International Behavioral
Neuroscience Society

Annual Meeting
Program and Abstracts

Villasimius, Sardinia, Italy
June 8-13, 2010

Abstracts of the International Behavioral Neuroscience Society, Volume 19, June 2010

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IBNS CENTRAL OFFICE

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PRESIDENTIAL WELCOME

Dear Conference Participants, Colleagues, and Friends,

It is my pleasure to welcome you to the 2010 International Behavioral Neuroscience Society Annual Meeting in beautiful Sardinia. I am thrilled to report that we have a record-breaking number of abstracts this year and a spectacular scientific program. As you look through the program highlights, you'll see that we have four world-renowned keynote speakers--Giovanni Biggio, Nicola Clayton, Thomas Insel and Michael Merzenich--addressing relevant topics such as hippocampal neuroplasticity, comparative cognition, translational research and effective therapeutic strategies for various mental illnesses. The scientific program is also supported by ten symposia on topics ranging from brain injury to maternal behavior, three oral sessions and two poster sessions. Supporting the continuing education of IBNS members, a grant workshop will feature Diane Witt from the National Science Foundation.

This exciting scientific program and beautiful meeting venue are the result of a lot of hard work by many individuals. IBNS is fortunate to have a wonderful Executive Coordinator, Marianne Van Wagner, who manages to channel and direct the efforts of IBNS members as she choreographs successful meetings year after year. We are all indebted to Marianne for her tireless efforts to make this meeting a success each year. A special thanks is also extended to our dedicated *Program Committee* (Wim Crusio-Chair, Sandra Kelly-Co-Chair, Betty Zimmerberg, Igor Branchi, Nancy Ostrowski, Helene David, Leonie de Visser, Francesca Cirulli, Etienne Coutureau, and John Bruno) who have produced such an outstanding program and to the *IBNS Council* (Simon Crowe, Elena Choleris, David Eilam, Giovanni Biggio, Shuji Aou, Rosalinda Guevara-Guzman, Jodi Lukkes, Byron Jones, Adrian Dunn and Larry Reid) who have provided valuable feedback about a multitude of questions that emerged during the planning process. We appreciate the hard work of the *Education and Training Committee* (Katerina Savelieva, Chair, Robert Benno, Jodi Gresack, Sarah Johnson, Peter Shiromani, Anders Agmo, and Matthew Skelton) for their contributions selecting the travel award recipients—as well as John Bruno's continued effort to secure funding to support our young IBNS members.

The *Local Organizing Committee's* (Giovanni Biggio, Alessandra Concas, Enrico Sanna, Laura Dazzi, Paolo Follesa) efforts are also appreciated as they have been helpful managing local arrangements for our members. Each year, we also appreciate the support of our valued sponsors: National Institute of Mental Health, Corporate Sponsors--Elsevier Science, Inc. and Stoelting Co. and our exhibitors--Blue Box Sensors, Campden Instruments, Clever Sys., Inc., Eicom, Noldus Information Technology, Panlab/Harvard Apparatus, San Diego Instruments, TSE Systems, UGO Basile, and Viewpoint Life Sciences. Finally, we appreciate the willingness of the Tanka Village Resort to work with us to provide the necessary resources for a successful scientific meeting against the beautiful setting of Sardinia.

If this is your first IBNS meeting, you are definitely in for a treat. I attended the very first IBNS meeting in 1992 and have been coming ever since! Each year, I look forward to learning more about the exciting discipline of Behavioral Neuroscience, as well as seeing valued colleagues from across the world. I hope you have a similar experience and will want to join us for future meetings.

Benvenuto to all IBNS participants… enjoy the meeting!!

Warmest regards,

Kelly Lambert, IBNS President

OFFICERS

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Secretary ..... Melanie Paquette
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TRAVEL AWARDS
(listed alphabetically)

We are pleased to announce the recipients of the IBNS Travel Awards for the 2010 meeting in Sardinia, Italy. Award winners will receive a cash award, certificate, and waiver of registration and banquet fees. Presentations given by the Travel Awardees are indicated in the program by the symbol †. Travel awardees are presenting orally in the Slide Blitz and will also have their research presented in a poster session.

Postdoctoral Travel Awards

Dr. Michael Vincent Baratta, MIT, Cambridge, MA USA
Dr. Jodi L. Pawluski, Maastricht University, Maastricht, THE NETHERLANDS
Dr. Kate Marie Wassum, University of California, Los Angeles, CA USA
Dr. Ingo Willuhn, University of Washington, Seattle, WA USA

Graduate Student Travel Awards

Ms. Cindy Kaur Barha, University of British Columbia, Vancouver, CANADA
Ms. Elizabeth Thomas Cox, UNC, Chapel Hill, NC, USA
Ms. Lauren Kristen Dobbs, Oregon Health & Science University, Portland, OR USA
Ms. Catherine Anne Marcinkiewcz, University of Florida, Gainesville, FL USA
Mr. Noam Miller, University of Toronto, Toronto, CANADA
Mr. Brandon Lance Pearson, University of Hawaii at Manoa, Honolulu, HI USA
Mr. Robert Raymond Rozeske, University of Colorado-Boulder, CO USA
Mr. Sandy Richard Shultz, University of Western Ontario, Ontario CANADA
Ms. Jessica Anne Siegel, Oregon Health & Science University, Portland, OR USA

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PRESIDENTIAL TRAVEL AWARDS

Dr. Leonie de Visser, Utrecht University, Urecht, THE NETHERLANDS
Dr. Melanie A. Paquette, Univ. of Texas Health Science Center, San Antonio, TX USA

Note: Presidential Travel Awards are new this year. They serve to recognize young scholars at early stages of their careers who not only have made an impact in behavioral neuroscience, but have also significantly contributed to the success of the Society. Presidential Travel Awards are funded by donations from the IBNS membership.

The IBNS would like to express our gratitude to the National Institute of Mental Health (NIMH) for financial support. This financial support enabled many students to attend the conference.

CORPORATE SPONSORS

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

Elsevier Science, Inc.
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EXHIBITORS

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

Blue Box Sensors
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Panlab/Harvard Apparatus
San Diego Instruments
TSE Systems
UGO Basile
Viewpoint Life Sciences

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

Program Committee

Wim Crusio, Chair
Sandra Kelly, Co-Chair
Igor Branchi
John Bruno
Francesca Cirulli
Etienne Coutureau
Helene David
Leonie de Visser
Nancy Ostrowski
Betty Zimmerberg

Education and Training Committee

Katerina Savelieva, Chair
Anders Agmo, Co-Chair
Robert Benno
Jodi Gresack
Peter Shiromani
Matthew Skelton
Sarah Johnson, Student

Local Organizing Committee

Giovanni Biggio, Chair
Alessandra Concas
Laura Dazzi
Paolo Follesa
Enrico Sanna
Mariangela Serra

Keynote Speakers

Giovanni Biggio, Ph.D., University of Cagliari, Italy
Neurosteroid modulation of GABAA receptor plasticity: Physiological and pharmacological conditions

Nicola S. Clayton, Ph.D., University of Cambridge, UK
Development and evolution of mental time travel

Thomas R. Insel, M.D., Director, NIMH, USA
Crossing the translational bridge: From behavioral neuroscience to public health

Presidential Invited Address

Michael Merzenich, Ph.D., University of California at San Francisco
Brain plasticity-based therapeutics

IBNS Workshop

Diane M. Witt, Ph.D., Program Director, National Science Foundation, Arlington, VA, USA

Special Symposia

THE ROLE OF THE BASAL GANGLIA IN LEARNING AND MEMORY.
Chairperson: Claudio Da Cunha

FAMILIAL PATTERNS IN SUBSTANCE USE DISORDERS: HOW MATERNAL PHENOTYPE INFLUENCES VULNERABILITY TO FUTURE DRUG USE.
Chairpersons: Josephine Johns and Elizabeth Byrnes

EARLY ENVIRONMENT SHAPES ADULT MENTAL DISORDERS: ANIMAL MODELS.
Chairperson: Mikhail V. Pletnikov and Co-chairperson: Paul H. Patterson

NEUROSTEROIDS IN THE TREATMENT OF BRAIN INJURY, STROKE AND NEURODEGENERATIVE MOTOR DISORDERS: MORPHOLOGICAL AND FUNCTIONAL OUTCOMES.
Chairperson: Donald G. Stein

NATURAL INTER-INDIVIDUAL DIFFERENCES IN BEHAVIOR TO EXPLORE COGNITIVE PROCESSES.
Chairperson: Françoise Dellu-Hagedorn

THE UNIQUE EFFECTS OF STRESS DURING ADOLESCENCE.
Chairpersons: Giovanni Laviola and Susan L. Andersen

ENDOGENOUS OPIOIDS AND ADDICTION.
Chairperson: Judith E. Grisel

TOP-DOWN MODULATION OF PREPULSE INHIBITION OF THE STARTLE REFLEX IN LABORATORY ANIMALS. Chairperson: Liang Li

UNDERSTANDING THE IMPACT OF EMOTIONAL EXPERIENCES ON BRAIN FUNCTION: INSIGHTS FROM ANIMAL AND CLINICAL STUDIES. (Sponsored by IBRO) Chairpersons: Patrizia Campolongo, Ph.D., Sapienza University, Rome, ITALY and Viviana Trezza, Ph.D., Rudolf Magnus Institute of Neuroscience, Utrecht, THE NETHERLANDS

TIME GOES BY: THE INTERPLAY BETWEEN EMOTION AND MEMORY. Chairperson: Antonella Gasbarri and Carlos Tomaz

Presidential Symposium

IN SEARCH OF EFFECTIVE ANIMAL MODELS IN BEHAVIORAL NEUROSCIENCE. Organizers: Robert Gerlai and Kelly Lambert

Special Satellite Meeting

INTEGRATIVE NEUROSCIENCE OF EXCESSIVE ALCOHOL DRINKING. Organizers: H.C. Becker and G. Biggio

WORKSHOP

A grant workshop will feature Diane Witt, Program Director, National Science Foundation, and a panel of experienced researchers. The workshop will focus on grant opportunities in different countries and on grant writing skills for the training and early independent stages of your career. ***Organizers:*** Nancy Ostrowski, Leonie De Visser, Betty Zimmerberg (Program Committee).

IBNS 2011 - CALL FOR SYMPOSIA and SATELLITE PROPOSALS

The Program Committee is now soliciting proposals for symposia and satellites for the 2011 Annual Meeting of the International Behavioral Neuroscience Society. The next IBNS meeting will be held May 24-29, 2011, at the Sheraton Steamboat Resort, Steamboat Springs, Colorado, USA.

A typical symposium includes four (4) speakers and is scheduled for two (2) hours. The time and date of symposia are set by the Program Committee. Satellites are structured and financed by the organizers. Satellite meetings and may be held either prior to or after the IBNS meeting dates. All proposals should include a title, the name of the chairperson(s), a substantive description of the topic and proposed talks, confirmed list of speakers, their affiliations, and tentative talk titles of their talks. Satellite proposals should also include the anticipated location and plans for financing. All proposals are reviewed by the Program Committee and then submitted to the IBNS Council for consideration.

The deadline for priority consideration of symposium proposals is September 1, 2010. Please send your proposal to the Program Committee Chair, Dr. Wim Crusio at wim_crusio@yahoo.com and COPY the IBNS Central Office at ibns@ibnshomepage.org. Please use subject line: Symposia/Satellite Proposal 2011.

PROGRAM NOTES:

- All main events, including Lectures, Symposia, Oral Sessions, Business Meeting, Poster Sessions, Slide Blitz, Student Workshop and Exhibits will be held in the Congress Center, Foyer and Courtyard. The Welcome Reception will be held at Giardino de Sapori. The Council meeting will start in the Oasys Restaurant. The Student Social will start in the Congress Center Foyer. The final Banquet will be at the Oasys Restaurant and dance will be at the Disco. A section of the Oasys Restaurant will be reserved for the IBNS participants, families and guests.
- Presenting authors are indicated in the program by **bold** type.
- † Indicates Travel Award recipient.

Monday, June 7

Special Satellite Meeting: INTEGRATIVE NEUROSCIENCE OF EXCESSIVE ALCOHOL DRINKING. Organizers: H.C. Becker and G. Biggio. ***Gardenia Room.***

8:00 **Introduction**. **Noronha, A.**

8:30 **Session I**

- EXCESSIVE DRINKING IN A MOUSE MODEL OF ETHANOL DEPENDENCE AND RELAPSE. **Becker, H.C.**
- EXCESSIVE DRINKING IN A MONKEY MODEL: RISKS AND CONSEQUENCES. **Grant, K.**
- NEUROADAPTATION TO ALCOHOL EXPOSURE IN HUMANS AND ANIMAL MODELS. **Pfefferbaum, A.**; Sullivan, E.V.; Zahr, N.M.

10:00 **Break**

10:30 **Session II**

- SYNAPTIC PLASTICITY IN THE CORTICOSTRIATAL SYSTEM: ROLES IN HABIT FORMATION AND ALCOHOL ADDICTION. **Lovinger, D.M.**
- ALCOHOL DEPENDENCE: NEUROADAPTATIONS IN THE AMYGDALA. Cruz, M.T.; **Roberto, M.**

- THE RELATIONSHIP BETWEEN DURATION OF INITIAL ALCOHOL EXPOSURE AND PERSISTENCE OF MOLECULAR TOLERANCE IN STRIATAL NEURONS IS MARKEDLY NON-LINEAR. **Treistman, S.N.**

12:00 **Lunch**

14:00 **Session III**

- NEUROACTIVE STEROID ADAPTATIONS FOLLOWING CHRONIC ALCOHOL CONSUMPTION. **Porcu, P.**; Morrow, A.L.; Adinoff, B.; Grant, K.A.

- ETHANOL MODULATION OF GABA-A RECEPTOR GENE EXPRESSION AND FUNCTION IN SOCIALLY ISOLATED ANIMALS. **Sanna, E.**; Follesa, P.; Mostallino, M.C.; Serra, M.; Biggio, G.

- SOCIAL STRESS AND NEURAL SENSITIZATION: ESCALATED COCAINE BINGING, A MODEL FOR ALCOHOL? **Miczek, K.**

15:30 **Session IV**

- GENE NETWORKS ASSOCIATED WITH ACUTE ETHANOL RESPONSES AND EXCESSIVE DRINKING: INTERACTIONS ACROSS THE MESOLIMBOCORTICAL SYSTEM. **Miles, M.F**.; Wolen, A.; Farris.; Wolstenholme, J.; Bruce, N.; Vorster, P.

16:30 **Brief Presentations**

- LACK OF EFFECT OF LOW CONCENTRATION ETHANOL ON $GABA_A$ RECEPTORS OF RAT CEREBELLAR GRANULES IN CULTURE: EXPLAINED BY THE ABSENCE OF CRITICAL RECEPTOR SUBTYPES? **Cupello, A.**, Gatta, E., Robello M.

- WITHDRAWAL OF LOW CONCENTRATIONS OF ETHANOL IS ASSOCIATED WITH CHANGES IN $GABA_A$ RECEPTOR GENE EXPRESSION AND FUNCTION IN RAT CEREBELLAR GRANULE NEURONS IN CULTURE. **Talani, G.,** Biggio, F., Utzeri, C., Olla, P., Obili, N., Sanna, E., Follesa, P.

- INNATE VULNERABILITY TO EXCESSIVE ALCOHOL DRINKING IN MSP RATS IS ASSOCIATED TO DYSREGULATION OF THE BRAIN CRF_1R SYSTEM. **Ciccocioppo, R.**, Roberto, M.

17:30 **Open Discussion**

Tuesday, June 8

Presidential Symposium: IN SEARCH OF EFFECTIVE ANIMAL MODELS IN BEHAVIORAL NEUROSCIENCE. Organizers: **Robert Gerlai** and **Kelly Lambert.** ***Gardenia Room.***

Immediate-past and current IBNS presidents (Gerlai and Lambert, respectively) have invited six highly recognized leaders in the field of behavioral neuroscience to join them in a pre-meeting Presidential Symposium. The focus of the Symposium is the use of animal models in translational research. The topics have been chosen to span a broad range of brain disorders and behavioral dysfunctions (from stress and anxiety to drug abuse and sleep) as well as behavioral neuroscience techniques (from psychophar-macology to molecular and developmental genetics). The talks are organized around two very different model organisms: rodents and zebrafish. The Presidential Symposium is open to all participants of the IBNS Annual Conference.

Session I: COPING WITH STRESS: ASSESSING ADAPTIVE AND MALADAPTIVE RESPONSES IN RODENT MODELS.

8:30-8:35 **Introduction** by **Kelly Lambert**

8:35-9:05 PREHISTORIC PROZAC: EXAMINING THE NEUROBIOLOGICAL CONSTITUENTS OF ADAPTIVE COPING STRATEGIES AND EFFORT-DRIVEN REWARD TRAINING. **Lambert, K.**

9:05-9:35 PRENATAL SOCIAL STRESS AND PROGRAMMED HYPER-SENSITIVITY TO STRESS IN ADULT OFFSPRING: GENDER-SPECIFIC MODULATION BY NEUROACTIVE STEROIDS IN THE RAT. **Russell, J.A.**; Brunton, P.J.

9:35-10:05 COPING WITH SOCIAL STRESS: NEUROBIOLOGY OF BEHAVIORAL RESPONSES TO SOCIAL DEFEAT. **Huhman, K.L.**

10:05-10:35 STRESS REVISITED: A CRITICAL EVALUATION OF THE STRESS CONCEPT. **Koolhaas, J.M.**

10:35-10:50 **Break**

Session II: FROM MOTOR FUNCTION TO EMOTION: ZEBRAFISH, A NEW TOOL FOR BEHAVIORAL NEUROSCIENCE.

10:50-10:55 **Introduction** by **Robert Gerlai**

10:55-11:25 GENETIC ANALYSIS OF BEHAVIORAL PLASTICITY AND LEARNING IN ZEBRAFISH. **Granato, M.**

11:25-11:55 THE CIRCADIAN CLOCK AND RESPONSES TO PSYCHOSTIMULANTS. **Zhdanova, I.V.**; Lopez-Patino, M.; Mabray, P.; Yu, L.

11:55-12:25 GENES, NEUROTRANSMITTERS AND BEHAVIOR: ZEBRAFISH STRAIN COMPARISON WITH A FOCUS ON ALCOHOLISM. **Gerlai, R.**

12:25-12:55 DECIPHERING GENETIC AND CELLULAR NETWORKS CONTROLLING EMOTION-RELATED BEHAVIORAL RESPONSES IN ZEBRAFISH. **Guo, S**.

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2:00-4:30 **Registration** – ***Congress Center Courtyard***

6:00-7:00 **Welcome Reception** – ***Giardino de Sapori***

7:00-8:30 **Student Social** – ***Ibisco Foyer***

Wednesday, June 9

All oral presentations will be held in the Ibisco Room in the Congress Center.

8:30-9:00 **Welcome:** IBNS President, **Kelly Lambert**.

9:00-10:00 **Presidential Invited Lecture:** BRAIN PLASTICITY-BASED THERAPEUTICS. **Merzenich, M.** Introduction: Kelly Lambert.

10:00-10:30 **Breaks/Exhibits**

10:30-11:30 **Keynote Lecture:** Development and evolution of mental time travel. **Clayton, N.** Introduction: Robert Gerlai.

11:30-12:30 **Oral Session 1:** STRESS AND ANXIETY. Chairperson: Rosa Almeida.

11:30-11:42 PRENATAL STRESS PRODUCES DIVERGENT PATTERNS OF ANXIETY- AND DEPRESSION-LIKE BEHAVIORS IN WKY AND WISTAR RATS. Sultany, T.; Schroeder, M.; **Weller, A.**

11:42-11:54 ROLE OF EARLY LIFE STRESS IN COCAINE-INDUCED LOCOMOTION AND ANXIETY-LIKE AND NOVELTY-SEEKING BEHAVIOR IN ADOLESCENCE. **Tschetter, K.E.**; Callahan, L.B.; Ronan, P.J.

11:54-12:06 ANTERIOR OLFACTORY NUCLEUS PLAYS AN IMPORTANT ROLE IN SOCIAL BUFFERING OF CONDITIONED FEAR RESPONSES. **Kiyokawa, Y.**; Takeuchi, Y.; Nishihara, M.; Mori, Y.

12:06-12:18 IMMUNE ACTIVATION AND DEFENSIVE BEHAVIOR. Dunn, A.J.; Wieczorek, M.; **Swiergiel, A.H.**

12:30-2:00 **Lunch Break**

2:00-4:00 **Symposium 1**: NEUROSTEROIDS IN THE TREATMENT OF BRAIN INJURY, STROKE AND NEURODEGENERATIVE MOTOR DISORDERS: MORPHOLOGICAL AND FUNCTIONAL OUTCOMES. Chairperson: **Donald G. Stein**

2:00-2:20 NEUROACTIVE STEROIDS AND DIABETIC NEUROPATHY. **Melcangi, R.C.**

2:20-2:40 PROTECTIVE EFFECTS OF PROGESTERONE. **Frye, C.**

2:40-3:00 ANTI-INFLAMMATORY ACTIONS OF ESTRADIOL AND ESTROGENIC COMPOUNDS AFTER BRAIN INJURY. **Garcia-Segura, L.M.**; Santos-Galindo, M.; Azcoitia, I.; Arevalo, M.A.

3:00-3:20 MOLECULAR AND BEHAVIORAL EVIDENCES FOR PROGESTERONE AND NEUROSTEROID PROTECTION IN MOTONEURON DEGENERATION. **De Nicola, A.F.**; Gonzalez Deniselle, M.C.; Meyer, M.; Gargiulo, G.; Guennoun R.; Schumacher, M.

3:20-3:40 PROGESTERONE AND ITS METABOLITES IN THE TREATMENT OF TRAUMATIC BRAIN INJURY AND OTHER CNS DISORDERS. **Stein, D.**

3:40-4:00 PROGESTERONE IN THE HEALTHY AND INJURED CENTRAL NERVOUS SYSTEM. **Guennoun, R.**; Labombarda, F.; Liu, A.; Delespierre, B.; Famose, S.; Meffre, D.; Liere, P.; Gonzalez Deniselle, M.C.; Stein, D.G.; De Nicola, A.F.; Schumacher, M.

4:00-6:00 **Workshop:** This workshop will feature Diane Witt, Program Director, National Science Foundation, and a panel of experienced researchers. The workshop will focus on grant opportunities in different countries and on grant writing skills for the training and early independent stages of your career.

6:00-8:00 **Symposium 2**: THE ROLE OF THE BASAL GANGLIA IN LEARNING AND MEMORY. Chairperson: **Claudio Da Cunha**

6:00-6:30 LEARNING NOVEL ACTIONS: FROM INTENT TO HABIT. **Dias-Ferreira, E.**

6:30-7:00 INTERACTIONS BETWEEN THE PEDUNCULOPONTINE AND BASAL GANGLIA AND THEIR ROLE IN LEARNING AND REINFORCEMENT. **Winn, P.**

7:00-7:30 LEARNING, MEMORY AND STRIATAL SYNAPTIC PLASTICITY IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS. **Di Filippo, M.**; Calabresi, P.

7:30-8:00 THE MOSAIC OF BROKEN MIRRORS MODEL. **Da Cunha, C.**; Wietzikoski, E.; Dombrowski, P.; Santos, L.; Bortolanza, M.; Boschen, S.; Miyoshi, E.

Thursday, June 10

8:30-10:30 Symposium 3: FAMILIAL PATTERNS IN SUBSTANCE USE DISORDERS: HOW MATERNAL PHENOTYPE INFLUENCES VULNERABILITY TO FUTURE DRUG USE. Chairpersons: **Josephine Johns** and **Elizabeth Byrnes**

8:30-8:54 COCAINES EFFECTS ON MOTHER AND INFANT PHENOTYPES: MODELS OF INTERGENERATIONAL AND TRANSLATIONAL MECHANISMS THAT MAY IMPACT OFFSPRING VULNERABILITY. **Johns, J.M.**; McMurray, M.S.; Williams, S.K., Cox, E.T.; Jarrett, T.M.; Walker, C.H.; Jamieson-Drake A.W.; Moy, S.S.

8:54-9:18 TRANSGENERATIONAL EFFECTS OF ADOLESCENT OPIATE USE. **Byrnes, E.M.**

9:18-9:42 MATERNAL COCAINE USE AND MOTHER-INFANT INTERACTIONS: DIRECT AND MODERATED EFFECTS. **Eiden, R.**

9:42-10:06 MALADAPTIVE MATERNAL EFFECTS IN RHESUS MONKEYS: IMPLICATIONS FOR DEVELOPMENTAL PSYCHOPATHOLOGY. **Maestripieri, D.**

10:06-10:30 SUBSTANCE USING MOTHERS' RESPONSE TO SALIENT INFANT CUES. Mayes, L.; Potenza, M.; **Landi, N.**; Greger-Moser, M.; Johns, J.

10:30-11:00 **Breaks/Exhibits**

11:00-12:00 **Keynote Lecture:** NEUROSTEROID MODULATION OF GABAA RECEPTOR PLASTICITY: PHYSIOLOGICAL AND PHARMACOLOGICAL CONDITIONS. **Biggio, G.** Introduction: Wim Crusio.

12:00-2:00 **Lunch Break/Meet the Professionals Lunches**

2:00-4:00 **Symposia 4:** Endogenous Opioids and Addiction. Chairperson: **Judith E. Grisel**

2:00-2:30 INVOLVEMENT OF THE ENDOGENOUS OPIOID SYSTEM IN NICOTINE ADDICTION. **Maldonado, R.**

2:30-3:00 ENDORPHIN AND ALCOHOL: FROM MOUSE TO HUMAN. **Rácz, I.**; Schürmann, B.; Zimmer, A.

3:00-3:30 b-ENDORPHIN AND NEGATIVE REINFORCEMENT. **Grisel, J.E.**

3:30-4:00 DETERMINANTS OF DESIRE: DISSOCIABLE OPIOID INVOLVEMENT IN PALATABILITY AND INCENTIVE LEARNING. **Maidment, N.T.**; Wassum, K.M.; Ostlund, S.B.; Balleine, B.W.

4:00-6:00 **Symposium 5**: NATURAL INTER-INDIVIDUAL DIFFERENCES IN BEHAVIOR TO EXPLORE COGNITIVE PROCESSES. Chairperson: **Françoise Dellu-Hagedorn**

4:00-4:24 GENETIC AND BEHAVIORAL REGULATION OF INTELLIGENCE IN GENETICALLY HETEROGENEOUS MICE. **Matzel, L.D.**; Kolata, S.

4:24-4:48 THE RELATIONSHIP BETWEEN WORKING MEMORY AND INTELLIGENCE IN HEALTHY YOUNG ADULTS. **Conway, A.R.A.**

4:48-5:12 INTER-INDIVIDUAL DIFFERENCES IN DECISION-MAKING IN THE RAT: RELATIONSHIPS WITH BEHAVIORAL TRAITS. Rivalan, M.; Fitoussi, A.; **Dellu-Hagedorn, F.**

5:12-5:36 PERSONALITY TRAITS IN THE PREDICTION OF PERFORMANCE IN LEARNING UNDER STRESS. **Sandi, C.**; Salehi, B.

5:36-6:00 ROLE OF PKMζ MEDIATING STRESS REACTIVITY DIFFERENCES BETWEEN SEXES: EFFECTS ON PLASTICITY AND COGNITION. **Serrano, P.**

6:00-8:00 **Poster Session 1.**

COGNITION

1. 6-HYDROXYDOPAMINE LESION IN THALAMIC RETICULAR NUCLEUS INHIBITS LEARNING IN MORRIS WATER MAZE. **Chuc-Meza, E.**; Avila, G.; Garcia-Ramirez, M.; Mireles, C., Limon, I.D.; Aceves, J.

2. COMPETITIVE FUNCTIONS OF THE RAT STRIATUM AND HIPPOCAMPUS IN SEQUENTIAL LEARNING. **Eckart, M.T.**; Huelse-Matia, M.C.; McDonald, R.S.; Loer, D.; Schwarting, R.K.W.

3. CORRELATIONS BETWEEN CORTICAL ACTIVITIES AND AUTONOMIC RESPONSES DURING THE PERFORMANCE OF EMOTIONAL WORKING MEMORY TASKS. **Garcia, A.**; Conde, S.; Uribe, C.; Tavares, M. C.; Tomaz, C.

4. BACK TO NATURE: DIFFERENTIAL EFFECTS OF NATURAL AND ARTIFICIAL ENRICHED ENVIRONMENTS ON COGNITION AND NEUROPLASTICITY IN CALIFORNIA DEER MICE (PEROMYSCUS CALIFORNICUS). **Huber, J.**; Franssen, C.L.; Bardi, M.; Shea, E.S.; Hampton, J.E.; Hyer, M.M.; Rhone, A.; Lambert, K.G.

5. MULTIPLE LEARNING EXPERIENCES IMPROVE COGNITION AND INCREASE NEUROGENESIS IN AN INDUCIBLE MOUSE MODEL OF NEURONAL LOSS. **Morroni, F.**; Kitazawa, M.; Caccamo, A.; Oddo, S.; LaFerla, F.M.

6. SIMULTANEOUS CONDITIONING OF "GAPING" AND TASTE AVOIDANCE IN RATS INJECTED WITH LITHIUM CHLORIDE AND SACCHARIN: EXAMINING THE ROLE OF CONTEXT AND TASTE CUES IN THE RODENT MODEL OF ANTICIPATORY NAUSEA. Cloutier, C.J.; Cross-Mellor, S.K.; Chan, M.Y.T.; Kavaliers, M.; **Ossenkopp, K.-P.**

7. IMPAIRED TEMPORAL ORDER RECOGNITION MEMORY IN NEUREGULIN 1 TYPE IV TRANSGENIC MICE. **Papaleo, F.**; Jenkins, K.A.; Chen, J.; Crawley, J.N.; Weinberger, D.R.; Law, A.J.

8. RAPID EFFECTS OF 17β-ESTRADIOL ON OBJECT PLACEMENT LEARNING IN FEMALE MICE. **Phan, A.**; Gabor, C.; MacLusky, N.; Choleris, E.

~~9. THE BEHAVIORAL EFFECTS OF THE METABOLIC ENHANCER METHYLENE BLUE ON DISRUPTED LATENT INHIBITION. **Puga, F.**; Gonzalez-Lima, F.~~ **NOT PRESENTED**.

10. FUNCTIONAL MAPPING OF THE PREVENTION OF IMPAIRED SPATIAL MEMORY IN AN ANIMAL MODEL OF MILD COGNITIVE IMPAIRMENT. **Riha, P.D.**; Rojas, J.C.; Gonzalez-Lima, F.

~~**11.** EFFECTS OF OXIDATIVE STRESS STATE ON MEMORY: ITS CORRELATION WITH INFLAMMATORY RESPONSE, AND ENDOTHELIAL CHANGES IN RATS EXPOSED CHRONICALLY TO LOW DOSES OF OZONE. **Rivas-Arancibia, S.**; Gallegos-Ríos, C.; Rodríguez-Ortiz, D.; Guevara-Guzmán, R.; Flores-Briceño, D.; Rodríguez-Martínez, E.~~ **NOT PRESENTED.**

~~12. OXIDATIVE STRESS EFFECT ON INFLAMMATORY RESPONSE PRODUCED BY ADMINISTRATION OF 3-NP ACID IN STRIATUM OF RATS. **Rodriguez-Martinez, E.**; Jalpa-Hernandez, E.; Miranda-Martinez, A.; Flores-Briseño, D.; Vite-Garcia, A.; Rivas-Arancibia; S.~~ **NOT PRESENTED**.

13. PERSISTENCE OF NEUROPSYCHIATRIC SYMPTOMS IN MILD COGNITIVE IMPAIRMENT OVER SIX MONTHS IN COMMUNITY DWELLING ELDERLY. **Ryu, S.H.**; Yu, J.H.

14. NEONATAL MDMA AND/OR CITALOPRAM EXPOSURE IN RATS PRODUCES LONG-TERM DEFICITS IN EGOCENTRIC LEARNING, BUT ONLY MDMA AFFECTS ALLOCENTRIC LEARNING. **Schaefer, T.L**.; Grace, C.E.; Graham, D.L.; Skelton, M.R.; Vorhees, C.V.; Williams, M.T.

15. HYPERACUSIS, INCREASED ANXIETY, AND DEFICITS IN MOTOR COORDINATION BUT NOT LEARNING AND MEMORY IN GTF2IRD1 KNOCKOUT MOUSE. **Schneider, T.**; Rawlins, J.N.P.; Tassabehji, M.

16. PKMζ EXPRESSION INCREASES WITH ACUTE STRESS AND NEGATIVELY AFFECTS MALE BUT NOT FEMALE MEMORY. **Serrano, P.**; Luine, V.L.; Schrott, L.M.

17. SEX DIFFERENCES IN AVERSIVE MEMORY IN RATS: POSSIBLE ROLE OF EXTINCTION AND REACTIVE EMOTIONAL FACTORS. **Silva, R.H.**; Barbosa, F.F.; Godinho, M.R.; Fernandes, V.S.; Munguba, H.; Melo, T.G.; Barbosa, M.T.; Ribeiro, A.M.

18. REVERSIBLE INACTIVATION OF MEDIAL PREFRONTAL CORTEX IMPAIRS DECISION-MAKING AND INCREASES ANXIETY IN RATS. **De Visser, L.**; Baars, J.M., Van t Klooster, J.G., Van den Bos, R.

19. DIFFERENTIAL RECRUITMENT OF CORTICAL AND LIMBIC AREAS IS RELATED TO PERFORMANCE IN A RAT MODEL OF DECISION-MAKING. **De Visser, L.**; Baars, J.M., Lavrijsen, M., Van den Bos, R.

20. SEX STEROID HORMONES AND NEUROPSYCHOLOGICAL FUNCTIONS: ROLE OF ESTROGEN IN WORKING MEMORY FOR EMOTIONAL FACIAL EXPRESSIONS, IN YOUNG WOMEN. Pompili, A.; dOnofrio, A.; Arnone, B.; Tavares, M.C.; Tomaz, C.; **Gasbarri, A.**

21. SEX-RELATED TALKATIVENESS AND EMOTIONAL MEMORY. **Gasbarri, A.**; Arnone, B.; Pompili, A.; Tavares, M.C.; Tomaz, C.

22. THE ROLE OF CONTEXT IN ACTIONS AND HABITS. Tran-Tu-Yen, D.; Holmes, N.; Di Scala, G., Marchand, A.R., **Coutureau, E.**

23. DECREASE IN NOVEL OBJECT RECOGNITION PERFORMANCE AFTER THE DOPAMINE DENERVATION OF THE THALAMIC RETICULAR NUCLEUS IN THE RAT. **Garcia-Ramirez, M.**; Chuc-Meza, E.; Avila-Velarde, G.; Aceves, J.

24. TOWARDS THE DEVELOPMENT OF AUTOMATED SOCIAL BEHAVIOURAL AND ANXIETY PARADIGMS IN ZEBRAFISH. **Luca, R.M.**; Gerlai, R.

25. EFFECTS OF METHAMPHETAMINE EXPOSURE DURING HIPPOCAMPAL DEVELOPMENT ON COGNITION AND THE CHOLINERGIC SYSTEM IN ADOLESCENT MICE. **†Siegel, J.**; Raber, J.

26. THETA IS MODULATED BY NOVELTY IN CA1 & SUBICULUM IN AWAKE BEHAVING MICE. **Huerta, P.T.**; Faust, T.W.; Chang, E.H.

27. MK-801 INDUCED IMPAIRMENTS OF VISUAL-DISCRIMINATION LEARNING AFFECT REVERSAL LEARNING IN RATS. Shao, F.; Li, N.-X.; Wang, W.-W.; **Li, L.**

28. ~~HUNGER SUBSTANCE OREXIN IMPAIRES SPATIAL PLASTICITY. **Oomura, Y.**; Aou, S.; Fukunaga, K.; Sasaki, K~~. **NOT PRESENTED**.

29. ~~MENTAL REPRESENTATION OF DISCOURSE WITH REPETITION: INEFFICIENCIES OF DISCOURSE PRODUCTION IN THE ELDERLY. **Saling, L.**; Laroo, N.; Saling, M.~~ **NOT PRESENTED**.

30. ENHANCED LEARNING AND MEMORY AFTER TOMOSYN OVEREXPRESSION IN THE DENTATE GYRUS OF THE MOUSE HIPPOCAMPUS. **Barak, B.**; Wang, Y.; Okun, E.; Norman, E.; Yizhar, O.; van Praag, H.; Mattson, M.P.; Ashery, U.

31. SENSORY PROCESSING IN TIMING MECHANISMS: IMPACT OF STIMULUS FREQUENCY IN AN AUDITORY DURATION PERCEPTION TASK. **Wiertelak, E.P.**; Coletto, N.L.

32. CREATINE TRANSPORTER KNOCKOUT MICE SHOW LEARNING AND MEMORY DEFICITS: MODELING HUMAN CRT DEFICIENCY. **Skelton, M.**; Schaefer, T.; Grace, C.; deGrauw, T.; Vorhees, C.; Williams, M.

33. TRANSITIONAL VERSUS SURGICAL MENOPAUSE IN A RODENT MODEL: ETIOLOGY OF OVARIAN HORMONE LOSS IMPACTS MEMORY AND THE ACETYLCHOLINE SYSTEM. **Acosta, J.I.**; Mayer, L.; Talboom, J.S; Tsang, C.W; Smith, C.J.; Enders, C.K.; Bimonte-Nelson, HA

34. ROUGH-AND-TUMBLE PLAY IMPROVES PERFORMANCE IN THE ATTENTION SET SHIFTING TASK. **Blake, C.**; Franssen, C.L.; Hampton, J.E.; Lambert, K.G.

SOCIAL BEHAVIOR

35. ANIMAL MODELS OF NEURODEVELOPMENTAL DISORDERS:MOUSE SOCIAL RESPONSES AS BIOMARKERS OF NEUROTOXICITY OF ENVIRONMENTAL CONTAMINANTS. Venerosi, A.; **Scattoni, M.**; Ricceri, L.; Calamandrei, G.

36. EFFECTS OF CHRONIC ESTRADIOL BENZOATE ON A SOCIALLY TRANSMITTED FOOD PREFERENCE IN OVARIECTOMIZED CD1 MICE. **Clipperton-Allen, A.E.**; Baheerathan, D.; Nadj, M.; Choleris, E.

37. IMPAIRMENT OF OLFACTORY FUNCTION BY beta-AMYLOID INJECTION IN THE HIPPOCAMPUS. **Guevara-Guzmán, R**.; Bernal-Mondragon, C.; Mercado Gomez, C.; Miranda, A.; Rivas Arancibia, S.

38. SOCIAL ISOLATION REDUCES SOCIAL ODOR INVESTIGATION AND AVOIDANCE OF SICKNESS-RELATED ODORS BY MALE RATS. **Kavaliers, M.**; Choleris, E.; Pisu, M. G.; Serra, M.

39. A ROLE OF THE PRIMATE MESENCEPHALIC TECTUM IN SOCIAL COGNITION AND RELATED DISORDERS. **Maior, R.**; Hori, E.; Barros, M.; Tomaz, C.; Nishijo, H.

40. EFFECTS OF HOUSING CONDITIONS IN THE REDUCTION OF SUBMISSIVE BEHAVIOR MODEL OF ANTIDEPRESSANT ACTIVITY. **Malatynska, E.**; Lane, B.; Van Brunt, C.; Rasmussen, K.

41. INHIBITORY ROLE OF THE MEDIAL PREFRONTAL CORTEX FOR SOCIAL TRANSMISSION OF AVOIDANCE. **Masuda, A.**; Aou, S.

42. THE EFFECTS OF ALCOHOL AND A DOPAMINE RECEPTOR ANTAGONIST ON SOCIAL BEHAVIOR OF ZEBRAFISH. **Scerbina, T.**; Chatterjee, D.; Gerlai, R.

43. NO INDUCTION OF SOCIAL EXPLORATORY ACTIVITY IN MALE μ-OPIOID RECEPTOR KNOCKOUT MICE BY PLAYBACK OF FEMALE ULTRASONIC VOCALIZATIONS. **Wöhr, M.**; Moles, A.; Schwarting, R.K.W.; D'Amato, F.R.

44. COMMUNAL NESTING ALTERS THE DEVELOPMENT OF AFFECTIVE AND SOCIAL BEHAVIOR IN RATS SELECTIVELY BRED FOR AN INFANTILE TRAIT. **Zimmerberg, B.**; Martinez, A.R.; Brunelli, S.A.

45. THE SOCIAL TRANSMISSION OF A FOOD PREFERENCE IS IMPAIRED IN SOCIALLY DEPRIVED MALE RATS. **Choleris, E.**; Loi, M.; Mameli, R.; Garau, A.; Pisu, M.G.; Dore, R.; Kavaliers, M.; Serra, M.

46. STRESS RESPONSIVENESS AND SPATIAL MEMORY IN SOCIALLY ISOLATED OFFSPRING. Pisu, M.G.; Dore, R,; Garau, A.; Arzedi, C.; Ruggeri, A.; Biggio, G.; **Serra, M.**

47. EFFECT OF METHAMPHETAMINE EXPOSURE AND POSTNATAL CARE ON BEHAVIOR OF ADULT MALE RATS. **Hruba, L.**; Schutova, B.; Rokyta, R.; Slamberova, R.

48. THE IMPACT OF ACUTE METHAMPHETAMINE ADMINISTRATION ON SOCIAL INTERACTION OF MALE AND FEMALE LABORATORY RATS. **Schutova, B.**; Hruba, L.; Mikulecka, A.; Pometlova, M.; Rokyta, R.; Slamberova, R.

~~49. THE EFFECT OF PERINATAL INFLAMMATION ON THE DEVELOPMENT OF PLAY BEHAVIOUR IN RATS. **Field, E.**; Spencer, S.; McLeod, S.; Kentner, A.; Pittman, Q.~~ **NOT PRESENTED**.

50. A SOCIAL ENCOUNTER WITH LIMITED PHYSICAL CONTACT PRODUCES CONDITIONED PLACE PREFERENCE IN MALE ADOLESCENT RATS. **Peartree, N.A.**; Hood, L.E.; Sanabria, F.; Thiel, K.J.; Neisewander, J.L.

51. MECHANISMS OF ABNORMAL AGGRESSION IN A NEW MODEL OF HUMAN VIOLENCE: EARLY SOCIAL DEPRIVATION OF RATS. **Tulogdi, A.**; Toth, M.; Mikics, E.; Haller, J.

52. CHARACTERIZATION OF SHOALING IN FREE SWIMMING ZEBRAFISH: A HIGH-THROUGHPUT BEHAVIORAL ASSAY. **†Miller, N.**; Gerlai, R.

53. CHARACTERIZATION OF THREE CHAMBER SOCIAL NOVELTY SEEKING IN C57BL/6J MICE. **†Pearson, B.L.**; Defensor, E.B.; Pobbe, R.L.H.; Blanchard, D.C.; Blanchard, R.J.

54. BTBR T+tf/J MICE SHOW SOCIAL DEFICITS IN SEMINATURAL VISIBLE BURROW SYSTEMS. **Blanchard**, **D.C.;** Bolivar, V.; Pobbe, R.; Defensor, E. Pearson, B.; Blanchard, R.J.

55. SCHOOLING FISH BEHAVIOR AND SOUNDS PRODUCED BY LOCOMOTION. **Larsson, M**.

56. MUTUALLY ANTAGONISTIC EEFECTS OF DOPAMINE AND ACETYLCHOLINE IN THE RAT BRAIN ON EXPRESSION OF ULTRASONIC VOCALIZATIONS. Silkstone, M.; **Brudzynski, S.M.**

57. UNUSUAL REPERTOIRE OF VOCALIZATIONS IN THE BTBR T+tf/J MOUSE MODEL OF AUTISM. **Scattoni, M.L.**; Crawley, J.N.; Ricceri, L.

58. RAPID EFFECTS OF ESTROGEN RECEPTOR ALPHA AND BETA AGONISTS ON HISTAMINE DEPOLARIZATIONS IN THE VENTROMEDIAL HYPOTHALAMIC NUCLEUS. **Phan, A.**; Pfaff, D.; Choleris, E.; Kow, L-M.

PSYCHIATRIC AND NEUROLOGIC DISORDERS

59. D1 AND D2 DOPAMINERGIC RECEPTORS MODULATE THE CONTEXTUAL FEAR CONDITIONING DEFICIT PRESENTED BY AN ANIMAL MODEL TO STUDY EMOTIONAL PROCESSING ABNORMALITIES IN SCHIZOPHRENIA. **Calzavara, M.B.**; Santos, C.M.; Medrano, W. A.; Levin, R.; Ablio, V.C.

60. BEHAVIORAL AND COGNITIVE EFFECTS OF PRENATAL FOLATE DEFICIENCY IN GLUTAMATE CARBOXYPEPTIDASE II HETEROZYGOUS MICE. **Eby, L.E.**, Schaevitz, L.R., Coyle, J.T., Berger-Sweeney, J.E.

61. EFFECTS OF ANTIPSYCHOTICS ON THE BEHAVIORAL DEFICITS IN HUMAN DOMINANT-NEGATIVE DISC1 TRANSGENIC MICE WITH NEONATAL POLYI:C TREATMENT. **Ibi, D.**; Nagai, T.; Kitahara, Y.; Nabeshima, T.; Sawa, A.; Yamada, K.

62. HYPOCRETIN GENE TRANSFER IN MICE MODELS OF NARCOLEPSY. Liu, M.; Blanco-Centurion, C.; **Shiromani, P.J.**

63. THE ROLE OF THE ENDOCANNABINOID SYSTEM IN A RAT MODEL OF DISTRACTION-INDUCED ANALGESIA. **Ford, G.K.**; Moriarty, O; Harhen, B; Tully, E; Mulcahy, A; Finn, D.P.

64. LITHIUM AND THIOCOLCHICOSIDE INTERACTION ON RAT DENTATE GYRUS NEURONAL NETWORK EXCITABILITY. **Talani, G.**; Obili, N; Fadda, E.; Uras, R.; Cordeddu, G.; Fois, C.; Prinzis, S.; Frau, A.; Piras, V.; Siuni, L.; Niola, P.; De Riu, P.L.; Sechi, G.P.; Sanna, E.

65. THE EFFECTS OF GRK6 DEFICIENCY IN THE MOUSE MODELS OF PARKINSONS. **Manago, F.**; Sotnikova, T.D.; Salahpour, A.; Caron, M.G.; Premont, R.T.; Gainetdinov, R.R.

66. PROMISCUOUS ANTI-DYSKINESIA DRUGS ACT AS 5-HT1A AGONISTS IN THE 6-OHDA RAT. **Paquette, M.A.**; Martinez, A.; Macheda, T.; Giuffrida, A.

67. ENHANCED RESPONSES TO L-DOPA IN THE TRACE AMINE ASSOCIATED RECEPTOR 1 (TAAR1) KNOCKOUT MICE. Sotnikova, T.D.; **Gainetdinov, R.R.**

68. ROLE OF DIFFERENT BRAIN STRUCTURES IN AN ANIMAL MODEL TO STUDY EMOTIONAL PROCESSING ABNORMALITIES IN SCHIZOPHRENIA: THE CONTEXTUAL FEAR CONDITIONING DEFICIT PRESENTED BY SHR (SPONTANEOUSLY HYPERTENSIVE RATS). Medrano, W.A.; Calzavara, M.B.; Levin, R.; Frussa-Filho, R.; **Abilio, V.C.**

~~69. DISRUPTION OF PREPULSE INHIBITION BY APOMORPHINE ACROSS PREPULSE STIMULUS MODALITY. **Mactutus, C.F.**; Moran, L.M.; Booze, R.M.~~ **NOT PRESENTED**.

~~70. THE EFFECT OF APOE ε 4 ALLELE ON GAIT VARIABILITY IN COMMUNITY-DWELLING ELDERS. **Moon, S.W.**; Choi, J.Y.; Kim, T.H.; Nam, B.W.~~ **NOT PRESENTED**.

71. SPINAL CERAMIDE MODULATES THE DEVELOPMENT OF MORPHINE ANTINOCICEPTIVE TOLERANCE VIA PEROXYNITRITE-MEDIATED NITROXIDATIVE STRESS AND NEUROIMMUNE ACTIVATION. **Cuzzocrea, S.**; Esposito E.; Masini, E.; Matuschak, G.M.; Salvemini, D.

72. PPAR-β/δ-MEDIATED PROTECTION ON IN VITRO COMPRESSION MODEL OF SPINAL CORD ORGANOTYPIC SLICE CULTURES. **Esposito, E.**; Paterniti, I.; Meli, R.; Bramanti, P.; Cuzzocrea, S.

73. COMBINING STRATEGIES TO DEVELOP BETTER ANIMAL MODELS FOR BIPOLAR DISORDER. Flaisher-Grinberg, S.; Ashkenazy-Frolinger, T.; Kronfeld-Schor, N.; **Einat, H.**

74. AN ANIMAL MODEL OF SPORTS-RELATED CONCUSSIONS: THE SHORT AND LONG-TERM EFFECTS OF REPEATED MILD FLUID PERCUSSION BRAIN INJURY IN THE RAT. **†Shultz, S.R.**; MacFabe, D.F.; Cain, D.P.

75. PROGESTERONE DECREASES CELL PROLIFERATION INDUCED BY TRAUMATIC BRAIN INJURY IN ADULT MALE RATS. **†Barha, C.K.**; Ishrat, T.; Epp, J.R.; Galea, L.A.M; Stein, D.G.

METABOLISM AND AUTONOMIC PROCESSES

76. IN THE MIDBRAIN, DURING PROESTRUS OR WITH PROGESTERONE ADMINISTRATION, EXPRESSION OF BIOSYNTHESIS AND METABOLISM ENZYME EXPRESSION ARE ENHANCED. **Frye, C.A.**; Osborne, D.M.; Walf, A.A.

77. WHEEL RUNNING ELIMINATES HIGH-FAT PREFERENCE AND ENHANCES LEPTIN SIGNALING IN THE VENTRAL TEGMENTAL AREA. **Scarpace, P.J.**; Tumer, N.; Matheny, M.; Zhang, Y.

~~78. VENTRAL PALLIDAL AND HYPOTHALAMIC COMPONENTS OF THE NUCLEUS ACCUMBENS SHELL FEEDING CIRCUIT. **Stratford, T.R.**; Wirtshafter, D.~~

79. REDUCTION IN RAT BODY WEIGHT AND FAT MASS WITHOUT AFFECTING FOOD INTAKE INDUCED BY VAGUS NERVE STIMULATION. **Olla, P.**; Biggio, F.; Utzeri, C.; Banni, S.; Marrosu, F.; Follesa, P.

80. HEART RATE AS A BIOINDEX TO ASSESS SENSORY PERCEPTIONS IN SIGHTED AND NON-SIGHTED CRAYFISH. **Robinson, M.**; Baker, M.; Cooper, R.L.; Bierbower, S.

Friday, June 11

8:30-10:30 **Symposium 6**: THE UNIQUE EFFECTS OF STRESS DURING ADOLESCENCE. Chairpersons: **Giovanni Laviola** and **Susan L. Andersen**

8:30-9:00 NEONATAL COMPETITION FOR MATERNAL RESOURCES ALTERS THE ONTOGENY OF STRESS-RELATED BEHAVIOR AND NEUROTROPHIC FACTORS. **Macri, S.**

9:00-9:30 MISGUIDED DEVELOPMENT: THE EFFECTS OF EARLY LIFE STRESS ON PRELIMBIC PREFRONTAL CORTEX CIRCUITRY AND WORKING MEMORY IN RATS. **Brenhouse, H.C.**; Andersen, S.L.

9:30-10:00 CHILDHOOD ABUSE: DELAYED PSYCHIATRIC AND ANATOMICAL EFFECTS IN HUMANS. **Andersen, S.**

10:30-11:00 **Breaks/Exhibits**

11:00-12:00 **Keynote Lecture:** CROSSING THE TRANSLATIONAL BRIDGE. **Insel, T.R.** Introduction: Kelly Lambert.

12:00-2:00 **Lunch Break/Meet the Professionals Lunches**

2:00-4:00 **Symposium 7**: EARLY ENVIRONMENT SHAPES ADULT MENTAL DISORDERS: ANIMAL MODELS. Chairperson: **Mikhail V. Pletnikov** and Co-chairperson: **Paul H. Patterson**

2:00-2:30 EPIGENETIC PROGRAMMING OF THE STRESS RESPONSE IN RATS BY PRENATAL RESTRAINT STRESS AN ANIMAL MODEL OF DEPRESSION. **Maccari, S.**; Mairesse, J.; Morley-Fletcher, S.

2:30-3:00 MATERNAL INFECTION: WINDOW ON NEUROIMMUNE INTERACTIONS IN FETAL BRAIN DEVELOPMENT AND MENTAL ILLNESS. **Patterson, P.H.**

3:00-3:30 ANIMAL MODELS OF EARLY LIFE STRESS: SEARCHING FOR THE EARLY DETERMINANTS OF ADULT PSYCHOPATHOLOGY. **Cirulli, F.**

3:30-4:00 PRENATAL AND POSTNATAL ADVERSE EVENTS INTERPLAY WITH GENETIC PREDISPOSITION IN MENTAL HEALTH: DISC1 MOUSE. **Pletnikov, M.**

4:00-6:00 **Symposium 8**: Top-Down Modulation of Prepulse Inhibition of the Startle Reflex in Laboratory Animals. Chairperson: **Liang Li**

4:00-4:20 MIDBRAIN CIRCUITS FOR PREPULSE INHIBITION AND STARTLE ACTIVATION SUGGEST FOREBRAIN CONTROL OF PREPULSE FUNCTIONS IN APPROACH BEHAVIORS. **Yeomans, J.**

4:20-4:40 ROLE OF PALLIDOTEGMENTAL GABAERGIC NEURONS IN PPI OF THE ACOUSTIC STARTLE REFLEX. **Yamada, K.**

4:40-5:00 IS PPI COGNITIVE? WHAT HAVE WE LEARNED FROM A CORRELATIVE APPROACH. **Yee, B.K.**; Peleg-Raibstein, D.; Hauser, J.; Singer, P.; Dubroqua, S.; Bitanihirwe, B.; LLano Lopez, L.; Gargiulo, P.A.; Feldon, J.

5:00-5:20 USE OF PRE-PULSE INHIBITION TO ASSESS COMPLEX ACOUSTIC PROCESSING IN RODENTS. **Cleary, C.E.**; Fitch, R.H.

5:20-5:40 EFFECTS OF NOISE EXPOSURE AND SALICYLATE ON AUDITORY CORTEX RESPONSE AND HYPERACUSIS BEHAVIOR. **Sun, W.**; Lu, J.; Deng, A.; Lobarinas, E.; Goodey, R.; Salvi, R.J.

5:40-6:00 EMOTIONAL LEARNING ENHANCES STIMULUS-SPECIFIC TOP-DOWN MODULATION OF SENSORIMOTOR GATING IN SOCIALLY REARED RATS BUT NOT ISOLATION-REARED RATS. **Li, L.**; Du, Y.; Li, N.-X.; Wu, X.-H.

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

ANXIETY, STRESS AND RELATED DISORDERS

81. FOS DISTRIBUTION IN THE MEDIAL TEMPORAL LOBE DURING CONTEXT-, AUDITORY- AND LIGHT-CUED CONDITIONED FEAR IN WISTAR RATS. **Albrechet-Souza, L.**; Borelli, K.G.; Almada, R.C.; Onusic, G.M.; Brandao, M.L.

~~82. A RE-EXAMINATION OF THE RELATIONSHIP BETWEEN THE FIRING RESPONSE OF THE AN2 INTERNEURON AND AVOIDANCE FLIGHT IN THE PACIFIC FIELD CRICKET, TELEOGRYLLUS OCEANICUS BY THE USE OF BAT-LIKE ACOUSTIC STIMULATION. **Asi, N.S.**; Jackson, M.E.; Fullard, J.~~ **NOT PRESENTED**.

83. THE NEUROPEPTIDE S RECEPTOR AS TARGET FOR NEUROSCIENCE DISORDERS. **Fendt, M.**; Buchi, M.; Brki, H.; Hoyer,D.; Langenegger, D.; Laurent, S.; Imobersteg, S.; Vanek, M.; Suply, T.; McAllister, K.H.; Zimmermann, K.; Sailer, A.W.

84. CRF RECEPTORS IN THE DORSAL RAPHE NUCLEUS MEDIATE ANXIETY STATES INDUCED BY POST-WEANING SOCIAL ISOLATION. **Forster, G.L.**; Bledsoe, A.C.; Oliver, K.M.; Scholl, J.L.

85. THEANINE MITIGATES CAFFEINE-INDUCED GLOBAL PROCESSING FOLLOWING EXPOSURE TO STRESS. Mahoney, C.R.; Brunye, T.T.; Giles, G.; **Kanarek, R.B.**

86. INTER-HEMISPHERIC MECHANISMS REGULATING THE MEDIAL PREFRONTAL GLUTAMATE RESPONSE TO STRESS. **Lupinsky, D.**; Moquin, L.; Gratton, A.

87. RECIPE FOR RESILIENCE: EXPLORATIONS OF COPING STRATEGIES AND EFFORT-DRIVEN REWARD TRAINING IN MALE LONG-EVANS RATS. **Rhone, A.**; Bardi, M.; Franssen, C.L.; Shea, E.S.; Hampton, J.E.; Hyer, M.M.; Huber, J.; Lambert, K.G.

88. BILATERAL INACTIVATION OF BASOLATERAL AMYGDALA IMPAIRS LEARNED (BUT NOT INNATE) FEAR RESPONSE IN RATS. **Ribeiro, A.M.**; Barbosa, F.F.; Silva, R.H.

89. EFFECTS OF NMA ON ANXIOLYTIC-LIKE BEHAVIOR INDUCED BY DORSAL HIPPOCAMPAL δ-OPIOIDERGIC SYSTEM. **Solati, J.**; Zarrindast, M-R.

~~90. An fMRI STUDY ABOUT EMOTIONAL PERSPECTIVE-TAKING IN KOREAN ADULTS. **Son, J.**; Oh, I.; Kim, H.; Lee, S.~~ **NOT PRESENTED**.

91. ANTAGONISM OF TRANSIENT RECEPTOR POTENTIAL VANILLOID TYPE-1 (TRPV1) RECEPTORS IN THE MEDIAL PREFRONTAL CORTEX REDUCES THE EXPRESSION OF CONTEXTUAL FEAR CONDITIONING IN RATS. **Terzian, A.L.**; Corrêa, F.M.; Guimarães, F.S.; Resstel, L.B.

92. LACK OF ANTIDEPRESSANT LIKE BEHAVIORAL EFFECTS OF CHRONIC VAGUS NERVE STIMULATION IN THE RAT DESPITE NEUROCHEMICAL END MOLECULAR ANTIDEPRESSANT LIKE EFFECTS. **Utzeri, C.**; Biggio, F.; Olla, P.; Marrosu, F.; Follesa, P.

93. EFFECTS OF SELECTIVE AND NOT SELECTIVE GABA-BENZODIAZEPINE AGONISTS ON IMMUNE-MEDIATED CUTANEOUS INFLAMMATORY DISEASES. **Freire-Garabal, M.**; Novio, S.; Tarrio, D.; Rodriguez, B.; Marino, J.C.; Dorado, T.; Nunez, M.J.

94. THE IMPACT OF STRESS IN POLICE: A STUDY OF STRESS-RELATED CAUSES. **Iglesias, M.**; Nunez-Iglesias, M.J.; Novio, S.; Freire-Garabal, M.

95. INHIBITORY EFFECTS OF FLUOXETINE ON THE PERMEABILITY BARRIER HOMEOSTASIS AND THE INFLAMMATORY RESPONSE IN VIVO IN A MOUSE MODEL OF PSORIASIS UNDER DEPRESSION CONDITIONS. **Novio, S.**; Nunez, M.J.; Tarrio, D.; Marino, J.C.; Dorado, T.; Rodriguez, B.; Freire-Garabal, M.

96. INHIBITORY EFFECTS OF ALPRAZOLAM ON THE DEVELOPMENT OF ACUTE EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS IN STRESSED RATS. **Nunez, M.J.**; Novio, S.; Freire-Garabal, M.

97. EFFECTS OF AN ADULT-ONSET CALORIE RESTRICTION ON FEAR BEHAVIOUR TOWARDS A PREDATOR ODOUR. **Kent, S.**; Govic, A.; Levay, E.A.; Penman, J.; Paolini, A.G.

98. FEAR-INDUCED ANTINOCICEPTION IN MICE: EFFECTS OF INTRA-PERIAQUEDUCTAL GRAY (PAG) INJECTIONS OF 5-HT2 RECEPTOR AGONIST AND ANTAGONIST. Baptista, D.; Nunes-de-Souza, R.L.; **Canto-de-Souza, A.**

99. EFFECTS OF DIFFERENT STRESSORS ON THE SEROTONERGIC ACTIVITY IN THE DORSAL RAPHE NUCLEUS (DRN). García-Saldívar, N.L.; González-López, M.R.A.; Castillo-Roberto, G.; Domínguez, R.; **Cruz-Morales, S.E.**

100. NITRIC OXIDE RELEASE WITHIN PERIAQUEDUCTAL GRAY MODULATES DEFENSIVE-LIKE BEHAVIORS AND NOCICEPTION IN MICE. **Miguel, T.T.**; Nunes-de-Souza, R.L.

101. NK3-RECEPTOR AGONIST SENKTIDE PROMOTES ANXIOLYTIC AND ANTIDEPRESSANT-LIKE EFFECTS, COMPONENTS OF EPISODIC-LIKE MEMORY AND IN VIVO ACh TRANSMISSION IN AGED RATS. **Schaeble, S.**; Buddenberg, T.; Topic, B.; Huston, J.P.; de Souza Silva, M.A.

102. ESCAPABLE AND INESCAPABLE STRESS DIFFERENTIALLY ALTER 5-HT1A RECEPTOR-MEDIATED INHIBITION OF NEURONAL FIRING RATES WITHIN THE DORSOMEDIAL DORSAL RAPHE NUCLEUS. **†Rozeske, R.R.**; Evans, A.K.; Watkins, L.R.; Lowry, C.A.; Maier, S.F.

103. STRESS DURING GESTATION ALTERS ANTEPARTUM ANXIETY-LIKE BEHAVIOR AND HIPPOCAMPAL CELL PROLIFERATION IN THE FEMALE. **†Pawluski, J.L.**; van den Hove, D.L.; Rayen, I.; Prickaerts, J.; Steinbusch, H.W.

104. PRIOR EXPOSURE TO STRESS FACILITATES FEAR RESPONDING TO PARTIAL AND PERFECT CUES. **†Baratta, M.V.**; Chow, B.Y.; Han, X.; Goosens, K.A.; Boyden, E.S.

105. THE ANANDAMIDE HYDROLYSIS INHIBITOR URB597 IN THE RAT BASOLATERAL AMYGDALA ENHANCES MEMORY CONSOLIDATION FOR EMOTIONAL EXPERIENCES. **Campolongo, P.**; Roozendaal, B.; Ratano, P.; Trezza, V.; Hauer, D.; Schelling, G.; McGaugh, J.L.; Cuomo, V.

106. IS THE CURE WORSE THAN THE DISEASE? EXPLORING THE ATYPICAL RESPONSE OF ADOLESCENTS TO PAROXETINE. **McGregor, I.S.**; Karanges, E.; Li, K.M.; Motbey, C.; Sarker, R.; Kashem, M.A.; Callaghan, P.D.

107. LIMBIC-CORTICAL NETWORK DIFFERENCES BETWEEN RESPONDERS AND NON-RESPONDERS TO FLUOXETINE ANTIDEPRRESSANT TREATMENT IN RATS. **Padilla, E.**; Shumake, J.; Barrett, D.; Sheridan, E.; Gonzalez-Lima, F.

