International Behavioral
Neuroscience Society

Annual Meeting
Program and Abstracts

Kailua-Kona, Hawaii, USA
June 5-10, 2012

Abstracts of the International Behavioral Neuroscience Society, Volume 21, June 2012

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IBNS CENTRAL OFFICE

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Aloha and Welcome to the 21st Annual Meeting of the International Behavioral Neuroscience Society, in Kona, Hawaii. The meeting is projected to be the largest meeting IBNS has ever had, and I look forward to an exciting and instructive program, in which recent developments in behavioral neuroscience will be described and discussed.

This site also provides lessons in history. The Kona coast is deeply embedded in the history of Hawaii. It was the site of first arrival of Europeans, under the command of Captain James Cook, who landed here in 1778. Returning to Hawaii after a brief expedition to what is now Alaska, Captain Cook was killed –again on this coast, at Kealakekua Bay—in 1779.

Kamehameha I ("the great") was born in Hawaii, at the northern tip of this coastline, and was a young man at the time of the Cook landings. Later, using western arms (he was an observant young man!) he conquered and united almost all of the islands, becoming the first King of Hawaii.

Aside from science and history, we have an extra event for attendees, one that will not be repeated for nearly 120 years. The transit of Venus across the sun will take place in the afternoon of June 5, the first day of our meeting. Hawaii and Alaska are the only parts of the US where the entire transit, lasting several hours, will be visible. (if you plan to view it, protect your eyes with eclipse shades)…as another point of connection to the history of Hawaii, Captain Cook's first voyage, in 1769, was to Tahiti, to observe---a transit of Venus! http://star.arm.ac.uk/history/transit.html

In sum, this meeting promises to be one that is totally without parallel! I sincerely hope that you find it deeply rewarding, and also a lot of fun, and that you come to appreciate Hawaii and its history, as we who live here do.

Sincerely,

D. Caroline Blanchard
President, International Behavioral Neuroscience Society

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We are pleased to announce the recipients of the IBNS Travel Awards for the 2012 meeting in Kona, Hawaii, USA. Award winners will receive hotel and travel reimbursement, certificate, and waiver of registration fees. Travel awardees are presenting orally and will also have their research presented in a poster session. Congratulations to all.

TRAVEL AWARDS

(listed alphabetically)

Postdoctoral Travel Awards

Alaine Keebaugh, Emory University, Atlanta, Georgia, USA

Alexxai Kravitz, Gladstone Institutes, San Francisco, California, USA

Erik Oleson, University of Maryland-School of Medicine, Baltimore, Maryland, USA

Tori Schaefer, Cincinnati Children's Research Foundation, Cincinnati, Ohio, USA

Moriel Zelikowsky, Caltech, Pasadena, California, USA

Graduate Student Travel Awards

Catherine Barrett, Emory University, Atlanta, Georgia, USA

Collin Challis, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Nina Donner, University of Colorado-Boulder, Colorado, USA

Stephanie Groman, University of California-Los Angeles, California, USA

Anna Phan, University of Guelph, Ontario, CANADA

Kartik Ramamoorthi, MIT, Cambridge, Massachusetts, USA

Adam Smith, Florida State University, Tallahassee, Florida, USA

Brandon Warren, Florida State University, Tallahassee, Florida, USA

IBNS Regional Travel Awards

Michael Bowen, University of Sydney, Australia

Áron Tulogdi, Institute of Experimental Medicine, Budapest, Hungary

The IBNS would like to express our gratitude to the following organizations that have given financial support to the 21st International Behavioral Neuroscience Society Conference. This financial support enabled many students to attend the conference.

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In addition to the sponsors above we are appreciative of our IBNS Members for their continued support and to those who donated this year: especially Student/Postdoctoral Members and an anonymous Member who covered the costs of the Regional Travel Awards.

**These companies will be onsite during the meeting. Please take time to stop by and thank them for their support.*

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

Program Committee

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Robert Blanchard, University of Hawaii, USA
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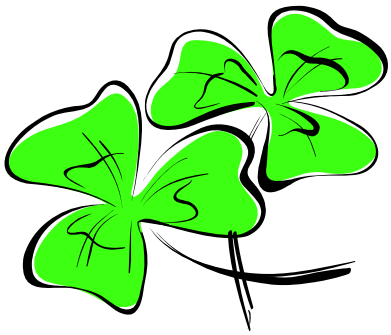
Any IBNS member who would like to become more involved in the Society may volunteer to serve on an IBNS committee. Committee details can be found on our website at http://www.ibnshomepage.org/committees.htm.

The Program Committee is now soliciting proposals for symposia and satellites for the 2013 Annual Meeting of the International Behavioral Neuroscience Society to be held at the Grand Hotel, Malahide, County Dublin, Ireland, June 25-30.

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, the list of speakers, their affiliations, and tentative 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 4, 2012. Please send your proposal to the IBNS Central Office at *ibns@ibnshomepage.org*. Please use subject line: Symposia/Satellite Proposal 2013.



IBNS 2013

Grand Hotel
Malahide, County Dublin, Ireland

JUNE 25-30

PROGRAM NOTES:

- Presenting authors are indicated in the program by **bold** type.
- Unless otherwise indicated in program, events will be held in the Convention Center - Keauhou II.

Tuesday, June 5, 2012

4:00-6:00 **Registration – *POOL TERRACE***

6:00-8:00 **Symposium:** THE NEUROBIOLOGY OF RESILIENCE: IMPLICATIONS FOR ADAPTIVE FUNCTIONS AND MENTAL HEALTH. Chair: **Kelly Lambert.** ***KEAUHOU II***

6:00 RODENT MODELS EXPLORING EFFECTIVE BEHAVIORAL THERAPIES FOR MENTAL HEALTH RESILIENCE: EVALUATION OF PREDISPOSED COPING STRATEGIES AND EFFORT-BASED REWARD CONTINGENCY TRAINING. **Lambert, K.**

6:25 A RODENT MODEL OF HUMAN BEHAVIORAL INHIBITION: DEVELOPMENTAL PRECURSORS AND ADULT NEURONAL CORRELATES OF PERI-WEANING INHIBITION. **Cavigelli, S.A.**; Ragan, C.M.

6:50 STRESS RESILIENCE AND VULNERABILITY: THE ASSOCIATION WITH REARING CONDITIONS, ENDOCRINE FUNCTION, IMMUNOLOGY, AND ANXIOUS BEHAVIOR. **Kent, S.**

7:15 Discussant: **Robert Blanchard**, University of Hawaii, Honolulu, HI, USA

8:00-10:00 **Welcome Reception – *BAYVIEW GROUNDS***
Educational Manta Ray talk – Christopher Blunt, Fair-Wind Tours
Appetizers, complimentary Manta Punch (alcoholic or non-alcoholic) and cash bar
Live Hawaiian Music – Keoni Thompson
Manta Ray viewing – Suites 1329 & 1425

Wednesday, June 6, 2012

8:45-9:00 **Welcome:** IBNS President, D. Caroline Blanchard. ***KEAUHOU II***

9:00-10:00 **Keynote Speaker:** Sarah F. Leibowitz, The Rockefeller University.
MATERNAL HIGH-FAT DIET, ALCOHOL AND FETAL PROGRAMMING

10:00-10:30 **Coffee/Snack Break - Exhibits**

10:30-12:30 **Symposium:** STRESS, INFLAMMATION, NEUROINFLAMMATION AND BEHAVIOR: CAUSES, CONSEQUENCES AND TREATMENT.
Chair: **Frederick Rohan Walker**

10:30 THE ROLE OF MICROGLIA IN THE REGULATION OF MOOD STATE AND COGNITIVE FUNCTION. **Walker, F.R.**

10:55 IMMUNE AND BEHAVIORAL CONSEQUENCES OF MICROGLIAL REACTIVITY FOLLOWING REPEATED SOCIAL DEFEAT. Wohleb, E.; Fenn, A.; Pacenta, A.; Powell, N.; Sheridan, J.; **Godbout, J.P.**

11:20 EXAMINING THE IMPACT OF CALORIE RESTRICTION UPON THE BEHAVIOURAL, PHYSIOLOGICAL, AND METABOLIC INDICATORS OF ILLNESS. **Kent, S.**

11:45 ISOLATION STRESS: RETHINKING THE MECHANISMS OF STRESS-IMPAIRED HEALING. **Engeland, C.G.;** Yang, L.; Pyter; L.M., McKenzie, C.

12:10 Discussant: **David Diamond**, University of South Florida, FL, USA

12:30-2:00 **Mid-Day Break - Exhibits**

2:00-4:00 **Symposium:** GENETIC AND EPIGENETIC FACTORS IN AUTISM.
Chair: **Joanne Berger-Sweeney**, Tufts University, USA. ***BAYVIEW ROOMS***

2:00 ADULT SOCIAL BEHAVIOR IN BTBR T+ TF/J MICE FOLLOWING NEONATAL ADMINISTRATION OF OXYTOCIN. **Benno, R.;** McKim, D.; Rendon, T.; Schanz, N.

2:25 DO ABNORMAL EXTRACELLULAR MATRIX SYSTEMS CONTRIBUTE TO EPIGENETIC FACTORS IN AUTISM? **Blanchard, D.C.**

2:50 DIETARY INTERVENTIONS IN MOUSE MODELS OF AUTISM SPECTRUM DISORDERS: THE CASE OF CHOLINE. **Ricceri, L**.

3:15 THE ONE-CARBON (C1) METABOLIC CYCLE, NEURAL CIRCUITS, AND COGNITIVE AND SOCIAL BEHAVIORS IN AUTISM. **Berger-Sweeney, J**.; Schaevitz, L.

3:40 Discussant: **Christine Hohmann**, Morgan State University, Baltimore, MD, USA.

2:00-4:00 **Symposium:** MODELING SCHIZOPHRENIA SYMPTOMS AND NEUROBIOLOGY IN MICE. Chair: **Francesco Papaleo** ***KEAUHAU II***

2:00 COGNITIVE AND NEUROIMAGING PHENOTYPES REVEAL BRAIN DYSFUNCTION IN DYSBINDIN-1 MUTANT MICE. **Jentsch, J.**

2:25 DEVELOPMENT OF COGNITIVE DEFICITS RELEVANT TO SCHIZOPHRENIA IN COMT AND DYSBINDIN MOUSE MUTANTS. **Papaleo, F.**

2:50 ULTRASONIC VOCALIZATIONS IN MICE: A TOOL TO MODEL NEGATIVE SCHIZOPHRENIA SYMPTOMS. **Scattoni, M.L.**

3:15 MODELING THE POSITIVE SYMPTOMS OF SCHIZOPHRENIA IN MICE: FOCUS ON DOPAMINERGIC AND GLUTAMATERGIC MECHANISMS. **Van den Buuse, M.**

3:40 Discussant: **Cyndi Shannon Weickert**, University of New South Wales, Sydney, Australia

4:00-4:30 **Snack Break - Exhibits**

4:30-7:00 **Symposium:** UNRAVELING THE CONTRIBUTION OF OXYTOCIN TO POSITIVE AFFECT AND DRUG-RELATED REWARD: A TRANSLATIONAL PERSPECTIVE. Chairs: **Femke Buisman-Pijlman** and **Jillian Broadbear**

4:30 PRENATAL AND GESTATIONAL DRUG EXPOSURE: EFFECTS ON THE OXYTOCIN SYSTEM, SOCIAL BEHAVIOR AND VULNERABILITY IN RATS. **Williams, S.K**.; McMurray, M.S.; Jarrett, T.M.; Cox, E.T.; Jameison-Drake, A..; Walker, C.H.; Robinson, D.L.; Johns, J.M.

4:52 OXYTOCINERGIC REGULATION OF ENDOGENOUS AS WELL AS DRUG-INDUCED MOOD. **Broadbear, J.H.;** Mak, P.; Beringer, K.

5:14 PREFRONTAL OXYTOCIN MEDIATES DRUG AND SOCIAL REWARD INTERACTION. **Wang, Z.;** Young, K.A.

5:36 A CONDITIONAL KNOCKOUT MOUSE LINE OF THE OXYTOCIN RECEPTOR: FINDINGS RELATING TO SOCIAL RELATIONS AND LEARNING. **Pagani, J.H.**; Young, W.S.

5:58 OXYTOCIN AS A REGULATOR OF ADDICTION: A NEURODEVELOPMENTAL PERSPECTIVE. **Buisman-Pijlman, F.T.A.;** Tops, M.

6:20 BREAKING THE LOOP: PRECLINICAL AND EARLY CLINICAL EVIDENCE FOR OXYTOCIN AS A TREATMENT FOR DRUG ADDICTION. **McGregor, I.**

6:42 Discussant: **Zoltan Sarnyai**, University of Cambridge and James Cook University, Australia.

7:00-8:00 **Evening Break**

8:00-10:00 **Exhibits**

8:00-10:00 **Poster Session 1:** ***Brain and Behavior. KEAUHOU I***

1. ROLE OF VENTRAL SUBICULUM IN CONTEXT-INDUCED REINSTATEMENT OF HEROIN SEEKING. **Bossert J.M**.; Eichenbaum, H; Wang, H.L.; Morales, M.; Shaham, Y.

2. THE COGNITIVE EFFECTS OF OVARIECTOMY TRANSITIONS FROM DETRIMENTAL TO BENEFICIAL WITH AGE. **Acosta, J.I.**; Engler, E.B.; Talboom, J.S.; Bimonte-Nelson, H.A.

