to improve. Subjects never achieved near-errorless performance over an extended period. These findings strongly support the view that mice do not achieve an abstract "rule-based" learning set in performing olfactory tests.
98. BEHAVIORAL AND ELECTROPHYSIOLOGICAL STUDIES OF CHRONIC ORAL ADMINISTRATION OF LTYPE CALCIUM CHANNEL BLOCKER VERAPAMIL ON LEARNING AND MEMORY IN RATS. Reza Lashgari a, b\*, Fereshteh Motamedi a, b, Saleh Zahedi Asl c aNeuroscience Research Center and Department of Physiology, Shaheed Beheshti University of Medical

Sciences, Tehran, Iran. b School of Cognitive Science, Institute for studies in Theoretical Physics and Mathematics, Tehran, Iran. cEndocrine Research Center, Shaheed Beheshti University of Medical Sciences . It has been shown that L-Type voltage dependent calcium channels (VDCCs) have important role in learning and memory. In vivo and in vitro electrophysiological recordings of hippocampal neurons have demonstrated their involvement in long term potentiation (LTP), which considers to be one possible cellular mechanism underlying learning and memory. The long term effect of VDCCs of hippocampal dentate gyrus (DG) so far on synaptic plasticity has not received much attention. In this study, the effect of chronic (60 days) oral administration of L-Type calcium channel blocker verapamil on learning and memory and synaptic plasticity of hippocampal dentate gyrus in rats has been investigated. L-Type calcium channel antagonist, verapamil chronically and orally at different doses (10, 20 and 50 mg/kg) was used to investigate learning and memory by passive avoidance learning. LTP in perforant-DG synapses was assessed (by either 200 or 400Hz tetanization) in order to investigate long term effect of verapamil on synaptic plasticity. In this case, Field excitatory postsynaptic potential (fEPSP) slope and population spike (PS) amplitude were measured. Our behavioral study has shown that chronic oral treatment of verapamil has no effect on learning whereas verapamil (50mg/kg) decreased memory retrieval. Verapamil (20 and 50mg/kg) inhibited EPSP-LTP induction at 400 Hz but not at 200 Hz tetanization. Furthermore only verapamil (50mg/kg) decreased PS-LTP with respect to control group. These data suggest that 400Hz LTP is required for activation of L-Type VDCCs and it seems that verapamil is more effective on L-Type calcium channels of DG dendrites than their soma

99. MEMORY SYSTEMS COMPETITION: THE HIPPOCAMPUS OVERSHADOWS OTHER NEURAL SYSTEMS FOR CONTEXT MEMORY. Lehmann H.; Sparks, F.T.; Hadikin, C.; Sutherland, R.J. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB. Hippocampal damage impairs context memories that were acquired before the onset of the damage, but does not impair the ability to establish new context memories. This dissociation has been interpreted as suggesting that other neural systems are capable of acquiring context memories, but that normally the hippocampus competes with and prevents these systems from doing so. We examined whether repeated contextual fear conditioning sessions would engage the other systems and mitigate the effects of post-training hippocampal damage. Rats were given 1 or 11 fear conditioning sessions followed, 24-48 hr later, by sham or neurotoxic-induced damage to the hippocampus. Following surgical recovery, rats were returned to the chamber for a retention test in which the amount of behavioural freezing was measured and used as an index of memory. Results indicate that sham rats, regardless of the number of training sessions, expressed robust freezing. Rats with hippocampal damage that previously received a single conditioning expressed minimal and significantly less freezing than their respective control group. In contrast, rats with hippocampal damage that received repeated conditioning sessions expressed high levels of freezing and did not significantly differ from their respective control group. Moreover, this freezing was specific to the conditioning context because the same rats did not freeze in an alternate context. These findings suggest that repeated conditioning sessions prevents hippocampal-induced retrograde amnesia for contextual fear conditioning and we present a model proposing that the hippocampus does not prevent other systems from acquiring the context memories, but that the hippocampus overshadows these systems. Supported by NIMH (MH61460) and AHFMR
  
100. ACUTE ADMINISTRATION OF INTERLEUKIN-1 $\beta$  DISRUPTS NON-HIPPOCAMPAL LEARNING. Hartle, K.D.\*; Ivanco, T.L.\*; Larson, S.J.†; \*Dept. of Psychology, University of Manitoba, Winnipeg, MB. & †Dept. of Psychology, Concordia College, Moorhead, MN. Proinflammatory cytokines and immune stimuli have been shown to disrupt consolidation of memory. Evaluation of the cognitive effects of immune stimuli have focused predominantly on the effect of cytokines on hippocampally-mediated learning. We sought to further understand the effects of cytokines on learning and memory by evaluating the effects of interleukin-1 $\beta$  (IL-1 $\beta$ ) on a motor learning task. In this task, rats were rewarded with a food pellet after they traversed a runway. The runway was either flat (control condition) or had up-ended dowels (motor learning condition). Subjects were trained to traverse the appropriate runway for 5 days, 10 trials per day, and were treated with either saline or 4  $\mu$ g/kg interleukin-1 $\beta$  immediately after each of the first two days of training. Rats that were given IL-1 $\beta$  after exposure to the motor learning condition were consistently slower at traversing the runway for the duration of training when compared to animals given saline. IL-1 $\beta$  did not impair performance in the control condition (i.e., rats in the flat conditioned performed similarly regardless

of whether they were treated with saline or IL-1 $\beta$ ). These data are the first evidence demonstrating that IL-1 $\beta$  can disrupt performance on a motor learning task.

101. THE DEVELOPMENT OF THE P300 EVENT RELATED POTENTIAL IN RATS DURING THE INITIAL STAGES OF SHAPING LEVER PRESSING. Klipec, W.D.; Blomgren, K.; Rozek, E.; Verlautz, S.; and Grinstead, K. Department of Psychology, Drake University, Des Moines, IA 50311 USA. Several experiments in our laboratory have shown that P300 ERP amplitude in rats is a decremental function of conditioned stimulus proximity to primary reinforcement in behavioral chains. We have also demonstrated robust P300 ERPs to stimuli predicting the occurrence as well as the omission of expected reinforcers. These findings support the hypothesis that the P300 is a correlate of the brain's response to recognizing a conditioned reinforcer. In all the experiments we have conducted, the P300 was measured well after the response was established. The present experiment investigated the growth of the P300 during the shaping of the response to food delivery magazine (click training) and subsequent lever pressing. During this training a target tone (5.5 KHz, 70 db SPL) predicted the click of the pellet delivery magazine while a random non-target tone (2.5 KHz, 70 db SPL) was presented on a 8:1 non-target to target ratio. Seven rats received this training across 12 training sessions that consisted of 60 target tone-click-food pairings and 480 non-target tones. The mean amplitude of the P300 ERP to the target tone increased significantly across the 12 days reaching 128  $\mu$ V and 95  $\mu$ V on Days 11 and 12 respectively. Latency of the peak amplitude was about 800 msec and did not change significantly across the training sessions. Since the P300 ERP amplitude increased gradually across the sessions, during the time that the target stimulus was acquiring conditioned reinforcing properties, these findings further support the working hypothesis that the P300 ERP is a correlate of the brains recognition of a conditioned reinforcing stimulus.
102. MUP-75 SAPORIN OLD AND NEW: EFFECTS ON BRAIN AND BEHAVIOUR. Brown, R.E.; Hoffman, N.; Currie, L.; Stamp, J.; Semba, K. Psychology Dept, Anatomy and Neurobiology Dept. and Neuroscience Institute. Dalhousie University, Halifax, NS Canada. B3H 4J1 [rebrown@dal.ca]. The destruction of cholinergic cells in the mouse brain using the cholinergic neurotoxin mup-75 saporin has been proposed as a mouse model of Alzheimer's Disease as it results in dose-dependent cell loss in the medial septum and deficits in spatial learning (Berger-Sweeney et al., 2001, J. Neuroscience, 21, 8164-73). In 2002-2004 we conducted two experiments, and found that bilateral i.c.v. injections 0.9, 1.8 and 3.6 mg/mL mup-75 saporin vs. a PBS control into male C57BL/6J mice reduced the number of cholinergic (VaChT positive) cells in the medial septum but not in the nucleus basalis magnocellularis (nBM) and there was no effect on performance in any of our battery of behavioural tests (Open Field, Elevated Plus Maze, Beam walking, Rotarod, Morris Water Maze, Win-Shift Radial Arm Maze task, Olfactory learning in an Olfactometer). In 2004 a new batch of mup-75 saporin was made available as the original batch had "lost its binding properties". In two experiments in 2004-2005 we examined the potency and selectivity of the new batch of mup-75 saporin (1.0, 1.5 or 2.0 mg/mL vs. a PBS control) for lesioning cholinergic neurons in male C57BL/6J mouse basal forebrain. The new mup-75 saporin reduced the number of cholinergic cells by 64% and 84% in the medial septum but only 32% and 23% in the nBM. In addition, non-cholinergic neurons in the medial septum and parts of the thalamus were also lesioned. There were no effects of mup-75 saporin on behavior in the Open Field or Rotarod, but latency to find the platform in the Morris Water Maze was significantly increased. This, however, appeared to be an effect on performance and not on cognitive function as swim speed was reduced by mup-75 saporin but swim distance and time spent in the correct quadrant in the probe trial were not affected. Mup-75 groups also showed a greater latency to reach the platform in the visible platform test and a slower swim speed. The results of these experiments suggest that mup-75 saporin is effective in reducing cholinergic neurons in the medial septum, but we have also found non-selective damage but no effects of this neurotoxin on cognitive function. Supported by grants from NSERC (REB) and CIHR (KS) of Canada.
103. ORBITOFRONTAL NEURONS CATEGORIZE FOOD AND SEX IN THE RHESUS MONKEY. Aou, S.; Inoue, T.; Lukats, B.; Sakai, K.; Mizuno, M. Department of Brain Science and Engineering, Kyushu Institute of Technology, Kitakyushu, Japan. To elucidate neuronal mechanisms of visual categorization related to feeding and sexual behaviors, neuronal responses to food and sex categories were analyzed in the orbitofrontal cortex (OBF) using a visual discrimination paradigm in rhesus monkeys. Three paired sets of visual categories consisted of: (1) foods and non-foods; (2) male and female monkeys; (3) geometrical figures and letters were used as visual cues. In food discrimination task, a picture of either food or non-food

object was randomly presented. In sex discrimination task, a picture from one of the sexes of Japanese monkeys was randomly presented. Geometrical figure/letter task were used as the control. Three monkeys were trained to press the lever to get water reward when the pre-determined "target" category was presented on a screen. During learning of the target category, monkeys understood the pre-determined category within the first 10 to 20 trials. Neurons showed wide variety of selectivity for these complex images. Although many neurons responded to all or some category in non-specific manner, some neurons responded in a category-specific or task-specific manner, e.g. responded to only food category but not others or to food/non-food task but not other tasks. In conclusion, OBF neurons are involved in various levels of categorization from individual category such as food, non-food, male and female to higher levels of categorization such as non-animal objects, sex. This work was supported by Grant-in-Aid for Scientific Research (A) (16209006, SA) and COE program in KIT from the MEXT.