108. SOCIAL DEFEAT AND ISOLATION: AUTONOMIC, ADRENOCORTICAL AND BEHAVIORAL EFFECTS IN RATS. **Pico-Alfonso, M.A.**; Mastorci, F.; Razzoli, M.I.; Arban, R.; Sgoifo, A.

109. INHIBITION OF nNOS AND sGC IN THE RAT DORSAL HIPPOCAMPUS INDUCES ANTIDEPRESSANT-LIKE EFFECTS. **Sato, V.A.H.**; Sales, A. J.; Joca, S.R.L.

110. A DEFINITION OF OPTIMAL DOSES OF CHRONIC ANTIDEPRESSANT TREATMENT BY PARAMETERS OF SUCROSE TEST, ANXIETY AND LOCOMOTION TESTS IN NAÏVE C57BL6 MICE. Gorenkova, N.; Dolgov, O.; Valenca, A.; Correia, M.; Nunes, J.; Bolkunov, A.; Bachurin, S.; Steinbusch, H.; **Strekalova, T.**

111. EARLY SOCIAL ENRICHMENT LEADS TO INCREASED FLOATING IN THE FORCED SWIM TEST AT ADULTHOOD: ARE THESE MICE MORE OR LESS VULNERABLE TO DEPRESSION? **Branchi, I.**; D'Andrea, I.; Cirulli, F.; Alleva, E.

112. SUBSTITUTION OF 8-OHDPAT IN QUINPIROLE MODEL OF OBSESSIVE-COMPULSIVE DISORDER. AlKhatib, A.; Beerepoot, P.; Jacklin, D.; Tucci, M.; Sharma, R.; Dvorkin, A.; Graham, D.; **Szechtman, H.**

113. DETERMINATION OF PRE-EXISTING ANXIETY DIFFERENCES BETWEEN C57BL/6 N AND J MICE TO INVESTIGATE FEAR EXTINCTION LEARNING DISPARITY RELATED TO POST TRAUMATIC STRESS DISORDER. **Landrau, S.**; Rodríguez, C.I.; Santos, I.; Peña de Ortiz, S.; Méndez-Merced, A.T.

114. SOCIAL DEFEAT STRESS DIFFERENTIALLY MODULATES HIPPOCAMPAL EXPRESSION OF THE ORGANIC CATION TRANSPORTER-3 IN RATS EXHIBITING BEHAVIORAL DEPRESSION. **†Marcinkiewcz, C.**; Devine, D.

115. TRANSLATIONAL STUDIES IN PIGS - VALIDATION OF A PORCINE MODEL FOR INFLAMMATORY PAIN. **Di Giminiani, P.**; Herskin, M.S.; Petersen, L.J.

116. AUTONOMIC STRESS REACTIVITY IN MICE LACKING 5-HT1A RECEPTORS. **Sgoifo, A.**; Mastorci, F.; Carnevali, L.; Audero, E.; Gross, C.

DEVELOPMENT

117. CHOLINERGIC HYPOFUNCTION AND ALTERED NGF LEVELS IN MECP2-308 MICE: BENEFICIAL OUTCOMES OF EARLY CHOLINE SUPPLEMENTATION. Ricceri, L.; De Filippis, B.; Fuso, A.; **Laviola, G.**

118. POST-WEANING SOCIAL ISOLATION SENSITIZES FEMALE RATS TO FG-7142-INDUCED INCREASES IN C-FOS EXPRESSION IN SEROTONERGIC NEURONS IN THE DORSAL RAPHE NUCLEUS. **Lukkes, J.L.**; Engelman, G.H.; Hale, M.W.; Lowry, C.A.

119. IMPACT OF EARLY OR LATE ADOLESCENT EXPOSURE TO NICOTINE ON RAT BRAIN DOPAMINERGIC FUNCTION. **McMillen, B.A.**; Williams, L.T.; Rogister, M.C.; Halsey, T.M.; Williams, H. L.

120. PRENATAL COCAINE'S EFFECT ON NEONATAL THERMOREGULATION AND ULTRASONIC VOCALIZATION. **McMurray, M.S.**; Meiners, S.M.; Zoghby, C.R.; Zeskind, P.S.; Johns, J.M.

~~121. DIFFERENTIAL EFFECTS OF ADOLESCENT SUBCHRONIC METHYLPHENIDATE AND ATOMOXETINE ON ADULT BEHAVIOR FOREBRAIN DOPAMINE, NOREPINEPHRINE AND SEROTONIN IN NAPLES HIGH-EXCITABILITY RATS. Ruocco, L.A.; Gironi Carnevale, U.A.; Treno, C.; **Sadile, A.G.**; Melisi, D.; Ibba, M.; Schirru., C.; Carboni, E.~~ **NOT PRESENTED.**

122. NEONATAL EXPOSURE TO ESTRADIOL ENHANCES ADULT DIAZEPAM SENSITIVITY. **Santoru, F.**; Mereu, V.; Rossi, F.; Langiu M.; Biggio, G.; Concas A.

123. ACETYL-L-CARNITINE IMPROVES GENERAL HEALTH IN A MOUSE MODEL OF RETT SYNDROME. **Schaevitz, L.R.**; Lopez, C.M.; DIddio, S.; Iannoni, E.; Nicolai, R.; Amato, A.; Berger-Sweeney, J.E.

124. PARENTAL BRAIN EMOTION CIRCUITS VARY WITH GENDER, CORRELATE WITH MOOD AND PREDICT BEHAVIOR. **Swain, J.E.**; Kim, P.; Feldman, R.; Mayes, L.C.; Leckman, J.F.

125. MECHANISMS AND CONSEQUENCES OF DISRUPTING CORTICAL DOPAMINE ACTIVITY DURING ADOLESCENCE. **Watt, M.J.**; Roberts, C.L.; Renner, K.J.; Scholl, J.L.; Haaland, E.J.; Forster, G.L.

126. INHIBITING NEONATAL METHAMPHETAMINE (MA)-INDUCED CORTICOSTERONE RELEASE IN RATS BY ADRENAL AUTOTRANSPLANTATION: EFFECTS ON LATER LEARNING, MEMORY, AND PLASMA CORTICOSTERONE LEVELS. **Williams, M.T.**; Grace, C.E.; Schaefer, T.L.; Graham, D.L.; Skelton, M.R.; Vorhees, C.V.

127. DIVERGENT EFFECTS OF EARLY CORTICOSTERONE EXPOSURE AND ADOLESCENT STRESS ON ADULT BEHAVIOURAL PATTERNS IN MALE AND FEMALE RATS. **Brummelte, S.**; Wong, J.H.K.; Lieblich, S.E.; Galea, L.A.M.

128. LONG-LASTING BEHAVIOURAL CONSEQUENCES OF CORTICOSTERONE ADMINISTRATION DURING THE FIRST POSTPARTUM PERIOD IN MULTIPAROUS DAMS. **Wong, J.H.K**.; Brummelte, S.; Lieblich, S.E.; Galea, L.A.M.

129. PATERNAL EXPERIENCE AND STRESS RESPONSES IN THE CALIFORNIA MOUSE (PEROMYSCUS CALIFORNICUS). Bardi, M.; Franssen, C.L.; **Hampton, J.E.**; Shea, E.A.; Fanean, A.;Lambert, K.G.

130. PATERNAL EXPERIENCE ALTERS NEUROPLASTICITY AND CELL PROLIFERATION IN CALIFORNIA DEER MICE (PEROMYSCUS CALIFORNICUS). Hampton, J.E.; Franssen, C.L.; **Bardi, M.**; Lambert, K.G.

131. DOPAMINE INVOLVEMENT IN THE REINDUCTION PHASE OF MATERNAL MEMORY IN FEMALE RATS. Bridges, R.S.; Peterson, D.B.; Carini, L.M.; Lovelock, D.L.; Byrnes, E.M.; **Byrnes, J.J.**

132. ~~MENTAL HEALTH: A NATURAL LIFE OUTLOOKS? AN ITALIAN TWIN STUDY ON HERITABILITY OF PSYCHOLOGICAL WELL-BEING (PWB) IN YOUNG ADULTS.~~ **~~Gigantesco, A.~~**~~, Fagnani, C~~. **NOT PRESENTED.**

133. BEHAVIOURAL AND COGNITIVE ALTERATIONS OF THE YOUNG MEGAENCEPHALY (BALB/cByJ-Kv1.1mceph/mceph) MOUSE. **Holst, S.**; Aberg, E.; Eriksson, T.; Ogren, S.O.; Lavebratt, C.

134. THE LONG-TERM CONSEQUENCES OF PRE- AND POST-NATAL ENVIRONMENTAL ENRICHMENT: EVALUATION OF ADULT RAT BEHAVIOUR. **Sparling, J.**; Baker, S.; Bielajew, C.

135. PRENATAL COCAINE EXPOSURE ALTERS HUMAN AND RODENT INFANT VOCALIZATIONS: IMPLICATIONS FOR MATERNAL CARE AND NEURAL INTEGRITY. **†Cox, E.**; Jones, G.; Williams, S.; McMurray, M.; Jamieson-Drake, A.; Zeskind, P.; Hodge, C.; Grewen, K.; Johns, J.

136. POSTNATAL MATERNAL SSRI EXPOSURE INCREASES DEPRESSIVE-LIKE BEHAVIOUR IN PRENATALLY STRESSED JUVENILE OFFSPRING. **Pawluski, J.L.**; van den Hove, D.L.; Rayen, I.; Prickaerts, J.; Steinbusch, H.W.

137. ~~EARLY EXPOSURE TO ENDOCRINE DISRUPTORS ALTERS SEX DIFFERENCES IN BEHAVIOR AND NEURAL CIRCUITS.~~ **~~Palanza, P.~~**~~; Parmigiani, S.; Gioiosa, L.; Ponzi, D.; Miceli, D.; Martini, M.; Panzica, G.~~ **NOT PRESENTED.**

138. BEHAVIORAL ALTERATIONS IN THE BIRD MODEL OF RETT SYNDROME. **Blue, M.E.**; Eyring, C.; Smith, D.

139. IRON, THE BRAIN AND GOLDILOCKS. **Jones, B.**

140. ACETYL-L-CARNITINE PREVENTS THE COGNITIVE IMPAIRMENT INDUCED BY MDMA IN ADOLESCENT RATS. **Magalhes, A.**; Alves, C.J.; Tavares, M.A.; de Sousa, L.; Summavielle, T.

141. SALIVARY TESTOSTERONE AND VISUAL INTEREST IN EARLY INFANCY. **Alexander, G. M.**; Wilcox, T.

REWARD AND ADDICTION

142. VOLUNTARY ETHANOL CONSUMPTION ALTERS HIPPOCAMPAL GABAA RECEPTOR GENE EXPRESSION IN C57BL/6J MICE. **Biggio, F.**; Utzeri, C.; Olla, P.; Follesa, P.

143. TRANSIENT HYPERDOPAMINERGIC TONE PRECEDES ATTENUATION OF DOPAMINE RELEASE AND BEHAVIORAL SENSITIZATION IN HIV PROTEIN TREATED RATS WITH A HISTORY OF COCAINE: IN VIVO MICRODIALYSIS IN THE NUCLEUS ACCUMBENS. **Booze, R.M.**; Ferris, M.J.; Frederick-Duss, D.; Fadel, J.; Mactutus, C.F.

144. ACUTE (+)-METHAMPHETAMINE (MA) EXPOSURE SELECTIVELY INCREASES BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AND MODULATES TRKB EXPRESSION IN THE ADULT RAT BRAIN. **Braun, A.A**.; Herring, N.R.; Schaefer, T.L.; Hemmerle, A.M.; Dickerson, J.W.; Seroogy, K.B.; Vorhees, C.V.; Williams, M.T.

145. NEUROSTEROID MODULATION OF CHRONIC ALCOHOL TOLERANCE IN ALCOHOL-PREFERRING MICE ON MEASURES OF FINE AND GROSS MOTOR COORDINATION. **Cronise, K.**; Henschen, C.; Sullivan, A.; Brown, K.; Dupre, N.; McNally, A.; Lee, K.; Morrison, A.; Saeed, F.; Maletsky, K.; Rose-Baker, M.

146. COMPARISON OF AMPHETAMINES FOLLOWING BINGE DOSING ON MULTIPLE-T WATER MAZE LEARNING. **Vorhees, C.V.**; He, E.; Skelton, M.R.; Graham, D.L., Schaefer, T.L.; Grace, C.E.; Braun, A.A.; Amos-Kroohs, R.; Williams, M.T.

147. THE USE OF PRESCRIBED MEDICINES TO IMPROVE MENTAL HEALTH BY COLLEGE STUDENTS. **Reid, L.D.**; Reid, M.L.

148. THE EFFECT OF PRIOR INTERMITTENT BINGEING ON HIGHLY PALATABLE FOODS ON SUBSEQUENT BEHAVIOURAL SENSITIZATION TO THE DOPAMINE AGONIST, QUINPIROLE. **Tenk, C.M.**; Campbell, A.; Ossenkopp, K.-P.

149. MORPHINE INDUCED LOCOMOTION AND ULTRASONIC VOCALIZATIONS IN M5 KNOCKOUT MICE RESCUED BY VIRAL TRANSFECTION OF M5 MUSCARINIC RECEPTORS IN VENTRAL TEGMENTUM. Wasserman, D.; Lee, E.; Wang, H.; Rashid, A.; Josselyn, S.; **Yeomans, J.**

150. ~~BLOCKADE OF THE MAPK/ERK KINASE BY SL327 PREVENTS THE ACQUISITION OF LITHIUM-ELICITED PLACE AVERSION. **Longoni R.**, Spina, L.; Vinci, S.; Ibba, F.; Gabba, S.; Mulas, G.; Spiga, S.; Acquas, E.~~ **NOT PRESENTED.**

151. ~~THE MEK INHINBITOR SL327 PREVENTS THE ACQUISITION OF ETHANOL-ELICITED PLACE PREFERENCE AND PLACE AVERSION. **Spina, L.**; Longoni, R.; Vinci, S.; Ibba, F.; Gabba, S.; Mulas, G.; Spiga, S.; Acquas, E.~~ **NOT PRESENTED.**

152. ADOLESCENT "DRINKING IN THE DARK". **Metten, P.**; Brown, L.L.; Crabbe, J.C.

153. MODERATE COCAINE EXPOSURE RESULTS IN INAPPROPRIATE INCENTIVE LEARNING VIA MU OPIOID RECEPTOR-RELATED PROCESSES IN THE BASOLATERAL AMYGDALA. **†Wassum, K.M.**; Cely, I.C.; Maidment, N.T.

154. SUBSECOND DOPAMINE RELEASE IN THE VENTRAL AND DORSOLATERAL STRIATUM DURING COCAINE SELF-ADMINISTRATION. **†Willuhn, I.**; Phillips, P.E.

155. LATERODORSAL TEGMENTAL ACETYLCHOLINE NEURONS DRIVE METHAMPHETAMINE STIMULATION OF LOCOMOTOR ACTIVITY AND NEUROCHEMICAL RESPONSES IN THE VENTRAL TEGMENTAL AREA. **†Dobbs, L.K.**; Mark, G.P.

156. EFFECTS OF THE COMBINATION OF METYRAPONE AND OXAZEPAM ON METHAMPHETAMINE SEEKING IN RATS. **Goeders, N.**; Keller, C.; Cornett, E.; Guerin, G.

~~157. THE EFFECTS OF THE AGONIST THERAPY IN ANXIUOS-DEPRESSED POSITIVE HCV DRUG-ABUSERS TREATED WITH IFN THERAPY. **Pieri, M.C.**~~ **NOT PRESENTED.**

158. OBSERVATIONAL STUDY AND FOLLOW-UP OF PATIENTS IN TREATMENT WITH OLAZAPINE AND SUBSTITUTIVE DRUG. **Pieri, M.C.**; Arfedele, D.R.; Comaschio, C.A.

159. FROM THE FEEDING TUBE TO THE ANIMAL MODELS OF AFFECTIVE DISORDERS **Pinhasov, A**.; Kuznetsov, Y.; Rylova, A.; Tikhonova T.; Nesher, E.

Saturday, June 12

8:30-10:30 **Symposium 9**: Understanding the impact of emotional experiences on brain function: insights from animal and clinical studies. Chairpersons: **Patrizia Campolongo**, Ph.D., Sapienza University, Rome, ITALY and **Viviana Trezza**, Ph.D., Rudolf Magnus Institute of Neuroscience, Utrecht, THE NETHERLANDS. ***(Sponsored by IBRO)***

8:30-8:54 SOCIAL DEFEAT EXPERIENCES WITH ENDURING IMPACT ON BDNF, ERK AND DOPAMINE-MEDIATED BEHAVIOR. **Miczek, K. A.**

8:54-9:18 ~~GLUCOCORTICOIDS AND THE REGULATION OF MEMORY OF EMOTIONALLY AROUSING EXPERIENCES. **Roozendaal, B.**~~ **NOT PRESENTED**.

9:18-9:42 NEUROBIOLOGICAL AND EPIGENETIC MECHANISMS INVOLVED IN THE IMPACT OF STRESS ON AGGRESSION AND DEPRESSION. **Sandi, C.**; Marquez, C.; Larsen, M.H.;Cordero, M.I.; Poirier, G.

9:42-10:06 OBSERVATIONAL FEAR LEARNING IN MICE IS DEPENDENT ON THE AFFECTIVE PAIN SYSTEM AND L-TYPE CALCIUM CHANNELS IN THE ANTERIO CINGULATE CORTEX. **Shin, H-S.**; Jeon, D.

10:06-10:30 THE PLAYFUL BRAIN: INSIGHTS INTO SOCIAL REWARD MECHANISMS. **Trezza, V.**; Damsteegt, R.; Baarendse, P.J.J.; Vanderschuren, L.J.M.J.

10:30-11:00 **Breaks/Exhibits**

11:00-12:00 **Travel Award Slide Blitz.** Chairperson: Jodi Lukkes.

11:00-11:07 PRIOR EXPOSURE TO STRESS FACILITATES FEAR RESPONDING TO PARTIAL AND PERFECT CUES. **†Baratta, M.V.**; Chow, B.Y.; Han, X.; Goosens, K.A.; Boyden, E.S.

11:07-11:14 STRESS DURING GESTATION ALTERS ANTEPARTUM ANXIETY-LIKE BEHAVIOR AND HIPPOCAMPAL CELL PROLIFERATION IN THE FEMALE. **†Pawluski, J.L.**; van den Hove, D.L.; Rayen, I.; Prickaerts, J.; Steinbusch, H.W.

11:14-11:21 MODERATE COCAINE EXPOSURE RESULTS IN INAPPROPRIATE INCENTIVE LEARNING VIA MU OPIOID RECEPTOR-RELATED PROCESSES IN THE BASOLATERAL AMYGDALA. **†Wassum, K.M.**; Cely, I.C.; Maidment, N.T.

11:21-11:28 SUBSECOND DOPAMINE RELEASE IN THE VENTRAL AND DORSOLATERAL STRIATUM DURING COCAINE SELF-ADMINISTRATION. **†Willuhn, I.**; Phillips, P.E.

11:28-11:35 PROGESTERONE DECREASES CELL PROLIFERATION INDUCED BY TRAUMATIC BRAIN INJURY IN ADULT MALE RATS. **†Barha, C.K.**; Ishrat, T.; Epp, J.R.; Galea, L.A.M; Stein, D.G.

11:35-11:42 PRENATAL COCAINE EXPOSURE ALTERS HUMAN AND RODENT INFANT VOCALIZATIONS: IMPLICATIONS FOR MATERNAL CARE AND NEURAL INTEGRITY. **†Cox, E.**; Jones, G.; Williams, S.; McMurray, M.; Jamieson-Drake, A.; Zeskind, P.; Hodge, C.; Grewen, K.; Johns, J.

11:42-11:49 LATERODORSAL TEGMENTAL ACETYLCHOLINE NEURONS DRIVE METHAMPHETAMINE STIMULATION OF LOCOMOTOR ACTIVITY AND NEUROCHEMICAL RESPONSES IN THE VENTRAL TEGMENTAL AREA. **†Dobbs, L.K.**; Mark, G.P.

12:00-2:00 **Lunch Break**

2:00-3:00 **Travel Award Slide Blitz.** Chairperson: Melanie Paquette.

2:00-2:07 SOCIAL DEFEAT STRESS DIFFERENTIALLY MODULATES HIPPOCAMPAL EXPRESSION OF THE ORGANIC CATION TRANSPORTER-3 IN RATS EXHIBITING BEHAVIORAL DEPRESSION. **†Marcinkiewcz, C.**; Devine, D.

2:07-2:14 CHARACTERIZATION OF SHOALING IN FREE SWIMMING ZEBRAFISH: A HIGH-THROUGHPUT BEHAVIORAL ASSAY. **†Miller, N.**; Gerlai, R.

2:14-2:21 CHARACTERIZATION OF THREE CHAMBER SOCIAL NOVELTY SEEKING IN C57BL/6J MICE. **†Pearson, B.L.**; Defensor, E.B.; Pobbe, R.L.H.; Blanchard, D.C.; Blanchard, R.J.

2:21-2:28 ESCAPABLE AND INESCAPABLE STRESS DIFFERENTIALLY ALTER 5-HT1A RECEPTOR-MEDIATED INHIBITION OF NEURONAL FIRING RATES WITHIN THE DORSOMEDIAL DORSAL RAPHE NUCLEUS. **†Rozeske, R.R.**; Evans, A.K.; Watkins, L.R.; Lowry, C.A.; Maier, S.F.

2:28-2:35 AN ANIMAL MODEL OF SPORTS-RELATED CONCUSSIONS: THE SHORT AND LONG-TERM EFFECTS OF REPEATED MILD FLUID PERCUSSION BRAIN INJURY IN THE RAT. **†Shultz, S.R.**; MacFabe, D.F.; Cain, D.P.

2:35-2:42 EFFECTS OF METHAMPHETAMINE EXPOSURE DURING HIPPOCAMPAL DEVELOPMENT ON COGNITION AND THE CHOLINERGIC SYSTEM IN ADOLESCENT MICE. **†Siegel, J.**; Raber, J.

3:00-5:00 **Symposium 10**: TIME GOES BY: THE INTERPLAY BETWEEN EMOTION AND MEMORY. Chairperson: **Antonella Gasbarri** and **Carlos Tomaz**

3:00-3:24 ESTROGEN AND WORKING MEMORY FOR EMOTIONAL FACIAL EXPRESSIONS IN YOUNG WOMEN. **Gasbarri, A.**; Pompili, A.; dOnofrio, A.; Arnone, B.; Tavares, M.C.; Tomaz, C.

3:24-3:48 EMOTIONAL WORKING MEMORY IN ELDERLY. **Tomaz, C.**; Satler, C.; Tavares, M.C.

3:48-4:12 PREFRONTAL/ACCUMBAL CATECHOLAMINE SYSTEM PROCESSES EMOTIONAL AND MOTIVATIONAL SALIENCE. **Puglisi-Allegra, S.**

4:12-4:36 EMOTIONAL MODULATION OF MULTIPLE MEMORY SYSTEMS. **Packard, M.G.**

4:36-5:00 EMOTIONAL MODULATION OF THE SYNAPSE. **McIntyre, C.K.**

5:00-6:00 **Oral Session 2:** REWARD AND ADDICTION. Chairperson: Leonie de Visser.

5:00-5:12 TRANSIENT NEURONAL SILENCING REVEALS OPPOSING ACTIONS OF INDIRECT AND DIRECT PATHWAY NEURONS. **Neumaier, J.F.**; Ferguson, S.M.

5:12-5:24 BREAKING THE ICE: OXYTOCIN SUPPRESSES METHAMPHETAMINE SELF-ADMINISTRATION AND ASSOCIATED C-FOS EXPRESSION IN RATS. **McGregor, I.S.**; Carson, D.S.; Guastella, A.J.; Barber, L.L.; Cornish, J.L.; Arnold, J.J.; Boucher, A.A.; Hunt, G.E.

5:24-5:36 THE NORADRENERGIC ALPHA-2 AGONIST CLONIDINE ATTENUATES CUE-INDUCED REINSTATEMENT OF COCAINE-SEEKING. **Smith, R.J.**; Aston-Jones, G.

5:36-5:48 VTA AFFERENTS CONTROLLING CUED REINSTATMENT OF COCAINE SEEKING. **Mahler, S.V.**; Aston-Jones, G.

6:00-7:00 **Oral Session 3:** PARENTAL CARE AND DEVELOPMENT. Chairperson: Francesca Cirulli.

6:00-6:12 PRENATAL COCAINE EXPOSURE ALTERS MATERNAL PREFERENCE FOR PUP-PRODUCED OLFACTORY CUES DURING THE EARLY POSTPARTUM PERIOD. **Williams, S.**; Barber, J.; Ross, B.; Thompson, B.; Jameison-Drake, A.; Enns, J.; Cox, E; Heaton, C.; Desai, N.; McMurray M.; Johns, J.

6:12-6:24 SEX-DIFFERENCE IN THE ASSOCIATION OF MATERNAL SMOKING DURING PREGNANCY AND COORDINATION IN OFFSPRING. **Larsson, M.**; Montgomery, S.M.

6:24-6:36 FATHERHOOD ENHANCES LEARNING AND MEMORY. **Franssen, C.L.**; Shea, E.S.; Hampton, J.E.; Bardi, M.; Huber, J.; Hyer, M.M.; Rhone, A.; Franssen, R.A.; Kinsley, C.H.; Lambert, K.G.

6:36-6:48 PRENATAL OXYCODONE EXPOSURE ENHANCES CONDITIONED PLACE PREFERENCE TO OXYCODONE IN ADULT MALE RATS BUT NOT FEMALES. **Schrott, L.M.**; Johnson, G.S.; Franklin, L.M.

7:00-7:30 **IBNS Business Meeting**. All members are encouraged to attend.

7:30-11:00 **Banquet/Dance.**

NOTES:

Monday, June 7

Special Satellite Meeting: Integrative Neuroscience of Excessive Alcohol Drinking. Organizers: H.C. Becker and G. Biggio.

EXCESSIVE DRINKING IN A MOUSE MODEL OF ETHANOL DEPENDENCE AND RELAPSE. Howard C. Becker; Charleston Alcohol Research Center, Departments of Psychiatry and Neurosciences, Medical University of South Carolina, Charleston, SC 29425 USA. We have developed a mouse model of ethanol dependence and relapse that demonstrates enhanced voluntary drinking as a consequence of repeated cycles of chronic ethanol exposure and withdrawal. In this model, C57BL/6J mice are trained to drink 15% (v/v) ethanol using a limited access (2 hr/day) 2-bottle choice paradigm. Once stable intake is established, mice are either exposed to repeated cycles of chronic intermittent ethanol vapor in inhalation chambers (16 hr/day x 4 days) or similarly treated in air chambers, with the weekly exposure cycles alternated with weekly limited access drinking sessions. Escalation of drinking in dependent mice produces a 2-3 fold increase in blood ethanol levels compared to more moderate and stable intake in nondependent mice. Additionally, the greater amount and faster rate of drinking exhibited by dependent mice compared to nondependent mice also results in significantly higher and more sustained brain ethanol concentrations. Use of operant procedures has demonstrated greater ethanol self-administration behavior and enhanced cue-induced reinstatement of ethanol responding following extinction in dependent compared to nondependent mice. There is also evidence for enhanced reinforcing efficacy of ethanol as well as reduced sensitivity to aversive effects of the drug in dependent compared to nondependent subjects. Studies are being conducted using this model to examine the role of stress mechanisms in mediating excessive ethanol drinking associated with dependence. Supported by AA14095, AA10761, AA18036.

EXCESSIVE DRINKING IN A MONKEY MODEL: RISKS AND CONSEQUENCES. Grant, K.A.; Ferguson B. Dept. of Behavioral Neurosciences, Oregon Health & Sciences University, Portland, OR 97027 USA Nonhuman primates add an important translational aspect to the study of alcohol abuse and alcoholism. Their genetic, anatomical, physiological, and behavioral similarity to humans offers unique opportunities for identifying risk factors that may predispose or accelerate the course of alcohol addiction. Using a standard procedure of schedule-induced polydipsia to induce the self-administration of gradually increasing doses of ethanol (0.5 g/kg, 1.0 g/kg, 1/5 g/kg with each dose given 30 consecutive days) and then open access (22 hrs/day) to ethanol (4% w/v) and water we have found macaque monkeys display high individual differences in ethanol self-administration. Average daily ethanol intake over 12 months of access to ethanol range from less than 1.0 to 4.0 g/kg/day and average blood ethanol concentrations range from 0-325 mg/dl. The purpose of this review is to highlight our current understanding of population characteristics of ethanol consumption that can be uniquely informative to alcohol research. Specific focus is given to behavioral, endocrine, genetic and developmental baseline variables that predict future excessive drinking as well as neurobiological and physiological variables that increase in proportion to chronic ethanol self-administration. Data from this model ethanol self- administration can be applied to prevention and treatment strategies. (supported by INIAstress AA13510)

NEUROADAPTATION TO ALCOHOL EXPOSURE IN HUMANS AND ANIMAL MODELS. [1,2]Adolf Pfefferbaum, M.D., [2]Edith V. Sullivan, Ph.D., [1,2]Natalie M. Zahr, Ph.D. [1]Neuroscience Program, SRI International, Menlo Park, California, U.S.A. [2]Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California, U.S.A. Chronic alcoholics are at risk for sustaining brain injury. Alcoholism is often associated with poor nutritional status, which can contribute to the observed brain abnormalities. Hematological indices reflective of nutritional, liver, and kidney function have been associated with MRI measures of alcoholism-related brain abnormalities. Longitudinal study of treatment-seeking alcoholics found that low hemoglobin values correlated with enlarged ventricular and smaller white matter volumes; change in these measures related to ventricular reduction with treatment. Diffusion tensor imaging has revealed degradation in integrity of white matter fibers myelin. Extent of regional fiber disrepair is predictive of poor performance on neuropsychological tests in sober alcoholics. Translational neuroimaging studies of alcoholism using animal models have extended human investigations because of the ability to control over factors not possible in naturalistic human study. Using MRI in a rat model of Wernicke Encephalopathy (WE), alcohol-preferring rats were scanned before and after receiving a thiamine deficient diet for 2 weeks. Compared with thiamine-treated rats, thiamine deficient rats had significantly enlarged ventricles and interstitial fluid accumulation in the thalamus and inferior colliculus; each abnormality showed a different pattern of recovery with thiamine repletion. This WE model was invaluable for identifying the separate contribution of nutritional deficiency and direct alcohol neurotoxicity in alcoholism-related brain damage. Using MRI and MRS we have tracked the chronic effects on selective brain metabolites of high doses of alcohol maintained over days and recovery following days of alcohol abstinence. Patterns of regional brain structural, functional, or biochemical insult associated with chronic alcoholism provide insight into the scope and limits of neural mechanisms responsible for alcoholism's dynamic

course on brain structure and function. Support: U.S. National Institute on Alcohol Abuse and Alcoholism (AA005965, AA013521-INIA)

SYNAPTIC PLASTICITY IN THE CORTICOSTRIATAL SYSTEM: ROLES IN HABIT FORMATION AND ALCOHOL ADDICTION. Lovinger, D.M. Lab. for Integrative Neuroscience, NIAAA, Rockville, MD 20852 USA. The striatum has crucial roles in control of action selection and performance, as well as the learning of skills and instrumental responses. The dorsolateral striatum/putamen nucleus is part of a cortical-basal ganglia system specialized for habit formation that has roles in habitual drug use and addiction. This presentation will describe forms of long-lasting synaptic plasticity in the striatum, and their potential roles in habit learning. Experiments examining effects of chronic alcohol exposure on synaptic transmission and plasticity in both mouse and monkey striatum will also be described. One consistent theme is that ethanol exposure reduces GABAergic transmission both when given acutely and chronically. Ethanol also alters long-term potentiation and depression, two prominent forms of synaptic plasticity at corticostriatal glutamatergic synapses. These findings will be discussed in relation to heavy alcohol drinking in mouse and monkey models. Interactions between ethanol and the striatal endocannabinoid system appear to contribute to the effects on GABAergic synaptic transmission and glutamatergic synaptic plasticity. Given the evidence for endocannabinoid participation in habit formation and addiction, it is tempting to speculate that ethanol/endocannabinoid interactions contribute to habitual and addictive ethanol drinking.

ALCOHOL DEPENDENCE: NEUROADAPTATIONS IN THE AMYGDALA. Cruz M.T.; Roberto M. Committee on Neurobiology of Addictive Disorders, The Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA 92037 Behavioral studies indicate that the GABAergic and corticotrophin-releasing factor (CRF) systems in the amygdala are important mediators of anxiety associated with stress and drug dependence. Nociceptin/orphanin FQ (nociceptin) peptide within the central amygdala (CeA) is implicated in regulating voluntary ethanol intake, participates in the response to acute stress exposure, and exerts marked antagonist effects on the endogenous CRF system. Behavioral and pharmacological studies suggest that amygdalar nociceptin and CRF are recruited during the transition to ethanol abuse and dependence. Here, we studied the role of nociceptin in ethanol- and CRF-induced GABA release at CeA synapses in an in vitro slice preparation using electrophysiological techniques. We found that CRF, like ethanol, increases GABAA receptor-mediated IPSPs via increased GABA release in the CeA. However, nociceptin decreases GABA release and opposes ethanol- and CRF-induced GABA release from CeA neurons. Ethanol dependence is associated with increased baseline GABAergic tone in the CeA. We found increased sensitivity to the effects of nociceptin and CRF on GABA release in CeA from dependent rats, indicating that neuroadaptation occurs in those systems during the development of ethanol dependence. Nociceptin and CRF may operate as reciprocal buffers within the CeA; nociceptin decreases GABA release while CRF and ethanol increase presynaptic release of GABA. Their opposing effects on GABA transmission and on ethanol-induced effects may mirror their opposing behavioral profiles in vivo. Understanding the cellular adaptations induced by chronic alcohol may provide insight into how the transition to alcoholism occurs and possible treatments for alcoholism. Supported by grants from NIH/NIAAA: AA015566, AA06420, AA016985, AA017447, INIA (Integrative Neuroscience Initiative on Alcoholism) AA013517, from Harold L. Dorris Neurological Research Institute, and from the Pearson Center for Alcoholism and Addiction Research.

THE RELATIONSHIP BETWEEN DURATION OF INITIAL ALCOHOL EXPOSURE AND PERSISTENCE OF MOLECULAR TOLERANCE IN STRIATAL NEURONS IS MARKEDLY NON-LINEAR. Steven N. Treistman, Institute of Neurobiology, UPR, San Juan, PR 00911. Why can some people use alcohol recreationally without developing dependency and alcoholism while others cannot? Elucidating the mechanisms underlying compensatory changes to alcohol exposure in individual molecules (molecular tolerance) may provide clues into this important question. The calcium- and voltage-activated BK potassium channel is a widely studied protein, whose activity is directly modulated by ethanol, and that plays a significant role in behavioral tolerance in both vertebrates and invertebrates. We examine the consequences of varying the temporal parameters of alcohol exposure on the characteristics of BK molecular tolerance in neurons from the ventral striatum. Striatal neurons were cultured from P8 rats, and BK channels in these neurons exhibited a two-component process of acute tolerance, similar to that reported for neurohypophysial channels. We discovered that that the duration of rapid tolerance is a function of exposure time. Persistence of rapid tolerance was surprisingly long. For example, after a 6 hr exposure to 20 mM ethanol, acute sensitivity was suppressed beyond 24 hrs withdrawal. However, after a 1 or 3 hr exposure, sensitivity had significantly recovered after only 4 hrs of withdrawal. This temporal switch is reflected by parallel changes in BK channel isoform profile. We found that after withdrawal from a 6 hr but not a 3 hr alcohol exposure, increases in mRNA levels of the alcohol insensitive STREX splice variant were observed. Moreover, the biophysical properties of BK channels during withdrawal from 6 hrs exposure were altered, and match the properties of STREX channels exogenously expressed in HEK 293 cells. Thus, our results suggest a temporally-triggered shift in BK isoform identity, with consequences for the persistence of molecular tolerance. Once activated, the switch does not require the continued presence of alcohol. These findings may be relevant in explaining how drinking patterns impact the development of alcohol dependence in humans.

NEUROACTIVE STEROID ADAPTATIONS FOLLOWING CHRONIC ALCOHOL CONSUMPTION Patrizia Porcu1, A. Leslie Morrow1, Bryon Adinoff2 and Kathleen A. Grant3 1Bowles Center for Alcohol Studies, University of North Carolina School of Medicine, Chapel Hill, NC, USA 2Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, USA 3Department of Behavioral Neurosciences, Oregon Health & Science University, Portland, OR, USA Neuroactive steroids contribute to alcohol sensitivity and regulate stress homeostasis in the central nervous system. The hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the pathology of alcoholism. A blunted HPA axis response has been found in both drinking and abstinent alcohol-dependent patients. We compared HPA axis regulation of the neuroactive steroid deoxycorticosterone (DOC) in cynomolgus monkeys and humans. Pharmacological challenges with naloxone, saline, corticotrophin releasing factor (CRF), dexamethasone, and adrenocorticotropic hormone (ACTH) were conducted in monkeys prior to and following 12 months of voluntary alcohol drinking, and in healthy humans vs. 1-month abstinent alcohol-dependent patients. DOC levels were measured in plasma samples by radioimmunoassay. Long-term alcohol self-administration increased basal DOC levels (+244%, $p<0.001$) in monkeys. DOC responses to CRF and dexamethasone challenges were blunted, responses to ACTH challenge were enhanced and responses to naloxone challenge were not altered by long-term alcohol exposure. In humans, basal DOC levels and DOC responses to HPA axis challenges did not differ in healthy subjects vs. abstinent alcohol-dependent patients, except for a delayed time to peak DOC response following CRF challenge in the alcohol-dependent patients. These data suggest different adaptations in HPA-mediated DOC responses in monkeys vs. humans. This is likely due to different alcohol exposure parameters (actively drinking state vs. 1-month abstinence) or to the induction procedure of alcohol self-administration in monkeys. Studies are underway to investigate if neuroactive steroid adaptations in monkeys are influenced by abstinence following long-term alcohol consumption. Supported by AA13515, AA13510 and AA11570.

ETHANOL MODULATION OF GABA-A RECEPTOR GENE EXPRESSION AND FUNCTION IN SOCIALLY ISOLATED ANIMALS Sanna E.; Follesa P.; Mostallino M.C.; Serra M.; Biggio G. University of Cagliari; Department of Experimental Biology, Section of Neuroscience; Institute of Neuroscience, C.N.R., Cittadella Universitaria; 09042 Monserrato, Cagliari, ITALY. Social isolation (SI) has been extensively shown to induce marked behavioral alterations, such as increase in locomotor activity, anxiety, depression, and aggression in laboratory animals, included mice and rats, suggesting that it may represent a stressful condition and that the abnormal behavioral response of rodents so reared is the product of prolonged stress. SI has also been shown to be associated with a decrease in brain and plasma concentrations of neuroactive steroids, and an abnormal response to acute stressful stimuli as well as an increased neurosteroidogenic effect induced by the acute administration of ethanol (EtOH). We have investigated in C57BL/6J mice the effect EtOH in the free-choice drinking paradigm on gene expression and function of GABAA receptor (GABAAR) in the hippocampus. Socially isolated (SI) and group-housed (GH) mice were exposed for 6 weeks to the two-bottle choice (EtOH/H2O). Specific GABAAR subunits expression were measured by RNase protection assay and immunohistochemistry. GABAAR function was evaluated by conventional whole-cell patch clamp recording in brain slices. We found a significant increase in the abundance of both 4 and subunits of the GABAAR in the hippocampus of SI mice compared to GH animals. On the contrary the abundance of the 1 subunit mRNA was unchanged in SI mice as compared to GH mice. Voluntary EtOH drinking resulted in a marked increase in subunit mRNA levels in GH mice, whereas in SI animals, it completely abolished the increase in 4 subunit mRNA but did not alter that of the subunit with respect to the SI mice that were exposed only to water. Patch clamp recording in dentate gyrus granule cells obtained from SI mice revealed a greater enhancement of tonic currents induced by THIP compared to that in GH animals. Voluntary EtOH consumption reduced the increase in tonic current associated with social isolation. These results suggest that voluntary EtOH drinking in SI mice has a selective influence on 4 subunit since blocks its enhanced expression but fails to alter the up-regulation of subunit. Sponsored by grant from NIAAA INIA-Stress Grant #1 U01 AA016670

SOCIAL STRESS AND NEURAL SENSITIZATION: ESCALATED COCAINE BINGEING, A MODEL FOR ALCOHOL. Miczek, Klaus; Tufts University, Medford, MA, USA. Traditionally, alcohol consumption has been interpreted to reduce tension and alleviate stress. Considerable anthropological and epidemiological data associate stress and the abuse of alcohol and other drugs, although it remains challenging to demonstrate a causal relationship between stress and alcohol. Systematic analysis have revealed that the conditions under which social stress engenders increased cocaine intake are characterized by brief, intermittent and escapable episodes of social defeat stress. These types of stress episodes induce behavioral cross-sensitization and activate the dopamine cells in the ventral tegmental area that project to the nucleus accumbens shell as measured via in vivo microdialysis and via fast scan voltametry. By contrast, prolonged inescapable social stress in the form of continuous subordination results in anhedonia-like deterioration of preference for sweets and intake of cocaine. Prolonged subordination stress induces a lessened response to a challenge with cocaine in terms of dopamine release and psychomotor stimulation. Suppressed intake is most often found in experimental studies on social stress and alcohol, suggesting that intermittency and controllability of social stress are critical features in engendering escalated alcohol drinking. Mechanistically, CRF modulation of the DA VTA system appears critical for social stress to escalate or suppress alcohol drinking, as illustrated by the effective change in escalated alcohol consumption after blockade of CRF 1 receptors in the VTA.

GENE NETWORKS ASSOCIATED WITH ACUTE ETHANOL RESPONSES AND EXCESSIVE DRINKING: INTERACTIONS ACROSS THE MESOLIMBOCORTICAL SYSTEM. Miles, M.F.; Wolen, A.; Farris.; Wolstenholme, J.; Bruce, N.; and Vorster, P. Depts. of Pharmacology/Toxicology and Neurology, Virginia Commonwealth University, Richmond, VA 23298 USA. Alcoholism is a complex trait likely governed by interaction between tens of genes and environmental factors. Molecular genetic approaches in humans and animal models have sought to identify genes governing predisposition to alcoholism or influencing ethanol behaviors. However, the complexity of the phenotype, small effect sizes of individual genes and limitations of the genetic architecture in animal models have hampered the identification of alcoholism and alcohol response genes (AARGs). Our laboratory has used whole genome expression profiling with microarrays and behavioral genetics to identify gene networks correlating with acute behavioral responses to ethanol and ethanol drinking behavior in mice. These networks have been further prioritized using bioinformatics approaches to identify genes containing functional connectivity to genes known from published studies to influence alcoholism risk or ethanol behaviors. In order to more fully understand the complexity of gene-gene interactions in modulation of ethanol phenotypes, we have also more recently studied interactions of gene expression across brain regions comprising the mesolimbocortical dopamine pathway. Our work has focused attention on several novel gene networks that appear to influence behavioral responses to ethanol and may play a role in conferring risk for alcoholism. *Supported by NIAAA grants U01AA016662, U01AA016667, P20AA017828, and R01AA014717 to MFM.*

LACK OF EFFECT OF LOW CONCENTRATION ETHANOL ON $GABA_A$ RECEPTORS OF RAT CEREBELLAR GRANULES IN CULTURE: EXPLAINED BY THE ABSENCE OF CRITICAL RECEPTOR SUBTYPES? Aroldo Cupello, Elena Gatta and Mauro Robello. Dipartimento di Fisica, Gruppo di Biofisica, Università di Genova, Italy. Previous experiments by our group showed that only high (≥ 100 mM) ethanol concentrations could enhance the activation by GABA of $GABA_A$ receptors of cerebellar granules put in culture from neonatal rats. This was unexpected since they were believed to express $GABA_A$ receptor subtypes which, according to the relevant scientific literature, are able to respond to concentrations of ethanol as low as 3 mM. The data discussed in this presentation suggest that the relatively low potency of ethanol in this model is due to absence of expression of $GABA_A$ receptors involved in the tonic component of GABA mediated inhibition. In particular, we describe the absence of the α_6 β_x δ subtype, a key player in tonic inhibition of mature granules. Overall, our data indirectly support, or at least do not contradict, the idea that ethanolic ataxia is related to excessive activity of δ subunit containing $GABA_A$ receptors, involved in cerebellar granule tonic inhibition.

WITHDRAWAL OF LOW CONCENTRATIONS OF ETHANOL IS ASSOCIATED WITH CHANGES IN $GABA_A$ RECEPTOR GENE EXPRESSION AND FUNCTION IN RAT CEREBELLAR GRANULE NEURONS IN CULTURE. Talani G., Biggio F., Utzeri C., Olla P., Obili N., Sanna E., Follesa P. Department of Experimental Biology, Sect. of Neuroscience, University of Cagliari. Cittadella Universitaria; 09042 Monserrato, Cagliari, ITALY. It is widely accepted that chronic exposure to ethanol (EtOH) and EtOH withdrawal (WDL) are associated with significant changes in $GABA_AR$ gene expression and function in different brain region. Such alterations, that generally have been described using relatively large concentrations of EtOH (50-200 mM), could be relevant for the development of tolerance and dependence. More recent studies, however, have suggested, although with some controversy, that α4β2δ and α6β2δ $GABA_ARs$, which mediate the tonic inhibitory currents, are extremely sensitive to very low concentrations of EtOH. An important question is whether $GABA_ARs$ can be altered also by lower concentrations (e.g., 1 – 50 mM) of EtOH. To address this question we used rat cerebellar granule cells (CGCs) in culture following a 6-day exposure to EtOH (1-100 mM) and after 3h WDL. Evaluation of $GABA_AR$ gene expression by RPA showed that prolonged EtOH exposure (with 50 mM or higher) resulted in a decrease (20%) in the a abundance of mRNAs for only the γ2 subunit compared to control. Three h WDL of 1 - 10 mM EtOH significantly decrease the abundance of α1, α6 and δ subunit mRNAs (36, 26, and 16%, respectively) with no change in those of the α4 subunit. To evaluate the function of $GABA_ARs$, whole-cell patch clamp experiments were performed. CGC membrane potential was clamped at -65 mV and Cl^- currents were evoked by the 60-s perfusion of GABA (0.5 μM) or the δ-receptor preferential agonist THIP (3 μM). WDL of 1 mM EtOH for 3 h was associated with a significant decrease in GABA- or THIP-evoked currents compared to control cells. This is the first report showing that prolonged exposure to low concentration of EtOH such as 1 mM can induce a decrease of gene expression and function of $GABA_ARs$.

INNATE VULNERABILITY TO EXCESSIVE ALCOHOL DRINKING IN MSP RATS IS ASSOCIATED TO DYSREGULATION OF THE BRAIN CRF_1R SYSTEM. [1]Ciccocioppo R,[2]Roberto M. [1] School of Pharmacy, University of Camerino, Italy. [2]Committee on the Neurobiology of Addictive Disorders, Scripps Research Institute, La Jolla, USA. Corticotropin-Releasing Factor 1 receptors (CRF_1R) mediate increased behavioral sensitivity to stress and excessive alcohol self-administration following a history of dependence. It was recently demonstrated that genetically selected alcohol preferring Marchigian Sardinian (msP), rats have an innate upregulation of the (CRF_1R) transcript which encodes the CRF_1R in several limbic areas of the msP rat brain. This upregulation is associated with genetic polymorphism of the CRF_1R promoter and is accompanied by increased CRF_1R density in these limbic regions. The msP rat line is highly sensitive to stress and stress-induced alcohol seeking, demonstrates an anxious phenotype, and has depressive-like symptoms that recover following ethanol consumption. Similar to postedependent rats the msP line is highly sensitive to treatment with CRF_1R

antagonists that reduced their alcohol drinking and potently prevented stress-induced reinstatement. Conversely, in nondependent Wistar rats CRF_1R antagonism plays only a marginal role in the regulation of drinking behaviour and relapse. Altogether these findings indicates that the innate dysregulation of the brain CRF_1R system, is responsible for the expression of the msP excessive-drinking phenotype. A corollary to this finding is that ethanol drinking in msP rats is motivated by negative reinforcement (e.g. ethanol-induced relief from the affective dysfunction associated with heightened CRF signaling). Accordingly, these animals may model drinking behavior in alcoholics that drink for tension relief and for self-medication purposes. *(Grant: AA017447 to MR, subcontract to RC*)

Tuesday, June 8

Presidential Symposium: IN SEARCH OF EFFECTIVE ANIMAL MODELS IN BEHAVIORAL NEUROSCIENCE. Organizers: **Robert Gerlai** and **Kelly Lambert**

PREHISTORIC PROZAC: EXAMINING THE NEUROBIOLOGICAL CONSTITUENTS OF ADAPTIVE COPING STRATEGIES AND EFFORT-DRIVEN REWARD TRAINING. Lambert, K.G., Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005 USA Chronic stress disrupts an organisms allostatic responses and leads to negative health effects such as cardiovascular disease, immunosuppression, and various forms of mental illnesses. Consequently, it is important to identify strategies that contribute to resilience in the midst of stressful contexts. Recent research in my laboratory suggests that repeated physical responses directed toward a meaningful goal (i.e., effort-driven reward training) enhance persistence in a novel challenge task and, correspondingly, lead to increased neuropeptide Y (NPY) immunoreactivity in the amygdala and hippocampus. Further, rats exhibiting variable, rather than consistent, coping responses also exhibit higher levels of NPY-ir in the amygdala (but not in the paraventricular hypothalamus) as well as context-dependent alterations in fecal corticosterone levels. In sum, certain acquired and innate behavioral strategies may alter relevant neurochemicals and neural circuits to reduce health-threatening responses to chronic stress and enhance emotional resilience.

PRENATAL SOCIAL STRESS AND PROGRAMMED HYPER-SENSITIVITY TO STRESS IN ADULT OFFSPRING: GENDER-SPECIFIC MODULATION BY NEUROACTIVE STEROIDS IN THE RAT. Russell, J.A.; Brunton, P. J. Laboratory of Neuroendocrinology, Centre for Integrative Physiology, University of Edinburgh, Edinburgh EH8 9XD, UK. Neuroendocrine responses to a range of types of stressor are strongly attenuated in late pregnancy, especially hypothalamo-pituitary-adrenal (HPA) responses [1]. The mechanism involves activation of an inhibitory opioid mechanism in the brain by allopregnanolone, a neuroactive progesterone metabolite [2,3]. Despite this mechanism, repeated brief exposure to social defeat stress in the last few days of pregnancy programmes the offspring, which show a phenotype involving gender-dependent hyper-anxiety, exaggerated HPA stress responses to emotional and physical stressors (restraint for 30 min; i.v. interleukin-1beta [IL-1b] challenge) and metabolic abnormalities [4]. The exaggerated HPA stress responses to IL-1b can be acutely reversed by neurosteroid metabolites of androgen or progesterone in males or females respectively. References: [1] Brunton PJ, Russell JA (2008) Nat Rev Neurosci. 9(1):11-25. [2] Brunton PJ et al. (2005) J Neurosci. 2005 25(21):5117-26. [3] Brunton PJ et al. (2009) J Neurosci. 29(20):6449-60. [4] Brunton PJ, Russell JA (2010) J Neuroend. DOI: 10.1111/j.1365-2826.2010.01969.x

COPING WITH SOCIAL STRESS: NEUROBIOLOGY OF BEHAVIORAL RESPONSES TO SOCIAL DEFEAT Kim Huhman, Neuroscience Institute, Georgia State University, Atlanta, GA USA 30303 Social stress plays an important role in the etiology of a variety of human psychopathologies, and the number of studies using animal models of social stress has increased substantially over the last several years. These studies have improved our understanding of behavioral responses to social stress as well as the neurobiological mechanisms subserving these responses. Syrian hamsters display a striking behavioral response to social defeat that has been termed conditioned defeat. Our work has begun to define the neural circuit that mediates this behavioral response and to determine which sites within this circuit are responsible for the actual plasticity that that underlies it. The question of whether the behavioral response to social stress is adaptive or maladaptive and whether this response is similar in humans and non-humans will also be explored.

STRESS REVISITED: A CRITICAL EVALUATION OF THE STRESS CONCEPT. Prof dr Jaap M. Koolhaas, Behavioral Physiology, University Groningen, P.O.Box 14, 9750 AA Haren, The Netherlands.The stress concept has been subject of much scientific debate. A comparison of the "stress" response to a positive and rewarding situation with that to a negative, aversive stimulus reveals no difference. Therefore, it will be argued that the stress concept should be restricted to uncontrollable and unpredictable situations to dissociate stress from the physiological support of behavior. It is not the magnitude of the HPA axis or sympathetic response that dissociates a stimulus from a stressor but rather the downward slope of these responses. This has important consequences, not only for the interpretation of experimental results, but also for the experimental approach of stress related questions. Much can be gained by more carefully exploiting the biological basis of animals and humans using ecologically relevant models. This allows a fundamental analysis of factors modulating the individual adaptive capacity and hence the individual vulnerability to disease. This paper will highlight a more biologically oriented framework of interpretation to evaluate both the adaptive and maladaptive nature of the stress response in relation to the existing environmental demands.

GENETIC ANALYSIS OF BEHAVIORAL PLASTICITY AND LEARNING IN ZEBRAFISH Granato, M.; Dept. of Cell and Developmental Biology, University of Pennsylvania, Philadelphia, USA. In response to experiences with their environment, animals constantly update their behavior through the processes of sensorimotor integration and learning. The simplest form of learning is non-associative learning, which is defined as a change in attention directed towards a stimulus. Abrupt sensory stimuli evoke an evolutionary conserved motor response, the startle reflex. The startle reflex is highly modifiable, such that repeated presentation of startling stimuli suppresses the startle response. This decrease in attention towards an irrelevant stimulus is defined as habituation and represents plasticity at the level of the circuit driving the suppressed behavior. Zebrafish show a remarkable capacity for behavioral plasticity, and using an automated high-speed video analysis and tracking system, we show that zebrafish larvae (5-14 days post fertilization) exhibit robust short-term habituation of the acoustic startle response with landmark behavioral and pharmacological characteristics. Importantly, our assay identifies habituation of a very specific sensorimotor behavior - only performed in response to startling stimuli - controlled by a well characterized and simple neural circuit that is easily visualized in an intact, freely behaving vertebrate organism. We will present data demonstrating that our habituation assay satisfies the nine behavioral characteristics commonly used to define habituation behavior. For example, we show that more frequent stimulation results in a more rapid and pronounced response decrement with more rapid spontaneous recovery and that habituation can be reversed through cross-modal stimulation (dishabituation). Finally, we will report on ongoing genetic and small molecule screens and the identification of the first zebrafish learning mutants.

THE CIRCADIAN CLOCK AND RESPONSES TO PSYCHOSTIMULANTS. Zhdanova, I.V.; Lopez-Patino, M.; Mabray, P.; Yu, L. Boston University School of Medicine, Boston, MA 02118 USA. There is growing evidence that the biological clock plays an important role in health and disease. Using zebrafish as a model, we study the relationship between the effects of a widely used psychostimulant, cocaine, and the circadian clock. Our data indicate a complex reciprocal relationship between the two. On the one hand, the effects of cocaine on gene expression, neuronal development, behavior and the cardiovascular system depend on the circadian phase and can be modified by the principal hormone of the circadian system, melatonin. On the other hand, cocaine can interfere with the functional state of the circadian system, causing temporal entrainment or desynchronization. Moreover, the interaction of the biological clock and psychostimulant effects is altered by the aging process.

GENES, NEUROTRANSMITTERS AND BEHAVIOR: ZEBRAFISH STRAIN COMPARISON WITH A FOCUS ON ALCOHOLISM. Gerlai, R. Department of Psychology, University of Toronto Mississauga, Mississauga ON, Canada L5L 1C6 Alcoholism is a major unmet medical need that has high costs both in terms of human suffering for the patient, his/her caregivers, families and coworkers and with regard to the actual financial loss at the society level. Appropriate treatment options for alcoholism and alcohol abuse are lacking mostly because of the complexity of alcohols actions in the brain. To unravel this complexity laboratory animals may be utilized as tools. Zebrafish has been proposed for this purpose for two main reasons. One, zebrafish responds to acute as well as chronic alcohol treatment with behavioral changes that show face validity. Second, zebrafish allows sophisticated genetic analysis, including DNA microarray and forward genetic mutagenesis studies. For successful genetic analyses, however, one needs to characterize zebrafish strains. Here we review our latest findings on two distinct strains of zebrafish and show differences in expression levels of numerous genes encoding neurotransmitter receptors and other proteins involved in neurotransmitter reuptake, metabolism and synthesis. We also demonstrate differences in levels of a variety of neurotransmitters as well as in the behavior of these strains including alcohol tolerance and withdrawal induced behavioral responses. Although at this point it is too early to draw causal conclusions about the gene expression, neurochemical and behavioral correlations, our results demonstrate the feasibility of zebrafish as a tool in the analysis of alcohol induced functional changes in the brain paving the way for future forward genetic and gene expression studies.

DECIPHERING GENETIC AND CELLULAR NETWORKS CONTROLLING EMOTION-RELATED BEHAVIORAL RESPONSES IN ZEBRAFISH Su Guo, Department of Biopharmaceutical Sciences University of California - San Francisco Emotional related behaviors such as fear/anxiety and aggression are evolutionarily conserved and important for the survival and well being of individuals. We employ zebrafish as model to study two innate behavioral responses: First is a camouflage response, which manifest at light/dark-controlled organelle movement in neural crest derived melanocytes, and second is a light dark choice behavior. We discuss the amenability of these behaviors to molecular genetic and cellular analysis, and how such understanding will provide insights into human emotions and emotion-related disorders.

Wednesday, June 9

9:00-10:00 **Presidential Invited Lecture: Merzenich, M.** Introduction: Kelly Lambert.

BRAIN PLASTICITY-BASED THERAPEUTICS. Merzenich, M. UCSF, Keck Ctr, San Francisco, CA, USA. Neuroplasticity science has provided us with an increasingly clear understanding of the brain plasticity-based origins of human ability, and of the operational 'self'. That science has also shown that brain plasticity processes are, by their general nature, reversible. We have employed this science to design brain plasticity-based training tools designed to progressively improve human neurological performance abilities, on the path to ameliorating the deficits that mark normal aging, or that accompany neurological or psychiatric illness. Design principles underlying the development of these new tools and strategies applied to validate their use shall be briefly described.

10:30-11:30 **Keynote Lecture: Clayton, N.** Introduction: Robert Gerlai.

THE DEVELOPMENT AND EVOLUTION OF MENTAL TIME TRAVEL. Professor Nicola S Clayton, University of Cambridge, UK. As humans, we spend much of our time thinking about the past and planning for our long-term future. Traditionally, it has been argued that only humans are capable of such mental time travel, the ability to cast one's mind forwards and backwards in time to reminisce about the past and imagine future scenarios. I shall argue, however, that some non-human animals are also capable of remembering the past and planning for the future, at least in a rudimentary form. Surprisingly, some of the most convincing evidence comes from a member of the crow family, the western scrub-jay. In this talk I shall also focus on the development of future planning in young children, and the distinction between episodic projection and semantic prospection.

11:30-12:30 **Oral Session 1:** STRESS AND ANXIETY. Chairperson: Rosa Almeida.

PRENATAL STRESS PRODUCES DIVERGENT PATTERNS OF ANXIETY- AND DEPRESSION-LIKE BEHAVIORS IN WKY AND WISTAR RATS. Sultany, T.; Schroeder, M.; Weller, A. Bar-Ilan University, Ramat-Gan, Israel. The behavioral effects of different prenatal stress (PNS) schedules were examined together with genetic predisposition, in male and female prepubertal depressive- and anxious-like Wistar Kyoto (WKY) and control Wistar rats. Groups: PS: Daily 1hr maternal restraint stress (gestational days 1420), RPS: 7-days of Random schedule restraint throughout pregnancy; Control: undisturbed. Offspring were tested on postnatal days 29-35 for exploration and novelty approach (or "anxiety-like" profiles), social play, swim-test immobility ("depressive-like" behavior) and corticosterone (CORT) levels (basal & post-stress). Results PNS induced an increase in anxiety-like behaviors in WKY, particularly in females, and decreased them among Wistar males compared to unstressed controls. On the other hand, PNS reduced immobility in the swim test and increased diving in WKY compared to control in both sexes. Within the Wistar strain there was only a minor effect in the swim test. Post stress CORT levels were elevated in WKY compared to Wistar and in males compared to females. Basal CORT levels in the PS group were lower than controls. PNS-Wistar performed more pinning, rearing and climbing the cage-cover than controls in a social interaction test, while WKY remained unaffected. Overall, RPS decreased Wistar and increased WKY body weight compared to controls. Thus, while prenatal stress induced opposite-direction effects within the WKY strain, its effects on the "normal control" Wistar strain exposed social hyperactivity and risk-taking behaviors. The results of the present study support the importance of the environment during gestation on long term anxiety and depressive like behaviors in the offspring. Support: Israel Science Foundation.

ROLE OF EARLY LIFE STRESS IN COCAINE-INDUCED LOCOMOTION AND ANXIETY-LIKE AND NOVELTY-SEEKING BEHAVIOR IN ADOLESCENCE. Tschetter, K.E.; Callahan, L.B.; Ronan, P.J. Basic Biomed. Sci. Neurosci. The Univ. of South Dakota Sanford Sch. of Med., Vermillion, SD 57069. Sioux Falls Veterans Admin. Res. Service, VA Hosp., Sioux Falls, SD 57105. Basic Res., Avera Mckennan, Sioux Falls, SD 57105. Early life stress is a risk factor for increased vulnerability to drug addiction during the particularly susceptible period of adolescence. Maternal separation (MS) is a widely used animal model of early life stress. Very few studies have evaluated the effects of MS on brain stress systems during adolescence. We sought to evaluate the effects of MS on anxiety-like behavior, novelty-seeking, and cocaine-induced locomotion during adolescence. We utilized two experimental groups: maternal separation for 15 min (MS15) and for 180 min (MS180) and two control groups: animal facility raised and non-handled. Elevated plus maze testing demonstrated females exposed to MS spent less time on the open arms. Also MS180 males spent less time on the open arms. In testing on the playground maze, MS females showed increased latency to approach and increased number of approaches to the novel object. Males exposed to MS showed decreased latency to approach and increased number of approaches to the novel object. Cocaine-induced locomotion testing demonstrated MS females showed significantly increased locomotion in response to novelty and cocaine. Maternally separated males exposed to a novel environment showed a trend toward increased locomotion and also showed this trend in response to cocaine. These results demonstrate that early life stress effects cocaine-induced locomotion and anxiety-like and novelty-seeking behavior during adolescence.

ANTERIOR OLFACTORY NUCLEUS PLAYS AN IMPORTANT ROLE IN SOCIAL BUFFERING OF CONDITIONED FEAR RESPONSES. Kiyokawa, Y.; Takeuchi, Y.; Nishihara, M.; Mori, Y. Graduate School of Agricultural and Life Sciences. The University of Tokyo, Tokyo 113-8657 JAPAN. In "social buffering", a phenomenon known in various species, stress responses are less distinct when an animal is exposed to a stressor with one or more conspecific animals. We have previously reported that the presence of an associate rat mitigates conditioned fear responses to an auditory conditioned stimulus (CS) via the main olfactory system in male rats. However, it is unclear how the signal is transmitted from the main olfactory bulb to the amygdala, the key site for the conditioned fear response. The anterior olfactory nucleus posterior region (AOP) is one of the nuclei that receive direct projections from the main olfactory bulb. In this study, we therefore investigated the role of the AOP with our social buffering model. The AOP of the subject was lesioned bilaterally four days before the conditioning. Twenty-four hours after the conditioning, the subjects were re-exposed to the CS either alone or with an associate. When the fear-conditioned subjects were exposed to the CS alone, both the lesioned- and sham operated (control)-subjects showed freezing. In contrast, social buffering was absent only if the subject with lesioned AOP. These results suggest that the AOP plays an important role in the social buffering of conditioned fear responses in male rats.