3. DIFFERENTIAL CONTRIBUTION OF MESOHABENULAR AND MESOACCUMBENS DOPAMINE NEUROTRANSMISSION TO BRAIN STIMULATION REWARD. Duchesne, V.; **Boye, S.M.**

4. D1 RECEPTORS IN THE NUCLEUS ACCUMBENS SHELL REGULATE THE EXPRESSION OF CONTEXTUAL FEAR CONDITIONING AND ACTIVITY OF THE ANTERIOR CINGULATE CORTEX IN RATS. Albrechet-Souza, L.; Carvalho, M.C.; **Brandao, M.L.**

5. MUSCARINIC M4 POSITIVE ALLOSTERIC MODULATION OF CIRCADIAN ACTIVITY RHYTHMS. **Gannon, R.**; Millan, M.J.

6. DOES FETAL HANDEDNESS REFLECT THE FUNCTIONAL MATURITY OF ITS BRAIN? **Hepper, P.G.**; Dornan, J.C.; Lynch, C.; Wells, D.L.

7. DEVELOPMENT OF A LABORATORY PARADIGM THAT ELICITS CHECKING UPON ACTIVATION OF SECURITY MOTIVATION. **Hinds, A.**; Van Ameringen, M.; Schmidt, L.; Woody, E.; Szechtman, H.

8. EVALUATING NEUROPSYCHOLOGICAL PERFORMANCE AMONG KHAT USERS. **Ismail, A.A**.; El-Setouhy, M.; El Sansoy, R.; Rohlman, D.S.

9. TEMPORAL INVOLVEMENT OF THE PERIRHINAL CORTEX IN CROSSMODAL OBJECT RECOGNITION. **Jacklin, D.L.**; Potvin, A.; Winters, B.D.

10. DISPLAY AND SEARCH DYNAMICS IN MULTI-ATTRIBUTE CHOICE. **Janowski, V.**; Madsen, E.; Willemsen, M.; Johnson, E.; Rangel, A.

11. OXYTOCIN SYNTHESIS IN THE HYPOTHALAMUS ARE INFLUENCED BY FASTING AND REFEEDING IN THE OXYTOCIN-MONOMERIC RED FLUORESCENT PROTEIN 1 TRANSGENIC RATS. **Katoh, A.;** Ishikura, T.; Yoshimura, M.; Ohkubo, J.; Onaka, T.; Suzuki, H.; Ueta, Y.

12. NATURAL ELEMENTS IN ENRICHED ENVIRONMENTS ENHANCE EMOTIONAL RESILIENCE IN MALE LONG EVANS RATS**. Kaufman, C.;** Brown, M.; Tschirhart, M.; Rzucidlo, A.; Hyer, M.; Bardi, M.; Lambert, K.

13. EXPERIENCE-BASED PREFERENCE FOR DRIED-BONITO DASHI (A TRADITIONAL JAPANESE FISH STOCK). **Kondoh, T.;** Matsunaga, T.

14. THE ROLE OF DORSAL AND VENTRAL HIPPOCAMPUS IN THE ACQUISITION, STRENGTHENING AND EXPRESSION OF OLFACTORY FEAR CONDITIONING IN RATS. **Kroon, J.A.V.;** Carobrez, A.P.

15. A COMPUTATIONAL MODEL OF FEAR CONDITIONING IN ANIMALS AND HUMANS: IMPLICATIONS FOR PTSD. **Moustafa, A.;** Gilbertson, M.W.; Orr, S. P.; Servatius, R. J.; Myers, C.E.

16. THE ROLE OF NEURONAL NITRIC OXIDE IN THE LONG-TERM MEMORY TO OLFACTORY FEAR LEARNING. **Pavesi, E.;** Heldt, S.A.; Fletcher, M.L.

17. SOCIETAL IMPACT OF DIETARY PHYTOESTROGEN AND LEARNED BEHAVIOR IN ANIMAL MODELS AND COLLEGE UNDERGRADUATES: PERSONALITIY AND PHYSIOLOGICAL ANXIOLYTIC REACTIONS. **Sanstrum, B.J.;** Totton, R.T.

18. A NEW TASKTO STUDY EXECUTIVE CONTROL IN MICE. **Scheggia, D.;** Bebensee, A.; Weinberger, D.; Papaleo, F.

19. BEHAVIORAL INHIBITION TRAIT AFFECTS FEEDBACK-BASED LEARNING WITH AN AVOIDANCE OPTION. **Sheynin, J.;** Shikari, S.; Ostovich, J.; Gluck, M.A.; Moustafa, A.A.; Servatius, R.J.; Myers, C. E.

20. BRAIN SPECIFIC DELETION OF THE CREATINE TRANSPORTER (CRT) LEADS TO SPATIAL LEARNING AND MEMORY DEFICITS WITHOUT REDUCTIONS IN BODY WEIGHT. **Skelton, M.;** Hautman, E.; Williams, M.; Vorhees C.

21. PARAVENTRICULAR OXYTOCIN REGULATES SOCIAL-MEDIATION OF THE STRESS RESPONSE IN FEMALE PRAIRIE VOLES. **Smith, A.S.;** Wang, Z.

22. DOES PROTEIN SYNTHESIS INHIBITOR (ANISOMYCIN) MODULATES STEP-DOWN INHIBITORY AVOIDANCE IN MICE? **Canto-de-Souza, L.;** Mattioli, R.

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29. MATERNAL BRAIN RESPONSES TO INFANT'S CRYING**. Noriuchi, M.;** Kikuchi, Y.

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34. DEFENSIVE AGGREGATION (HUDDLING) IN LABORATORY RATS IN RESPONSE TO PREDATOR ODORS: GENERAL CHARACTERISTICS AND NEURAL CORRELATES. **Bowen, M.T.;** Kevin, R.; Kendig, M.D.; McGregor, I.S.

35. AROMATASE INHIBITION IN THE ZEBRA FINCH HIPPOCAMPUS DECREASES ACQUISITION AND PERFORMANCE IN A SPATIAL MEMORY TASK. **Bailey, D.J.;** Saldanha, C.J.

36. EMBRACING COMPLEXITY: TIME SERIES, LONG-RANGE CORRELATIONS, AND DIMENSIONAL SCALING AS ALTERNATIVE BEHAVIORAL ASSESSMENTS IN BEHAVIORAL NEUROSCIENCE. **Bardi, M.**; Lambert, K.G.

37. FUNCTIONAL ANTAGONISM BETWEEN EMISSION OF 50 kHz AND 22 kHz ULTRASONIC VOCALIZATIONS. Silkstone, M.; **Brudzynski, S.M.**

38. ADOLESCENT STRESS HORMONE EXPOSURE AFFECTS HIPPOCAMPAL NEUROGENESIS IN MALE AND FEMALE RATS. **Brummelte, S.**; Duarte-Guterman, P.; Crozier, T.M.; Lieblich, S.E.; Galea, L.A.M.

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49. SEXY PREDATORS; A TWO PRONGED MANIPULATION OF VASOPRESSIN-SOCIAL SYSTEM DRIVES TOXOPLASMA INDUCED BEHAVIOR CHANGES. **Hari Dass, S.A.;** Vyas, A.

50. EFFECTS OF ADOLESCENT SOCIAL DEFEAT ON COGNITION AND PREFRONTAL CORTEX DOPAMINE FUNCTION. **Novick, A.M.**; Forster G.L.; Watt, M.J.

51. TOXIN-INDUCED GUSTATORY CONDITIONING IN RATS: THE EFFECTS OF ORAL INGESTION OF LOW LEVELS OF A TOXIN (LITHIUM CHLORIDE) ON DRINKING BEHAVIORS. Good, A.N.; Kavaliers, M.; **Ossenkopp, K.-P.**

52. ACUTE RESTRAINT DIFFERENTLY ALTERS DEFENSIVE RESPONSES AND FOS IMMUNOREACTIVITY IN THE RAT BRAIN. Andrade, J.S.; Abrao, R.O.; Cespedes, I.C.; Garcia, M.C.; Nascimento, J.O.G.; Spadari-Bratfisch, R.C.; Melo, L.L.; da Silva, R.B.; **Viana, M.B.**

53. AN EXAMINATION OF PREDISPOSED COPING STRATEGIES AND NEUROBIOLOGICAL RESPONSES IN MALE RATS EXPOSED TO VARIOUS PROBLEM-SOLVING TASKS. **Brown, M.**; Kaufman, C.; Tschirhart, M.; Rzucidlo, A.; Hyer, M.; Bardi, M.; de Silva, I.; Lambert, K.

54. NEURONAL ACTIVATION PATTERNS ASSOCIATED WITH HYPER-EMOTIONAL AGGRESSION IN RATS SOCIALLY ISOLATED FROM WEANING. **Tulogdi, A.;** Toth, M.; Biro, L.; Soros, P.; Haller, J.

55. NPAS4 REGULATES A TRANSCRIPTIONAL PROGRAM IN CA3 REQUIRED FOR CONTEXTUAL MEMORY FORMATION. **Ramamoorthi**, K.; Fropf, R.; Belfort, G.M.; Fitzmaurice, H.L.; McKinney, R.M.; Neve, R.L.; Otto, T.; Lin, Y.

56. NEURONAL ENSEMBLES IN CA1 AND MPFC DIFFERENTIALLY REPRESENT RECENT AND REMOTE CONTEXTUAL FEAR MEMORIES. **Zelikowsky, M.;** Fanselow, M.S.

Thursday, June 7, 2012

9:00-10:00 **Presidential Lecture:** *BEHAVIORAL NEUROSCIENCE: A VIEW FROM DOWN UNDER.* **Stephen Kent,** La Trobe University; **Iain McGregor**, University of Sydney

10:00-10:30 **Coffee/Snack Break - Exhibits**

10:30-12:30 **Symposium:** PLASTICITY IN THE MATERNAL BRAIN: EFFECTS OF STRESS, DRUGS AND MEDICATION. Chair: **Jodi Pawluski**

10:30 MATERNAL CORTICOSTERONE: DIFFERENCES IN PRE- VERSUS POST-PARTUM EXPOSURE IN THE DAM AND HER OFFSPRING. **Galea, L.A.M.;** Brummelte, S.

10:55 EFFECT OF GESTATIONAL STRESS AND SSRI MEDICATION USE ON HIPPOCAMPAL NEUROGENESIS IN THE MOTHER. **Pawluski, J.**

11:20 EFFECTS OF GESTATIONAL COCAINE ON SPINE DENSITY IN PREGNANT RAT DAMS. **Liuine, V.**; Frankfurt, M.

11:45 MOTHERHOOD AND AGING: THE EFFECTS OF DIFFERENT ESTROGENS ON HIPPOCAMPAL NEUROGENESIS AND COGNITION IN MIDDLE-AGED FEMALES. **Barha, C.K.;** Lieblich, S.L.; Chow, C.; Galea, L.A.M.

12:10 Discussant: **Kelly Lambert**, Randolph-Macon College, Ashland, VA, USA

12:30-2:00 **Mid-Day Break - Exhibits**
Meet the Profs – *CONVENTION CENTER LAWN*

2:00-4:00 **Oral Session 1:** Psychiatry and Cognition. Chair: Jared Young. ***KEAUHOU BALLROOM***

2:00 DIFFERENCES IN FEEDBACK-BASED LEARNING AND PREFRONTAL DOPAMINE UTILIZATION ARE ASSOCIATED WITH VARIATION IN THE DRD4 GENE. **Groman, S.M.;** Feiler, K.; Seu, E.; Woods, J.A.; Jentsch, J.D.

2:15 MEASUREMENT OF A SCHIZOPHRENIA ENDOPHENOTPE IN A RODENT MODEL: MISMATCH NEGATIVITY (MMN) TO FREQUENCY DEVIANTS. Hodgson, D.M.; **Harms, L.**; Nakamura, T.; Fulham, W.R.; Todd, J.; Schall, U.; Michie, P.T.

2:30 IMPAIRED ATTENTION OF DOPAMINE TRANSPORTER (DAT) KNOCKDOWN (KD) MICE IN A CONTINUOUS PERFORMANCE TEST: SIMILARITIES TO PATIENTS WITH BIPOLAR DISORDER (BD). **van Enkhuizen, J.**; Geyer, M.; Young, J.

2:45 SUBSECOND MESOLIMBIC DOPAMINE RELEASE PREDICTS THE AVOIDANCE OF PUNISHMENT. **Oleson, E.B.;** Gentry, R.N.; Cheer, J.F.

3:00 DISTINCT NEURAL SUBSTRATES FOR REINFORCEMENT AND PUNISHMENT IN THE STRIATUM. **Kravitz, A.V.;** Tye, L.D.; Kreitzer, A.C.

3:15 MEDIAL SEPTAL-DIAGONAL BAND (MSDB) AND HIPPOCAMPAL INVOLVEMENT IN THE CLASSICALLY CONDITIONED EYEBLINK RESPONSE. **Roland, J.J.**; Gluck, M.A.; Myers, C.; Pang, K.C.H.; Servatius, R.J.

3:30 NPAS4 REGULATES A TRANSCRIPTIONAL PROGRAM IN CA3 REQUIRED FOR CONTEXTUAL MEMORY FORMATION. **Ramamoorthi, K**.; Fropf, R.; Belfort, G.M.; Fitzmaurice, H.L.; McKinney, R.M.; Neve, R.L.; Otto, T.; Lin, Y.