104. TIME-DEPENDANT EFFECTS OF SYSTEMIC MUSCIMOL ON EXTINCTION (EXT) OF A CONDITIONED TASTE AVERSION (CTA). Mickley, G.A.; Hoxha, Z.; Bacik, S. Department of Psychology and the Neuroscience Program, Baldwin-Wallace College, Berea, OH 44017 USA. GABA ( $\bar{\alpha}$ -aminobutyric acid) receptor manipulation has been proposed as an important mediator of EXT. The current experiments paired 0.3% saccharin (SAC) with 81 mg/kg Lithium Chloride (LiCl; i.p.) to establish a strong CTA in adult, male Sprague-Dawley rats. During extinction, subsequent opportunities to drink SAC were either preceded, or followed, by an injection of the GABA agonist muscimol (1.0 mg/kg, i.p.). Muscimol given 0.75 hr after SAC exposure significantly impaired EXT learning in rats compared to either, (a) rats that received muscimol 0.5 hr before SAC exposure or, (b) control rats that received no muscimol. The days required to reach asymptotic EXT did not differ between rats that received muscimol before daily SAC drinking and those that received no muscimol. A second study tested the hypothesis that muscimol given after CS exposure can act as a US and cause a CTA. This experiment paired rat SAC drinking with muscimol (1.0 mg/kg, i.p.), instead of LiCl. Each subsequent exposure to SAC during the acquisition phase resulted in approximately the same consumption of SAC as on the first day of exposure. Thus, these rats neither developed a strong aversion nor did they overcome the initial neophobia (natural avoidance of a novel taste) and readily accept the SAC. These data suggest that the GABA agonist muscimol can impair EXT of a CTA but this phenomenon depends on the timing of the drug administration relative to CS re-exposures. The exact mechanism by which muscimol retards EXT is currently unknown. The drug may be, (a) acting as a weak US, (b) impairing sensory processing of the SAC taste, (c) blocking the taste memory itself, or (d) having direct effects on EXT memory formation. Current studies are addressing these possibilities. Supported by NIMH Award 1-R15-MH63720-02.
105. INFLUENCE OF SEX AND AGE ON AN AMYGDALA-DEPENDENT MEMORY TASK. Rubinow, M.J.,<sup>1</sup> Hagerbaumer, D. A., <sup>1</sup> & Juraska, J.M.<sup>1,2</sup> <sup>1</sup>Dept. of Psychology and <sup>2</sup>Neuroscience Program. The University of Illinois at Urbana-Champaign, Champaign, IL 61820 USA. Both age and sex influence the anatomy of the rat basolateral amygdala (Rubinow, Drogos and Juraska, IBNS abstract 2005). To investigate concomitant effects of these variables on amygdala-dependent learning and memory, we are testing male and female Long-Evans rats in adolescence (day 35), adulthood (3-5 months), and old age (18-21 months) on the conditioned place preference (CPP) task. In the task, food-restricted rats are confined, on alternating days, to one of two distinct compartments of the CPP apparatus, only one of which is paired with a Froot Loops reward. Following habituation to the apparatus and 6 days of training (3 confinements to each chamber), rats are placed in an alleyway connecting the two chambers and given free access to both (now food-free) compartments. Memory for the chamber paired with food is indexed by time spent in the food-paired chamber vs. the non-paired chamber. Preliminary data suggest an effect of age, with adolescent rats showing impaired memory compared to older ages. Since this task has been shown to depend on the basolateral amygdala (Schroeder & Packard, 2002), effects of age and any sex differences in performance will be discussed in light of other known age- and sex-related differences in the structure and function of the rat basolateral amygdala. Supported by NSF IBN 01-36468 and NIA AG 022499 and NIH HD07333 (MJR)
106. EFFECTS OF MODAFINIL ON RADIAL ARM MAZE PERFORMANCE AFTER TWELVE HOURS OF REM SLEEP DISRUPTION Mery, L; McQuade, JA; and Wayner, MJ University of Texas at San Antonio, Brooks City-Base USAF, San Antonio, TX. The radial arm maze (RAM) is an accepted behavioral test of working memory, and may be used to detect performance impairments in rats. Numerous

studies have implicated the involvement of the hippocampus in navigation of the radial arm maze. It has been reported that long term potentiation (LTP) measured in the dentate gyrus (DG) of the hippocampus is decreased after 12 hours of REM sleep disruption. We hypothesized 12 hours of REM sleep disruption will impair RAM performance and decrease induced LTP. We have tested one dose of modafinil, to determine if this drug ameliorates the performance impairments in animals trained to criterion and then sleep disrupted. In this study, male Sprague-Dawley rats were food restricted to 80% of body weight, and trained in the eight arm RAM. To reach criterion the animal learned to investigate each arm of the maze once to retrieve the food. This study utilized the modified flowerpot method, in which REM sleep disruption occurs when an animal is placed on a small platform during the light phase from 7:00 am to 7:00 pm. Animals were injected intraperitoneally with either vehicle or 150mg/kg of modafinil at 6:30 pm, thirty minutes prior to the final maze trial. The animals were tested in the maze immediately after the 12 hours of sleep disruption ended. After the final maze trial, animals were anesthetized with urethane, and LTP in the dentate gyrus was measured. Sleep disrupted animals made more mistakes in the maze than cage controls. LTP in animals placed on the small platform was decreased compared to cage controls. The results suggest the REM sleep stage is required to maintain performance in the RAM and normal LTP in the DG of the hippocampus. However, preliminary data so far does not appear to support the hypothesis that modafinil will improve impaired performance due to sleep disruption in rats. This study was funded by the Air Force Office of Scientific Research.

107. DIFFERENTIAL EFFECTS OF MEMANTINE AND MK-801 ON THE AMPHETAMINE-INDUCED CARRIER-MEDIATED DOPAMINE RELEASE AND BEHAVIORAL SENSITIZATION. David, H.N.; Marc Ansseau ; Abiraini, J.H. NNOXe Pharmaceuticals, Québec, Canada; Unité de Psychologie Médicale, CHU Sart-Tilman, Liège, Belgium; UMR 6185, Université de Caen – CNRS, Centre CYCERON, Caen, France Amphetamine raises extracellular dopamine levels in limbic structures such as the nucleus accumbens (NAcc), a critical event that is thought to be involved in its psychostimulant action. This occurs because amphetamine promotes redistribution of vesicular dopamine within the cytoplasm, induces stimulation-independent dopamine release via reverse dopamine transport, and further inhibits dopamine uptake. Amphetamine also decreases stimulation-dependent vesicular dopamine release. These effects may involve possible indirect glutamatergic mechanisms. We investigated the effects of memantine which have been shown to possess potentially neuroprotective and therapeutic properties due to their antagonistic action at the NMDA receptor – on amphetamine-induced changes in carrier-mediated- and KCl-evoked dopamine release in the NAcc, using differential pulse amperometry that allows real-time measurements of dopamine release. The low affinity NMDA receptor antagonist memantine, but not the prototypical compound MK-801, blocked the amphetamine-induced increase in carrier-mediated dopamine release. However, both memantine and MK-801 blocked locomotor sensitization to amphetamine. In contrast with what generally found using prototypical NMDA receptor antagonists, our findings support a causal link between activation of certain NMDA receptors (possibly those composed of the NR1a/NR2D subunit), enhanced dopamine release, and the development of behavioral sensitization to amphetamine. Memantine may be of therapeutic interest for treating drug dependence.
108. GUT BACTERIA ALTERS THE STRESS SYSTEM: IMPACT ON LEARNING. Neufeld, K.A., Bienenstock, J., Foster, J.A. Brain Body Institute, St. Joseph's Healthcare; Department of Psychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada. Germ-free (GF) mice have no intestinal microflora and as such exhibit an undeveloped immune system. Research has demonstrated an altered hypothalamic-pituitary-adrenal (HPA) axis in this animal model, with elevated plasma adrenocorticotropin hormone (ACTH) and corticosterone in response to restraint stress. These animals exhibit reduced basal levels of hippocampal brain derived neurotrophic factor (BDNF) and NMDA receptor subunit NR-2A expression. Little is known regarding the contribution of gut bacteria to nervous system development, or the role of the immune system in the functionality of the nervous system. Our research aims to understand the influence of these factors on brain development and function as reflected in behavioural responses to stress, using the GF model. We examined the anxiety and learning behaviours of Swiss Webster GF vs. Swiss Webster conventional mice through use of activity chambers, elevated plus maze and fear conditioning, under stressed and non-stressed conditions. We found increased levels of anxiety, and impaired cued and contextual learning in the GF mice as compared to controls under stressed conditions. In an unstressed paradigm, GF mice exhibited less anxiety than conventional, but persistent deficits in contextual learning. These initial studies provide strong evidence that intestinal microflora

influences brain development leading to an altered stress axis in the adult. This work also points to the link between an exaggerated stress response and learning deficits. Future studies are planned to ask innovative questions about the role of the immune system on CNS development and function and to dissect whether observed effects are dependent on the immune system per se or whether direct pathways exist between the intestinal microflora and the brain.

### ***Models of schizophrenia, mania and OCD***

109. TOPIRAMATE REVERSES APOMORPHINE-MEDIATED DISRUPTION OF PREPULSE INHIBITION. Bortolato M, Frau R, Orru' M, Casti A, Manunta M, Gessa GL Dept. Pharmacology, University of California, Irvine, USA; Dept. Neuroscience, University of Cagliari, Cagliari, Italy. The anticonvulsant topiramate (TPM) has been recently proposed as a novel adjuvant therapy for bipolar disorder and schizophrenia, yet its efficacy remains controversial. Since both disorders are characterized by gating deficits, we tested the effects of TPM on the behavioral paradigm of prepulse inhibition (PPI) of the acoustic startle response, a validated animal model of sensorimotor gating. TPM (10, 18, 32, 58, 100 mg/kg, intraperitoneal, IP) enhanced PPI in rats in a dose-dependent fashion, prevented the PPI reduction mediated by the dopaminergic agonist apomorphine (0.25 mg/kg, subcutaneous, SC) and potentiated the effects of the antipsychotic drugs haloperidol (0.05, 0.1 mg/kg, IP) and clozapine (2.5, 5 mg/kg, IP). Conversely, TPM elicited no significant effect on the PPI disruption mediated by the NMDA receptor antagonist dizocilpine (0.05, 0.1 mg/kg, SC) and surprisingly antagonized the attenuation of dizocilpine-induced PPI disruption mediated by clozapine (5 mg/kg, IP). Our results suggest that TPM may exert diverse actions on the neural substrates of sensorimotor gating. While the pharmacological mechanisms of such effects are still elusive, our findings might contribute to shed light on some controversies on the therapeutic action of TPM, and point to this drug as a putative novel adjuvant therapy for some clusters of gating disturbances.
110. ANTIPSYCHOTIC-LIKE PROFILE OF 5-ALPHA REDUCTASE INHIBITORS. Bortolato, M; Frau, R; Orru', M; Casti, A; Manunta, M; Bourov, Y; Gessa, GL Dept. Neuroscience, University of Cagliari, Cagliari, Italy. Brain steroidogenesis is known to play a key role in the modulation of many behavioral properties. In particular, recent studies suggest that the enzyme 5-alpha-reductase, one of the main rate-limiting steps in steroidogenesis, might be involved in some metabolic pathways regulating dopaminergic activity. In view of these premises, we investigated whether 5-alpha-reductase inhibitors could possess antipsychotic activity in two animal models relevant to psychotic behavior: the prepulse inhibition of the startle (PPI) and the stereotyped behavior. While finasteride (30, 60, 100 mg/kg, i.p.) had no significant intrinsic effects on either paradigm, it dose-dependently antagonized PPI deficits and stereotyped activities induced by apomorphine (0.25 mg/kg, s.c.). Conversely, finasteride failed to prevent the effects of dizocilpine (0.1 -1 mg/kg, s.c.) on prepulse inhibition. Similar results were observed with the 5-alpha-reductase inhibitors dutasteride (40 mg/kg, i.p.) and SKF 105,111 (30 mg/kg, i.p.). Furthermore, when tested in the open field test, 5-alpha-reductase did not alter spontaneous motor activity, nor did they induce catalepsy in the elevated-bar test. Our results suggest that 5-alpha reductase blockade elicits antipsychotic-like effects, and encourage further investigations to qualify the putative role of this enzyme as a new target in the management of psychotic disorders.
111. ROLE OF DOPAMINE D1 AND D2 RECEPTORS IN CRF-INDUCED ALTERATIONS IN STARTLE PLASTICITY. Risbrough, V.<sup>1</sup>; Vinkers, C.<sup>1</sup>; Geyer, M.<sup>1</sup>; Caldwell, S.<sup>1</sup>; Low, M.<sup>2</sup>; Hauger, R.<sup>1</sup>. <sup>1</sup>Dept. of Psychiatry, University of California, San Diego, La Jolla, CA. <sup>2</sup>Center for the Study of Weight Regulation and Dept. of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR. Inhibition of startle by sensory stimuli (i.e. prepulse inhibition or PPI) is disrupted in patients with panic or post traumatic stress disorders where corticotropin-releasing factor (CRF) neurotransmission may be abnormal. CRF, a neuropeptide released during stress, has been reported to modulate PPI in rodents, although the mechanism for this effect is unclear. CRF administration increases dopamine (DA) turnover and CRF receptors are expressed at neuronal circuits required for DA effects on PPI. In rats, CRF effects on PPI are attenuated by antipsychotic treatments, which have D2 receptor antagonist properties. Hence, we hypothesized that DA D1 and D2 receptor activation may contribute to the effects of CRF on PPI. We examined the effects of r/h-CRF (1-3 µg, ICV) on PPI in mice with either D1 or D2 null mutations or after administration of the respective D1 and D2 receptor antagonists SCH23390 (1 mg/kg, SC) or haloperidol (1

mg/kg, IP). D1 and D2 KO mice exhibited no significant differences in their sensitivity to CRF-induced disruptions of PPI. Similarly, SCH23390 and haloperidol treatment had no effect on CRF-induced disruption in PPI, although both increased PPI at baseline. These results indicate that neither D1- nor D2-receptor activation is necessary for CRF to exert its effects on acoustic startle and PPI, and support the hypothesis that CRF effects on startle and PPI may be via non-dopaminergic systems.