IMMUNE ACTIVATION AND DEFENSIVE BEHAVIOR. Dunn, A.J.; Wieczorek, M.; Swiergiel, A.H. Louisiana State University Health Sciences Center, Shreveport, LA 71130, & University of Hawaii, Honolulu, HI 96822. Administration of interleukin-1 (IL-1) to rats and mice induces many behavioural, physiological and neurochemical responses. Regardless of the route of administration, it decreases overall behavioural activity, exploration and feeding, as well as sexual activity, and increases slow-wave sleep. It also stimulates the activity of hypothalamo-pituitary-adrenocortical axis (HPAA) indicative of stress, while also increasing the activity of noradrenergic and serotonergic systems in the brain, and increasing free tryptophan concentrations. It is believed that the noradrenergic response may be instrumental in activating the HPAA. The behavioural changes are very similar to those observed during illness (slowness, aversion to novel stimuli, anhedonia), and are referred to as 'sickness behaviour.' These responses may be regarded as adaptive, allowing animals to cope with disease and possibly protect them against potential predators and pathogens. Changes in the activity of the immune system produced by infections or inflammatory events result in the production of IL-1, which can thus be regarded as the mediator of these adaptive responses. Lipopolysaccharide (LPS) has very similar effects, most likely because LPS is a potent stimulator of IL-1 production both peripherally and centrally. However, the mechanisms by which IL-1 and LPS elicit these effects are not fully understood. Cyclooxygenase (COX) enzymes which are involved in the production of prostaglandins have been shown to be important in signalling from the periphery to the brain. COX inhibitors, such as indomethacin impair this signalling, as do lesions of vagal afferents to the CNS. However, neither procedure completely prevents the brain responses. Thus both the vagus nerve and COX appear to be involved in signalling peripheral immune system activation to the brain. In the present experiments, we examined the effects of COX inhibition (by indomethacin), and subdiaphragmatic vagotomy of rats on the HPAA responses to peripherally injected IL-1 and LPS. Supported by NIH NS35370

2:00-4:00 **Symposium 1**: NEUROSTEROIDS IN THE TREATMENT OF BRAIN INJURY, STROKE AND NEURODEGENERATIVE MOTOR DISORDERS: MORPHOLOGICAL AND FUNCTIONAL OUTCOMES.
Chairperson: **Donald G. Stein**

NEUROACTIVE STEROIDS AND DIABETIC NEUROPATHY. Melcangi, R.C. DEFIB-CEND, University of Milan, via Balzaretti 9, 20133, Milano Italy. Peripheral neuropathy represents an important complication of diabetes involving a spectrum of structural, functional and biochemical alterations in peripheral nerves. We have observed that neuroactive steroids, such as progesterone (PROG), testosterone (T) and their reduced metabolites, are able to counteract nerve damage induced by diabetes. Indeed, in the experimental model of streptozotocin-treated rats, neuroactive steroids counteracted the impairment of nerve conduction velocity and thermal threshold, restored skin innervation density, and improved Na+K+-ATPase activity and mRNA levels of myelin proteins (Leonelli et al, Neuroscience 144:1293-1304, 2007; Roglio et al. Cell. Mol. Life Sci. 64:1158-1168, 2007). Moreover, they was able to counteract the increase in the number of fibers with myelin infoldings observed in the sciatic nerve (Veiga et al. Neurosci. Lett. 402:150-153, 2006). Finally, treatment with a ligand of translocator protein-18 kDa (TSPO), such as Ro5-4864, was able to reduce the severity of diabetic neuropathy (Giatti et al., Neuroscience 164:520-529, 2009) and to increase the low levels of neuroactive steroid levels observed in the peripheral nerves (Caruso et al., Neurochem Int. 52:560-568, 2008; Pesaresi et al. Horm. Behav. 57:46-55, 2010). Altogether, these findings suggest that neuroactive steroids may represent potential therapeutic tools for the treatment of diabetic neuropathy.

PROTECTIVE EFFECTS OF PROGESTERONE. Frye, C. Depts. of Psychology and Biology, Ctrs. for Life Science and Neuroscience Research. The University at Albany, State University of New York, Albany, NY, 12222 USA. Growing evidence supports a role for gonadal hormones in explaining some gender/sex differences. Among females, the majority of studies that have examined effects of gonadal steroids have focused on estradiol. Yet, progesterone varies over reproductive cycles. Emerging evidence suggests that progesterone may exert profound and diverse effects to protect the brain from stress-related pathologies, drug effects, and/or neurodegeneration. Findings from this lab which suggest that progesterone is integral for normal neural and cognitive development, and novel actions of progesterone for these effects, will be discussed.

ANTI-INFLAMMATORY ACTIONS OF ESTRADIOL AND ESTROGENIC COMPOUNDS AFTER BRAIN INJURY. Garcia-Segura, L.M.; Santos-Galindo, M.; Azcoitia, I.; Arevalo M.A. Instituto Cajal, C.S.I.C., Madrid E-28002 Spain. Glial cells are directly or indirectly affected by estradiol and by different estrogenic compounds, such as selective estrogen receptor modulators (SERMs). Acting on astrocytes and microglia, estrogens regulate the reorganization of brain tissue after injury and after inflammatory challenge, reducing the number of reactive astrocytes, the number of reactive microglia and the release of pro-inflammatory molecules. The anti-inflammatory actions of estrogenic compounds involve classical estrogen receptors and the inhibition of NFkappaB p65 transactivation. Estradiol and some SERMs reduce reactive gliosis in males and females, in young and older individuals and after short or prolonged depletion of ovarian hormones. Therefore, estradiol and SERMs are potential candidates for the control of reactive gliosis and brain inflammation. Supported by BFU 2008-02950-C03-01/02 from the Spanish Ministerio de Ciencia e Innovacin.

MOLECULAR AND BEHAVIORAL EVIDENCES FOR PROGESTERONE AND NEUROSTEROID PROTECTION IN MOTONEURON DEGENERATION De Nicola, A.F., Gonzalez Deniselle, M.C., Meyer, M., Gargiulo, G., Guennoun R., Schumacher,M. Instituto de Biologia y Medicina Experimental-CONICET, Buenos Aires, and UMR 788 INSERM Paris. The effects of progesterone in nervous system diseases are of increasing interest due to their potential clinical applications. We have studied progesterone neuroprotection in Wobbler mouse spinal cord degeneration. Wobblers present motoneuron vacuolation, astrogliosis, atrophic limbs, tremor and ambulatory difficulty that worsens with disease progression. Wobbler motoneurons show impaired expression of brain-derived neurotrophic factor (BDNF), choline acetyltransferase (ChAT) and Na,K-ATPase and increased expression of nitric oxide synthase (NOS). Mitochondria show vacuolation, edema and crystolysis, decreased activity of respiratory chain complex I activity and increased expression of mitochondrial NOS (mtNOS). In 5-8 month-old Wobblers, at the established stage of the disease, progesterone reverses these abnormalities. Progesterone effectiveness has also been studied at early (12 months) and late (12 months) stages of neurodegeneration. In untreated Wobblers, vacuolated motoneurons are initially abundant, experience a slight reduction at the established stage and dramatically diminish during the late period. ChAT and BDNF are reduced at all stages of the Wobbler disease. Progesterone significantly reduces motoneuron vacuolation, enhances ChAT immunoreactivity during the early progressive and established stages, whereas up regulation of BDNF occurs at the established and late periods. Untreated Wobblers show high density of glial fibrillary acidic protein (GFAP) astrocytes, which are down-regulated by progesterone at all stage periods. Long-term progesterone treatment enhances survival and muscle strength, according to the time spent on a vertical grid and on a horizontal rope test. Therefore, progesterone may constitute a novel therapeutic tool to attenuate the course of neurodegeneration. Studies are in progress to study progesterone effects in patients with amyotrophic lateral sclerosis.

PROGESTERONE AND ITS METABOLITES IN THE TREATMENT OF TRAUMATIC BRAIN INJURY AND OTHER CNS DISORDERS Donald G. Stein, Ph.D. Emory University School of Medicine Atlanta, Georgia Research on the role of neurosteroids in the treatment of brain injury started in the 1960s but began to take hold only in the early 1990s. Today there are over 100 publications from more than 25 laboratories around the world using 22 different injury or disease models in four different species including humans, demonstrating that progesterone and its metabolites can promote morphological and functional recovery. Recently, two independent Phase II trials for moderate to severe TBI have shown that progesterone has no serious side effects and can reduce mortality and improve functional outcomes 30 days and 6 months after injury. Two large national and international Phase III trials for moderate to severe TBI will soon begin, so the progress over the last decade in bringing this neurosteroid to clinical application has been substantial. The clinical work is backed by many studies examining the genomic, molecular and physiological mechanisms of neurosteroid action in the nervous system and our understanding of these processes continues to improve. Researchers are also beginning to evaluate neurosteroid effects in other diseases that affect the brain and spinal cord. For instance, growing evidence indicates that progesterone and its metabolite allopregnanolone may be differentially effective in the treatment of ischemic stroke or spinal cord injuries. Our laboratory is now focusing on this question and whether the neurosteroids can be combined with other therapies such as the clotbuster tPA, or vitamin D, to improve stroke outcome. We are also exploring a prophylactic progesterone treatment to address ischemia and edema caused by pediatric cardiovascular surgery.

PROGESTERONE IN THE HEALTHY AND INJURED CENTRAL NERVOUS SYSTEM.Guennoun. R.1; Labombarda, F.2; Liu, A.1; Delespierre, B.1; Famose, S.1; Meffre, D.1; Liere, P.1; Gonzalez Deniselle, M.C.2; Stein, D.G3; De Nicola, A.F.2; Schumacher, M.1. 1- UMR788 Inserm and University Paris-Sud 11, Kremlin-Bictre, France; 2- Instituto de Biologia y Medicina Experimental-CONICET, Buenos Aires; 3- Emory University School of Medicine Atlanta, Georgia. USA. Progesterone and its metabolites promote the viability of neurons in the brain and spinal cord. Their neuroprotective effects have been documented in different lesion models, including traumatic brain injury, experimentally induced ischemia, spinal cord lesions and a genetic model of motoneuron disease. I will summarize our recent findings concerning the synthesis, metabolism, and receptors of progesterone in the healthy and injured nervous system. Emerging evidence from our studies, suggest that the increase in neurosteroid synthesis may be part of the mechanisms by which nerve cells cope with injury, and that different mechanisms of progesterone signalling are activated in the intact and injured nervous system. Recent selected references - Labombarda F, Meffre D, Delespierre B, Krivokapic-Blondiaux S, Chastre A, Thomas P, Pang Y, Lydon JP, Gonzalez SL, De Nicola AF, Schumacher M, Guennoun R (2010). Neuroscience 166(1):94-106. - Guennoun R, Meffre D, Labombarda F, Gonzalez SL, Deniselle MC, Stein DG, De Nicola AF, Schumacher M (2008). Brain Res Rev 57:493-505 - Meffre D, Pianos A, Liere P, Eychenne B, Cambourg A, Schumacher M, Stein DG, Guennoun R (2007). Endocrinology 148:2505-2517. - Schumacher M, Guennoun R, Ghoumari A, Massaad C, Robert F, El-Etr M, Akwa Y, Rajkowski K, Baulieu EE (2007). Endocr Rev 28:387-439. - Labombarda F, Pianos A, Liere P, Eychenne B, Gonzalez S, Cambourg A, De Nicola AF, Schumacher M, Guennoun R (2006). Endocrinology 147:1847-1859.

6:00-8:00 **Symposium 2**: THE ROLE OF THE BASAL GANGLIA IN LEARNING AND MEMORY. Chairperson: **Claudio Da Cunha**

LEARNING NOVEL ACTIONS: FROM INTENT TO HABIT Dias-Ferreira, E.Champalimaud Neuroscience Program at Instituto Gulbenkian de Cincia, Rua da Quinta Grande, 2780-156 Oeiras, Portugal. The process of perfecting an action through repetition may change the nature of the action. For example, extensive training on an instrumental task where animals lever press for particular outcomes can lead to a shift from goal-directed responding, that is sensitive to changes in the value of the outcome, to habitual responding, that is insensitive to outcome devaluation. We have previously found that extended training on a skilled task lead to subregion-specific circuit plasticity in the dorsal striatum, with dynamics consistent with previous studies showing that goal-directed actions are dependent on the associative striatum, while habits are dependent on the sensorimotor striatum. Endocannabinoid receptors (CB1) are highly expressed in the sensorimotor striatum which is important for habit formation, and previous studies showed that amphetamine sensitization, which depends upon endocannabinoid signaling, predisposes for habit formation. Using both genetically targeted mice that lack CB1 receptors, and pharmacological antagonists of CB1 receptors, we found that endocannabinoid signaling is critical for habit formation. Furthermore, using cre-mediated deletion of NMDA receptors in different midbrain dopamine neurons, we uncovered that nigral but not mesolimbic dopamine is important for habit formation. Finally, we developed a within-subject behavioral task in mice and recorded multiple single units within the frontal cortex and the associative and sensorimotor striatum to uncover activity related to goal-directed versus habitual behavior. These studies indicate that different cortico-striatal circuits mediate the learning and performance of different behavioral strategies. Supported by ERC

INTERACTIONS BETWEEN THE PEDUNCULOPONTINE AND BASAL GANGLIA AND THEIR ROLE IN LEARNING AND REINFORCEMENT. Winn, P. Strathclyde Institute of Pharmacy and Biomedical Science, University of Strathclyde, Glasgow G4 0NR, Scotland. The pedunculopontine tegmental nucleus (PPTg) has a complex relationship with the basal ganglia: posterior PPTg receives novel polymodal sensory information and projects to VTA dopamine (DA) containing neurons. The anterior PPTg is connected to substantia nigra pars compacta DA neurons and receives descending input from basal ganglia and extended amygdala. PPTg cholinergic neurons change firing patterns across the sleep-wake cycle, but the regulation of behavioural state is not the only PPTg function. In a series of studies we demonstrated that excitotoxic lesions of the PPTg do not have significant impact on locomotor activity, feeding and drinking, or emotional state (as measured by the elevated plus maze). Rather, PPTg loss disrupts rats' ability to learn. We hypothesize that a key property of the PPTg is to enable formation of action-outcome associations, and that posterior PPTg is more important for this than anterior. In recent studies we examined the abilities of rats to learn to bar press for both natural rewards and drugs; these studies suggest strongly that the PPTg is critical for action-outcome association. In addition, in order to determine the effect that PPTg cholinergic neurons have on the VTA, we studied intra-cranial self-administration of the cholinergic agonists nicotine and carbachol into the VTA. Data suggest that cholinergic control over the VTA is functionally concerned with reinforcement enhancement. Overall these studies highlight the fact that PPTg has higher order functions than was previously thought, and that it is critical for normal learning.

LEARNING, MEMORY AND STRIATAL SYNAPTIC PLASTICITY IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS. Massimiliano Di Filippo, MD and Paolo Calabresi, MD. Clinica Neurologica, Università di Perugia, Perugia, Italy and IRCSS Fondazione S Lucia, Rome, Italy. The striatum is the major division of the basal ganglia, representing the input station of the circuit and arguably the principal site within the basal ganglia where information processing occurs. Striatal activity critically control motor function and learning and many parts of the striatum are also involved in reward processing and cognitive functions. The crucial role played by the striatum in learning and cognitive processes is thought to be based on changes in neuronal activity when specific behavioral tasks are being learned. Accordingly, excitatory corticostriatal synapses onto both striatal projecting spiny neurons and interneurons are able to undergo the main forms of synaptic plasticity, including long-term potentiation (LTP), long-term depression (LTD), short-term forms of intrinsic plasticity and spike timing-dependent plasticity. Striatal LTP and LTD, the two main forms of synaptic plasticity, strongly depend on the activation of dopamine receptors. LTD is thought to be initiated postsynaptically but expressed through a presynaptic reduction in neurotransmitter release and it requires dopamine D2 receptors, group I mGluRs, L-type calcium channels, and CB1 receptor activation, but notably, not NMDA receptors. Conversely, LTP at glutamatergic synapses onto striatal medium spiny neurons involves activation of NMDA-type glutamate receptors and D1 dopamine receptors. In physiological conditions striatal neuroplasticity is thought to allow the short-term and long-term selection and differential amplification of cortical neural signals modulating the processes of motor and behavioral selection within the basal ganglia neural circuit. Following pathological insults and in different experimental models of neurological diseases such as basal ganglia neurodegenerative disorders, stroke and epilepsy, striatal synaptic plasticity has found to be altered suggesting that, at least in part, plastic abnormalities at striatal synapses may underlie symptoms onset and/or disease progression in human pathological conditions.

THE MOSAIC OF BROKEN MIRRORS MODEL. Da Cunha, C. ; Wietzikoski, E.; Dombrowski, P.; Santos, L.; Bortolanza, M.; Boschen, S.; Miyoshi, E. Dep. Farmacologia, UFPR, Curitiba, Brazil. The Mosaic of Broken Mirrrors Model (BBR 199:157,2009) proposes that the body and its surrounding environment are represented in the striatum in a fragmented and repeated way, like a mosaic consisting of the fragmented images of broken mirrors. Each fragment forms a functional unit representing a body part, objects of the environment which the subject can approach or manipulate, and locations the subject can move to. These units integrate the sensory properties and movements related to them. The repeated and widespread distribution of such units amplifies the combinatorial power of the associations among them. These associations depend on the phasic release of dopamine in the striatum triggered by the saliency of stimuli and will be reinforced by the rewarding consequences of the actions related to them. Dopamine permits synaptic plasticity in the corticostriatal synapses. The striatal units encoding the same stimulus/action send convergent projections to the internal segment of the globus pallidus and to the substantia nigra pars reticulata that stimulate or hold the action through a thalamus-frontal cortex pathway. According to this model, this is how the basal ganglia select actions based on environmental stimuli and store adaptive associations as procedural memories, such as motor skills and memories for goal-directed actions and stimulus-response habits, formed by instrumental conditioning.

Thursday, June 10

8:30-10:30 Symposium 3: FAMILIAL PATTERNS IN SUBSTANCE USE DISORDERS: HOW MATERNAL PHENOTYPE INFLUENCES VULNERABILITY TO FUTURE DRUG USE. Chairpersons: **Josephine Johns** and **Elizabeth Byrnes**

COCAINES EFFECTS ON MOTHER AND INFANT PHENOTYPES: MODELS OF INTERGENERATIONAL AND TRANSLATIONAL MECHANISMS THAT MAY IMPACT OFFSPRING VULNERABILITY. Johns, J.M.; McMurray, M.S.; Williams, S.K., Cox, E.T.; Jarrett, T.M.; Walker, C.H.; Jamieson-Drake A.W. and Moy, S.S. Depts. of Neurobiology, Psychiatry and Behavioral Neuroscience. University of North Carolina, Chapel Hill, NC 27599 USA. Our lab has previously demonstrated intergenerational effects of cocaine associated with (a) differential rearing environments resulting from maternal drug treatment, (b) prenatal exposure condition of pups, or (c) the interactive effects of both prenatal exposure environment of pups (cocaine or not) and rearing experience (drug treated or non treated mother). These factors, either individually, or in concert, are correlated with differences in next generation offspring maternal/social behavior and neurobiological processes during development. Other studies report that offspring neglect or abuse and drug exposure history, are also correlated with later increased substance use by offspring. This talk will briefly summarize some of the behavioral and biological effects of cocaine on rodent mothers and offspring from our studies. We will also introduce a new model of human and animal research projects designed to identify potentially important translational mechanisms through which cocaine may influence maternal-infant interactions and thus possibly alter later vulnerability of offspring to substance use. Supported by NIH grants DA13362, DA13283, 1P01DA022446-01A2 (JMJ)

TRANSGENERATIONAL EFFECTS OF ADOLESCENT OPIATE USE. Byrnes, E.M. Department of Biomedical Sciences, Tufts University, Cummings School of Veterinary Medicine, North Grafton, MA 01536, USA. Using a rat model, we have observed significant transgenerational effects following limited morphine exposure in adolescent females. For example, the adult offspring of adolescent-exposed mothers rapidly sensitize to the locomotor effects of morphine, demonstrate differential sensitivity to both the sedative and analgesic effects of morphine, and develop tolerance more quickly than offspring of control mothers. As morphine-exposed females are withdrawn from the drug several weeks prior to mating, their offspring are never directly exposed to opiates. Thus, some mechanism for maternal transmission must underlie these effects. This presentation will discuss potential alterations in maternal phenotype that may trigger transgenerational effects and explore how such effects may be mediated by alterations in histone acetylation in brain regions critical for maternal and addiction-related behaviors. These results may further our understanding of familial patterns of drug abuse.

MATERNAL COCAINE USE AND MOTHER-INFANT INTERACTIONS: DIRECT AND MODERATED EFFECTS. Rina D. Eiden, Research Institute on Addictions, State University of New York, Buffalo, NY 14203, USA. There is a growing consensus that the teratological effects of prenatal cocaine exposure are subtle, and may occur through several pathways. One such pathway may be through problematic mother-infant interactions. This study examined the associations between prenatal substance exposure and quality of mother-infant play interactions at 13 months of infant age. We investigated whether maternal psychological distress and infant reactivity mediated or moderated this association. Participants consisted of 220 mother-infant dyads participating in an ongoing longitudinal study of prenatal cocaine exposure. Mother-infant dyads were asked to spend some time in a room filled with toys and spend some time as they normally would at home. Maternal and infant behaviors were videotaped and coded by blinded observers. Results indicated that mothers who used cocaine during pregnancy displayed higher negative affect and lower sensitivity toward their infant during play interactions at 13 months, and that their infants were less responsive toward them. Results also indicated that as hypothesized, infant reactivity moderated the association between maternal cocaine use during pregnancy and maternal warmth/sensitivity at 13 months of age. Cocaine using mothers who perceived their infants as being more reactive in early infancy were less warm/sensitive toward them in later infancy. Results have implications for parenting interventions that may be targeted toward improving maternal sensitivity among cocaine using mothers with more reactive infants.

MALADAPTIVE MATERNAL EFFECTS IN RHESUS MONKEYS: IMPLICATIONS FOR DEVELOPMENTAL PSYCHOPATHOLOGY. Maestripieri, D. Institute for Mind and Biology, The University of Chicago, Chicago, IL 60637 USA. In evolutionary biology, maternal effects refer to effects of the maternal phenotype on the offspring phenotype, which occur independent of the offspring genotype. Maternal effects have been demonstrated in both plants and animals and they can be adaptive or maladaptive. Research with animal models of maladaptive maternal effects has important implications for understanding the early determinants of vulnerability to stress, psychiatric disorders, and substance abuse. Studies of rodents and nonhuman primates have shown that maternal stress (gestational or postpartum) and abusive or neglectful parenting result in long-term neuroendocrine and neurochemical alterations in the offspring, which represent risk factors for developmental psychopathology. We have shown that rhesus monkey infants exposed to abusive maternal behavior in the first few months of life exhibit long-term alterations in the activity of the hypothalamic-pituitary-adrenal axis including greater cortisol responses to stress and to exogenous CRH, and blunted ACTH responses to CRH during their first 3 years of

life. Infants exposed to maternal abuse and high rates of maternal rejection also exhibit reduced brain serotonergic activity, as reflected in lower CSF concentrations of the serotonin metabolite 5-HIAA, as well as increased anxiety and impulsivity. Cross-fostering studies have demonstrated the crucial role of experience in these maternal effects and their transmission across generations. Other studies of rhesus monkeys have shown that infants exposed to other traumatic early experiences, such as maternal separation and social deprivation, develop behavioral and neurobiological profiles similar to those of abused infants and that individuals with these profiles are more likely to engage in drug and alcohol abuse. The study of maladaptive maternal effects in nonhuman primates provides the opportunity to understand the biological mechanisms underlying these effects as well as to develop early intervention strategies that minimize the risk of developmental psychopathologies including substance abuse.

SUBSTANCE USING MOTHERS' RESPONSE TO SALIENT INFANT CUES. Mayes, L.; Potenza, M.; Landi, N.; Greger-Moser, M.; Johns, J. Yale Child Study Center, New Haven, CT. 06520 USA. Substance abuse involves a dysregulation of stress and reward systems such that individuals seek rewarding stimuli such as drugs to downregulate negative emotional and stressful experiences. Social attachment is also a process based on the balance between reward and stress. It may be that the dysregulation in these neural systems conveyed by addictive processes directly impact parenting such that stimuli salient for eliciting parenting behaviors such as an infant cry are sufficiently stressful to the addicted adult to elicit instead avoidant behavior toward the infant and increased craving for drugs. This presentation will present neuroimaging data relevant to this model and address the relevance of these data in familial patterns of substance abuse.

11:00-12:00 **Keynote Lecture: Biggio, G.** Introduction: Wim Crusio.

NEUROSTEROID MODULATION OF GABAA RECEPTOR PLASTICITY: PHYSIOLOGICAL AND PHARMACOLOGICAL CONDITIONS. Biggio, G. Dept. of Experimental Biology, Sect of Neuroscience and Center of Excellence for the "Neurobiology of Dependence", University of Cagliari, Cagliari, Italy. Research of the past decades has clearly demonstrated that neurosteroids, pregnane steroids that are synthesized de novo in the brain, act in a nongenomic manner to potently and selectively facilitate the interaction of the inhibitory neurotransmitter GABA with the GABAA receptor, contributing to the control of neuronal excitability. Thus, neurosteroids such as 3alpha,5alpha-TH Prog and THDOC are endowed with anxiolytic, anticonvulsant, hypnotic, and anesthetic properties. In this presentation, experimental data obtained in vitro and in vivo models will be illustrated that show how fluctuations in the brain concentrations of these neurosteroids, for example in response to stress, during pregnancy and after the acute or chronic administration of ethanol, may regulate both the expression and function of GABAA receptors. The results are in agreement with the notion that fluctuation in the levels of neurosteroids play a major role in the temporal pattern of expression of specific subunits of the GABAA receptor. Thus, rapid and long-lasting increases or decreases in the concentrations of these hormones observed in physiological as well as pathophysiologicals conditions, or induced by pharmacological treatments, might elicit selective changes in GABAA receptoc gene expression and function in specific neuronal populations. Because of both the relevant physiological role of GABAA receptors in the regulation of neuronal excitability and the large fluctuations in the plasma and brain levels of neurosteroids associated with physiological conditions and the response to environmental stimuli, these compounds are likely among the most important endogenous modulators that could affect emotional and affective behaviors.

2:00-4:00 **Symposia 4:** Endogenous Opioids and Addiction. Chairperson: **Judith E. Grisel**

INVOLVEMENT OF THE ENDOGENOUS OPIOID SYSTEM IN NICOTINE ADDICTION. Maldonado, R; Berrendero, F. Laboratory of Neuropharmacology, Health & Life Sciences School, Pompeu Fabra University, Barcelona, Spain. The endogenous opioid system plays an important role in the behavioural effects of nicotine. In this study, we evaluated the role of b-endorphin and delta-opioid receptors in the pharmacological effects of nicotine by using knockout mice. The rewarding effects of nicotine evaluated in the conditioned place-preference paradigm were blocked in mice lacking b-endorphin and delta-opioid receptors. In addition, in vivo microdialysis studies revealed that the enhancement in dopamine extracellular levels in the nucleus accumbens induced by nicotine was also reduced in delta-opioid receptor knockout mice. The behavioural expression of nicotine withdrawal was similar in wild-type and mutant animals. Therefore, b-endorphin through the activation of mu- and delta-opioid receptors seems to be involved in the modulation of the rewarding properties of nicotine.

ENDORPHIN AND ALCOHOL: FROM MOUSE TO HUMAN. Ildik Rácz, Birtta Schürmann, Andreas Zimmer. Institute of Molecular Psychiatry, University of Bonn, Germany. Introduction: The endogenous opioid system has been implicated in various aspects of alcohol addiction and in the regulation of stress responses. Because stress is one of the most important factors contributing to drug dependence and relapse, we have now studied ethanol preference in β-endorphin deficient mice under baseline conditions and after stress exposure. We performed an association analysis to clarify whether β-endorphin contributes to alcohol dependence in humans. Methods: We first used a two-bottle choice paradigm to study ethanol consumption and stress-induced ethanol preference. Next, we examined alcohol withdrawal symptoms in animals that have received ethanol as their only fluid source for three weeks. Animal studies were complemented with an association analysis in two case-control samples of alcohol addicts. Results: Ethanol consumption was significantly reduced in the absence of β-endorphin, particularly in female knockout animals. Stress exposure resulted in an increased ethanol consumption in wild type mice, but did not influence ethanol drinking in β-endorphin knockouts. In the human association study we found a two-marker haplotype in the POMC gene that was associated with alcohol dependence in females in both cohorts. Discussion: Our results identified a contribution of -endorphin to behaviours associated with alcoholism. -endorphin seems to be involved in ethanol preference and in the mediation of the stress effect on ethanol consumption. In line with that we found a significant role of POMC in female subjects in the human study.

b-ENDORPHIN AND NEGATIVE REINFORCEMENT. Grisel, J.E. Department of Psychology and Neuroscience Program. Furman University, Greenville SC 29613. Drug use is mediated by both positive and negative reinforcement. Generally the pleasurable effects of drugs are emphasized during the initiation of a habit, and dependence is characterized as a drive to escape aversive states consequent to chronic use. Most researchers agree that positive reinforcement is less likely and less robust with prolonged use, but there are few basic studies on the role of negative reinforcement in the initiation of drug abuse and dependence. However, clinical studies indicate that psychopathology often predicts drug abuse. For instance, mood disorders are highly co-morbid with alcoholism, and this observation contributes to the idea that even initial exposure to alcohol may be particularly reinforcing in some individuals as it medicates an aversive anxious or depressed state. Endogenous opioid peptides have been implicated in all three of these disorders, and may be one common predisposing factor. The studies presented here focus on that relationship using transgenic mice with low or absent b-endorphin. These mice show more anxiety-like behavior than control subjects in a number of laboratory measures, supporting the idea that this peptide, synthesized and released in response to stress, inhibits activity of the stress axis. Despite a hyper-anxious basal state, low b-E mice are especially sensitive to the anxiety-reducing effects of EtOH. Though basal self-administration and conditioned place preference for EtOH (two standard animal models for assessing reward) dont seem to depend much on b-E, when stress is introduced into the home cage where EtOH is available for consumption, or when it is incorporated into the conditioned place experimental paradigm, subjects with low b-E appear to find EtOH especially reinforcing. These data suggest that b-endorphin may mediate EtOH negative reinforcement via actions on the stress axis, and may have implications for understanding the common neural substrate for alcoholism and anxiety.

DETERMINANTS OF DESIRE: DISSOCIABLE OPIOID INVOLVEMENT IN PALATABILITY AND INCENTIVE LEARNING. Maidment, N.T; Wassum, K.M; Ostlund, S.B; Balleine, B.W. Dept. of Psychiatry & Biobehavioral Sciences, UCLA, USA and Brain & Mind Research Institute, University of Sydney, Australia. Endogenous opioids may mediate some of the affective qualities of both natural and drug rewards and, based on the conditioned aversive qualities of naloxone, they may also mediate a basal affective tone. However, evidence also points to their involvement in motivational processes. Using an instrumental paradigm for sucrose reward incorporating an index of reward palatability, we found dual, doubly dissociable roles for opioids in palatability, or liking, and the assignment of incentive value used to direct instrumental actions. Blockade of opioid receptors in the ventral pallidum and nucleus accumbens shell prevented the palatability-enhancing effect of food restriction, whereas disruption of opioid function in the basolateral amygdala (BLA) during reward consumption in the food-deprived state blocked the normally ensuing increase in reward-seeking actions, without affecting palatability. Data from use of selective antagonists implicate BLA mu receptors in facilitating incentive learning and we are currently examining the

specific peptides mediating this effect using precursor-deficient mice. Interestingly, encoding of downward shifts in value was not BLA opioid-dependent, neither was the retrieval of reward value once learned. A dual role of endogenous opioids in both the affective experience associated with drug taking and the incentive learning process involved in reward seeking may underlie the intensely addictive property of opiates as well as other substances that induce release of opioid peptides.

4:00-6:00 **Symposium 5**: NATURAL INTER-INDIVIDUAL DIFFERENCES IN BEHAVIOR TO EXPLORE COGNITIVE PROCESSES. Chairperson: **Françoise Dellu-Hagedorn**

GENETIC AND BEHAVIORAL REGULATION OF INTELLIGENCE IN GENETICALLY HETEROGENEOUS MICE. Matzel, L.D.; Kolata, S. Dept. of Psychology, Program in Behavioral Neuroscience. Rutgers University, Piscataway, NJ 08854 USA. Accumulating evidence indicates that the storage and processing (e.g., selective attention) capacities of the human working memory system co-vary with individuals performance on a wide range of cognitive tasks. The ubiquitous nature of this relationship suggests that variations in these processes may underlie individual differences in intelligence. Data from our laboratory indicates that genetically heterogeneous mice also express a trait that is qualitatively and quantitatively analogous to intelligence, and that the expression of this cognitive trait varies across individuals. As in humans, the expression of general cognitive abilities in mice is strongly correlated with individual animals capacity for selective attention. Moreover, we find that training-induced modulation of selective attention has a direct commensurate impact on animals general cognitive abilities, suggesting the possibility that selective attention is the latent variable that establishes intelligence. From this behavioral foundation, we have begun to characterize RNA expression profiles of mice characterized as exhibiting high or low cognitive abilities. Consistent with selective attention as the substrate for intelligence, work to date has indicated that the principal genetic correlates of intelligence reside in the prefrontal cortex, and are primarily attributable to variations in the expression of a small number of genes that regulate dopamine transport, sensitivity, and cycling. We will discuss this work in the context of normal cognitive abilities, as well as age-related impairments in general cognitive function.

THE RELATIONSHIP BETWEEN WORKING MEMORY AND INTELLIGENCE IN HEALTHY YOUNG ADULTS. Conway, A. R. A., Dept. of Psychology, Princeton University, Princeton, NJ 08540 USA. Working memory is a construct developed by cognitive psychologists to explain the role of short-term memory in complex cognitive tasks, such as reasoning, reading, and problem solving. Working memory is required to maintain access to mental representations and concurrently process new information. Working memory is also a limited capacity system, such that only a small amount of information can be maintained at one time. Recent research indicates that the capacity of working memory is strongly correlated with intelligence, accounting for over half the variance in test scores among young adults. I will review studies that have demonstrated this relationship and discuss the cognitive and neural mechanisms underlying the relationship between working memory and intelligence.

INTER-INDIVIDUAL DIFFERENCES IN DECISION-MAKING IN THE RAT: RELATIONSHIPS WITH BEHAVIORAL TRAITS. Rivalan M., Fitoussi A., Dellu-Hagedorn F. Lab. MAC, UMR CNRS 5227; Universits Bordeaux 2 et Bordeaux 1, Bordeaux, France. Most psychiatric symptoms seem to occur across a continuum and can be conceptualized as extreme manifestations of behavioral dimensions. Based on this concept, excessive or inadequate behaviors observed within a healthy rat population could accurately model some of key aspects of psychiatric conditions. We designed a Rat Gambling Task (RGT) analogous to the IGT that provides rapid and specific measurement of the ongoing decision-making process. This process depends on the integrity of distinct prefrontal cortex areas. Like in humans, the majority of a group of healthy subjects can evaluate and deduce favorable choices. However, some individuals systematically choose disadvantageously, immediate gratification prevailing over long-term gain. These interindividual differences are stable and reproducible over time. Similar performances between humans and rodents in the task suggest the involvement of similar cognitive processes. We have revealed that poor decision makers exhibit a combination of distinct behavioral characteristics: they almost always displayed risk-taking associated with higher motivation for reward, behavioral inflexibility, as shown by perseverative and compulsive-like behaviors, as well as motor impulsivity, contrarily to good decision-makers that only expressed up to two of these characteristics. The traits and behaviours that accurately predict poor decision-making in healthy individuals are reminiscent of symptoms observed in several decision-making related psychiatric disorders such as attention deficit hyperactivity disorder, substance abuse or mania. This work shows that integrating information across distinct behavioral paradigms provides a promising framework for understanding the mechanisms that underlie poor decision-making from normal to pathological states. The potential endophenotypes that we have revealed could be risk factors of mental disorders, thereby enabling further investigations for the understanding of the neural systems involved.

PERSONALITY TRAITS IN THE PREDICTION OF PERFORMANCE IN LEARNING UNDER STRESS. Sandi, C.; Salehi B. Laboratory of Behavioral Genetics, Brain Mind Institute, Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland. Stress is a potent modulator of memory function, including learning, memory and retrieval processes. However, there is important variability both in the susceptibility of individuals to stress and in individuals performance in learning tasks. Our work, in rodents, aims to investigate whether personality traits can help predicting individual differences in learning under stress and whether this approach could allow a better understanding of the neurobiological mechanisms involved in learning-related variability. Using outbred strains of rats, we have developed a battery of tasks that allows categorizing animals simultaneously for several personality traits that have been termed anxiety, exploration and activity. In the hippocampus-dependent radial arm water maze task (RAWM), we firstly found that, when the whole population is considered, training animals under different stress intensities (water at either 16, 19 or 25 C) lead to an inverted U-shape in

performance, with animals trained under high low (25 C) and high (16 C) stress conditions showing impaired learning when compared with those trained at 19 C. However, certain profiles related to the interaction between anxiety and exploration traits performed well under low or high stress conditions. We also found that highly explorative animals display better reversal learning abilities in the RAWM as well as stronger memory and facilitated extinction of conditioned fear memories than low explorative animals. These findings suggest that highy explorative animals are better at both memorizing and extinguishing emotional cues. On its turn, anxiety trait was also related to performance in the extinction task, with highly anxious animals exhibiting an extinction deficit even in the absence of the tone. These results indicate that certain behavioral styles or personality-like traits in rats are strong predictors of individuals learning under stress as well as of learning, memory and extinction capabilities.

ROLE OF PKMζ MEDIATING STRESS REACTIVITY DIFFERENCES BETWEEN SEXES: EFFECTS ON PLASTICITY AND COGNITION Serrano, P. Dept of Psychology and Neuroscience Program. Hunter College, New York, NY 10065 It is becoming increasingly apparent that problems of stress and anxiety including post-traumatic stress disorders are differentially expressed between sexes within the population. One of the main effects of stress is the decline of cognitive functioning. Recently, the constitutively active, atypical protein kinase, M zeta (PKMζ has been found to be critical for maintaining long-term memory. Spatial learning increases PKMζ protein activity in the cytosol and redistributes it to the post-synaptic density (PSD), an important mechanism affecting the length of time a spatial memory is maintained. A similar pattern of PKMζ expression and distribution occurs to varying degrees after stress that compromises subsequent learning and memory processing. This effect is differentially expressed between sexes such that males appear more negatively affected by stress than females. We hypothesize that stress-induced PKMζ saturates synapses preventing memory-induced PKMζ expression from occurring. The differential affects of stress on learning and memory between sexes will be discussed in the context of stress and anxiety disorders.

6:00-8:00 **Poster Session 1.**

COGNITION

1. 6-HYDROXYDOPAMINE LESION IN THALAMIC RETICULAR NUCLEUS INHIBITS LEARNING IN MORRIS WATER MAZE. Chuc-Meza E1, Avila G1, Garcia-Ramirez M1, Mireles C1, Limon ID2, Aceves J3. 1Departamento de Fisiologia, Escuela Nacional de Ciencias Biologicas IPN, 2 Benemerita Universidad de Puebla,3Departamento de Fisiologia Biofisica y Neurociencias, CINVESTAV-IPN. Paying attention to external cues is basic for the right performance in tests of the spatial learning as Morris water maze. The denervation of dopamine in Thalamic Reticular Nucleus (TRN) induces deficits in anxiety (Picazo et al, 2009) and in novel object recognition tests suggesting some kind of dysfunction in attention to external cues. To investigate this hypothesis a group of Wistar rats with unilateral denervation of TRN made with 100 nL of 6-OHDA (15 g/L) and a sham-lesioned group were tested for place navigation within the Morris water maze. Lesion was behaviorally confirmed inducing ipsilateral turning with apomorphine (0.5 mg/kg s.c.) 8 days postsurgery. After 30 days of the turning test, trial sessions of the Morris test were made for 5 days. Each session included 4 searches for the platform from different starting positions and this position was randomly chosen day to day. The results showed that lesioned rats learned significantly less than sham-operated. The latency to find the hidden platform was higher in lesioned rats between 4 to 11 trial respect sham rats. There was no significant change in the mean swim speed between groups during the study period. So it is reasonable to suspect that dopamine in TRN modulates the attention to external cues needed for spatial learning. Supported by COFAA-IPN and CONACyT grant (50427) to JA

2. COMPETITIVE FUNCTIONS OF THE RAT STRIATUM AND HIPPOCAMPUS IN SEQUENTIAL LEARNING. Eckart, M.T.; Huelse-Matia, M.C.; McDonald, R.S.; Loer, D.; Schwarting, R.K.W.; Experimental and Physiological Psychology, Philipps-University of Marburg, Marburg, Germany; Sequential behaviour, a type of procedural behaviour, has been intensively investigated in humans using the so-called serial reaction time task (SRTT), which was first introduced by Nissen and Bullemer (Cognitive Psychology 19, 1987). In the SRTT, subjects have to respond to visual stimuli by key pressing. Decreases in reaction times to sequential compared to random stimulus presentation are taken as an indicator of sequential learning. Theories that postulate a crucial role of dopaminergic processes in the basal ganglia in sequential learning are widely accepted and find empirical support from human and animal research. The role of the hippocampus in sequential learning however remains unclear. There are three conflicting major hypotheses: interaction, competition or dissociation between hippocampus and striatum. Evidence for each of these theories is found in human and animal experiments. In our research we used an analogous rat model of the human SRTT which was recently developed by Domenger and Schwarting (behav brain res 160; 2005). In the rat SRTT, the animals have to respond to visual stimuli by nose poking. As in the human SRTT, stimuli are either presented randomly or in a sequential order. Rats with striatal 6-OHDA lesions showed inferior sequential learning while rats with dorsal hippocampal ibotenic acid lesions showed superior SRTT performance in terms of reaction time and accuracy, as compared to controls. Based on the fact that the rat hippocampus is strongly involved in spatial learning, we suggest that the occurrence of competition between hippocampus and striatum results from the spatial requirements of a given tests. Since our rat SRTT only has minor spatial requirements (as compared to the Morris water maze for instance), the hippocampal processes interfere with the basal ganglia.

3. CORRELATIONS BETWEEN CORTICAL ACTIVITIES AND AUTONOMIC RESPONSES DURING THE PERFORMANCE OF EMOTIONAL WORKING MEMORY TASKS. Garcia, A.; Conde, S.; Uribe, C.; Tavares, M. C.; Tomaz, C. Department of Physiological Sciences, Institute of Biology, Laboratory of Neurosciences and Behavior, University of Braslia, Brazil. Executive function is considered to be a product of dynamic interactions between brain frontal systems and other processes they interact with. Furthermore, other neuronal substrates including the autonomic nervous system can give more in face of some emotional issue. The present study aims to investigate the correlations between cortical activities and autonomic responses in adult subjects (age: 18-24;~19,5+/-0,582). Changes in cortical activity during executive function test were examined with electroenphalogram (EEG) recorded simultaneously with a frequency cardiac (FC) monitoring system during the performance of delayed (non) matching-to-sample tasks (DMTS/DNMTS) using pictures from the International Affective Picture System (neutral and emotional) and others of geometric figures as stimuli. The results demonstrated by means of a repeated measures ANOVA a significant difference between the tasks (DNMTS>DMTS; p= 0,041), considering the average of power of frontals and parietals derivations of EEG record, and about heart rate variability (HRV) parameters - pNN50 (DMTS>DNMTS; p=0,038), LF/HF (DNMTS>DMTS; p=0,012). These analyses indicate a trend of the task DNMTS to express higher cortical activation concomitantly with the excitability as a result of heart rate. Taken together, these findings indicate a close relationship between the

fronto-parietal cortical activity and the autonomic nervous system in the performance of the emotional working memory task used in this study.

4. BACK TO NATURE: DIFFERENTIAL EFFECTS OF NATURAL AND ARTIFICIAL ENRICHED ENVIRONMENTS ON COGNITION AND NEUROPLASTICITY IN CALIFORNIA DEER MICE (PEROMYSCUS CALIFORNICUS). Huber, J.[1]; Franssen, C.L.[1]; Bardi, M.[2]; Shea, E.S.[1]; Hampton, J.E.[1]; Hyer, M.M.[1]; Rhone, A.[1]; Lambert, K.G.[1]. [1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005, USA; [2]Dept. of Psychology, Marshall University, Huntington WV 25755 USA. Enriched environments are beneficial to neurobiological development; specifically, rodents exposed to novel stimuli exhibit increased neuronal complexity and enhanced neuronal production. While enriched laboratory environments have been found to enhance neurobiological factors, these environments have consistently used artificial stimuli (e.g., plastic blocks and balls) and have failed to consider the impact of exposure to elements characteristic of the natural environment in which the animal evolved. Consequently, the purpose of the current study was to compare cognitive responses and neuroplasticity in mice housed in a Naturally Enriched (NE) environment, containing relevant natural elements (e.g., dirt, rocks, branches), a standard Lab Enriched (LE) environment containing standard laboratory artificial elements (e.g., plastic toys, synthetic nesting material), and a standard laboratory environment (SL) with no enrichment. Male and female California deer mice were housed in one of these three environments for four weeks. NE mice had the shortest latencies to reach a baited well in the Dry-Land Maze (DLM), a test of spatial memory, which suggest more efficient foraging responses. Assessment of videotapes of the animals in their habitats at night indicated that SL males displayed more maladaptive behavioral stereotypes (e.g., repeated back flips) than the NE or LE males. Neurobiological results reveal a significant interaction between sex and environment indicating that females in the LE and SL conditions had a greater quantity of staining for Ki-67. Semi-quantitative analysis shows more nestin-immunoreactivity in NE animals. Thus, both cognition and neuroplasticity seem to be differentially affected by these different environments.

5. MULTIPLE LEARNING EXPERIENCES IMPROVE COGNITION AND INCREASE NEUROGENESIS IN AN INDUCIBLE MOUSE MODEL OF NEURONAL LOSS. Morroni, F.[1]; Kitazawa, M. [2]; Caccamo, A. [3]; Oddo, S. [3]; LaFerla, F.M. [2] 1. Dept. of Pharmacology, University of Bologna, Italy. 2. Dept. of Neurobiology and Behavior, University of California Irvine, California, USA. 3. Dept. of Physiology, UTHSCSA, San Antonio, Texas, USA. Hippocampus plays a central role in learning and memory, and neuronal loss and atrophy in this area are key pathological changes in Alzheimer disease. Here, we utilized an inducible transgenic mouse model of neuronal injury in which the site of diphtheria toxin-induced neuronal cell ablation was temporally and spatially regulatable. We primarily ablated neurons in the CA1 region of hippocampus and examined whether repeated learning experiences modulated cognitive impairments in this model. After the CA1 ablation, a group of mice were trained in the Morris water maze (MWM) once a month for 3 months, while another group of mice did not receive any training for the same period. Repeatedly trained mice with CA1 ablation performed significantly better than non trained mice not only in MWM but also other hippocampal-dependent memory tasks. The improvement of cognitive function appeared to be correlated with significant increases in neurogenesis in the subgranular zone of dentate gyrus and in synaptophysin and post-synaptic density 95, indicative of functional synapses in the CA1 region. These findings suggest that repeated learning experiences stimulate brain functions to compensate neuronal injuries and cognitions.

6. SIMULTANEOUS CONDITIONING OF GAPING AND TASTE AVOIDANCE IN RATS INJECTED WITH LITHIUM CHLORIDE AND SACCHARIN: EXAMINING THE ROLE OF CONTEXT AND TASTE CUES IN THE RODENT MODEL OF ANTICIPATORY NAUSEA. Cloutier,C.J.; Cross-Mellor,S.K.; Chan,M.Y.T.; Kavaliers,M.; Ossenkopp,K.-P. Dept. of Psychology and Graduate Neuroscience Program. The University of Western Ontario, London, ON N6A 5C2 Canada. Systemic administration of lithium chloride (LiCl) will induce nausea and vomiting in humans and other emetic species and conditions robust taste avoidance/aversion in rodents. LiCl will also condition place avoidance of a distinctive context, a frequently used paradigm to index negative hedonic states. Rats, a non-emetic species, that experience the toxic effects of LiCl in a distinctive context will also show a conditioned gaping response after several pairings of the toxin and the context. The gaping response has been proposed to reflect nausea and this conditioning procedure has been suggested as a rodent model of anticipatory nausea. In the present study we examined the conditioning of both context and taste cues to the aversive properties of LiCl by injecting rats with a LiCl plus saccharin mixture and subsequently assessing conditioned gaping to the context and conditioned avoidance to the saccharin taste. On 4 conditioning days spaced 72 h apart, male Long-Evans rats received i.p. injections of either LiCl (0.15 M, 127 mg/kg), sodium saccharin (Sacc 2%), LiCl plus saccharin (LiCl + Sacc), or isotonic saline (Sal), followed immediately by exposure to a distinctive context for 30 min. 72 h after the last conditioning trial conditioned gaping and other spontaneous orofacial behaviors were videotaped in each of the 4 groups (n = 8/gr.) during a 10 min Test with the animals in a drug free state. The animals were then returned to their home cages for 4 days. Taste avoidance was assessed with a two-bottle choice test where

one bottle contained water and the other a 0.2% saccharin solution. Fluid intake was measured at 6 and 24 h and saccharin preference ratios were calculated for each animal. Both of the LiCl treated groups (LiCl and LiCl + Sacc) exhibited significantly higher levels of gaping responses ($p < 0.01$) on the Test Day relative to the Sal and Sacc treated groups, which displayed almost no gapes. Other spontaneous orofacial behaviors, such as rhythmical mouth movements and tongue protrusions did not differ significantly among the 4 groups. Thus, treatment with LiCl conditioned the expected gaping responses, indicative of anticipatory nausea. In contrast, only the LiCl + Sacc group exhibited a significantly reduced saccharin preference ratio (at both the 6 and 24 h period, $p < 0.05$) relative to the other 3 groups; evidence of a conditioned taste avoidance in the LiCl + Sacc group. These findings show that both context and taste cues can be conditioned at the same time in the rodent anticipatory nausea model and provides a paradigm for further exploration of the relative roles that context (external cues) and taste (internal cues) have in this phenomenon.

7. IMPAIRED TEMPORAL ORDER RECOGNITION MEMORY IN NEUREGULIN 1 TYPE IV TRANSGENIC MICE Francesco Papaleo1,2, Kimberly A. Jenkins1, Jingshan Chen1, Jacqueline N. Crawley3, Daniel R. Weinberger1, Amanda J. Law1 1Clinical Brain Disorders Branch; Genes, Cognition and Psychosis Program, National Institute of Mental Health, Bethesda, MD, USA. 2Department of Neuroscience and Brain Technologies, The Italian Institute of Technology, Genova, Italy. 3Laboratory of Behavioral Neuroscience, National Institute of Mental Health, Bethesda, MD, USA Genetic variation in neuregulin 1 (NRG1), a gene that plays critical roles in neural development, has been associated with schizophrenia. NRG1 is expressed in the prefrontal cortex (PFC), hippocampus, cerebellum, and substantia nigra. Recently, a schizophrenia-risk associated variant in the NRG1 gene was established as a functional promoter polymorphism that regulates expression of a novel isoform of the NRG1 gene, termed NRG1 type IV. Elevated expression of NRG1 type IV was associated with genetic risk for schizophrenia. To determine the biological and behavioral consequences of increased NRG1 type IV we created transgenic mice engineered to overexpress the human NRG1 type IV gene. Testing the general health of these mice showed no physical abnormalities. Schizophrenia is a psychiatric disorder characterized by impairments in cognitive function and PFC deregulations. Furthermore, genetic variation in NRG1 has been associated with altered prefrontal cortical function in normal human individuals. Thus, we tested NRG1 type IV transgenic mice and control littermates in a temporal order object recognition, which is dependent on the PFC. Control and transgenic mice showed equal exploration of the objects in the different phases of the test suggesting no genotype effects on motivation, curiosity, motor, olfactory, tactile, or visual functions relevant to object recognition. However, NRG1 type IV transgenic mice were unable to discern between the two sample objects, indicating recency discrimination deficits. These data show that overexpression of NRG1 type IV, impairs temporal order object recognition memory abilities.

8. RAPID EFFECTS OF 17β-ESTRADIOL ON OBJECT PLACEMENT LEARNING IN FEMALE MICE. Phan, A.[1]; Gabor, C.S.[2]; MacLusky, N.J.[2]; Choleris, E.[1] [1]Dept of Psychology, [2]Biomedical Sciences, University of Guelph. Estrogens effects on learning and memory are typically studied hours to days after their administration when transcriptional responses predominate. In addition to these genomic effects, estrogens also have very rapid effects on neuronal electrophysiology and morphology, which occur within minutes to an hour of estrogen application. 17β-estradiol application to hippocampal tissue was reported to enhance long-term potentiation and glutamate depolarization within minutes, suggesting that it may act in a rapid fashion to improve learning and memory. Rapid estrogen effects on neuronal electrophysiology, morphology, as well as other behaviours tend to be reported at drug doses much higher than needed for their genomic effects. Thus, there is concern as to whether these rapid estradiol effects are physiologically relevant. Therefore, we determined whether a physiological dose of 17β-estradiol can rapidly affect spatial learning, a type of learning that is hippocampus dependent. Young adult, ovariectomized, female CD1 mice were injected subcutaneously with vehicle, 1.5μg/kg, 2μg/kg, or 3μg/kg of 17β-estradiol, 15min prior to testing in an object placement paradigm. This paradigm was completed within 40min of drug injections and the results were ethologically analyzed. We found that administration of 2μg/kg of 17β-estradiol improved object placement learning in these female mice within the rapid 40min time frame. This dose of 17β-estradiol has been shown to produce physiological levels of plasma estradiol in rats. Therefore, 17β-estradiol can rapidly improve object placement learning, and these rapid effects can occur within the physiological range of estradiol levels. Funded by NSERC.

9. THE BEHAVIORAL EFFECTS OF THE METABOLIC ENHANCER MRTHYLENE BLUE ON DISRUPTED LATENT INHIBITION. Puga, F.; Gonzalez-Lima, F. Department of Psychology. The University of Texas, Austin, TX 78712 USA. Latent inhibition is a form of latent learning in which preexposure or familiarity with a stimulus disrupts the formation of subsequent associations with that stimulus. There has been increased interest in the neural mechanisms underlying latent inhibition due to its potential to model behavioral deficits associated with schizophrenia, specifically the inability to ignore irrelevant stimuli. Thus, studying latent inhibition can provide

insight into how learned behavior is affected by prior experience and disrupted in specific mental disorders. The aim of the present study was to investigate the facilitating effects of the methylene blue, a known metabolic enhancer, on disrupted latent inhibition. Behaviorally latent inhibition can be disrupted in various ways, such as decreasing the number of stimulus preexposures or increasing the number of stimulus-reinforcement pairings. In this study disruption of latent inhibition was achieved by reducing the number of tone-alone presentations mice received prior to tone-footshock fear conditioning. The disrupted latent inhibition led to a significant increase in freezing behavior relative to animals that received a greater number of tone-alone presentations. Administration of methylene blue immediately following stimulus preexposure facilitated the disrupted latent inhibition effect as evident by a significant decrease in freezing behavior relative to animals receiving saline. These results demonstrate methylene blues ability to enhance memory for the preexposed stimulus in latent inhibition which provides a useful model of facilitated memory in a disrupted learning paradigm.

10. FUNCTIONAL MAPPING OF THE PREVENTION OF IMPAIRED SPATIAL MEMORY IN AN ANIMAL MODEL OF MILD COGNITIVE IMPAIRMENT. Riha, P.D.; Rojas, J.C.; Gonzalez-Lima, F. Department of Psychology, University of Texas, Austin, TX 78712 USA. Spatial memory involves the coordination of several brain regions, notably the hippocampus proper, rhinal cortex, anterior thalamic regions, and the posterior cingulate cortex (PCC). As previously reported, metabolic inhibition of the PCC with sodium azide results in impaired spatial memory in a food-rewarded spatial task. Co-administration with the metabolic enhancer, methylene blue, prevents spatial memory deficits caused by PCC inhibition. However, the memory-enhancing effects of methylene blue were not mediated by local increases in brain metabolism or decreases in cell death in the PCC. Here, we report that co-administration of methylene blue reduced the lesion size within the PCC. To further elucidate the mechanism of action by which methylene blue prevented spatial memory deficits, we applied structural equation modeling to examine the influences of direct anatomical connections between brain structures involved in spatial memory, and how these influences changed under conditions of impaired PCC and methylene blue co-administration. Functional models were created based on both known anatomical connections between brain structures and regional metabolic activity data measured by cytochrome oxidase activity. The interregional covariances of activity were used to calculate path coefficients that represent the magnitude of the influence of each directional path. The analysis revealed that the pathway between the posterior cingulate and entorhinal cortices was conserved in the rats treated with methylene blue. In agreement with published findings in both the human and animal literature, the results confirm that this pathway is important in spatial memory.

11. EFFECTS OF OXIDATIVE STRESS STATE ON MEMORY: ITS CORRELATION WITH INFLAMMATORY RESPONSE, AND ENDOTHELIAL CHANGES IN RATS EXPOSED CHRONICALLY TO LOW DOSES OF OZONE. Rivas-Arancibia, S.; Gallegos-Rios, C.; Rodriguez-Ortiz, D.; Guevara-Guzmán, R.; Flores-Briceno, D.; Rodriguez-Martinez, E. Departamento de Fisiologa, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Mexico D.F. Mexico. The objective of this work was to study the effect of oxidative stress in a passive avoidance test, inflammatory response and endothelial changes in rats chronically exposed to low doses of ozone. Seventy-two male Wistar rats, with free access to water and food, were randomly divided in 6 groups (n= 12): 1)Control group, exposed to ozone free air stream, 2) 7 days of ozone exposure, 3) 15 days of ozone exposure, 4) 30 days of ozone exposure, 5) 60 days of ozone exposure; and 6) 90 days of ozone exposure. Ozone exposure was carried out daily for 4 hours at a 0.25 ppm dose. Two hours after the last exposition to ozone, all the animals were trained in an avoidance passive test conditioning; and it was measured retention 24 hours after. Hippocampus of six animals of each group was processed to carry out the western blot technique, 6 remaining animals of each group were anesthetised and perfunded to carry out immunohistochemistry technique against blood brain barrier, guanylyl cyclase alpha 1, FOXO 1a, NFkB, COX2. Results show a deficit in long-term memory since 15 days to ozone exposure, and this alteration increases whit a chronic exposure to this gas. It is observed morphological changes of capillaries, lost of the continuity of blood brain barrier, thickness of endothelium; and there is no expression of guanylyl cyclase alpha 1, FOXO and NFkB at 30 days to ozone exposure. With these results, we can conclude that chronic exposure to low doses of ozone per se, causes an oxidative stress state, which induces deficit in memory and learning processes associated with a dysregulation of inflammatory response and degenerative changes in vascular endothelium. Supported by DGAPA-IN215408 to S.R-A

12. OXIDATIVE STRESS EFFECT ON INFLAMMATORY RESPONSE PRODUCED BY ADMINISTRATION OF 3-NP ACID IN STRIATUM OF RATS. Rodriguez-Martinez, E.; Jalpa-Hernandez, E.; Miranda-Martinez, A.; Flores-Briseno, D.; Vite-Garcia, A.; Rivas-Arancibia; S. Departamento de Fisiologa, Facultad de Medicina, UNAM. Oxidative stress plays an important role in the development of neurodegenerative diseases. These processes occur together with inflammation because free radicals, produced during oxidative stress, oxidize cellular membranes and induce the activation of eicosanoid pathway producing an increase of inflammatory mediators. There are several pharmacological models for the study of neurodegenerative diseases like Huntington Disease (HD), acute

administrations of 3-nitropropionic acid (3-NP) in rodents show biochemical alterations similar to the ones that occur in HD. The objective of this work is to evaluate different inflammation markers and its relation with neurodegenerative process caused by oxidative stress produced by 3-NP in striatum of rats. We use 24 male Wistar rats (300 g) divided in tow groups: 1) Control (ip. injection of saline solution 0.9% during 4 days), 2) Ip.3-NP (20mg/kg, during 4 days). The day before the last injection, 6 animals of each group were anesthetised and perfunded, brains were processed to carry out histological techniques (H&E) and immunohistochemistry (COX-2 and TNF-alpha). Striatum of the 6 remaining animals of each group was processed to carry out the western blot technique (Malondialdehyde). Our results show an increase on lipid peroxidation levels in group treated with 3-NP against control group. In terms of morphology, control group presents a neuropile and cellular bodies conserved in contrast to the group treated with 3-NP, in which it is observed damaged cells with pyknotic nucleus. We also observed an increase in the expression of COX-2 in groups treated with 3-NP against control group. Oxidative stress induced by administration of 3-NP produces morphological changes, as well as the activation of inflammatory pathways that could be involved in the development of Huntington Disease. DGAPA IN215408 to S. R-A

13. PERSISTENCE OF NEUROPSYCHIATRIC SYMPTOMS IN MILD COGNITIVE IMPAIRMENT OVER SIX MONTHS IN COMMUNITY DWELLING ELDERLY. Ryu S.H.; Yu J.H. Dept. of Psychiatry. Konkuk University Medical Center. Objectives: Mild cognitive impairment (MCI) may be a transitional state between normal aging and Alzheimers disease (AD). Several studies for neuropsychiatric symptoms (NPS) in patients with MCI have revealed that this population suffer from various NPS as in patients with dementia. It is important in terms of management to know their natural history and course. We aimed to determine the persistence and change in severity of neuropsychiatric symptoms over 6 months in participants with MCI. Method: Neuropsychiatric Inventory (NPI) was used to rate the severity of neuropsychiatric symptoms on 241 participants with MCI at baseline and on 220 at 6-month follow-up. We also collected information about cognition and quality of life of patients and their caregiver. Results: 44.1% of MCI participants who completed 6-month follow-up exhibited at least on or more neuropsychiatric symptoms in the previous month. Depression (22.3%), anxiety (19.5%), irritability (13.6%), apathy (11.8%), and agitation/aggression (10.0%) were most common. 72.1% of whom had at least one persistent NPS at 6-month follow-up. 27.3% of participants who completed 6-month follow-up had clinically significant neuropsychiatric symptoms (each NPI score4 at any NPI domain). Those with persistent symptoms had more severe baseline symptoms ($p<0.00$). Those with at least one clinically significant symptom had poorer quality of life in both patients and caregivers ($p<0.05$). Conclusions: NPS were highly persistent overall in the elderly with MCI. Persistence was predicted by having more severe symptoms at baseline. Clinically significant levels of neuropsychiatric symptoms were associated with quality of life. We conclude that it is important to assess and manage neuropsychiatric symptoms in patients with MCI.