3:45 ON MAKING ZEBRAFISH SAD AND ANXIOUS: DEVELOPING NOVEL AQUATIC MODELS OF AFFECTIVE DISORDERS. Kyzar, E.; Roth, A.; Gaikwad, S.; Green, J.; Collins, C.; El-Ounsi, M.; Davis, A.; Pham, M.; Stewart, A.M.; Cachat, J.; Zukowska, Z.; **Kalueff, A.V.**

2:00-4:00 **Oral Session 2:** Stress and the Environment. Chair: Nancy Ostrowski. ***KEAUHOU II***

2:00 MEDIAL SEPTAL-DIAGONAL BAND (MSDB) AND HIPPOCAMPAL INVOLVEMENT IN THE APPEASING PHEROMONE MEDIATES SOCIAL BUFFERING OF CONDITIONED FEAR RESPONSES. **Kiyokawa, Y.**; Takahashi, Y.; Takeuchi, Y.; Mori, Y.

2:15 BEHAVIOURAL CHANGES OF MALE MICE PERINATALLY EXPOSED TO FLUOXETINE**. Kiryanova, V.;** Smith, V.M.; Antle, M.C.; Dyck, R.H.

2:30 NEONATAL PROGRAMMING OF THE AUTONOMIC NERVOUS SYSTEM BY IMMUNOLOGICAL CHALLENGE: IMPLICATIONS FOR ANXIETY. Sominsky, L.; Fuller, A.E.; Bondarenko, E.; Ong, L.K.; Clark, V.R.; Bobrovskaya, L.; Dunkley, P.; Nalivaiko, E.; **Hodgson, D.M.**

2:45 INDIVIDUALLY VENTILATED CAGE SYSTEMS: A NOVEL HOUSING TYPE CAUSING PROBLEMS FOR MOUSE MODEL RESEARCH. Logge, W.; Kingham, J.; **Karl, T.**

3:00 EXERCISE PROTECTS AGAINST APOPTOSIS INDUCED BY CHRONIC RESTRAINT STRESS. **Gerecke, K.M.;** Kolobova, A.; Allen, S.

3:15 ANXIOGENIC-LIKE EFFECTS INDUCED BY CRF RECEPTOR ACTIVATION WITHIN THE AMYGDALA IN MICE. Cipriano, A.C.; Gomes, K.S.; **Nunes-de-Souza, R.**

3:30 GENETIC ANALYSIS OF CHRONIC MILD STRESS IN MICE. **Jones, B.C.**; Lu, L.; Williams, R.W.; Cavigelli, S. A.; Mormede, P.

3:45 WHAT BETWEEN OBSESSIVE-COMPULSIVE (OCD) RITUALS, SPORT RITUALS, AND DAILY MOTOR TASKS? A POSSIBLE ADAPTIVE VALUE FOR SEEMINGLY UNNECESSARY ACTS. **Eilam, D.**; Keren, H.; Mort, J.; Weiss, O.

4:00-4:30 **Snack Break - Exhibits**

4:30-6:30 **Student Slide Blitz**

4:30 Introduction: Robert Gerlai, Chair

4:40 OXYTOCIN RECEPTOR KNOCKDOWN PRAIRIE VOLES DISPLAY SOCIAL DEFICITS AND PROVIDE NOVEL MODELS FOR THE SCREENING OF PHARMACOTHERAPUTICS**. Keebaugh, A.;** Barrett, C.; Jenkins, J.; Young, L.

4:50 DEVELOPMENTAL METHAMPHETAMINE EXPOSURE ALTERS NEUROTRANSMITTER SYSTEMS: POTENTIAL NEUROBIOLOGICAL MECHANISMS OF LEARNING AND MEMORY DEFICITS IN RATS. **Schaefer, T.L.;** Graham, D.L.; Amos-Kroohs, R.M.; Braun, A.A.; Grace, C.E.; Skelton, M.R.; Williams, M.T.; Vorhees, C.V.

4:60 RESILIENCE TO EARLY LIFE STRESS IN FEMALE PRAIRIE VOLES (MICROTUS OCHROGASTER): POTENTIAL MODERATION BY OXYTOCIN RECEPTORS. **Barrett, C.E.;** Modi, M.; Young, L.J.

5:00 TOP DOWN CONTROL OF SEROTONERGIC SYSTEMS IN DEPRESSIVE-LIKE BEHAVIORS. **Challis, C.;** Boulden, J.; Beck, S.G.; Berton, O.

5:10 INESCAPABLE TAIL SHOCK AND COLD SWIM STRESS INTERACT TO ELEVATE TPH2 MRNA EXPRESSION IN AN ANXIETY-RELATED SUBSET OF SEROTONERGIC NEURONS. **Donner, N.C.;** Kubala, K.H.; Drugan, R.C.; Maier, S.F.; Lowry, C.A.

5:20 THE NATURE OF HIPPOCAMPAL INVOLVEMENT IN ESTROGEN-MEDIATED LEARNING ENHANCEMENT. **Phan, A.;** Suschkov, S.; Pecchioli, N.; Seguin, L.; Winters, B.D.; Choleris, E.

5:30 PARAVENTRICULAR OXYTOCIN REGULATES SOCIAL-MEDIATION OF THE STRESS RESPONSE IN FEMALE PRAIRIE VOLES. **Smith, A.S.;** Wang, Z.

5:40 BEHAVIOR AND DYSREGULATES GENE EXPRESSION WITHIN THE VTA. **Warren B.L.;** Alcantara L.F.; Wright, K.N.; Vialou, V.; Iiguez, S.D.; Nestler, E.J.; Bolaos-Guzman, C.A.

5:50 DEFENSIVE AGGREGATION (HUDDLING) IN LABORATORY RATS IN RESPONSE TO PREDATOR ODORS: GENERAL CHARACTERISTICS AND NEURAL CORRELATES. **Bowen, M.T.;** Kevin, R.; Kendig, M.D.; McGregor, I.S.

6:00 NEURONAL ACTIVATION PATTERNS ASSOCIATED WITH HYPER-EMOTIONAL AGGRESSION IN RATS SOCIALLY ISOLATED FROM WEANING. **Tulogdi, A.;** Toth, M.; Biro, L.; Soros, P.; Haller, J.

6:30-8:00 **Evening Break**

8:00-10:00 **Exhibits**

8:00-10:00 **Poster Session 2:** ***Pharmacology***. ***KEAUHOU I***

57. THE ENDOCANNABINOID SYSTEM CRITICALLY MODULATES THE EXPRESSION OF SOCIAL BEHAVIORS IN ADULT MALE MICE. Pietropaolo, S.; Le Maire, V.; Bellocchio, L.; **Crusio, W.E.;** Marsicano, G.

58. RELATIVELY BRIEF EXPOSURE TO AN ENRICHED ENVIRONMENT EFFECTIVELY BLOCKS SUCROSE SEEKING AND REDUCES SUCROSE SELF-ADMINISTRATION IN RATS. **Grimm, J.W.**; Weber, R.; Barnes, J.; Koerber, J.; Dorsey, K.; Deuse, L.; Glueck, E.; Collins, S.; North, K.

59. CHRONIC TREATMENT WITH FLUOXETINE IMPAIRS THE FACILITATORY EFFECT PRODUCED BY 5-HT2C RECEPTOR ACTIVATION WITHIN THE DORSAL PERIAQUEDUCTAL GRAY (DPAG) ON ELEVATED PLUS MAZE (EPM)-INDUCED ANTINOCICEPTION IN MICE. **Baptista, D.**; Nunes-de-Souza, R.L.; Canto-de-Souza, A.

60. DIMINISHED NICOTINE BEHAVIORAL SENSITIZATION IN GHRELIN RECEPTOR NULL RATS. **Wellman, P.J.**; Clifford, P.S.; Rodriguez, J.A.

61. SOCIAL CONTEXT ENHANCES INITIAL REINFORCING EFFECTS OF NICOTINE. **Peartree, N.A.**; Chandler, K. N.; Goenagga, J.; Whillock, C. L.; Neisewander, J.L.

62. EFFECTS OF KETOGENIC DIET ON MOTOR PERFORMANCE AND BEHAVIOR IN MOUSE MODELS OF ALZHEIMER'S DISEASE. D'Agostino, D.; Brownlow, M.; Leif Benner, L.; Gordon, M.N.; Morgan, D.

63. DEVELOPMENT, TESTING AND THERAPEUTIC APPLICATIONS OF KETONE ESTERS (KE) FOR CNS OXYGEN TOXICITY (CNS-OT); I.E., HYPERBARIC OXYGEN (HBO2)-INDUCED SEIZURES. **D'Agostino, D.P.**; Pilla, R.; Held, H.; Landon, C.S.; Ari, C.; Arnold, P.; Dean, J.B.

64. THE USE OF AGOMELATINA IN DRUG ADDICTED PATIENTS WITH PSYCHIATRIC DISORDERS. **Pieri, M.C.**; Comaschi, A.C.

65. THE EFFECTS OF THE AGONIST THERAPY IN ANXIOUS-DEPRESSED POSITIVE HCV DRUG-ABUSERS TREATED WITH IFN THERAPY. **Pieri, M.C.;** Comaschi, A.C.

66. CB1-RECEPTOR LIGAND PRE-TREATMENT INFLUENCES BEHAVIORAL EFFECTS INDUCED BY REPEATED COCAINE ADMINISTRATIONS IN MARMOSET MONKEYS. Cagni, P.; Netto, G.C.M.; Jesus, A.G.L.; **Barros, M**.

67. THE ATYPICAL ANTIPSYCHOTIC DRUG ARIPIPRAZOLE ENHANCES COGNITION AFTER EXPERIMENTAL TRAUMATIC BRAIN INJURY. Phelps, T.I.; Cheng, J.P.; **Kline, A.E**.

68. ELECTROACUPUNCTURE AT JOKSAMNI AND PUNGNYUNG ACUPOINTS ALLEVIATES POLOXAMER 407-INDUCED HYPERLIPIDEMIA THROUGH THE REGULATION OF SREBP-2 EXPRESSION IN RATS. **Park, J.**; Lee, B.; Yin, C.S.; Shim, I.; Lee, H.; Hahm, D.H.

69. INHIBITORY EFFECT OF IXERIS DENTATE ON DEVELOPMENT AND EXPRESSION OF BEHAVIORAL LOCOMOTOR SENSTIZATION TO NICOTINE IN RATS**. Park J.H.**; Lee, B.; Shim, I.; Lee, H.; Hahm, D.H.

70. CRF2 RECEPTORS MEDIATE ANXIETY STATES DURING AMPHETAMINE WITHDRAWAL. **Scholl, J**.; Reinbold, E.; Oliver, K.; Watt, M.; Forster, G.

71. ETHANOL DOSE GENERALIZATION CURVES FOLLOWING MULTIPLE DISCRIMINATION TRAINING CONDITIONS IN ADOLESCENT AND ADULT RATS. **Anderson, R.I.**; Spear, L.P.

72. ADOLESCENT CB1 RECEPTOR AGONISM, BUT NOT ANTAGONISM , ENHANCES ADULT MALE SEXUAL PERFORMANCE. **Gorzalka, B.;** Lee, T.-Y.T.

73. THE ROLE OF THE BASOLATERAL AMYGDALA IN CONDITIONED CUE-INDUCED ALTERATIONS IN ALCOHOL-SEEKING. **Deehan, G.A. Jr.;** Hauser, S.R.; Engleman, E.A.; Ding, Z-M.; McBride, W.J.; Rodd, Z.A.

74. THE GALANIN-3 RECEPTOR ANTAGONIST, SNAP 37889, REDUCES BREAKPOINT AND CUE-INDUCED RELAPSE TO ETHANOL IN ALCOHOL-PREFERRING RATS. Ash, B.L.; Tsegay, S.; Williams, S.J.; Lawrence, A.J.; **Djouma, E**.

75. CAN THE COMBINATION OF MORPHINE AND THE NON-OPIOID ANALGESIC FLUPIRTINE, REDUCE MORPHINE'S ABUSE POTENTIAL? **Elkman, L.;** Goodchild, C.S.; Kolosov, A.; Broadbear, J.H.

76. DEVELOPMENT OF A DISCRETE TRIALS TASK TO ASSESS SEROTONERGIC MODULATION ON INTERVAL TIMING IN MICE. **Halberstadt, A.L.;** Young, J.W.; Geyer, M.A.

77. THE EFFECTS OF GENE KNOCKOUT OF CADHERIN 13 (CDH13) ON NICOTINE CONSUMPTION. **Hall, F.S.;** Arnold, E.R.; Deshmukh, A.A.; Perona, M.T.G.; Drgonova, J.; Ranscht, B.; Uhl, G.R.

78. THE EFFECT OF COCAINE ON ROTOROD PERFORMANCE IN MALE AND FEMALE C57BL/6J MICE. **Heyser, C.J.;** Vishnevetsky, D. Berten, S.

79. *IN VIVO* CHARACTERISATION OF SOC-1: A NOVEL PROSOCIAL COMPOUND. **Hicks, C.;** Bowen, M.T.; Ramos, L.; Jorgensen, W.; Kassiou, M.; Hunt, G.E.; McGregor, I.S.

80. SHORT-TERM AND ENDURING BEHAVIORAL EFFECTS OF CHRONIC RISPERIDONE IN THE ADOLESCENT AND ADULT RAT. **Karanges, E.;** Caminer, A.; McGregor, I.S.