112. LOSS OF OUABAIN BINDING IN THE  $\alpha 2$  ISOFORM OF NA, K-ATPASE AFFECTS LOCOMOTOR AND STARTLE BEHAVIOR. Tori L. Schaefer<sup>1</sup>, Amy E Moseley<sup>2</sup>, Jerry B. Lingref<sup>2</sup>, Charles V. Vorhees<sup>1</sup>, Michael T. Williams<sup>1</sup>, <sup>1</sup>Neurology, Cincinnati Children's Res. Foundation; <sup>2</sup>Molecular Genetics, Univ of Cincinnati, College of Medicine Cincinnati OH 45229. Na, K-ATPases are ubiquitous, participate in osmotic balance and membrane potential, and are composed of  $\alpha$ ,  $\beta$ , and  $\gamma$  subunits. There are 4 known  $\alpha$  isoforms; 3 that are expressed in the CNS in a regional and cell specific manner. These enzymes are integral components of membrane pumps and contribute to neurotransmitter, amino acid, and glucose uptake. The  $\alpha 2$  isoform is most commonly found in astrocytes and perhaps Purkinje cells of the cerebellum in adulthood and in neurons during early development. Ouabain, a proposed stress-related hormone, modulates the activity of the  $\alpha 2$  isoform, however the impact of this modulation is largely unknown. Wild-type  $\alpha 2$  isoform is normally ouabain sensitive. Therefore, to test the role of ouabain, knock-in mice were generated that are  $\alpha 2$  ouabain insensitive, however, these mice retain basal Na, K-ATPase function. In the present study we found the adult knock-in mice to exhibit decreased locomotor activity relative to wildtype. Time in the periphery was increased in the knock-in mice as well as a trend toward decreased distance traveled in the center. These mice also demonstrated a blunted startle reflex. Nonetheless, knock-in mice were not anxious in the elevated zero maze nor were they impaired during the acquisition phase of the Morris water maze. While preliminary, these data suggest that the expression of  $\alpha 2$  in Purkinje cells may be involved in ouabain-mediated changes in locomotor behavior and startle reactivity and are consistent with the finding that these mice show a 23% decrease in ouabain binding.
113. MODELING CHOLINERGIC-RELATED COGNITIVE IMPAIRMENTS IN SCHIZOPHRENIA: DISRUPTION OF LATENT INHIBITION BY SCOPOLAMINE AND ITS RESTORATION BY ANTIPSYCHOTIC DRUGS AND AN ACETYLCHOLINESTERASE INHIBITOR. Barak, S. and Weiner, I. Department of Psychology. Tel-Aviv University, Tel-Aviv 69978, Israel. Administration of muscarinic antagonists may evoke a psychotic state ("antimuscarinic psychosis") including hallucinations, delusions, and impaired attention and thinking. The similarity of this syndrome to psychosis in schizophrenia, along with findings of cholinergic alterations in schizophrenia patients, have kindled an interest in the involvement of acetylcholine in this disease. Latent inhibition (LI) is the slower conditioning to a stimulus which is seen when the stage of conditioning is preceded by a stage of repeated nonreinforced preexposure to that stimulus. Amphetamine-induced LI disruption and its reversal by antipsychotic drugs (APDs) is a well established model of positive symptoms of schizophrenia. Here, we tested if the muscarinic antagonist scopolamine would disrupt LI and if this disruption could be reversed by APDs and by the acetylcholinesterase inhibitor physostigmine. We found that scopolamine at doses of 0.15 and 0.5 mg/kg disrupted LI, similarly to 1 mg/kg amphetamine. Unlike amphetamine however, which disrupts LI when given in the conditioning but not in the preexposure stage, scopolamine disrupted LI when injected in preexposure but not in conditioning. This points to distinct mechanisms underlying LI disruption by scopolamine and amphetamine, and by corollary, scopolamine and amphetamine-induced psychoses. In addition, both the typical and atypical APDs, haloperidol and clozapine, reversed scopolamine-induced LI disruption when given in conditioning or both stages, but not in preexposure, suggesting distinct mechanisms of action of scopolamine and APDs. Finally, physostigmine (0.05 and 0.15 mg/kg) reversed scopolamine- but not amphetamine-induced LI disruption. We propose scopolamine-induced LI disruption as a model of cholinergic-related cognitive impairments in schizophrenia.
114. STIMULATION OF CENTRAL BETA NORADRENERGIC RECEPTORS DISRUPTS PPI. Alsene, K.M; Bakshi, V.P. University of Wisconsin-Madison, Dept. of Psychiatry and Neuroscience Training Program, Madison, WI 53719 USA. Prepulse inhibition (PPI) refers to the ability of a weak stimulus (the prepulse) to inhibit the magnitude of the startle response to a subsequent, intense stimulus (the pulse). PPI is deficient in a number of psychiatric illnesses including schizophrenia. There is evidence that the norepinephrine (NE) system may be important in regulating PPI. The NE system has traditionally been divided into  $\alpha 1$ ,  $\alpha 2$  and  $\beta$  receptor subtypes and recent studies have found that PPI is disrupted by either



stimulation of central postsynaptic  $\alpha 1$  NE receptors or blockade of pre-synaptic  $\alpha 2$  receptors. The role of  $\beta$  receptors in regulating PPI however, remains largely unexplored. This study examined the effects of intracerebroventricular (ICV) administration of the mixed  $\beta$  receptor agonist, isoproterenol (ISO), on PPI. Male Sprague-Dawley rats (N=9) were surgically prepared with cannulae aimed at the lateral ventricle. Following recovery from surgery rats were given ICV infusions of ISO (0, 3, 10, or 30  $\mu\text{g}/5\mu\text{L}$ ) and immediately thereafter tested in startle chambers for assessment of PPI and baseline startle reactivity. ISO significantly and dose-dependently disrupted PPI. Importantly, this disruption in PPI was independent from changes in baseline startle responses as ISO did not alter baseline startle at any of the doses tested. The results therefore indicate that stimulation of central  $\beta$  receptors disrupts PPI. This finding supports the general hypothesis that stimulation of postsynaptic NE receptors can disrupt PPI. Studies examining the ability of  $\beta 1$  and  $\beta 2$  receptor antagonists to block the ISO-induced deficits in PPI are underway.

115. NEONATAL NITRIC OXIDE SYNTHASE INHIBITION IN RATS: A NOVEL NEURODEVELOPMENTAL MODEL OF NEGATIVE SYMPTOMS IN SCHIZOPHRENIA. De Levie, A.; Zuckerman, L.; Weiner, I. Dept. of psychology. Tel-Aviv University, Tel Aviv 69978, Israel. Based on evidence for abnormalities in nitric oxide (NO) system in schizophrenia, such as abnormal distribution of the nicotinamide-adenine dinucleotide phosphate-diaphorase (NADPH-d) neurons and reduced plasma nitrate and NO metabolites levels, we investigated the effects of neonatal administration of the NO synthase (NOS) inhibitor, L-Nitroarginine on the development of latent inhibition (LI). LI refers to retarded conditioning to a stimulus as a consequence of its nonreinforced pre-exposure. We found that neonatal NOS inhibition did not affect LI at prepubertal age, but led to the emergence of an abnormally persistent LI at adulthood in male but not in female rats. Because NMDA receptor antagonists produce abnormally excessive LI, modeling a specific aspect of negative symptomatology, namely, attentional perseveration, we suggested that the abnormally excessive LI following neonatal NOS inhibition may provide a neurodevelopmental model of negative symptoms in schizophrenia. Consistent with clinical pharmacology of schizophrenia, abnormally excessive LI was reversed by the atypical antipsychotic drug (APD) clozapine and the NMDAR agonists, glycine and D-cycloserine, but not by the typical APD haloperidol, supporting the model's relevance for negative symptoms. In addition, we found that NOS inhibition led to decreased sensitivity to the locomotor-stimulating effects of amphetamine and this effect was evident already at prepubertal age, possibly representing a "prodromal state" fully expressed in adulthood. These results suggest that neonatal NOS inhibition may provide a neurodevelopmental model of negative symptoms of schizophrenia that mimics its temporal course and predicts responsiveness to atypical APDs and putative drugs.
116. A SELECTIVE INTRACELLULAR SIGNALING PATHWAY IN THE ANTERIOR CINGULATE CORTEX REGULATES MANIA-RELATED BEHAVIOR. Creson, T.; Hao, Y.; Engel, S.; Yuan, P.; Manji, H.; Chen, G. The extracellular signal-regulated kinase (ERK) and phosphatidylinositol 3 kinase (PI3K) intracellular pathways are important regulators of balances between cell survival and death and cell proliferation and growth in the brain. Abnormalities of these pathways have been implicated in the pathophysiology of mood disorders and may contribute to brain region-specific volume reductions detected in imaging studies. Evidence supports the involvements of mood stabilizers lithium and valproate in the regulation of these pathways as well as their involvement in attenuation or reversal of brain region volume reductions in bipolar patients on a mood stabilizer regimen. Data from our group and others indicate that lithium and valproate differentially activate the ERK and PI3K pathways and, through these pathways, enhance neuronal growth in cultured primary cortical neurons and neuroblastomal neurons as well as specific rodent brain regions related to mood regulation in humans. Several studies have implicated pathological abnormalities in the left anterior cingulate cortex (ACC) of bipolar patients. In the present study we show that continuous infusions of an ERK pathway inhibitor or single injections of an ERK  $\Delta$ -lentiviral construct, but not a PI3K pathway inhibitor or control, in the left ACCs of male Sprague-Dawley rats, initiate manic-like behaviors as evidenced by heightened activities in a battery of tests including increased ambulation and rearing in automated activity boxes, increased mobility in the forced swim test, and increased responses to an amphetamine challenge hyperactivity test. These effects could not be attributed to differences in anxiety-related behaviors among the groups as measured by parameters of the elevated plus maze. Our work implicates the ERK pathway in the regulation of manic-like behaviors.