14. HYPERACUSIS, INCREASED ANXIETY, AND DEFICITS IN MOTOR COORDINATION BUT NOT LEARNING AND MEMORY IN GTF2IRD1 KNOCKOUT MOUSE. Schneider, T. (1); Rawlins, J.N.P. (1); Tassabehji, M. (2). (1)Dept. of Experimental Psychology, University of Oxford, Oxford OX1 3UD, UK. (2) Genetic Medicine, University of Manchester, St Marys Hospital, Manchester M13 9WL, UK. Williams-Beuren syndrome (WBS) is an autosomal dominant disorder, caused by a hemizygous deletion of 1.55 Mb on chromosome 7q11.23 spanning 28 genes. These candidate genes include a novel three-member family of general transcription factors, one of which, GTF2IRD1 was suggested to be linked to the specific cognitive profile and craniofacial features in WBS patients. We have already shown craniofacial abnormalities in gtf2ird1 knockout mice. Here we present data showing that mice with homozygous disruption of gtf2ird1 exhibit increased sensitivity to low-intensity sounds and decreased sensitivity to high-intensity sounds, motor coordination problems, and increased anxiety but normal learning and memory measured in the object recognition test. Hyperacusis was also observed in heterozygous animals. These findings are reminiscent of the increased anxiety, problems with motor coordination and hyperacusis observed in WBS; however, one of the core features of WBS, disturbed learning and memory was not present in the targeted mice. These results suggest that hemizygosity for GTF2IRD1 may play a role in the complex neurological phenotype seen in patients with WBS, either individually, or in combination with other genes.

15. NEONATAL MDMA AND/OR CITALOPRAM EXPOSURE IN RATS PRODUCES LONG-TERM DEFICITS IN EGOCENTRIC LEARNING, BUT ONLY MDMA AFFECTS ALLOCENTRIC LEARNING Schaefer, T.L; Grace, C.E.; Graham, D.L.; Skelton, M.R.; Vorhees, C.V.; Williams, M.T. Division of Neurology, Dept. of Pediatrics, Cincinnati Childrens Research Foundation, Cincinnati, OH 45229-3039, USA. Neonatal exposure to 3,4-methylenedioxymethamphetamine (MDMA) in rats, a period analogous to second half of human gestation, produces allocentric learning deficits in the Morris water maze and egocentric learning deficits in the Cincinnati water maze. The underlying mechanism for these effects is unknown; however it may involve perturbations to the serotonergic system since P11-20 MDMA exposure (10 mg/kg/day x4/d at 2 h intervals) acutely reduces 5-HT by ~50% during the exposure period. During development 5-HT is a neurotrophic factor and influences neurogenesis,

synaptogenesis, migration, and the development of target regions. We hypothesized that these early 5-HT decreases set in motion later changes that result in cognitive deficits. To test this, we administered citalopram (CIT), a selective serotonin reuptake inhibitor (SSRI), 30 min. prior to the 1st and 4th dose during each day of P11-20 MDMA treatment. 5 mg/kg CIT administered two times daily + MDMA on P12 (after P11 exposure), 16 (after P11-15 exposure), and P21 (after P11-20exposure) attenuated 5-HT depletions in the hippocampus, neostriatum, and entorhinal cortex compared with animals treated with MDMA alone. Behavioral analysis of a similarly treated group as adults showed no cognitive protection as a result of the CIT treatment. Interestingly, CIT alone produced egocentric learning deficits in the Cincinnati water maze without depleting 5-HT. Together with the 5-HT depletions in MDMA-only treated animals, the developmental CIT-induced learning deficits suggest that developmental alterations to 5-HT such as prolonged synaptic 5-HT release may lead to increased 5-HT receptor activation or alterations to other pathways resulting in later learning impairment. (NIH DA021394 ES07051)

16. PKMζ EXPRESSION INCREASES WITH ACUTE STRESS AND NEGATIVELY AFFECTS MALE BUT NOT FEMALE MEMORY. [1]Serrano, P.; [1]Luine, V.L.; [2]Schrott, L.M. [1]Department of Psychology, Hunter College, New York, NY. [2]Department of Pharmacology, Toxicology, and Neuroscience, Louisiana State University, Health Science Center, Shreveport, LA. The constitutively active, atypical protein kinase, M zeta (PKMζ) has been found to be critical for maintaining long-term memory. Spatial learning increases PKMζ expression in the cytosol and redistributes it to the post-synaptic density (PSD), an important mechanism affecting the length of time a spatial memory is maintained. We investigated the sex effects on stress-induced PKMζ and subsequent memory ability. Our results show that males given an acute stress (1 h platform stress) had higher corticosterone concentrations than similarly-stressed females ($p<0.05$). Moreover, only stressed males increased PKMζ within the PSD and cytosol, compared to stressed females ($p<.05$). Stress effects on memory were tested using the object placement (OP) task. Rats are initially exposed to the OP task with two identical objects placed in an arena. During testing, one object is moved to a novel location. Rats that remember the old location show increased exploration of the object in the new location compared to the object in the old location. Males given the acute stress 3h prior to OP test were impaired, but female rats, given the same acute stress, had intact OP memory. These results show that stress increases PKMζ expression in the cytosol and redistribution to the PSD in males but not females, which negatively affects male spatial memory. We hypothesize that stress-induced PKMζ saturates synapses preventing memory-induced PKMζ expression from occurring. Further studies will examine these molecular mechanisms in the context of predatory scent stress, a model for post-traumatic stress disorder. Supported by NCRR grant RR003037 and Department of Defense PT073569 to PAS

17. SEX DIFFERENCES IN AVERSIVE MEMORY IN RATS: POSSIBLE ROLE OF EXTINCTION AND REACTIVE EMOTIONAL FACTORS. Silva, R.H.; Barbosa, F.F.; Godinho, M.R.; Fernandes, V.S.; Munguba, H.; Melo, T.G.; Barbosa, M.T.; Ribeiro, A.M. Dept. of Physiology. Universidade Federal do Rio Grande do Norte, Natal, RN 59071970, Brazil. Studies in humans and animals usually show better spatial learning in males and stronger emotional memory in females. Differences in spatial memory could relate to diverse strategies, while dissimilar stress reactions could cause emotional memory differences. We compared male and female rats in two emotional (classical emotional conditioning and aversive memory task with concomitant emotional evaluation) and two emotionally neutral tasks. The rats were tested in: (1) Plus-maze discriminative avoidance, containing two open and two enclosed arms, one of which presenting aversive stimuli (light / noise). While no differences were found in learning or retrieving (performance at test 24h later, in the absence of stimuli), only male rats presented extinction (exploration of the previously aversive arm by the end of the test). No differences were found in open-arm exploration, indicating similar emotional levels. (2) Contextual fear conditioning - a cage was paired to mild foot shocks. Upon reexposure, freezing behavior was decreased in females compared to males. (3) Spontaneous alternation - the animals were expected to alternate among the arms of a four-arm maze. No differences between genders were found. (4) Open field habituation was addressed in an arena which the rats were allowed to explore for 10 minutes. Habituation (decreased exploratory activity during second exposition) was similar between genders. Differences were found only in tasks with strong emotional contexts, where different fear responses and stress effects could be determinant. The lack of extinction of discriminative avoidance by females points out to stronger consolidation and/or impaired extinction of aversive memories.

18. REVERSIBLE INACTIVATION OF MEDIAL PREFRONTAL CORTEX IMPAIRS DECISION-MAKING AND INCREASES ANXIETY IN RATS. De Visser, L. de; Baars, J.M., Van t Klooster, J.G, Van den Bos, R. Dept. of Animals in Science and Society, Div. Neurobiology of Behavior, Utrecht University, Utrecht, The Netherlands. Anxiety is an adaptive emotion, aimed at adequately directing an individuals response towards a possible threatening stimulus or situation. However, anxiety may become maladaptive and develop into a psychological disorder disrupting daily functioning. An essential part of daily functioning is decision-making, which involves both the emotional and cognitive processing of different and varying costs and benefits, ultimately converging into a

successful choice strategy. Common neural substrates can be identified in anxiety and decision-making in humans, such as the medial prefrontal cortex (mPFC), anterior cingulate cortex and the amygdala. We previously found that high levels of anxiety impair decision-making in both healthy human subjects and male rats. To investigate the neurobiological mechanisms underlying the interaction between anxiety and decision-making, we manipulated mPFC activity in male rats and studied the effects on both anxiety-related behaviour and decision-making. Rats were bilaterally injected with a mixture of the GABA-agonists muscimol and baclofen (0.1 and 1.0 nmol/side) through surgically implanted canulae located in the mPFC. Injections were given prior to testing on the elevated plus maze for anxiety (EPM), and during the second phase of training in a rodent analogue of the Iowa Gambling Task (r-IGT) for decision-making. Rats treated with muscimol/baclofen showed a decrease in the time spent on the open arm of the EPM, in the absence of changes in the number of closed arm entries. Furthermore, mPFC inactivation during testing in the r-IGT impaired performance, reflected by a decreased number of advantageous choices and increased undirected exploration. The findings suggest an important role for the mPFC in both anxiety and decision-making in rats, in line with similar findings from imaging studies in humans. The study further established the relevance of using a rat decision-making task for the understanding of neural substrates underlying complex cognitive processes and their relation to neuropsychiatric conditions.

19. DIFFERENTIAL RECRUITMENT OF CORTICAL AND LIMBIC AREAS IS RELATED TO PERFORMANCE IN A RAT MODEL OF DECISION-MAKING. De Visser, L. de; Baars, J.M., Lavrijsen, M., Van den Bos, R. Dept. of Animals in Science and Society, Div. Neurobiology of Behavior, Utrecht University, Utrecht, The Netherlands. Decision-making plays a pivotal role in daily life. When disrupted, severe problems may occur in social and financial affairs. Moreover, impaired decision-making is a common symptom in psychiatric disorders such as addiction, mood and anxiety disorders and pathological gambling. We recently developed a rat model of decision-making (r-IGT), analogous to the human Iowa Gambling Task, to study underlying neural substrates of decision-making and increase understanding of the pathophysiology of cognitive impairments in psychiatric disorders. In this study, we investigated the involvement of different cortical and limbic brain areas in relation to individual differences in decision-making performance. For this purpose, we measured the expression of the immediate early gene c-fos in brain areas involved in decision-making. Male Wistar outbred rats were tested in the r-IGT during 10 days, after which they showed an overall preference for the advantageous . C-fos immunostaining was performed for subareas of the prefrontal cortex (cingulate area 1, prelimbic and infralimbic), striatum (caudate putamen, nucleus accumbens shell and core) and amygdala (basolateral, central nucleus). Rats were divided in two groups using a split medium approach, resulting in a group of rats showing good performance (0.86 % choices for advantageous) and a group of rats showing a relatively poor performance (0.50 % choices for advantageous option). C-fos expression was increased in poor performers compared to good performers for the prelimbic cortex, caudate putamen and nucleus accumbens shell. Activity in the nucleus accumbens core was higher in good performers compared to poor performers. Together the findings suggest that poor performers were still in a more exploratory phase of the task compared to good performers, recruiting areas related to immediate choice outcomes and the integration of affective value of choice options into behavioural programmes. This study confirms findings obtained in human studies and indicate an interesting development from exploration to exploitation during decision-making that is accompanied by ventral-dorsal shift of underlying neural circuits.

20. SEX STEROID HORMONES AND NEUROPSYCHOLOGICAL FUNCTIONS: ROLE OF ESTROGEN IN WORKING MEMORY FOR EMOTIONAL FACIAL EXPRESSIONS, IN YOUNG WOMEN. Pompili, A(1); dOnofrio, A(1); Arnone B.(1); Tavares, M.C. (2) ; Tomaz, C. (2); Gasbarri, A.* (1). (1) Dept. Biomed. Sci & Technol, Univ. LAquila, Italy (2) Dept. Physiol. Sci, Lab. Neurosci. & Behav, Univ. Braslia, Brazil. Previous studies indicate that the influence of sex steroid hormone estrogen on nervous system extends beyond its role in the control of the reproductive function. Moreover, the hormonal influence on cognitive functions, such as learning and memory, was also reported. Across the menstrual cycle, the performance in memory tasks can oscillate according to the hormonal levels. Therefore, in this study we evaluated in young women, during the different phases of their menstrual cycle, the performance in a Delayed Matching-to-Sample (DMTS) working memory task for emotional facial expressions. The results of this study suggest that high levels of estrogen in the follicular phase could have a negative effect on DMTS with emotional stimuli. In addition, in the follicular phase, compared to the menstrual phase, the percent of errors was significantly higher for sadness and disgust facial expressions. The evaluation of the times of answer for each emotional facial expression evidenced a statistically significant difference between follicular and luteal phases, relatively to sadness. Moreover, high levels of estrogen in the follicular phase can impair the performance of working memory for selective facial expressions suggesting that, during the menstrual phases at high conception risk, women give less importance to emotional expressions with negligible reproductive significance, such as sadness and disgust. Our data show that fluctuations of ovarian hormones across the menstrual cycle affect several behaviors and could contribute to identify therapies for the treatment of disorders related to menstrual cycle phases and menopause in women.

21. SEX-RELATED TALKATIVENESS AND EMOTIONAL MEMORY. Gasbarri, A.*(1); Arnone, B. (1); Pompili, A. (1); Tavares, M.C. (2) ; Tomaz, C. (2) . (1) Dept. Biomed. Sci & Technol, Univ. LAquila, Italy. (2) Dept. Physiol. Sci, Lab. Neurosci. & Behav, Univ. Braslia, Brazil. Emotionally arousing events are more likely to be recalled compared to non-arousing events. Moreover, recent studies have begun to reveal seemingly large, but previously unsuspected, sex-related influences on this mechanism, and sex differences in cognition are consistently reported. Sex-related differences in language processing are well known from everyday life, as well as from the scientific literature. Our previous studies indicated that both sex and cerebral hemisphere constitute important interacting influences on neural correlates of emotion and emotional memory. Moreover, many data evidenced sex-related differences in language processing and conversational behaviour. Therefore, the aim of the present study was to evaluate possible talkativeness differences between the two sexes in the recollection of emotional stimuli, recording the number of words that men and women use when they are submitted to a declarative memory test, using two kinds of emotional stimuli: the International Affective Picture System (IAPS), a set of calibrated picture stimuli, and an Italian adaptation of two versions of a story, differing for their arousal characteristics (neutral and emotional), both widely used for investigating emotion and emotional memory. The evaluation of the number of words, utilized by men and women during the free recall of both kind of stimuli, showed that women used always an higher number of words compared to men. In conclusion, according to previous studies indicating that men and women process emotional stimuli differently, our findings suggest the existence of gender-related neural responses to emotional stimuli and could also contribute to the understanding of mechanisms underlying the gender disparity of neuropsychiatric diseases, such as mood disorders.

22. THE ROLE OF CONTEXT IN ACTIONS AND HABITS Tran-Tu-Yen, D. ; Holmes, N. ; Di Scala G., Marchand A. R., Coutureau E. CNRS/ Universit de Bordeaux, Centre de Neurosciences Intgratives et Cognitives, UMR 5228, Talence, F-33405, France A current view of response control in instrumental conditioning suggests that it relies upon two dissociable associative processes. Early in acquisition actions are thought to be mediated by a goal-directed action-outcome (A-O) association, which requires both the encoding of the instrumental contingency and the representation of the outcome as a goal, which can experimentally be assessed using contingency degradation and outcome devaluation procedures respectively. The content of the A-O association is still poorly known. The present experiments aimed at contributing to this question, and particularly questioned context dependency of the A-O association. In a first experiment, rats were initially trained to press a lever in order to obtain a food reward. The food reward was later devalued through pairings with a digestive malaise (i.p. injection of LiCl) which occurred either in the instrumental training context or an alternative context. When tested in extinction in the initial training context, only devaluation that had been performed in the same context affected instrumental responding, thus indicating that goal-directed responding is sensitive to context change. In a second experiment, we found that this context effect did not result from simple aversive context conditioning since an unpaired group displayed normal responding when given a reacquisition test. In a third experiment we assessed the role of context change on incentive learning about the outcome value. Taken together, these results suggest that the context plays a central role in response control by actions or habits.

23. DECREASE IN NOVEL OBJECT RECOGNITION PERFORMANCE AFTER THE DOPAMINE DENERVATION OF THE THALAMIC RETICULAR NUCLEUS IN THE RAT. Garcia-Ramirez M1; Chuc-Meza E1; Avila-Velarde G1; Aceves J2. 1Depto. de Fisiologa ENCB-IPN, 2.Depto. de Fisiologa Biofsica y Neurociencias, CINVESTAV-IPN. In a previous study we showed that bilateral dopamine denervation of the thalamic reticular nucleus (TRn) induced anxiolysis (Picazo et al., 2009). Since TRn has a role in a wide variety of process, including attention, memory and integration of sensory information, here we studied the effect of DA denervation of TRn on novel object recognition performance (NOP). One group of male Wistar rats were unilaterally lesioned by administration of 100 nL of 6-OHDA (15 g/L) into the TRn, another group of rats was administrated with of saline solution (sham). All the tests were done after 30 days from surgery and only rats with ipsilateral turning behavior elicited by apomorphine (0.5mg/Kg sc) were used. Furthermore NOP, other behavioral test were determinate such; elevated plus maze and rotarod performance. Dopamine loss of dopamine in the TRn reduces more than 90% time spend in recognition of novel object. These rats showed also decrease anxiety as judge by increased percentage of the time spent in the open arms as well as increase in open arm entries. No effect was observed upon rotarod performance. The NOP has been developed as a task which can be configured to measuring working memory, attention and preference for novelty in rodents. These results suggest the involvement of dopamine in the TRn in processing working memory and confirm its participation in anxiety behavior. Supported by COFAA-IPN and CONACyT grant (50427) to JA

24. TOWARDS THE DEVELOPMENT OF AUTOMATED SOCIAL BEHAVIOURAL AND ANXIETY PARADIGMS IN ZEBRAFISH Luca, R. M.; Gerlai, R. Dept. of Psychology. University of Toronto, Mississauga, ONT. Zebrafish, a novel vertebrate model organism, has been successfully utilized in genetics and embryology. The high nucleotide sequence homology of its genes with that of human genes, its small size, prolific nature, and sophisticated behavioural repertoire confer an advantage. Despite the excellent genetic tools, linking genes and behaviour has proven difficult with zebrafish because of the paucity of behavioural paradigms available for this species. Analysis of behaviour is expected to be an efficient method with which mutation-induced phenotypical changes in brain function may be detected. Abnormal social behaviour and anxiety represent major unmet medical needs in humans. Social preference and group forming (shoaling) as well as antipredatory behaviours (avoidance or fear reactions) are species-specific characteristics of the natural behavioural repertoire of zebrafish. We focus on these behaviours and develop and optimize tests to quantify shoaling with conspecifics and fear responses to natural and artificial predators. We investigate how computer generated moving images may be utilized in eliciting these behaviours. Our goal is to find characteristics of images that induce the most robust and reliable behavioural responses. We are at the early phase of test optimization but our results demonstrate that shoaling behaviours and fear responses can be successfully induced in an automated manner using the computer images. Previous findings that utilized live conspecifics and natural predators are also replicated. Thus, computer-animated images will help standardize behavioural tests in zebrafish and will lead the way to more sophisticated, and better controlled automated screening for mutations.

25. EFFECTS OF METHAMPHETAMINE EXPOSURE DURING HIPPOCAMPAL DEVELOPMENT ON COGNITION AND THE CHOLINERGIC SYSTEM IN ADOLESCENT MICE Siegel J. and Raber J. Departments of Behavioral Neuroscience, Oregon Health & Science University, Portland OR USA. Exposure to methamphetamine (MA) in utero leads to deficits in spatial learning and memory in 7-9 year old children. Similarly, deficits in hippocampal-dependent spatial learning and memory are observed in adult mice exposed to MA during the first three weeks of life when the hippocampus is formed. However, the neurobiological mechanisms underlying the cognitive effects of MA exposure during brain development remain unknown. In addition, little is known about the effects of MA exposure during brain development on cognitive function during adolescence in mice. MA detrimentally affects many neurotransmitter systems in the adult brain, including the cholinergic system. As the cholinergic system is intimately involved in cognition, potential MA-induced cholinergic alterations may be related to the MA-induced cognitive deficits. We tested the hypothesis that MA exposure during hippocampal development would adversely affect cognition and cholinergic integrity in adolescent mice. C57BL/6J mice were exposed to a single injection of MA (5 mg/kg) or saline from postnatal day 11-20, during rodent hippocampal development. MA-exposed adolescent mice showed impairments in novel location and novel object recognition and impaired memory in the water maze compared to saline-exposed adolescent mice. Current experiments are ongoing to study the effects of MA exposure from postnatal day 11-20 on measures of cholinergic function in adolescent mice, and how these cholinergic effects correlate with MA-induced cognitive impairments.

26. THETA IS MODULATED BY NOVELTY IN CA1 & SUBICULUM IN AWAKE BEHAVING MICE. Huerta, P.T.; Faust, T.W.; Chang, E.H. Dept. Neurosci., Burke Med.Res.Inst., Weill Med. Coll. of Cornell Univ., White Plains, NY 10605 USA. Network oscillations reflect the collective activity of neurons and offer a link from neural ensembles to ongoing behavior. Theta (4-12Hz) is seen in the hippocampus and correlates with exploratory and cognitive behavior. The subiculum (SUB) is the major output of the hippocampus but little is known about its

functional role. To examine SUB and CA1 network activity, we implanted BALB/cJ mice (n=15, female, 4-6 mo old) with moveable electrodes and performed in vivo awake-behaving recordings (Neuralynx, Cheetah software, sampling at 10kHz). As mice were exposed to several contexts, we found that theta was robust in the SUB albeit smaller in amplitude than CA1-theta. While CA1-theta decreased in power as mice were familiarized to a context, SUB-theta did not change during familiarization suggesting it was modulated by different contingencies than CA1-theta. We tested the mice in 2 cognitive tasks: novel-object recognition (NOR) and object-place recognition (OPR). For NOR, in a total of 62 trials we found that on most trials (73%) SUB-theta was very strong when mice explored novel objects. This novelty-modulated SUB-theta may reflect the encoding of a novelty signal. For OPR, CA1-theta showed an upward shift in frequency (11-14Hz) while decreasing in power in the 8-10Hz range, only during object exploration. When an object was moved from a familiar to a novel location, high-band theta power increased further. These results show that high-band theta may contribute specifically to cognitive processing during spatial novelty, whereas low-band theta may reflect spatial exploration.

27. MK-801 INDUCED IMPAIRMENTS OF VISUAL-DISCRIMINATION LEARNING AFFECT REVERSAL LEARNING IN RATS. Shao, F.; Li, N.-X.; Wang, W.-W.; Li, L. Dept. of Psychology, Peking University, Beijing 100871, China. Although NMDA receptors contribute to a wide range of learning/memory activities, it remains largely unclear whether there are NMDA-receptor-mediated functional connections between initial discrimination learning and subsequent reversal learning. In this study, visual-discrimination learning in a rotating T-maze was retarded in rats by NMDA-receptor antagonist MK-801 (0.25 mg/kg) administrated either 120 minutes before or immediately after a training session. Pre-training MK-801 treated rats needed much more trials than post-training MK-801 treated rats to reach the initial-learning criterion. In succeeding reversal learning without MK-801 treatment, rats that were treated with pre-training MK-801 during initial learning needed less trials than both their saline controls and post-training MK-801 treated rats to inhibit the response strategy acquired in initial learning. Then in the new-acquisition phase of reversal learning, both groups of MK-801 treated rats needed more trials than their respective saline controls to reach the reversal-learning criterion, and post-training MK-801 treated rats needed even more trials than pre-training MK-801 treated rats. These results indicate that pre-training and post-training MK-801 treatments cause different initial-learning impairments, which in turn affect reversal learning differently. Thus, NMDA receptors may mediate functional connections between discrimination learning and cognitive flexibility.

28. HUNGER SUBSTANCE OREXIN IMPAIRES SPATIAL PLASTICITY. Oomura Y., Aou S., Fukunaga, K., Sasaki, K. Dept. Integrative Physiol., Kyushu Univ., Life Sci., Inst., Kyushu Inst. Teck., Dept. Pharmacol., Tohoku Univ., Dept. Bio- Inform., Toyama Univ. The glucose-sensitive neurons in the rat lateral hypothalamic area of feeding center produce orexin-A and send their axons to the hippocampus which predominantly expresses orexin receptor-1 showing a high sensitivity to orexin. Orexin released during food intake facilitates food intake by the activation of glucose-sensitive neurons and inhibition of the glucoreceptor neurons in the ventromedial nucleus, satiety center. The released orexin then reaches to the hippocampus and suppresses spatial learning and memory. Namely the Morris water maze tests showed that 1-10mM orexin administered icv retarded spatial learning and memory. A probe tests showed also an impairment. LTP of CA1neurons in vitro experiments was suppressed by 1-10 mM orexin dose dependently, but no effect on LTD. The paired pulse facilitation experiments indicated that the orexin effects were postsynaptic and not presynaptic transmitter release. The post-synaptic responses to NMDA and GABA applied electrophoretically to the apical dendrites of CA1 neurons were also suppressed. The phosphorylations of presynaptic synapsin I-3 was not influenced by oresin but those of postsynaptic PKC, CaMKII, ERK etc. were suppressed dose dependently. These results indicate that orexin impairs behavioral spatial plasticity with suppressions of CA1 LTP.

29. MENTAL REPRESENTATION OF DISCOURSE WITH REPETITION: INEFFICIENCIES OF DISCOURSE PRODUCTION IN THE ELDERLY Saling, L.L.; Laroo, N. School of Psychology, Charles Sturt University, Wagga Wagga, NSW, 2650 Australia. Saling, M.M. School of Behavioural Science, University of Melbourne, Victoria, 3010, Australia. When young adults tell the same story repeatedly, their narratives become more concise. Changes in narrative production with repetition have not been investigated in elderly adults, however. 30 young (aged 18-49 years) and 30 elderly (aged 65+ years) adults completed a discourse production task elicited using an eight-frame cartoon. Narratives were repeated 4 consecutive times. Variables analysed were narrative duration, word count, fluency (words/sec) and hesitancy (pause to speech ratio). Additionally, errors associated with the narratives were extracted. Results revealed that, in contrast to the increasingly concise narratives of young adults, the narratives of elderly adults become more verbose and of longer duration with repetition. Fluency associated with the narratives of both groups increased with repetition, although elderly adults were less fluent than their younger counterparts. Greater hesitancy was associated with elderly adults discourse for every cycle. It seems that elderly adults have a

reduced capacity to coordinate discourse planning and storage and hence to generate an adequate discourse representation. Possible neural correlates of this phenomenon are discussed.

30. ENHANCED LEARNING AND MEMORY AFTER TOMOSYN OVEREXPRESSION IN THE DENTATE GYRUS OF THE MOUSE HIPPOCAMPUS Boaz Barak1, Yue Wang2, Eitan Okun2, Eric Norman2, Ofer Yizhar3, Henriette van Praag2, Mark P. Mattson2 and Uri Ashery1 1 Department of Neurobiology, Life Sciences Institute, Tel Aviv University, Tel Aviv, Israel, 69978 2 Laboratory of Neurosciences, National Institute on Aging, NIH, Baltimore, MD, USA, 21224 3 Department of Bioengineering, Stanford University, Stanford, California, USA, 94305 Tomosyn is a syntaxin-binding protein that inhibits vesicle priming and synaptic transmission. To characterize tomosyn's roles and physiology in the mouse hippocampus, we transcranially injected lentivirus overexpressing YFP-tomosyn into the dentate gyrus of the hippocampi in adult mice. Virus expression was verified by the expression of YFP and immunohistochemistry. 2-3 weeks after the injection, YFP-tomosyn overexpressing mice and control mice, which were injected only with lentivirus expressing YFP, were subjected to behavioral tests and electrophysiological measurements. Our results show that tomosyn-overexpressing mice, but not YFP-overexpressing mice performed significantly better in hippocampus-dependent behavioral tests. These improvements include steeper learning curves and better memory retention in the Morris water maze test and in the contextual learning paradigm of the fear conditioning test. In contrast, no significant differences were noticed in motoric and exploration abilities in the rotarod and open field exploration tests. Additionally, electrophysiological measurements of brain slices derived from tomosyn-overexpressing mice revealed that mossy fibers to CA3 synapses have impaired synaptic transmission. One explanation for these results is that tomosyn overexpression enhances learning and memory by decreasing the input-output ratio in the dentate gyrus. As a result, increase in neuronal gain in this region is associated with a decrease in local network activity; consequently small changes related to the learning paradigm will have larger effects in this "silenced network", and will result in better learning and memory abilities in behavioral tests.

31. SENSORY PROCESSING IN TIMING MECHANISMS: IMPACT OF STIMULUS FREQUENCY IN AN AUDITORY DURATION PERCEPTION TASK. Wiertelak, E. P.; Coletto, N. L. Cognitive & Neuroscience Studies, Macalester College, St. Paul, MN 55105 USA. Controversy exists whether temporal perception results from central or local modality-specific sensory processing, and different processes seem involved in timing short intervals of sub- and supra-second durations. In study one, participants reproduced 450ms and 3.3s tones, presented at 250Hz and at 2200Hz to examine the influence of auditory frequency on duration perception. A common modality-specific mechanism to the timing of both durations may exist, as 2200Hz tones were reproduced with shorter intervals than for 250Hz tones. To our knowledge, temporal perception of sub- to several-second durations had not been studied with visual frequency (color) stimuli; other research found that at longer durations, red light appears to produce a shorter perceived duration than blue light at 180 but not 90s. In a second study now underway, we compared durations of intervals reproduced in response to red and blue squares (450ms, 3.3s duration) presented on a computer screen. Durations reproduced in response to color were compared to those in response to tones (same durations; presented at different frequencies). If color has opposite effects on timing processes from auditory frequency, such a finding would support the idea that modality specific processing of sensory features is needed for duration judgments, suggesting reliance on sensory cortices, rather than lower-level cerebellar and thalamic processes suggested by many central timer models. The results of these studies may provide further insight into where temporal processing occurs and, duration information is segregated from other modality specific sensory features.

32. CREATINE TRANSPORTER KNOCKOUT MICE SHOW LEARNING AND MEMORY DEFICITS: MODELING HUMAN CRT DEFICIENCY Matthew R. Skelton, Tori L. Schaefer, Curtis E. Grace, Ton J. deGrauw, Charles V. Vorhees and Michael T. Williams Div of Neurology, Cincinnati Childrens Res Found and Dept. of Pediatrics, U. of Cincinnati College of Medicine, Cincinnati, OH 45229 Creatine (Cr) is involved in maintaining readily available phosphate pools for replenishing ATP levels during times of high energy demand. Mutations in the creatine transporter (CrT; *Slc6a8*) gene leads to an absence of brain Cr and in intellectual disability, loss of speech, and behavioral abnormalities. The CrT gene is located on the X chromosome and CrT deficiency follows an X-linked pattern of inheritance. In order to model this disorder, we created conditional CrT knockout mice (CrT flox/y) that were then crossed with mice that express Cre recombinase driven by the CMV promoter, creating ubiquitous CrT knockout mice. Male CrT $^{-/y}$ (affected) mice lack Cr in the brain with significant reductions of Cr in other tissues including heart and muscle. Adult mice showed no differences in acoustic startle reflex or pre-pulse inhibition between genotypes. CrT$^{-/y}$ mice showed increased latency and cumulative distance from the platform during each phase of the Morris water maze (MWM). During MWM probe trials, CrT$^{-/y}$ mice showed an increase in average distance from the platform. CrT$^{-/y}$ mice did not show a preference for the novel object during a novel object recognition task while controls showed preference. Animals are also to be examined in the radial arm

maze and latent inhibition in a conditioned fear paradigm. The results thus far suggest that CrT knockout mice have learning and memory deficits that appear to resemble several key aspects of human CrT deficiency. (Supported by funds from the Division of Neurology at CCRF)

33. TRANSITIONAL VERSUS SURGICAL MENOPAUSE IN A RODENT MODEL: ETIOLOGY OF OVARIAN HORMONE LOSS IMPACTS MEMORY AND THE ACETYLCHOLINE SYSTEM Acosta, J.I.; Mayer, L.; Talboom, J.S; Tsang, C.W; Smith, C.J.; Enders, C.K.; Bimonte-Nelson, HA Department of Psychology, Arizona State University, Tempe, AZ 85287 Clinical research suggests that type of ovarian hormone loss at menopause influences cognition. Until recently, ovariectomy (OVX) has been the primary rodent model to examine effects of ovarian hormone loss on cognition. This model limits evaluations to abrupt and complete ovarian hormone loss, modeling less than 13% of women that receive surgical menopause. The majority of women undergo transitional hormone loss via ovarian follicular depletion. 4-vinylcyclohexene-diepoxide (VCD) produces gradual ovarian follicular depletion in the rodent, with hormone profiles more similar to naturally menopausal women versus OVX. We directly compared VCD and OVX models to examine whether type of hormone loss (transitional vs surgical) impacted cognition as assessed on a maze battery, as well as the cholinergic system tested via scopolamine mnemonic challenge and brain AChE activity. Middle-aged rats received either SHAM surgery, OVX surgery, VCD, or VCD then OVX to assess effects of removal of residual ovarian output after transitional menopause and follicular depletion. VCD-induced transitional menopause impaired learning of a spatial recent memory task; surgical removal of residual ovarian hormones by OVX abolished this negative effect of transitional menopause. Further, transitional menopause before OVX was better for memory than an abrupt loss of hormones via Ovx only. Surgical ovarian hormone loss, regardless of menopause history, increased hippocampal AChE activity. Circulating gonadotropin and androstenedione levels were related to cognitive competence. Collectively, findings suggest that in the rat initiation of transitional menopause before surgical ovary removal can benefit mnemonic function, and could obviate some negative cognitive consequences of surgical menopause alone.

34. ROUGH-AND-TUMBLE PLAY IMPROVES PERFORMANCE IN THE ATTENTION SET SHIFTING TASK. Blake, C.; Franssen, C.L.; Hampton, J.E.; Lambert, K.G. Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005, USA. Three to five percent of children worldwide are diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and the rates of diagnosis have been increasing since the 1970s. Interestingly, it has been hypothesized that the rise in ADHD may be related to decreased rates of natural self-generated social play, also referred to as rough-and-tumble (RT) play (Panksepp, 2007 & 1998). Accordingly the aim of the current study was to explore the effect of RT play on attention in a rodent model. Beginning at 23 days of age, sixteen male Long-Evans rats were given two 30-minute play sessions with one age-matched rat each day for two weeks; as a control, eight of these rats were separated from partners by a wire screen, allowing visual, auditory, and olfactory communication without providing the opportunity for RT play. To determine the effects of RT play on attentional processes, rats were subsequently exposed to the attention set-shifting task (ASST). Specifically, rats were trained to dig in a dish for a Froot Loop reward before encountering simple, complex, intradimensional and extradimensional discrimination challenges/shifts for four days. Results indicated that the RT rats performed more efficiently in the habituation digging training and, subsequently, exhibited shorter latencies to obtain the reward (and fewer errors) in test trials. The brains of RT and control animals are currently being processed for an assessment of fos-activation, tyrosine hydroxylase-immunoreactivity, and hippocampal neuroplasticity. In sum, the behavioral results confirm that RT play enhances attentional processes in rodents.

SOCIAL BEHAVIOR

35. ANIMAL MODELS OF NEURODEVELOPMENTAL DISORDERS: MOUSE SOCIAL RESPONSES AS BIOMARKERS OF NEUROTOXICITY OF ENVIRONMENTAL CONTAMINANTS. Venerosi, A.; Scattoni, M.L.; Ricceri, L.; Calamandrei G. - Department of Cell Biology and Neurosciences, Istituto Superiore di Sanit, Viale Regina Elena 299 I-00161 Rome (Italy) Concerns about the risk for childrens health of sub toxic exposures to pesticides are increasing, as their role in enhanced vulnerability to neurodevelopmental disorders is supported by both experimental and clinical data in US and Europe. Chlorpyrifos (CPF), one of the most widely used organophosphorous insecticide worldwide, elicits developmental neurotoxicity at doses well below the threshold for systemic toxicity, exerting subtle but disruptive effects on neural cell development. In the past years we have studied extensively the neurobehavioral effects of developmental exposure to CPF in the mouse species, focusing on end points related to social/communicative behaviors from early development till adulthood. In utero exposure to CPF modified the profile of ultrasound emission in neonate mice and had pro-aggressive effects in adolescent and adult mice in a social interaction test. In adult females, prenatal CPF altered the pattern of social interaction, either with same-sex partners or with a male intruder during nest defense test. The behavioral changes induced by developmental CPF are accompanied by permanent alteration in expression of the hypothalamic neuropeptides

oxytocin and vasopressin, and by reduced responsiveness to antidepressant drugs acting on serotonin neurotransmission. These findings support epidemiological evidences and suggest that developmental low-dose exposure to a widely diffused pesticide interferes with maturation of important brain pathways modulating social responses. Detailed analysis of mouse social behavior repertoire at different life stages and in the two sexes may provide sound experimental models for proper risk evaluation in public health.

36. EFFECTS OF CHRONIC ESTRADIOL BENZOATE ON A SOCIALLY TRANSMITTED FOOD PREFERENCE IN OVARIECTOMIZED CD1 MICE. Clipperton-Allen, A.E.[1], Baheerathan, D.[2], Nadj, M.[1], Choleris, E.[1] [1]Dept Psychology, [2]Dept Human Hlth & Nutr Sci, University of Guelph, Guelph, Ontario, Canada N1G 2W1. One advantage of social living is that it allows for learning from ones conspecifics, thus reducing reliance on more hazardous trial-and-error learning. The social transmission of food preferences (STFP) paradigm examines the evolutionary advantage of learning food-related information socially. In this task, an observer animal is given a choice between the two flavoured foods after interacting with a demonstrator animal that ate one of the foods. Observer mice typically consume more of the food that was on the demonstrators breath during the social interaction. Previous studies have shown an involvement of estrogens in this learning process. Mice in high estradiol phases of the estrous cycle show a prolonged preference for the demonstrated food. Administration of acute estradiol benzoate (EB) or an estrogen receptor beta (ERβ) agonist to ovariectomized (ovx) mice also prolonged the observers preference for the demonstrated food, while ERα agonist administration blocked social learning. To date, the effects of chronic administration of estrogens on the STFP are unknown. In the current study, ovx observer mice were implanted with Silastic capsules containing sesame oil vehicle or EB (1.25g, 12.5g, 25g, or 50g per capsule) 13-15 days prior to testing. Observers were tested as described above. Results of an 8 hour choice test show that EB prolonged the observers preference for the demonstrated food in a similar manner to both acute estradiol and an ERβ agonist, suggesting similar mechanisms in the acute and chronic involvement of estradiol in social learning. Supported by NSERC.

37. IMPAIRMENT OF OLFACTORY FUNCTION BY beta-AMYLOID INJECTION IN THE HIPPOCAMPUS. Guevara-Guzmán, R.; Bernal-Mondragón, C.; Mercado Gómez, C.; Miranda, A.; Rivas-Arancibia, S. Departamento de Fisiologa, Facultad de Medicina, Universidad Nacional Autónoma de México. Apdo. Postal 70250, Delegación Coyoacán, 04510 México, D.F. México rguevara@servidor.unam.mx. The effect of intrahippocampal (HIPPO) or olfactory bulb (OB) administration of beta-AMY (25-35) was studied on a social recognition memory and a spatial memory in adult female Wistar rats. Twenty four h later beta-AMY injection in HIPPO, animals showed impairment in the social recognition memory, since the animals were unable to discriminate between familiar from the unfamiliar juvenile conspecific 60 minutes after exposure to a juvenile stimulus animal, but 15 days later a complete recover was observed. They also showed impaired speed in locating a buried chocolate chip for 48 h post injection, indicating some loss of olfactory perception. However if the animals were feed with chocolate 24 h before the HIPPO beta-AMY injection they do find the buried chocolate chip with a latency similar to control group. These results indicate that if a memory was stored, the beta-AMY was not able to disrupt it. Habituation-dishabituation test to different odors confirm that HIPPO beta-amyloid injection animals were unable to discriminate between two or more odors. HIPPO beta-amyloid group showed also impairment in a spatial memory task as long as 8 days after the injection. On the other hand, OB beta-AMY injection group did not present any impairment in the social recognition memory using the same tests as described before. On the other hand, lipoperoxidation was measured in both HIPPO and OB after beta-amyloid injection in HIPPO or OB. We found that levels of lipoperoxidation were higher in HIPPO than in OB independently the place of the injection HIPPO or OB. Western blot experiment confirms lipoperoxidation results. Finally our result point out the role of HIPPO in the social recognition memory and the oxidative stress as a mechanism responsible of olfactory impairment being the OB less sensitive to oxidative stress. Grants: IN-216907 and 24784-M

38. SOCIAL ISOLATION REDUCES SOCIAL ODOR INVESTIGATION AND AVOIDANCE OF SICKNESS-RELATED ODORS BY MALE RATS. Kavaliers, M.1.; Choleris, E.2.; Pisu, M.G.3.; Serra, M.3. 1Dept. Psychology, University of Western Ontario, London Canada, 2Dept. Psychology, University of Guelph, Guelph, Canada, 3Dept. Experimental Biology, University of Cagliari, Cagliari, Italy. Olfactory cues play a fundamental role in the determination of social behavior. The ability to recognize individuals and their condition (health, infection status) is essential to most aspects of social behavior. Rodents can distinguish between infected and uninfected individuals on the basis of odor, displaying aversive responses to, and avoidance of, the odors of infected individuals. Avoidance of the odors cues of infected and sick individuals reduces the likelihood of social interactions reducing the risk of contagion. However, an individuals response to the threats in their environment is also affected by the social context and their prior experience. Rearing rat pups from weaning in isolation to prevent social contact produces a variety of behavioral and neurochemical changes that can impact on social behavior. Whether social isolation affects responses to sickness associated social odors is unclear. We examined the responses of adult male

rats (75 days of age)) that were either socially isolated from weaning (25 days of age) or grouped housed to the aversive odor cues associated with acute illness. Group housed male rats displayed a discrimination of, and normal avoidance of, the odors of male rats treated with lipopolysaccharide, a nonreplicating component of gram-negative bacterial cell walls (LPS, 100 ug/kg). In contrast, socially isolated rats showed a reduced investigation of social odors and did not display an enhanced avoidance of the odors of LPS treated males. This suggests that early social isolation impacts on the responses to social odors and the discrimination and avoidance of aversive sickness associated odors. Supported by NSER and RAS (Program Visiting Professor) Italy.

39. A ROLE OF THE PRIMATE MESENCEPHALIC TECTUM IN SOCIAL COGNITION AND RELATED DISORDERS. Maior, R; Hori, E; Barros, M; Tomaz, C; Nishijo, H. Laboratory of Neuroscience and Behavior, Institute of Biology, University of Brasilia, Brazil. In primates, social cues are processed even before sophisticated cortical processing is fully developed. Newborn infants are known to preferentially orient to facial expressions and this is thought to rely on subcortical structures. Recently a few sub-cortical structures in the Mesencephalic Tectum have been suggested to be involved in the processing of social and emotional information. In the present study, we have been assessing the behavioural effect of bilateral neurotoxic lesion of the superior colliculus in young capuchin monkeys (Cebus spp.). Six infants (4 lesion and 2 sham) have been under behavioral observation in their home cages. Subjects social cognition is tested in terms of directed social behavior among peers in the home cage, directed social behavior towards an unfamiliar adult and danger recognition in the Predator confrontation paradigm. Preliminary results show that lesion to the Superior Colliculus reduces the frequency of directed social behavior among home cage peers and unfamiliar adults as well as impairing the assesment of danger. If confirmed, these results will suggest an important role for the Superior Colliculus in early social behavior and defense systems. The implications of this structure on developmental disorders will therefore require further analysis.

40. EFFECTS OF HOUSING CONDITIONS IN THE REDUCTION OF SUBMISSIVE BEHAVIOR MODEL OF ANTIDEPRESSANT ACTIVITY. Malatynska, E.; Lane, B.; Van Brunt, C.; Rasmussen, K. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN. To improve the translation of preclinical findings to clinical outcomes for depressed patients, better preclinical models are needed. The Reduction in Submissive Behavior Model (RSBM) was recently developed to predict antidepressant activity (Malatynska & Knapp, Neurosci Biobeh Rev, 2005). In this model, a subset of randomly-paired rats forms dominant-submissive relationships (DSR) when subjected to competition for a food reward in a specially designed apparatus. If the submissive animal of the pair is treated with antidepressant drugs (and the dominant animal is treated with vehicle) over a three week period, the DSR is altered and the submissive and dominant animal eventually spend equal time consuming the food. In an effort to improve the utility of this model, we examined the effects of housing conditions on the stability of the DSR. Methods: Randomly paired male, Sprague-Dawley rats were housed in separate groups (four animals per cage) or together (two animals per cage) over the course of the five-week period of the RSBM. Time spent on the feeder was measured by computer software (TopScan, Cleversys Inc.). Results: No significant difference in the number of pairs formed, or the stability of the DSR over time, was observed between the two groups. Administration of the MAOI phenelzine produced a significant decrease in dominance level for paired-housed animals. Conclusion: Housing paired-animals together or separately did not alter the stability of the DSR in the RSBM. The effects of phenelzine and other antidepressants in the assay will be discussed.

41. INHIBITORY ROLE OF THE MEDIAL PREFRONTAL CORTEX FOR SOCIAL TRANSMISSION OF AVOIDANCE. Masuda, A.; Aou, S. Dept of Brain Sciences and Systems Engineering. Kyushu Institute of Technology. Kitakyushu, 8080196 JAPAN. Animals receive information through interaction with other conspecifics and effectively adapt to their environment. This transmission of information is called "social transmission" and found in many animals including rats. Avoidance learning is essentially important for living, but neural mechanisms for "social transmission of avoidance" are largely unknown. Previous studies found that avoidance behavior (step-through inhibitory avoidance) is regulated by social partners in both inhibitory and facilitatory ways under safe and dangerous situations, respectively. Using this paradigm, we investigated the effect of bilateral mPFC lesions by NMDA injections on social transmission of avoidance in rats. The medial prefrontal cortex (mPFC) is thought to support social functions in humans, primates and rodents. Under interactive safe situations, social inhibition of avoidance was not affected by mPFC lesions. Lesioned animals displayed normal social inhibition in the first trial of interaction. Then, the sustained effect was evaluated in the second consecutive trial. Unexpectedly, we found more strongly sustained inhibition in mPFC lesions than in controls. Under dangerous situations, the social facilitation of avoidance was found only in animals with mPFC lesion. The present study suggests that mPFC in rodents have an inhibitory role for social transmission of avoidance.

42. THE EFFECTS OF ALCOHOL AND A DOPAMINE RECEPTOR ANTAGONIST ON SOCIAL BEHAVIOR OF ZEBRAFISH. Scerbina, T.; Chatterjee, D.; Gerlai, R. Dept. of Psychology. University of Toronto, Mississauga, ON L5L 1C6, Canada Alcoholism is a devastating public health problem, a disease whose mechanisms are not well understood. Dopamine, a key neurotransmitter system involved in alcoholism and reward, acts via a number of dopamine receptors (D1-D5) and pharmacological manipulation of these receptors have significant effects on drug of abuse induced behaviors. Social stimuli, e.g. the sight of conspecifics, also have rewarding properties and thus the dopaminergic system may be involved too. Here, two strains of adult zebrafish (AB and SF) were exposed to acute treatment with a D1 receptor antagonist, 3H-SCH23390 (30 minutes in 0.0, 0.1 or 1.0 mg/L) and a subsequent acute treatment with alcohol (one hour in 0.00, 0.25, 0.50 or 1.00 % vol/vol). The question we wanted to address with this 2x3x4 experimental design was whether D1-R antagonism can modify the social behaviour by altering the effects of alcohol and whether D1-R antagonism alone can modify social behaviour, and last, whether the drug effects are strain dependent. Behavioral responses of zebrafish to computerized animated images of a zebrafish shoal were quantified using videotracking. The results demonstrated D1 receptor antagonist-dependent and alcohol-dependent behavioral changes. For instance, the distance of control zebrafish from the stimulus screen decreased in response to the presentation of the shoal image, whereas zebrafish exposed to high concentration of alcohol, or to high doses of the D1-R antagonist, did not show this response. These findings suggest that high doses of alcohol or the dopamine antagonist elicit similar behavioral responses. We also detected a significant interaction between these two drugs: dopamine significantly reduced the social response impairing effect of alcohol, i.e. it reinstated the social response (moving closer to the shoal image). Finally, several of the drug and alcohol induced behavioural changes were strain dependent as AB showed robust behavioural changes whereas SF was mainly resistant to both alcohol and the D1-R antagonist. The results imply that zebrafish is an excellent tool for the analysis of the behavioral and biological effects of drugs of abuse.

43. NO INDUCTION OF SOCIAL EXPLORATORY ACTIVITY IN MALE μ-OPIOID RECEPTOR KNOCKOUT MICE BY PLAYBACK OF FEMALE ULTRASONIC VOCALIZATIONS. Wöhr, M.; Moles, A.; Schwarting, R.K.W.; D'Amato, F.R. Experimental and Physiological Psychology, Philipps-University of Marburg, 35032 Marburg, Germany. Behavioral Neuroscience, CNR Institute of Neuroscience, 00143 Rome, Italy. The opioid system controls social behavior and it was hypothesized that it therefore plays a role in neuropsychiatric disorders such as autism. Besides abnormal reciprocal social interactions and repetitive behaviors, qualitative impairments in communication such as delayed language and poor communication skills are fundamental to the diagnosis of autism. Mice communicate via auditory signals in the ultrasonic range, so called ultrasonic vocalizations. As pups, they produce ultrasonic vocalizations when isolated from dam and littermates. These calls serve an important adaptive biological purpose, namely the induction of maternal search and retrieval behavior. Administration of μ-opioid-receptor-agonists such as morphine diminishes isolation-induced ultrasonic vocalizations and μ-opioid-receptor knockout mouse pups (Orpm -/-) emit fewer ultrasonic vocalizations during isolation than intact wildtype controls (Orpm +/+). In adulthood, male and female mice produce ultrasonic vocalizations during social interactions. While it was shown that male ultrasonic vocalizations elicit social approach behavior in females, little is known about occurrence and function of ultrasonic vocalizations produced by adult females. Here, we conducted a playback experiment in order to assess whether female ultrasonic vocalizations elicit changes in the recipients behavior and whether a possible change in behavior is dependent on a functioning opioid system by comparing Orpm -/- mice with wildtype controls. Our results showed that female ultrasonic vocalizations elicited social exploratory activity in male recipients and that its elicitation in response to female ultrasonic vocalizations is dependent on an intact opioid system, since no such response was seen in Orpm -/- mice. The lack of social exploratory activity seen in Orpm -/- mice supports their phenotypic relevance for the study of autism.

44. COMMUNAL NESTING ALTERS THE DEVELOPMENT OF AFFECTIVE AND SOCIAL BEHAVIOR IN RATS SELECTIVELY BRED FOR AN INFANTILE TRAIT. Zimmerberg, B.; Martinez, A.R.; Brunelli, S.A., Psychology Dept, Williams College, Williamstown, MA 01267 The social environment has been shown to alter behavioral phenotypes of rodents via epigenetic mechanisms. In this study, Communal Nesting (CN), where dams are housed together during pregnancy and lactation, was examined in rats selectively bred for an infantile affective trait: rates of ultrasonic calls (USVs) after brief maternal separation. High and Low male and female offspring raised in CN groups were compared to standard housed (SH) controls on five measures of social and affective behavior at three critical ages. All CN subjects vocalized less than SH subjects at one week. High line subjects vocalized more than Lows, as expected, and had greater USV reductions if housed in CN. In adulthood, CN subjects entered an open field more quickly, spent more time in the center squares, and had greater general activity compared to SH subjects. CN also reduced immobility on the Porsolt forced swim task relative to SH subjects. CN litters showed increased social behaviors in tests of juvenile parenting and play. These findings support the role of social contact during pregnancy and lactation in reducing affect and enhancing prosocial behavior. In addition, an epigenetic effect of the CN paradigm was seen in measures of anxiety behavior, but not in measures of depression or social behavior.

45. THE SOCIAL TRANSMISSION OF A FOOD PREFERENCE IS IMPAIRED IN SOCIALLY DEPRIVED MALE RATS. Choleris, E.1; Loi, M.2; Mameli, R.2; Garau, A.2; Pisu, M.G.3; Dore, R.2; Kavaliers, M.4; Serra, M.2,3 1Dept Psycol, Univ Guelph, ON, Canada; 2Dept Exper Biol, Sez Neurosci, Univ Cagliari, Italy; 3 Natl Res Council, Inst Neurosci, Cagliari , Italy; 4Dep Psycol Univ Western Ontario, London, ON, Canada Social learning, the acquisition of novel information from others, adaptively allows bypassing trial-and-error individual learning. Being it social in nature, social learning is likely affected by the degree of sociality and level of social skills displayed by interacting individuals. In rats and mice postweaning social deprivation causes heightened aggression, impaired social recognition as well as marked changes in brain biochemistry (e.g. progesterone metabolites, GABA). Whether social learning is also affected by early social deprivation is currently unknown. In the present study 2-mo old male Sprague-Dawley CD rats that since weaning had been either group (5) or individually housed were tested for the social transmission of food preferences, where a rat acquires a food preference during a 30-min social interaction with a recently fed demonstrator. Diluted (25%) whole milk flavored with either 0.03% anise or 0.015% mint essential oils was used. Results show that while group housed rats acquired a preference for their demonstrators flavored milk that lasted as long as 24 hr, the individually-housed rats showed minimal ($p=0.11$) socially acquired flavor preference and only at the first hour of testing. These results suggest that trust in the information carried by a conspecific may be lower in socially deprived rats. Further studies will investigate whether this reduced social learning is associated with changes in brain steroids and aspects of social interactions. Funded by NSERC and RAS, Program "Visiting Professor".

46. STRESS RESPONSIVENESS AND SPATIAL MEMORY IN SOCIALLY ISOLATED OFFSPRING. Pisu, M.G.1; Dore, R,2; Garau, A.2; Arzedi, C.2; Ruggeri, A.2; Biggio, G.1,2; Serra, M.1,2 1C.N.R., Institute of Neuroscience, Unit of Neuropsychopharmacology and 2Department of Experimental Biology, University of Cagliari, Cagliari, Italy. Social isolation of male rats at weaning is associated to a reduction in the brain basal levels of allopregnanolone. Moreover, acute foot shock stress increased in these animals the brain concentrations of allopregnanolone by a greater percentage than in group-housed animals suggesting an increase in the responsiveness of HPA axis to new stimuli. In agreement, isolated female rats showed a significant decreases in the cerebrocortical concentrations of allopregnanolone compared with the corresponding values for group-housed animals and exhibited an anxiety-like profile. Isolated male and female were breeding and male offspring at weaning were stabulated in group as group-housed offspring. Isolated female dams did not differ in their frequency of licking/grooming and arched-back nursing, while showing a decreased frequency in passive nursing and an increase in the frequency of pup-independent actions. In contrast to their parents, two month-old male offspring of isolated rats showed a significant increase in the brain basal levels of allopregnanolone comparing to group-housed offspring. Moreover, in these animals, the increase in brain concentrations of allopregnanolone induced by acute foot shock stress, was blunted compared to offspring of group-housed animals. In the Morris Water Maze, no differences in spatial learning, examined during 5 days, was found between the two groups. However, the probe trial revealed a significant decrease in the latency and a significant increase in the frequency of platform crossing, in the time spent in the platform quadrant and in the percentage of quadrant crossing in isolated offspring comparing to group-housed offspring. Studies are in progress to investigate if the observed effects are associated to changes in the neuroendocrine axis.

47. EFFECT OF METHAMPHETAMINE EXPOSURE AND POSTNATAL CARE ON BEHAVIOR OF ADULT MALE RATS. Hruba, L.; Schutova, B.; Rokyta, R.; Slamberova, R. Charles University in Prague, Third Faculty of Medicine, Department of Normal, Pathological and Clinical Physiology, Prague, Czech Republic. Our previous studies demonstrated that methamphetamine (MA) administered during gestation and lactation periods impairs maternal behavior, alters the functional development of rat pups and affects cognitive functions in adulthood. The aim of the present study was to investigate the impact of MA exposure and postnatal care on behavior and anxiety in adult male rats. Mothers were daily exposed to injection of MA (5 mg/kg) or saline (S): prior to impregnation and throughout gestation and lactation periods. On postnatal day 1, pups were cross-fostered so that each mother received some of her own and some of the pups of mother with the opposite treatment. Based on the prenatal and postnatal exposure 4 experimental groups (S/S, S/MA, MA/S, MA/MA) were tested in the Open field (OF) and in the Elevated plus maze (EPM). Locomotion, exploration, comforting behavior and anxiety were evaluated in the OF, while anxiety and exploratory behavior were assessed in the EPM. Our results showed that adult male rats fostered by mother exposed to MA (S/MA and MA/MA) had decreased locomotion and exploratory behavior in the OF compared to rats fostered by mothers exposed to saline (S/S and MA/S). Further, S/MA and MA/MA showed increased anxiety in the OF as well as in the EPM. In conclusion, the present study demonstrates that postnatal care of mothers exposed to MA decrease locomotion, exploration but increase anxiety to novel environment. On the other hand, decreased psychomotor activity and increased anxiety are not demonstrated in rats prenatally exposed to MA and fostered by saline dams. Supported by: GACR 305/09/0126, GACR P303/10/0580 and MSM 0021620816

48. THE IMPACT OF ACUTE METHAMPHETAMINE ADMINISTRATION ON SOCIAL INTERACTION OF MALE AND FEMALE LABORATORY RATS. Schutova, B.1; Hruba, L.1; Mikulecka, A.2; Pometlova, M.1; Rokyta, R.1; Slamberova, R.1 1. Charles University in Prague, Third Faculty of Medicine, Department of Normal, Pathological and Clinical Physiology, Prague, Czech Republic, 2. Academy of Sciences of the Czech Republic. In our previous study we demonstrated that methamphetamine (MA) administration reduces social interaction in a dose- and stress environment condition-specific manner. In the present study we aimed to investigate if male and female gonadal hormones influence the effect of MA on social interaction. Adult gonadectomized male and female Wistar rats were divided into groups with subcutaneous (s.c.) administration of testosterone, estradiol or oil. Each group was tested for social interaction (SI) in an Open field arena. Thirty minutes prior to testing, rats were administered MA (1 mg/kg), saline (S) s.c. or did not get any injection (C). SI of two strange animals with the same pretreatment and hormonal condition was recorded for 5 min and manually analyzed by using ODLog software. Duration and frequency of social and non-social activities were evaluated. Our results showed that MA decreased total SI in both sexes. Sexual differences were observed for mutual sniffing, so that females sniffed less than males. However, this difference was not observed in rats pretreated with MA. Moreover, we found that estradiol increased genital investigation and vertical activity in C and S female rats while these changes were not present in MA pretreated females. On the other hand, testosterone did not alter either social or non-social behavior in males. In conclusion, our present study demonstrated that MA decreases SI regardless of sex and diminishes the differences in SI caused by female gonadal hormones. Supported by: MSM 0021620816; GACR 305/09/0126; GACR P303/10/0580

49. THE EFFECT OF PERINATAL INFLAMMATION ON THE DEVELOPMENT OF PLAY BEHAVIOUR IN RATS. Evelyn Field(1,2) Sarah Spencer(3) Scott McLeod(1) Amanda Kentner(1,2) and Quentin Pittman(2). (1)Department of Psychology, Mount Royal College, Calgary, AB Canada; (2)Hotchkiss Brain Institute, Faculty of Medicine, University of Calgary, Calgary, AB Canada; (3)Department of Physiology, Faculty of Medicine, Monash University, Melbourne, Victoria, Australia Altered social interactions are a common behavioural marker of several neurodevelopmental disorders. Recent work in rodents has shown that perinatal inflammation/infection, via various routes of initiation, can alter behaviour in adulthood. What has not been addressed is whether exposure to perinatal inflammation alters play behaviour in male and female juvenile rodents. Pregnant female rats on gestational day 15, or neonates on postnatal day (P)14, were administered either a single low-dose injection of the bacterial endotoxin lipopolysaccharide (LPS 100g/kg), or saline. Frequency of attack and styles of playful defense during juvenile play behaviour were assessed between P30 and P40. Exposure to LPS induced inflammation led to a reduction in the likelihood of playful defense during the juvenile period in male and female animals from each treatment condition. In addition, the LPS treated neonates when they did respond to a playful attack, were significantly more likely to turn towards the attacking animal and use a defensive upright stance which is often associated with antagonistic behaviour - to prevent nape attacks. Thus, a single exposure to a low-dose of LPS, during the early perinatal period can alter play behaviour in juvenile rodents. This work has significant implications for the study of how exposure to perinatal inflammation may affect the developing CNS and its control of social behaviour during early childhood. Research supported by AHFMR and CIHR.

50. A SOCIAL ENCOUNTER WITH LIMITED PHYSICAL CONTACT PRODUCES CONDITIONED PLACE PREFERENCE IN MALE ADOLESCENT RATS. Peartree, N.A.; Hood, L.E.; Sanabria, F.; Thiel, K.J.; Neisewander, J.L. Adolescence is a period of enhanced sensitivity to social rewards. The present study tested whether rats exhibit conditioned place preference (CPP) following exposure to another rat on the opposite side of a mesh barrier that limits physical contact. The CPP apparatus contained 2 distinctive main compartments separated by a removable solid partition, each with an additional smaller area added onto the outer wall, resulting in 4 separate compartments in series (i.e., small, main, main, small). The bottom half of the walls that separated the small end compartments from the main compartments was a wire mesh that allowed social investigation without full physical contact. Adolescent male rats were first tested for baseline preference. Subsequently, the rats were given 2 conditioning sessions/day over the next 8 consecutive days. During one of the daily sessions, the rats were placed alone into their initially preferred side with nothing in the small adjacent compartment. During the other daily session, the rats were placed into their initially nonpreferred side under one of 4 conditions: 1) with another rat and nothing in the small compartment; 2) alone with another rat in the small compartment; 3) alone with a tennis ball and nothing in the small compartment; or 4) alone with a tennis ball in the small compartment. The tennis ball controlled for rewarding effects of a novel object. The results from a post-conditioning test indicated that all rats exhibited a preference shift (i.e., more time spent in the initially nonpreferred side), except for those that had been alone in the initially nonpreferred side with a tennis ball in the small compartment. These results demonstrate that a social encounter is rewarding in male adolescent rats even when physical contact is limited, suggesting that other aspects of social interaction apart from play behavior are sufficient to produce social reward-CPP. Supported by DA023123 and DA023746

51. MECHANISMS OF ABNORMAL AGGRESSION IN A NEW MODEL OF HUMAN VIOLENCE: EARLY SOCIAL DEPRIVATION OF RATS Tulogdi, A.; Toth, M.; Mikics, E.; Haller, J. Department of Behavioural Neurobiology, Institute of Experimental Medicine of the Hungarian Academy of Sciences, Budapest, Hungary. Serious psychopathologies and violence in adulthood are often correlated with early social disturbances in humans. Various animal species showed increased aggressive behavior after social deprivation. Our model was the first that showed the qualitative changes in aggressive behavior of rats after early social deprivation, i.e. attacks that are not signaled, are more frequent, stronger, and are aimed at vulnerable body parts (head, throat and belly; Toth et al., 2008). The aim of the present experiments was to investigate the underlying mechanisms of this abnormal, violent behavior. We studied the autonomic responses by in vivo biotelemetry. Increased reactivity of heart rates of socially deprived rats during aggressive encounter indicates that, in lines with many human studies, socially deprived rats showed a marked autonomic hyperarousal. Increased corticosterone reactivity was also seen during aggressive encounter in socially deprived rats. We also measured the aggression-induced neuronal activation patterns by means of immunolabeling c-Fos and cell type-specific markers in brain regions relevant for aggression. Altered activation patterns were seen in the prefrontal cortex and in amygdalar nuclei in socially deprived rats.