81. ANALYSIS BY AUTORADIOGRAPHY FOLLOWING MEPHEDRONE (4-METHYLMETHCATHINONE) INDUCED SELF ADMINISTRATION BEHAVIOUR IN ADOLESCENT RATS. Motbey, C.P.; **Karanges, E.**; Apetz, N.; Callaghan, P.D.; Clemens, K.; Cornish, J.; McGregor, I.S.

82. PROGESTERONE DECREASES COCAINE CHOICE IN FEMALE RATS. **Kippin, T.E.**; Kerstetter, K.A.; Carr, A.E.; Lee; J.I.; Togal, V.L.

83. THE ROLE OF MIDBRAIN DOPAMINE IN PREDICTIVE FEAR LEARNING. **Li, S**.; McNally, G.P.

84. CONTEXT-INDUCED RELAPSE TO ALCOHOL SEEKING AFTER PUNISHMENT IN A RAT MODEL. **Marchant, N. J.**; Khuc, T. N.; Bonci, A.; Shaham, Y.

85. COMBINATIONS OF SKF 38393 WITH MEMANTINE DO NOT HAVE AN ADDITIVE EFFECT TO REDUCE THE VOLITIONAL CONSUMPTION OF ETHANOL BY THE MYERS MHEP RAT. **McMillen, B. A.;** Lommatzsch, C.L.; Sayonh, M.J.; Williams, H.L.

86. DEVELOPMENTAL FLUOXETINE EXPOSURE, BUT NOT PRENATAL STRESS, DEMASCULINIZES SEXUAL BEHAVIOR IN MALES, BUT HAS NO EFFECT ON SEXUAL BEHAVIOR IN FEMALES. **Rayen, I.;** Charlier, T.D.; Balthazart, J.; Steinbusch, H.W.M.; Pawluski, J.L.

87. EFFECTS OF SHORT-TERM TREATMENT WITH LOW DOSE OF FLUOXETINE ON THE EXTRACELLULAR LEVELS OF SEROTONIN IN THE PERIAQUEDUCTAL GRAY MATTER OF FEMALE RATS IN LATE DIESTRUS. **Santos, J.M.**; Carvalho, M.C.; Lovick, T.A.; Brandao, M.L.

88. DEVELOPMENTAL METHAMPHETAMINE EXPOSURE ALTERS NEUROTRANSMITTER SYSTEMS: POTENTIAL NEUROBIOLOGICAL MECHANISMS OF LEARNING AND MEMORY DEFICITS IN RATS. **Schaefer, T.L.;** Graham, D.L.; Amos-Kroohs, R.M.; Braun, A.A.; Grace, C.E.; Skelton, M.R.; Williams, M.T.; Vorhees, C.V.

89. DOES PRENATAL METHAMPHETAMINE EXPOSURE INDUCE CROSS-SENSITIZATION TO OTHER DRUGS IN ADULT MALE RATS? **Slamberova, R.**; Pometlova, M.; Schutova, B.; Hruba, L.; Deykun, K.

90. NOREPINEPHRINE ANTAGONISM IN THE EXTENDED AMYGDALA REDUCES THE APPROACH-AVOIDANCE BEHAVIOR OF RATS RUNNING AN ALLEY FOR IV COCAINE. **Wenzel, J.M.;** Su, Z.-I.; Haber, Z.M.; Ettenberg, A.

91. GIT1 IS ASSOCIATED WITH ADHD. **Won, H**.; Mah, W.; Kim, E.

92. ADOLESCENTS ARE AT GREATER RISK FOR COCAINE ADDICTION THAN ADULTS. **Wong, W.C.**; Bamman, M.T.; Ford, K.A.; McCutcheon, J.M.; Marinelli, M.

93. ADOLESCENTS ARE INSENSITIVE TO PUNISHMENT-INDUCED SUPPRESSION OF COCAINE SELF-ADMINISTRATION. **Wong, W.C.**; Lamoureux, L.; Bamman, M.T.; Marinelli, M.

94. THE MULTIPLE PARTNER CHOICE ARENA SATISFIES THE CONSTRUCT VALIDITY OF AN ANIMAL MODEL TO STUDY PREMETURE EJACULATION. **Ferreira-Nuno, A.;** Olayo-Lortia, J.; Cruz-Benites, A.; Velazquez-Moctezuma, J.; Morales-Otal, A.

95. TRANSIENT CRF OVEREXPRESSION IN THE FOREBRAIN DURING EARLY LIFE INCREASES STARTLE REACTIVITY AND ANXIETY IN ADULTHOOD. Gresack, J.E.; **Toth, M.;** Gross, M.; Vicentini, E.; Mangiarini, L.; Mansuy, I.M.; Merlo-Pich, E.; Risbrough, V.B.

96. ENDURING EFFECTS OF METHYLPHENIDATE: THE ROLE PLAYED BY ROUTE OF DRUG ADMINISTRATION. **Bigney, E.;** Taukulis, H.

97. EARLY ADOLESCENT IMPULSIVITY PREDICTS LATE ADOLESCENT BINGE IN FEMALE RATS. **McClure, J.R.;** Richardson, H.N.

98. EFFECTS OF DIFFERENT HALLUCINOGENIC NMDA ANTAGONISTS AND XYLAZINE ON FEAR EXTINCTION. **Padilla, E.;** DeMis, J.; Seo, D.; Adkins, D.; Monfils, M.

99. ACUTE PROSOCIAL EFFECTS OF PERIPHERALLY ADMINISTERED OXYTOCIN IN RATS: REVERSAL BY THE V1A ANTAGONIST SR49059. **Ramos, L.;** Hicks, C.; Kevin, R.; McGregor, I.S.

100. INCREASE IN THE SENSITIVITY OF NICOTINE WITHIN THE POSTERIOR VENTRAL TEGMENTAL AREA PRODUCED BY CHRONIC ETHANOL CONSUMPTION. Hauser, S.; Deehan, G.; Toalston, J.; Truitt, W.; McBride, W.; **Rodd, Z.**

101. FUCOIDAN AMELIORATES SCOPOLAMINE-INDUCED NEURONAL IMPAIRMENT AND MEMORY DYSFUNCTION IN RATS VIA ACTIVATION OF CHOLINERGIC SYSTEM AND REGULATION OF CREB AND BDNF EXPRESSION. **Sur, B.J.;** Lee, B.; Kwon, S.; Shim, I.; Yin, C.S.; Lee, H.; Hahm, D.H.

102. INVOLVEMENT OF KAPPA OPIOD RECEPTOR IN DSL AND PDSM STRIATUM DURING HABITUAL AND GOAL DIRECTED COCAINE SEEKING. **Wang, Y.;** Zapata, A.; Minney, V.; Shippenberg, T.

103. RESILIENCE TO EARLY LIFE STRESS IN FEMALE PRAIRIE VOLES (MICROTUS OCHROGASTER): POTENTIAL MODERATION BY OXYTOCIN RECEPTORS. **Barrett, C.E.;** Modi, M.; Young, L.J.

104. EFFECTS OF A DYSFUNCTIONAL BRAIN SEROTONERGIC SYSTEM ON SOCIAL BEHAVIORS IN MALE PET-1 KNOCKOUT MICE. **Can, A.;** Piantadosi, S.C.; Gould, T.D.

105. INESCAPABLE TAIL SHOCK AND COLD SWIM STRESS INTERACT TO ELEVATE TPH2 MRNA EXPRESSION IN AN ANXIETY-RELATED SUBSET OF SEROTONERGIC NEURONS. **Donner, N.C.;** Kubala, K.H.; Drugan, R.C.; Maier, S.F.; Lowry, C.A.

106. PLATELET SEROTONIN FUNCTION AND ITS RELATIONSHIP TO ADOLESCENT SUICIDAL IDEATION AND HISTORIES OF SUICIDE ATTEMPTS. **Dougherty, D.;** Mathias, C.; Hill-Kapturczak, N.; Tian, P.; Javors, M.

107. DOPAMINE MANIPULATIONS IN THE ORBITOFRONTAL CORTEX MODULATE REVERSAL LEARNING DEFICITS OF SPONTANEOUSLY HYPERTENSIVE RATS IN AN ATTENTIONAL SET-SHIFTING TASK. **Li, J.-S.;** Cheng, J.-T.

108. G PROTEIN-COUPLED RECEPTOR KINASE 6 DEFICIENCY AND MOUSE MODELS OF PARKINSON'S DISEASE. **Manago', F.;** Espinoza, S.; Salahpour, A.; Sotnikova, T.D.; Caron, M.G.; Premont, R.T.; Gainetdinov, R.R.

109. EXERCISE DOES NOT PROTECT AGAINST EXPERIMENTAL PARKINSONISM IN MICE DEFICIENT IN BDNF. **Gerecke, K.**; Jiao, Y.; Pagala, V.; Pani, A.; Smeyne, R.

110. DISTINCT NEURAL SUBSTRATES FOR REINFORCEMENT AND PUNISHMENT IN THE STRIATUM. **Kravitz, A.V.;** Tye, L.D.; Kreitzer, A.C.

111. SUBSECOND MESOLIMBIC DOPAMINE RELEASE PREDICTS THE AVOIDANCE OF PUNISHMENT. **Oleson, E.B.;** Gentry, R.N.; Cheer, J.F.

112. STRUCTURAL NEUROANATOMY CORRELATES WITH FUNCTIONAL MOTOR-RELATED NETWORKS IN STROKE PATIENTS. Liew, S-L.; Garrison, K.; Haldar, J.; Winstein, C.; Damasio, H.; **Aziz-Zadeh, L.**

Friday, June 8, 2012

9:00-10:00 **Keynote: David M. Diamond**, University of South Florida
A NOVEL PERSPECTIVE ON THE INVOLVEMENT OF THE HIPPOCAMPUS IN FLASHBULB AND TRAUMATIC MEMORIES.

10:00-10:30 **Coffee/Snack Break - Exhibits**

10:30-12:30 **Symposium:** USE OF OPTOGENETICS IN BEHAVIORAL NEUROSCIENCE. Chair: **Peter Shiromani**, Ralph H. Johnson VA and the Medical University of South Carolina, Charleston

10:30 SHINING LIGHT ON WAKEFULNESS AND AROUSAL USING OPTOGENETICS. **Carter, M.E.;** de Lecea, L.

10:55 DISSECTING ADDICTION CIRCUITRY WITH OPTOGENETICS. **Moorman, D.E.;** Vazey, E.M.; Aston-Jones, G.

11:20 SEEING IS BREATHING. **Feldman, J.L.**

11:45 SLEEP INDUCTION BY OPTOGENETIC INHIBITION OF HYPOCRETIN NEURONS: IMPLICATIONS FOR INSOMNIA. **Kilduff, T.S.**

12:10 Discussant: **Peter Shiromani**

12:30-2:00 **Mid-Day Break - Exhibits**
Grant Workshop – *KEAUHOU II*

2:00-3:35 **Symposium:** BRAIN HEALTH: THE ESSENTIAL NATURE OF OMEGA-3 FATTY ACIDS. Chairs: **Corina O. Bondi** and **Michael J. Weiser**

2:00 DOCOSAHEXAENOIC ACID (DHA) IS ESSENTIAL FOR NEURAL DEVELOPMENT: A BEHAVIORAL PERSPECTIVE. **Weiser, M.J**.; Salem, N.; Dahms, I.

2:25 OMEGA 3 FATTY ACIDS: LIMITING DIETARY NUTRIENTS WITH CRITICAL ROLES IN BRAIN DEVELOPMENT. **Innis, S.M.**

2:50 DIETARY DEFICIENCY IN OMEGA-3 FATTY ACIDS PRODUCES ALTERATIONS IN RAT BEHAVIOR AND BRAIN MARKERS OF MONOAMINERGIC INNERVATION**. Bondi, C.O.;** Tock, J.L.; Moghaddam, B.

3:15 Discussant: **David Jentsch**, University of California, Los Angeles, CA, USA

3:35-4:30 **Coffee/Snack Break - Exhibits**

4:30-6:30 **Symposium:** AGGRESSION, NEUROMODULATION, AND SOCIAL ADAPTATION: LESSONS FROM MULTIPLE ANIMAL MODELS. Chairs: **Gary R. Ten Eyck** and **Cliff H. Summers.** ***BAYVIEW ROOMS***

4:30 SOCIAL ADAPTATION IN THE MOUSE. **Blanchard, R.J.;** Pearson, B.L.

4:55 THE NEUROENDOCRINOLOGY OF SEXUAL BEHAVIOR AND SEX CHANGE IN CORAL REEF FISHES. **Godwin, J.**; Slane, M.A.

5:20 CHOICES IN SOCIAL ADAPTATION TO AGGRESSION: NEUROMODULATORY MECHANISMS IN DECISION MAKING. **Summers, C.H.;** Summers, T.R.; Arendt, D. H.; Smith, J.P.; Carpenter, R.E.

5:45 AGGRESSION, DEFENSE, AND PATERNAL CARE IN THE INVASIVE PUERTO RICAN COQUÍ FROG, ELEUTHERODACTYLUS COQUI. **Ten Eyck, G.R.;** Calibuso, M.J.

6:10 Discussant: **Lorey K. Takahashi**, University of Hawaii at Manoa, HI, USA

4:30-6:30 **Symposium:** CONTEXTUAL CONTROL OVER FEAR BEHAVIORS: RECENT ADVANCES AND MOLECULAR MECHANISMS. Chair: **Gavan P. McNally**, University of New South Wales, Sydney, Australia. ***KEAUHOU II***

4:30 ELECTRICAL SYNAPTIC CONTROL OVER FEAR BEHAVIORS. **Bissiere, S.**

4:55 NEURONAL ENSEMBLES IN CA1 AND MPFC DIFFERENTIALLY REPRESENT RECENT AND REMOTE CONTEXTUAL FEAR MEMORIES. **Zelikowsky, M.;** Fanselow, M.S.