117. MOUSE STRAIN DIFFERENCES IN LITHIUM ATTENUATION OF D-AMPHETAMINE HYPERLOCOMOTION. Gould, T.D.; O'Donnell, K.C.; Picchini, A.M.; Manji, H.K. Laboratory of Molecular Pathophysiology, NIMH, Bethesda, MD, 20892-3711, USA. Recent advances in neurobehavioral genetics have increased our awareness of the behavioral patterns of different mouse strains, and have characterized essential neural processes that are influenced by strain-dependent inheritable traits. Lithium attenuation of stimulant-induced hyperlocomotion represents a rodent model for the mechanism of the therapeutic action of lithium, and for the development of novel lithium-mimetic compounds; this hyperlocomotion also models a putative clinical endophenotype (mania in response to a dopamine agonist). We studied 12 (3 outbred) mouse strains (129S6/SvEv, A/J, C3H/HeJ, C57BL/6J, C57BL/6NTac, CBA/J, DBA/2J, FVB/NJ, SWR/J, Black Swiss, CD-1, NIH Swiss). Mice received either 1) no drugs, 2) lithium only, 3) d-amphetamine only, or 4) d-amphetamine and lithium. Lithium chloride (100mg/kg) was administered 15 minutes prior to d-amphetamine (2mg/kg). There was a large degree of strain variation in the effects of lithium in this model. For example, d-amphetamine hyperlocomotion was attenuated by lithium chloride in C57/BL6J, C57BL/6Tac, Black Swiss, and CBA/J mice, while CD-1, FVB/NJ, SWR/J and NIH Swiss mice, which were responsive to amphetamine, showed no significant effect of lithium. D-amphetamine hyperlocomotion in the C3H/HeJ strain was enhanced by pretreatment with lithium. Four weeks of lithium administration prior to d-amphetamine produced locomotion effects identical to acute administration in C57/BL6J (decrease), C3H/HeJ (increase) and FVB/NJ (no change) strains. The results are not explained by brain lithium levels, suggesting that the behavioral differences are under the control of inherent genetic or other biological mechanisms specific to the effects of lithium on brain function.
118. EFFECTS OF KAPPA OPIOID RECEPTOR STIMULATION IN AN ANIMAL MODEL OF OBSESSIVE-COMPULSIVE DISORDER. Perreault, M.L.; Seeman, P.; Szechtman, H. Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, ON L8N 3Z5 Canada. Dept. Pharmacology, University of Toronto, Toronto, ON M5S 1A8 Canada. In small activity chambers activation of the kappa-opioid system by U69593 enhances locomotor sensitization to the D2/D3 dopamine agonist quinpirole (QNP). However, in addition to locomotor sensitization QNP induces compulsive checking when rats are tested in a large open field, a phenomenon that may constitute an animal model of obsessive-compulsive disorder (OCD). Therefore, the present study examined how U69593 may affect QNP-induced compulsive checking, and whether changes in drug-induced behaviour are related to alterations in dopamine receptors. A 2x2 design with two fully crossed factors was employed, chronic dose of QNP (0 vs 0.5 mg/kg) and chronic dose of U69593 (0 vs 0.3 mg/kg). Rats were administered fourteen biweekly injections and behavioural activity monitored after each treatment. Results showed that U69593 co-treatment enhanced locomotor sensitization to QNP, altered the topography of motion through space, and accelerated the development of compulsive checking compared to rats treated with QNP alone; U69593 alone had no effect on compulsive checking. Despite the differences in behaviour, similar increases in the levels of D2High in the striatum and nucleus accumbens (NAC) were observed in rats treated with either U69593 or QNP or the two drugs together. Moreover, although there were elevations in D1High and D3High in the NAC, these changes also did not discriminate among the drug groups. These results suggest that the opioid system may accelerate development of OCD-like behaviours but this effect does not simply reflect an increase in dopamine receptor activity.
119. COGNITIVE-DISRUPTIVE EFFECTS OF THE PSYCHOTOMIMETIC PHENCYCLIDINE AND ATTENUATION BY ATYPICAL ANTIPSYCHOTICS. Amitai, N.1,2; Semenova, S.1; Markou, A.1,2. 1Molecular and Integrative Neurosciences Dept., The Scripps Research Institute, and 2Graduate Program in Neurosciences, University of California at San Diego, La Jolla, CA 92037 USA. Cognitive deficits in schizophrenia are pervasive and respond poorly to current antipsychotic treatments. The development and validation of animal models of cognitive schizophrenia symptoms is crucial for the study of these deficits and the discovery of better treatments. We investigated disruptive effects of phencyclidine (PCP), a non-competitive N-methyl-D-aspartate receptor antagonist, on cognitive performance in a test of attention, as well as the potential attenuation of this disruption with atypical antipsychotics. Rats were trained on the 5-choice serial reaction time task (5-CSRTT). The effects of PCP (2 mg/kg s.c.) injected either acutely or subchronically on task performance were assessed. Further, the effects of the atypical antipsychotics clozapine, risperidone, quetiapine, and olanzapine and the typical antipsychotic haloperidol in the 5 CSRTT under baseline conditions were investigated. We then explored the effects of acute clozapine or

risperidone, as well as chronic clozapine, on PCP-induced attentional disruption. Acute PCP had nonspecific response-depressing effects in the 5-CSRTT. Subchronic PCP administration caused selective performance disruption, characterized by decreased accuracy and increased impulsivity. Under baseline conditions, atypical antipsychotics did not affect attentional accuracy except at high doses, and dose-dependently reduced impulsivity. The response depression induced by acute PCP was exacerbated by acute clozapine or risperidone, and was unaffected by chronic clozapine. Importantly, chronic clozapine significantly attenuated the performance disruption caused by subchronic PCP. In conclusion, the effects of subchronic PCP in the 5-CSRTT may constitute a useful animal model for cognitive symptoms of schizophrenia that is sensitive to reversal by atypical antipsychotics and may aid discovery of novel targets for medications ameliorating attentional deficits in schizophrenia.

***Motor behaviors, exercise, and circadian rhythms***

120. EXPERIENTIAL THERAPY IMPROVES SKILLED MOTOR FUNCTION IN 6-OHDA DOPAMINE-DEPLETED RATS. Nafisa M. Jadavji, Bryan Kolb, Gerlinde A. Metz, Canadian Centre for Behavioural Neuroscience. University of Lethbridge. Experiential therapies have been shown to influence the neurodegenerative processes that underlie Parkinson's disease (PD). Furthermore, earlier reports have indicated that experiential therapy, such as environmental enrichment, promotes the survival of dopaminergic grafts in dopamine-depleted rats. Here we investigated whether an enriched environment (EE) affects the severity of dopamine depletion and the development of motor impairments in the unilateral 6-hydroxydopamine (6-OHDA) rat model of PD. Adult, female Long-Evans rats were pre-trained and tested daily in a skilled reaching task. One group of rats was placed in an EE while one group was housed in standard conditions. During this time period, reaching success of EE animals improved as compared to animals living in standard conditions. The animals remained in the two housing conditions for six weeks prior to receiving unilateral infusion of the neurotoxin 6-OHDA into the nigrostriatal bundle. The daily behavioral testing continued up to four weeks after lesion. The observations showed that EE rats developed a significantly higher reaching success during the first three weeks after lesion as compared to rats housed in the standard condition. A separate experiment compared the benefit of EE prior to versus after 6-OHDA lesion. The results indicated that EE only improves skilled motor function when pre-exposure is combined with post-treatment. These data will be discussed in relation to possible mechanisms of experience-dependent modulation of the pathology of PD and in relation to implications for rehabilitation programs in patients with PD. Supported by: Alberta Heritage Foundation for Medical Research, National Institutes of Health Grant# 1R21NS043588-01A1, the Lethbridge Public Interest Research Group, and the National Parkinson Foundation.
121. EXERCISE, ETHOLOGY, AND MONOAMINERGIC ACTIVITY IN MICE SELECTED FOR INCREASED VOLUNTARY WHEEL-RUNNING. Pringle, R.B.<sup>1,2</sup>; Forster, G.L.<sup>2</sup>; Renner, K.J.<sup>1,2</sup>; Waters, R.P.<sup>1</sup>; Garland, T. Jr.<sup>3</sup>; Malisch, J.L.<sup>3</sup>; Swallow, J.G.<sup>1</sup> Dept. of Biology<sup>1</sup> and Basic Biomed. Sci.<sup>2</sup>, U. of South Dakota, Vermillion, SD 57069, USA. Dept. of Biology<sup>3</sup>, U. of California-Riverside, Riverside, CA 92521, USA. The neural circuitry and neurochemistry that regulates the execution of voluntary exercise is not well understood. Our goal was to evaluate neurochemical differences between mice selected (S) for increased voluntary wheel-running and controls (C) in selected brain nuclei. Wheel-running was monitored for 8 weeks in S and C mice, with behavioral evaluations during the last 4.5 weeks. Selected mice ran considerably more than C mice as reflected by both increased speed and time spent on wheels. Selected mice were also behaviorally more active during the dark period, devoting very little time to sleep. Levels of corticosterone did not differ between the lines, but substantial differences were found in basal monoamine levels. Increased striatal dopamine (DA) was found in S mice, and lower DA and serotonin (5HT) concentrations were found in DA and 5HT cell body regions. Serotonin levels in S mice were also lower in brain regions associated with emotive state (amygdala), learning (hippocampus), and motivation (nucleus accumbens). Our finding of altered DA and 5HT systems in S mice reveal marked changes in behavior and neurochemistry. Support: NIH P20 RR-015567, NSF 0091948, IBN-0212567.
122. CONDITIONED LOCOMOTOR ACTIVITY FOLLOWING REPEATED INTERMITTENT ACTIVATION OF NEUROTENSIN RECEPTORS: COMPARISON BETWEEN FISCHER 344, LEWIS, AND LONG EVANS RATS. Rompré, P.-P.; Baucó, P. Psychiatry, University of Montreal, Montreal, Quebec, Canada. Neurotensin (NT) is a neuropeptide localized in limbic regions involved in the

homeostatic control of neurovegetative functions. In a previous study we have shown that central injections of the NT analog [D-Tyr11]-NT produces opposite behavioral effects in Fischer 344 (F344) and Lewis (Lew) rats; it also sensitizes Lew more than F344 rats to the locomotor-stimulant effects of d-amphetamine. This study was aimed at determining whether repeated activation of central NT receptors produces conditioned locomotor activity, an effect that may account, in part, for the sensitized response previously observed in the two strains and in Long Evans. Male adult rats were implanted with a guide cannula above the left cerebral ventricle. In Phase 1, activity was assessed on alternate days for two hours following ICV injection of [D-Tyr11]-NT (18 nmol/10  $\mu$ l), or saline (Days 1,3,5, and 7) in separate groups of animals. One week after the end of Phase 1 (Day 14), activity was assessed in all rats for two hours (conditioning test) following a single injection of saline (icv or ip). Results show that repeated activation of NT receptors produces a conditioned locomotor response, the amplitude of which was very similar in all strains tested even though differential locomotor responses were observed during Phase 1. These findings show that i) when injected centrally, [D-Tyr11]-NT produces psychostimulant-like effects, ii) its acute behavioral effect is not predictive of its long-term effect and iii) the previously reported sensitized response to amphetamine may be partly attributed to conditioned locomotion. Supported by: CIHR to P.B. & P.-P.R.

123. DOPAMINERGIC RECEPTORS DIFFERENTIALLY REGULATE THE HYPERACTIVITY OBSERVED IN AN EXCITOTOXIC MODEL OF HUNTINGTON'S DISEASE. Vázquez I., Mendoza M.S., Giordano M., Instituto de Neurobiología, UNAM, Querétaro, Qro. 76230, México. The striatum regulates the activity of the output nuclei, through two pathways according to the current hypothesis of basal ganglia function. The direct pathway GABAergic cells express predominantly type D1 dopaminergic receptors, and regulate the activity of the internal segment of the globus pallidus, and the substantia nigra reticulata. The indirect pathway neurons express predominantly D2 receptors, and regulate the activity of the external segment of the globus pallidus (Smith, 1998). Excitotoxic models of Huntington's disease result in a short term increase in nocturnal spontaneous locomotor activity in rodents (Mena-Segovia, 2002) The purpose of this experiment was to determine the role of the dopaminergic system in this behavior. Male Sprague-Dawley rats were implanted with cannulae directed to the anterodorsal striatum. Control animals received intra-striatal administration of vehicle (PBS, 0.1M), and experimental animals received kainic acid (5 nmoles/0.5  $\mu$ l). Locomotor activity was measured at 7 days post-lesion using an automated system (AccuScan Electronics, Columbus OH). Briefly, animals received bilateral intra-striatal administration of 15  $\mu$ g/kg SKF 38393 (D1 agonist), 5  $\mu$ g/kg quinpirol (D2 agonist), 10  $\mu$ g/kg SCH233990 (D1 antagonist), or 10  $\mu$ g/kg eticloptide (D2 antagonist) in one session, and vehicle on another session. At the end of the experiment, animals were intracardially perfused, and the presence of the lesion was evaluated. Results showed that KA-lesioned animals were more active than controls, both groups showed increased activity with the D1 agonist, and decreased activity with the D1 antagonist, suggesting a role for the direct pathway. However both the D2 agonist and antagonist decreased locomotor behavior in control and experimental animals. This work was supported by IN225305-3 from DGAPA-UNAM, CONACYT 46161-M, and scholarship No. 189355 to I.V.
124. MOTOR SKILL LEARNING MEDIATED BY D1 DOPAMINE RECEPTORS IN THE STRIATUM: FACILITATION BY COCAINE. Willuhn, I.; Steiner, H. Dept. of Cell. & Mol. Pharmacol. RFUMS/Chicago Medical School, North Chicago, IL 60064. Motor learning is implicated in the transition from casual to compulsive cocaine use. Our previous studies indicate that cocaine enhances gene regulation in the striatum associated with learning of wheel running. We investigated the role of striatal D1 dopamine receptors in this motor skill learning and the effects of cocaine. The rat's ability to control/balance the wheel ("wheel skills") was tested before and after a 2-day running wheel training under the influence of cocaine (25 mg/kg, i.p.), or vehicle. Both cocaine- and vehicle-treated rats displayed improved wheel skills for up to 26 days after training (long-term memory). The D1 receptor antagonist SCH-23390 (3 or 10  $\mu$ g/kg, i.p.) given alone before each training session blocked this wheel skill learning. In contrast, animals treated with the lower dose of SCH-23390 (3  $\mu$ g/kg) plus cocaine improved and retained their wheel skills throughout the 26 days, whereas rats treated with the higher dose (10  $\mu$ g/kg) plus cocaine initially improved, but then lost their skills by day 18 after training. Intra-striatal infusion of the D1 antagonist (0.3-1  $\mu$ g) had similar effects. These results suggest that striatal D1 receptors play at least 2 dissociable roles in this motor skill learning. First, dopamine tone at the D1 receptor contributes to initial (short-term) processes of learning. Second, striatal D1 receptors are critical for consolidation of such long-term memory. Our results further indicate that cocaine enhances both short-term and long-term motor memory

formation. These mechanisms may participate in aberrant motor learning proposed to contribute to compulsive drug taking. Supported by NIDA Grants DA011261, DA015439.