52. CHARACTERIZATION OF SHOALING IN FREE SWIMMING ZEBRAFISH: A HIGH-THROUGHPUT BEHAVIORAL ASSAY. Miller, N.Y.; Gerlai, R.G. Department of Psychology. University of Toronto, Toronto, Ontario, M5S 3G3, Canada. High-throughput, automated, behavioral assays often suffer from simplistic or insufficient endpoints, thus limiting their usefulness for uncovering subtle and complex behavioral changes. Shoaling in zebrafish, like other forms of collective motion, is particularly complex and flexible and currently available software applications and analysis techniques cannot handle multiple interacting subjects. We present a novel software application and method of analysis for multiple subjects in an open-field arena. Our software automatically tracks multiple interacting targets and our analysis method extracts multiple spatiotemporal characteristics of the dynamically changing shoal and quantifies these characteristics as a set of endpoints that can be easily compared between groups of, for example, mutagenized or drug-exposed fish. The system identifies both social and individual, complex and basic, measures such as speed distributions, excursions away from the shoal, and positional preferences within the shoal. We use novel mathematical and statistical techniques to analyze the complex temporal dynamics of the shoal. We present a sample analysis to exemplify the ability of the system to detect subtle behavioral changes resulting, in this particular experiment, from repeated exposures to the enclosure. Our system will allow, in the future, for screening hundreds of mutagenized fish, ultimately leading to the identification of novel genes involved in vertebrate social cognition and navigation.

53. CHARACTERIZATION OF THREECHAMBER SOCIAL NOVELTYSEEKING IN C57BL/6J MICE. Pearson, B.L.; Defensor, E.B.; Pobbe, R.L.H.; Blanchard, D.C.; Blanchard, R.J. Dept. of Psychology and Pacific Biosciences Research Center, University of Hawaii at Manoa, Honolulu, HI 96822 USA. Mouse models of autism and other pervasive developmental disorders depend upon tasks in which mice display preference for an unfamiliar conspecific. The automated three chamber sociability and social novelty task has proven to be effective in distinguishing strain and genotype differences in social investigation. Previous findings have demonstrated that, in the second phase of this task, mice seemingly prefer a novel over familiar mouse. However, the sensory modalities and specific motivation for approach in this paradigm have yet to be characterized. To determine whether novelty preference is specific to the identity of the stimulus mouse or to the location, we reversed the typical stimulus orientation for half of the C57Bl/6J (B6) subject mice such that novel mice were placed where the familiar mouse was previously presented, predicting that subject mice would spend more time associating with the novel stimulus mouse independent of the location of its presentation. Duration in association with an unfamiliar B6 or outbred CD1 stimulus, and relative preference for those mice over a novel mouse of the same strain was assessed with both possible novel stimulus presentation arrangements in the second phase. In phase one, mice spent significantly more time in the chamber associated with the unfamiliar B6 and CD1 mice compared to an empty cup. However, in the second phase, subject mice preferred the novel mouse over the familiar only when it was presented in the opposing, previously empty cup for both strains of stimulus mice. These results suggest the need for additional analysis or interpretation of social novelty preference in the three chamber task.

54. BTBR T+tf/J MICE SHOW SOCIAL DEFICITS IN SEMINATURAL VISIBLE BURROW SYSTEMS. D. Caroline Blanchard, Valerie Bolivar, Roger Pobbe, Erwin Defensor, Brandon Pearson, and Robert J. Blanchard, University of Hawaii. Autism spectrum disorders (ASD) are a group of increasingly prevalent neurodevelopmental disorders defined by social interaction and communication deficits and ritualistic-repetitive behaviors. They show extremely high concordance between monozygotic twins, but likely involve an interaction between multiple genes and possible environmental factors during development. As their primary diagnostic indices are behavioral, animal models need to demonstrate social deficits related to core ASD symptoms. Previous studies on BTBR T+tf/J (BTBR) mice have shown a range of social deficits, as well as high levels of self-grooming, in tasks specifically

designed to evaluate these behaviors. The Visible Burrow System (VBS) is a semi-natural habitat in which groups of mice or rats live for extended periods in situations affording "burrows" based on those constructed in nature, as well as "open space"; maintained under a 12:12 hr. light/dark cycle. Same-strain groups of 3 male BTBR or c57Bl/6J (B6) mice were maintained in VBS for 4 days, with videorecordings of each group for 24 hrs/colony (total = 192 hrs) over this period. Time samplings of behaviors indicated that BTBRs showed an extremely robust pattern of reduced approach, huddling, allogrooming, and chase/follow, with enhanced flight, alone, and self-grooming. These findings are in agreement with earlier data on the BTBR mice, and validate their reduced sociality and enhanced self-grooming in a semi-natural situation in which behaviors and a behavioral time-budget are self-generated. This research was supported by R01 MH 081845

55. SCHOOLING FISH BEHAVIOR AND SOUNDS PRODUCED BY LOCOMOTION. Larsson, M. Dept. of Respiratory Medicine. rebro University Hospital, SE -701 85 rebro, Sweden. If moving fishes are closely situated, the hydrodynamic signals they produce will overlap, and this may result in difficulties in perceiving the single source (i.e. the single prey). Individual rey must be approx. five body widths apart to produce separate signals in electrosensory systems. Hence, I suggest that schooling may confuse the octavolateralis system as well as electrosensory systems of predators, and that this may have influenced the evolution of schooling behavior. Although sounds produced during locomotion (SOL) will be perceived throughout life in most animals, its possible interactions with hearing perception and behavior have been little discussed. However, theoretical models imply that SOL may mask critical signals of the environment and moreover that the discrimination of tone frequencies, perception of pitch, sequential grouping, and the excellent temporal resolution abilities of fish could aid in discrimination of SOL from other sound sources. Synchronized movements of a group will produce relatively concurrent SOL, which may improve sound-source discrimination. In addition, aforementioned hearing skills may increase the ability to synchronize group movements, which in turn may improve predator/prey detection since one outcome of synchronized movements will be more silent intervals. Adaptations to reduce masking caused by own locomotion may have influenced the evolution of perception and behavior in other ways. Its unlikely that sonic signals in fish developed before acute hearing existed to receive these (or some similar) sounds. Its suggested that perceiving and discriminating SOL may have been vital in the evolutionary priming of hearing systems to perceive the sonic signals fish use to communicate, and that this might have ramifications for the behavior and hearing perception in terrestrial animals including humans.

56. MUTUALLY ANTAGONISTIC EEFECTS OF DOPAMINE AND ACETYLCHOLINE IN THE RAT BRAIN ON EXPRESSION OF ULTRASONIC VOCALIZATIONS. Silkstone, M.; Brudzynski, S.M., Department of Psychology, Brock University, St. Catharines, Ontario, Canada. It has been established that intraaccumbens application of dopamine agonists in the rat can induce 50 kHz type of ultrasonic calls indicating appetitive state of the animal. Also, it was shown that intrapreoptic injection of muscarinic cholinergic agonists can induce 22 kHz type of calls, which signals an aversive and defensive state. It was postulated that these drugs activate the mesolimbic system and the aversive system known as the medial cholinoceptive vocalization strip. The goal of the present study was to provide evidence that these two brain systems work in a mutually antagonistic manner. Fifteen Long Evans rats were bilaterally implanted with cannulae in the shell of the nucleus accumbens and in the medial preoptic area. Apomorphine (0.5 μg in 0.3 μl) was injected into the accumbens, while carbachol (1.0 μg in 0.3 μl) was injected into the medial preoptic area. Apomorphine in the accumbens pretreated with saline in the preoptic area induced high numbers of 50 kHz calls (both flat and frequency-modulated types) and no 22 kHz calls. Carbachol in the preoptic area pretreated with saline in the accumbens induced very high numbers of 22 kHz and no 50 kHz calls. The number of 50 kHz calls induced by apomorphine from accumbens significantly decreased after pretreatmenet with carbachol in the preoptic area ($p < 0.0005$). The number of 22 kHz calls induced by carbachol from the preoptic area also significantly decreased after pretreatment with apomorphine in the accumbens ($p < 0.0005$). The results confirmed the hypothesis that activities of the mesolimbic dopamine and medial cholinoceptive systems have a mutually antagonistic relationship. Supported by NSERC of Canada.

57. UNUSUAL REPERTOIRE OF VOCALIZATIONS IN THE BTBR T+tf/J MOUSE MODEL OF AUTISM. Maria Luisa Scattoni1,2, Jacqueline N. Crawley2, Laura Ricceri1. 1Neurotoxicology and Neuroendocrinology Section, Department of Cell Biology and Neurosciences, Istituto Superiore di Sanit, Rome, Italy; 2Laboratory of Behavioral Neuroscience, National Institute of Mental Health, NIH, Bethesda, MD, USA. BTBR T+tf/J (BTBR) is an inbred mouse strain that displays social deficits and repetitive behaviors analogous to the first and third diagnostic symptoms of autism, a neurodevelopmental disorder. During the first two weeks of postnatal life, BTBR pups emitted ultrasonic vocalizations more loudly and more frequently when separated from their mothers and siblings. A detailed sonographic analysis of these vocalizations revealed an unusual pattern in BTBR as compared to C57BL/6J (B6), FVB and 129 X1. BTBR emitted low numbers of complex, upward, chevron, short, and frequency steps calls, along with high harmonics and composites. The present study investigated the social and vocal repertoire in adult

BTBR mice to investigate the vocal repertoire at adulthood in different social settings: a. male-female interactions (5 min direct interaction of a male with a sexually receptive female of the same strain); b. male resident-intruder interactions (3 min interaction of a resident male with an unfamiliar male), and c. female reciprocal interactions (3 min interaction of a resident female with an unfamiliar female). Behavioral responses and ultrasonic vocalizations were simultaneously recorded for BTBR and B6 mice. BTBR displayed lower levels of vocalizations and social investigation in all three social contexts as compared to B6. As seen previously in BTBR pups, we discovered that adult BTBR also displayed an unusual vocal repertoire as compared to B6. Our findings suggest that atypical vocalizations in the BTBR mouse model of autism may be relevant to the unusual prosody, speech intonation and rhythm in children and adults with autism.

58. RAPID EFFECTS OF ESTROGEN RECEPTOR ALPHA AND BETA AGONISTS ON HISTAMINE DEPOLARIZATIONS IN THE VENTROMEDIAL HYPOTHALAMIC NUCLEUS. Phan, A.[1]; Pfaff, D.[2]; Choleris, E.[1]; Kow, L-M.[2] [1]Dept of Psychology, University of Guelph, ON. [2]Laboratory of Neurobiology and Behavior, The Rockefeller University, NY. Histamine induces excitatory responses in the ventromedial hypothalamic nucleus (VMN), potentially modulating VMN dependent behaviors (e.g., sexual behaviors). Rapid (minutes) application of 17β-estradiol to the VMN potentiates histamine-induced membrane depolarizations. Thus histamine and estrogens may interact to influence sexual arousal. The rapid effects of estrogens on neurons can be mediated through both estrogen receptor (ER)α and ERβ, although behavioral studies indicate that ERα is more important than ERβ in mediating sexual behaviors. Therefore we used selective ER agonists PPT (ERα) and DPN (ERβ) to investigate whether estradiols effects on histamine-induced depolarizations were mediated by either or both subtypes. Whole cell patch-clamp was performed on VMN neurons from female Sprague-Dawley rats, 11-25 days old. Membrane potentials were recorded as a picospritzer delivered histamine (10mM in ejecting pipette) at 5min intervals before, during and after 5-15min of PPT (100nM) or DPN (100nM) bath application. PPT replicated the findings of 17β-estradiol, potentiating histamine-induced depolarizations in 8/9neurons. However, DPN had a range of effects, potentiating (3/12neurons), attenuating (2/12neurons) or having no effect (7/12neurons) on histamine-induced depolarizations. These effects of DPN are not likely due to random variation in the recordings. When both DPN and PPT were applied to the same neurons in 2 instances, DPN had no effect or attenuated the response, while PPT potentiated the histamine depolarizations. Therefore, the rapid effects of 17β-estradiol on histamine depolarizations in the VMN appear to be mediated through ERα. While ERβ is also capable of rapidly influencing histamine depolarizations, the functional significance of this is not clear. NIH and ERA funded.

PSYCHIATRIC AND NEUROLOGIC DISORDERS

59. D1 AND D2 DOPAMINERGIC RECEPTORS MODULATE THE CONTEXTUAL FEAR CONDITIONING DEFICIT PRESENTED BY AN ANIMAL MODEL TO STUDY EMOTIONAL PROCESSING ABNORMALITIES IN SCHIZOPHRENIA Calzavara, M. B. 1, 2; Santos, C.M. 2; Medrano, W. A1.; Levin, R. 1; Ablio, V.C. 1, 2 1Department of Pharmacology, Federal University of Sao Paulo, 2 Laboratrio Interdisciplinar de Neurocincias Clnicas LiNC, Department of Psychiatry, Federal University of Sao Paulo. We have described that spontaneously hypertensive rats (SHR) present a contextual fear conditioning (CFC) deficit that is specifically reverted by antipsychotics and potentiated by proschizophrenia manipulations. Based on these findings, we suggested that this could be a useful animal model to study abnormalities in emotional processing in schizophrenia. Recently, we also have observed that inactivation of nucleus accumbens as well as activation of prefrontal cortex attenuated the deficit presented by SHR. These results are in accordance with the proposed overactivity of the mesolimbic system and hypoactivity of prefrontal cortex that underlie the pathophysiology of schizophrenia. The aim of this work was to investigate the role of dopaminergic D1 and D2 receptors in the prefrontal cortex and nucleus accumbens, respectively, in the CFC deficit presented by this strain. For this purpose, quinpirole and raclopride (D2 receptor agonist and antagonist, respectively) were injected in the prefrontal cortex and SKF38393 and SCH23390 (D1 receptor agonist and antagonist, respectively) were injected in the nucleus accumbens previous to the acquisition of the CFC. The D2 receptors blockade in the nucleus accumbens as well as the D1 receptors stimulation in the prefrontal cortex attenuated the deficit presented by SHR. In this context, these results reinforce the intersections between CFC deficit in SHR and emotional processing abnormalities in schizophrenia.

60. BEHAVIORAL AND COGNITIVE EFFECTS OF PRENATAL FOLATE DEFICIENCY IN GLUTAMATE CARBOXYPEPTIDASE II HETEROZYGOUS MICE Eby LE, Schaevitz LR, Coyle JT, Berger-Sweeney JE. Dept. of Biological Sciences, Wellesley College, Wellesley MA, USA and Dept. of Psychiatry, McLean Hospital, Harvard Medical School, Belmont MA, USA. Schizophrenia (SZ) is a complex disorder that likely has both genetic and environmental etiology. We have developed a model of SZ that replicates glutamatergic hypofunction using mice heterozygous for a null mutation of enzyme glutamate carboxypeptidase II (GCPII). These mice express some but not all symptoms of SZ. To create a better model of SZ, by combining genetic and environmental deficits, we

deprived GCPII mice of the nutrient folate in adulthood. In humans, folate deficiency in pregnant women is associated with increased rates of SZ in the offspring. We have found that mice with either a GCPII mutation or folate deficiency in adulthood display SZ-like symptoms; however, surprisingly, mice with both performed similarly to wildtypes. We hypothesized that prenatal folate deficiency would model SZ better than deficiency in adulthood. In a second study, dams were folate-deprived prior to breeding and offspring were given a folate-deficient diet after birth. Four groups of mice were tested: wildtype, folate-deprived wildtype, GCPII heterozygous, and folate-deprived GCPII heterozygous. Mice were assessed for general health and tested on tasks relevant to symptoms of SZ, including locomotor, rotorod, and pre-pulse inhibition. Four out of 5 wildtype animals on the folate-deficient diet displayed severe developmental abnormalities, whereas no folate-deprived GCPII heterozygous mice (n=6) displayed these abnormalities. Due to the severe effects of folate-deprivation on wildtype animals, it was difficult to analyze behavioral data. We are currently conducting a study limiting folate deficiency to the early postnatal period (birth to weaning), attempting to model nutritional deficiency during the third trimester in humans. We predict that this combination will better model the human disorder with less severe consequences to general health.

61. EFFECTS OF ANTIPSYCHOTICS ON THE BEHAVIORAL DEFICITS IN HUMAN DOMINANT-NEGATIVE DISC1 TRANSGENIC MICE WITH NEONATAL POLYI:C TREATMENT. Ibi, D_1;Nagai, T_1; Kitahara, Y_1; Nabeshima, T_2; Sawa, A_3; Yamada,K_1; $_1$Dept. of Neuropsychopharmacology and Hospital Pharmacy, Nagoya University Graduate School of Medicine, Nagoya 4668560, Japan. $_2$Dept. of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, Meijo University, Nagoya 468-8503, Japan. $_3$Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. We have recently reported an animal model of schizophrenia with gene-environment interaction by inducing immune activation during perinatal period in transgenic mice with human dominant-negative form of disrupted-in-schizophrenia 1 (DN-DISC1). In the present study, we investigated the effects of antipsychotics on the behavioral deficits in this animal model. From postnatal day 2 to 6, neonatal DN-DISC1 mice were repeatedly injected polyI:C. An atypical antipsychotic clozapine or a typical antipsychotic haloperidol was administered orally once a day for 7 consecutive days before the start of the series of behavioral tests. Memory impairment in polyI:C-treated DN-DISC1 mice was ameliorated by administration of clozapine but not haloperidol. Both antipsychotics suppressed the potentiation of MK-801-induced hyperactivity although they had no effect on deficit of social interaction in polyI:C-treated DN-DISC1 mice. These results suggest that polyI:C-treated DN-DISC1 mice may be useful in evaluating the effects of antipsychotics.

62. HYPOCRETIN GENE TRANSFER IN MICE MODELS OF NARCOLEPSY. Meng Liu, Carlos Blanco-Centurion and PJ. Shiromani. VA Boston Healthcare System and Harvard Medical School, West Roxbury, MA 02132. Narcolepsy is now considered a neurodegenerative disorder characterized by the loss of neurons containing the neuropeptide hypocretin, also known as orexin. As with other diseases where CNS neurons die it is necessary to explore new strategies to transfer genes to restore function. At the 2008 IBNS meeting we presented evidence that an HSV-1 amplicon vector mediated transfer of the gene for mouse prepro hypocretin together with reporter genes into hypocretin null mice decreases symptoms of narcolepsy. That vector was short-lived and expressed the hypocretin gene for only 4d. We have now created a vector that expresses the hypocretin gene for at least 30days. We have injected this gene into the brains of the ataxin-hypocretin mice, which are a model of narcolepsy. In these mice, the hypocretin neurons are dead, and thus the gene is transferred to other surviving neurons. Gene transfer was also made in hypocretin knockout mice. In both groups of mice 30 days after hypocretin gene transfer we find a robust expression of the hypocretin peptide in the lateral hypothalamus. We also find dense innervation of target sites in the locus coeruleus, tuberomammillary nucleus, pons and other brain regions relevant to sleep and arousal. This study demonstrates feasibility of methods to stably transfer the gene for HCRT. Our long-term strategic intent is to deliver the gene for hypocretin-2 receptor to reverse the symptoms in the canine model of narcolepsy where the HCRT-2 receptor gene is mutated. Supported by NIH and VA Research Service.

63. THE ROLE OF THE ENDOCANNABINOID SYSTEM IN A RAT MODEL OF DISTRACTION-INDUCED ANALGESIA. Ford, G.K; Moriarty, O; Harhen, B; Tully, E; Mulcahy, A; Finn, D.P. Pharmacology and Therapeutics, Centre for Pain Research and NCBES Neuroscience Cluster, National University of Ireland, Galway, Ireland.Distraction interventions are used clinically to relieve pain. Attention is a limited capacity and exposure to another attention-demanding stimulus causes withdrawal of attention away from a painful stimulus and thus reduces perceived pain. We have recently established and validated a rat model of distraction-induced analgesia where exposure to a novel, non-aversive object resulted in a suppression of formalin-evoked nociceptive behaviour (Ford et al., 2008 Eur J Pain 12; 970-979). Given its role in pain and attention, we investigated the hypothesis that the endocannabinoid system is involved in mediating distraction-induced antinociception. Intraplantar injection of formalin was used to evoke nociceptive behaviour in male Lister-Hooded rats which was scored for a 30-minute period (30-60min post-formalin in an arena containing a novel object distractor or no object). Immediately following formalin, animals received an intra-peritoneal injection of either the fatty acid amide hydrolase inhibitor URB597

(0.3mg/kg), the cannabinoid-1 receptor antagonist/inverse agonist rimonabant (1mg/kg), URB597 (0.3mg/kg)+rimonabant (1mg/kg) or vehicle. Post-mortem hippocampal endocannabinoid/fatty acid amide concentrations were determined by LC-MS/MS. Exposure to novel object reduced formalin-evoked nociceptive behaviour and was associated with increased hippocampal levels of anandamide, 2-arachidonoyl glycerol, oleoylethanolamide and palmitoylethanolamide. Rimonabant prevented distraction-induced antinociception, an effect accompanied by reduced levels of anandamide, oleoylethanolamide and palmitoylethanolamide. In rats not exposed to distractor, URB597 significantly reduced nociceptive behaviour and increased oleoylethanolamide and palmitoylethanolamide levels, effects that were blocked by co-administration with rimonabant. These data suggest that increasing endocannabinoid tone is antinociceptive in a rat model of tonic persistent pain. Pharmacological blockade of CB1 receptors attenuates both the expression of URB597-induced and distraction-induced antinociception. These results provide evidence that the hippocampal endocannabinoid system may be an important neural substrate subserving attentional modulation of pain. Acknowledgments: This work was supported by grants from Science Foundation Ireland and the Irish Higher Education Authority (PRTLI4).

64. LITHIUM AND THIOCOLCHICOSIDE INTERACTION ON RAT DENTATE GYRUS NEURONAL NETWORK EXCITABILITY Talani G., Obili N, Fadda E., Uras R., Cordeddu G., Fois C., Prinzis S., Frau A., Piras V., Siuni L., Niola P., *De Riu PL, *Sechi GP, Sanna E. Dep. of Experimental Biology, Sect of Neuroscience, University of Cagliari; *Department of Neurosciences, University of Sassari, Italy The muscle relaxant thiocolchicoside (TCC) is commonly used in clinical practice also for its anti-inflammatory and analgesic effects. Several previous studies have proposed that TCC as a competitive antagonist of GABAARs, and in vivo exerts a proconvulsant and convulsant activity in rats and humans. Preliminary data suggest that pre treatment of rats with concentration of lithium similar to those found in humans under clinical conditions, markedly enhances the convulsant effects of TCC. To better understand the nature of the interaction between lithium and TCC, we performed extracellular electrophysiological recordings of fEPSPs and evaluated the neuronal excitability in rat dentate gyrus (DG) slices. After 6 h of LiCl (1 mM) incubation the I/O responses of fEPSPs were markedly enhanced compared to control. Application of 1 μM TCC potentiated fEPSPs with a greater efficacy in slices after LiCl incubation. Patch-clamp recordings in DG granule cells revealed that LiCl incubation enhanced the frequency of mEPSCs and reduced paired-pulse facilitation ratio suggesting an increased probability of glutamate release. Taken together these results indicate that treatment of slices with LiCl increases fEPSP recorded from DG granule cells, and markedly potentiates the effects of TCC. The strong increase of DG neuronal excitability induced by the association of lithium and TCC is consistent with the pharmacological observation of an enhanced convulsant activity in rats and suggests that particular attention should be taken when such drug combination is used in clinical practice.

65. THE EFFECTS OF GRK6 DEFICIENCY IN THE MOUSE MODELS OF PARKINSONS Manag, F.1; Sotnikova, T.D.1; Salahpour, A.2; Caron, M.G.2; Premont, R.T.3; Gainetdinov, R.R. 1,2 1-Neuroscience and Brain Technologies Department, Italian Institute of Technology, Genova, Italy; 2-Cell Biology Department, Duke University, Durham NC, USA; 3- Gastroenterology, Department, Duke University, Durham NC, USA. G Protein-Coupled Receptor Kinase 6 (GRK6) belongs to a family of seven serine/threonine protein kinases (GRKs) critically involved in the regulation of GPCRs and this kinase is the most highly expressed GRK in the striatum. It has been reported that some animal models of Parkinsons disease (PD) and PD patients have an increased levels of GRK6 in the striatum. GRKs, in general, phosphorylate agonist-activated GPCRs thereby blocking the activation of G proteins and leading to rapid desensitization. Moreover, phosphorylation of GPCRs by GRKs and recruitment of arrestin proteins can also promote novel G-protein-independent signaling events. In particular, it has been shown that GRK6 has a role in regulating D2-class dopamine receptor desensitization. In fact, GRK6 knockout (GRK6-KO) mice are supersensitive to several direct and indirect dopaminergic agonists including cocaine and amphetamine. Thus, it is important to understand how GRK6 deletion can affect the behavioral manifestations of dopamine deficiency and responses to L-DOPA in mouse models of PD. For this purpose we evaluated: 1) the cataleptic response to D2 dopamine antagonist haloperidol (pharmacological model of PD) in GRK6-KO mice; 2) the role of GRK6 in the regulation of locomotor activity in mice with persistently increased dopaminergic tone by crossing GRK6 deficient mice to dopamine transporter knockout (DAT-KO) mice; 3) the role of GRK6 in acute responses to L-DOPA by crossing these mutants to dopamine transporter knockout (DAT-KO) mice and developing an acute model of absolute dopamine deficiency, DDD mice; 4) the role of GRK6 in chronic responses to L-DOPA in hemiparkisonian 6-OHDA mouse model. The results indicate that GRK6 deletion significantly modulates dopaminergic responses in animal models of PD and causes a reduction in cataleptic behavior, increase in dopaminergic sensitivity and potentiation of the effect of L-DOPA. Thus, the inhibition of GRK6 activity could be a novel approach to improve efficacy of L-DOPA therapy.

66. PROMISCUOUS ANTI-DYSKINESIA DRUGS ACT AS 5-HT1A AGONISTS IN THE 6-OHDA RAT. Paquette, M.A.; Martinez, A.; Macheda, T.; Giuffrida, A. Dept. of Pharmacology, UTHSCSA, San Antonio, TX 78229 USA. The 6-hydroxydopamine (6-OHDA) rat model of Parkinsons disease (PD) develops Abnormal Involuntary Movements (AIMs) after repeated L-DOPA, similar to the L-DOPA-induced dyskinesia (LID) observed in human PD patients. Amantadine and dextromethorphan (DM) suppress AIMs and LID, supporting the models predictive validity. However, the mechanism by which these promiscuous drugs work is unclear, as they are noncompetitive NMDA antagonists and indirect serotonin (5-HT) agonists. We used a pharmacological blockade approach in the 6-OHDA rat to determine whether the anti-dyskinetic effect of DM was dependent on NMDA agonism or 5-HT1A agonism. We also tested BMY-14802, a sigma-1 ligand and 5-HT1A agonist that suppresses AIMs. These drugs were compared to the 5-HT1A agonists buspirone and flesinoxan and the noncompetitive NMDA antagonist MK-801. The anti-dyskinetic effects of DM were prevented by a 5-HT1A antagonist, but not an NMDA agonist. Likewise, the anti-dyskinetic effects of BMY-14802 were prevented by 5-HT1A antagonism. As expected, selective 5-HT1A agonists had anti-dyskinetic effects, and sensorimotor testing identified 5-HT1A agonist doses of that suppressed AIMs without preventing L-DOPAs therapeutic effects. Conversely, MK-801 suppressed AIMs only at doses that exacerbated parkinsonism. Our results suggest that selective 5-HT1A agonists should be pursued as anti-dyskinesia treatments in PD.

67. ENHANCED RESPONSES TO L-DOPA IN THE TRACE AMINE ASSOCIATED RECEPTOR 1 (TAAR1) KNOCKOUT MICE. Sotnikova T.D.; Gainetdinov R.R. Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genoa, 16163, Italy. Trace amines are endogenous amines of unknown function that are structurally related to dopamine and other monoamines and normally found at low concentrations in the brain. Recently, specific GPCR receptors for trace amines, designated as Trace Amine Associated Receptors (TAARs), have been discovered. The best characterized TAAR1 is particularly interesting since it can be activated by a variety of monoaminergic compounds including trace amines, amphetamines and dopamine metabolites. These receptors represent attractive potential mediators of certain aspects of movement control. By using various experimental paradigms aimed to model Parkinsons disease in mice lacking TAAR1 we investigated role of TAAR1 in movement control. In particular we used three approaches: 1) pharmacological model of PD (haloperidol catalepsy); 2) a novel model of acute dopamine deficiency, DDD mice; 3) 6-OH-DA model of PD. TAAR1-KO mice demonstrated significantly altered responses in all these models, thus indicating important role of TAAR1 in the movement control and actions of antiparkinsonian drugs. These observations suggest that TAAR1 may represent a novel target for the pharmacology of Parkinsons disease.

68. ROLE OF DIFFERENT BRAIN STRUCTURES IN AN ANIMAL MODEL TO STUDY EMOTIONAL PROCESSING ABNORMALITIES IN SCHIZOPHRENIA: THE CONTEXTUAL FEAR CONDITIONING DEFICIT PRESENTED BY SHR (SPONTANEOUSLY HYPERTENSIVE RATS) . Medrano, W. A. ; Calzavara, M. B.; Levin, R. ; Frussa-Filho, R. ; Ablio, V.C. , Department of Pharmacology, Federal University of Sao Paulo Laboratrio Interdisciplinar de Neurocincias Clnicas LiNC, Department of Psychiatry, Federal University of Sao Paulo. Recently, we have described that spontaneously hypertensive rats (SHR) present a contextual fear conditioning (CFC) deficit that is specifically reverted by antipsychotics and potentiated by proschizophrenia manipulations. Based on these findings, we suggested that this could be a useful animal model to study abnormalities in emotional processing in schizophrenia. The aim of this work was to investigate the role of basolateral amygdala, prefrontal cortex and nucleus accumbens in the CFC deficit presented by this strain. These structures were chosen because they are related both to emotional processing and schizophrenia. For this purpose, tetrodoxine and veratridine (that inactivates and activates neuronal functioning, respectively) were injected in these structures previous to the acquisition of the CFC. Inactivation of nucleus accumbens as well as activation of prefrontal cortex attenuated the deficit presented by SHR. These results are in accordance with the proposed overactivity of the mesolimbic system and hypoactivity of prefrontal cortex that underlie the pathophysiology of schizophrenia. In this context, they reinforce the intersections between CFC deficit in SHR and emotional processing abnormalities in schizophrenia.

69. DISRUPTION OF PREPULSE INHIBITION (PPI) BY APOMORPHINE (APO) ACROSS PREPULSE STIMULUS MODALITY. Mactutus, C.F.; Moran, L.M.; Booze, R.M. Dept. of Psychology, University of South Carolina, Columbia, SC 29208 USA. Schizophrenia and other neuropsychiatric disorders show deficient sensorimotor gating, which can be measured with PPI. It is well-established that APO, a dopamine agonist, disrupts PPI of the auditory startle response (ASR) at low prepulse intensities (5-10 dB > background) at an interstimulus interval (ISI) of 100msec. It was hypothesized that disruption of PPI by APO would also occur with a visual prepulse stimulus, and further, that a range of ISIs would provide a more precise index of such disruption. It was also hypothesized that PPI of the ASR would be disrupted by APO with a relatively high intensity prepulse (15 dB > background), when assessed with a range of ISIs. Sensorimotor gating was measured with visual and auditory

prepulse stimuli in the PPI paradigm (ISIs of 0, 8, 40, 80, 120, 4000 msec, 6-trial blocks, Latin-square design). Adult male Sprague-Dawley rats (n=12) were tested (within-subjects design) 5 min after a s.c. injection of saline or apomorphine (APO) (0.1, 0.25, and 0.5 mg/kg) in an ascending series with 48 hr between assessments. In replication of prior studies, auditory PPI with a low prepulse intensity (75dB) was disrupted by APO at the 100 msec ISI; also as expected, such disruption was not seen with the high prepulse intensity (85 dB). However, the use of a range of ISIs revealed a flattening of the ISI curve as a function of increasing APO dose; a effect observed with both auditory and visual prepulse stimuli. Thus, APO has clear effects on the temporal domain of PPI, independent of its effects on prepulse detectability, an effect which also generalizes across prepulse stimulus modality. (NIH HD043680, DA013137, DA014401)

70. THE EFFECT OF APOE 4 ALLELE ON GAIT VARIABILITY IN COMMUNITY-DWELLING ELDERS. Moon S.W. ; Choi J.Y. ; Kim T.H. ; Nam B.W. Dept. of Neuropsychiatry. The Konkuk Univ., Chungju, South korea. Background and Aims: Gait variability increases with age and in the elderly affected by subclinical subcortical changes. The brain anatomical correlates of gait variability associated with the occurrence of the APOE 4 allele have not been studied in community-dwelling normal elders. Methods: Gait variability were assessed in 200 men and women (mean age = 75.9). They have been free of cerebrovascular diseases, dementia, delirium, Parkinson's disease and depression. Subclinical brain vascular abnormalities were measured on brain MRIs as small infarcts and white matter hyperintensities. Genomic DNA was extracted from the venous blood and APOE genotyping was done in the normal elderly group. Results: Gait variability was associated with subcortical volume of small infarcts and white matter hyperintensities, independent of age, gender and cognitive function. There were relationships between gait variability and the occurrence of the APOE 4 allele. Conclusion: A greater variability was associated with subclinical brain vascular changes as defined by MRI and the occurrence of the APOE 4 allele.

71. SPINAL CERAMIDE MODULATES THE DEVELOPMENT OF MORPHINE ANTINOCICEPTIVE TOLERANCE VIA PEROXYNITRITE-MEDIATED NITROXIDATIVE STRESS AND NEUROIMMUNE ACTIVATION Cuzzocrea, S.; Esposito E.; Masini, E.; Matuschak, G.M.; Salvemini, D. Dept. of Clinical and Experimental Medicine and Pharmacology, School of Medicine, University of Messina, Messina, Italy; Istituto di Ricovero e Cura a Carattere Scientifico Centro Neurolesi Bonino-Pulejo, Messina, Italy; Dept. of Preclinical and Clinical Pharmacology, University of Florence, Florence, Italy; Dept. of Internal Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, Saint Louis University School of Medicine, St. Louis, MO 63104, USA. The effective treatment of pain is typically limited by a decrease in the pain-relieving action of morphine that follows its chronic administration (tolerance). Therefore, restoring opioid efficacy is of great clinical importance. In a murine model of opioid antinociceptive tolerance, repeated administration of morphine significantly stimulated the enzymatic activities of spinal cord serine palmitoyltransferase, ceramide synthase, and acid sphingomyelinase (enzymes involved in the de novo and sphingomyelinase pathways of ceramide biosynthesis, respectively) and led to peroxynitrite-derive nitroxidative stress and neuroimmune activation [activation of spinal glial cells and increased formation of tumor necrosis factor-α, interleukin (IL)-1β, and IL-6]. Inhibition of ceramide biosynthesis with various pharmacological inhibitors significantly attenuated the increase in spinal ceramide production, nitroxidative stress, and neuroimmune activation. These events culminated in a significant inhibition of the development of morphine antinociceptive tolerance at doses devoid of behavioral side effects. Our findings implicate ceramide as a key upstream signaling molecule in the development of morphine antinociceptive tolerance and provide the rationale for development of inhibitors of ceramide biosynthesis as adjuncts to opiates for the management of chronic pain.

72. PPAR-β/δ-MEDIATED PROTECTION ON IN VITRO COMPRESSION MODEL OF SPINAL CORD ORGANOTYPIC SLICE CULTURES Esposito, E.; Paterniti, I.; Meli, R.; Bramanti, P.; Cuzzocrea, S. Dept. of Clinical and Experimental Medicine and Pharmacology, School of Medicine, University of Messina, Messina, Italy; Istituto di Ricovero e Cura a Carattere Scientifico Centro Neurolesi Bonino-Pulejo, Messina, Italy; Dept. of Experimental Pharmacology, University of Naples Federico II, Naples, Italy. The aim of the present study was to evaluate the contribution of PPAR-β/δ in in vitro compression model of spinal cord organotypic slice cultures performed to simulate in vivo compressive trauma. To this purpose we developed in vitro compression model dropping a weight from a prescribed height onto organotypically cultured spinal tissue. This model produced many of the pathophysiological changes documented after in vivo SCI. In the present study with organotypic slice cultures of spinal cord derived from the adult mouse, we have demonstrated, by western blot analysis, a significant increase in COX-2 expression in injured slices compared with control cultures. The signal transduction mechanism involved in this upregulation was related to activation of the protein serine/threonine kinases. In particular, the MAPK activation observed in the study was correlated with the phosphorylation of p38 and c-jun N-terminal kinase (JNK). It's well known that neurotrophic factors resulted in improvement in neuronal survival, and regeneration of fibers in the spinal cord. Brain-derived neurotrophic factor (BDNF) is one of the best-characterized neurotrophic factors, that is important in early phase long-term potentiation, neural survival, differentiation, and synaptogenesis and plays

important roles in activity-dependent forms of synaptic plasticity in the CNS. The decrease in the neurotrophin levels observed in our experiments was likely to reflect, at least in part, the neuronal death and down-regulation of their synthesis by these cells. The spinal cord injury could also have interrupted some of the ascending and descending tracts, resulting in a decreased transportation of neurotrophins. Significantly increased levels of BDNF and GDNF were observed after treatment with GW0742, a high affinity PPAR-β/δagonist. These results are consistent with recovery of locomotor function observed after GW0742 treatment in vivo and supports the pragmatic application of cell-based therapies in correcting damaged circuitry after spinal cord injury. Our results, recognizing that neuroprotective drugs can maintain their neuroprotective efficacy in this in vitro injury model, suggest that it would be a valuable tool to assess novel therapeutic agents.

73. COMBINING STRATEGIES TO DEVELOP BETTER ANIMAL MODELS FOR BIPOLAR DISORDER. [1]Flaisher-Grinberg, S.; [2]Ashkenazy-Frolinger, T.; [2]Kronfeld-Schor, N.; [1,3*]Einat, H. [1]College of Pharmacy, University of Minnesota, USA; [2]Dept. of Zoology, Tel-Aviv University, Israel; [3]Dept. of Psychology, Tel-Hai College, Israel. * heinat@d.umn.edu; haime@telhai.ac.il. The limited availability of appropriate animal models for bipolar disorder (BPD) is repeatedly mentioned as one critical factor hindering research of its underlying biology as well as the ability to develop new treatments. As part of the molecular revolution in psychiatry, there is a growing emphasis on development of animal models through targeted gene mutations. Indeed, mutation based models provide promise but have their own shortcomings and need to be combined with additional approaches. Some of these additional strategies include attempts to develop better tests to evaluate BPD-like behaviors in animals, identification of models for disease endophenotypes, and the utilization of comparative biology approaches to explore model animals based on strains comparison or nontraditional animal species with a biology that is more relevant to the disorder. Combining strategies and enhancing strong collaborations between clinicians, animal behavior scientists, animal physiologists and molecular scientists might be the best way to achieve predictive and etiologically valid models.

74. AN ANIMAL MODEL OF SPORTS-RELATED CONCUSSIONS: THE SHORT AND LONG-TERM EFFECTS OF REPEATED MILD FLUID PERCUSSION BRAIN INJURY IN THE RAT. Shultz, S.R.; MacFabe, D.F.; Cain, D.P. The University of Western Ontario, Canada. Brain concussion is a serious public health concern. In particular, athletes are at an increased risk of suffering repeated concussions within short time periods. Initial studies from our laboratory indicate a single mild fluid percussion injury (mFPI) in the rat results in behavioral and pathological changes consistent with those seen in humans suffering a concussion. Multiple concussions in humans result in cognitive impairments and it has been suggested that repeated concussion injury increases the risk of developing several neurological diseases (e.g. chronic traumatic encephalopathy). The current study investigated the effects of repeated mFPI in the rat in an attempt to model the multiple concussions experienced by athletes. Male Long-Evans rats received sham, one, three, or five mFPIs spaced 5 days apart. Following the final injury, rats received either short (24 hours) or long-term (8 weeks) recovery periods. Rats then underwent detailed behavioral analyses. Following testing rats were sacrificed and brains were examined immunohistochemically. Results indicate that rats receiving repeated mFPIs displayed significant short and long-term cognitive impairments in the water maze. In addition, rats suffering five mFPIs displayed increased short and long-term anxiety levels compared to sham-control rats. Initial neuropathological findings suggest a widespread neuroinflammatory response and diffuse axonal injury in rats suffering repeated mFPI. These findings are similar to symptoms associated with multiple concussions in humans and support the use of repeated mFPI in the rat as a model of sports-related concussion.

75. PROGESTERONE DECREASES CELL PROLIFERATION INDUCED BY TRAUMATIC BRAIN INJURY IN ADULT MALE RATS Cindy K. Barha 1; Tauheed Ishrat 4; Jonathan R. Epp 2; Liisa AM. Galea 1,2,3; Donald G. Stein 4 1 Department of Psychology, 2 Graduate Program in Neuroscience, 3 Brain Research Centre, University of British Columbia, Vancouver British Columbia, Canada. 4 Department of Emergency Medicine, Brain Research Laboratory, Emory University School of Medicine, Atlanta, Georgia, USA. Traumatic brain injury (TBI) increases cell death in the hippocampus and produces deficits in hippocampus-dependent cognition. The hippocampus is the site of ongoing neurogenesis throughout the lifespan. Progenitor cells in the dentate gyrus (DG) of the hippocampus retain the ability to produce neurons during adulthood in most mammalian species studied including humans. These new neurons are involved in hippocampus-dependent learning and memory. TBI is associated with an increase in hippocampal cell proliferation and although counterintuitive these new neurons may play a role in the deficits in learning and memory seen with TBI, as they do in seizure-related deficits in cognition. Progesterone is neuroprotective and treatment with progesterone improves behavioral recovery, reduces apoptosis, lesion volume, and edema after TBI. Therefore the aim of the present study was to determine whether treatment with progesterone altered cell proliferation and short-term survival in the DG following TBI. Male Sprague-Dawley rats with bilateral contusions of the frontal cortex or sham operations were given a single injection of bromodeoxyuridine (BrdU) 48 hours after injury and were treated with either progesterone or vehicle for 7 days before perfusion. Brains were

processed for Ki67 (endogenous marker of cell proliferation), BrdU (short-term cell survival), and Fluoro-jade (marker of degenerating neurons). Results indicate that injury increased cell proliferation compared to shams, and progesterone decreased cell proliferation in injured rats but increased cell proliferation in sham rats. Interestingly injury and/or progesterone treatment did not influence short-term cell survival of BrdU-ir cells. Furthermore, injury increased cell death and progesterone treatment decreased cell death back to levels seen in sham rats. Therefore it may be that the beneficial behavioral effects seen with progesterone treatment after TBI may be associated with the ability of progesterone to reinstate neurogenic homeostasis in the hippocampus.

METABOLISM AND AUTONOMIC PROCESSES.

76. IN THE MIDBRAIN, DURING PROESTRUS OR WITH PROGESTERONE ADMINISTRATION, EXPRESSION OF BIOSYNTHESIS AND METABOLISM ENZYME EXPRESSION ARE ENHANCED Frye, C.A.; Osborne, D.M.; Walf, A.A. The University at Albany, State University of New York, Albany, NY 12222. Progesterone (P) has actions in the midbrain of rodents to mediate reward, social, and affective behaviors. Some actions of P are due, in part, to its neuroactive product, allopregnanolone. Allopregnanolone can be formed via metabolism by 5alpha-reductase of P from peripheral and central sources, or following local biosynthesis. Biosynthesis may involve the Pregnane Xenobiotic Receptor (PXR), a nuclear receptor that regulates gene transcription for cytochrome P450 enzymes. The PXR gene, RNA, and protein are expressed in the midbrain of proestrous rats. Our hypothesis was that activity of progestogen metabolism and/or biosynthesis factors in the midbrain may change with endogenous hormone milieu (Exp. 1), extirpation of the ovaries, and/or hormone replacement (Exp. 2). We characterized the expression of metabolism (5alpha-reductase) and biosynthesis (PXR, StAR, P450) enzymes in the midbrain of adult rats using Westerns. In Exp. 1, proestrous rats, which have high endogenous levels of estradiol and P, had increased expression of biosynthesis, but not metabolism, enzymes in the midbrain compared to control (male) rats. In Exp. 2, there were robust changes in biosynthesis and metabolism enzyme expression in the midbrain of rats administered P compared to vehicle. These data suggest that changes over the estrous cycle in the midbrain are associated with biosynthetic factors, whereas P administration increased progestogen biosynthesis and metabolism factors in the midbrain. Thus, there may be different roles of progestogen biosynthesis and metabolism in the midbrain during hormonal cycles and hormone administration.

77. WHEEL RUNNING ELIMINATES HIGH-FAT PREFERENCE AND ENHANCES LEPTIN SIGNALING IN THE VENTRAL TEGMENTAL AREA. Scarpace, P. J.; Tumer, N.; Matheny, M; Zhang Y. Dept. Pharmacology, Univ. of Florida, Gainesville, FL 32610. We examined the effects of voluntary wheel running (WR) on dietary preference and the potential role of leptin. In a two-diet choice paradigm, palatable high-fat (HF) food and standard chow were provided ad libitum. Rats chose to eat almost exclusively the HF diet over chow in sedentary conditions. With WR, however, rats exhibited no preference for HF food and consumed equal gram amounts of both chow and HF. Total daily caloric consumption during WR was equivalent whether in the two-choice protocol, with only chow or with only HF diet available, yet significantly less than sedentary chow caloric intake. Two days after initiating WR, leptin signaling was examined in multiple brain sites following leptin injection into the third cerebral ventricle. The maximal leptin-stimulated STAT3 phosphorylation was enhanced in the ventral tegmental area (VTA), but not in the arcuate nucleus, lateral hypothalamus, dorsal medial or ventral medial hypothalamus, or substantia nigra. In conclusion, WR appears to act either as an independent reinforcing factor or as a more favored activity to substitute for the consumption of a palatable HF diet, thus eliminating the preference for the HF food. Moreover, WR enhances leptin signaling specifically in the VTA, suggestive of a WR-evoked mechanism of heightened leptin function in the VTA to curb the drive to consume palatable HF food.

78. VENTRAL PALLIDAL AND HYPOTHALAMIC COMPONENTS OF THE NUCLEUS ACCUMBENS SHELL FEEDING CIRCUIT. Stratford, T.R.; Wirtshafter, D., Dept. Psych. and Lab. Integrative Neuroscience, U. Illinois at Chicago, Chicago, IL 60607 USA. Injections of the GABA agonist muscimol (M) or the -opioid agonist DAMGO into the nucleus accumbens shell (AcbSh) elicit intense feeding in sated rats. The AcbSh projects to several brain regions involved in feeding, including the medial ventral pallidum (VPm) and lateral hypothalamus (LH). To examine whether the AcbSh mediates feeding through projections to these structures, we compared the effects of unilateral excitotoxic lesions on feeding elicited by unilateral injections of M or DAMGO. Following unilateral lesions of the LH, the response to injections of either M or DAMGO was significantly larger when made on the side opposite to the lesion than when made on the side of the lesion. These data indicate that the LH is an essential component of a lateralized pathway through which GABA and opioids in the AcbSh control food intake. Similarly, M injections produced a larger response when made contralateral to a VPm lesion than when made ipsilaterally, indicating that the VPm is also part of the circuit mediating the response to GABA in the AcbSh. In contrast, after unilateral VPm lesions, DAMGO failed to induce significant feeding when injected into the AcbSh on either side. Since there are no major connections between the AcbSh and the contralateral VPm, these results suggest that VPm

lesions produce some nonspecific effect sufficient to abolish the response to DAMGO injected on either side. The presence of a nonspecific effect of this magnitude means that the question of whether the VPm is an essential direct mediator of the DAMGO response cannot be answered using the current methodology; it does not indicate that the VPm is not such a mediator.

79. REDUCTION IN RAT BODY WEIGHT AND FAT MASS WITHOUT AFFECTING FOOD INTAKE INDUCED BY VAGUS NERVE STIMULATION. Olla, P.; Biggio, F.; Utzeri, C.; Banni, S.; Marrosu, F.; Follesa, P. Among the many effects of vagus nerve stimulation (VNS), which is used to treat drug-resistant epileptic seizures, moderate loss of body weight has been observed in some individuals. The mechanism of this effect of VNS has remained unclear, although VNS increases the expression of brain-derived neurotrophic factor (BDNF) in the brain of rats and hypothalamic BDNF regulates metabolism and energy balance. We have now investigated the possible effects of VNS on food intake, body weight, adipose tissue metabolism, and hypothalamic BDNF gene expression in rats. Whereas chronic treatment with VNS for 4 weeks did not affect food intake, it induced an ~20% decrease in body weight and an ~45% decrease in the amount of perirenal adipose tissue compared with those apparent in sham-operated animals. Such VNS treatment also increased the levels of nonesterified fatty acids (NEFAs) in plasma and visceral adipose tissue by ~50 and 80%, respectively, without affecting the NEFA content of the liver. Moreover, the mRNA levels encoding for exon 9 of the BDNF gene was significantly increased in the hypothalamus of rats treated for 30 days with VNS. Chronic VNS thus induces loss of body weight and visceral fat mass in association with an increase in NEFA levels in both plasma and visceral adipose tissue of rats, with these effects appearing to be independent of food intake and rather the result of increased energy expenditure probably elicited by BDNF.

80. HEART RATE AS A BIOINDEX TO ASSESS SENSORY PERCEPTIONS IN SIGHTED AND NON-SIGHTED CRAYFISH. Robinson, M.; Baker, M.; Cooper, R.L.; Bierbower, S. Dept. of Biol, Univ KY, Lexington, KY 40506-0225 USA. Most organisms show diversity in the type and amount of peripheral sensors allowing for detection of different sensory stimuli within and across multiple sensory modalities. Most invertebrates possess chemosensory neurons which enable identification of many chemicals in the environment, and thus are able to behave differentially among chemical compounds based upon the sensory pathway stimulated (i.e. attractive or repellant). Crayfish are decapod crustaceans reliant on visual and chemical environmental cues. Behavior studies alone often exclude fight or flight internal readiness changes and may conclude a lack of environmental awareness. Therefore, a sympathetic-like autonomic response (i.e. HR, heart rate and VR, ventilation rate) in crayfish, (surface) *Procambarus clarkii* and (cave) *Orconectes australis packardi*, during chemical introduction establishes chemical and modality sensitivities that may be species-specific. Initial findings suggest crayfish demonstrating no behavioral response show an internal response through changes in HR/VR. Also, crayfish show an increased HR with attractant chemical introduction (i.e. cysteine) suggesting a natural response to a potential food source, while showing a more pronounced response to toxic/warning compounds. Future research will entail using chemical stimuli identified as significant to induce electrical impulses to be recorded within the antennular olfaction neurons. Investigation of antennular sensillae and associated nerve cluster structure will supplement such experimentation. Funded by G. Ribble Fellowship & Arnold and Mabel Beckman Foundation (MR).

Friday, June 11

8:30-10:30 **Symposium 6**: THE UNIQUE EFFECTS OF STRESS DURING ADOLESCENCE. Chairpersons: **Giovanni Laviola** and **Susan L. Andersen**

NEONATAL COMPETITION FOR MATERNAL RESOURCES ALTERS THE ONTOGENY OF STRESS-RELATED BEHAVIOR AND NEUROTROPHIC FACTORS. Macri, S. Sect. Behavioural Neuroscience, Dept. Cell Biology & Neuroscience, Istituto Superiore di Sanit, Roma, Italy. The maternal mediation hypothesis poses that variations in the environmental conditions adjust maternal styles, and that these, in turn, regulate the development of adult offspring defensive systems. Maternal separation studies in rodents are often advocated to support such hypothesis, whereby the removal of the dam from the cage often modifies dam-pup interaction and this results in permanent neuro-behavioural adjustments in the offspring. Yet, such interpretation is spurious in the light of the fact that, beside maternal care, separation procedures per se directly affect both pups and dams physiology through massive experimenters intervention. This hampers clear-cut mapping of environment-dependent modulation of maternal care on the offspring. Here, we studied maternal care and offspring development in young, adolescent and adult SD rats reared in a communal nursing situation (two dams delivering their offspring four days apart and communally caring for them until weaning). Offspring of the second-born litter received less maternal care compared to older cage-mates. Additionally, compared to first-born and to animal facility reared rats, second-born offspring showed increased anxiety-related behaviour in a plus-maze and abnormal developmental trajectories in terms of social interaction and BDNF levels in the amygdala and hippocampus.

MISGUIDED DEVELOPMENT: THE EFFECTS OF EARLY LIFE STRESS ON PRELIMBIC PREFRONTAL CORTEX CIRCUITRY AND WORKING MEMORY IN RATS. Brenhouse, H.C.; Andersen, S.L. Harvard Medical School, McLean Hospital, Belmont MA 02478 USA. Early adverse experience plays an important role in psychopathology by altering memory and motivational processes. These effects typically manifest during adolescence, in parallel with the later-developing prefrontal cortex (PFC). The PFC mediates motivational salience and decision-making, partially through its connectivity with the nucleus accumbens (NAc). While it is likely that the PFC is involved in delayed effects of early life stress, little is known about how environmental events modulate its development. Here, we will discuss effects of early life stress on PFC development in rats. From postnatal day (P)2-20, rats received maternal separation stress (MS) or facility rearing (CON). Brains from MS and CON males were taken at three ages: juvenile (P25), adolescent (P40), and adult (P100). Five days previously, rats received microinjections of retrograde tracer into the NAc to identify PFC-NAc projections. The prelimbic (pl) PFC was analyzed with immunohistochemistry and Western blot for expression of the D2 dopamine receptor (D2R) and parvalbumin (a marker of fast-spiking interneurons). A separate set of rats was tested at P50 for working memory performance on the win-shift task. During adolescence, D2R were transiently over-expressed on plPFC-NAc projection neurons in CON but not MS animals. Moreover, MS adolescents had reduced parvalbumin-positive interneurons. In late adolescence, MS rats made more errors in the win-shift task compared with CON rats. These results will be discussed in the context of mechanistic changes caused by early life stress that could help explain delayed vulnerability to psychopathology.

CHILDHOOD ABUSE: DELAYED PSYCHIATRIC AND ANATOMICAL EFFECTS IN HUMANS. Andersen SL. McLean Hospital/Harvard Medical School, 115 Mill Street, Belmont, MA 02478 USA. Depression is debilitating and typically emerges during late adolescence. However, exposure to early adversity during childhood not only increases the prevalence of depression, but accelerates the age at which it first manifests. In a retrospective study, we found that young adult females with a history of childhood sexual abuse developed depression an average of 9.2 years after the initial exposure to abuse (Teicher et al., 2009). This delay in symptoms suggests that exposure to maltreatment interacts with brain development to alter its trajectory. In morphometric MRI studies, we found that the timing of abuse produces selective effects in the brain. Specifically, exposure to abuse early in life (e.g., 3-5 years of age) is strongly associated with changes in the hippocampus. Exposure to abuse during adolescence (e.g., 15-17 years) is associated with selective changes in the prefrontal cortex. Preclinical studies in the rat that utilize age-appropriate stressors have found identical regional effects within the hippocampus and prefrontal cortex. Similar to the delayed emergence of depression, our animal work shows that these neuroanatomical changes do not appear until adolescence or young adulthood. Taken together, these data suggest a window of opportunity to intervene. While children with a history of abuse may not report or demonstrate any symptomatic behaviors, our research suggests that the brain may be rewiring in such a way to increase vulnerability in their teenage years. Identifying predictive markers or novel intervention approaches would likely have a significant impact on this population.

11:00-12:00 **Keynote Lecture:** CROSSING THE TRANSLATIONAL BRIDGE. **Insel, T.R.** Introduction: Kelly Lambert.

CROSSING THE TRANSLATIONAL BRIDGE. Insel, T.R. NIMH/NIH, Bethesda, MD 20892 USA. The basic science for psychiatry, previously spread across schools of psychology and neuropharmacology, increasingly needs to include behavioral neuroscience. The public health challenge is both formidable and urgent. In the developed world, mental illnesses are the largest source of disability from all medical causes for people ages 18 -45. Suicide rates are nearly double homicide rates. And the prevalence of childhood disorders, from autism to serious mood dysregulation, has increased markedly in the past decade. How can behavioral neuroscience elucidate the pathophysiology of these mysterious illnesses? Mental disorders are increasingly understood as developmental brain disorders, the result of genetic risk combined with developmental exposures. The clues for solving the mystery of mental illness will come from understanding (a) how genetic variation and experience influence neural circuit formation and (b) the principles by which neural circuits mediate fundamental behavioral and cognitive processes from learning and memory to social behavior. This will require shifting the focus from animal model studies to studies of model animals; from a focus on studies that use behavior to understand drugs to using drugs as tools to understand behavior; and from a singular focus on abnormal behaviors to a deep understanding for the mechanisms of individual and species differences in fundamental aspects of behavior and cognition. With the tools of high throughput biology, stem cell technology, and neuroimaging, there has never been a better time for translating the basic science of brain and behavior to the needs of millions of people disabled by mental illness.

2:00-4:00 **Symposium 7**: EARLY ENVIRONMENT SHAPES ADULT MENTAL DISORDERS: ANIMAL MODELS. Chairperson: **Mikhail V. Pletnikov** and Co-chairperson: **Paul H. Patterson**

EPIGENETIC PROGRAMMING OF THE STRESS RESPONSE IN RATS BY PRENATAL RESTRAINT STRESS AN ANIMAL MODEL OF DEPRESSION. Maccari, S.; Mairesse, J.; Morley-Fletcher, S. Neuroplasticity Team, UMR 8576 CNRS North Lille University of France. Life events occurring during the perinatal period have strong permanent long-term effects on the behavioural and neuroendocrine response to stressors. In rats, repeated restraint stress of the pregnant dam during the last week of pregnancy (PRS) produces long lasting changes in the HPA axis function and behaviours in the offspring. The HPA dysfunctions have been reported in infant, young adult and aged animals, therefore suggesting a permanent effect of early stress. PRS produces high anxiety levels and depressive-like behaviour during adulthood including sleep disorders related to depression. Despite the permanent imprinting induced by stress in utero, the dysfunctions observed after PRS can be reversed by environmental or pharmacological strategy. For example, early adoption or environmental enrichment attenuated some HPA dysfunctions produced by PRS. We have recently shown that the enduring changes in endocrine, behavioral and neuroplasticity found in adult PRS rats can be corrected by antidepressant medication. Mechanisms underlying the PRS effects on the offspring remain largely unknown. However, previous works demonstrated that maternal glucocorticoids during pregnancy may play an important role in the HPA disturbances reported. Thus, in the offspring of stressed mothers, the HPA response to stress is normalised by maternal adrenalectomy. Finally, during lactating period, stressed mothers show an impairment of maternal care and low aggressive behaviour against a male intruder. Given that, several evidences suggest that changes in maternal care may durably program offsprings HPA function and behaviours, it could be postulated that the alterations of the maternal behaviour during the early postnatal period may also strongly contribute to the long-term effect described after PRS.

MATERNAL INFECTION: WINDOW ON NEUROIMMUNE INTERACTIONS IN FETAL BRAIN DEVELOPMENT AND MENTAL ILLNESS. Patterson, P.H. Biology Division, Caltech, Pasadena, CA 91125 USA. Several types of maternal infection are associated with increased risk of schizophrenia and autism in the offspring. In a mouse model, infection with influenza virus at mid-gestation leads to behavioral abnormalities and neuropathologies in the offspring that are consistent with these disorders. The cause of these abnormalities is maternal immune activation (MIA), as evoking an anti-viral-like immune response in uninfected, pregnant mice with the dsRNA, polyI:C, mimics the effects of infection. It is therefore of interest to discover the anatomical and molecular pathways through which MIA alters fetal brain development. Blocking IL-6 activity during development or inactivating its gene strongly attenuates the effects of MIA on the offspring. Conversely, a single injection of IL-6 in pregnant mice can mimic many of the effects of maternal infection on the behavior of the offspring. Regarding the site of IL-6 action, MIA induces IL-6 mRNA and a series of IL-6 response genes in the placenta as well as in a subpopulation of neurons in the fetal brain. This raises the possibility that the rise in maternal IL-6 induced by MIA induces sustained changes in the brains of the offspring through feed-forward dysregulation. Permanent immune dysregulation is, in fact, observed in young and adult brains of autistic and schizophrenic human subjects. MIA also leads to significant elevation of pro-inflammatory cytokines IL-6 and IL-17 in CD4+ T cells from the spleen and mesenteric lymph node of adult offspring. These observations support the hypothesis that MIA can cause permanent changes in immune status of the offspring, both in the brain and in the periphery. The MIA model has face and construct validity for schizophrenia and autism, and is useful for exploring the mechanism of how the maternal infection risk factor alters fetal brain development and subsequent changes in behavior in the offspring.

ANIMAL MODELS OF EARLY LIFE STRESS: SEARCHING FOR THE EARLY DETERMINANTS OF ADULT PSYCHOPATHOLOGY. Cirulli, F. Section of Behavioural Neuroscience, Department of Cell Biology and Neurosciences, Istituto Superiore di Sanit, Rome, Italy. Early adverse events can enhance stress responsiveness and lead to greater susceptibility for psychopathology at adulthood. The epigenetic factors involved in transducing specific features of the rearing environment into stable changes in brain function and behavior have only begun to be elucidated. Neurotrophic factors, such as Nerve Growth Factor (NGF) and Brain-derived neurotrophic factor (BDNF), are good candidates for mediating the effects of early adverse experiences since they are affected by stress and play a major role in brain development and in the trophism of specific neuronal networks involved in cognitive function and in mood disorders. Disruption of the mother infant relationship has been used to model early adverse experiences from rodents to primates. Data obtained from animal models will be discussed to indicate that early maternal deprivation stress is able to affect neurotrophin levels both in the central nervous system and in the peripheral circulation. Changes in the levels of NGF and BDNF following maternal deprivation suggest that neurotrophins might be enlisted among the neurobiological mediators regulating attachment behavior, in addition to representing novel neuroendocrine signals involved in the response to early adversity. Activation of these neurotrophic factors early during postnatal life might influence stress sensitivity at adulthood and increase vulnerability for stress-related psychopathology.

PRENATAL AND POSTNATAL ADVERSE EVENTS INTERPLAY WITH GENETIC PREDISPOSITION IN MENTAL HEALTH: DISC1 MOUSE MODEL. Mikhail Pletnikov. Depts. of Psychiatry, Neuroscience, and Molecular Pathobiology, Johns Hopkins University School of Medicine, Baltimore, MD 21287. Gene-environment interactions play a major role in the pathogenesis of mental diseases. We evaluated interactions between mutant Disrupted-In-Schizophrenia-1 (DISC1) and adverse effects of microbial pathogens or drug of abuse implicated in schizophrenia and mood disorders. We studied adult psychopathological consequences of prenatal immune activation by polyinosinic:polycytidylic acid (Poly I:C) at gestation day 9. Prenatal interaction produced anxiety, depression-like responses, altered pattern of social behaviors and decreased reactivity of the HPA axis, attenuated enlargement of lateral ventricles, decreased volumes of amygdale and periaqueductal gray matter and linear density of spines on dendrites of granule cells of the dentate gyrus of the hippocampus. Prenatal interaction also altered secretion of pro- and anti-inflammatory cytokines in fetal brains, and changed levels of mutant DISC1, endogenous mouse DISC1 and GFAP. We found that the phenotypic effects of interaction required prenatal expression of mhDISC1. Another instance of interaction included evaluation of the synergistic effects of methamphetamine (METH) and mutant DISC1 on cognitive and drug-related behaviors in mice. We found that escalating, non-toxic doses of METH produced more pronounced cognitive impairments and delayed sensitization to the stimulant. Our experiments indicate that alteration in the ERK pathway may be an underlying convergent pathway of interaction between METH and mutant DISC1. Taken together, we will propose that our DISC1 mouse model is a valuable system to study the molecular pathways of gene-environment interplay relevant to mental illnesses.