5:20 CONTEXTUAL INFLUENCE IN CONDITIONED FEAR IN JUVENILE RATS: FORGETTING VS. EXTINCTION**. Kim, J.H.**

5:45 TRACES OF MEMORY: WHY RELEARNING FEAR FOLLOWING FORGETTING IS AN NMDAR-INDEPENDENT PROCESS. **Li, S.;** Langton, J.M.; Richardson, R.

6:10 Discussant: **Gavan P. McNally**

6:30-8:00 **Evening Break**

8:00-10:00 **Exhibits**

8:00-10:00 **Poster Session 3:** ***Disease Models. KEAUHOU I***

113. LOCAL OREXINERGIC ACTIVATION AND THE INFLUENCE ON THE FORCED SWIM TEST. **Arendt, D.**; Oliver, K.; Summers, C.

114. NEUREGULIN 1 AND REPEATED RESTRAINT STRESS INTERACT TO PROMOTE DEFICITS IN SENSORIMOTOR GATING AND GROWTH OF DENDRITIC SPINES IN ADOLESCENT MICE. **Arnold, J.C.;** Chohan T.W.; Boucher A.A.; Karl, T.; Bennett M.R.

115. WHAT DRIVES A FISH TO DIVE? MOTIVATION AND DEFENSIVE BEHAVIOR IN ZEBRAFISH. **Blaser, R**.; Goldsteinholm, K.

116. DISTINCT NEUROBEHAVIOURAL PROFILE OF P2X7-/- MICE: IMPLICATIONS FOR MANIA, ANXIETY AND AGGRESSION. **Boucher, A.A.;** Todd, S.; Bennett, M.; Kassiou, M.; Arnold, J.C.

117. EFFECTS OF MATERNAL SEPARATION ON SOCIAL INTERACTION. **Diehl, L.A.;** Henriques, T.P.; Corrêa, C.N.; Lucion, A.B.; Dalmaz, C.

118. IMPAIRED CONTEXT DISCRIMINATION AND NMDA RECEPTOR EXPRESSION AND FUNCTION IN THE DENTATE GYRUS OF A MOUSE MODEL OF FRAGILE X SYNDROME. **Eadie, B.;** Majaess, N.; Bostrom, C.; Cushman, J.; Kannangara, T.; Fanselow, M.; Christie, B.

119. PRENATAL EXPOSURE TO PROPIONIC ACID PRODUCES DEVELOPMENTAL DELAY, HYPER-SENSITIVITY TO ACOUSTIC STARTLE, AND SOCIAL IMPAIRMENT IN ADOLESCENT RATS. **Foley, K.A.;** MacFabe, D.F.; Kavaliers, M.; Ossenkopp, K.-P.

120. CHEMOPROTECTIVE POTENTIAL OF COCCINIA INDICA AGAINST CYCLOPHOSPHAMIDE INDUCED OXIDATIVE STRESS AND GENOTOXICITY IN BONE MARROW. **Hirani, K.;** Nitharwal, R.; Singh, K.; Patel, H.; Ugale, R.R.

121. LIPOPOLYSACCHARIDE ALTERS HYPOTHALAMIC NEUROPEPTIDE EXPRESSION AND INDUCES A STATE OF NEGATIVE ENERGY BALANCE THROUGH THE CYCLO-OXYGENASE-2 DEPENDENT PRODUCTION OF PROSTAGLANDINS. Ganegala, H.; Parkington, H.; **Hollis, J.**

122. EXTENDED EXPOSURE TO NATURAL AND ARTIFICIAL ENRICHED ENVIRONMENTS: NEUROBIOLOGICAL AND BEHAVIORAL RESPONSES IN MALE LONG EVANS RATS. **Hyer, M.;** Rzucidlo, A.; de Silva, I.; Bardi, M.; Lambert, K.

123. BEHAVIORAL DISCREPANCY BETWEEN GIT1-/- AND GIT1+/- MICE. **Lee, J.**

124. INHIBITORY EFFECT OF PHELLODENDRI CORTEX ON LIPOPOLYSACCHARIDE-INDUCED MEMORY IMPAIRMENT IN RATS. **Lee, B.;** Sur, B.J.; Shim, I.; Lee, H.; Hahm, D.H.

125. WHAT ARE WE ASSESSING IN JUVENILE PLAY BEHAVIOR? **Lewter, L.**; Hohmann, C.F.

126. GIT1 KNOCK-OUT MICE DISPLAY IMPAIRED HABITUATION AND ANXIOLYTIC BEHAVIORS. **Mah, W**.; Won, H.; Kim. E.

127. THE EFFECT OF EMBRYONIC ALCOHOL EXPOSURE ON SOCIAL BEHAVIOR AND NEUROCHEMISTRY IN TWO DIFFERENT ZEBRAFISH STRAINS. **Mahabir, S.;** Chatterjee, D.; Buske, C.; Gerlai, R.

128. ABNORMAL NEURONAL ACTIVATION IN RESPONSE TO NOVELTY AND SOCIAL INTERACTION IN BTBR T+tf/J MICE. **Meyza, K.Z.;** Pearson, B.L.; Pobbe, R.L.H.; Blanchard, D.C.; Blanchard, R.J.

129. ELEVATED BRAIN HEPARAN SULFATES IN THE NEUROGENIC LATERAL VENTRICLE WALL OF MECP2 MUTANT MICE. **Pearson, B.L.;** Corley, M.J.; Blanchard, D.C.; Blanchard, R.J.

130. OXYTOCIN RECEPTOR AND MECP2(308/Y) KNOCKOUT MOUSE STRAINS DISPLAY ALTERED EXPRESSION OF AUTISM-RELATED SOCIAL BEHAVIORS. **Pobbe, R.L.;** Pearson, B.L.; Blanchard, D.C.; Blanchard, R.J.

131. DEPRESSION & ANXIETY DIFFERENTIALLY PREDICT HPA REACTIVITY TO COUPLE CONFLICT. **Powers, S.;** Laurent, H.; Gunlicks-Stoessel, M.; Balaban, S.; Bent, E.

132. PRENATAL EXPOSURE TO BACTERIAL LPS LEADS TO LONG-LASTING PHYSIOLOGICAL CONSEQUENCES IN MALE OFFSPRING. **Solati, J.** ; Asiaei, M.

133. TAIL-PINCH-INDUCED EATING IS ASSOCIATED WITH EMOTIONALITY AND ACTIVATION OF HYPOTHALAMIC-PITUITARY-ADRENAL AXIS. **Someya, N.;** Narikiyo, K.; Masuda, A.; Hata, T.; Tsuneyoshi, D.; Aou, S.

134. MATERNAL SEPARATION AND POSTNATAL OXYTOCIN ADMINISTRATION ALTER SOCIAL RECOGNITION MEMORY IN ADOLESCENT FEMALE MICE. **Thomas, N.R.;** Cornwell, C.A.

135. VICARIOUS SOCIAL DEFEAT INDUCES DEPRESSION- AND ANXIETY-LIKE BEHAVIOR AND DYSREGULATES GENE EXPRESSION WITHIN THE VTA. **Warren, B.L.;** Alcantara, L.F.; Wright, K.N.; Vialou, V.; Iiguez, S.D.; Nestler, E.J.; Bolaos-Guzman, C.A.

136. KAOLIN-INDUCED VENTRICULOMEGALY AT WEANING PRODUCES LONG-TERM LEARNING AND MEMORY DEFICITS IN RATS. **Williams, M.T.;** Lindquist, D.M.; McAllister, J.P.; Mangano, F.T.; Yuan, W.; Vorhees, C.V.

137. FACILITATION OF PANIC-RELATED DEFENSIVE BEHAVIORS AFTER CORTICOTROPHIN-RELEASING FACTOR (CRF) INJECTION IN THE RAT DORSOLATERAL PERIAQUEDUCTAL GRAY. **Zangrossi, H.;** Sergio, T.O

138. MORPHOLOGICAL AND FUNCTIONAL DEFECTS OF NEUROTRANSMITTER AND NEUROTROPHIN RECEPTORS CAUSED BY EG5 MOTOR PROTEIN INHIBITION IN ALZHEIMER`S DISEASE. **Ari, C.;** Borysov, S.I.; Wu, J.; Padmanabhan, J.; Potter, H.

139. BCL9 AND C9ORF5 ARE ASSOCIATED WITH NEGATIVE SYMPTOMS IN SCHIZOPHRENIA: META-ANALYSIS OF TWO GENOME-WIDE ASSOCIATION STUDIES. **Xu, C.**; Aragam, N.; Villla, E.C.; Posada, Y.; Mao, C.X.; Camarillo, C.; Mao, Y.; Escamilla, M.A.; Wang, K-S.

140. SEIZURE 6-LIKE GENE ASSOCIATED WITH BIPOLAR DISORDER I. **Xu, C.;** Mullersman, J.; Wang, L.; Su, B.B.; Mao, C.X.; Posada, Y.; Mao, Y.; Escamilla, M.A.; Wang, K-S.

141. EXECUTIVE FUNCTIONS IN AGENESIS OF THE CORPUS CALLOSUM: WORKING MEMORY AND SUSTAINED ATTENTION IN BTBR MICE. **Gregg, M.;** Sample, H.; Neal, H.; Branson, N.; Martin, L.A.

142. QUANTITATIVE ASSESSMENT OF SOCIAL MOTIVATION IN BTBR AND C57BL/6J MICE THROUGH NOVEL OPERANT CONDITIONING PARADIGMS. Wood, C.; Sample, H.; Neal, H.; Gregg, M.; Branson, N.; **Martin, L.A.**

143. MATERNAL PROBIOTIC INTERVENTION PROTECTS AGAINST NEUROENDOCRINE AND IMMUNE DYSFUNCTIONS AND DISRUPTION OF GUT MICROFLORA BALANCE PROVOKED BY NEONATAL AND SUBSEQUENT ADULT STRESS IN WISTAR RATS. Barouei, J.; **Hodgson, D.**

144. NEONATAL LIPOPOLYSACCHARIDE EXPOSURE ALTERS NOCICEPTION. Zouikr, I.; Tadros, M.A.; Callister, R.J.; Nakamura, T.; Beagley, K.; Clifton, V.; **Hodgson, D.M.**

145. COMMUNICATION AND STEREOTYPED BEHAVIORS OF MICE EXPOSED TO MATERNAL IMMUNE ACTIVATION. **Defensor, E.B.**; Jensen, A.L.; Miske, M.M.; Yamamoto, L.H.L.; Blanchard, D.C.; Blanchard, R.J.

146. SOCIAL BEHAVIOR OF MICE EXPOSED TO MATERNAL IMMUNE ACTIVATION. **Jensen, A.L.;** Defensor, E.B.; Yamamoto, L.H.L.; Miske, M.M.; Blanchard, D.C.; Blanchard, R.J.

147. DETERMINATION OF ANXIETY DIFFERENCES BETWEEN C57BL/6 N AND J MICE TO INVESTIGATE EMOTIONAL PERSEVERATION. Landrau, S.; Rodríguez, C.; Vilarchao, J.; Sáez, E.; Santos, I.; López, O.; Budet, A.; Hernández, G.; Peña De Ortíz, S.; Méndez-Merced, A.T.

148. GENETIC BASES OF DIFFERENCES RELATED TO EMOTIONAL PERSEVERATION IN MOUSE SUBSTRAINS. Sáez, E.; Budet, A.; Landrau, S.; Hernández, G; Peña de Ortíz, S.; Méndez-Merced, A.T.

149. PREDATOR EXPOSURE INDUCES INHIBITED EXPLORATORY BEHAVIOR AND INCREASED AVOIDANCE OF TRAUMA-ASSOCIATED CUES. **Toth, M.;** Gross, M.; Adamec, R.; Risbrough, V.

150. BEHAVIORAL AND NEUROCHEMICAL ANALYSIS OF HDC-KO MICE, A MODEL OF A GENETIC FORM OF TOURETTE SYNDROME. **Baldan Ramsey, L.C.;** Crowley, M.J.; Hughes, Z.A.; Gorczyca, R.; Ohtsu, H.; De Araujo, I.; State, M.; Mayes, L.C.; Pittenger, C.

151. TOP DOWN CONTROL OF SEROTONERGIC SYSTEMS IN DEPRESSIVE-LIKE BEHAVIORS. **Challis, C.;** Boulden, J.; Beck, S.G.; Berton, O.

152. KLP-1 RESCUES PREPULSE INHIBITION DISRUPTIONS AND SOCIAL WITHDRAWAL INDUCED BY NMDA CHANNEL BLOCKERS: A POTENTIAL ANTIPSYCHOTIC. **Chiou, L.-C.;** Lee, H.-J.; Chen, H.-L.; Chou, R.-F.; Mouri, A.; Huang, W.-J.; Nabeshima, T.

153. RESTRAINT STRESS RELIEVES DEPRESSION-LIKE BEHAVIOR AND INDUCES ADULT NEUROGENESIS VIA OREXIN 2 RECEPTORS IN MICE. **Chiu, S.-Y.;** Teng, S.-F.; Chang, L.-Y.; Chiou, L.-C.