125. **BIDIRECTIONAL SELECTION FOR ENDURANCE CAPACITY INFLUENCES GENERALIZED ANXIETY LEVEL AND STRESS COPING MECHANISMS IN NIH RATS.** RP Waters, JL Scholl, RB Pringle, B Seiler, CH Summers, MJ Watt, GL Forster, KJ Renner, LG Koch, SL Britton, JG Swallow. Department of Biology. University of South Dakota, Vermillion, SD 57069. Evidence suggests prolonged physical exercise ameliorates anxiety levels in humans and animal models. Previous research suggests these effects are due to changes in HPA axis and central monoaminergic activity. Whether these effects are mediated by genetic as well as environmental factors is not established. To investigate possible genetic influence on this relationship we obtained NIH rats bi-directionally selected for endurance capacity that exhibit positively correlated changes in voluntary wheel running activity. Response to stress was tested using the elevated plus maze (EPM) before and after restraint stress, forced swim test, light dark box, and dexamethasone suppression test. Behavioral and endocrine response to EPM following restraint and recovery suggests better stress coping mechanisms in low endurance animals than in high endurance animals, in that they exhibited higher levels of maze exploration, and lower corticosterone levels following restraint stress. These results suggest an interaction of the genes that determine endurance capacity and stress coping ability. This project was funded by USDMS Center of Biomedical Research Excellence to JGS, RPW, KJR (NIH P20 RR15567), and NSF EPSCoR in South Dakota to JGS (0091948).
126. **GLUTAMATERGIC AND NICOTINIC MECHANISMS OF L-DOPA-INDUCED DYSKINESIAS IN THE HEMIPARKINSON RAT.** Paquette, M.A.; Brudney, E.G.; Putterman, D.B.; Anderson, A.; Johnson, S.W.; & Berger, S.P. Laboratory of Translational Behavioral Neuroscience, Oregon Health & Science University and the Department of Veteran's Affairs Medical Center, Portland, OR 97239 The NMDA antagonist dextromethorphan (DM) has been demonstrated to reduce L-dihydroxyphenylalanine (L-DOPA)-induced dyskinesias in animal models of Parkinson's Disease, as well as clinically. However, DM also acts as a nicotinic antagonist, and sub-clinical doses of NMDA and AMPA/kainate antagonists reduce dyskinesias when co-administered. To investigate the roles of glutamatergic and nicotinic 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. Co-administration of MK-801 (0.1 mg/kg) with L-DOPA for 5 weeks did not prevent development of dyskinesias, assessed using the Abnormal Involuntary Movement Scale (AIMS). Acute treatment with MK-801 (0.1 mg/kg) or the AMPA/kainate antagonist CNQX (3 mg/kg) did not affect expression of dyskinesias. However, treatment with the NMDA antagonists DM (45 mg/kg) or amatadine (40 mg/kg) or with the AMPA/kainate antagonist topiramate (30 mg/kg), significantly reduced AIMS with differential effects on the AIMS subscales. The nicotinic antagonist mecamylamine (3 mg/kg) did not reduce total AIMS, but did inhibit axial dyskinesias at a dose that reduced contralateral rotation. These data suggest that NMDA, AMPA/kainate, and nicotinic receptors may mediate L-DOPA-induced dyskinesias and could serve as therapeutic targets. Supported by the VA Merit Grant #07-1003.
127. **EXPOSURE TO CHRONIC STRESS LIMITS MOTOR RECOVERY AFTER FOCAL ISCHEMIC STROKE IN THE RAT MOTOR CORTEX.** Scott W. Kirkland, Adrian K. Coma and Gerlinde A. Metz. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB T1K 3M4, Canada. Stress has been shown to exacerbate cell death and cognitive deficits after stroke, however, little is known of the effects of stress on motor recovery after stroke. The objective of this study was to examine the effects of stress on skilled movement after focal ischemia in rats. Rats were pretrained in a skilled reaching task and assigned to one of the following groups. One group was exposed to daily immobilization stress for two weeks prior to the lesion (PRE), one group received daily immobilization stress for two weeks after the lesion (POST), and a third group served as non-stress controls. Focal ischemia of the motor cortex was induced via devascularization. Reaching success in the skilled reaching task was assessed on a daily basis throughout the study, and video recordings were made for qualitative movement analysis. The results showed that stress significantly impaired skilled reaching performance in the PRE group prior to the lesion compared to the POST group and controls. After stroke, both the PRE and POST groups showed significantly lower skilled reaching success compared to non-stress controls. These findings indicate that stress both prior and after ischemic lesion impairs skilled movement performance and recovery. This data suggests that chronic stress might limit the compensatory capacity of the motor system and alter the

pathological processes of stroke. Additional analyses of motor performance and histological evaluations of lesion size are currently being performed. This research was supported by: Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, and the Alberta Heritage Foundation for Medical Research.

128. NEUROBEHAVIORAL CHANGES IN A RAT MODEL OF MAMMARY ADENOCARCINOMA: EFFECTS OF MELATONIN INGESTION. Wilson M.A.; Meekins C.; Ford K.; Junor L.; Crapse T. Department of Pharmacology, Physiology & Neuroscience, Univ South Carolina School of Medicine & University of South Carolina Honors College, Columbia SC 29208. Melatonin, a hormone produced in the pineal gland primarily at night, has been shown to decrease the size, number, occurrence and growth rate of tumors as well as have anxiolytic and antidepressant properties. This study investigated if mammary adenocarcinoma can induce changes in anxiety-like and depression-like behaviors in a tumor-bearing rat model, and to ascertain if melatonin can attenuate both the development and progression of mammary adenocarcinomas and altered mood behaviors. Female Fisher 344 rats were handled and monitored daily for food and water intake, and melatonin intake was initiated 2 days prior to tumor cell injection at a dose of 4mg/kg/day in the drinking water. Estrous cycles were also tracked daily by vaginal lavage. Animals were injected subcutaneously in a mammary pad with either serum free medium or MTLn3 rat adenocarcinoma cells for tumor growth. Once significant tumor growth occurred palpable tumor size was recorded daily. For the assessment of anxiety-like behaviors, animals were tested on the elevated plus maze 19-20 days following control or MTLn3 cell injections. Two days later, depression-like behaviors and the antidepressant effects of melatonin ingestion were evaluated using the Porsolt forced swim test. Results showed both circulating and brain melatonin levels were higher, even in daylight hours, in animals treated with melatonin compared with controls. Melatonin-treated animals also showed attenuated tumor progression compared with control rats. The presence of tumors induced modest increases in anxiety and depression-like behaviors in both testing paradigms, although these changes appeared to be attenuated with nocturnal melatonin supplementation consistent with the anxiolytic and antidepressant profile of this hormone. Supported by the Cancer Complementary and Alternative Medicine Center (CCCAM) Biomedical Research Initiative at USC (MAW) & a Howard Hughes Fellowship to CM.
129. FOS EXPRESSION IN THE STRIATUM AFTER MODAFINIL ADMINISTRATION IN KAINIC ACID LESIONED ANIMALS. Mendoza-Trejo M.S; Mena-Segovia J; Giordano M. Dept. of Behavioral and Cognitive Neurobiology, Institute for Neurobiology, Campus UNAM-Juriquilla, Querétaro, México 76230. The striatum may play a significant role in mediating cortical activation required for behavioral arousal, and this function may be independent from the motor function classically associated with the basal ganglia. Modafinil, a recently discovered wake-improving substance induces prolonged wakefulness in a number of species, apparently without inducing locomotor stimulation. The underlying mechanisms of the effects of modafinil remain unknown, particularly with regard to the brain targets involved in its wake-promoting effects, although it has been found that systemic modafinil increases striatal extracellular dopamine. We have observed that striatal administration of modafinil (0.5, 1, 10 and 50 mM) does not increase locomotor activity, nor does it increase total waking time or number of bouts; and it does not modify slow-wave sleep or REM sleep. Number of Fos+ cells increased but the increase was not statistically significant. In this study we examined the effect of striatal administration of modafinil on Fos expression in control and kainic acid (KA) lesioned animals. Briefly, animals were lesioned (KA 3 nmol/0.5 $\mu$ l), and allowed to recover for 7 days; after one hour of intrastriatal administration of modafinil (50mM, 2 $\mu$ l/min) or its vehicle (CMC; 2 $\mu$ l/min), they were perfused, and their brains processed for Fos immunohistochemistry. Another group of control and lesioned animals received intraperitoneal administration of modafinil (200 $\mu$ g/kg), and their locomotor behavior, and cortical activity were monitored. Stronger Fos expression was observed in the lesioned animals; while locomotor behavior, was not affected by modafinil administration. Electrocardiographic recordings are being analyzed. These results will help determine if the striatum is involved in modafinil's effect. We thank Cephalon for providing Modafinil, this work was supported by IN225305-3 from DGAPA-UNAM, and CONACYT 46161-M.
130. CHRONIC STRESS AND GLUCOCORTICOID TREATMENT SUPPORT RECOVERY OF MOTOR FUNCTION IN A RAT MODEL OF FOCAL CEREBRAL ISCHEMIA. Smith, L.K.; Kirkland, S.W.; Metz, G.A. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB T1K 3M4, Canada. One possible reason for the failure to develop effective therapies for stroke is that

intrinsic factors, such as stress, might critically influence pathologic mechanisms and recovery. Acute stress or corticosterone (CORT) treatment prior to ischemic stroke have been shown to exacerbate neuronal death and cognitive deficits. The objective of this study was to examine the effects of chronic stress and elevated levels of CORT on motor function after focal cerebral ischemia in adult rats. Groups of rats received daily restraint stress or oral doses of CORT for a period of two weeks prior to receiving a focal ischemic lesion of the motor cortex via devascularization. Another group served as lesion controls. After surgery, the stress and CORT treatments were continued for three weeks. Motor performance was assessed at weekly intervals in tasks of skilled (tray reaching, skilled walking) and non-skilled (open field, cylinder, swimming) movement. All three groups demonstrated behavioral deficits following surgery, however, the treated groups showed more improvement over time than the control group. For example, restraint and CORT animals were more successful in the tray reaching task following surgery than control rats and showed no impairments in ipsilateral-to-lesion limb use in the skilled walking task. These results suggest that chronic restraint stress and CORT treatment may improve motor recovery after ischemia. While there were no significant group differences in infarct size, restraint animals showed a tendency to develop larger lesions. These data suggest that chronic stress might alter pathological processes of stroke and support motor recovery after focal ischemia.