4:00-6:00 **Symposium 8**: Top-Down Modulation of Prepulse Inhibition of the Startle Reflex in Laboratory Animals. Chairperson: **Liang Li**

MIDBRAIN CIRCUITS FOR PREPULSE INHIBITION AND STARTLE ACTIVATION SUGGEST FOREBRAIN CONTROL OF PREPULSE FUNCTIONS IN APPROACH BEHAVIORS. Yeomans, J. Dept. of Psychology, University of Toronto, Toronto, ON M5S 3G3 Canada. The startle reflex is elicited by strong tactile, acoustic or vestibular stimuli that sum to excite caudal pontine (PnC) giant neurons critical for startle. These mechanisms suggest that startle protects the brain and body during concussive blows. Moderate-intensity acoustic, visual and tactile prepulses inhibit startle at interstimulus intervals (ISIs) from 20-1000 ms via midbrain pathways. In particular, prepulse inhibition (PPI) is mediated by GABA and cholinergic receptors in PnC at specific times. Pedunculopontine cholinergic neurons inhibit PnC giant neurons so that fast nicotinic and slower muscarinic receptors mediate PPI from 20-100 ms and 100-1000 ms, respectively. GABAa receptors contribute to PPI at ISIs near 100 ms, while GABAb receptors contribute from 100-1000 ms. Stimulation and lesion studies show that inferior colliculus mediates fast acoustic PPI. PPI is elicited in intermediate layers of the superior colliculus where contraversive approach turns to acoustic, visual and tactile stimuli are evoked. These mechanisms suggest that PPI functions to inhibit startle-mediated eye closure during the execution of approach turns, i.e. while foveating targets of interest. Startle is elicited, however, by stimulation of deep layers of the superior colliculus where uncrossed pathways mediate avoidance responses. Colliculi and pedunculopontine cholinergic neurons are activated by descending basal ganglia, cortical and limbic systems important for approach responses, sensory-motor gating and PPI.

ROLE OF PALLIDOTEGMENTAL GABAERGIC NEURONS IN PPI OF THE ACOUSTIC STARTLE REFLEX. Yamada, K. Dept. of Neuropsychopharmacology and Hospital Pharmacy Nagoya University Graduate School of Medicine, Nagoya 466-8560, JAPAN. Prepulse inhibition (PPI) of the startle reflex is a measure of the inhibitory function and time-linked information processing by which a weak sensory stimulus (the prepulse) inhibits the startle response caused by a sudden intense stimulus. Deficits in PPI are observed in patients suffering from schizophrenia and other psychiatric disorders, and can be induced in rodents by administration of psychotomimetics such as methamphetamine (METH) and phencyclidine (PCP). Disrupted PPI in rodents can be normalized with antipsychotics, and thereby the PPI model has been used for evaluating the effects of novel antipsychotic drugs. Despite the usefulness of PPI model, however, the neuronal mechanisms and circuits that are involved in PPI have not yet been completely elucidated. In this symposium, I will show that pallidotegmental GABAergic neurons play a crucial role in PPI of the startle reflex in mice, through the activation of $GABA_B$ receptors in pedunculopontine tegmental neurons (PPTg). Furthermore, acute treatment with METH and MK-801 significantly disrupts PPI in mice, which is accompanied by a suppression of c-Fos expression in lateral globus pallidus (LGP) induced by PPI and an increase in c-Fos expression in the caudal pontine reticular nucleus (PnC). Baclofen, a $GABA_B$ receptor agonist, dose-dependently ameliorates PPI impairment induced by METH and MK-801, and decreases the METH- and MK-801-stimulated c-Fos expression in PnC to the basal level. We propose that $GABA_B$ receptors may constitute a putative new target in treating neuropsychiatric disorders with sensorimotor gating deficits, such as schizophrenia and METH psychosis.

IS PPI COGNITIVE? WHAT HAVE WE LEARNED FROM A CORRELATIVE APPROACH. Yee, B.K.; Peleg-Raibstein, D.; Hauser J.; Singer, P.; Dubroqua, S.; Bitanihirwe, B.; LLano Lopez, L.[2]; Gargiulo, P.A.[2]; Feldon, J., Laboratory of Behavioural Neurobiology, Swiss Federal Institute of Technology Zurich, Schorenstrasse 16, CH-8603 Schwerzenbach, Switzerland, [2]Laboratorio de Neurociencias y Psicologa Experimental, Universidad Nacional de Cuyo, Mendoza, Argentina. Prepulse inhibition (PPI) is a common translational paradigm for evaluating sensorimotor gating, whereby a weak prepulse stimulus impedes response to a succeeding pulse stimulus. Typically a startle-eliciting acoustic pulse stimulus is employed, and PPI is defined as the diminution of the startle reaction when the pulse stimulus was shortly preceded by a weak prepulse stimulus. Possible links between PPI and other controlled attention systems as well as performance in other cognitive domains are of obvious interest but remain contentional. Attempts have been made to identify possible associations between PPI impairment and specific cognitive deficits characteristic of different diseases or personality traits, as well as concomitant changes in cognitive functions induced by PPI-disruptive or -enhancing treatments. We have attempted to address this issue using a correlative approach in healthy unperturbed laboratory mice. No evidence of a link between PPI expression and memory processes was revealed. Surprisingly, PPI predicts choice accuracy rather than speed of processing or response time in a test of visual vigilance. PPI also appear to predict proneness to develop amphetamine sensitization, and brain content of specific neurochemicals.

USE OF PRE-PULSE INHIBITION TO ASSESS COMPLEX ACOUSTIC PROCESSING IN RODENTS. Cleary C.E.; Fitch R.H. Department of Psychology, University of Connecticut, Storrs CT 06269 USA. Prepulse inhibition (PPI, also called startle reduction or reflex modification) provides an efficient and accurate method to assess both simple and complex acoustic discrimination in rodents. Although PPI has traditionally been used to assess primary mechanisms of sensory-motor gating, the application of modified versions of this task to subjects with normal baseline PPI allows for the assessment of higher-order acoustic discrimination -- specifically by incorporating increased prepulse cue complexity (e.g., variable duration silent

gaps, tone-sequences, and FM sweeps). Such modified versions of PPI borrow from principles of oddball mismatch negativity paradigms by employing a repeating background stimulus, and a stimulus reversal as the prepulse cue. Cross-session modification of stimulus parameters (e.g., shortening the duration of repeating FM sweeps) can further be used to assess group thresholds for cue discrimination (i.e., the point at which the prepulse cue no longer serves to attenuate the startle response). Neural mechanisms underlying these modified PPI tasks likely reflect cortical input, given evidence that cortical disruption and/or deactivation substantially impairs performance. Importantly, PPI procedures allow for data acquisition from the first day of testing, thus avoiding the time-consuming requirements of operant conditioning paradigms more typically used for assessment of complex acoustic discrimination in rodents. Finally, PPI can be used on rats as young as P21, making the paradigm ideally suited to assessment of both normally developing and neurodevelopmentally impaired rodent models.

EFFECTS OF NOISE EXPOSURE AND SALICYLATE ON AUDITORY CORTEX RESPONSE AND HYPERACUSIS BEHAVIOR Sun, W.; Lu, J.; Deng, A.; Lobarinas, E.; Goodey, R.; Salvi, R.J. Center for Hearing & Deafness, Department of Communicative Disorders and Sciences, SUNY State University at Buffalo, Buffalo, NY 14214 USA Department of Surgery, University of Auckland, New Zealand. Hyperacusis, a marked intolerance to ordinary environmental sound, is a common symptom associated with a variety of neurological diseases. Although severe hyperacusis can significantly degrade the quality of life, the mechanisms that give rise to hyperacusis are poorly understood. In this study, we examined the relationship between a hyperacusis-like behavior, specifically an enhanced startle reflex amplitude, and neural hyperactivity in auditory cortex (AC) which occurred after acoustic overstimulation or high-dose salicylate treatment. Bilateral noise exposure (120 dB SPL, narrow band noise, 12 kHz, 1 h) significantly enhanced startle reflex amplitude 1 day post-exposure, indicative of hyperacusis. The firing rates of AC neurons also increased after the noise exposure consistent with previous reports. Local or systemic salicylate treatment also significantly increased sound-evoked AC neural activity and significantly enhanced the amplitude of the startle reflex, a behavioral manifestation of increased loudness and neural gain. S-baclofen and R-baclofen, GABA-B receptor agonists, strongly suppressed the AC firing rates and sound-evoked local field potentials and reduced the salicylate-induced enhancement of AC firing rate. Importantly, S-baclofen also reduced the exaggerated startle reflex response induced by noise exposure and salicylate. Collectively, these results suggest that noise and salicylate induced hearing loss reduced cortical inhibition which in turn leads to enhanced AC responses and hyperacusis-like behavior. Our results suggest that increasing GABA-medicated inhibition with baclofen reduces AC central gain and reverses the exaggerated neural and behavioral responses evoked by noise exposure and high doses of salicylate (Supported by NIH, RNID and AFAR).

EMOTIONAL LEARNING ENHANCES STIMULUS-SPECIFIC TOP-DOWN MODULATION OF SENSORIMOTOR GATING IN SOCIALLY REARED RATS BUT NOT ISOLATION-REARED RATS. Li, L.; Du, Y.; Li, N.-X.; Wu, X.-H. Dept. of Psychology, Peking University, Beijing 100871, China. Prepulse inhibition (PPI), the suppression of the startle reflex by a preceding sensory stimulus (prepulse), can be top-down modulated in humans. This talk describes a series of recent studies on emotional-learning-induced enhancement of PPI in laboratory ratsand particularly, shows that top-down modulation of PPI in rats is prepulse-stimulus specific and based on selective attention. Specifically, PPI elicited in socially reared rats by a narrowband-noise prepulse on the broadband-noise background (masker) is enhanced after the prepulse becomes fear conditioned. This fear-conditioning-modulated PPI is further enhanced by introducing an attention-related perceived spatial separation between the conditioned prepulse and the broadband-noise masker. These PPI enhancements disappear if the conditioned prepulse is replaced by a different narrowband-noise prepulse which is not fear conditioned. In contrast, in isolation-reared rats, neither fear conditioning of the prepulse nor perceived spatial separation enhances PPI. Since the deficiency of attentional modulation of PPI in schizophrenic patients is significantly correlated with the symptom severity, the deficiency of stimulus-specific emotional-learning-induced enhancement of PPI in isolation-reared rats is useful for modeling schizophrenia. Supported by the National Natural Science Foundation of China (30950030) and the 973 National Basic Research Program of China (2009CB320901).

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

ANXIETY, STRESS AND RELATED DISORDERS

81. FOS DISTRIBUTION IN THE MEDIAL TEMPORAL LOBE DURING CONTEXT-, AUDITORY- AND LIGHT-CUED CONDITIONED FEAR IN WISTAR RATS. Albrechet-Souza, L.; Borelli, K.G.; Almada, R.C.; Onusic, G.M.; Brandao, M.L. Laboratorio de Neuropsicofarmacologia and Instituto de Neurociencias e Comportamento (INeC), FFCLRP, Universidade de Sao Paulo, SP, Brazil. Independent brain circuits underlie different forms of conditioned fear and, within a particular memory domain, the involvement of specific structures may depend upon the type of conditioning, such as a context or explicit cues paired with footshocks. Several clinical reports have associated the damage to the medial temporal lobe (MTL) with retrograde amnesia. Although much has been done to disclose the neural circuits underlying the conditioned fear, the involvement of the MTL in the aversive conditioning paradigm is still unclear. To address this issue we assessed the Fos protein distribution in the MTL of rats following exposure to a context, a tone or a light previously paired with footshocks. Twenty-four hours after the conditioning, the rats were exposed to the same chamber or to a distinct context and presented with tone or light, without footshocks. The results showed comparable percentage of freezing response in the three types of conditioned fear but a distinct pattern of Fos distribution. Although the groups exposed to specific cues showed no differences in Fos expression, the group exposed to context-paired footshocks presented a selective activation of the entorhinal, perirhinal and ectorhinal cortices, with no changes in the ventral hippocampus. These findings suggest that contextual and explicit stimuli endowed with aversive properties through conditioning recruit distinct brain areas and the cortico-hippocampal circuitry appears to be critical for storing context but not explicit cue footshocks associations. Financial support: CNPq

82. A RE-EXAMINATION OF THE RELATIONSHIP BETWEEN THE FIRING RESPONSE OF THE AN2 INTERNEURON AND AVOIDANCE FLIGHT IN THE PACIFIC FIELD CRICKET, TELEOGRYLLUS OCEANICUS BY THE USE OF BAT-LIKE ACOUSTIC STIMULATION. Asi, N.S.; Jackson, M.E.; Fullard, J.H. Dept. of Biology. University of Toronto Mississauga, Mississauga, ON L6S 4M3 Canada. Nolen and Hoy (1984) determined that a spike rate of 220 Hz averaged over 100 ms in the AN2 interneuron elicits avoidance steering to ultrasonic stimuli in female Teleogryllus oceanicus,. Recent studies however, suggest that instantaneous rather than averaged spike activity is a more realistic predictor of how neural circuits operate. Also, bats sympatric with this Australian cricket never produce echolocation calls of 100 ms. We examined the instantaneous spike rates (ISRs) of AN2 responses corresponding to the threshold spike train response reported by Nolen and Hoy (1984) to elicit avoidance steering (behavioural threshold (BT)) within the first 10 ms (i.e., a typical natural duration of echolocation calls) and 33 ms (i.e., the minimum latency between the first AN2 spike and muscle activation) by generating AN2 neural response traces using the same stimulus criteria as used by Nolen and Hoy (1984). Our re-estimation of these responses shows that the ISR at BT approaches 450 Hz for the first four spikes (defined as bursting), which reduces to less than 220 Hz after 13 spikes. When relating AN2 spike responses to the natural echolocation call durations of sympatric bats we suggest that avoidance steering in T. oceanicus may be elicited by bursting followed by a spike train firing at sufficiently high rates with lower duration calls requiring greater intensity to produce such a response.

83. THE NEUROPEPTIDE S RECEPTOR AS TARGET FOR NEUROSCIENCE DISORDERS. Fendt, M.; Buchi, M.; Brki, H.; Hoyer,D.; Langenegger, D.; Laurent, S.; Imobersteg, S.; Vanek, M.; Suply, T.; McAllister, K.H.; Zimmermann, K.; Sailer, A.W. Novartis Institutes for BioMedical Research, Basel, Switzerland. Neuropeptide S (NPS) and its cognate receptor (NPSR) are a recently identified receptor/ligand pair. Central administration of NPS strongly induced locomotor hyperactivity, suppressed all stages of sleep, reduced food intake, potentiated drug-seeking behavior, and had anxiolytic-like effects in several animal models of fear and anxiety. A detailed characterization of the NPS system is therefore crucial for the understanding of its physiological role in health and disease. In the present study, we investigated the (1) in vitro pharmacology of the NPSR antagonist SHA68, (2) effects of intra-amygdala NPS injections on fear-potentiated startle, and (3) phenotype of hetero- and homozygous NPSR-deficient mice. We found that (1) one of the two stereoisomers of SHA68 is much more potent on NPSR than the other stereoisomer, (2) intra-amygdala injections of NPS dose-dependently reduce the expression of fear-potentiated startle, and (3) homozygous NPSR-deficient mice show a reduction of locomotor activity, as well as a weak increase of fear behavior. These findings support an important role of NPS and NPSR in fear and anxiety and suggest that NPSR agonists would have fear-reducing effects. However, NPSR agonism may also have effects which would not be acceptable for an anxiolytic compound.

84. CRF RECEPTORS IN THE DORSAL RAPHE NUCLEUS MEDIATE ANXIETY STATES INDUCED BY POST-WEANING SOCIAL ISOLATION. Forster, G.L.; Bledsoe, A.C.; Oliver, K.M.; Scholl, J.L. Neuroscience Group, Division of Basic Biomedical Sciences, Sanford School of Medicine, University of South Dakota, Vermillion, SD, USA. Post-weaning social isolation of rats is utilized as a model of early life stress. We have previously demonstrated that rats exposed to post-weaning social isolation exhibit greater anxiety-like behaviors as adults. Furthermore, these rats exhibit greater density of corticotropin-releasing factor (CRF) type 2 receptors in the dorsal raphe nucleus (dRN). Therefore, we examined whether antagonism of CRF2 receptors in the dRN reverses the effects of post-weaning social isolation on anxiety states. Male rats were reared in isolation or in groups from day of weaning (postnatal day [P] 21) to mid-adolescence (P42) and then allowed to develop to early adulthood housed in groups. At P62, rats were either infused with vehicle, the CRF1 receptor antagonist antalarmin (0.25-0.5 g) or the CRF2 receptor antagonist antisauvagine (2 g) into the dRN, 20 minutes prior to being introduced to the elevated plus maze. Within vehicle-treated rats, isolation-reared rats showed reduced open arm behavior compared to group-reared rats, confirming the anxiogenic effects of post-weaning social isolation. Infusion of the CRF2 receptor antagonist, but not the CRF1 receptor antagonist, into the dRN of isolation-reared rats increased open arm behavior to that of group-reared rats. Overall, the findings suggest that CRF2 receptors within the dRN mediate anxiety-like states following post-weaning social isolation, and CRF2 receptors may represent an important target for the treatment of anxiety disorders following early-life stressors. Supported by: NIH grants R01 DA019921 and P20 RR015567. A.B. was a University of South Dakota UDiscover scholar.

85. THEANINE MITIGATES CAFFEINE-INDUCED GLOBAL PROCESSING BIASES FOLLOWING EXPOSURE TO STRESS. Mahoney, C.R.; Brunye, T.T.; Giles, G.; Kanarek, R.B. Department of Psychology, Tufts University, Medford, MA 02155. USA. Tea is perceived to be less arousing than coffee, even though both contain behaviorally significant amounts of caffeine. This perceived difference may be attributed to the fact that theanine, which is present in tea but not coffee, has calming effects and may influence brain activity, blood pressure, cortisol, cognition and mood. The purpose of this work was to determine if theanine, alone or with caffeine, would result in a reduced stress response (reduced heart rate, cortisol levels, and feelings of anxiety) following exposure to stressful stimuli and consequently impact performance on a visual attention task known to be influenced by emotional and physiological arousal. Participants (n=36) completed 4 test sessions, crossing caffeine (0 mg, 200 mg) with theanine (0 mg, 200 mg) consumption (capsule form), each following an overnight fast, separated by 3 days, using a double-blind, within-subjects design. To control for caffeine withdrawal, participants were low caffeine consumers. During each session, one of four treatments was administered; participants then viewed a 45 min. highly arousing and negatively valenced video, and finally completed a visual attention task. Heart rate, salivary cortisol, mood and arousal were assessed at three time-points pre and post treatment. Results from the visual attention task revealed a main effect of treatment ($p = .001$), showing a significant global processing bias with caffeine alone, but this bias was mitigated when caffeine was consumed with theanine, such that performance with caffeine and theanine was no different than with placebo or theanine alone. Given the popularity of coffee and tea and that the doses employed are commonly found in commercially available products, results have significant implications for the way in which people process information under stress.

86. INTER-HEMISPHERIC MECHANISMS REGULATING THE MEDIAL PREFRONTAL GLUTAMATE RESPONSE TO STRESS. Lupinsky, D.; Moquin, L.; Gratton, A. Integrated Program in Neuroscience. Douglas Mental Health University Institute/McGill University, Montreal, QC H4H1R3 Canada. While stressors are known to increase medial prefrontal cortex (PFC) levels of glutamate (GLU) the mechanism(s) subserving this response remains to be elucidated. We used in vivo microdialysis and local drug application to investigate the possibility that the PFC GLU stress response reflects increased interhemispheric communication by pyramidal callosal projection neurons. We found that tail-pinch stress elicited comparable increases in GLU levels in the left and right PFC which were sodium- and calcium-dependent and insensitive to local glial cystine-GLU exchanger blockade ([S]-4-carboxyphenylglycine). Unilateral ibotenate-induced PFC lesions abolished the GLU stress response in the opposite hemisphere, as did contralateral microinjections of LY379268, an mGlu2/3 receptor agonist. Local dopamine (DA) D1 receptor blockade (SCH 23390) in the left PFC potently and dose-dependently enhanced the right PFC GLU stress response whereas the same treatment applied to the right PFC produced a much weaker enhancement of the left PFC GLU stress response. Finally, the PFC GLUT stress response was attenuated and potentiated, respectively, following a1-adrenoreceptor blockade (benoxathian) and GABAB (baclofen) receptor activation in the opposite hemisphere. These findings indicate that the PFC GLU stress response reflects, at least in part, activation of GLU-containing callosal neurons located in the opposite hemisphere and that the activity of these neurons is under the control of GLU-, DA-, norepinephrine- and GABA-sensitive mechanisms. In the case of DA, this control was found to be asymmetrical in that the DA input to the left PFC exerts a relatively stronger influence on GLU transmission in the right PFC than does the right PFC DA input on the left PFC GLU stress response. Funded by the Canadian Institutes for Health Research.

87. RECIPE FOR RESILIENCE: EXPLORATIONS OF COPING STRATEGIES AND EFFORT-DRIVEN REWARD TRAINING IN MALE LONG-EVANS RATS. Rhone, A. [1]; Bardi, M. [2]; Franssen, C.L. [1]; Shea, E.S. [1]; Hampton, J.E. [1]; Hyer, M.M. [1]; Huber, J. [1]; Lambert, K.G. [1]. [1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005, USA; [2]Dept. of Psychology, Marshall University, Huntington WV 25755 USA. Effective coping strategies build resilience against stress-induced pathology. Here we explore both predisposed and acquired coping strategies to determine their impact on subsequent stress responsiveness. Our laboratory previously investigated effort-driven reward (EDR) training (building associations between physical effort and rewards) and reported that this training enhanced persistence in an unsolvable task (Hyer et al., 2009). Further, using the back-test assessment, we identified three predisposed coping profiles in young rats (i.e., passive, active, and flexible (variable) coping) and found that flexible coping animals exhibited more effective coping strategies and enhanced NPY-immunoreactivity in the amygdala and BNST (Hawley et al., 2010). In the current study we explored the effects of EDR training on stress responsiveness in rats profiled as passive, active and flexible copers. Following the back-test assessment, 28 male Long-Evans rats were exposed to either EDR training or non-contingent training in the same apparatus for four weeks. Behavioral results indicated that the EDR animals persisted longer than the non-contingent rats in the problem-solving task. Additionally, when challenged by a forced swim, an interaction was found indicating that the EDR-trained flexible copers exhibited the most efficient responses (i.e., conserved floating on the second swim). Further, EDR training and coping profile influenced DHEA/CORT ratios; specifically EDR training and flexible coping groups had higher ratios than the other groups. Additionally, the flexible copers had increased NPY-immunoreactivity in the CA1 region of the hippocampus. In sum, the results suggest that EDR training interacts with predisposed coping strategies to produce enhanced resilience.

88. BILATERAL INACTIVATION OF BASOLATERAL AMYGDALA IMPAIRS LEARNED (BUT NOT INNATE) FEAR RESPONSE IN RATS. Ribeiro, A. M., Barbosa, F. F., Silva, R. H. Department of Physiology, Universidade Federal do Rio Grande do Norte, Natal, Brazil. Studies have suggested that the amygdala has a crucial role in acquisition of aversive memories. However, the possibility that amygdala is merely related to any kind of fear sensation or response, indirectly modulating memories based on fearful situations has been not tested. We investigated the effects of bilateral inactivation of the amygdaloid complex in rats tested in the plus maze discriminative avoidance task. This task concomitantly evaluates aversive memory (by discrimination of the two enclosed arms) and innate fear (by open arm exploration). Wistar rats (3-5 months-old) were implanted with bilateral guide cannulae into basolateral amygdala. After surgery, all subjects were given one week to recover before behavioral experiments. Afterwards, in experiment 1, fifteen minutes prior to training, 0.5 μl of saline or muscimol (1 mg/ml) was infused in each side via microinjection needles. In experiment 2 the animals received injections after the training session and in experiment 3 rats were injected prior to testing session 24 hours after training. The main results showed that (1) pretraining muscimol induced acquisition (evaluated by aversive arm exploration along the training) and memory (evaluated by aversive arm exploration in the test session) deficits, but did not alter innate fear (evaluated by percent time in open arms; (2) post-training muscimol impaired consolidation, inducing increased percent in aversive arm exploration in the test session; (3) pretesting muscimol induced retrieval deficits (evaluated by aversive enclosed arm exploration in the test session), but also did not alter innate fear response. The results suggest that amygdala inactivation specifically modulated the acquisition, consolidation and retrieval of the aversive task, since innate fear was not affected.

89. EFFECTS OF NMA ON ANXIOLYTIC-LIKE BEHAVIOR INDUCED BY DORSAL HIPPOCAMPAL d-OPIOIDERGIC SYSTEM. Jalal Solati1; Mohammad-Reza Zarrindast2 1Department of Biology, Islamic Azad University-Karaj branch, Karaj, Iran 2Department of Pharmacology, Tehran University of Medical Sciences, Tehran, Iran. Dorsal hippocampus is one brain region that plays an important role in anxiety. In present study we have investigated effects of injections of NMDA receptor agonist; NMA on d-opioid receptor agents induced anxiety-like behaviour in rats, using the elevated plus maze test of anxiety. Bilateral administration of d opioid receptor agonist, [D-Pen 2,5]-enkephalin acetate hydrate (enkephalin; 1, 2, 5 and 10 g/rat; 1 l/rat; 0.5l/rat in each side) into dorsal hippocampus (CA1) induced an anxiolytic-like effect, shown by specific increases in the percentage of open arm time (OAT%) and percentage of open arm entries (OAE%). Intra-CA1 injection of d opioid receptor antagonist, naltrindole hydrochloride (0.25, 0.5, 1 and 2 g/rat) produced significant anxiogenic-like behaviour. Furthermore, the intra-CA1 injection of NMDA glutamatergic receptor agonist, NMA (0.125, 0.25, 0.5 and 0.75 g/rat) increased OAT% and OAE%, indicating anxiolyticlike behaviour. However, administration of NMDA glutamatergic antagonist, MK801 (0.125, 0.25, 0.5 and 1 g/rat) has no significant effects on OAT% and decreased OAE% significantly. The ineffective dose of NMA (0.125 g/rat) when co-administred with enkephalin (1, 2, 5 and 10 g/rat), did not decrease the anxiety behavior significantly. An effective dose of NMA (0.5 g/rat) in combination with naltrindole hydrochloride (0.25, 0.5, 1 and 2 g/rat) showed no interactions on OAT%, OAE% and locomotor activity. These results demonstrated that the dorsal hippocampal d opioid and NMDA glutamatergic systems may modulate anxiety behaviours independently.

90. An fMRI STUDY ABOUT EMOTIONAL PERSPECTIVE-TAKING IN KOREAN ADULTS. Son J ; Oh I ; Kim H ; Lee S. Department of Neuropsychiatry, Chungbuk National University Hospital. Purpose ; Emotional perspective-taking, that is, the ability of taking either one's own emotional perspective or the perspective of others is very important for people to live in social community. This study aimed to investigate the difference of brain activity in viewing common emotional situation according to perspective-taking in Korean adults. Methods ; Using fMRI, brain activities were measured while performing the task viewing common emotional situation(happy, anger, sad, neutral) on either his own perspective(self-perspective) or the perspective of his mother(third-person perspective) in fourteen healthy adult Korean. The relatively activated brain area on either self-perspective or third-person perspective were investigated, especially according to each emotional situation. Results ; 1) The common relatively activated brain area on self-perspective in each emotional situation were right precentral gyrus(BA 4) and left superior temporal gyrus(BA 22). 2) But, there were some difference of relatively activated brain area on other-perspective in each emotional situation. In happy emotional situation, the activated brain regions were those including the prefrontal areas. But in either sad or angry emotial situation, the activation of prefrontal areas were not observed. Conclusions ; This study demonstrate that the activated brain region according to emotional perspective-taking would be different according to each emotional situation.

91. ANTAGONISM OF TRANSIENT RECEPTOR POTENTIAL VANILLOID TYPE-1 (TRPV1) RECEPTORS IN THE MEDIAL PREFRONTAL CORTEX REDUCES THE EXPRESSION OF CONTEXTUAL FEAR CONDITIONING IN RATS Terzian, A.L; Corrêa, F.M; Guimarães, F.S; Resstel, L.B. Dept of Pharmacology, FMRP – USP Introduction: Contextual fear conditioning is evoked by animal re-exposure to an environment that has been previously paired with an aversive or unpleasant stimulus. This model causes in rodents freezing immobility and cardiovascular changes such as increases in mean arterial pressure (MAP) and heart rate (HR). And it is associated with a marked increase in neuronal activity in structures involved with defense reactions, such as the ventral portion of medial prefrontal cortex. Previous studies indicate that glutamate-mediated neurotransmission into the vMPFC is involved in these changes. Since TRPV1 receptors can modulate glutamate release and are expressed in the vMPFC, the present work tested the hypothesis that TRPV1 antagonism would inhibit the behavioral expression. Methods: Male Wistar rats (weight between 230-260g) with cannulae aimed at the vMPFC, received bilateral microinjections of the TRPV1 receptor antagonist capsazepine in different doses (1, 10 and 60 nmol/200 nL) and were placed again in the experimental chamber where they had received footshocks 48h before. Freezing behavior and cardiovascular responses alteration were recorded for 10 min. Results: Capsazepine at the higher dose (60 nmol, n=8) reduced freezing duration (F3,25= 12.55; $p<0.05$) and cardiovascular responses (MAP: $_{F16,238}$= 228.9; $p<0.001$. HR: $F_{16,238}$= 270.8; $p<0.001$) in conditioned animals when compared to vehicle-injected animals (n=8). The other doses of 1 (n=6, $p>0.05$) and 10 (n=7, $p>0.05$) nmol of capsazepine did not have any effect on these responses when compared to vehicle group. Conclusions: The present results suggest that TRPV1 receptors present in the vMPFC play an important role on behavior and cardiovascular changes related to the expression of contextual fear conditioning. Financial support: Fapesp, CNPq

92. LACK OF ANTIDEPRESSANT LIKE BEHAVIORAL EFFECTS OF CHRONIC VAGUS NERVE STIMULATION IN THE RAT DESPITE NEUROCHEMICAL END MOLECULAR ANTIDEPRESSANT LIKE EFFECTS. Utzeri, C.; Biggio, F.; Olla, P.; Marrosu, F.; Follesa, P.Vagus nerve stimulation (VNS) is used to treat pharmacotherapy-resistant epilepsy and depression. The mechanisms underlying the therapeutic efficacy of VNS remain unclear, however. We examined the effects of VNS on hippocampal neuronal plasticity and behavior in rats. Cell proliferation in the hippocampus of rats subjected to acute (3 h) or chronic (1 month) VNS was examined by injection of bromodeoxyuridine (BrdU) and immunohistochemistry. Expression of doublecortin (DCX) and brain-derived neurotrophic factor (BDNF) was evaluated by immunofluorescence staining. The dendritic morphology of DCX+ neurons was measured by Sholl analysis. Our results show that acute VNS induced an increase in the number of BrdU+ cells in the dentate gyrus that was apparent 24 h and 3 weeks after treatment. It also induced long-lasting increases in the amount of DCX immunoreactivity and the number of DCX+ neurons. Neither the number of BrdU+ cells nor the amount of DCX immunoreactivity was increased 3 weeks after the cessation of chronic VNS. Chronic VNS induced long-lasting increases in the amount of BDNF immunoreactivity and the number of BDNF+ cells as well as in the dendritic complexity of DCX+ neurons in the hippocampus. In contrast to chronic imipramine treatment, chronic VNS had no effect on the behavior of rats in the forced swim or elevated plus-maze tests. Both chronic and acute VNS induced persistent changes in hippocampal neurons that may play a key role in the therapeutic efficacy of VNS. However, these changes were not associated with evident behavioral alterations characteristic of an antidepressant or anxiolytic action.

93. EFFECTS OF SELECTIVE AND NOT SELECTIVE GABA-BENZODIAZEPINE AGONISTS ON THE OXIDATIVE STATUS OF PERIPHERAL BLOOD LYMPHOCYTES, GRANULOCYTES AND MONOCYTES UNDER THE IMPACT OF HIGH ANXIETY LEVEL IN MICE. Balboa, J; Novio, S.; Nunez, M.J.; Tarrio, D.; Dorado, T.; Rodriguez, B.; Marino, J.C.; Freire-Garabal, M. Dept. of Pharmacology. School of Medicine. University of Santiago de Compostela. C/ San Francisco, s/n. 15782 Santiago de Compostela. SPAIN. In this study, we investigated the effects of selective and not selective GABAbenzodiazepine agonists on the levels of intracellular reactive oxygen species in lymphocytes, granulocytes and monocytes from the peripheral blood of mice subjected to a high anxiety model by using a 2',7'-dichlorofluorescein diacetate (DCFH-DA) probe. The behavioural light/dark choice test was used to distinguish highly anxious from less anxious mice. Our results showed that a high anxiety level significantly increased the generation of reactive oxygen species in the peripheral blood lymphocytes, granulocytes and monocytes and these effects were significantly reduced by the treatment with GABAbenzodiazepine agonists, especially with alprazolam.

94. EFFECTS OF SELECTIVE AND NOT SELECTIVE GABA-BENZODIAZEPINE AGONISTS ON IMMUNE-MEDIATED CUTANEOUS INFLAMMATORY DISEASES. Freire-Garabal, M.; Novio, S.; Tarrio, D.; Rodriguez, B.; Marino, J.C.; Dorado, T.; Nunez, M.J.; Dept. of Pharmacology. School of Medicine. University of Santiago de Compostela. C/ San Francisco, s/n. 15782 Santiago de Compostela. SPAIN. Psychologic stress (PS) is well recognized to provoke, exacerbate, and propagate many cutaneous inflammatory diseases (CID) associated with abnormal epidermal barrier function via hypothalamic-pituitary-adrenal (HPA) axis activation with subsequent modulation of the inflammatory response. Corticotropin Releasing Hormone (CRH) and CRH-skin receptor over-expression is usually associated with the severity of the disease. In this study we evaluated the effects of a full agonist at the benzodiazepine receptor that binds to four alpha-subtypes of the receptor (alpha-1,-2,-3,-5) (alprazolam 1 mg), and of an agonist selective for the alpha-1 subtype of the gamma amino butyric acid-receptor subtype A (GABA-A) receptor (zolpidem 5 mg), on an experimental model of CID in stressed mice. Our studies showed that GABAbenzodiazepine agonists, mainly, alprazolam reduced the PS-induced increase in the permeability barrier homeostasis and the inflammatory response in vivo in a mouse model of psoriasis. Plasma and skin CRH levels were also calculated and found that alprazolam significantly reduced the PS-induced increases. These results suggest that anxiolytic treatment with benzodiazepines may effectively counteract the adverse effects of PS on cutaneous dermatoses associated with abnormal epidermal barrier function, such as psoriasis and atopic dermatitis.

95. THE IMPACT OF STRESS IN POLICE: A STUDY OF STRESS-RELATED CAUSES. Iglesias, M.; Nunez-Iglesias, M.J.; Novio, S.; Freire-Garabal, M. Dept. of Pharmacology. School of Medicine. University of Santiago de Compostela. C/ San Francisco, s/n. 15782 Santiago de Compostela. SPAIN. Police work tends to be regarded as inherently stressful. This study assessed responses to the Occupational Stress in the Civil Guard Police. A cross-sectional questionnaire survey was conducted by administering a postal questionnaire to 600 within a county police force (Asturias, Spain). These ranks were selected for the survey on the basis both of their predominance within the organization, constituting 80% of the police force, and indications from our experience* of increased liability to strain. The questionnaire was designed to assess levels of strain associated with a series of potential home and work related stressors, health and job satisfaction, in addition to demographic information. The organization of the service and environmental influences were found to be major determinants of stress. Police expressed greater job-related pressure from "organizational structure and climate" than from "intrinsic factors to the job". Negative correlation was found between stress, job satisfaction and health score. *AUGC (Civil Guard Unified Association) Safety and Health at Work coordinator.

96. INHIBITORY EFFECTS OF FLUOXETINE ON THE PERMEABILITY BARRIER HOMEOSTASIS AND THE INFLAMMATORY RESPONSE IN VIVO IN A MOUSE MODEL OF PSORIASIS UNDER DEPRESSION CONDITIONS. Novio, S.; Nunez, M.J.; Tarrio, D.; Marino, J.C.; Dorado, T.; Rodriguez, B.; Freire-Garabal, M. Dept. of Pharmacology. School of Medicine. University of Santiago de Compostela. C/ San Francisco, s/n. 15782 Santiago de Compostela. SPAIN. Corticotropin Releasing Hormone (CRH) over-expression is usually associated with the severity of the disease under depression conditions via hypothalamic-pituitary-adrenal (HPA) axis activation. CRH-skin receptor activation can provoke and exacerbate abnormal epidermal barrier function with subsequent modulation of the inflammatory response that is on the basis of most of the cutaneous inflammatory diseases. Our studies showed that fluoxetine reduced the unpredictable chronic mild stress (UCMS)-induced increase in the permeability barrier homeostasis and the immune response in vivo in a mouse model of psoriasis. Skin CRH activity was also evaluated and found that fluoxetine significantly inhibited UCMS-induced over-expression. These results suggest that antidepressant treatment with fluoxetine may effectively counteract the adverse effects of PS on cutaneous dermatoses associated with abnormal epidermal barrier function, such as psoriasis.

97. INHIBITORY EFFECTS OF ALPRAZOLAM ON THE DEVELOPMENT OF ACUTE EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS IN STRESSED RATS. Nunez, M.J.; Novio, S.; Freire-Garabal, M. Dept. of Pharmacology. School of Medicine. University of Santiago de Compostela. C/ San Francisco, s/n. 15782 Santiago de Compostela. SPAIN. The progression and development of multiple sclerosis (MS) an inflammatory demyelinating and neurodegenerative disease with a presumed T-cell driven autoimmune origin has long been hypothesized to be associated with stress. Benzodiazepines have been observed to reduce negative consequences of stress on the immune system in experimental and clinical models, but there is no data on their effects on MS, or experimental autoimmune encephalomyelitis (EAE), a model for human MS. We designed experiments conducted to ascertain whether alprazolam could modify the clinical, histological and neuroendocrine manifestations of acute EAE in Lewis rats exposed to a chronic auditory stressor. EAE was induced by injection of myelin basic protein (MBP) emulsified in complete Freunds adjuvant (CFA). Stress application and treatment with drugs (placebo or alprazolam) were initiated 5 days before inoculation and continuing daily for the duration of the experiment (days 14 or 28 postinoculation). Our results show significant increases in the severity of neurological symptoms, the histological lesions of the spinal cord (inflammation and demyelination), and the corticosterone plasmatic levels in stressed rats compared to those non-stressed ones. Treatment with alprazolam reversed the adverse effects of stress. These findings could have clinical implications in patients suffering from MS treated with benzodiazepines, so besides the psychopharmacological properties of alprazolam against stress, it has beneficial consequences on EAE.

98. EFFECTS OF AN ADULT-ONSET CALORIE RESTRICTION ON FEAR BEHAVIOUR TOWARDS A PREDATOR ODOUR. Kent, S.; Govic, A.; Levay, E.A.; Penman, J.; Paolini, A.G. School of Psychological Science, La Trobe University, Bundoora, VIC 3086, Australia. Calorie restriction (CR) can modulate the expression of anxiety and fear behaviour. The effect of various levels of calorie restriction on fearfulness towards a predatory odour was assessed in adult hooded Wistar rats. Two treatment groups were examined: a chronic 25% (CR25%) and a chronic 50% (CR50%) restriction group, calorie restricted for four weeks before testing. All groups demonstrated defensive behaviour when exposed to a cloth saturated with tom cat urine. Only the CR25% group demonstrated an enhancement of fear responses compared to controls. This was demonstrated by the longer latency and fewer entries into the zone closest to the predator odour, the greater time taken to make first contact with the odour, and overall fewer contacts with the cat urine throughout the duration of the test. Further, the CR25% group also exhibited more risk assessment behaviours; flat-back approach and attention was significantly higher in this group compared to controls. Non-defensive grooming behaviour was also significantly diminished in the CR25% when compared to controls. Although calorie restriction typically has anxiolytic effects in anxiety tests of forced exploration, reactions to potential threats have not yet been characterised in animals administered a moderate and substantial calorie restriction. These findings indicate that moderately restricting calories can enhance the display of defensive behaviour elicited by the presence of a predator odour.

99. FEAR-INDUCED ANTINOCICEPTION IN MICE: EFFECTS OF INTRA-PERIAQUEDUCTAL GRAY (PAG) INJECTIONS OF 5-HT2 RECEPTOR AGONIST AND ANTAGONIST. 1,3Baptista, D.; 2,3Nunes-de-Souza, R.L.; 1,3Canto-de-Souza, A. Dept Psychology-Psycobiology group/UFSCar, Pharmacol, FCF/Unesp/Araraquara, 3Program of Physiological Sciences-CCBS-Federal University of So Carlos-UFSCar, Brazil. A single exposure in the elevated plus maze (EPM), an animal model of anxiety, induces antinociception in mice (Psychopharmacol., v.150, p. 300-310, 2000). In addition, the anxiolytic-like effect produced by intra-PAG injections of mCPP (a 5-HT2B/2C receptor agonist) was blocked by local pretreatment with 5-HT2A/2C receptor antagonist, ketanserin, suggesting a mediation of the 5-HT2C receptors in the anxiety (Behav. Brain Res., v.187, p.7279, 2008). In the present study we investigated the effects of intra-PAG mCPP (0.01, 0.03 and 0.1 nmol/0.1 μl) and ketanserin (10 nmol/0.1 l) on the EPM open arm confinement-induced antinociception (OAA) in mice. Nociception was assessed by the writhing test (intraperitoneal injection of 0.6% acetic acid; 0.1 ml/10g) in mice confined in the open or enclosed arms of the EPM. Intra-PAG mCPP increased OAA [$F(3,80)=11,31$, $P < 0,0001$] only at the lower dose (0.01 nmol) (Experiment 1). In Experiment 2, this enhancement in the antinociceptive response was selectively and completely blocked by local pretreatment with ketanserin ($p < 0.007$). Although intra-PAG mCPP (0.01 nmol) also produced antinociception in enclosed arm confined mice (Exp. 1), this effect was not confirmed in the Experiment 2. Present results corroborate previous studies showing that open arm confinement induces antinociception and suggest that the 5-HT2C receptors located within the PAG play a role in this type of fear-induced pain inhibition in mice. Financial Support: UFSCar, CAPES.

100. EFFECTS OF DIFFERENT STRESSORS ON THE SEROTONERGIC ACTIVITY IN THE DORSAL RAPHE NUCLEUS (DRN). Garcia-Saldivar, N.L.; Gonzalez-Lopez, M.R.A.; Castillo-Roberto, G.; Dominguez, R.; Cruz-Morales, S.E. Psychopharmacology, FES-Iztacala and FES-Zaragoza, UNAM, Mexico. Serotonin (5-HT) plays a critical role in stress related behaviors, and in anxiety. Stress induced by inescapable shock activates DRN and increase the 5-HT. The objective of present study was to analyze the effects of stress induced by restraint (R), training in the elevated T maze (ETM) and the combination of R+ETM on the serotonergic activity in the DRN in male rats. Male Wistar rats (250-270 g) were assigned to 10 independent groups: a control group (C), 3 trained in the ETM, 3 exposed to R 60 min (these groups were sacrificed 0, 1, or 24 hr after procedures), and 3 groups exposed to R and trained 0, 1, or 24 hr later in the ETM (R+ETM) and sacrificed immediately. Samples of the DRN were obtained; the [5-HT] and [5-HIAA] were quantified by HPLC. Activity was calculated as [5-HIAA]/ [5-HT]. Statistics: Independent analyses of variance (ANOVA) were used to determine any significant differences for [5-HT], [HIAA] and the activity. Immediately after R, activity was higher than C, while 5-HT was lower. One hr later, 5-HT was higher in R+ETM than in ETM; activity was higher in ETM than in C and R+ETM. In those sacrificed 24 hr later, the activity of ETM was higher than C. The higher activities observed results from the lower 5-HT observed in those groups. The results indicate that the effects of R, ETM and R+ETM on serotonergic activity varies with the interval between treatment and sacrifice, and that the changes are related with the neurotransmitter amount and not with its metabolite, implying that stress could modify 5-HT synthesis and/or transport. Supported by PAPCA63, UNAM, FES-Iztacala.

101. NITRIC OXIDE RELEASE WITHIN PERIAQUEDUCTAL GRAY MODULATES DEFENSIVE-LIKE BEHAVIORS AND NOCICEPTION IN MICE. Miguel, T.T.1; Nunes-de-Souza, R.L.1,2. 1. Interinstitutional Graduate Program in Physiological Sciences, Federal University of Sao Carlos and Univ Estadual Paulista - UNESP; 2. Pharmacology, UNESP, Araraquara, SP, Brazil. Chemical stimulation of the midbrain periaqueductal gray matter (PAG) elicits defensive behaviors (flight, jumps) and antinociception. In addition, intra-PAG injection of SIN-1, a nitric oxide (NO) donor, produces flight in rats. However, intra-PAG SIN-1 provoked seizures and death (excitotoxicity & peroxynitrite synthesis) in mice. Here we investigated the effects of intra-PAG NOC-9 (N9), a new NO donor (peroxynitrite production free) on defensive behavior and nociception. Mice (n= 12-15) received intra-PAG N9 (75 nmol) or vehicle (veh) and were placed in an arena (30x21x25 cm) to recording the frequency of jumping and rearing; duration (seconds) of running, freezing and locomotion (5-min). Two other groups (n= 8 each) received 2.5% formalin injection in the hind paw (nociception test) and 25 minutes later intra-PAG injection (see above) and the time (seconds) spent on licking the paw was recorded (10-min). N9 induced defensive behaviors [running (veh: 0; N9: 9.5 +/- 2.4); freezing (veh: 0; N9: 53.5 +/- 15.0); jump (veh: 0; N9:3 +/- 1)], decreased exploratory behavior [rearing (veh: 46 +/- 6; N9: 16 +/- 5); locomotion (veh: 101.9 +/- 8.9; N9: 38.3 +/- 11.3)] and decreased nociceptive response (veh: 84.5 +/- 13.1; N9: 12.5 +/- 4.8). These results indicate that NO release within the PAG modulates defensive behaviors and nociception in mice, suggesting that this gas neurotransmitter plays a role in the mediation of pathologies related to defensive reaction (e.g., anxiety disorders) as well as in some types of fear-induced pain inhibition.

102. NK3-RECEPTOR AGONIST SENKTIDE PROMOTES ANXIOLYTIC AND ANTIDEPRESSANT-LIKE EFFECTS, COMPONENTS OF EPISODIC-LIKE MEMORY AND IN VIVO ACh TRANSMISSION IN AGED RATS. Schaeble, S.; Buddenberg, T.; Topic, B.; Huston, J.P.; de Souza Silva, M.A. Center for Behavioral Neuroscience, Heinrich-Heine-University, Duesseldorf, Germany. The neurokinin3 receptor (NK3-R), has been identified in brain regions which have been implicated in processes related with learning and memory as well as emotionality. The effects of NK3-R agonism on emotionality (anxiety and depression), learning and memory performance and ACh neurotransmission in aged rats have not been determined. Our aim in this study was to assess the effects of 0.2 mg/kg and 0.4 mg/kg senktide, a highly potent NK3 receptors agonist, in the aged (24 months old) Wistar rat on: (a) parameters of anxiety in an open field test, (b) antidepressant-like action in the forced swimming test, (c) episodic-like memory and (d) the activity of cholinergic neurons of the basal forebrain by in vivo microdialysis and HPLC. Results: Senktide produced dose-dependently anxiolytic and antidepressant-like effects as assessed by the open field test and the forced swimming test, respectively. Senktide did not establish episodic-like memory in aged rats, but reinstated components of episodic-like memory, namely object-memory for temporal order and for spatial displacement. Treatment with senktide also increased ACh levels in the frontal cortex, amygdala and hippocampus. The results advance our understanding of the behavioural and neurochemical functions of the NK3-R in learning and memory processes and anxiety and antidepressant-like behaviour in aged rats. Supported by DFG grant DFG DE 792/2-4

103. ESCAPABLE AND INESCAPABLE STRESS DIFFERENTIALLY ALTER 5-HT1A RECEPTOR-MEDIATED INHIBITION OF NEURONAL FIRING RATES WITHIN THE DORSOMEDIAL DORSAL RAPHE NUCLEUS. Rozeske, R.R.1; Evans, A.K2.; Watkins, L.R.1; Lowry, C.A.2; Maier S.F.1 1: Dept. of Psychology, University of Colorado-Boulder, USA 2: Dept. of Integrative Physiology, University of Colorado-Boulder, USA Traumatic experiences can profoundly enhance the development of mental disorders. However, not all organisms react similarly to aversive or traumatic experiences. Whether an organism can exert behavioral control during a stressful experience is an important factor determining the behavioral and physiological impact of the stressor. For example, uncontrollable (inescapable, IS), but not controllable (escapable, ES) stress, potently activates the dorsal raphe nucleus (DRN) and sensitizes serotonin (5-HT) neurons within the DRN for a number of days. However, the mechanism underlying this sensitized 5-HT response has not been elucidated. It has been suggested that the high levels of extracellular 5-HT within the DRN produced by IS desensitizes 5-HT1A inhibitory somatodendritic autoreceptors within the DRN for a period of time, thereby yielding sensitized DRN neurons due to a reduction in this source of inhibitory control. To examine this hypothesis extracellular single unit recordings within the dorsomedial region of the DRN were performed 24 hrs following ES, IS, or homecage control (HC) treatment. Slices were perfused with varying concentrations of the 5-HT1A receptor agonist ipsapirone and 5-HT. Prior IS, but not ES, decreased the ability of 5-HT and ipsapirone to reduce baseline neuronal firing rate, compared to HC, at a number of doses. Additionally, rats were given ES 24 hrs prior to IS, a procedure termed behavioral immunization because a prior experience with ES blunts the usual behavioral and neurochemical consequences of IS. 5-HT1A receptor mediated inhibitions following behavioral immunization were investigated. Together these results suggest a desensitization or downregulation of the 5-HT1A receptor in the DRN following IS, but not ES, offering a possible mechanism for the sensitized 5-HT response observed following IS, but not ES.

104. STRESS DURING GESTATION ALTERS ANTEPARTUM ANXIETY-LIKE BEHAVIOR AND HIPPOCAMPAL CELL PROLIFERATION IN THE FEMALE. Pawluski, J.L.; van den Hove, D.L.; Rayen, I.; Prickaerts, J.; Steinbusch, H.W. Department of Neuroscience, Faculty of Health, Medicine and Life Sciences, Maastricht University, The Netherlands. Recent estimates document that 10-20% of women have mood disorders, such as depression and anxiety, during the perinatal period yet little is known about the mechanisms behind these alterations in mood. In animal models gestational stress is commonly used to determine how stress during pregnancy may affect offspring outcomes. However, very little research has investigated the effect of gestational stress on maternal 'mood' and neural correlates of these behaviors. Therefore the aim of the present study was to determine whether gestational stress alters anxiety- and depressive-like behaviors and hippocampal neurogenesis in the mother during pregnancy. Age-matched pregnant and virgin adult Sprague-Dawley females were divided into four conditions: 1) Cage Control, 2) Behavioral Control, 3) Early Stress, and 4) Late Stress. Females in the stress conditions were restrained under bright light on gestation days (GD) 5-11 (Early Stress) or GD11-17 (Late Stress) and at matched time points in virgin females. To assess 'mood' females were tested on the elevated zero maze and forced swim test on GD 18-20 and at matched points in virgin females. Results demonstrate that pregnant females restrained during early gestation tend to exhibit increased anxiety-like behavior. Additionally, pregnant females subject to stress have increased cell proliferation in the hippocampus compared to non-stressed pregnant females. Further work will determine the effect of stress on new cell survival in the hippocampus of the virgin and pregnant female.

105. PRIOR EXPOSURE TO STRESS FACILITATES FEAR RESPONDING TO PARTIAL AND PERFECT CUES. Baratta, M.V.; Chow, B.Y.; Han, X.; Goosens, K.A.; Boyden, E.S. Media Lab, McGovern Institute for Brain Research, and Department of Brain and Cognitive Sciences, MIT, Cambridge, MA 02139 USA. Animals must learn how to respond to cues that predict aversive events, to survive. However, in the natural world the predicted value of cues varies over time, and thus neural circuits that implement such learning likely invokes other information, including those derived from earlier unrelated experiences, to attempt an optimal strategy of learning and action. It is known that in Pavlovian fear conditioning the fear response is weakened when CSs and USs are not perfectly paired during acquisition (CS-US contingency <100%). We explored the effects of prior immobilization stress on a contingency reduction protocol in which the percentage of tone-footshock pairings is varied across groups but the total number of tones and shocks is held constant. In EXP 1, mice conditioned to either 25% or 50% CS-US contingency displayed reduced freezing during a retrieval tone test compared to 75% and 100% groups. In EXP 2, prior immobilization stress increased fear responding to the tone in all contingency groups. In EXP 3, exposure to stress after conditioning had no effect on later fear responding which suggests that the observed stress enhancement resulted from modulating the acquisition rather than the expression of fear. In order to characterize the neural inputs that mediate the stress effects on acquisition, we adapted a light-sensitive proton pump (termed Arch from H. sodomense) to enable in vivo cell-type specific silencing in a temporally precise fashion. This novel opsin and other optical neural control tools that we have developed offer the ability to precisely parse out the interaction between prior experience and aversive learning.

106. THE ANANDAMIDE HYDROLYSIS INHIBITOR URB597 IN THE RAT BASOLATERAL AMYGDALA ENHANCES MEMORY CONSOLIDATION FOR EMOTIONAL EXPERIENCES Campolongo P.1; Roozendaal B.2; Ratano P.1; Trezza V.1; Hauer D.3; Schelling G.3; McGaugh J.L.4; Cuomo V.1 1Dept. Physiology and Pharmacology, Sapienza Univ. of Rome, Italy; 2Dept. Neuroscience, Univ. Medical Center Groningen, The Netherlands; 3Dept. Anaesthesiology, Ludwig Maximilians Univ. Munich, Germany; 4Center for the Neurobiology of Learning and Memory, Univ. of California, Irvine, CA, USA Extensive evidence indicates that the basolateral complex of the amygdala (BLA) modulates the consolidation of memories for emotionally arousing experiences, an effect that involves the activation of the glucocorticoid system. We have recently shown that the CB1 receptor agonist WIN55,212-2 (5-50 ng/0.2 μL per side), infused bilaterally into the BLA of male Sprague-Dawley rats immediately after inhibitory avoidance training, enhances memory consolidation; this effect is dependent on activation of CB1 cannabinoid receptors. Furthermore, we have shown that CB1 activity within the BLA mediates glucocorticoid effects on memory consolidation. The use of drugs that directly bind and activate brain cannabinoid receptors is limited by their abuse liability. Nowadays, more innovative and selective pharmacological approaches exist to enhance endocannabinoid signalling in the brain. Several lines of evidence identify, indeed, indirect cannabinoid agonists as a novel therapeutic approach for the treatment of central nervous system disorders. We therefore tested whether the anandamide hydrolysis inhibitor URB597 influenced memory consolidation for emotional events. Post-training intra-BLA infusions of URB597 (3-30 ng/0.2 μL per side) enhanced 48-h inhibitory avoidance retention performance. Intra-BLA infusions of a low and non-impairing dose of the CB1 antagonist AM251 (0.14 ng/0.2 μL per side) blocked the memory enhancement induced by concurrent administration of URB597. This result suggests that the memory enhancing effect of URB597 is dependent on anandamide-mediated activation of CB1 cannabinoid receptors. The present findings further support the notion that the activation of the endocannabinoid system in the BLA enhances memory consolidation for emotional experiences.

107. IS THE CURE WORSE THAN THE DISEASE? EXPLORING THE ATYPICAL RESPONSE OF ADOLESCENTS TO PAROXETINE. McGregor, IS; Karanges, E; Li, KM; Motbey, C; Sarker, R; Kashem, MA; Callaghan, PD. Schools of Psychology and Pharmacology, University of Sydney, Australia. Antidepressant drugs lack efficacy, and can promote suicidal ideation and anxiogenic effects in human adolescents. It is widely acknowledged that one of the worst drugs for causing adverse adolescent effects is the SSRI antidepressant paroxetine. However it is unclear what causes the paradoxical response of adolescents to this drug. In the present study we compared the effects of chronic paroxetine in adolescent (PND 28+) versus adult (PND 60+) Wistar rats. The drug was continuously administered in drinking water for 3 weeks at a target dose of 10 mg/kg. Drug treatment caused no significant loss in body weight in adolescent or adult rats relative to placebo treated controls. However during drug administration adolescent rats on paroxetine showed greater anxiogenic effects of the drug relative to adults, particularly on the social interaction and novelty suppressed drinking tests. Adolescent rats also failed to show an antidepressant-like effect of paroxetine on the forced swim test (FST), while adult rats given the drug showed a typical decrease in immobility and increase in active escape behaviors on this test. Two adolescent rats on paroxetine died unexpectedly after the FST suggesting a compromised response to physical stress. Analysis of plasma paroxetine levels showed that adolescents had significantly lower plasma levels of the drug than adults, despite showing a greater adverse reaction to the drug. Ex vivo analysis at the end of dosing showing equivalent effects of drug treatment on brain 5-HT (normal) and 5-HIAA levels (decreased) in adolescent and adult rats. However markers of dopamine function in the striatum were decreased in adolescents while being increased in adults. Proteomic analysis of the hippocampus showed upregulation of apoptosis related proteins (e.g. BH-3 interacting domain death agonist) in adolescents rats only and upregulation of neurotrophic proteins (e.g. neurogenin 1) only in the adults. Overall these results suggest that rats can be used to model the unusual response of human adolescents to antidepressant drugs and provide some interesting clues as to the neural mechanisms underlying this atypical response.

108. LIMBIC-CORTICAL NETWORK DIFFERENCES BETWEEN RESPONDERS AND NON-RESPONDERS TO FLUOXETINE ANTIDEPRRESSANT TREATMENT IN RATS. Eimeira Padilla, Jason D. Shumake, Douglas W. Barrett, Eva C. Sheridan, and F. Gonzalez-Lima. Institute for Neuroscience, Departments of Psychology and Pharmacology, University of Texas at Austin, 1 University Station A8000, Austin, TX 78712, USA. Neural network effects of antidepressant treatment with the selective serotonin reuptake inhibitor (SSRI) fluoxetine were investigated using Holtzman rats. Animals underwent the forced swim test (FST) and immobility time was scored. On the next day, animals began receiving two weeks of fluoxetine (5 mg/kg) or vehicle and were retested in the FST at the end of treatment. Antidepressant behavioral effects of fluoxetine were analyzed using a ratio of immobility during pre- and post-treatment FST sessions. Brains were analyzed for regional metabolic activity and network interactions using quantitative cytochrome oxidase histochemistry and structural equation modeling. Fluoxetine exerted a protective effect against FST-induced immobility behavior in Holtzman rats. The mean regional metabolism of the nucleus accumbens shell differentiated fluoxetine-treated from vehicle-treated subjects, but not

treatment responders from non-responders. The metabolic activities of infralimbic cortex and medial septum were predictive of antidepressant behavioral response, but these regions contributed opposite influences as evidenced by their opposite relationship to FST-induced immobility. A cortico-cortical correlogram revealed complex interactions among frontal cortex regions in fluoxetine responders that were less evident among non-responders and absent in the vehicle-treated group. Structural equation modeling of cortico-subcortical interactions revealed that direct path influences between the dorsal raphe nucleus and the lateral habenula and prelimbic cortex switched from negative to positive between fluoxetine-responders and non-responders, respectively. The observed differences in limbic-cortical interactions may represent an important neural network mechanism mediating the antidepressant SSRI response via modulation of the effective connectivity between the dorsal raphe and the lateral habenula and prelimbic cortex.

109. SOCIAL DEFEAT AND ISOLATION: AUTONOMIC, ADRENOCORTICAL AND BEHAVIORAL EFFECTS IN RATS. Pico-Alfonso, M.A.1; Mastorci, F.1; Razzoli, M.I.2; Arban, R.2; Sgoifo, A1. 1) Dept. Evolutionary and Functional Biology, University of Parma, Italy. 2) GlaxoSmithKline, Verona, Italy. Unfavourable social environments play a relevant role in the onset and progression of depressive disorders. The present study aimed at establishing a rodent model of depression based on a negative social episode followed by prolonged social isolation in rats. Adult male rats were implanted with telemetry transmitters for ECG, temperature (T) and activity (Act) recordings. Treated animals were exposed to a social defeat episode followed by 4-week isolation (SDI, n=22), while control counterparts (CTR, n=22) remained undisturbed with female partners. During the isolation period, cardiac sympathovagal balance in the open-field test (day 9 and 23 post-defeat) and hypothalamic-pituitary-adrenocortical axis (HPAA) reactivity to dexamethasone suppression test (day 10 post-defeat) were assessed. Before and after defeat, hedonic behavior (% sucrose solution consumption) was measured and heart rate (HR), T, and Act sampled around-the-clock to assess their circadian rhythmicity. At sacrifice, adrenal glands were removed and weighed. Unlike CTR rats, SDIs did not show habituation of cardiac autonomic responsivity (tachycardia and vagal withdrawal) to the open field test. HPAA function appeared to be altered in SDI rats as compared to CTR counterparts, as shown by significantly higher plasma corticosterone levels following dexamethasone injection and adrenal weight increase. SDIs also exhibited a significant decrement of sucrose solution consumption (anhedonia) 3 weeks after defeat, as well as a reduction in the amplitude of HR and Act daily rhythms across the first week of isolation. In conclusion, social defeat and a prolonged period of isolation produced a set of physiological and behavioral changes in rats which resemble those observed in depressed and chronically stressed subjects.

110. INHIBITION OF nNOS AND sGC IN THE RAT DORSAL HIPPOCAMPUS INDUCES ANTIDEPRESSANT-LIKE EFFECTS Sato, V.A.H.*; Sales, A. J.*; Joca, S.R.L*. *Laboratory of Pharmacology, Department of Physics and Chemistry. School of Pharmaceutical Sciences of Ribeiro Preto University of So Paulo. Introduction: Nitric oxide (NO) is thought to be involved on the neurobiology of depression. The injection of NO synthase (NOS) inhibitor into the dorsal hippocampus (DH) induces antidepressant-like effects in rats, thus, implicating local NO levels in the development of depressive-like behaviors. Therefore, the aim of the present study was to investigate the involvement of the hipocampal neuronal NOS isoform and of the guanylyl ciclase (GC), main NO target, in the modulation of the depressive-like behavior in the rat forced swimming test (FST). Methods: After a stereotaxic surgery, male Wistar rats with guide-canulas aimed at the DH were submitted to pretest (PT: 15 min of swimming) and received a local injection of n-propyl-L-ω-arginine (NPLA, selective nNOS inhibitor: 0,00001, 0.0001, 0.01 or 1 nmol/0.5 L), ODQ (sGC inhibitor: 0.1, 1.0 or 10 nmol/0.5 L) or saline (0.5 L). One day later, the immobility time (IT) were registered at a 5 min of swimming. All protocols were approved by a local ethical committee (Proc. N. 08.1.1133.53.4).Results: Intra-DH administration of NPLA and of ODQ significantly reduced the IT in the FST ($F_{4,30} = 5{,}807$, $p<0.01$; $F_{3,21} = 7.88$, $p<0.01$; respectively), an antidepressant-like effect in the FST.Discussion: These results indicate that inhibition of nNOS and of sGC in the DH induces antidepressant-like effects. It suggests that stress leads to nNOS activation and NO synthesis in the DH, what may trigger sGC activation and behavioral consequences, such as the behavioral despair in the FST. The involvement of 5HT in such effects is now under investigation.Finnancial Support: CNPq, FAPESP.