154. GIT1+/- MICE DISPLAY DIFFERENT CELLULAR PHENOTYPES IN BRAIN FROM GIT1-/- MICE WHICH ARE AN ADHD MOUSE MODEL. **Chung, C.**

155. IMPLICATION OF THE TRANSCRIPTION FACTOR NPAS4 IN COGNITIVE AND SOCIAL FUNCTIONS. **Coutellier, L.;** Beraki, S.; Saw, N.L.; Shamloo, M.

156. NEONATAL EXPOSURE TO ANTIDEPRESSANT RESULTED IN ADULT DECREASE OF NEUROLIGIN 1 IN THE PREFRONTAL CORTEX IN RATS. **Feng, P.;** Zhang, J.; Akladious, A.; Hu, Y.

157. CANNABINOIDS: A RISK FACTOR FOR A NEUREGULIN 1 MOUSE MODEL OF SCHIZOPHRENIA? **Karl T.;** Long L.; Boucher A.; McGregor I.; Huang X.-F.; Arnold J.

158. OXYTOCIN RECEPTOR KNOCKDOWN PRAIRIE VOLES DISPLAY SOCIAL DEFICITS AND PROVIDE NOVEL MODELS FOR THE SCREENING OF PHARMACOTHERAPUTICS**. Keebaugh, A.;** Barrett, C.; Jenkins, J.; Young, L.

159. SLEEPING IN CLASS: ARE STUDENT SCHEDULES PHYSIOLOGICALLY INHIBITING LEARNING? **Baynard, M.;** McEachron, D.L.

160. ACTIVATION OF B1-ADRENERGIC RECEPTOR AS A POTENTIAL MEMORY ENHANCEMENT STRATEGY IN NEURO COGNITIVE DISORDERS. Saw, N.L.; **Coutellier, L.;** Shamloo, M.

161. HYPOCRETIN GENE TRANSFER IN MICE MODELS OF NARCOLEPSY. Konadhode, R.; Pelluru, D.; Blanco-Centurion, C.; Liu, M.; **Shiromani, P.J.**

162. ANTI-INFLAMMATORY EFFECTS OF GLUCOSYLCERAMIDE IN LPS-INDUCED RAW 264.7 CELLS. **Park, J.;** Yeom, M.; Kim, S.; Kim, M.; Han, J.J.; Yin, C.S.; Park, H.J.; Lee, H.; Hahm, D.H.

163. INVOLVEMENTS OF CORTICOTROPIN-RELEASING FACTOR, BUT NOT GLUCOCORTICOID IN THE RESTRAINT-INDUCED CONDITIONED PLACE PREFERENCE. Mei, Y.Y.; **Li, J.S**.

164. DIFFERENCES IN FEEDBACK-BASED LEARNING AND PREFRONTAL DOPAMINE UTILIZATION ARE ASSOCIATED WITH VARIATION IN THE DRD4 GENE. **Groman, S.M.**; Feiler, K.; Seu, E.; Woods, J.A.; Jentsch, J.D.

165. SPATIAL LEARNING DEFICITS IN MOUSE MODELS OF CONGENITAL MUSCULAR DYSTROPHIES. **Yu, M.;** Liu, Y.; Bampoe, K.; Hu, H.

Saturday, June 9, 2012

9:00-10:00 **Bench-to-Bedside Lecture: David L. McKinzie**, Eli Lilly, Indianapolis, IN, USA
FROM BENCH TO CLINIC: DEVELOPMENT OF METABOTROPIC GLUTAMATE-2/3 RECEPTOR AGONISTS FOR THE TREATMENT OF SCHIZOPHRENIA

10:00-10:30 **Coffee/Snack Break - Exhibits**

10:30-12:30 **Symposium:** THE PROMISE AND POTENTIAL PITFALLS OF TRANSLATIONAL RESEARCH. Chair: Eva Ihle, University of California, San Francisco, USA

10:30 RESEARCH IN TRANSLATION: TOWARD CLARITY IN COMMUNICATION BETWEEN BASIC AND CLINICAL SCIENCES. **Ihle, E.**

10:55 TRANSLATIONAL RESEARCH: FINDING THE "SWEET SPOT". **Blanchard, D.C.**

11:20 MIND THE GAP: A REPORT CARD ON TRANSLATIONAL TREATMENT ATTEMPTS IN AUTISM AND NEURODEVELOPMENTAL DISORDERS. **McCracken, J. T.**

11:45 WHAT ARE THESE THINGS CALLED WORKING MEMORY: TRANSLATIONAL PITFALLS IN DEVELOPING PROCOGNITIVE TREATMENTS. **Young, J.W.**

12:10 Discussant: **Eva Ihle**

12:30-2:00 **Mid-Day Break - Exhibits**
Meet the Profs - *CONVENTION CENTER LAWN*

2:00-4:00 **Symposium:** NEW ANIMAL MODELS OF BIPOLAR DISORDER.
Chairs: **Francisco Gonzalez-Lima** and **Eimeira Padilla**

2:00 REDUCED DOPAMINE TRANSPORTER FUNCTION: A MODEL OF MANIA WITH CROSS-SPECIES TRANSLATIONAL VALIDITY. **Young, J.W.**; van Enkhuizen, J.; Geyer, M.A.

2:25 MUTANT *POLG1* TRANSGENIC MICE AS A MODEL OF BIPOLAR DISORDER. **Kubota-Sakashita, M.;** Kasahara, T.; Kato, T.

2:50 FORCED DESYNCHRONIZATION AS A BEHAVIORAL MODEL OF BIPOLAR DISORDER. **Koike, B.D.V.;** Ribeiro, J.M.; Gonalves, B.S.B.; Araujo, J.F.

3:15 BIPOLAR-DEPRESSIVE BEHAVIOR IN HOLTZMAN RATS. **Padilla, E.;** Shumake, J.; Auchter, A.; Barrett, D.; Gonzalez-Lima, F.

3:40 Discussant: **Francisco Gonzalez-Lima,** University of Texas, Austin, TX, USA

4:00-4:30 **Snack Break - Exhibits**

4:30-6:30 **Symposium:** THE ROLE OF NEUROINFLAMMATION IN THE ETIOLOGY OF AUTISM SPECTRUM DISORDERS (ASD). Chairs: **Christine F. Hohmann** and **Judy Van de Water**

4:30 NEUROINFLAMMATION AND NEUROIMMUNE ABNORMALITIES IN CHILDREN WITH ASD. **Van de Water, J.**; Ashwood, P.

4:55 VALIDATING IMMUNE FINDINGS IN ANIMAL MODELS OF AUTISM. **Ashwood, P.;** Van de Water, J.

5:20 SEROTONIN AS POSSIBLE MODULATOR OF NEUROINFLAMMATION IN THE FOREBRAIN: STUDIES IN A MOUSE MODEL FOR ASD**. Hohmann, C.F**.; Blue, M.E.

5:45 PROGRAMMING INNATE IMMUNITY: IMPLICATIONS FOR NEURAL AND BEHAVIORAL DEVELOPMENT. **Bilbo, S.D.**

6:10 Discussant: **Robert Benno**, William Paterson University of New Jersey, Wayne, NJ, USA

6:30-7:00 **Business Meeting – *KEAUHOU II***

7:00-9:00 **Luau – *HAWAII LAWN***

7:00-8:00 Luau (buffet dinner)
7:30 Live Music starts
8:00-9:00 Cultural Show

9:00-12:00 Dance and music – ***KEAUHOU I***
Live band featuring LT Smooth

Sunday, June 10, 2012

9:00-11:00 **Symposium:** NEW INSIGHTS INTO THE NEUROBIOLOGY OF ADDICTION: NEUROCHEMICAL AND BEHAVIOURAL ADAPTATIONS TO LONG TERM DRUG EXPOSURE. Chairs: **Christian P. Müller** and **Tomasz Schneider**

9:00 PRENATAL NICOTINE EXPOSURE AND ADHD: CURRENT CONTROVERSIES AND ANIMAL MODELS. **Schneider, T.**

9:25 SHIFT OF DRUG CUE-INDUCED PHASIC DOPAMINE RELEASE FROM LIMBIC TO SENSORIMOTOR STRIATUM DURING THE PROGRESSION OF DRUG TAKING. **Willuhn, I.**; Everitt, B.J.; Phillips, P.E.

9:50 A HISTORY OF EXTENDED ACCESS TO COCAINE PRODUCES ANOMALIES IN CORTICO-ACCUMBENS GLUTAMATE: IMPLICATIONS FOR ADDICTION THERAPY. **Szumlinski, K.K.**

10:15 CALMODULIN-DEPENDENT KINASES IN THE ACQUISITION AND EXPRESSION OF ADDICTION RELATED BEHAVIOUR IN MAN AND MICE. **Müller, C.P.**

10:40 Discussant: **Aaron Ettenberg,** University of California, Santa Barbara, CA

11:00-11:30 **Coffee/Snack Break**

11:30-1:30 **Symposium:** EXAMINING A LEARNING DIATHESIS MODEL FOR ANXIETY DISORDERS. Chairs: **Xilu Jiao** and **Kevin C.H. Pang**

11:30 LEARNING DIATHESIS AS A MODEL FOR THE ETIOLOGY OF ANXIETY DISORDERS. **Servatius, R.J.**

11:50 ANIMAL MODELS OF ANXIETY VULNERABILITY: INFLUENCE OF RISK FACTORS ON AVOIDANCE LEARNING. **Pang, K.**

12:10 NEUROBIOLOGY OF FASTER ACQUISITION AND PERSEVERATION IN ANIMALS**. Jiao, X.**

12:30 COMPUTATIONAL MODEL OF AVOIDANCE LEARNING: MECHANISMS OF BEHAVIORAL INHIBITION. **Myers, C.E.**

12:50 BEHAVIORAL AND NEURAL MARKERS OF ANXIETY VULNERABILITY IN HUMANS. **McAuley, J.D.**

1:10 Discussant: **Israel Liberzon**, University of Michigan, Ann Arbor, MI, USA

Tuesday, June 5, 2012

6:00-8:00 **Symposium:** THE NEUROBIOLOGY OF RESILIENCE: IMPLICATIONS FOR ADAPTIVE FUNCTIONS AND MENTAL HEALTH. Chair: **Kelly Lambert**

RODENT MODELS EXPLORING EFFECTIVE BEHAVIORAL THERAPIES FOR MENTAL HEALTH RESILIENCE: EVALUATION OF PREDISPOSED COPING STRATEGIES AND EFFORT-BASED REWARD CONTINGENCY TRAINING. Lambert, K. G. Department of Psychology. Randolph-Macon College, Ashland, VA 23005 USA. Our laboratory has previously reported that post-weaned rats exhibit passive, active and variable coping strategies (Hawley et al., 2010). In contrast to the more consistently responding passive and active copers, variable coping rats exhibit situation-dependent, as opposed to fixed, behavioural responses to various stressors. Additionally, more adaptive neurobiological responses (e.g., increased NPY-immunoreactivity in stress-related brain areas) have been observed in the variable coping animals. Further, we have reported that rats exposed to five weeks of contingency training [i.e., Effort-Based Reward (EBR) Training; Lambert, 2006] exhibit more resilient responses (e.g., more persistent attempts in problem-solving tasks, lower CORT/DHEA ratios, more adaptive/conservative responses to repeated swim tests). Interestingly, when rats representing the various coping strategies are exposed to either contingent EBR training or non-contingent training, variable copers exhibit enhanced resiliency in the contingent training group whereas variable copers lose their advantage in the non-contingent group. Thus far we have not observed contingency training to alter the responses of passive and active animals in such a dramatic fashion. These results suggest that the variable copers are differentially prepared to respond to contingency training and, in the absence of behavioral control, exhibit higher stress hormone levels and less adaptive behavioural responses (Bardi et al., 2012), making them more susceptible to experiencing allostatic load. In sum, the combined coping profile assessment and EBR training models may be used as an approach to explore the effectiveness of behavioural therapies for building emotional resilience in rodents, allowing the investigation of differential effects on animals exhibiting varying types of coping responses.

A RODENT MODEL OF HUMAN BEHAVIORAL INHIBITION: DEVELOPMENTAL PRECURSORS AND ADULT NEURONAL CORRELATES OF PERI-WEANING INHIBITION. Cavigelli, S.A.; Ragan, C.M. Dept. of Biobehavioral Health, Pennsylvania State University, University Park, PA 16802; Dept. of Psychology, Michigan State University, East Lansing, MI 48824 USA. Childhood behavioral inhibition (or dysregulated fear) is an important predictor of adult anxiety (particularly social anxiety). Although behavioral inhibition often predicts adult anxiety, the early environmental and neurological underpinnings are not understood. To identify potential long-term biological and health consequences of early behavioral inhibition and to test how early life experiences may influence the trajectory of a fearful temperament, we have been developing a rodent model of behavioral inhibition. In this talk, we will: (1) review the rodent model, (2) present results on glucocorticoid, cardiovascular, and longevity correlates of the behavioral fear trait, (3) identify maternal-neonate interactions that predict this trait, and (4) identify some adult neuronal processes mRNA expression of corticotropin releasing hormone receptor 1 in the hippocampus and serotonin transporters in the dorsal raphe associated with pre-adult inhibition in mice and rats. The findings suggest a useful rodent model of human behavioral inhibition and identify some interesting areas of future investigation (in humans and animal models) on the causes and consequences of human childhood behavioral inhibition/dysregulated fear.