131. **STRESS AND GLUCOCORTICOIDS EXAGGERATE MOTOR IMPAIRMENTS IN A RAT MODEL OF PARKINSON'S DISEASE.** Smith, L.K.; Jadavji, N.M.; Colwell, K.L.; Pehudoff, S.K.; Metz, G.A. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB T1K 3M4, Canada. Parkinson's disease (PD) is a common neurological condition of the motor system caused by loss of dopaminergic neurons in the substantia nigra. Stress has been one of the earliest proposed causes of PD and both acute and chronic stress may lead to earlier onset or more debilitating symptoms. The goal of this study was to examine the effects of both acute and chronic stress on motor function and dopamine loss in the 6-hydroxydopamine (6-OHDA) rat model of PD. Animals were exposed to restraint stress or oral corticosterone (CORT) treatments either following the unilateral 6-OHDA lesion or both before and after surgery. Another group of animals served as lesion controls. Performance in both skilled (single pellet reaching, ladder rung walking task) and non-skilled motor tasks (open field, cylinder, apomorphine rotations) was monitored at regular intervals. While the 6-OHDA lesion itself reduced the animals' ability to perform the tasks, stress and CORT had additional effects, particularly on skilled movements. Acute stress after lesion did not significantly alter reaching success, but disturbed reaching movement performance. Chronic stress, on the other hand, significantly decreased reaching success both prior to and after surgery. Skilled walking was also negatively influenced by the stress treatments at both time periods. The CORT treatment increased the use of the contralateral forelimb in the cylinder task and activity in the open field. These findings show that stress and elevated levels of stress hormones affect the function of both the intact and compromised motor system and might represent key factors in the pathogenesis of PD.
132. **THE USEFULNESS OF THE SUNFLOWER SEED TEST IN EVALUATING FORELIMB MOTOR DYSFUNCTION AFTER BRAIN ISCHEMIA IN MICE.** Gomez C; Santiago-Mejia J; Ventura-Martinez R; Rodriguez R. Department of Pharmacology, Faculty of Medicine, National University of Mexico, Mexico City, Mexico. 04510. Motor incoordination and forelimb paralysis are two of the most common and persistent neurological alterations produced by sequential common carotid artery sectioning (SCAS) in mice. In this study we assessed the ability of the sunflower seed test to reveal forelimb motor dysfunction in SCAS animals. Male middle-aged mice (37-40 weeks) underwent sequential common carotid artery sectioning at an interval of 32 days. Behavioral testing was done immediately before (baseline) and 24, 48, 72 and 96 hours after first, and second carotid artery sectioning. We recorded the latency to react (sniffing and biting) to food, and the time spent in manipulating, opening and consuming the seed. We found that unilateral carotid artery sectioning produced mild increases in time to reach and successfully consume the seed. After the second surgery (bilateral sectioning) the velocity of seed-reaching was significantly reduced, and the time to successfully consume the seed increased markedly with no evidence of recovery (96 h). The total amount of time needed to successfully consume the seed is mainly due to impairments in forepaw and finger movements required for holding and dexterously manipulating the sunflower seed. Results of this study show that forelimb motor function after SCAS can be easily quantified using the sunflower seed test. We view this test as a sensitive, simple, and economic method in which the degree and progression of the forelimb impairment after brain ischemia can be quantified, as well as any interaction with potential neuroprotective drug therapies.

133. HIPPOCAMPAL NOREPINEPHRINE (NE) LEVEL AND EXERCISE BEHAVIOR IN SPORTS RATS. Morishima, M.; Harada, N.; Hara, S.; Takahashi, A.; Nakaya, Y. Dept. of Nutrition and Metabolism, Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima, Japan. Here we examined the running activity of Spontaneously-Running-Tokushima-Shikoku (SPORTS) rat, a novel hyper-running rat on wheel, and its relation with the hippocampal NE system including the levels of NE, adrenergic receptors (ARs), and degradation enzymes for monoamines. In the hippocampus of SPORTS rats, the level of NE in extracellular fluid was augmented, whereas the level in the homogenate of the whole tissue was decreased even for sedentary conditions. Elevated extracellular NE caused downregulation of  $\alpha$ 2-ARs in the hippocampus of SPORTS rats. Local administration of  $\alpha$ 2-ARs antagonist yohimbine, but not of  $\alpha$ 2-agonist clonidine, into the hippocampus suppressed high running activity in SPORTS rats. The protein expression and the activity levels of monoamine oxidase A (MAOA), a critical enzyme for the degradation of NE, were decreased in the hippocampus of SPORTS rats to increase extracellular NE level. Thus, the inhibition of MAOA in normal Wistar rats markedly increased wheel-running activity. These results indicate that decreased MAOA activity, elevation of extracellular NE, and  $\alpha$ 2-ARs in the hippocampus determine the neural basis of the psychological regulation of exercise behavior in SPORTS rats.
134. DIFFERENTIAL ROLE OF HIPPOCAMPAL GLUTAMATERGIC AFFERENTS IN ACCUMBAL DOPAMINERGIC LOCOMOTOR RESPONSES IN RATS. Rouillon, C.; David, H.N.; and Abbraini, J.H. Centre CYCERON, CNRS UMR 6185, University of Caen, Boulevard H. Becquerel, BP 5229, 14074 Caen, FRANCE. The nucleus accumbens is the main ventral input structure of the basal ganglia, which provide a major neural system involved in the integration and regulation of sensorimotor, limbic and cognitive pathways. The nucleus accumbens is considered to be involved in the limbic-motor interface. Among others, the nucleus accumbens receives major glutamate projections from the frontal cortex and limbic structures such as hippocampus and amygdala, and dopamine projections 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 behaviours. In the present study, we characterize the role of the dorsal hippocampus and the ventral subiculum in the locomotor response induced by activation of the D1-like receptors alone and in the locomotor response produced by activation of both D1-like and D2-like receptors in the nucleus accumbens. Infusion of lidocaine alone either into the ventral subiculum or into the dorsal hippocampus showed no significant 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 dorsal hippocampus as well as in the ventral subiculum amplified locomotor activity induced by SKF 38393. Furthermore, administration of lidocaine in the dorsal hippocampus increased the locomotor response induced by co-infusion of SKF 38393 + quinpirole, while application of lidocaine in the ventral subiculum decreased it. Our results show that ventral subiculum and dorsal hippocampus differentially modulate accumbal dopaminergic locomotor responses.
135. ELECTROPORATION OF THE WILD-TYPE CASEIN KINASE 1-EPSILON GENE INTO THE SUPRACHIASMATIC NUCLEUS OF TAU MUTANT HAMSTERS LENGTHENS CIRCADIAN PERIOD. Wang, H.; Ko, C.H.; Ralph, M.R.; Yeomans, J.S. Dept. of Psychology. University of Toronto, Toronto ON, Canada. Tau mutant hamsters show circadian activity periods near 20 hrs. Mutations of the casein kinase 1e (CK1e) gene appear to cause the tau mutation, presumably by regulating the turnover of proteins in neurons of the suprachiasmatic nucleus (SCN). To test this hypothesis, we added wild-type CK1e to the SCN by electroporation. First, a plasmid vector was constructed with the CK1e gene and a green fluorescent protein (GFP) gene. The plasmid was bilaterally infused into the SCN, followed by electrical stimulation (10 mA, 2 ms pulses at 10 Hz over 5 sec). Circadian periods were measured for at least 2 weeks before and after electroporation. After 3-7 days of activity disruption due to surgery, the circadian rhythm reappeared. The period, however, was lengthened over the next few weeks by a mean of 22.3 min, and by 40.2 min for the 3 sites showing most GFP expression in the SCN. Control tau mutant hamsters electroporated with plasmids lacking the CK1e gene showed no change in circadian period. The data support the conclusion that CK1e gene expression changes in the SCN can change circadian periods in hamsters. (Supported by CIHR and NSERC grants to JY or MRR.)



136. EFFECTS OF THE D2 ANTAGONIST RACLOPRIDE ON SUCROSE FEEDING, LOCOMOTOR ACTIVITY, AND BEHAVIORAL SENSITIZATION TO THE D2/D3 AGONIST QUINPIROLE. K.A. Foley, M. Kavaliers, K.-P. Ossenkopp. Neuroscience Program, Dept. of Psychology, Univ. of Western Ontario, London, CAN. Natural rewards (e.g., food) and drugs of abuse involve similar neural targets and may share common neural mechanisms. Previous work investigating the effects of pre-exposure to sucrose on the behavioral sensitization to the D2/D3 agonist, quinpirole, found that sucrose facilitates the excitatory locomotor effects of quinpirole. The present study examined the effects of the D2 antagonist, raclopride, in this paradigm. Male Long-Evans rats received 30 min access to 0.3M sucrose or water over 9 consecutive days. 20 minutes prior to each drinking session, animals were injected with raclopride (0.1 mg/kg, i.p.) or saline (0.9%). Locomotor activity was assessed for 45 min on days 1, 5, and 9. After a 5-day rest period, behavioral sensitization was examined with the rats receiving a quinpirole (0.5 mg/kg, s.c.) or saline injection every 2 days for 10 injections. Locomotor activity was assessed for 60 min following injections 1, 2, 4, 6, and 10. Animals receiving raclopride consumed less water than controls, with no drug effect seen on sucrose consumption. Repeated injections of quinpirole produced locomotor sensitization. Pre-treatment with raclopride or sucrose did not affect the level of quinpirole-induced sensitization, but did affect activity levels in saline controls. Supported By: NSERC.

*Saturday, May 27, 2006*

**8:45-10:45**

***Symposium 7: Explorations of the parental brain***

THE ADAPTIVE NATURE OF PARENTAL RESPONSIVENESS: LESSONS FROM THE RAT RACES, WILD-CAUGHT RATS, AND DEADBEAT DADS. Kelly G. Lambert, Randolph-Macon College, Ashland, VA 23005 USA. It is well established that effective parenting responses contribute to the development of offspring. Conversely, recent research has also established that stimulation provided by the offspring contributes to the development of the maternal animal by altering responses that have not been traditionally viewed as maternal behaviors. For example, maternal rats in our labs have exhibited enhanced foraging and exploratory behavior when compared to their virgin counterparts. In another study, maternal rats were more successful in a social competition (i.e., the rat race) than virgin rats. Outside of the laboratory, larger amygdalar cell bodies were observed in pregnant and lactating wild-caught rats than in non-reproductive wild-caught rats, suggesting an effect on emotional responsiveness in the wild animals. Thus, in addition to playing a role in the evolution of the mammalian brain (as proposed by Paul MacLean), the maternal response appears to contribute to the development of the maternal brain in adaptive ways. In an attempt to assess the influence of parental responsiveness on the male brain, *Peromyscus californicus* has been used as a paternal model. Corroborating our maternal rat findings, *P. californicus* dads exhibited enhanced foraging ability and exploration. Further, when compared to uniparental *Peromyscus maniculatus* (i.e., deadbeat dads), *californicus* virgin males exhibited more nurturing responses in the presence of foster pups than their *maniculatus* counterparts, and this behavioral effect was accompanied by alterations in vasopressin and fos immunoreactivity in relevant brain areas. We are currently collecting data indicating that, even in the *maniculatus* model, first-time fathers exhibited increased affiliative responses toward foster pups enclosed in "pup tents" than their virgin counterparts. In sum, our data provide empirical support for offspring-induced neurobiological alterations in the parental brain.

PARITY AND MOTHERING AFFECT WORKING/REFERENCE MEMORY AND HIPPOCAMPAL NEUROGENESIS Galea, L.A.M.; Pawluski, J.L. Department of Psychology, Neuroscience Program and Brain Research Centre, The University of British Columbia, Vancouver, BC, CANADA. Pregnancy and motherhood are life-changing events resulting in marked alterations in the psychology and physiology of the female. There are dramatic fluctuations during pregnancy and lactation in steroid and peptide hormones that are known to alter hippocampus-related behaviour and morphology. It is therefore perhaps not too surprising that pregnancy and mothering affect hippocampus-mediated behaviours and morphology. We have found recently that primiparous (given birth and mothered once) and multiparous (given birth and mothered twice) rats have better spatial working memory compared to nulliparous (never pregnant) rats. Primiparous, but not multiparous, rats also have better spatial reference memory than nulliparous rats. Furthermore, in terms of hippocampal morphology, primiparous, but not multiparous, rats show evidence of reduced dendritic arbor in the CA3 and CA1 regions of the hippocampus compared to nulliparous rats. We will also present recent findings suggesting that primiparous rats have reduced hippocampal neurogenesis during lactation compared to nulliparous and multiparous rats. Our results clearly show

that primiparity is a time of maximal plasticity in female reproductive experience and that this plasticity exists beyond the traditional maternal circuit into the hippocampus.