111. A DEFINITION OF OPTIMAL DOSES OF CHRONIC ANTIDEPRESSANT TREATMENT BY PARAMETERS OF SUCROSE TEST, ANXIETY AND LOCOMOTION TESTS IN NAÏVE C57BL6 MICE. Gorenkova N.#; Dolgov O.; Valenca A.&; Correia M.&; Nunes J.&; Bolkunov A.;Bachurin S.; Steinbusch, H.*; Strekalova T&*. Kings College London, Dept. of Neuroscience, London SE5, UK#; Anokhin Inst. of Normal Physiology, Baltiyskaya 8, Moscow, Russia; Center for Environmental Biology, Lisbon University, Campo Grande 1749-016, Portugal &; Institute of Physiol. Active Compounds, Chernogolovka, Severnii pr.1, Moscow Region, Russia; Dept. of Neuroscience, Maastricht University, Universiteitssingel 50, NL 6229 ER Maastricht, Netherlands*. Animal models of human disorders need a pharmacological validation with clinically efficient drugs. However, while planning such studies, species-specific differences in response to selected standard pharmaca and their doses have to

be taken into consideration. Our experiments with a 4-week administration of imipramine, a tricyclic antidepressant, and antidepressant citalopram, a Selective Serotonin Reuptake Inhibitor, show that optimal doses of these drugs can be defined in naïve animals. Here, we investigated effects of imipramine and citalopram (7 or 15 mg/kg/day, p.o.) in naïve C57BLN male mice in series of tests for exploration, locomotion, anxiety and two-bottle sucrose drinking test. We found a lasting increase of vertical activity and home cage locomotion, a reduction of anxiety scores and body weight, as well as a profound elevation of a total liquid intake and sucrose intake in mice treated with high dose of imipramine. Lower dose of imipramine evoked some of these effects. Citalopram induced none of these changes causing a significant increase in body weight in high dose. Our data suggest that chronic administration of imipramine in dose 15 mg/kg/day, as commonly applied in pre-clinical studies with models of depression can compromise behavioral testing of parameters reflecting depressive-like features in mice. Thus, relatively simple behavioral assay in naïve animals can be beneficial in defining the optimal reference drug and its dose to be used in animal paradigms of psychiatric disorders.

112. EARLY SOCIAL ENRICHMENT LEADS TO INCREASED FLOATING IN THE FORCED SWIM TEST AT ADULTHOOD: ARE THESE MICE MORE OR LESS VULNERABLE TO DEPRESSION? Branchi, I.; D'Andrea, I.; Cirulli, F.; Alleva, E. Dept. Cell Biol and Neurosci, Istituto Superiore di Sanita', Rome, Italy. In order to study the role of early experiences in shaping vulnerability and resilience to psychopathology at adulthood, we exposed mouse pups to an early social enrichment: the Communal Nest (CN). CN consists in a single nest where three mothers keep their pups together and share care-giving behavior from birth to weaning. In the CN, maternal behavior and peer interactions are markedly increased. At adulthood, mice reared in CN display phenotypic traits having face validity with reduced vulnerability to depression. When compared to mice reared in standard laboratory conditions (SN), CN mice display more elaborate social skills, reduced anhedonia following social stress, lower activation of the hypothalamic-pituitary-adrenal axis after social challenge and higher brain BDNF levels. By contrast, in the forced swim test, CN mice display longer floating time, usually considered as a depression-like response. These apparently discordant results may be put coherently together when the forced swim test is performed according to the original pharmacological protocol. Indeed, while acute fluoxetine administration reduces immobility in both CN and SN mice, chronic fluoxetine administration -- which is effective in humans -- increases immobility in SN mice up to the level shown by CN group, confirming that CN mice appear less vulnerable to depression-like behavior. Overall, the present findings suggest that caution should be used when interpreting forced swim test results obtained without drug administration and indicate CN mouse as a coherent model of reduced vulnerability to depression.

113. SUBSTITUTION OF 8-OHDPAT IN QUINPIROLE MODEL OF OBSESSIVE-COMPULSIVE DISORDER. AlKhatib, A; Beerepoot, P; Jacklin, D; Tucci, M; Sharma, R; Dvorkin, A; Graham, D; Szechtman, H; Dept Psychiatry & Behav Neurosc. McMaster University, Hamilton, Canada. In the quinpirole sensitization model of OCD, compulsive checking behavior is induced by repeated injections of the D2/D3 dopamine receptor agonist quinpirole to rats exploring a large open field (Szechtman et al., 1998), suggesting a role for dopaminergic stimulation in OCD. In contrast, a role for serotoninergic activity in OCD is suggested by another animal model of OCD in which an injection of 8-OHDPAT (a 5-HT1a receptor agonist) induces perseveration of spontaneous alternation behavior, a preparation that shares many pharmacologic properties of the human disorder (Yadin et al., 1991). In the present study, we asked whether 8-OHDPAT can substitute for quinpirole in the quinpirole model of compulsive checking since positive findings would suggest that this compulsive behavior could be driven by stimulation of receptors of either dopamine or serotonin neurotransmitter systems. After induction of compulsive checking using our standard protocol, half of the rats in the chronic quinpirole and the chronic saline groups received an injection of 8-OHDPAT (1 mg/kg) while the other animals received their regular injection of quinpirole or saline. Results showed that 8-OHDPAT produced compulsive checking when substituted for quinpirole, suggesting that compulsive behavior can be triggered and driven by serotonin or dopaminergic hyperactivity. Supported by CIHR (MOP-64424).

114. DETERMINATION OF PRE-EXISTING ANXIETY DIFFERENCES BETWEEN C57BL/6 N AND J MICE TO INVESTIGATE FEAR EXTINCTION LEARNING DISPARITY RELATED TO POST TRAUMATIC STRESS DISORDER. Landrau1, S.; Rodríguez1, C.I.;Santos2, I.; Peña de Ortiz2, S.; Méndez-Merced1, A.T. 1Universidad del Este, Escuela de Ciencias y Tecnologa, Carolina, PR, USA 00984; 2Universidad de Puerto Rico, Departamento de Biologa, Ro Piedras, PR, USA 00931. We are interested in studying the cellular and molecular neurobiological bases for individual differences related to anxiety disorders, in particular Post Traumatic Stress Disorder (PTSD). PTSD has been singled out as a health disparity issue among Hispanic American minorities by the United States Surgeon General. We are using as model animals the C57BL/6 N and J mouse substrains to approach individual mental health disparities related to PTSD. Previous investigations using the Pavlovian fear conditioning paradigm has shown that J mice are able to extinguish previously acquired fears more efficiently than N mice. The persistent

execution of fear related behaviors of N mice, in relation to J animals, is similar to what is displayed in PTSD patients. However, it is not known whether these two mouse substrains differ in terms of pre-existing anxiety, which has been reported to increase the susceptibility for PTSD. To address potential differences in innate anxiety between N (poor fear extinguishers) and J (good fear extinguishers) mice, we ran experiments using the Elevated-Plus Maze (EPM). This paradigm consists in an elevated plusshaped maze apparatus with two open and two enclosed arms. Innately anxious animals will spend more time in the closed arms than in the open arms and vice versa. We tested naive mice with a videotape tracking of time spent within the hub (center) and particular arms, open and closed arms entries, number of arms explorations while in the hub and, risk assessment behaviors including; rearing, head dipping, stretch-attend postures and grooming. Our data showed that N animals spend significantly more time in the open arms and have a greater number of open arms entries compared to J mice. J mice spend significantly more time in the hub and had a greater number of explorations and grooming behavior compared to N animals. It seems that N mice are willing to engaged in more risky behaviors, i.e. spend more time in the mazes open spaces, compared to J mice. Furthermore, J mice behaved precautious in relation to N mice, by remaining and exploring within the hub, which could parallels to the animals burrow entrance. Therefore, N mice impairment in fear extinction learning in relation to J mice might not be related to pre-existing anxiety which would have prevented their engagement in risky behavior. We will further test our results by measuring post-EPM corticosterone blood levels, as an indication of the physiological anxiety response within these animals. Supported by:URGREAT-MBRS-RISE 2R25GM066250-05A1 and NCMHD-RIMI-NIH, IP20MD003355-01.

115. SOCIAL DEFEAT STRESS DIFFERENTIALLY MODULATES HIPPOCAMPAL EXPRESSION OF THE ORGANIC CATION TRANSPORTER-3 IN RATS EXHIBITING BEHAVIORAL DEPRESSION. [1]Marcinkiewcz, C.A.; [1,2]Devine, D.P. Depts. of Neuroscience and Psychology. University of Florida, Gainesville, FL 32611 USA. The organic cation transporter-3 (OCT3) is a corticosterone-sensitive monoamine transporter that has recently been implicated in a variety of psychiatric disorders. The OCT3 participates in serotonin clearance in limbic regions the brain and occlusion by corticosterone increases extracellular serotonin, an important neuromodulator of mood states. Expression of the OCT3 is associated with anxiety- and depressive-like behavior in rodents and may be influenced by genetic and environmental factors. In this study, we quantified relative expression of the OCT3 in the Wistar-Kyoto (WKY) rat, an animal model of depressive-like behavior, using Long-Evans (LE) rats as a comparison strain. Neural expression of the OCT3 was quantified by real time RT-PCR and Western blot in rats exposed to chronic social defeat followed by acute restraint stress. Our results indicate that the OCT3 is elevated in the hippocampus of WKY rats compared to LE rats and that stress upregulates expression of the OCT3 in WKY rats, which may partially account for their poor adaptive response to stress and tendency toward depressive-like behavior. Conversely, social defeat robustly downregulates OCT3 expression in LE rats, which may reflect the relative stress resilience of this particular strain. These findings suggest that the OCT3 may be an important biomarker of stress vulnerability and selective responsiveness to a new class of drugs targeting the OCT3. Studies are currently underway in our laboratory to evaluate the antidepressant efficacy of pharmacological inhibition of the OCT3 in WKY rats.

116. TRANSLATIONAL STUDIES IN PIGS - VALIDATION OF A PORCINE MODEL FOR INFLAMMATORY PAIN. Di Giminiani, P. [1]; Herskin, M.S.[1]; Petersen, L.J.[2] [1] Univ of Aarhus, Dept of Anim Health and Biosci, Tjele, Denmark [2] Lab of Exp Physiol and Inflamm, Viborg Hospital, Denmark. *Why pigs?* Spontaneous pain and hyperalgesia as a result of inflammation and tissue damage are commonly studied in rodents as animal models for humans. However, these species show limited resemblance in the anatomical structure and in the functioning of nerve fibers and receptors. Pigs are considered highly relevant due to their greater anatomical homology, and are used increasingly as animal model species. Porcine skin is comparable to human. Recently laser thermal stimulation has been validated as a new tool for measuring pain threshold; increased flare reaction in inflamed skin and the confirmation of striking similarities in functional properties of cutaneous C-fibers in pigs and humans through single-fiber neurography. *Aim* This project is developed in order to establish a new animal model of translational research and provide information on cutaneous inflammatory pain that can apply to human medical conditions. *Methods* Induction: 3 models of local inflammation with different mechanisms of action and clinical presentation: 1. capsaicin-induced neurogenic inflammation through topical and intradermal administration 2. localized UVB inflammation 3. cellular model of inflammation via injection of nerve growth factor Quantification: spontaneous behaviour and nociceptive responses via physical impact stimulation with mechanical von Frey and radiant heat (CO2 laser) as well as axon reflex vasodilation (Doppler imaging). Validation: (1) Repeatability tested via stimulation of normal skin on three different parts of the body (flank, hind leg and tail); (2) All pigs receive UVB, capsaicin and placebo inflammation at three different sites within the flank; (3) Sensitivity determined via use of different dosages of inflammatory agents. *So far...* New application for the Von Frey anesthesiometer Optimization of set-up for an electronic IITC-von Frey anesthesiometer in the tail region. The test was performed in freely moving animals and early results suggest that mechanical stimulation can be applied without the need to stressful

confinement. Effective habituation is necessary in order to exclude responses due to stimuli other than selectively nociceptive.

117. AUTONOMIC STRESS REACTIVITY IN MICE LACKING 5-HT1A RECEPTORS. Sgoifo, A.1; Mastorci, F.1; Carnevali, L.1; Audero, E.2; Gross, C.2. 1) Department of Evolutionary and Functional Biology, University of Parma, Italy; 2) Mouse Biology Unit, EMBL Monterotondo, Italy. Previous studies indicate that the exogenous activation of central 5-HT1A receptors has sympatholytic effects, but it is still unclear whether this represents a physiological mechanism preventing exaggerated stress responsivity or rather a pharmacological artifact. This study evaluated cardiac autonomic modulation in mice lacking 5-HT1A receptors, both in baseline conditions and following the exposure to acute and chronic stressors. Male KO (n=22) and WT (n=17) mice were implanted with transmitters for ECG, temperature (T) and activity (Act) recordings and exposed to chronic social stress (CSS), consisting in 15 consecutive days of forced physical/sensory contact with a dominant male. Before CSS, mice were injected with a 5-HT1A agonist (8-OH-DPAT); before and after CSS, they were subjected to a restraint test associated with sympathetic or vagal pharmacological blockade. Before and during CSS, HR, T, and Act were sampled around-the-clock to assess their circadian rhythmicity. From ECGs, heart rate and vagal input to the heart were quantified via R-R interval variability indexes. Mice lacking 5-HT1A receptors showed a higher tachycardic stress response and a larger reduction of vagal modulation during vehicle+restraint test, both before and after CSS, whereas autonomic blockades associated with restraint did not reveal group differences. 8-OH-DPAT administration produced significantly higher heart rates and lower values of vagal activity in KOs. CSS determined a reduction in the amplitude of HR rhythm that was significantly larger in KO mice during the second week as compared to WTs. These results suggest that the lack of 5-HT1A receptors enhances stress-induced tachycardia and vagal withdrawal, and sensitizes to chronic stress induced alterations in circadian rhythmicity of heart rate.

DEVELOPMENT

118. CHOLINERGIC HYPOFUNCTION AND ALTERED NGF LEVELS IN MECP2-308 MICE: BENEFICIAL OUTCOMES OF EARLY CHOLINE SUPPLEMENTATION. ^Ricceri, L.; *De Filippis, B.; Fuso A.; *Laviola, G. ^Sect. Neurotoxicology & Neuroendocrinology, *Sect. Behavioural Neuroscience, Dept. Cell Biology & Neuroscience, Istituto Superiore di Sanit, Roma, Italy; Dept. Surgery Pietro Valdoni, Sapienza University, Roma, Italy. Rett syndrome (RTT) is a rare neurodevelopmental disorder caused by mutations in the X-linked gene MeCP2. RTT causes severe cognitive, social, motor and physiological impairments. We investigated the efficacy of supplementation with choline (25mM in dam water) from birth to weaning in a RTT mouse model which expresses a truncated form of MeCP2 (MeCP2-308). When adult, male mutant hemizygous (hz) mice exhibited a prominent reduction of locomotor activity compared to wild type (wt) littermates. Early choline treatment restored wt-like levels. In response to the specific cholinergic muscarinic antagonist scopolamine (2 mg/kg ip) wt subjects exhibited the expected hyperactivity profile whereas hz mice were not affected, indicating an alteration of central cholinergic tone. Consistently, lower striatal choline acetyl-trasferase activity and decreased levels of cortical NGF were found in hz mice. Early choline supplementation efficaciously counteracted these genotype-related alterations and also enhanced NGF and BDNF expression in the same brain regions. Supported by ERARE-EuroRETT network and ISSNIH grant 7NR1.

119. POST-WEANING SOCIAL ISOLATION SENSITIZES FEMALE RATS TO FG-7142-INDUCED INCREASES IN C-FOS EXPRESSION IN SEROTONERGIC NEURONS IN THE DORSAL RAPHE NUCLEUS. Lukkes, J.L; Engelman, G.H.; Hale, M.W.; Lowry, C.A. Department of Integrative Physiology and Center for Neuroscience, University of Colorado, Boulder, CO, USA. Our previous studies have shown that post-weaning social isolation of male rats leads to alterations in serotonergic activity and anxiety-like behavior in adulthood. Although evidence from studies in humans suggests that females have an increased sensitivity to stress and risk for the development of neuropsychiatric illnesses, most studies have been done on males while females have been insufficiently studied. Therefore, we investigated how post-weaning social isolation of female rats, in combination with a challenge with the anxiogenic drug, N-methyl-beta-carboline-3-carboxamide (FG-7142; a partial inverse agonist at the benzodiazepine site on the GABAA receptor), affects topographically organized subpopulations of serotonergic neurons in the dorsal raphe nucleus (DR) in adulthood using dual immunohistochemical staining for c-Fos and tryptophan hydroxylase. Juvenile female rats were reared in isolation or groups of three for a 3-week period from weaning to mid-adolescence, after which all rats were group-reared for an additional 2 weeks. Isolation-reared rats injected with FG-7142 had increased c-Fos expression in serotonergic neurons in the shell region of the dorsal part of the DR, the ventrolateral part of the DR, and the caudal part of the DR compared to isolation-reared rats injected with saline. In contrast, no treatment differences were observed in group-reared rats. These data suggest that post-weaning social isolation of female rats sensitizes a subpopulation of serotonergic neurons within the DR to stress-

related stimuli, which may lead to an increased vulnerability to stress- and anxiety-related responses in adulthood. Supported by F32MH084463 (JLL) and R01MH086539 (CAL) from the NIMH.

120. IMPACT OF EARLY OR LATE ADOLESCENT EXPOSURE TO NICOTINE ON RAT BRAIN DOPAMINERGIC FUNCTION. McMillen B.A.; Williams L.T.; Rogister M.C.; Halsey T.M.; Williams H. L. Dept. of Pharmacol. & Toxicol., Brody Sch. of Med., E. Carolina Univ., Greenville, NC 27858 USA. The administration of 0.4 mg/kg i.p. nicotine to rats once daily for the 10 days that brackets the onset of puberty (P35 P44) results in a heterologous sensitization to the rewarding effects of nicotine, cocaine and diazepam in the adult. Our hypothesis is that the early adolescent exposure to nicotine has resulted in a lasting change in dopaminergic activity. The nicotine exposure paradigm was used with one group of rats beginning at P35 and another group at P60 and then at P80 the rats used for a behavioral test, the stimulant response to 1.0 mg/kg s.c. amfonelic acid (AFA), followed by 0.1 mg/kg haloperidol after 45 min. and then after another 45 min. the brain dissected for the striatum and the medial prefrontal cortices. AFA produced a mixture of hyperlocomotion and stereotyped behaviors at 45 min, 3.0 on a 4.0 scale, in all rats regardless of exposure or age of treatment. Haloperidol reversed the hyperactivity. Control striatal concentrations of DOPAC in V/V-P35, N/V-P35, V/V-P60 and N/V-P60 were 3.770.33, 3.510.18, 2.970.37 and 3.200.26 ug/g (NS). Control concentrations of DOPAC in the prefrontal cortices in V/V-P35, N/V-P35, V/V-P60 and N/V-P60 were 0.2280.030, 0.2990.056, 0.3200.049 and 0.258 0.058 ug/g (NS). Haloperidol by itself significantly increased by 75% - 100% the concentration of DOPAC in all groups. Injection of AFA before haloperidol had little affect on the increase in DA metabolism. Although the early exposure to nicotine, P35 44, increases the reward responses to drugs, the behavioral response to a stimulant and the metabolism of DA were not affected. The altered reward responses may be due to some other change in the neurotransmitter control of the brains reward system.

121. PRENATAL COCAINE'S EFFECT ON NEONATAL THERMOREGULATION AND ULTRASONIC VOCALIZATION. McMurray, MS; Meiners, SM; Zoghby, CR; Zeskind, PS; Johns, JM. Depts of Psychology, Psychiatry, and Pediatrics. University of North Carolina, Chapel Hill, NC 27599 USA. Rat pup prenatal cocaine exposure (PCE) alters the postnatal care received, likely caused by alterations in pup-produced stimuli that elicit early postnatal maternal care, including pup thermal state and ultrasonic vocalizations (USVs). PCE may affect thermogenesis through its reduction of birth weight (and brown adipose tissue) and its cardiac effects. Laryngeal breaking can also be used to increase thermogenesis, the byproduct of which is a USV. Alterations in thermogenesis would be reflected in USVs, and when combined, could alter the care elicited by pups. Following PCE (gestation days 1-20), male and female pups were first exposed to an hour of no thermal challenge, then an hour of mild, and lastly an hour of moderate thermal challenge on postnatal days 3 and 5. Interscapular and back temperatures, as well as USVs were recorded during the three hour test. Inequality in interscapular and back temperatures is reflective of brown fat tissue thermogenesis. A variety of sonographic characteristics of USVs were analyzed and paired with the thermal data. Results indicated that PCE altered patterns of USVs compared to controls, reflective of altered thermogenic ability. These findings implicate a variety of cocaine-induced alterations in auditory and thermal cues of pups, potentially responsible for altering the care received.

122. DIFFERENTIAL EFFECTS OF ADOLESCENT SUBCHRONIC METHYLPHENIDATE AND ATOMOXETINE ON ADULT BEHAVIOR FOREBRAIN DOPAMINE, NOREPINEPHRINE AND SEROTONIN IN NAPLES HIGH-EXCITABILITY RATS. Ruocco, L.A.; Gironi Carnevale, U.A.; Treno, C.; Sadile, A.G.; 2Melisi, D; 3Ibba, M; 3Schirru, C; 3Carboni,E.Dept. of Exptl. Med., II Univ.; 2 Pharmaceut. and Toxicol. Chem., Univ. of Naples Federico II, Naples; 3 Dept. of Toxicology, Univ. of Cagliari, Italy Attention-deficit hyperactivity disorder (ADHD) can be studied in animal models such as Naples High-Excitability (NHE) rats, a genetic model for the mesocortical variant of the disorder. This study aimed at investigating the long-term effects of adolescent subchronic methylphenidate (MPH) and atomoxetine (ATX) on adult behavior and the forebrain neurotransmitter and metabolite content of NHE rats. Male NHE rats were given a daily i.p.(1.0 mg/kg) of MPH, ATX or vehicle in the 5th and 6th. At age of 7075, rats were tested in two spatial novelties (Làt and Olton mazes). Behavior: indices of horizontal, vertical, non-selective (NSA) and selective spatial attention (SSA) revealed that only MPH reduced horizontal activity 39% in the Làt and 16% in the Olton and increased NSA. Neurochemistry: tissue content of dopamine (DA),norepinephrine (NE), serotonin and metabolites assessed by HPLC, in forebrain areas showed a MPH induced decrease in i) DA, DOPAC, NE and MHPG in the Prefrontal cortex (PFC), ii) DA, DOPAC, HVA, serotonin, 5-HIAA in the Dorsal Striatum (DS), iii) DA, DOPAC, HVA and MHPG (but increased NE) in the Ventral Striatum (VS). ATX increased DA and decreased MHPG in the PFC. Like MPH, decreased DA, DOPAC, HVA, serotonin and 5-HIAA in the DS, but decreased MHPG in the VS. Therefore, only MPH gave long term effects on adult brain and behaviour but ATX only on the former.(Supported by:Young Investigator project 2009-12, to LAR).

123. NEONATAL EXPOSURE TO ESTRADIOL ENHANCES ADULT DIAZEPAM SENSITIVITY. Santoru, F.; Mereu, V.; Rossi, F.; Langiu M.; Biggio, G.; Concas A. Dept of Exp. Biology, Centre of Excellence for the Neurobiology of Dependence, University of Cagliari, Italy. Estradiol affects GABAergic transmission, especially during early development, when GABA acts as an excitatory neurotransmitter. We have previously shown that neonatal estradiol (NE) administration to female rats induces a marked and persistent change in the expression of specific GABAA receptor subunits (1, 2, and 2) in the cerebral cortex of adult rats. Given that these subunits are required for GABAA receptors to show sensitivity to benzodiazepines, the object of this study was to evaluate whether NE administration to female rats can affect in adulthood sensitivity to diazepam in several behavioural tests. Administration of -estradiol 3-benzoate (10 microg/50 microl sesam oil/animal) to female rats on the day of birth did not affect the locomotor activity and the behaviour of adult rats in the elevated plus maze. On the contrary, administration of diazepam produced a more pronounced anxiolytic-like behaviour in the elevated plus maze test and an higher reduction in the locomotor activity in NE-treated females compared to control rats. In the Morris water maze, NE-treated females displayed a decreased latency to find the submerged platform and the effect of diazepam on the retention, but not on the acquisition, of place learning in these animals was more evident compared to control-treated rats. On the contrary, diazepam showed a similar anticonvulsant activity against pentylenetetrazole-induced seizures in both groups. Given that the anxiolytic, sedative and amnesic effects of benzodiazepines seem to be mediated by specific GABAA subunits, the higher sensitivity of NE-treated females to diazepam could be related to the changes in the expression of GABAA receptor subunits observed in the brain of NE-treated females.

124. ACETYL-L-CARNITINE IMPROVES GENERAL HEALTH IN A MOUSE MODEL OF RETT SYNDROME. Schaevitz, L.R.; Lopez, C.M.; DIddio, S.; Iannoni, E.; Nicolai, R.; Amato, A.; Berger-Sweeney, J.E. Department of Biological Sciences, Wellesley College, Wellesley, MA, USA; Sigma Tau SpA, Pomezia, Rome, Italy. Rett Syndrome (RTT) is a devastating developmental disorder on the autistic spectrum caused by mutations in the X-linked gene encoding methyl-CpG-binding protein 2 (MeCP2). Girls with RTT and mouse models of RTT suffer from behavioral and metabolic deficits including weight abnormalities and severe breathing irregularities (increases in hyperventilation and apneas) that result in a drastically reduced lifespan. We hypothesized that improving cholinergic and metabolic functioning with acetyl-L-carnitine (ALCAR) treatment during critical periods in development would improve general health including weight and breathing deficits in *MeCP2*^{1lox} null mice. In this study, we examined whether daily ALCAR supplementation beginning on postnatal day (PN) 1 could improve weight gain, metabolic function (O_2 consumption/CO_2 production measured by calorimetry) and respiratory rhythms and volumes (measured by whole body pletysmography). We found that null mice gained significantly less weight, exhibited a decrease in O_2/CO_2 exchange, and showed increasingly irregular breathing between PNs 21 and 42, as compared to wildtypes. ALCAR dramatically mitigated this time-dependent weight loss and decrease in gas exchange in the null mice. Currently, we are examining whether ALCAR also rescues breathing irregularities in null mice. Overall, the data support the hypothesis that ALCAR significantly improves general health in a mouse model of RTT and suggests that metabolic abnormalities may underlie both the weight and breathing irregularities. Although ALCAR may not directly rescue the genetic mutation, it appears to be dramatically more effective than

choline, another treatment we tested (Neurobiol Dis. 26:473, 2007), at improving RTT-like symptoms and may provide a safe non-invasive treatment for RTT.

125. PARENTAL BRAIN EMOTION CIRCUITS VARY WITH GENDER, CORRELATE WITH MOOD AND PREDICT BEHAVIOR. Swain J.E.; Kim P., Feldman R., Mayes L.C., Leckman J.F. University of Michigan, Ann Arbor, MI, 48105 USA. Parenting requires social cognitive and affective circuits to regulate thoughts and behaviors for reciprocal interactions with their infants that contribute to infant development. We hypothesized that discrete parental brain regions, differing from non-parents, respond to baby-stimuli modulate mood-regulation circuits and predict infant-directed parental behavior. Methods: We scanned and interviewed non-mothers (n=10), non-fathers (n=10) as well as mothers (n-18) and fathers (n=16) at 2-4 weeks and 3-4 months postpartum. At each time point, fMRI scans assessed brain activity while attending to their own baby-cries pictures. In addition to interviews, parent-infant interaction video-tapes were assessed at 4 months postpartum. Results: Newest analyses replicate parental brain-response findings in emotion regulation circuits and focus on comparisons with non-parents, gender differences and correlations. Cortical responses were markedly increased in parents compared to non-parents. First-time parents activate more in mothers than fathers at 2-4 weeks, but over 3 months, alarm responses in mothers shift to hypothalamus (metabolic control), nucleus accumbens (reward), and frontal cortical (planning) activations as the parent-infant bond develops. Psychometric data indicate significantly higher preoccupations in moms compared to dads ($p<0,001$), and correlations of pre-occupations with depression ($p<0.001$), and brain activity in the amygdala and basal ganglia (fear, worry, and OCD circuits) with anxiety and frontal circuits with depression at 2 weeks; brain activity in amygdala predicts parental sensitivity 3 months later. Conclusions: Parental brains respond to baby stimuli vary with gender and correlate with concurrent mood and later behavior linking parental brain function with behavior and offspring outcome.

126. MECHANISMS AND CONSEQUENCES OF DISRUPTING CORTICAL DOPAMINE ACTIVITY DURING ADOLESCENCE. Watt MJ; Roberts CL; Renner KJ; Scholl JL; Haaland EJ; Forster GL. Basic Biomedical Sciences, University of South Dakota, Vermillion SD USA. Adolescence is a critical period of behavioral and neural development, making adolescents vulnerable to effects of negative social experiences such as bullying. We showed that male rats exposed to social defeat in adolescence exhibit decreased medial prefrontal cortex (mPFC) dopamine (DA) content as adults, which is associated with heightened sensation-seeking. Accordingly, rats defeated in adolescence show enhanced novelty responses as adults compared to non-defeated controls. We hypothesize that reductions in mPFC DA content and subsequently enhanced novelty responses result from heightened defeat stress-induced activation of DA synthesis-controlling D_2 autoreceptors in the mPFC during adolescence. Using rats not exposed to social defeat, we investigated whether repeated pharmacological activation of mPFC D_2 autoreceptors during mid-adolescence would result in increased novelty responses as associated with altered mPFC DA activity. Male rats received daily bilateral infusions of the D_2 receptor agonist quinpirole (100 ng in 0.3 l per side) or vehicle (aCSF) into the mPFC, from postnatal day (P) 35 to 39. Subjects were then tested for responses to a novel object either in adolescence (P40) or upon reaching early adulthood (P56). Quinpirole-treated rats displayed both greater time in close proximity and more approaches to the novel object compared to vehicle-treated controls, with this effect appearing in adolescence and persisting into adulthood. This enhanced novelty-seeking was associated with decreased mPFC DA content in adolescent rats and reduced mPFC DA activity in adults. These findings suggest that disruption of adolescent mPFC DA activity via D_2 autoreceptor activation results in both immediate and enduring alterations to neural substrates underlying novelty seeking.

127. INHIBITING NEONATAL METHAMPHETAMINE (MA)-INDUCED CORTICOSTERONE RELEASE IN RATS BY ADRENAL AUTOTRANSPLANTATION: EFFECTS ON LATER LEARNING, MEMORY, AND PLASMA CORTICOSTERONE LEVELS Williams, M.T.; Grace, C.E.; Schaefer, T.L.; Graham, D.L.; Skelton, M.R.; Vorhees, C.V. Div Neurology, Cincinnati Childrens Research Foundation and Univ Cincinnati College of Medicine Neonatal MA exposure in rats, which corresponds to the second-half of human pregnancy, has been shown to cause long-term behavioral impairments similar to those observed following early stress. The MA induced impairments may therefore be related to early increases in corticosterone (CORT) release. We developed a method to attenuate MA-induced CORT release using adrenal autotransplantation (ADXA) in neonatal rats and used this to determine if neonatal MA-induced increases in CORT are associated with the long-term behavioral deficits. Animals (ADXA or sham with surgery on postnatal day (P)9) were treated from P11-20, 4 times daily with 10 mg/kg of MA or saline. ADXA successfully attenuated MA-induced CORT increases by ~50% during treatment but did not alter the long-term behavioral deficits of MA-treatment. MA-treated rats, regardless of surgery, showed deficits in the Cincinnati water maze and in three phases of Morris water maze testing. MA-treated offspring were also hypoactive and had reduced open zone entry latency in the elevated zero maze but no light-dark test effects. ADXA had no effect on MA-induced reductions in 5-HT or 5-HIAA in multiple brain regions. Although 50% attenuation of MA-induced elevations in CORT did not mitigate later learning deficits or other behavioral effects of exposure, the data

cannot rule out the possibility that a more complete block of CORT release might prove to be effective. NIH grants R01 DA006733 and T32 ES7051.

128. DIVERGENT EFFECTS OF EARLY CORTICOSTERONE EXPOSURE AND ADOLESCENT STRESS ON ADULT BEHAVIOURAL PATTERNS IN MALE AND FEMALE RATS. Brummelte, S.; Wong, J.H.K.; Lieblich, S.E. and Galea L.A.M. Department of Psychology, University of British Columbia, Vancouver, BC, Canada. Early adverse experiences such as stress can have long lasting effects on the development of the individual. Previous studies from our laboratory have shown that high levels of maternal corticosterone (CORT) during the postpartum period can be transferred to the offspring and can induce life-long changes in the cognitive and behavioural abilities of the affected offspring. However, while the adverse effects of early stressful experiences may be attenuated by providing environmental enrichment, they may also be exacerbated by further challenges such as adolescent stress. Therefore, the current study was conducted to investigate the effect of postpartum exposure to elevated maternal corticosterone levels and adolescent stress on adult behaviour in male and female offspring. Dams either received sesame oil (control) or CORT (40mg/kg) during the postpartum period and after weaning (day 23) the offspring were assigned to either a stress or no-stress group. Rats in the stress group were given restraint stress for 1 hr/ d every other day from postnatal day 30-52, while rats in the no-stress group were left undisturbed. All rats were tested in a serious of behavioural tests in adulthood including the forced swim test (depressive-like behaviour), open field test (locomotor activity), hot plate test (pain sensitivity) and elevated plus maze (anxiety). Results revealed that early corticosterone exposure and adolescent stress affect adult offspring differently but not necessarily in an accumulative way. For instance, only non-stressed, but not stressed CORT-exposed rats show more thigmotaxis behaviour in the OFT compared to oil controls. Female CORT-exposed rats exhibited less anxiety in the elevated plus maze and male and female rats exposed to maternal CORT had lower thresholds for pain sensitivity. In summary early CORT and adolescent stress exposure can affect the developmental outcome in a highly complex and sex-dependent matter. These results may help us to better understand different predispositions or vulnerabilities for stress during different phases in life between males and females.

129. LONG-LASTING BEHAVIOURAL CONSEQUENCES OF CORTICOSTERONE ADMINISTRATION DURING THE FIRST POSTPARTUM PERIOD IN MULTIPAROUS DAMS. Wong, J.H.K; Brummelte, S; Lieblich, S.E.; Galea, L.A.M. Department of Psychology, Program in Neuroscience and Brain Research Centre. University of British Columbia, Vancouver, BC, Canada. Postpartum depression affects 15% of new mothers and previous experience of depressive episodes increases the risk for postpartum depression. To better understand the causes and progress of this common affective disorder we examined a corticosterone (CORT)-induced rodent model of postpartum depression. In the present study, we aimed to investigate the effects of CORT treatment in the dams first postpartum period on maternal mood after a subsequent pregnancy. Sprague-Dawley female rats received either sesame oil (control) or CORT (40 mg/kg) injections for 23 days during their first postpartum period. The dams were observed for "depressive-like" behaviour on the Forced-Swim Test (FST) from postpartum day 21-22. Following a second pregnancy, dams were again tested on the FST apparatus at postpartum day 4 and 21. During the first postpartum period, CORT-treated dams displayed an increase in immobility in the FST compared to oil controls, indicative of "depressive-like" behaviour. However, the effect was reversed in the second postpartum period with the CORT dams showing less immobility than control dams in the FST. Interestingly, control dams had an increase in time spent immobile during second postpartum period compared to first. This implied that the conditions of the first motherhood have a substantial influence on the second postpartum period; in particular, it hinted that the CORT dams may had a dampened stress response. Further investigations are necessary to fully understand the effect of parity on postpartum depression.

130. PATERNAL EXPERIENCE ALTERS NEUROPLASTICITY AND CELL PROLIFERATION IN CALIFORNIA DEER MICE (PEROMYSCUS CALIFORNICUS). Hampton, J.E.[1]; Franssen, C.L.[1]; Bardi, M.[2]; Lambert, K.G.[1]. [1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005, USA; [2]Dept. of Psychology, Marshall University, Huntington WV 25755 USA. Past research on the female reproductive model has shown that gonadal hormones influence neurogenesis in the adult hippocampal dentate gyrus (Galea et al. 2006) and gestation can induce cell proliferation in the subventricular zone (SVZ) of rats and mice (Shingo et al., 2003; Furata & Bridges, 2005). However, the impact of reproduction on neurogenesis and cell proliferation has not been described in males. In this study, we examined hippocampal sections taken from the brains of male California deer mice (Peromyscus californicus), a monogamous, biparental species. Dads (n=8) were sacrificed 5 days following the birth of their first litter of pups, having been housed with their female mate throughout pregnancy. Pup-exposed Virgins (PEVs; n=7) were given 5 days of pup exposure. Virgins without pup exposure (n=9) served as a control. Preliminary data reveal a complex profile of neuroplasticity among these groups. For instance, cell proliferation (Ki-67 immunofluorescence) is elevated in the SVZ of PEVs versus other groups, yet GFAP-immunoreactivity in the dentate gyrus indicate greater restructuring in Virgins than males with paternal experience. Still another marker of plasticity, doublecortin, showed no difference in the SVZ of the three groups. To further elucidate the potential changes in the paternal brain, hippocampi were immuno-stained with nestin (restructuring neurons), NeuN (neurogenesis), and cresyl violet (cell bodies). This examination of neurogenesis and neuroplasticity in the paternal brain is the first of its kind and will shed further light on the neurological impact of parenthood.

131. PATERNAL EXPERIENCE AND STRESS RESPONSES IN THE CALIFORNIA MOUSE (*PEROMYSCUS CALIFORNICUS*). Bardi, M.[1]; Franssen, C.L.[2]; Hampton, J.E.[2]; Shea, E.A.[2]; Fanean, A.[1];Lambert, K.G.[2]. [1]Marshall University, Huntington, WV -USA; [2]Randolph-Macon College, Ashland, VA -USA. The transition from nulliparity to motherhood has been associated with profound alterations of the female's behavioral and motivational repertoire. However it is not known if the same effect is true for males in a biparental monogamous species (*Peromyscus californicus*). In this study we tested the hypothesis that paternal experience can induce long-term changes in the behavioral and motivational responses of California mouse fathers. Adult males with (Dads, n=8) and without (Pup-Exposed Virgins (PEVs), n=8) parental experience were exposed to unfamiliar pups for three days. A third group of adult males (Virgins, n=8) were never exposed to pups and therefore served as the control group. Behavioral and hormonal stress responsiveness was assessed in two experiments. In experiment 1, animals were acutely exposed to 2,5-dihydro-2,4,5-trimethylthiazoline (TMT), a component of fox feces widely used to stimulate fear response in mice. In experiment 2, animals were introduced to a novel open field (OF) with an unfamiliar object located in the center. Corticosterone and DHEA were measured non-invasively by collecting fecal samples. Preliminary behavioral results showed that Dads were less anxious than both PEVs and Virgins in the OF test. Interestingly, PEVs were somewhat intermediate in their level of anxiety. Dads also had higher hormonal levels during the OF test, whereas PEVs secreted intermediate levels. No difference related to parental experience was found in animals exposed to TMT, however we observed widely varying behavioral responses toward TMT exposure, suggesting that this stimulus may be an unreliable anxiety test for this species. These data suggest that paternal experience can induce long-term changes in the stress responsiveness of California mouse males.

132. DOPAMINE INVOLVEMENT IN THE REINDUCTION PHASE OF MATERNAL MEMORY IN FEMALE RATS. Bridges, R.S.; Peterson, D.B.; Carini, L.M.; Lovelock, D.L.; Byrnes, E.M.; Byrnes, J.J. Dept. of Biomedical Sciences. Tufts University -Cummings School of Veterinary Medicine, North Grafton, MA 01536 USA. Mothers form a long-term potentiation of maternal responsiveness (maternal memory) during the immediate postpartum period. Maternal memory consists of two phases: (1) the initial consolidation phase during the postpartum period and (2) the reinduction phase when subsequently tested for the retention of maternal behavior. The consolidation phase in rats is mediated in part by dopamine (DA) acting through known reward pathways. The neurochemical mediation of the reinduction phase has received limited attention. In the present study we investigated the involvement of DA and the DA D2 receptor in this phase. Previously parous females were given 2 days of postpartum experience followed by 20-25 days of separation from pups. Subjects were then treated with either the DA D2 agonist, bromocriptine (injected twice daily at 1 mg/kg), or the DA D2 antagonist, raclopride administered chronically via sc implants (Alzet minipumps - 0.3 and 1.0 mg/kg/day). Drug treatments started 2 days prior to daily testing for maternal memory (using foster young). Two main findings emerged. First, treatment with bromocriptine resulted in a faster rate of reinduction of maternal behavior, stimulating maternal memory. Second, chronic exposure to raclopride, while not delaying the reinduction of maternal care in the home cage test, resulted in reduced levels of responsiveness to pup cues in an elevated plus maze test once maternal behavior was reestablished. These findings indicate that the DA D2 receptor may modulate the incentive value of pup stimuli during the reinduction phase of maternal memory, a role similar to its established actions during the consolidation phase. Supported by NIH Grant R37 HD19789 (RSB).

133. MENTAL HEALTH: A NATURAL LIFE OUTLOOKS? AN ITALIAN TWIN STUDY ON HERITABILITY OF PSYCHOLOGICAL WELL-BEING (PWB) IN YOUNG ADULTS.Gigantesco A, Fagnani C.,Italian National Institute of Health. One of the most significant developments of recent decades has been the emergence of empirically validated assessments of Psychological Well-being (PWB). Researchers increased interest in this topic and articulated a conception of PWB from an eudaimonic perspective that was concerned with self-realization (Ryff, 1898) and emphasized human potentials (e.g., living a life rich in purpose and meaning, continued growth, and quality ties to others). PWB was partitioned into six dimensions: autonomy, positive relations, purpose in life, self-acceptance, environmental mastery and personal growth. Research on factors influencing individual differences in these dimensions has mainly focused on psychosocial environmental characteristics. To date, none genetic studies targeted the dimensions of PWB. The aim of this study was to examine the contribution of genetic and environmental factors to variation in these dimensions. This is the first twin study to explore the origins of individual differences in PWB. For the purpose, we used the SPWB in their shortest form. The genetic analyses complemented the phenotypic analyses by providing a greater understanding of the sources of co variation among the six dimensions. This study provides evidence that the observed correlations between the six dimensions of PWB can be attributed to largely shared genetic influences. Furthermore, unshared environmental factors unique to the individual also influence PWB and influence each phenotype, with exception of autonomy.

134. BEHAVIOURAL AND COGNITIVE ALTERATIONS OF THE YOUNG MEGAENCEPHALY (BALB/cByJ-Kv1.1mceph/mceph) MOUSE. Holst, S*.; Aberg, E#.; Eriksson, T §.; Ogren, SO*.; Lavebratt, C# .* Department of Neuroscience, Karolinska Institute, Solna, Sweden. #Department of Molecular Medicine and Suregery, Karolinska University Hospital, Solna, Sweden. §Department of Physiology and Pharmacology, Karolinska Institute, Solna, Sweden. The transgenic mouse BALB/cByJ-Kv1.1mceph/mceph (mceph/mceph) is homozygous for a mutation truncating the Shaker-like voltage gated potassium channel, Kv1.1 (KCNA1), which causes defects in potassium channels function. From 3 weeks of age the mceph/mceph mice develop epileptic seizures and a pathological overgrowth of the hippocampus and the ventral cortex whereas the heterozygots are normal (present study). Locomotor and anxiety-related behaviours were studied in Elevated Plus Maze, Open field and Novel Cage tests. Body weight and frequency of vocalisation and teary eyes were recorded. Since the hippocampus and nearby regions are involved in cognition, the emotional memory was investigated in the Passive Avoidance (PA). The motor coordination was examined in the Rota-Rod. Compared to heterozygots and wild types the mceph/mceph mice had reduced body weight and vocalisation frequency, higher frequency of teary eyes and displayed reduced frequency and duration of rearing, wall-rearing, walking and defensive burrowing in the Novel Cage test. In the PA test there was a significant effect of genotype on memory retention, mceph/mceph had a tendency to a decreased retention latency compared to heterozygots but not to wild types. Further, the mceph/mceph had a decreased frequency of risk assesment behavior and higher duration in the dark compartment, while the duration and number of feces in the bright compartment was decreased. This suggests that the mceph/mceph prefer the dark compartment despite the

aversive cue received 24h earlier. In conclusion, the mceph/mceph mice have less explorative, locomotor and risk assessment behavior as well as a deficit in emotional memory.

135. THE LONG-TERM CONSEQUENCES OF PRE- AND POST-NATAL ENVIRONMENTAL ENRICHMENT: EVALUATION OF ADULT RAT BEHAVIOUR. Sparling, J.; Baker, S.; Bielajew, C. University of Ottawa, Ontario, Canada. Environmental enrichment housing provides complex experiences that engage cognitive and motor circuitry, resulting in a greater repertoire of species appropriate behaviours. As unprecedented periods of physiological development, the pre- and post-natal periods are particularly sensitive to environmental changes. Long-Evans rats were bred in-house from mothers co-housed in an enriched social colony or in standard laboratory housing. The social colony consisted of a network of seven cages interconnected using tubes that facilitated locomotion between cages. The social colony offered interaction with both inanimate objects and conspecifics. Offspring from social colony mothers were enriched from conception until offspring juvenile age. In order to evaluate the long-term effects of early life enrichment, weight was monitored as well as adult offspring behaviour (80 days) in either the elevated-plus maze or the Morris water maze. Enriched offspring maintained a leaner body weight from postpartum through until adulthood. In the elevated-plus maze, the enriched group displayed more stretch attend behaviour and the enriched females showed a greater percentage of open arm entries over time. Results from the Morris water maze probe test showed that enriched adults frequented the past location of the submerged platform and the maze center significantly more often. Although additional group differences were found at an earlier age based on housing group (reported elsewhere), this study shows that some effects of enrichment are present until adulthood.

136. PRENATAL COCAINE EXPOSURE ALTERS HUMAN AND RODENT INFANT VOCALIZATIONS: IMPLICATIONS FOR MATERNAL CARE AND NEURAL INTEGRITY. Cox E.; Jones G.; Williams S.; McMurray M.; Jamieson-Drake A.; Zeskind P.; Hodge C.; Grewen K.; Johns J. Depts of Neuro., Psychology, and Psychiatry, UNC-Chapel Hill, NC, USA. Maternal cocaine use is associated with increased child neglect. Infant vocalizations promote maternal response and may be altered following prenatal cocaine exposure (PCE). This study examined human and rodent infants to determine if PCE alters vocalizations and if altered vocalizations correlate with infant neural integrity. Four week old human infants (+4 days) of healthy control mothers and mothers who used cocaine or other drugs during pregnancy were placed on a cold scale and 35 seconds of crying was recorded and analyzed. Pregnant rats were left untreated or treated chronically throughout gestation (GD 1-20) with cocaine HCl (30mg/kg/day) or with saline. Bromodeoxyuridine (10mg/kg) was injected on GDs 13-15 to label proliferating cells in the periaqueductal gray (PAG) in developing offspring. On postnatal day 14, one male and female offspring from each litter was tested for vocalizations by placement on a cold scale mirroring human elicitation. Results indicate PCE alters vocalizations in both species. Rodent brains are being assessed using immunohistochemistry for neuronal differentiation in the PAG to correlate with vocalization differences. Vocalizations may serve as a behavioral and biological marker for infants with developmental vulnerability to maternal neglect.

137. POSTNATAL MATERNAL SSRI EXPOSURE INCREASES DEPRESSIVE-LIKE BEHAVIOUR IN PRENATALLY STRESSED JUVENILE OFFSPRING. Pawluski, J.L.; van den Hove, D.L.; Rayen, I.; Prickaerts, J.; Steinbusch, H.W. Department of Neuroscience, Faculty of Health, Medicine and Life Sciences, Maastricht University, The Netherlands. Stress during gestation has marked effects on offspring development and results in postpartum depressive-like behavior in the mother. Postpartum depression (PPD) is a growing health problem, which affects 15% of women worldwide. Currently, selective serotonin reuptake inhibitor (SSRIs) medications are commonly used for treatment of PPD. Unfortunately there is very little research on the effect of maternal depression and perinatal SSRI exposure in juvenile offspring. Therefore the aim of this study was to determine how postnatal maternal SSRI (fluoxetine) exposure affects the development of anxiety- and depressive-like behavior in prenatally stressed juvenile offspring. In order to investigate this, gestationally stressed or non-stressed mothers were divided into 3 groups: 1) fluoxetine treated (5mg/kg/day), 2) vehicle and 3) cage control. On postnatal day 1 (PD1) treatment was administered to mothers via minipump implants (Alzet). Offspring were weaned at PD 21 and five groups of male and female offspring were used used for behavioral testing: 1) prenatal stress+maternal fluoxetine, 2) prenatal stress+vehicle, 3) maternal fluoxetine alone, 4) vehicle alone, and 5) no treatment. Offspring between 30-35 days of age were tested on the open field test and the forced swim test to assess anxiety- and depressive-related behaviors. Preliminary results demonstrate that postnatal maternal fluoxetine exposure significantly increases depressive-like behavior in prenatally stressed juvenile offspring. This research provides some of the first evidence that postnatal SSRI exposure affects depressive-like behavior in juvenile offspring of prenatally stressed mothers. Further research will determine the role of postnatal SSRIs on anxiety-related behavior and neural correlates of these changes in juvenile offspring.

138. EARLY EXPOSURE TO ENDOCRINE DISRUPTORS ALTERS SEX DIFFERENCES IN BEHAVIOR AND NEURAL CIRCUITS. Palanza, P.; Parmigiani, S.; Gioiosa, L.; Ponzi, D.; Miceli D.; Martini M.; Panzica G. Dept of Evolutionary and Functional Biology, Parma University (I). Bisphenol A (BPA) is an estrogenic plastic-derived pollutant and is considered an endocrine disruptor. We assessed the effects of maternal exposure during pregnancy and/or lactation to BPA at a concentration within the range of human exposure and not patently teratogenic (10, 20, 40 ug/kg/day), on behavior and neural circuits of male and female mice, tested before and after puberty in different behavioral paradigms. As a general result, we found that while control mice showed sex differences on a number of behavioral responses at both ages and in many test paradigms, mice perinatally exposed to BPA showed decreased or no sex differences. Maternal exposure to BPA mostly affected female mice on exploration, emotional and cognitive behaviors, and maternal behavior, while males were more sensitive to BPA as far as the development of aggression and social interactions. We examined neural circuits possibly associated to the observed behavioral changes: BPA altered the noradrenergic systems in the locus coeruleus and in the preoptic area of the hypothalamus and affected the number of nNOS immunoreactive cells in the medial preoptic nucleus in a sex-oriented and dose-dependent way. The high sex dimorphism of kisspeptin expression found in controls was reduced by BPA exposure in some nuclei. These findings are evidence of long-term consequences of maternal exposure to low-dose BPA at the level of neurobehavioral development in mice. Possible mechanisms of the BPA effects on sex differentiation processes, and implications for human health need to be carefully assessed.

139. BEHAVIORAL ALTERATIONS IN THE BIRD MODEL OF RETT SYNDROME. Blue, M.E.; Eyring, C.; Smith, D.; Hugo W. Moser Research Institute at Kennedy Krieger and Johns Hopkins University, Baltimore, MD. Rett Syndrome (RTT) is a development disorder caused by mutations in MECP2 that results in mental retardation, seizures, autonomic irregularities and hand stereotypies. We evaluated behavior in Bird Model Mecp2 KO and HET mice in 2 cohorts, one had 5-7 week old WT, HET and KO mice, the other had 3-6 month old HET and WT mice. The levels of general activity and the behavior of each mouse was recorded and analyzed while in a home cage setting. 5-7 week old KO mice had significantly fewer bouts of hanging from the cage top ($p<0.05$) and spent more time grooming ($p<0.001$) than WT and HET mice. At 3-6 months, HET mice also spent significantly more time grooming than the WT mice ($p<0.003$), but did not differ from WT in hanging behavior. We think the increased grooming is a repetitive behavior that is a mouse correlate of repetitive, non-purposeful hand wringing behaviors in girls with RTT. Rotorod testing revealed significant changes in motor learning/performance among the different genotypes (group effect) at both ages. Open field testing showed comparable levels of locomotion in all genotypes and all ages. At 5-7 weeks, the WT and HET exhibited a similar amount of rearing, while the KO group showed less. In the older group HETs showed less rearing ($p<0.05$) and did not habituate. The changes in the rotorod and open field test suggest non-ambulatory motor deficits. Our results indicate that this model exhibits behavioral similarities to RTT. Supported by PO1 HD24448 and HD24061.

140. IRON, THE BRAIN AND GOLDILOCKS. Jones B.C., Department of Biobehavioral Health. The Pennsylvania State University, University Park, PA 16802, USA. Iron is a trace element necessary for a variety of biological functions including oxygen transport, intermediate metabolism, catalytic actions, immunity and a host of others. In the brain, iron is a co-factor for enzymes, such as tyrosine hydroxylase and plays a critical role in cognitive, affective and motor development. Over the years, our laboratory in collaboration with others has shown that too little iron during development can alter the trajectory of central dopamine system development. It is clear that iron deficiency during critical periods during development can result in permanent damage in rodents and in humans. We have new data that show that the attentional deficits produced by iron deficiency in infancy in rats can be reversed with methylphenidate treatment. Alternatively, in other work in our laboratory we are showing that the commonly applied herbicide, paraquat causes neurodegeneration in the subsantia nigra, but to varying extent in mouse strains and perhaps related to iron content. So, like Goldilocks, the task of the brain is to avoid the porridge containing too much or too little iron and to choose the porridge whose iron content is just right.

141. ACETYL-L-CARNITINE PREVENTS THE COGNITIVE IMPAIRMENT INDUCED BY MDMA IN ADOLESCENT RATS. Magalhes, A.1, Alves, C.J.1, Tavares, M.A.1, de Sousa, L.1,2, Summavielle, T.11 IBMC Neuroprotection Lab, Porto, Portugal; 2 ICBAS, Porto, Portugal. We have previously shown that acetyl-L-carnitine (ALC) prevents the long-term serotonergic depletion induced by 3,4-Methylenedioxymethamphetamine (MDMA) in adolescent rats. Here, we aimed to evaluate the role of ALC in preventing also the long term cognitive damage associated to MDMA exposure in the same animal model. Adolescent male Wistar rats were assigned to four groups: control saline solution, isovolumetric to the MDMA solution, administered intraperitoneally (i.p.); MDMA (4x10mg/Kg MDMA, i.p.); ALC/MDMA (100mg/Kg 30 min of ALC prior to MDMA, i.p.) and ALC (100mg/Kg, i.p.). Working and reference memory were assessed simultaneously in the radial maze, through a fixed position reward task, in which half of the arms were baited and their positions were fixed throughout the training. Rats were killed at the end of the testing period. Levels of monoamines were assessed in dissected brain regions by HPLC-EC.

Neurochemical data revealed a highly significant ($p<0.001$) protection by ALC in the levels of DA and 5-HT, at the ventral mesencephalon, the prefrontal cortex and the hippocampus. In the radial maze, pre-treatment with ALC exerted an effective neuroprotection against the MDMA-induced neurotoxicity by reducing the number of working and reference errors in the first five trials. However, animals from the ALC group also showed a higher number of working and reference memory errors in the same trials. Therefore, while ALC seems to be beneficial in reducing MDMA-induced neurotocixity, it also seems to impair the cognitive function in the healthy brain. All together these results highlight the relevance of understanding the molecular mechanisms involved in the action of ALC. Moreover, the period of ALC administration, ie, before or after a damage, may be of crucial relevance.

142. SALIVARY TESTOSTERONE AND VISUAL INTEREST IN EARLY INFANCY. Alexander, G. M.; Wilcox, T. Dept. of Psychology, Texas A&M University, College Station, TX 77843 USA.Testosterone levels in infant boys predict visual preferences for gender-linked stimuli (Alexander, Wilcox, & Farmer, 2009). In this research, we measured salivary hormone levels in sixty-two male and female infants (3-4 months of age) who watched a video depicting three-dimensional shapes (ball, cube). For both, a fast moving figure and slow moving figure were presented simultaneously, each object appearing once on the left side and once on the right side. Infants were positioned in car seats and eye-moments were measured using an infra-red eye-tracker with remote optics (Model R6, Applied Science Laboratories). Saliva (<15 ml) was collected by a sterile DeLee suction catheter from each infant at the end of the session. The slow moving and fast moving objects (ball pairs, cube pairs) were each defined as an area of interest (AOI). Measures of visual attention (fixation number, looking times) in the AOI were analyzed using MANCOVA for repeated measures, with shape (cube,ball) and speed (fast, slow) as repeated measures, sex (male, female)as a grouping factor, and age as a covariate. That analysis showed a speed by sex effect $F(1, 59) = 6.29$, $P < .01$ such that measures of visual attention on slower moving figures did not differ between male and female infants (Cohens $d = .03$) but attention on faster moving figures was greater in female infants compared to male infants ($d = .54$). In female infants, salivary testosterone levels were unrelated to visual attention on fast or slow moving figures. In male infants, higher androgen levels predicted greater visual attention on slow moving figures. These data provide additional evidence for a role for postnatal hormones in early human development.

REWARD AND ADDICTION

143. VOLUNTARY ETHANOL CONSUMPTION ALTERS HIPPOCAMPAL GABAA RECEPTOR GENE EXPRESSION IN C57BL/6J MICE. **Biggio, F.**; Utzeri, C.; Olla, P.; Follesa, P. Gamma-amino butyric acid type A receptors (GABAAR) are sensitive to ethanol in distinct brain regions and are involved in ethanol tolerance, ethanol dependence and ethanol self-administration. It has been postulated that ethanol tolerance and dependence may be the result of changes in GABAAR gene expression and related function. To further elucidate this possible molecular mechanism we used the social isolation paradigm, an experimental animal model in which GABAAR gene expression is already altered. Thus, we here used socially isolated (SI) C57BL/6J mouse strain to investigate the effect EtOH in the free-choice drinking paradigm on gene expression of GABAAR in the hippocampus. Both groups of mice SI and control group-housed (GH) were exposed for 6 weeks to the two-bottle choice (EtOH versus water); during the whole period of isolation free access to EtOH for 2 h in their home cage, beginning at 0.5 h prior the start of the dark cycle. Mice from both experimental groups were individually housed for the 2-h procedure. Specific GABAAR subunits gene expression was measured by RNase protection assay. We found a significant increase in the abundance of both 4 and subunits of the GABAAR in the hippocampus of SI mice (+20 and 26% respectively $p<0.001$) compared to GH animals. On the contrary the abundance of the 1 subunit mRNA was unchanged in SI mice as compared to GH mice. Voluntary EtOH drinking resulted in a marked increase (89%, $p < 0.01$) in subunit mRNA levels in GH mice, whereas in SI animals, it completely abolished the increase in 4 subunit mRNA but did not alter that of the subunit with respect to the SI mice that drank water. These results suggest that voluntary EtOH drinking in SI mice has a selective influence on 4 subunit since blocks its enhanced expression but fails to alter the up-regulation of subunit.

144. TRANSIENT HYPERDOPAMINERGIC TONE PRECEDES ATTENUATION OF DOPAMINE RELEASE AND BEHAVIORAL SENSITIZATION IN HIV-PROTEIN TREATED RATS WITH A HISTORY OF COCAINE: IN VIVO MCIRODIALYSIS IN THE NUCLEUS ACCUMBENS. Booze, R.M.; Ferris, M.J.; Frederick-Duss, D.; Fadel, J.; Mactutus, C.F. Program in Behavioral Neuroscience, University of South Carolina, Columbia, SC, 29208, USA and Department of Pharmacology, Physiology, and Neuroscience, University of South Carolina School of Medicine, Columbia, SC, 29208, USA. HIV positive drug abusers have higher rates of cognitive and motor dysfunction in comparison to non-drug abusers; however, the neurobiological consequences of drug use and HIV infection remain unclear and pharmacotherapy unsuccessful. Recent human imaging studies find that the dopamine transporter (DAT) is reduced in HIV patients, especially in those with cognitive/motor deficits and those with co-morbid cocaine abuse. The current investigation used quantitative in vivo microdialysis following an intra-accumbal

administration of the HIV-1 protein, Tat, in drug nave rats, compared to cocaine treated rats. We found that cocaine pretreated rats, showed an early hyperdopaminergic state following Tat-treatment, relative to non-treated controls. This early hyperdopaminergic state is transient as the DA response and cocaine-induced locomotor activity is blunted during a late testing phase in Tat + cocaine treated animals. A robust and persistent decrease in DA metabolite levels was found in Tat-treated animals regardless of experience with cocaine. Thus, the combination of neurotoxic HIV-1 proteins and cocaine results in a hyperdopaminergic state. The preservation of DAT uptake kinetics and homeostatic DA concentrations may break the pathological feedback loop in HIV-1, providing a targeted neuropharmacologic approach for dopaminergic dysfunction and neurocognitive deficits in HIV+ drug abusers. supported by NIH DA014401; DA013137; HD043680

145. ACUTE (+)-METHAMPHETAMINE (MA) EXPOSURE SELECTIVELY INCREASES BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) AND MODULATES TRKB EXPRESSION IN THE ADULT RAT BRAIN Braun, A.A; Herring, N.R.; Schaefer, T.L.; Hemmerle, A.M; Dickerson, J.W.; Seroogy, K.B.; Vorhees, C.V.; Williams, M.T. Div Neurology, Cincinnati Childrens Research Foundation and Dept. of Neurology, Univ Cincinnati College of Medicine. MA is an abused stimulant which at sufficient doses can result in cognitive deficits and monoamine depletions. Animal models of neurotoxic MA exposure show reductions in dopamine (DA), serotonin (5-HT), and their associated transporters and rate limiting synthetic enzymes. MA abuse can also result in long-term attention, working memory, and executive function deficits in humans, and with deficits in route-based egocentric learning and novel object recognition in rodents. Furthermore, MA can modulate BDNF in humans and rodents. This experiment examined the effects of a neurotoxic binge dosing regimen (10 mg/kg x 4 at 2 h intervals, s.c.) of MA in Sprague-Dawley rats on BDNF, TrkB, and tyrosine hydroxylase (TH) mRNA expression as well as plasma corticosterone (CORT) levels. Tissues were collected 1, 7, and 24 h after MA dosing. mRNAs were analyzed using in situ hybridization with cRNA probes. BDNF mRNA was particularly susceptible to MA exposure with increased expression in frontal, parietal, and entorhinal cortices at all time points, and alterations in other regions at select time points. TrkB expression was modified in the hippocampus, PFC, and striatum. Plasma CORT levels were increased at all time points. The findings suggest that BDNF and TrkB may be upregulated as a compensatory mechanism shortly after MA exposure. How long these changes last is unknown. Support by NIH grants R01 DA006733 and T32 ES07051.