STRESS RESILIENCE AND VULNERABILITY: THE ASSOCIATION WITH REARING CONDITIONS, ENDOCRINE FUNCTION, IMMUNOLOGY, AND ANXIOUS BEHAVIOR. Kent, S. School of Psychological Science, La Trobe University. Melbourne (Bundoora), VIC 3086 Australia. Background: The current study explored the underlying behavioural, endocrine, and immune markers of vulnerability to stress-induced depression, and the impact of rearing environments on adult functioning. Method: Adult Sprague-Dawley rats (n=195) were reared in either Maternal Separation (MS), Early Weaning and Isolation (EWI), or Non-Handled (NH) conditions. Anxiety behaviour was assessed using the emergence test at mean postnatal day (PND) 60. Stress-induced depressive behaviour was measured at mean PND 86 using intermittent cold water swim stress and swim escape test (SET) paradigm. Immediately following the SET, and in a sample of nave controls (N=31), trunk blood was collected to assay for serum corticosterone (CORT) and spleens were removed for determination of Concanavalin A (Con-A) stimulated T-cell proliferation. Results: Stress vulnerable rats (top tertile of SET swim time) were characterised by increased anxiety-like behaviour, greater post-stress CORT concentrations, and a significantly higher Con-A induced T-cell proliferative response compared to stress resilient rats (bottom tertile of SET swim time). The EWI rearing condition was a contributing factor in predicting total swim escape time, however MS was not. MS offspring did have double the basal level of CORT than NH offspring, suggestive of a hyperfunctioning HPA axis. Conclusion: The swim stress animal model enabled observation of stress vulnerability and resilience; results point towards the existence of distinct behavioural, endocrine, and immunological profiles of the vulnerable and resilient animal, which may have important implications for mental health and stress research.

Wednesday, June 6, 2012

9:00-10:00 **Keynote Speaker:** Sarah F. Leibowitz, The Rockefeller University.
MATERNAL HIGH-FAT DIET, ALCOHOL AND FETAL PROGRAMMING

MATERNAL HIGH-FAT DIET, ALCOHOL AND FETAL PROGRAMMING. Leibowitz, S.F. Maternal consumption of a fat-rich diet or alcohol during pregnancy has been shown, in both human and preclinical studies, to increase the offspring's appetite for dietary fat and alcohol. The mechanisms underlying these phenomena have yet to be identified. Our recent studies in rodents demonstrate that *in utero* exposure to a high-fat diet (HFD), as compared to a balanced diet, stimulates the birth of excess neurons that express specific neurochemicals, such as the peptides galanin (GAL), orexin (OX), and opioid enkephalin (ENK), that are potent stimulants of both fat consumption and alcohol drinking. The density at birth of these peptide-expressing neurons in the hypothalamus is markedly increased. This phenomenon, which occurs in close association with higher blood lipids caused by the HFD, persists postnatally long after the diet is removed, suggesting that the neuronal changes at this early age are permanent. This is supported by evidence showing that a HFD during pregnancy simulates the proliferation of neuroepithelial and neuronal precursor cells of the embryonic hypothalamic third ventricle, the proliferation and differentiation of neurons, and the migration of these neurons toward hypothalamic areas where the peptides act. Remarkably, very similar results are obtained with maternal consumption of a low dose of alcohol, which also increases circulating lipids. Together with other disturbances in opioid and dopamine receptor systems in extra-hypothalamic areas, these neuronal changes associated with maternal hyperlipidemia may contribute to the increased appetite for fat and alcohol observed in the offspring.
Research supported by USPHS grants: DA 21518 and AA 12882

10:30-12:30 **Symposium:** STRESS, INFLAMMATION, NEUROINFLAMMATION AND BEHAVIOR: CAUSES, CONSEQUENCES AND TREATMENT.
Chair: **Frederick Rohan Walker**

THE ROLE OF MICROGLIA IN THE REGULATION OF MOOD STATE AND COGNITIVE FUNCTION. Walker, F.R. University of Newcastle, NSW, Australia. Several recent reports have identified that psychological stress can both structurally and functionally alter microglia, cells that are pivotal to the production and maintenance of a neuroinflammatory state in the brain. The ability of stress to modulate microglial activity is of interest for two main reasons (a) stress is major risk factor in the emergence of depression and (b) depression appears to be characterised by enhanced levels of neuroinflammation. These two facts have led to the hypothesis that psychological stress may elicit changes in mood state and cognitive function by driving microglial mediated neuroinflammatory events. In investigating this hypothesis our research group, using a variety of behavioural approaches, has previously found that chronic stress sufficient to induce an increase in anhedonia and a decline in cognitive performance co-occurred with an increase in microglial activation within mood regulatory forebrain nuclei (notably the medial prefrontal cortex and amygdala). We have now subsequently, established that targeting stress induced microglial activation with anti-inflammatory agents improves stress induced cognitive decline. Moreover, using a variety of immunohistochemical techniques we have identified at a cellular level that microglial activity is intimately linked with neuronal activity. Interestingly, we have also observed that the stress induced changes in microglial activity are not clearly associated with signs of neurodegeneration. Indicating that the stress induced increase in microglial activation is occurring via a non classical mechanism. Currently, our group is now functionally characterizing, using a variety of ex-vivo techniques, the inflammatory status of microglia within the mood regulatory nuclei where we have observed differences following exposure chronic stress. Collectively, these findings may prove to be relevant in furthering our understanding of the neurobiology of depression.

IMMUNE AND BEHAVIORAL CONSEQUENCES OF MICROGLIAL REACTIVITY FOLLOWING REPEATED SOCIAL DEFEAT. Wohleb, E.; Fenn, A.; Pacenta, A.; Powell, N.; Sheridan, J.; Godbout, J.P. The Ohio State University, Columbus, OH.Repeated social defeat (RSD) activates neuroendocrine pathways that have a significant influence on immunity and behavior. Our work indicates that social defeat in mice enhances the inflammatory capacity of CD11b+ cells in the brain and promotes anxiety-like behavior in an interleukin (IL)-1 and beta-adrenergic receptor manner. These previous data will be highlighted in the presentation. In addition, new data will be presented showing that mice subjected to RSD are more responsive to a secondary immune challenge. In these experiments, RSD or control mice were injected with saline or lipopolysaccharide (LPS) and activation of brain CD11b+ cells (e.g., microglia and CNS macrophages) and behavioral responses were determined. Peripheral LPS injection caused an extended sickness response with exaggerated weight loss and prolonged social withdrawal in socially defeated mice. LPS injection also amplified mRNA expression of inflammatory mediators including IL-1β, tumor necrosis factor (TNF)-α, inducible nitric oxide synthase (iNOS), and CD14 in enriched CD11b+ cells isolated from socially defeated mice. In addition, IL-betą mRNA levels in enriched CD11b+ cells remained elevated in socially defeated mice 24 h and 72 h after LPS. Moreover, microglia and CNS macrophages isolated from socially defeated mice had the highest CD14 expression after LPS injection. Both social defeat and LPS injection increased

the percentage of CD11b+/CD45hi macrophages in the brain and the number of inflammatory macrophages (CD11b+/CD45hi/CCR2+) was highest in RSD-LPS mice. Anxiety-like behavior was increased by social defeat, but was not exacerbated by the LPS challenge. Nonetheless, reduced locomotor activity and increased social withdrawal were still present in socially defeated mice 72 h after LPS. Last, LPS-induced microglia activation was most evident in the hippocampus of socially defeated mice. Taken together, these findings demonstrate that repeated social defeat enhanced the neuroinflammatory response and caused prolonged sickness following innate immune challenge.

EXAMINING THE IMPACT OF CALORIE RESTRICTION UPON THE BEHAVIOURAL, PHYSIOLOGICAL, AND METABOLIC INDICATORS OF ILLNESS. Kent, S. School of Psychological Science, La Trobe University. Melbourne (Bundoora), VIC 3086 Australia. The physiological outcomes of a diet reduced in calories have been well established. However, there has been limited research on the impact of calorie restriction (CR) on sickness behaviour including fever. Recently, we have explored the relationship between a CR diet and behavioural, physiological, molecular, and metabolic indicators of illness. Initially we determined that a 50% CR for 28 days in mice and rats attenuated fever after administration with lipopolysaccharide (LPS). In addition, in the CR mice there was a shift towards a central anti-inflammatory bias as indicated by several hypothalamic immune and diet related markers changing at two and four hours post-LPS. In the CR rats there was a significant increase in peripheral corticosterone at two hours post-LPS and also a significant attenuation of the increase in interleukin-6 at two hours post-LPS. In addition, it was demonstrated that the rats CR to 50% for 28 days demonstrated a reduction in metabolic rate after the CR period and no change in metabolism post-LPS. In the final experiment the 50% CR rats selected a higher ambient temperature (Ta) compared to control rats. Further, the CR rats were able to produce a febrile response post-LPS once at this heightened Ta; however, other measures of sickness behaviour remained attenuated in the CR rats. These findings suggest that a 50% CR leads to altered inflammatory pathways (namely a bias towards anti-inflammatory) and that when the CR animals are able to self-select their preferred Ta it possibly becomes less metabolically costly for them to increase their Tb post-LPS. Funding was provided by the Australian Research Council Grant (LP 0775284) and Jims Group Pty Ltd.

ISOLATION STRESS: RETHINKING THE MECHANISMS OF STRESS-IMPAIRED HEALING Engeland, C.G., Yang, L., Pyter, L.M., McKenzie, C. Center for Wound Healing and Tissue Regeneration, University of Illinois at Chicago, Chicago IL USA. Wound healing in humans and rodents is impaired by exposure to chronic stress. Isolation stress, which is akin to loneliness/isolation in humans, has been shown to negatively affect immunity. This is important to many scientific studies in which, to prevent potentially confounding interactions, mice are often separated. In a series of studies, we investigated the effects of isolation stress on gene expression and healing rates in skin wounds of mice. 160 male and female hairless SKH-1 mice were divided into two groups: isolate-housed (ISO), and group-housed controls (GRO). ISO mice were individually housed from 3 weeks before wounding. Under anesthesia, two 3.5mm biopsy punch wounds were placed dorsally on each mouse and harvested at day 1, 3, 5 or 7 post-wounding. Wound closure was assessed through daily pictures. Biopsies were analyzed by RT-PCR for gene expression of proteins important to early tissue repair including keratinocyte growth factor (KGF), important for re-epithelialization, and -smooth muscle actin (-SMA) which correlates with fibroblast contractile ability. Isolation stress significantly delayed wound closure rates ($p<0.001$ each sex). Female ISO mice had lower KGF gene expression at days 1&3. Male ISO mice had lower gene expression for KGF at days 1&3, and -SMA at days 3&5. Surprisingly, ISO mice had less bacteria in the wounds than controls ($p<0.01$). Unlike other stress models in mice, a high bacterial burden was not necessary to induce stress-impaired healing in this relatively naturalistic model. These findings, which differ from other models of stress-impaired wound healing, suggest that isolation affects tissue repair through alterations in re-epithelialization and wound contraction independent of infection.

2:00-4:00 **Symposium:** GENETIC AND EPIGENETIC FACTORS IN AUTISM.
Chair: **Joanne Berger-Sweeney**, Tufts University, USA

ADULT SOCIAL BEHAVIOR IN BTBR T+ tf/J MICE FOLLOWING NEONATAL ADMINISTRATION OF OXYTOCIN. Benno, R.; McKim, D.; Rendon, T.; Schanz, N. William Paterson University of NJ, Wayne NJ, 07470 USA. Numerous studies have shown the importance of oxytocin in social behavior. It has been suggested that abnormal regulation of oxytocin function may be in part responsible for the expression of autisticlike behaviors. There is conflicting data whether or not the BTBR mouse has significant differences in the levels of oxytocin and/or oxytocin receptors compared to control mice and if so whether these differences are related to the expression of the autistic-like symptoms in this strain. In this study we have sought to determine if postnatal manipulation of oxytocin function can normalize social behaviors in the BTBR strain. The background for this approach is based on studies reviewed by Carter (2003) which showed that neonatal administration of oxytocin to the montane vole altered the brain levels of oxytocin and produced monogamous like behaviors in this species similar to that which is observed in the nave prairie vole. The subjects of this mixed litter design study were C57BL/6J and BTBR T+tf/J mice. Litters consisting of three male and three females pups received either saline, oxytocin or atosiban (an oxytocin antagonist). Drugs were administered either acutely (one single intraperitoneal injection on postnatal

day 1) or chronically (days 1-7 postnatal). The pups were tested as adults using a three chambered social apparatus during which we measured both sociability (1st trail) and social novelty preference (2nd trial). In addition, we recorded grooming during the trials. The results of this study show that postnatal manipulation of oxytocin has only minimal effects upon autistic like symptoms in the BTBR mouse. In addition, there were also minimal effects upon social behaviors in the C57 mice. As expected, there were significant strain differences in most of the behaviors analyzed, but for the most part this was independent of drug or length of treatment. Grooming behavior appeared to be somewhat more effected by the drug treatments with both strains increasing grooming following chronic drug treatment. In summary, it appears that manipulation of oxytocin during the postnatal period does not alleviate the autistic like symptoms demonstrated by the BTBR mouse. Our findings lend support to the belief that the abnormal social behaviors exhibited by BTBR mice are independent of any potential differences in oxytocin function which might exist between them and C57 mice. Carter, S. (2003). Developmental consequences of oxytocin. Physiology and Behavior, 79(3): 383-397.