**WHEN THINGS GO WRONG; COCAINE'S DISRUPTION OF MATERNAL/SOCIAL BEHAVIOR IN RAT DAMS AND THEIR OFFSPRING: THE OXYTOCIN CONNECTION** Johns, J. M.; McMurray, M. S.; Jarrett, T.M. Depts. of Psychiatry and Psychology. University of North Carolina, Chapel Hill, N.C.27599-7096 USA. Over the past twelve years, our laboratory has been studying the effects of different regimens of cocaine treatment in rat dams, during pregnancy or in the postpartum period, on pup directed maternal behavior and maternal aggressive behavior towards intruders in the nest. Recently we have completed studies on the intergenerational effects of cocaine on maternal/social behavior in rat dams and their offspring based on both prenatal exposure condition of the offspring and rearing environment condition. Additionally, we have attempted to determine if cocaine might be mediating behavior through changes in the oxytocin system of dams and/or offspring, either directly or indirectly. Some of our conclusions are that: depending on the regimen and dose of cocaine, maternal behavior and aggression are disrupted in rat dams in a non-adaptive manner; that cocaine-induced alterations of the oxytocin system are a likely mediator of some of these effects; and that next generation offspring maternal/social behavior and oxytocin system dynamics are affected by either prenatal exposure to cocaine, rearing environment (drug treated/non-treated dam) or both. This presentation is an overview of some of the studies that have led us to these conclusions. This work was supported by NIH DA R01-13283 and R01 13362 awarded to Dr. Johns.

**THE EMOTIONS OF MOTHERHOOD: HOW REPRODUCTIVE EXPERIENCE REGULATES ANXIETY-LIKE RESPONSES IN RATS.** Byrnes, E.M.; Scanlan V.S.; Bridges, R.S. Dept. of Biomedical Sciences. Tufts University, Cummings School of Veterinary Medicine, North Grafton, MA 01536, USA. Reproductive experience, including pregnancy, lactation and caring for young, has long lasting effects on the brain. One way in which the flexibility of the maternal brain can be demonstrated is by examining how reproductively experienced females shift their behavioral responses under various conditions. To this end, we have examined the impact of prior reproductive experience on anxiety-like behaviors using the elevated plus maze and open field tasks in female rats. The results of these studies indicate that significant alterations in anxiety-like behavior are observed in reproductively experienced females; however, the direction and magnitude of these effects are dependent upon several factors, including the endocrine status and the age of the female. Moreover, changes in anxiety-like behavior are modulated by the presence of pups during testing. Interestingly, the influence of the pups on anxiety-like behavior is observed in females that have given birth, but not in virgin females induced to behave maternally. The neural and/or endocrine changes that underlie these shifting behavioral responses likely facilitate enhanced reproductive success in the experienced female throughout her adult lifespan.

**THE INDUCTION, MAINTENANCE & MEANING OF MATERNAL NEUROPLASTICITY.** Kinsley, C.H. Dept. Psych.-Ctr. for Neuroscience, Univ. Richmond, VA, 23173, USA. Sexual behavior is a transient means to an end, as are the endocrine events that regulate it. The consequences, however, (viz., pregnancy and the rearing of young), are permanent. In mammals motherhood focuses on and benefits the offspring, whose lives would be in peril otherwise. For the mother, though, might the experiences of pregnancy and the care of young confer advantages beyond reproductive fitness and that linger well into senescence? Young parous females display significantly better maze acquisition and memory compared to nulliparous females, effects that depend, in part, on steroidal stimulation of hippocampus, and on robust alterations therein induced by the neuropeptide oxytocin, which also reorganizes synapses in other limbic structures. Because the mother is faced with novel challenges which require new learning, any improvement in the behaviors on which she relies for sustenance and security would be advantageous to her and her offspring. What neuroplasticity may underlie the behavioral changes early and over the lifespan? Compared to age-matched NULLs, parous females perform significantly better in a spatial task, and demonstrate little loss in such abilities, through 24-months of age. Similar females also show marked differences in hippocampal amyloid precursor protein, dendritic spine, and glial concentrations, and in neurotrophic factors. Parity and the presence of young, therefore, collectively an "enriching environment," may modify the brain's basic plasticity, up-regulating its ability to respond to the exigencies of survival. Flexibility in behavioral responses, therefore, appears to be accompanied by a brain that is itself more plastic. These enhancements may spur the female to better and more efficient maternal care, thereby increasing the likelihood of offspring survival and quality and, hence, better offspring outcomes.

**11:00-12:00 Keynote Speaker: James L. McGaugh**

**EMOTIONAL AROUSAL AND AMYGDALA ACTIVATION: THE MAKING OF LASTING MEMORY.** McGaugh, J.L. Center for the Neurobiology of Learning and Memory and Department of Neurobiology and Behavior. University of California, Irvine, Irvine, CA 92697-3800. Emotionally arousing experiences tend to be well-remembered. There is extensive evidence that the basolateral complex of the amygdala (BLA) plays a critical role in modulating the consolidation of memories of emotionally arousing experiences. I will summarize findings from my laboratory indicating that stress hormones regulate memory consolidation, via converging influences on  $\alpha$ -noradrenergic activation within the BLA, and that such activation influences memory for many different types of training via projections to other brain regions including the hippocampus, striatum, and cortical regions. Such findings are consistent with extensive evidence that BLA activation is critically involved in regulating neuroplasticity in the hippocampus and cortex. Human brain imaging findings provide additional evidence that emotional arousal-induced amygdala activation modulates the consolidation of long-term memory through interactions with other brain regions. Thus, the findings of animal and human studies provide compelling evidence that the activation of emotionally activated neuromodulatory systems affecting the BLA and its projections to other brain regions involved in processing memory for different kinds of experiences plays a critical role in insuring that significant experiences are well-remembered.

**14:15-16:15 Symposium 8: Sex, steroids and environment affect recovery from brain injury**

**EFFECTS OF AGE, SEX, AND EXPERIENCE ON RECOVERY CEREBRAL INJURY.** Kolb, B. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB, T1K 3M4, Canada. Damage to the cerebral cortex of rats leads chronic behavioral deficits that are modulated by precise age at injury, precise locus of injury, and pre- and postinjury experience, all of which interact with sex. Overall, males show better spontaneous recovery than females after prefrontal injuries whereas females show better recovery than males after motor cortex injury. Experiences that facilitate recovery (e.g., complex environments, tactile stimulation) provide greater benefits to females whereas experiences that interfere with recovery (e.g., prenatal nicotine) have greater effects on males. The sex differences are correlated with sexually dimorphic changes in dendritic arborization and spine density.

**SEX AND ESTRADIOL IN EARLY BRAIN INJURY: A TALE OF TWO FACTORS.** Nuñez, J.L. Department of Psychology and Neuroscience Program. Michigan State University, East Lansing, MI 48824 USA. Males are more susceptible than females to early brain insult. Hypoxia-ischemia, stroke, periventricular leukomalacia and seizures all result in more devastating effects in the developing male brain, and lead to greater incidence of pathologies such as chronic epilepsy, cerebral palsy and ADHD. My initial exploration into this field involved looking at the effect of sex in an animal model of brain injury common in premature human infants. Subsequent work attempted to dissect the hormonal contributions to this sex difference by investigating the effects of altering the levels of estradiol during the neonatal period. Contradictory to the effects in adult models of brain injury, estradiol exacerbates damage in my model of brain injury. Regardless, estradiol alone was not able to account for the sex difference in susceptibility to brain and behavioral repercussions. My recent work has begun to investigate the role of androgens, with promising data documenting their contribution to sex differences in early brain injury.

**NEUROSTEROIDS IN THE TREATMENT OF TRAUMATIC BRAIN INJURY AND STROKE.** Stein, D. My lab studies how progesterone and its precursors and metabolites can enhance functional and structural recovery in the damaged brain. Recently our team completed an NIH-sponsored Phase II (a), single-center trial for safety and efficacy of progesterone in 100 traumatically brain-injured patients, and these data will be discussed. I will also discuss the functional, physiological and genomic mechanisms underlying progesterone's beneficial effects and still being discovered. Some of the background to this research, as well as newer findings on the neurosteroid's salutary actions in the treatment of TBI and ischemic stroke, will be described. There is now growing experimental and clinical evidence that progesterone and its metabolites play a substantial role in reducing the metabolic and functional deficits in stroke and TBI. We are currently examining these injury models in an effort to develop low-cost, safe and effective treatments for brain and spinal cord injuries in humans.

**NEUROPROTECTION BY ESTRADIOL IN A MODEL OF NEONATAL BRAIN INJURY.** Hilton, G.D., Dept. of Neuroscience, Georgetown University, Washington, D.C. The immature brain is particularly susceptible to hypoxic/ischemic (H/I) injury, which may be associated with death and long term neurologic disability, including epilepsy, mental retardation and learning disorders. In the adult, H/I results in the massive release of glutamate,

resulting in increased intracellular calcium and eventual cell death. The mechanisms underlying this injury in the neonate, however, remain elusive and are confounded by the rapid neurologic and hormonal changes that occur during early development. In order to explore possible mechanisms of neonatal brain injury, we have examined the effect of glutamate receptor activation in the newborn rat, with emphasis on the potential neuroprotective role of estradiol.

**16:30-18:30 Oral Session 2: Learning, reward and drug abuse**

ETHANOL AND MDMA: THE COMBINED EFFECT IS MORE THAN MDMA PLUS ETHANOL. Byron C. Jones<sup>1</sup>, Sami Ben Hamida<sup>2</sup>, Erin L. Hute<sup>1</sup>, Céline Riegert<sup>2</sup>, Christian Kelche<sup>2</sup> and Jean-Christophe Cassel<sup>2</sup>  
<sup>1</sup>Biobehavioral Health, The Pennsylvania State University, University Park, PA 16802 USA <sup>2</sup>LN2C FRE 2855 CNRS-Université Louis Pasteur, Strasbourg France. For recreational drug users, polydrug use is the rule rather than the exception. The most frequent combination is marijuana and alcohol; cocaine-alcohol use is also commonly reported. 3,4-methylenedioxymethamphetamine (MDMA), or ecstasy, is also taken frequently with alcohol in the club scene, however the basic science of the combination in animals has been little studied heretofore. Earlier studies by this group has shown that ethanol greatly potentiates spontaneous activity actions of MDMA in rats, while ethanol alone at 1.5 g/kg ip either produces no increase in or slightly decreased spontaneous activity. Moreover, on the first day of a series of daily administrations, ethanol has a protective effect against MDMA-induced hypothermia. This effect, however, was seen only on the first day. The fact that it was transient was not due to tolerance towards ethanol, as this effect was also found after several days of administration of ethanol alone prior to administration of the combination. In addition, when the ethanol+MDMA treatments were spaced by 2 days at least, the protective effects of ethanol were observed after each of them. These results suggest to us that co-administration of ethanol with MDMA produces effects attributable to activation of the mesolimbic dopamine system and that the combination may have some emergent properties as seen with the combination of ethanol and cocaine. Supported in part by USPHS grants NS 35088 and AG 21190 and by Professeur Invité award from ULP to BCJ.

MIDBRAIN PATHWAYS FOR PREPULSE INHIBITION OF THE STARTLE REFLEX. Yeomans, J.S. Dept. of Psychology, University of Toronto, Toronto ON, Canada. The startle reflex is strongly inhibited if a noise, or midbrain stimulation, precedes the eliciting stimulus by 20-100 ms. Based on lesions, the inferior colliculus, superior colliculus and pedunculopontine tegmentum have been proposed to mediate prepulse inhibition by a serial circuit. The time of the prepulse inhibition elicited by low-current midbrain stimulation, however, is inconsistent with a serial pathway, but is consistent with a fast auditory pathway from the inferior colliculus to the pedunculopontine tegmentum, and a second 5-ms-slower pathway from the superior colliculus to the tegmentum for multimodal processing. The refractory periods and sites of the directly stimulated neurons mediating prepulse inhibition are similar to those mediating approach turning responses from the superior colliculus (i.e., 0.6-1.0 ms). By contrast, at higher currents, startle is elicited in the same sites by neurons with shorter or longer refractory periods (i.e., 0.3-0.5 ms, or 1-2 ms). This clearly distinguishes the pathways that mediate startle potentiation (from the amygdala to the brain stem) from those that mediate startle inhibition by activating approach responses in the midbrain. (Supported by NSERC grants to JSY and his students.)