146. NEUROSTEROID MODULATION OF CHRONIC ALCOHOL TOLERANCE IN ALCOHOL-PREFERRING MICE ON MEASURES OF FINE AND GROSS MOTOR COORDINATION. Cronise, K.1, 2, Henschen, C.2, Sullivan, A.2, Brown, K.1,3, Dupre, N.2, McNally, A.3, Lee, K.1,2 Morrison, A.2, Saeed, F. 2, Dept. of Psychology1, Prog. of Neuroscience2 and Dept. of Molecular Biology3, Middlebury College, Middlebury, VT 05753 These studies assessed the effects of the neurosteroids epipregnanolone (EPI) and pregnenolone sulfate (PS), allosteric modulators of the GABAA receptor, on the development of chronic tolerance to ethanol-induced ataxia in C57BL/6J (alcohol-preferring) mice. EPI was hypothesized to block tolerance development, while PS would facilitate it. Challenging measures of fine motor coordination, such as the balance beam, were predicted to be better assessments of altered ethanol tolerance than measures of gross motor coordination, such as the rotarod. Male C57BL/6J mice were injected (IP) with 0.3 or 1 mg/kg EPI, 0.15 mg/kg PS, or saline, 30 minutes before a 3 g/kg injection of ethanol or saline, daily, for 5 days. On day 6, mice were injected with 2.25 g/kg ethanol or saline and tested for ataxia on the fixed-speed rotarod followed by balance beam testing. On both apparatus, mice pre-treated with ethanol showed less ataxia than ethanol-nave mice, indicating tolerance. On the rotarod, no effects of the neurosteroids on tolerance were seen. On the balance beam, EPI/ethanol pre-treatment affected performance dose dependently. Mice pre-treated with 1 mg/kg EPI made more foot-slips and were less tolerant than mice pre-treated with ethanol only. While strong effects of neurosteroids on tolerance in Swiss Webster mice have been shown, the effect may be either very modest or more difficult to assess in the C57BL/6J strain. Sensitive measures of ataxia and higher doses of neurosteroids are necessary to demonstrate the putative modulation of tolerance in C57BL/6J mice. Support: NIH/AREA (1R15AA18216-1) and VGN/INBRE 2009 Award.

147. COMPARISON OF AMPHETAMINES FOLLOWING BINGE DOSING ON MULTIPLE-T WATER MAZE LEARNING Vorhees, C.V.; He, E.; Skelton, M.R.; Graham, D.L., Schaefer, T.L.; Grace, C.E.; Braun, A.A.; Amos-Kroohs, R.; Williams, M.T. Division of Neurology, Cincinnati Childrens Hospital Medical Center and University of Cincinnati Phenylethylamines [(+)-methamphetamine (MA), ()-3,4-methylenedioxymethamphetamine (MDMA), (+)-amphetamine (AMPH), and ()-fenfluramine (FEN)] cause reductions of 5-HT and/or dopamine (DA) at high doses. Although cognitive impairments have been found in human MA and MDMA abusers, modeling these deficits in rats has proven difficult. Rats treated with MA (10 mg/kg x 4 at 2 hr intervals) show impaired Cincinnati multiple-T water maze (CWM) learning under infrared lighting (to eliminate distal cues and promote reliance on egocentric cues); whereas allocentric learning (Morris water maze) was unaffected (Herring et al. 2008; Psychopharmacology, 199: 637-650). Adult male Sprague-Dawley rats were treated with 4 subcutaneous doses at 2

h intervals on 1 day with MA = 10 or 12.5, AMPH = 25 (to match MA-induced hyperthermia), MDMA = 15 mg/kg (hyperthermic dose), and FEN = 16.5 mg/kg/dose (equimolar to MA) or Saline and tested 2 weeks later in the CWM (2 trials/day for 21 days). AMPH and MA increased errors and latency to find the goal. Errors and latency were not significantly affected by MDMA or FEN. None of the drugs affected swimming speed or motivation to escape in a straight swimming channel. FEN selectively and MDMA preferentially affects 5-HT whereas AMPH selectively and MA preferentially affects DA, hence the data suggest that DA plays a larger role in this form of learning than 5-HT. (NIH grants R01 DA006733 and T32 ES07051)

148. THE USE OF PRESCRIBED MEDICINES TO IMPROVE MENTAL HEALTH BY COLLEGE STUDENTS. Reid, L.D.; Reid, M.L. Rensselaer Polytechnic Institute, Troy, NY 12180 USA. Samples of students (n = 912) from five colleges, in the USA, were surveyed concerning their use of prescription medicines to treat various disorders. They were asked whether they had ever been prescribed, by a professional health care provider, medicines to treat (a) depression, (b) anxiety, (c) bipolar disorder, (d) insomnia, (e) chronic pain and (f) attention deficit/hyperactivity disorder. Subsequently, a smaller sample was asked about schizophrenia. They were also asked to estimate the % of the students on their campus who had ever been prescribed the same kinds of medicine. In addition, they were asked if they were currently taking the prescribed medicines and asked to estimate the % of their fellow students who were currently taking the medicines. They were asked their age and sex. The incidence of prescriptions for a disorder were similar to the reported incidence rates for the disorder among adults in the USA (e.g., about 1% for bipolar disorder), except for schizophrenia (exceptionally low levels of prescriptions for medicines to treat schizophrenia). The students estimates of their fellow students rates of being prescribed, and currently taking psychotropic drugs, are much larger than the students reports of being prescribed and currently taking. Women's estimates were larger than mens. College students have totally unrealistic estimates of the use of prescription drugs by their fellow students.

149. THE EFFECT OF PRIOR INTERMITTENT BINGEING ON HIGHLY PALATABLE FOODS ON SUBSEQUENT BEHAVIOURAL SENSITIZATION TO THE DOPAMINE AGONIST, QUINPIROLE. Tenk, C.M.; Campbell, A.; Ossenkopp, K.-P.. Psych Dept. Brescia University College at University of Western Ontario; Psych Dept & Graduate Prog in Neurosci. University of Western Ontario, London, CANADA. Sensitization of neural reward circuits, including the mesolimbic dopamine system, is hypothesized to contribute to the development of addiction. Highly palatable foods activate these same areas and binge eating produces brain and behaviour changes that resemble aspects of addiction. This study examined the effects of intermittent bingeing on highly palatable foods (sugar or sugar-fat) on these circuits by measuring subsequent locomotor sensitization to the dopamine (D2/D3) agonist, quinpirole. Free-feeding male Long-Evans rats were given 2hr access to one of four diets (sugar, sugar-fat, chow-pellet, chow-mash) 3x per week for four weeks. Locomotor sensitization was then examined 10 days after scheduled feeding. Rats were injected with quinpirole (0.5mg/kg, s.c.) every other day for a total of 10 injections. Locomotor activity was assessed using an automated open-field. There was evidence of bingeing in all diet groups except for the chow-pellet group. Chow-mash rats consumed significantly more than all other groups while sugar-fat rats consumed significantly more than the sugar and chow-pellet rats. Despite these large differences in prior bingeing, there were no significant effects on quinpirole-induced locomotor sensitization. However, there was a trend such that sugar animals showed the highest level of sensitization to quinpirole administration, sugar-fat animals the lowest and chow-pellet and chow-mash animals intermediate levels. These data suggest that the effect of prior bingeing on highly palatable foods on subsequent locomotor sensitization is a complex interaction that may depend on factors such as palatability and reward, amount consumed and/or caloric intake. Supported by NSERC and Brescia University College.

150. MORPHINE INDUCED LOCOMOTION AND ULTRASONIC VOCALIZATIONS IN M5 KNOCKOUT MICE RESCUED BY VIRAL TRANSFECTION OF M5 MUSCARINIC RECEPTORS IN VENTRAL TEGMENTUM. Wasserman, D.; Lee, E.; Wang, H.; Rashid, A.; Josselyn, S.; Yeomans, J. Depts. of Psychology and Physiology, University of Toronto, Toronto, ON M5S3G3 Canada. Mesopontine cholinergic neurons activate tegmental dopamine neurons via nicotinic and M5 muscarinic receptors. In rats, ventral tegmental area (VTA) muscarinic receptors are needed for brain-stimulation reward, food reward sensitivity, and morphine-induced dopamine output. M5 knockout mice emit fewer ultrasonic vocalizations (USVs) during mating, and show less locomotion or dopamine output in response to morphine than wild-type mice. Using a Herpes simplex virus, the M5 receptor gene was transfected into the VTA or rostromedial tegmentum (RMT) of M5 knockout mice along with a green fluorescent protein (GFP) marker gene (HSV-M5-GFP). M5 transfection into VTA dopamine and non-dopamine neurons fully restored mating-induced USVs and increased morphine-induced locomotion and stereotypy. M5 transfection into RMT inhibited USVs and morphine-induced locomotion, consistent with activation of RMT GABA or median raphe serotonin neurons that tonically inhibit VTA dopamine neurons. These M5 transfection studies help identify which tegmental neurons are responsible for deficits in M5 knockout mice, and show that these deficits are reversed in adult mice with a single localized transfection.

151. BLOCKADE OF MAPK/ERK KINASE BY SL327 PREVENTS THE ACQUISITION OF LITHIUM-ELICITED PLACE AVERSION Longoni R.1, Spina L. 1, Vinci S. 1, Ibba F. 1, Gabba S. 2, Mulas G. 2, Spiga S.2 and Acquas E.1,3,4 1Department of Toxicology, 2Department of Animal Biology and Ecology, 3INN National Institute of Neuroscience, 4Centre of Excellence on Neurobiology of Addiction, University of Cagliari, I-09100 Cagliari, Italy The place conditioning paradigm is a method that allows the characterization of intrinsic motivational properties of drugs. These are transferred to an otherwise neutral environment by a process of associative learning and both positive and negative motivational properties of drugs can be studied, respectively, by conditioned place preference (CPP) and conditioned place aversion (CPA) experiments. ERKs are intracellular kinases particularly enriched in the mesolimbic system that have been shown to play a role in the acute effects of addictive drugs and in the associative learning processes. However, while the role of MAPK/ERK kinases (MEK) in the motivational properties of drugs has been assessed by CPP experiments with drugs such as cocaine, ecstasy and amphetamine, little is know on the role of MEK in CPA learning. Aim of our study was therefore to verify whether blockade of MEK by SL327 would affect the acquisition of CPA. Male C57BL6J mice were used for this study. Mice were tested for their spontaneous preference in an unbiased apparatus and, during conditioning, were administered with saline + saline (SAL) or saline + lithium chloride (LITH, 150 mg/kg i.p.) before being paired, with the assigned compartment. To study the role of MEK inhibition, SL327 was administered, at the dose of 50 mg/kg i.p., unable per se to modify mice spontaneous preference, before SAL or LITH. Conditioning took place every day for 4 days. At the end of conditioning mice were tested, in a drug-free condition, for LITH-elicited side preference shift. In agreement with previous data, LITH elicited a significant CPA and blocakade of MEK during conditioning prevented LITH-elicited CPA. The results demonstrate that LITH elicits CPA in mice and demonstrate for the first time, to our knowledge, that blockade of MEK prevents the acquisition of aversive conditioning as assessed by CPA.

152. THE MEK INHINBITOR SL327 PREVENTS THE ACQUISITION OF ETHANOL-ELICITED PLACE PREFERENCE AND PLACE AVERSION Spina L. 1, Longoni R.1, Vinci S. 1, Ibba F. 1, Gabba S. 2, Mulas G. 2, Spiga S.2 and Acquas E.1,3,4 1Department of Toxicology, 2Department of Animal Biology and Ecology, 3INN National Institute of Neuroscience, 4Centre of Excellence on Neurobiology of Addiction, University of Cagliari, I-09100 Cagliari, Italy Under appropriate experimental conditions ethanol has been shown able to elicit both conditioned place preference (CPP) and conditioned place aversion (CPA). The role of ERK in drug-elicited place conditioning has been demontrated for a number of drugs of abuse and in a recent study we demonstrated that, similarly to other addictive compounds, ethanol activates ERK phosphorylation in the nucleus accumbens and nuclei of the extended amygdala. Aim of the present study was to assess the role of activated ERK in the acquisition of ethanol elicited CPP. In addition, since the role of activated ERK in CPA has not been addressed, aim of the present study was to determine whether blockade of MEK would result also in prevention of ethanol-elicited CPA. Male CD-1 mice were used in these experiments with an unbiased place conditioning apparatus. Ethanol (2 g/kg i.p.) was administered either immediately before or immediately after 5 minutes pairings with an assigned compartment. The MEK inhibitor SL327 was administered, at the dose of 50 mg/kg i.p. unable per se to affect spontaneous preference, before ethanol or saline. The results confirm that ethanol, in these conditions, is able to elicit significant CPP and CPA. Interestingly, SL327 administration not only prevented ethanol-elicited CPP but also significantly prevented ethanol-elicited CPA. Overall these results indicate that phosphorylated ERK plays a critical role in the acquisition of place conditioning, irrespective of their motivational valence, and cast new light on the role of ERK in the acquisition of conditioned responses.

153. ADOLESCENT DRINKING IN THE DARK. Metten, P., Brown, L.L., Crabbe, J. C. Portland Alcohol Research Center, Oregon Health & Science Univ, Dept Behavioral Neuroscience, and VA Medical Center, Portland, OR USA. We studied limited access drinking of ethanol during the dark cycle (DID) in a genetically heterogeneous stock of mice (HS/Npt). We studied the developmental onset of DID and whether ethanol drinking during adolescence in this model would lead to enhanced drinking during adulthood. HS/Npt mice of 7 age groups (3 9 wks at testing onset) were tested for DID for 4 days. 3 hrs into the dark cycle, water bottles were removed and replaced by a single tube containing 20% v/v ethanol. Ethanol consumed in 2 hrs was measured, tubes removed and water restored. On Day 4, ethanol was left on for 4 hrs. Mice then were left undisturbed for 3 days. Mice of each age cohort were tested in this procedure for two consecutive wks (ie, mice of the 3 wk old group were tested at 3 wks and at 4 wks). Mice then were undisturbed until all mice were aged 9 wks and were retested for 2 more consecutive wks. Results showed that mice aged 5-6 wks drank more in their 2nd consecutive week than initial values, suggesting a developmental period of susceptibility to high ethanol drinking. Groups aged 4 & 8 wks drank more ethanol at 10 wks of age than during earlier periods, suggesting that repeated DID may lead to greater consumption later. Supported by the Dept of Veterans Affairs, and AA107860 and AA13519 from the NIH.

154. MODERATE COCAINE EXPOSURE RESULTS IN INAPPROPRIATE INCENTIVE LEARNING VIA MU OPIOID RECEPTOR-RELATED PROCESSES IN THE BASOLATERAL AMYGDALA Wassum, K.M.; Cely, I.C.; Maidment, N.T. Semel Institute for Neuroscience and Human Behavior. University of California Los Angeles, Los Angeles, CA 90095, USA. In addiction, it is often the case that the addict seeks out the abused substance with consistent or increasing vigor despite a decline in the actual experienced high or negative consequences associated with use. We tested the hypothesis that addictive substances result in incentive value attributions inconsistent with affective experience by examining the impact of cocaine on the hedonic experience and incentive value of a sucrose solution. Rats maintained relatively sated were trained to seek sucrose using a procedure in which they had to press a (seeking) lever to gain access to a second lever that delivered sucrose. This task has been found to establish a reward seeking action sensitive specifically to incentive value. Rats were given an incentive learning opportunity by allowing them to consume the sucrose after cocaine injections. We show that cocaine inflated the value of the sucrose as evidenced by an increase in subsequent reward seeking actions towards it. Importantly cocaine increased sucrose reward seeking actions in a manner that was inconsistent with its current affective properties. Moreover, we show this effect of cocaine, to inflate the value and therefore reward seeking actions, to be dependent upon basolateral amygdala mu opioid receptors. When cocaine-sucrose pairings were conducted under basolateral amygdala mu opioid receptor blockade, cocaine showed no significant effect on subsequent reward seeking activity; i.e. reward seeking actions remained consistent with affective experience. These data indicate that cocaine exposure may result in a disruption of incentive learning, via basolateral amygdala mu opioid receptor-related processes, whereby incentive value is altered without respect to actual hedonic impact.

155. SUBSECOND DOPAMINE RELEASE IN THE VENTRAL AND DORSOLATERAL STRIATUM DURING COCAINE SELF-ADMINISTRATION. Willuhn, I.; Phillips, P.E. Dept. of Psychiatry & Behavioral Sciences. University of Washington, Seattle, WA 98195 USA. Dopamine neurotransmission in the ventral striatum is known to control the intake of abused drugs. Over time, the control of drug taking is thought to become increasingly dependent on the dorsolateral striatum. In a previous study, we characterized subsecond dopamine release in the ventral striatum at an early time point during cocaine self-administration training. Here, we extended this work by assessing changes in phasic dopamine signaling in the ventral and dorsolateral striatum simultaneously over the course of weeks. Electrodes for fast-scan cyclic voltammetry were chronically implanted in the striatum of rats outfitted with intravenous catheters for cocaine self-administration. Rats were allowed access to cocaine in an operant chamber for one hr/day for 20 days. During a self-administration session, a nose poke elicited a cocaine infusion (0.5 mg/kg) that was accompanied by a 20-second presentation of an audiovisual stimulus (delivery cue). After this 20-second time-out, a separate cue signaled the availability of additional infusions (availability cue). Consistent with our previous studies, we observed phasic dopamine release in the ventral striatum associated with the presentation of the delivery cue throughout training. Additionally, dopamine release in this brain region associated with the presentation of the availability cue was augmented after repeated training. In the dorsolateral striatum, cue-related dopamine signals developed only during later stages of training. These results show that phasic dopamine signaling in the striatum in response to drug cues is region-specific and changes dynamically over time. Furthermore, these data suggest that dopamine release in the dorsolateral striatum may only be involved in the control of drug taking after repeated drug experience.

156. LATERODORSAL TEGMENTAL ACETYLCHOLINE NEURONS DRIVE METHAMPHETAMINE STIMULATION OF LOCOMOTOR ACTIVITY AND NEUROCHEMICAL RESPONSES IN THE VENTRAL TEGMENTAL AREA. Dobbs, L. K.; Mark, G. P. Department of Behavioral Neuroscience, Oregon Health & Science University, Portland, OR 97239, USA. Methamphetamine (MA) reward is in part mediated by the activity of dopamine (DA) neurons within the ventral tegmental area (VTA). Acetylcholine (ACh) modulates DA release within the mesocorticolimbic pathway. The laterodorsal tegmental nucleus (LDT) is the primary source of ACh to the VTA and has been implicated in psychostimulant activation and reward-related behavior. The current study examined the role of LDT-derived ACh in MA locomotor activation. LDT ACh neurons were reversibly inhibited with bilateral microinjections of the M2 receptor agonist oxotremorine (OXO) in the LDT. Mice were given OXO (0, 0.1, or 0.01 nmol/side) immediately prior to IP saline or MA (2 mg/kg). MA-induced locomotor activity was significantly inhibited by the highest OXO dose (0.1 nmol/side). The 0.01 nmol/side dose and aCSF were without effect. In a second experiment we used microdialysis in the VTA to clarify the role of LDT-derived ACh in MA-induced levels of ACh and DA. Extracellular ACh increased to 433% of baseline following LDT microinjection of aCSF+ IP MA (2 mg//kg). Intra-LDT OXO (0.01 and 0.1 nmol/side) reduced the MA-induced increase in VTA ACh to 290% and 171% of baseline, respectively. Somatodendritic DA levels in the VTA were not significantly increased (127% of baseline) after LDT microinjection of OXO (0.01 nmol/side) + IP MA. The effects of higher OXO doses (0.05 and 0.1 nmol/side) on MA-induced VTA DA levels are currently being tested. These data suggest that LDT ACh is important in behavioral and neurochemical responses to systemic MA. Future experiments will analyze the potential role of LDT-derived ACh on MA self-administration and MA-seeking behavior.

157. EFFECTS OF THE COMBINATION OF METYRAPONE AND OXAZEPAM ON METHAMPHETAMINE SEEKING IN RATS. Goeders, N.E.; Keller, C.; Cornett, E.; Guerin G.F. Dept. of Pharmacology, Toxicology & Neuroscience. Louisiana State University Health Sciences Center in Shreveport, Shreveport, LA 71130 USA. We have previously reported that combining low doses of metyrapone (a corticosterone synthesis inhibitor) and oxazepam (a benzodiazepine receptor agonist) reduces intravenous cocaine self-administration and the cue-induced reinstatement of extinguished cocaine seeking in rats. This experiment was designed to investigate whether or not the combination of metyrapone and oxazepam would also block cue reactivity associated with methamphetamine self-administration in rats. Adult male rats were implanted with jugular catheters and trained to self-administer methamphetamine (0.06 mg/kg/infusion) during daily 2-h sessions. During training, methamphetamine delivery was paired with the presentation of a tone and the illumination of a houselight. Once stable baselines of self-administration were observed, rats were placed into forced abstinence, where the rats remained in their home cages for 14 days. During cue reactivity testing on the 15th day, the rats were placed in the operant chambers and responding only resulted in the presentation of the conditioned reinforcer (i.e., the houselight and tone previously paired with methamphetamine self-administration); no methamphetamine was delivered. The response-contingent presentation of the conditioned reinforcer reliably maintained methamphetamine seeking (i.e., lever pressing) following vehicle pretreatment. Pretreatment with combinations of metyrapone and oxazepam (25mg/kg metyrapone/5 mg/kg oxazepam or 50mg/kg metyrapone/10 mg/kg oxazepam, ip) resulted in a dose-related attenuation of methamphetamine seeking. These data suggest that the combination of metyrapone and oxazepam may be useful in blocking the ability of environmental cues to stimulate methamphetamine seeking.

158. THE EFFECTS OF THE AGONIST THERAPY IN ANXIUOS-DEPRESSED POSITIVE HCV DRUG-ABUSERS TREATED WITH IFN THERAPY. Pieri, M-C., Bologna, Italy. The substances of abuse and / or stressful events can activate CREB, the results is an increase in gene transcription of dynorphin, which increases the activity of kappa receptor mediated and development of a dysphoric state. HCV infection is associated with psychiatric disorders, like depression, and drug abusers with this infection have these disorders more frequently than abusers without HCV. In patients with hepatitis C, a rebalancing, with opioid agonist drugs, in addition to improving mood, but also improves quality of life and has the effect of immuno - stimulation in response to treatment of HCV. In patients heroin addicts and with hepatitis C, a rebalancing with opioid agonist drugs, improving mood but also improves quality of life and has the effect of immuno - stimulation in response to treatment of HCV. A group of patients addicted to heroin and HCV positive charge at the Sert EST and treated with opioid agonists and PEG-INF-RIBA, was observed over a period of one year. Monthly Test was administered on the HAM-D, for the assessment of depression by the physician, have made surprise checks of urine, blood chemistry checks at the beginning and end of the observation and evaluation of potential side effects present and the monitoring of the weight. Patients, who test Hamilton appeared to have a depression is moderate and severe were treated with antidepressant SSRIs at different doses, all patients in the group have completed the treatment with interferon, taking into depression under control.

159. OBSERVATIONAL STUDY AND FOLLOW-UP OF PATIENTS IN TREATMENT WITH OLAZAPINE AND SUBSTITUTIVE DRUG. Dott Del Re Arfedele; Dott Claudio Antonio Comaschio. In our study, we want to verify: The aim of the treatment with olanzapine to patients who take methadone like substitutive drug; the difference of gravity between patients who take methadone and patients who take buprenorphine. Valuations of craving on the use of substances and the course of the weight of the patients from every 2 months until six months and then every the T/0 time six months until 30 months. We have divided the patients in 3 groups: 1) take methadone and after the T/0 time Scales BRMES and BRMAS after 30 months of observation still do not show meaningful differences of score total or single items regarding the visit to a 6 months, denoting a decreasing course. Analyzing it turns out to you obtained from the three groups of famous treatment like, newly are not present meaningful differences after the T/4 that is to the six months for both the scales, but that the olanzapine association - methadone it concurs to obtain turns out better to you and in short times and than to maintain them for longer times. The weight has been another variable studied. As far as the champion total, some meaningful difference between the beginning of the observation and the visit to 30 months is not observed. The analysis of the VAS in the champion total concurs to observe a decreasing course, statistically meaningful ($p<0.0001$) in the first 6 months of treatment and to the term of the observation, to 30 months. The compliance of the patients he has been good, all have finished the study, the association of two drugs like the methadone and the olanzapine also in presence of psychiatric symptomatology under level significance improves in our champion the adherence of the patient drug addict to the treatment also in absence of one statistics results.

160. FROM THE FEEDING TUBE TO THE ANIMAL MODELS OF AFFECTIVE DISORDERS Pinhasov, A.; Kuznetsov, Y.; Rylova, A.; Tikhonova T.; Nesher, E. Ariel University Center of Samaria, Israel Dominant-Submissive Relationship (DSR) based tests were developed for mood stabilizing or antidepressant drug testing. In our current DSR model, pairs of animals compete for food during daily 5-min sessions. The relationship of animals was defined as dominant-submissive when one animal of a pair spent a significantly longer time on the feeder (dominant) than the other (submissive). Under such conditions only 25-30% of animal pairs form DSRs. Using selective breeding approach and based on DSR test we developed populations of Sabra mice with prominent dominant and submissive characteristics. The frequency of DSR formation gradually increased across generations of outbred Sabra mice, when animals inbred for the dominant trait were paired with those inbred for the submissive trait. Thus, more than 95% of animals of F9 generation developed strong and stable DSRs. Treatment of submissive animals with known antidepressants significantly reduced submissive behavior in a dose- and time-dependent manner. Mood-stabilizing agent lithium, selectively influenced on animals with dominant background. Furthermore, submissive pups suckled by dominant dams and dominant pups suckled by submissive females maintained their genetically specified features. Thus, our accumulating data demonstrate that 1) selectively bred dominant and submissive mice have different genetic background; 2) may serve as a potential model for screening of antidepressant and antimanic compounds 3) may aid in a better understanding of the genetic basis of dominant and submissive behavior, important elements in the etiology of affective disorders.

8:30-10:30 **Symposium 9**: Understanding the impact of emotional experiences on brain function: insights from animal and clinical studies. Chairpersons: **Patrizia Campolongo**, Ph.D., Sapienza University, Rome, ITALY and **Viviana Trezza**, Ph.D., Rudolf Magnus Institute of Neuroscience, Utrecht, THE NETHERLANDS. ***(Sponsored by IBRO)***

SOCIAL DEFEAT EXPERIENCES WITH ENDURING IMPACT ON BDNF, ERK AND DOPAMINE-MEDIATED BEHAVIOR. Miczek, K. A., Dept. of Psychology, Pharmacology, Psychiatry and Neuroscience. Tufts University, Medford and Boston, MA 02215, USA. An apparent paradox in need of resolution is the neural link between ostensibly aversive stress experiences and intensely rewarding drug taking. Epidemiological data associate stress and the abuse of various drugs, and experimental data identify the conditions that determine how episodic social stress intensifies the motivation for cocaine and the actual self-administration of cocaine. Two types of social stress have been the focus of experimental study in Long-Evans rats, since they engender divergent changes in drug- or sugar-rewarded behavior and in neuroadaptation. Episodic social defeat stress consists of four brief confrontations between the experimental rat and an aggressive resident rat of the Long-Evans strain over the course of 10 days. Subordination stress involves the continuous exposure to an aggressive resident for five weeks, while living in a protective cage within the resident's home cage with daily brief confrontations. These stress experiences result in (1) increased intravenous cocaine self-administration under fixed and progressive ratio schedules with prolonged binge-like access in episodically defeated intruder rats, but suppressed cocaine intake by continuously subordinate rats; (2) deteriorated sugar preference and intake and decreased exploratory behavior in subordinate, but not intermittently defeated rats; (3) a sensitized dopamine response in the n. accumbens via in vivo microdialysis and fast scan voltametry, increased tegmental BDNF and phosphorylated ERK and CREB in episodically defeated rats, whereas the continuously subordinate rats show suppression of the DA, BDNF, ERK and CREB responses. These divergent neuroadaptations to social stress may represent the substrates for the intensification of cocaine "bingeing" relative to the anhedonia-like deterioration of reward processes during subordination stress.

GLUCOCORTICOIDS AND THE REGULATION OF MEMORY OF EMOTIONALLY AROUSING EXPERIENCES Roozendaal, B Dept. of Neuroscience, Section Anatomy, University Medical Center Groningen, Groningen, The Netherlands Extensive evidence indicates that stress hormones released from the adrenal glands are critically involved in memory consolidation of emotionally arousing experiences. Epinephrine or glucocorticoids administered after exposure to emotionally arousing experiences enhance the consolidation of long-term memories of these experiences. Our findings indicate that adrenal stress hormones influence memory consolidation via interactions with arousal-induced activation of noradrenergic mechanisms within the basolateral complex of the amygdala (BLA). In turn, the BLA regulates memory consolidation via its efferent projections to many other brain regions. In contrast to the enhancing effects on consolidation, high circulating levels of stress hormones impair memory retrieval and working memory. Such effects also require noradrenergic activation of the amygdala and interactions with other brain regions. These apparently dual effects of glucocorticoids on memory consolidation versus memory retrieval and working memory appear to be related in terms of function and neurobiological substrate. The BLA is a key structure in a memory-modulatory system that regulates, in concert with other brain regions, stress and glucocorticoid effects on these different memory functions.

NEUROBIOLOGICAL AND EPIGENETIC MECHANISMS INVOLVED IN THE IMPACT OF STRESS ON AGGRESSION AND DEPRESSION. Sandi, C.; Marquez, C.; Larsen, M.H.; Cordero, M.I.; Poirier, G. Laboratory of Behavioral Genetics, Brain Mind Institute, Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland. Stress is a potent modulator of brain function and cognition, and can have a major impact on social interactions. Epidemiological data in humans indicates that early life stress can have long-term consequences in individuals personality, including increased aggression and vulnerability to develop depression. We will present an animal model developed in our lab in which male rats stressed around puberty show pathological aggression and depression-like behaviours in adulthood. These alterations are accompanied by hyperactivity in several amygdala nuclei and hypoactivity in the orbitomedial prefrontal cortex, as well as by changes in the expression of genes of the serotonin family in the prefrontal cortex. Evidence for the implication of epigenetic mechanisms will be presented. Finally, I will show how, eventually, stress has a profound impact not only in the directly stressed individuals but also in their interacting partners and offspring. These results will be discussed within a broader context implying stress as a strong modulator of social interactions.

OBSERVATIONAL FEAR LEARNING IN MICE IS DEPENDENT ON THE AFFECTIVE PAIN SYSTEM AND L-TYPE CALCIUM CHANNELS IN THE ANTERIOR CINGULATE CORTEX. Shin, H-S.; Jeon, D. Center for Neural Science, Korea Institute of Science and Technology, Seoul, Korea. Fear can be acquired via empathy through social observation of others suffering from aversive stimuli. We show here that a mouse (observer) develop freezing behavior by observing another (demonstrator) receiving repetitive foot shocks. Observers displayed higher fear responses when demonstrators were socially related to themselves, such as siblings or mating partners. Inactivation of anterior cingulate

cortex (ACC), and parafascicular or mediodorsal thalamic nuclei, which comprise the medial pain system representing pain affection, significantly impaired this observational fear learning, whereas inactivation of sensory thalamic nuclei had no effect on this learning. The ACC neuronal activities were increased and synchronized with those of the lateral amygdala at the theta rhythm frequency during this learning. Furthermore, an ACClimited deletion of Cav1.2 Ca2+ channels in mice impaired observational fear learning as well as reduced behavioral pain responses. These results demonstrate the involvement of the affective pain system and Cav1.2 in the ACC in observational social fear by empathy.

THE PLAYFUL BRAIN: INSIGHTS INTO SOCIAL REWARD MECHANISMS. V. Trezza, R. Damsteegt, P.J.J. Baarendse, L.J.M.J. Vanderschuren. Rudolf Magnus Institute of Neuroscience, Dept. of Neuroscience and Pharmacology, University Medical Center Utrecht, Utrecht, The Netherlands. Social play behavior, also known as rough-and-tumble play, is the most characteristic and energetic social behavior displayed by young mammals. This form of social behavior is highly conserved throughout evolution, and it is essential to develop behavioral and mental flexibility, and to acquire cognitive and social competence. In line with its importance for proper development of brain and behavior, social play is a natural reinforcer. Although the neural underpinnings of social play behavior are largely unknown, accumulating evidence suggests that neurotransmitter systems involved in positive emotions and motivation modulate social play behavior in adolescent rats. Thus, previous studies have shown that the opioid receptor agonist morphine enhances social play, whereas opioid receptor antagonists suppress it. Our recent studies have shown that indirect cannabinoid agonists, that increase endocannabinoid signalling by inhibiting endocannabinoid inactivation, enhance social play, through interaction with opioid and dopaminergic neurotransmission. Interestingly, other drugs that act on brain reward mechanisms, such as ethanol and nicotine, also increased social play, acting through opioid, cannabinoid and dopamine receptors. Investigation of the brain regions involved has thus far identified the nucleus accumbens and amygdala as important sites for opioid and cannabinoid modulation of social play. Together, our data indicate that interacting opioid, cannabinoid and dopaminergic systems within the corticolimbic circuits underlying incentive motivation and reward modulate the expression of social play behavior.

3:00-5:00 **Symposium 10**: TIME GOES BY: THE INTERPLAY BETWEEN EMOTION AND MEMORY.
Chairperson: **Antonella Gasbarri** and **Carlos Tomaz**

ESTROGEN AND WORKING MEMORY FOR EMOTIONAL FACIAL EXPRESSIONS IN YOUNG WOMEN. Gasbarri A.*(1);Pompili A.(1);dOnofrio A.(1);Arnone B.(1);Tavares M.C.(2);Tomaz C.(2). (1) Dept.Biomed.Sci. & Technol.,Fac.Sci.Education,Univ. LAquila, Italy;(2) Dept. Physiol. Sci., Lab. Neurosci. & Behav.,Univ. Braslia, Brazil. Physiological hormonal fluctuations during the menstrual cycle, postpartum, and menopause have been implicated in the modulation of mood, cognition, and affective disorders. Taking into account that womens performance in memory tasks can also fluctuate with circulating hormones levels across the menstrual cycle, the cognitive performance in a working memory (WM) task for emotional facial expressions, using the six basic emotions as stimuli in the delayed matching-to-sample task (DMTS), was evaluated in young women in different phases of the menstrual cycle. Our findings suggest that high levels of estradiol in the follicular phase (FP) could have a negative effect on DMTS WM task, using stimuli with emotional valence. Moreover, in the FP, compared to the menstrual phase, the percentage of errors was significantly higher for the expressions of sadness and disgust. The evaluation of the response times for each expression showed a significant difference between FP and luteal phase, in reference to the expression of sadness, suggesting that high levels of estradiol in the FP could impair the performance of WM. However, this effect is specific to selective facial expressions suggesting that, across the phases of the menstrual cycle, in which conception risk is high, women could give less importance to the recognition of sadness and disgust. This study is in agreement with research conducted on non-human primates, showing that fluctuations of ovarian hormones across the menstrual cycle influence a variety of social and cognitive behaviors. Our data could also represent a useful tool for investigating emotional disturbances linked to menstrual cycle phases and menopause in women.

EMOTIONAL WORKING MEMORY IN ELDERLY. Tomaz, C.; Satler, C.; Tavares, M.C.H. Lab. of Neuroscience & Behavior. University of Brasilia, Brasilia, DF, 70910-900 Brazil. For many years studies investigating the neuropsychology of elderly were principally focused on cognitive impairments related to long-term memory function. However, a growing number of studies emphasized the impairments in other cognitive domains. Among these, executive functions are interesting because they may have repercussions on everyday life activities, as suggested by clinical observations. Working memory (WM) has been suggested as an essential component of higher cognitive processes, such as decision making, reasoning, problem solving, learning, and aspects of language. This paper report differences in WM for emotional information in Alzheimers disease (AD) patients and normal aging controls using a computerized delayed (non) matching-to-sample (DMTS/DNMTS) task with trial-unique stimuli and short delay interval. Thirty-six IAPS photographs were grouped in pairs into 3 sets of 12 pictures (neutral, highly pleasant-arousing/relaxing and highly unpleasant-arousing), plus 12 geometric figures for each task. Pairs of stimuli, classified as congruent/divergent, showed an interaction with the factor task displaying more correct responses for congruent condition in DMTS and divergent condition in DNMTS, regardless of groups. Considering the sample stimuli (emotional/neutral), controls but not AD, in both tasks, showed a better performance when the sample was Emotional. These findings suggest a WM deficit in AD subjects, indicating a lack of benefit of emotion for this paradigm. We correlate these results with those showing that WM depends on integrity of medial temporal lobe structures and the evidence implicating prefrontal cortex, particularly ventral and medial regions, in performance of both tasks in monkeys and humans.

PREFRONTAL/ACCUMBAL CATECHOLAMINE SYSTEM PROCESSES EMOTIONAL AND MOTIVATIONAL SALIENCE. Puglisi-Allegra, S. Dipartimento di Psicologia and Centro Daniel Bovet, Sapienza University of Rome and Fondazione Santa Lucia, IRCCS, Rome, Italy. Motivational salience regulates the strength of goal seeking, the amount of risk taken, and the energy invested from mild to extreme. Neural mechanisms mediating motivational salience attribution are, therefore, very important for individual and species survival and for well-being. However, pathological neuro-adaptation by these mechanisms could be implicated in attribution of extreme motivational salience to different stimuli leading to maladaptive compulsive seeking or avoidance. We have offered the first evidence that prefrontal cortical norepinephrine transmission is a necessary for motivational salience attribution to both reward and aversion related stimuli, through modulation of dopamine in the nucleus accumbens, a brain area involved in all motivated behaviors. Intense emotional experiences promote highly persistent memories. Although this phenomenon is adaptive in some conditions, experiences with extremely high levels of motivational salience can promote development of traumatic memories that can be re-experienced intrusively for long time. Prefrontal-accumbal catecholamine system determines approach or avoidance responses to both reward- and aversion-related natural stimuli only when the salience of the unconditioned natural stimulus is high enough to induce sustained catecholamine activation, thus affirming that this system processes motivational salience attribution selectively when intense motivational salience is processed. Moreover, memories underlying high motivational salience are sustained by expression of transcription factors c-Fos within the mesocorticolimbic system and by intracellular signaling cascade of cyclic adenosin monophosphate (cAMP).

EMOTIONAL MODULATION OF MULTIPLE MEMORY SYSTEMS Packard, M.G., Department of Psychology, Texas A & M University College Station, Texas, 77845 mgp@psyc.tamu.edu. Animal studies employing localized brain lesions and intracerebral drug infusions have differentiated the roles of the hippocampus and dorsal striatum in cognitive and habit learning and memory, respectively. In addition, activation of the basolateral amygdala, a brain structure implicated in mammalian emotion, can modulate memory processes occurring in other brain structures. In this context, we have investigated the manner in which emotional state may influence the relative use of multiple memory systems. In dual-solution tasks that can be acquired using hippocampus-dependent or dorsal striatal-dependent learning, a pre-training stress regimen, or peripheral or intra-basolateral amygdala injection of anxiogenic drugs bias rats towards the use of habit memory. This influence of drug-induced anxiety on the relative use of multiple memory systems is observed when drugs are administered prior to training, post-training, or prior to retrieval. In single-solution tasks that require the use of either cognitive or habit learning, intra-amygdala infusions of anxiogenic drugs result in a behavioral profile that is consistent with an impairing effect on hippocampus-dependent memory. In a task in which hippocampal function interferes with task acquisition, intra-amygdala infusions of anxiogenic drugs eliminate interference between cognitive and habit memory systems, producing enhanced habit learning. Overall, these findings suggest that the emotional state(s) produced by stress or anxiogenic drugs can influence the relative use of multiple memory systems in a manner that favors habit learning. Moreover, intra-basolateral amygdala infusion of anxiogenic drugs is sufficient to produce this modulatory influence of emotional state on the use of multiple memory systems. The general hypothesis that anxiogenic or stressful emotional states may result in the dominant use of habit memory may have implications for the role of learning and memory in various human psychopathologies.

EMOTIONAL MODULATION OF THE SYNAPSE. McIntyre, C.K. School of Behavioral and Brain Sciences. The University of Texas at Dallas, Richardson, TX 75080 USA. Long-term memories can be formed after a single emotionally arousing experience whereas more neutral memories require rehearsal to be stored for the long-term. Decades of research have established that stress hormones can enhance or impair the consolidation of memories. This effect requires activation of -adrenoceptors in the basolateral complex of the amygdala (BLA) which, in turn, influences synaptic plasticity through interactions with other areas of the brain. However, the cellular mechanisms supporting this BLA-influenced plasticity remain to be identified. According to our research, memory-modulating manipulations of BLA -adrenoceptors influence hippocampal expression of the activity-regulated cytoskeletal-associated protein (Arc) through posttranscriptional mechanisms. Arc is a synaptic plasticity-associated protein that is translated in stimulated synapses. Blockade of Arc translation impairs long-term plasticity and long-term memory without affecting induction or acquisition. Taken together, these findings suggest that amygdala modulation of local translation of Arc in the hippocampus may determine whether a memory is rapidly forgotten, or stored for the long-term. Our recent results indicate that stress and actions on BLA -adrenoceptors can also influence Arc protein expression in synapses of the anterior cingulate cortex and the medial prefrontal cortex. These findings support the hypothesis that stress-induced amygdala activation may modulate memory by influencing the translation of synaptic plasticity-associated proteins in areas of the brain that are engaged during memory encoding.

5:00-6:00 **Oral Session 2:** REWARD AND ADDICTION. Chairperson: Leonie de Visser.

TRANSIENT NEURONAL SILENCING REVEALS OPPOSING ACTIONS OF INDIRECT AND DIRECT PATHWAY NEURONS. Neumaier, J.F., Ferguson, S.M. Depts. of Psychiatry and Pharmacology. University of Washington, Seattle, WA USA. The striatum is a key site for many of the behavioral and neurobiological adaptations thought to underlie the development of addiction. However, the direct (striatonigral) and indirect (striatopallidal) medium spiny neurons, respectively, have not been previously targeted in rat behavioral models. In order to address this, we have developed HSV viral vectors that use the preprodynorphin and preproenkephalin promoters to target transgene expression to the direct or indirect pathway, respectively. We used these new vectors to express either GFP or novel engineered DREADD receptor that can be selectively activated by a synthetic and otherwise inert ligand, clozapine-N-oxide (CNO). Based on gene expression and retrograde tracing, these vectors are highly selective for these target pathways. Using functional and electrophysiological strategies, the hM4D receptor transiently silenced targeted neurons only when activated by CNO. Transient silencing of striatopallidal neurons in rat dorsal striatum facilitates the development of locomotor sensitization to amphetamine whereas silencing striatonigral neurons attenuates the development of this behavior; yet acute locomotor responses were intact. Silencing striatonigral neurons inhibits learning a simple operant task; operant experiments with striatopallidal silencing and with cocaine self-administration are beginning. Engineered receptors can be used to alter cellular signaling in specific neuron phenotypes transiently or chronically. This can be used to elucidate the roles of specific neuron phenotypes in a variety of behavioral models in a variety of species.

BREAKING THE ICE: OXYTOCIN SUPPRESSES METHAMPHETAMINE SELF-ADMINISTRATION AND ASSOCIATED C-FOS EXPRESSION IN RATS. McGregor, IS; Carson, DS; Guastella, AJ; Barber, LL; Cornish, JL; Arnold, JJ; Boucher, AA; Hunt, GE. School of Psychology and Brain and Mind Research Institute, University of Sydney. Recent preclinical evidence indicates that the neuropeptide oxytocin may have potential as a treatment for drug dependence and drug withdrawal. In recent work we have found that peripherally administered oxytocin reduces methamphetamine self-administration, conditioned place preference, and hyperactivity in rodents. Repeated treatment with oxytocin also appeared to increase sociability in rats and caused lasting decreases in the tendency to self-administer drugs. However, it is unclear how oxytocin acts in the brain to produce such effects. The present study examined how patterns of neural activation produced by methamphetamine were modified by co-administered oxytocin. Male Sprague-Dawley rats were pre-treated with either 2 mg/kg oxytocin (IP) or saline and then injected with either 2 mg/kg methamphetamine (IP) or saline. After injection, locomotor activity was measured for 80 minutes prior to perfusion. As in previous studies, co-administered oxytocin significantly reduced methamphetamine-induced locomotor activity and rearing. Strikingly, oxytocin significantly reduced methamphetamine-induced Fos expression in two regions of the basal ganglia: the subthalamic nucleus and the nucleus accumbens core. The subthalamic nucleus is of particular interest given emerging evidence for this structure in compulsive, addiction-relevant behaviors. When administered alone, oxytocin increased Fos expression in several regions, most notably in the oxytocin-synthesizing neurons of the supraoptic nucleus and paraventricular nucleus of the hypothalamus. We hypothesize that stimulation of these neurons may lead to long-term upregulation of brain oxytocin levels. This study provides new evidence for central actions of peripheral oxytocin and suggests a self-stimulatory effect of exogenous oxytocin on its own hypothalamic circuitry. Overall these results give further insight into the way in which oxytocin might moderate compulsive behaviors and demonstrate the capacity of peripherally administered oxytocin to induce widespread central effects.

THE NORADRENERGIC ALPHA-2 AGONIST CLONIDINE ATTENUATES CUE-INDUCED REINSTATEMENT OF COCAINE-SEEKING. Smith, R.J.; Aston-Jones, G. Dept. of Neurosciences, Medical University of South Carolina, Charleston, SC 29425 USA. The central noradrenergic (NA) system has a critical role in stress-induced relapse of cocaine-seeking. However, its involvement in relapse triggered by drug-associated stimuli has not been extensively explored. Here, we tested this role of the NA system. Male SD rats self-administered cocaine (i.v.) paired with discrete tone and light cues for 10 days, underwent extinction in the absence of cocaine and cues, and were tested for cue-induced reinstatement of responding. Systemic administration of the NA alpha-2 agonist clonidine blocked cue-induced reinstatement of extinguished cocaine-seeking. However, it is unclear if this effect is due to clonidine binding at: a) alpha-2 receptors that act as autoreceptors for the NA system, b) alpha-2 receptors that function as heteroreceptors and regulate release of non-NA transmitters, and/or c) imidazoline-1 (I1) receptors, which are involved in the control of blood pressure. Post-synaptic NA agents were administered to test the first possibility. Propranolol (beta antagonist) and prazosin (alpha-1 antagonist) had no significant effect on reinstatement, indicating that clonidines effect on reinstatement may be unrelated to an autoreceptor function at NA terminals. The more selective alpha-2 agonist UK-14,304 (slightly greater affinity for alpha-2 over I1) significantly attenuated cue-induced reinstatement but required larger doses, indicating I1 binding may be involved in the actions of clonidine. Current studies are aimed at further exploring the contribution of alpha-2 vs. I1 binding in clonidines ability to block cue-induced reinstatement.

VTA AFFERENTS CONTROLLING CUED REINSTATMENT OF COCAINE SEEKING. Stephen V. Mahler & Gary Aston-Jones Neurosciences, Medical University of South Carolina While VTA dopamine cells are thought to be involved in the ability of cues to reinstate drug seeking after extinction, little is known about which brain areas control VTA firing and resulting drug seeking and/or craving. Here we injected the retrograde tracer cholera toxin B subunit (CTb) in VTA, and examined Fos expression in a wide variety of reward-related structures projecting to VTA. Animals were trained to intravenously self-administer 0.2mg/kg cocaine infusions paired with a light/tone CS+ cue for 10 days, extinguished of this behavior for 7 days, then given one 2 hour test session after which they were sacrificed and their brains were processed for CTb and Fos immunohistochemistry. For cued reinstatement animals, test-day lever presses resulted in CS+ presentations but no cocaine infusions, which caused animals to robustly reinstate extinguished lever pressing. Control animals experienced an additional day of extinction training, exposure to a novel environment, or exposure to a control CS- cue that was explicitly unpaired with cocaine on test days. We found Fos activation in VTA afferents in hypothalamus, extended amygdala, accumbens, ventral pallidum, and other structures in cued reinstatement but not control animals, indicating that these areas may be important inputs controlling firing of VTA dopamine neurons and relapse to drug use caused by conditioned cues.

6:00-7:00 **Oral Session 3:** PARENTAL CARE AND DEVELOPMENT. Chairperson: Francesca Cirulli.

PRENATAL COCAINE EXPOSURE ALTERS MATERNAL PREFERENCE FOR PUP-PRODUCED OLFACTORY CUES DURING THE EARLY POSTPARTUM PERIOD Williams, S.; Barber, J.; Ross, B.; Thompson, B.; Jameison-Drake, A.; Enns, J.; Cox, E; Heaton, C.; Desai, N.; McMurray M.; Johns, J. University North Carolina, Chapel Hill, NC, 27599 Gestational cocaine use is associated with maternal neglect in human and preclinical models. Neglect is correlated with disruptions in infant produced cues, thought to be important for elicitation of normal maternal care. This study determined whether gestational cocaine treatment alters maternal preference for pup olfactory stimuli produced by control or cocaine exposed pups. Pregnant rats were designated as untreated (UN), chronic saline (CS), or chronic cocaine (CC). CC and CS dams were given cocaine (30 mg/kg/day) or saline respectively throughout gestation. Dams were tested for olfactory preference of pup urine from UN or CC pups on postpartum days (PPDs) 1, 3 and 5. Urinalysis assessed several biochemical measures. All control (UN, CS) and CC dams preferred to be in the presence of CC compared to UN pup urine on PPD1 and the same trend was observed on PPD5. CC pups had higher urinary glucose, ketones and proteins on PPD1, suggesting malnutrition and lower pH on PPD5, possibly impacting cue detection. Although, urine preference did not differ between dam treatment groups, dams exhibited a dynamic preference for pup urine. Prenatal CC exposure altered dam preference for pup cues, potentially explaining neglectful care received by CC pups during this critical time

SEX-DIFFERENCE IN THE ASSOCIATION OF MATERNAL SMOKING DURING PREGNANCY AND COORDINATION IN OFFSPRING. Larsson, M ; Montgomery, SM. Dept. of Respiratory Medicine. Clinical Epidemiology and Biostatistics Unit, rebro University Hospital, rebro, Sweden. BACKGROUND. To examine if smoking during pregnancy is associated with poorer motor competence among offspring, indicating impact on neurological function. The measures may be less susceptible to socioeconomic confounding than cognition tests. METHODS. Data were from 13,207 members of the National Child Development Study, born in Great Britain in 1958. Maternal smoking during pregnancy was recorded prospectively. Tests of physical control and coordination administered by a school doctor at age 11 years were: time to pick up 20 matches (PUM), number of squares marked (NSM) and copying designs (CD). PUM and NSM were tested for left and right hand. Test scores were dependent variables in linear regression analysis, with adjustment for maternal smoking during pregnancy, sex, birth weight standardised for gestational age, breast-feeding, social class, parental education, mothers age, laterality and pubertal development. RESULTS. After adjustment, heavy smoking during pregnancy was statistically significantly associated with PUM (non-dominant hand) and CD, but not NSM; particularly among boys. The regression coefficients (and 95% confidence intervals) for PUM (non-dominant hand) are1.474 (0.47 to 2.48, p=0.004) and 1.203 (0.15 to 2.26, p=0.026) for boys and girls, respectively: higher scores indicate poorer performance. The coefficients for CD are -0.185 (-0.32 to -0.05, p=0.006) for boys and 0.020 (-0.11 to 0.15, p=0.753) for girls: lower scores indicate poorer performance. CONCLUSIONS. Smoking during pregnancy is associated with subtly reduced motor competence, particularly on the non-dominant side in boys.

FATHERHOOD ENHANCES LEARNING AND MEMORY. Franssen, C.L.[1]; Shea, E.S.[1]; Hampton, J.E.[1]; Bardi, M.[2]; Huber, J.[1]; Hyer, M.M.[1]; Rhone, A.[1]; Franssen, R.A.[3]; Kinsley, C.H.[3]; Lambert, K.G.[1]. [1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005, USA; [2]Dept. of Psychology, Marshall University, Huntington WV 25755 USA; [3]Dept of Psychology, University of Richmond, Richmond, VA 23173 USA. In addition to enhancing traditional maternal behavior in the rat, maternal experience modifies ancillary behaviors (e.g., efficient foraging) important for the survival of offspring. Aside from pregnancy, the mere exposure to pupsand the associated sensory and physical cuesalso modifies spatial/foraging ability (Lambert et al., 2005). However, the female parental model, with its associated hormonal and physiological modifications, presents a plethora of methodological challenges. Thus, we focused on paternal behavior in the biparental mouse Peromyscus californicus and examine the effects of fatherhood or conspecific pup exposure on spatial learning in the dry land maze (DLM) as well as hippocampal responsiveness and plasticity. During the 7-day DLM assessment, Dads exhibited more exploratory behavior than pup-exposed virgins (PEV) and Virgins. On the acquisition test day, Dads exhibited shorter latencies to approach the baited well, demonstrating superior memory for the task; additionally, PEVs approached the baited wells faster than Virgins. Focusing on the neurobiological data, compared to PEVs and Virgins, Dads had significantly more Fos-immunoreactivity in the hippocampal CA1, CA3, and DG regions. We also found significantly more Nestin-immunoreactivity in the CA1 region of the hippocampi of PEVs than Dads or Virgins. In accordance with previous findings with maternal rats (Kinsley et al., 1999), paternal experience enhanced foraging effectiveness and hippocampal activation. These results confirm that the paternal California mouse is a valuable model for assessing the neurobiological effects of parental experience.

PRENATAL OXYCODONE EXPOSURE ENHANCES CONDITIONED PLACE PREFERENCE TO OXYCODONE IN ADULT MALE RATS BUT NOT FEMALES. LM Schrott, GS Johnson, and LM Franklin. Dept. of Pharmacology, Toxicology, and Neuroscience, Louisiana State University Health Sciences Center, Shreveport, LA USA. Abuse of prescription opioid analgesics for non-medical conditions is a growing public health problem in the United States. There are multiple factors that influence vulnerability to drug abuse and in the present study we examined development history (exposure to opiates *in utero*) and sex. The measure of interest was conditioned place preference (CPP) to oxycodone in adulthood. To generate opiate-exposed offspring, adult female Sprague-Dawley rats were treated for 28 days via oral gavage with ascending doses of oxycodone HCl up to a final dose of 15 mg/kg/day, which was maintained during breeding and gestation. Oxycodone is the active ingredient in the widely prescribed analgesic Oxycontin. Controls were treated with water. Oxycodone was well tolerated during pregnancy, and the pups underwent a mild withdrawal after birth. As adults male and female rats exposed to water or oxycodone (n=6 per group) were assessed in an unbiased version of CPP. Following a 30 min baseline assessment, there were four 30 min conditioning sessions, alternating water vehicle and oxycodone (15 mg/kg oral). Preference was tested on the day following the final conditioning session. There was an overall Sex effect ($p<0.002$), with males displaying a stronger preference to oxycodone as compared to females. There was a marginal Prenatal Treatment x Sex interaction. Analyses were conducted within each sex, and in the males exposure to oxycodone *in utero* led to a 2.5-fold greater preference than the water controls. There was no effect of prenatal oxycodone exposure in the females. These data indicate that sex and developmental history interact to affect abuse prescription drug vulnerability in adulthood, and that males may be more sensitive than females. Supported in part by USPHS DA018181 (NIDA, NIH).

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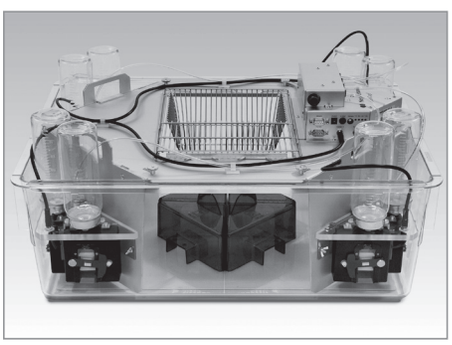

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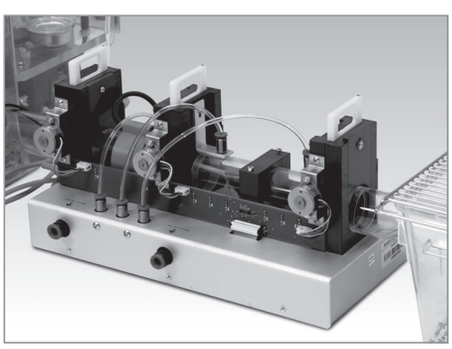

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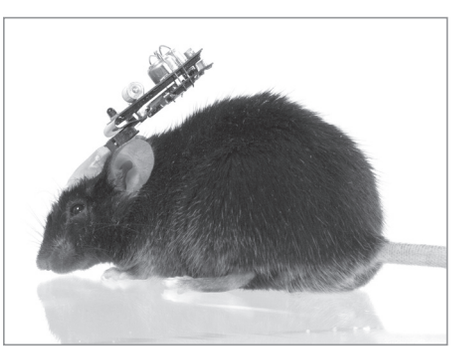

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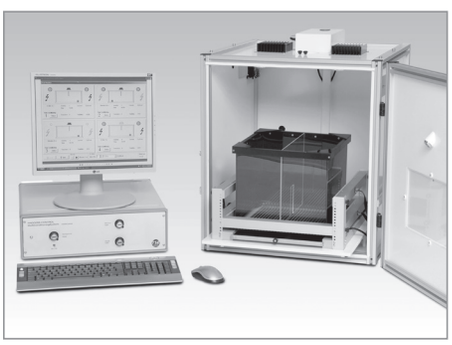

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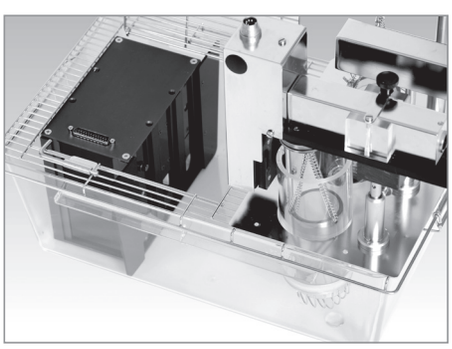

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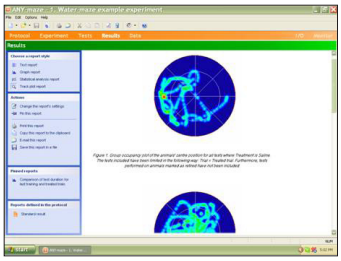

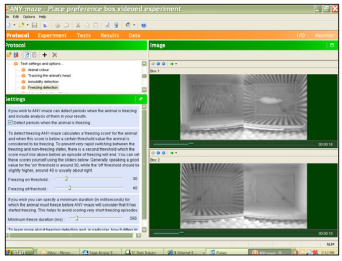

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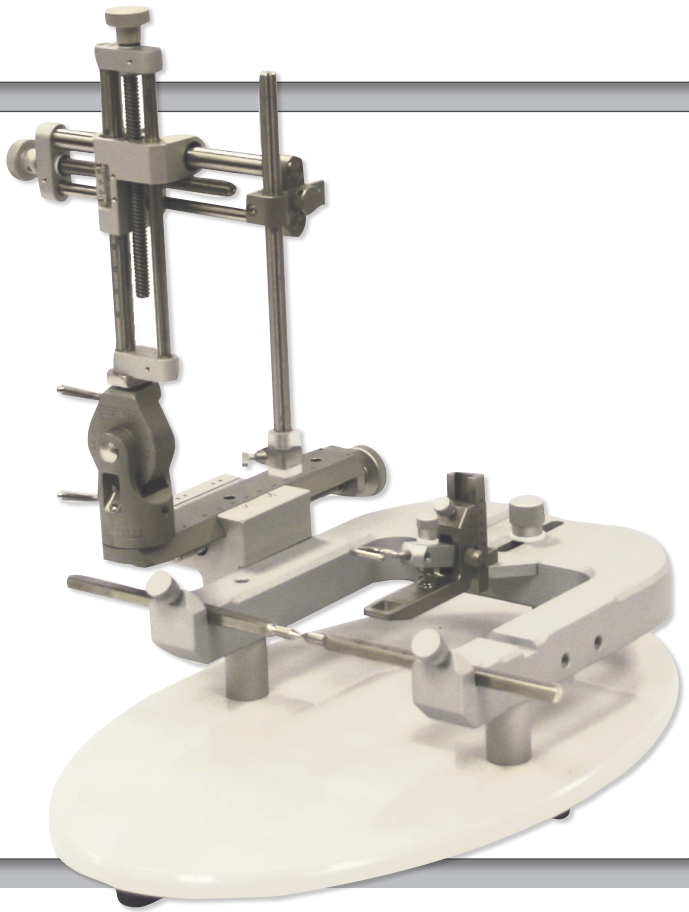

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8:00						
8:15						
8:30	**Special Satellite**	**Presidential Syposium**	8:30-9:00 Welcome	8:30-10:30	8:30-10:30	8:30-10:30
8:45						
9:00			9:00-10:00 Presidential Lecture	Symposium 3	Symposium 6	Symposium 9
9:15	Organizers:	Organizers:				
9:30				**J. Johns & E. Byrnes**	**G. Laviola & S.L. Andersen**	**P. Campolongo & V. Trezza**
9:45						
10:00	Giovanni Biggio	Robert Gerlai	Break - Exhibits			
10:15						
10:30			10:30-11:30 Keynote **N.S. Clayton**	Break - Exhibits	Break - Exhibits	Break - Exhibits
10:45		Kelly Lambert				
11:00	Howard Becker			11:00-12:00 Keynote **G. Biggio**	11:00-12:00 Keynote **T.R. Insel**	11:00-12:00 Student Slide blitz
11:15						
11:30			11:30-12:30 Oral Session 1 Stress and anxiety			
11:45		8:30-1:00				
12:00	8:00-6:00			12:00-2:00 Lunch Break	12:00-2:00 Lunch Break	12:00-2:00 Lunch Break
12:15						
12:30			12:30-2:00 Lunch Break			
12:45						
13:00				Meet the Professionals Lunches	Meet the Professionals Lunches	
13:15						
13:30						
13:45						
14:00						
14:15		2:00-4:30 Registration	2:00-4:00 Symposium 1	2:00-4:00 Symposium 4	2:00-4:00 Symposium 7	2:00-3:00 Student Slide blitz
14:30						
14:45						
15:00						
15:15			**D.G. Stein**	**J.E. Grisel**	**M.V. Pletnikov & P.H. Patterson**	3:00-5:00 Symposium 10
15:30						
15:45						
16:00			4:00-6:00 Workshop	4:00-6:00 Symposium 5	4:00-6:00 Symposium 8	**A. Gasbarri & C. Tomaz**
16:15						
16:30						
16:45						
17:00		6:00-7:00 Welcome Reception				5:00-6:00 Oral Session 2 Reward & addiction
17:15				**F. Dellu-Hagedorn**	**L. Li**	
17:30						
17:45						
18:00			6:00-8:00 Symposium 2	6:00-8:00 Poster Session 1	6:00-8:00 Poster Session 2	6:00-7:00 Oral Session 3 Parental care & development
18:15						
18:30						
18:45						
19:00		7:00-8:30 Student Social				Business Mtg. 7:00-7:30
19:15						
19:30			**C. Da Cunha**			7:30-11:00 Banquet Awards Dance
19:45						
20:00			Council Meeting 8:00-10:00	Meals are included with your room rate and served at the Oasys Restaurant. **Meal times are:** Breakfast 7:30-9:40 Lunch 12:30-14:00 Dinner 19:30-21:30		
20:15						
20:30						
20:45						
21:00						
21:15						
21:30						
21:45						
22:00						

Next IBNS Meeting:

May 24-29, 2011
Sheraton Steamboat Resort
Steamboat Springs, Colorado, USA