GENERAL THEORY OF PSYCHOLOGICAL RELATIVITY AND COGNITIVE EVOLUTION. Bailey, Charles E. M.D. General Psychiatrist and Medical Director at Accurate Clinical Trials Inc., Cognitive Neuroscientist, and Clinical Research Psycho-pharmacologist, in Orlando, Florida. There is no existing unifying theory of brain, behavior, and Psychology with an established reference point. This theory presents a unifying Psychological theory utilizing a reference point of cognitive accuracy and rational bias, including the tenets of Rational Emotive and Cognitive Behavioral Science and our current general knowledge of brain functioning. The theory ties together emotions, brain function, and cognition. Cognitive thought processes are delineated in relationship to cognitive accuracy; information accuracy, thought process accuracy, and time space continuum accuracy. The evolution of the human frontal lobes is compared to the evolution of our thought processes relative to cognitive accuracy. Generally our thinking is fraught by cultural belief systems that tend to utilizing rigid inaccurate irrational thinking. These irrational thought processes lag behind the evolution of our frontal lobe potential to utilize flexible accurate rational thinking. This irrationality in our thinking inhibits accurate executive functioning which in turn diminishes our rational thought and behaviors, along with decreased rational outcomes, and promotes further irrational thought and behavior in the future that are passed down as cultural belief systems from generation to generation. The theory offers a timely reference point for implementation of cognitive accuracy along with our current knowledge of

general brain functioning in order to increase our rational thought and behavior along with improved adaptability, harmony, and survival.

**BRAIN REGION-DEPENDENT EFFECTS OF GLUCOSE ON MEMORY.** Parent, M.B.; Krebs, D.L. Center for Behavioral Neuroscience and Department of Psychology, Georgia State University, Atlanta, GA, 30303 USA. We have demonstrated repeatedly that glucose infusions into the medial septum (MS) exacerbate memory deficits produced by co-infusions of  $\gamma$ -aminobutyric acid (GABA) receptor agonists. In contrast to these negative effects, we showed recently that hippocampal glucose infusions reverse spontaneous alternation deficits produced by co-infusions of the GABA agonist muscimol. Emerging evidence suggests that extracellular (ECF) glucose concentrations vary by brain region, raising the possibility that there may be differences in ECF glucose in the MS versus the hippocampus. Such differences could affect the dose-response properties of glucose and contribute to its brain region-dependent effects on memory. Experiment 1 determined whether the positive effects of glucose in the hippocampus are task-dependent. Fifteen min prior to inhibitory avoidance training, rats were given hippocampal infusions of vehicle (1.0  $\mu$ L), glucose (33 or 50 nmol), muscimol (3  $\mu$ g), or a combination of glucose with muscimol in one solution. Memory of the training was tested 48 hr later. Experiment 2 quantified ECF glucose levels in the MS and hippocampus of freely-moving rats using no net flux in vivo microdialysis procedures. Our results show that, as in spontaneous alternation, hippocampal infusions of glucose (50 nmol) reverse the avoidance memory deficits produced by hippocampal muscimol infusions. We also found that ECF glucose levels in the hippocampus and MS are comparable (~1.2 mM). Collectively, our results show that the opposite effects of glucose in the MS and hippocampus generalize to two memory tasks and are not likely due to differences in basal ECF glucose concentrations. Supported by NINDS-NIDDK-JDF & the STC Program of the NSF under Agreement IBN-9876754.

**DISCOVERY AND FUNCTIONAL EXPRESSION OF BRAIN CANNABINOID CB2 RECEPTORS INVOLVED IN DEPRESSION AND DRUG ABUSE.** Onaivi, E. S. Department of Biology, William Paterson University, Wayne, NJ USA. Two well-characterized cannabinoid receptors (CBs), CB1 and CB2 mediate the effects of cannabinoids and marijuana. In mice the effects of CB2 antisense oligonucleotide injection into the brain and i.p treatment with JWH015 in motor function and plus-maze tests were evaluated. We used RT-PCR, immunoblotting, immunohistochemistry, and hippocampal cultures to determine the expression of CB2 CBs in rat brain and in mice brain exposed to chronic mild stress (CMS) or those treated with cocaine or heroin. JWH015 reduced locomotor activities while CB2 antisense oligonucleotide microinjection induced anxiolysis. In CMS animal's expression of CB2 CBs was enhanced and modified in brains of cocaine and heroin treated rats. Abundant iCB2 in neuronal and glial processes were detected in brain. Contrary to the prevailing view that CB2 CBs is restricted to peripheral tissues, we demonstrate that CB2 CBs and their gene transcripts are present in brain. The presence and functional expression of CB2 CBs in brain may be exploited as new target in the treatment of depression and substance abuse.

**THE FLUCTUATION OF LATENT INHIBITION ALONG THE ESTROUS CYCLE: DIFFERENT SENSITIVITY TO TYPICAL AND ATYPICAL NEUROLEPTICS IN INTACT AND OVARIECTOMIZED FEMALE RATS.** Arad M.; Weiner I. Dept. of Psychology, Tel-Aviv University, Tel-Aviv 69978, Israel. The estrogen hypothesis of schizophrenia derives from findings that relapse rates in schizophrenic women are elevated when estrogen levels are low during the follicular phase, postpartum and perimenopausal periods. Latent inhibition (LI) is slower conditioning to a stimulus seen when conditioning is preceded by a repeated nonreinforced preexposure to that stimulus; LI disruption in rats models the impaired ability to ignore irrelevant stimuli in schizophrenia. The study of LI and its loss in rats was done almost solely using males. Given that gender differences are reported in schizophrenia, our aim was to study the LI phenomenon and its modulation by female steroid sex hormones in intact and ovariectomized (OVX) female rats. Here we demonstrate that: 1) females showed LI only if preexposure took place during estrous and conditioning took place during the metestrous phase (estrous-metestrous), whereas no LI was seen during the remaining sequential phases of the estrous cycle; 2) both typical and atypical neuroleptics haloperidol and clozapine restored LI in the proestrous-estrous group, and failed to restore LI in the diestrous-proestrous group, while only clozapine restored LI in the metestrous-diestrous group; 3) LI was disrupted in OVX rats and both  $17\beta$ -estradiol and clozapine restored it. Our study suggests that LI expression in female rats is correlated with hormonal fluctuation and that neuroleptics-induced restoration of LI depends on rats' estral state. Given the link between estrogen and psychotic outbreaks, and that LI is disrupted in acute schizophrenia, the elucidation of the role of feminine steroid sex hormones in LI may shed light on their role in schizophrenia as well as on gender differences in this disorder.

ROLE OF CRF IN THE NEGATIVE AFFECTIVE ASPECTS OF NICOTINE WITHDRAWAL. Bruijnzeel, A.W.; Zislis, G.; Wilson, C.; Gold, M.S. Department of Psychiatry, University of Florida, Gainesville, FL 32611 USA. Nicotine dependence is a chronic mental illness that is characterized by a negative affective state upon tobacco smoking cessation and relapse after periods of abstinence. It has been hypothesized that cessation of nicotine administration results in the activation of brain CRF systems that leads to the negative affective state of withdrawal. The aim of our experiments was to investigate the role of brain CRF systems in the deficit in brain reward function associated with the cessation of nicotine administration in rats. The intracranial self-stimulation procedure was used to assess to negative affective aspects of nicotine withdrawal. In the first experiment, mecamylamine induced a dose- dependent elevation in brain reward thresholds in nicotine-treated rats. In the follow-up experiment, it was shown that pretreatment with the corticotropin-receptor antagonist D-Phe CRF(12-41) prevents the elevations in brain reward thresholds associated with precipitated nicotine withdrawal. In the third experiment, the effect of D-Phe CRF(12-41) on the elevations in brain reward thresholds associated with spontaneous nicotine withdrawal was investigated. Administration of D-Phe CRF(12-41) 6 hours after the explantation of the nicotine pumps, did not result in a lowering of the brain reward thresholds. These findings indicate that antagonism of CRF receptors prevents, but not reverses, the deficit in brain associated with nicotine withdrawal. These data provide support for the hypothesis that a hyperactivity of brain CRF systems may at least partly mediate the initiation of the negative affective aspects of nicotine withdrawal.

DEVELOPMENTAL EXPOSURE TO MDMA RESULTS IN LONG-TERM DEFICITS IN SPATIAL VS. PATH INTEGRATION LEARNING AS A FUNCTION OF DOSE DISTRIBUTION. Vorhees, C.V.; Schaefer, T.L.; Williams, M.T. Div. of Neurology, Cincinnati Children's Res. Found. and Univ. of Cincinnati, Cincinnati, OH 45229. We previously demonstrated a critical period when MDMA exposure results in path integration (Cincinnati water maze, CWM) and spatial (Morris water maze, MWM) learning impairments. We tested whether the same dose of MDMA administered in different patterns on P11-20 differentially affects later behavior. Using a within-litter design, offspring from 20 litters were injected 4 times/day with saline or MDMA (10x4, i.e., 10 mg/kg MDMA x 4/day), or a combination of MDMA and saline: 40x1 (40 mg/kg MDMA x 1/day and saline x 3) or 20x2 (20 mg/kg MDMA x 2/day and saline x 2). All injections were spaced 2 h apart. All three MDMA groups exhibited reduced locomotor activity independent of dose group. No MDMA effects were found on novel object recognition or pre-maze swimming ability, however the 40x1 and 20x2 MDMA groups were most impaired on path integration learning, whereas the 10x4 MDMA group was most impaired on spatial learning. Hence, the type of impairment depends on the pattern of MDMA administration. Were comparable dose-pattern-dependent effects to occur in humans, it suggests that pattern as well as dose and stage of brain development must be accounted for in understanding the long-term effects of early drug exposures.

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Zislis, G. ....	28,100
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## ***IBNS Program (short version)***

### ***Wednesday, May 24, 2006***

- 08:15-08:45 **President's Welcome.** Frontenac Ballroom AB.  
08:45-10:45 **Symposium 1:** *The underappreciated importance of the aversive properties of drugs of abuse.* Frontenac Ballroom AB.  
10:45-11:00 Break/**Exhibitors' Display.** Frontenac Ballroom C.  
11:00-12:00 **Presidential Lecture:** Robert Adamec. Frontenac Ballroom AB.  
12:15-14:15 **Council Meeting.** Montebello Room.  
14:30-16:30 **Oral Session 1:** Stress, fear and emotion. Frontenac Ballroom AB.  
16:30-16:45 Break/**Exhibitors' Display.** Frontenac Ballroom C.  
16:45-18:45 **Symposium 2:** *Genes Meet Behavior: a joint symposium between the International Behavioral Neuroscience Society and International Behavioural and Neural Genetics Society.* Frontenac Ballroom AB.  
19:00-20:00 **Reception** Mallard Lounge.

### ***Thursday, May 25, 2006***

- 08:45-10:45 **Symposium 3:** *Vocalization as an emotional indicator.* MacDonald Ballroom DEF.  
10:45-11:00 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
11:00-12:00 **Keynote Speaker: Michael J. Meaney.** MacDonald Ballroom DEF.  
14:00-16:00 **Symposium 4:** *Relation of dominant-submissive behavior to mania and depression; parallels between animal behavior and human disease.* MacDonald Ballroom DEF.  
16:00-16:15 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
16:15-17:45 **Student Travel Award Slide Blitz.** MacDonald Ballroom DEF.  
18:00-19:45 **Poster Session 1. Exhibitors' Display.** MacDonald Ballroom ABC.

### ***Friday, May 26, 2006***

- 08:45-10:45 **Symposium 5:** *Behavioural Neuroscience - Quo Vadis.* MacDonald Ballroom DEF.  
10:45-11:00 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
11:00-12:00 **The Matthew J. Wayner/NNOXe Pharmaceuticals Award: William T. Greenough** MacDonald Ballroom DEF.  
14:30-15:30 **Grant Workshop.** MacDonald Ballroom DEF.  
15:30-15:45 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
15:45-17:45 **Symposium 6:** *The pharmacological and neural modulation of defensive behavior.* MacDonald Ballroom DEF.  
18:00-19:45 **Poster Session 2. Exhibitors' Display.** MacDonald Ballroom ABC.

### ***Saturday, May 27, 2006***

- 08:45-10:45 **Symposium 7:** *Explorations of the parental brain.* MacDonald Ballroom DEF.  
10:45-11:00 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
11:00-12:00 **Keynote Speaker: James L. McGaugh.** MacDonald Ballroom DEF.  
12:00-13:45 **Student Workshop.** MacDonald Ballroom DEF.  
14:15-16:15 **Symposium 8:** *Sex, steroids and environment affect recovery from brain injury.* MacDonald Ballroom DEF.  
16:15-16:30 Break/**Exhibitors' Display.** MacDonald Ballroom ABC.  
16:30-18:30 **Oral Session 2:** *Learning, reward and drug abuse.* MacDonald Ballroom DEF.  
18:30-19:00 **Business Meeting.** ALL IBNS members. MacDonald Ballroom DEF.  
19:15- **Banquet and Presentation of Awards.** Frontenac Ballroom ABC.