DO ABNORMAL EXTRACELLULAR MATRIX SYSTEMS CONTRIBUTE TO EPIGENETIC FACTORS IN AUTISM? Blanchard, D.C., University of Hawaii, USA. Attempts to model an autism-relevant behavioral phenotype in laboratory animals have increased in recent years, in line with dramatic increases in diagnoses of this disorder. Reverse genetics approaches are complicated by the plethora of potentially relevant genes, and by potential specificities in the gene-experiential challenge interactions that may be involved in the etiology of autism. Using behavior alone to select a relevant model has yielded one, the BTBR T+tf/J strain, that provides excellent parallels to all three defining symptom groupings for autism, whereas other genetic models have tended to show either inconsistent or partial parallels. BTBR mice are also beginning to reveal neural and molecular differences that may provide clues to the biology of these autism-like behavior changes. They show differences from C57BL/6J (B6) controls in regional levels and turnover of several neurotransmitters; early gene expression in a wide variety of brain sites; and reductions in plasma sulfates; the latter parallel reductions reported in autistic children. BTBR also show a significant reduction in heparan sulfate –a cell-surface and extracellular molecule that modulates the activity of a host of growth and guidance factors. Heparan sulfate distribution, as well as amount, was altered in the subventricular zone of the lateral ventricles, one of two neurogenic zones in the adult mammalian brain. These differences provide potential links between factors altering odds ratios for autism, and aberrant neuronal connectivity in the nervous system.

DIETARY INTERVENTIONS IN MOUSE MODELS OF AUTISM SPECTRUM DISORDERS: THE CASE OF CHOLINE. Ricceri, L. Dept. of Cell Biology and Neuroscience. Istituto Superiore di Sanit, Rome ITALY. Choline is a dietary component essential for normal function of all cells. Choline, or its metabolites, is needed for the structural integrity and signaling functions of cell membranes; it is one of the sources of methyl-groups in the diet (one of choline metabolites, betaine, participates in the methylation of homocysteine to form methionine), and it directly affects cholinergic neurotransmission, trans-membrane signaling and lipid metabolism. Changes in choline availability during the neonatal period profoundly (and permanently) affect brain development: perinatal choline supplementation enhances transmission at cholinergic synapses, protects against neurodegeneration, improves performance on several behavioural tasks and, importantly for exploitation of the treatment in the context of neurodevelopmental disorders, upregulates expression of different growth factors. Studies in a knock-out mouse models of Rett syndrome (RTT), an autism-spectrum disorder primarily caused by mutations in the X-linked gene encoding methyl-CpG-binding protein 2 (MeCP2), have shown that developmental choline supplementation ameliorates RTT symptoms. We extended these results showing that postnatal choline supplementation attenuates some of the behavioural and neurobiological abnormalities also in the truncated Mecp2-308 mouse line: choline treatment (from birth till weaning) restored wt-like locomotor activity levels in hemyzygous (hz) mice. Lower striatal choline acetyl-trasferase (ChAT) activity and decreased levels of cortical mRNA NGF were found in hz mice: choline supplementation increased striatal ChAT activity and enhanced NGF and BDNF expression in cortical and hippocampal regions. In preclinical studies developmental choline supplementation thus exerts beneficial effects on the RTT phenotype accompanied by increases in BDNF and NGF expression: these results could be translationally relevant for development of dietary therapeutic approaches for neurodevelopmental disorders.

THE ONE-CARBON (C_1) METABOLIC CYCLE, NEURAL CIRCUITS, AND COGNITIVE AND SOCIAL BEHAVIORS IN AUTISM. Berger-Sweeney, J.; Schaevitz, L. Increasing evidence makes it clear that both genetic and epigenetic factors are critical in the etiology of developmental disorders such as autism. With so many genetic and epigenetic influences in neurological disorders, recent studies focus on elucidating common underlying pathways, and determining how specific genetic and epigenetic factors may interact within a given pathway. A variety of environmental factors can influence epigenetic programming and DNA methylation including nutrition, stress, maternal care, or toxins; the focus of our work has been on nutritional factors such as choline and folate. In the brain, epigenetic programming appears to be most sensitive to nutritional influences *in utero* and early in postnatal life, which also correspond to critical periods of synaptic refinement in cortical circuitry. As such, epigenetic programs can set the stage for neural circuitry that underlie complex cognitive and social behaviors later in life. In this talk, we will examine the interaction between genetic and epigenetic factors in the one-carbon (C_1) metabolic cycle and implications for autism spectrum disorders. We hypothesize that alterations in C_1 metabolic

function *in utero* and during early postnatal development lead to changes in cholinergic and glutamatergic synaptic transmission, which act as neuromodulators in the developing cerebral cortex. Models for how these alterations (though combinations of genetic and epigenetic factors) could lead to dysfunctional neural circuits that result in an autistic phenotype will be explored. The C_1 metabolic cycle utilizes nutrients to establish and maintain DNA methylation patterns. Alterations in C_1 metabolites affect widespread functions that include acetylcholine biosynthesis, NMDA receptor functions, as well as DNA methylation rates. Alterations of key neuromodulators, such as acetylcholine and glutamate, during critical periods in cortical development can perturb the formation of normal neural networks that support complex cognitive and social behaviors later in life that are likely disturbed in autism.

2:00-4:00 **Symposium:** MODELING SCHIZOPHRENIA SYMPTOMS AND NEUROBIOLOGY IN MICE. Chair: **Francesco Papaleo**

COGNITIVE AND NEUROIMAGING PHENOTYPES REVEAL BRAIN DYSFUNCTION IN DYSBINDIN-1 MUTANT MICE. Jentsch, J. UCLA, Los Angeles, CA. Multimodal neuroimaging approaches and measures of cognition are increasingly powerful tools for interrogating patterns of brain dysfunction in schizophrenia. That said, mouse models that are used to examine putative genetic and pathophysiological mechanisms that are causal for syndromal aspects of the disorder are often assessed with unsophisticated tools or with approaches that lack translational appeal. Here, we report the results of studies that begin with cognitive and neuroimaging measurements to determine validity of a particular genetic model for schizophrenia - reduced expression of the candidate risk gene, dysbindin-1. These studies have uncovered specific patterns of brain dysfunction that span from frontal cortical to hippocampal networks, while also implicating midbrain dopaminergic circuitry. Mechanistic studies directed at these brain regions have revealed cellular and synaptic phenotypes consistent with both compromised pre-synaptic mechanisms (reduced neurotransmitter release under high frequency conditions), impaired synaptic plasticity and compromised post-synaptic glutamate receptor function. The use of translational cognitive and neuroimaging methodologies, as described above, allow us to both validate the models and connect cellular dysfunction with human phenotypes in increasingly powerful and informative ways.

DEVELOPMENT OF COGNITIVE DEFICITS RELEVANT TO SCHIZOPHRENIA IN COMT AND DYSBINDIN MOUSE MUTANTS. Papaleo, F. Istituto Italiano di Tecnologia, Genova, Italy.
Development of cognitive deficits relevant to schizophrenia in COMT and Dysbindin mouse mutants F. Papaleo, Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Via Morego 30, 16163 Genova - Italy Cognitive abnormalities are core manifestations of schizophrenia that precede the onset of the diagnostic psychosis, dramatically contribute to poor functional outcomes in patients, and are currently not effectively treatable. Cognitive dysfunctions in schizophrenia have been linked to genetic susceptibility for the illness. I will then illustrate cognitive abnormalities in mutant mice bearing targeted, clinically-relevant mutations of two schizophrenia-susceptibility genes, catechol-O-methyl transferase (COMT) and dysbindin. COMT and dysbindin are both involved in cortical dopamine signaling. The dysregulation of this system is implicated in the schizophrenia pathophysiology, including attendant cognitive deficits. Special attention will be given to the study in mice of working memory and extra-dimensional shifting abilities. These are among the cognitive functions mainly affected in schizophrenia and which greatly depend on the prefrontal cortex.

ULTRASONIC VOCALIZATIONS IN MICE: A TOOL TO MODEL NEGATIVE SCHIZOPHRENIA SYMPTOMS. Scattoni, M.L.; Dept. of Cell Biology and Neuroscience. Istituto Superiore di Sanit, I-00161 Rome, ITALY. Patients with schizophrenia often display a lack of spontaneous seeking to share interests with other people, abnormal hedonic behavior and low social reciprocity, while the ability to recognize different individuals is intact. Mus musculus is a social species that engages in high levels of reciprocal social interactions, communal nesting, sexual and parenting behaviors, territorial scent marking and aggressive behaviors. In these social contexts, mice communicate predominantly in the ultrasonic range of sound frequencies. Pups separated from the nest emit vocalizations, signals which the parents use to locate the straying pup and retrieve it to the nest. Adult mice of both sexes produce complex ultrasonic vocalization patterns in different experimental/social contexts such as play, aggressive or sexual interactions. This talk will focus primarily on the evaluation of negative schizophrenia symptoms in mice through the detailed spectrographic analysis of ultrasonic vocalizations emitted during infant social isolation, adult dyadic interactions and sniffing of estrus female urine by male mice, a novel approach for monitoring reward-seeking behavior in rodents. Ultrasonic emission is a consistent and robust phenomenon in rodents during adult social interactions, and can be considered an index of social interest and motivation. Experimental evidence indicates as vocalizations are a valuable tool for identifying alterations in several mouse models of human neurodevelopmental disorders, starting from those in which deficits in social communication are a primary core symptom e.g. schizophrenia and autism spectrum disorders.

MODELING THE POSITIVE SYMPTOMS OF SCHIZOPHRENIA IN MICE: FOCUS ON DOPAMINERGIC AND GLUTAMATERGIC MECHANISMS M. van den Buuse Behavioural Neuroscience Laboratory, Mental Health Research Institute, University of Melbourne, Australia. Hyperactivity of the subcortical dopamine system has been suggested as a core feature of psychosis. All antipsychotic drugs share blockade of the dopamine D2 receptor as their core mechanism of action. In addition, in schizophrenia hypoactivation of the glutamate NMDA receptor has been postulated. These main neurotransmitter alterations and their modulation by other factors, such as serotonin and neuropeptides, have been widely modeled in rat and mouse studies. This presentation will include an overview of commonly used animal behavioural approaches for psychotic symptoms, including locomotor hyperactivity and prepulse inhibition (PPI), and how these relate to human findings. I will also outline some of the advantages as well as pitfalls which are associated with this experimental methodology and include studies in mice with mutations in schizophrenia candidate genes. For example, neuregulin-1 hypomorphic mice showed mild baseline locomotor hyperactivity but no changes in the effects of the dopamine releaser, amphetamine, or the NMDA receptor antagonist, MK-801. On the other hand, reelin heterozygous mutant mice showed markedly enhanced locomotor hyperactivity induced by MK-801, but not amphetamine. Notably, this effect was only seen in male mice and not in female mice, illustrating how straightforward experimental factors, such as the sex of the animals, can influence the results. Developmental environmental factors and treatments can further interact with genetically-induced changes in behaviour. For example, chronic young-adult treatment with methamphetamine leads to sensitization to the locomotor hyperactivity-inducing effects of amphetamine in adulthood and this has been used as a model of psychosis development. We recently found that this sensitization is absent in mice heterozygous for a mutation in the brain-derived neurotrophic factor gene (BDNF Hets). Strikingly, again this interaction was only observed in male mice. Further details and examples of gene effects and gene-environment interactions will be discussed.

4:30-7:00 **Symposium:** UNRAVELING THE CONTRIBUTION OF OXYTOCIN TO POSITIVE AFFECT AND DRUG-RELATED REWARD: A TRANSLATIONAL PERSPECTIVE. Chairs: **Femke Buisman-Pijlman** and **Jillian Broadbear**

PRENATAL AND GESTATIONAL DRUG EXPOSURE: EFFECTS ON THE OXYTOCIN SYSTEM, SOCIAL BEHAVIOR AND VULNERABILITY IN RATS. Williams, S.K.; McMurray, M.S.; Jarrett, T.M.; Cox,E.T.; Jameison-Drake, A.; Walker,C.H.; Robinson, D.L.; Johns, J.M. University of North Carolina, Chapel Hill, NC 27599 USA. Drug abuse during pregnancy is major public health concern, with negative consequences throughout development. Prenatal cocaine exposure (PCE) in rats produces deficits in social behavior with corresponding changes in neuroendocrine and monoaminergic signaling. The relevance of parental care in social behavior maturity cannot be ignored, and gestational exposure to cocaine severely disrupts parental care, thus impacting the early environment of the offspring. Oxytocin (Oxt) is critical in regulating social behaviors and central levels are disrupted following acute and chronic cocaine (CC) treatment in postpartum rat dams, coincident with deficits in maternal care. We will discuss studies aimed to determine the relative contribution of PCE and CC-induced deficits in maternal care to social behaviors and Oxt signaling across development. Our animal model entails either bidaily injections on cocaine (15 mg/kg) from gestational day 1-20 or intermittent injections throughout pregnancy and lactation. Pups were either cross-fostered to drug-free rat dams or remained with their biological dams until testing. PCE results in decreased social (including parental) behaviors in adolescence and adulthood. PCE is also associated with increased aggression in adults. Rearing by CC-exposed mothers synergistically increases the behavioral effects of PCE. Rearing by CC-exposed mothers, but not PCE, disrupts Oxt levels and mRNA in regions relevant to social behavior, but does not affect receptors in postpartum adult offspring. Preliminary work indicates PCE/CC rearing has dynamic effects on Oxt levels and receptors in neonatal rat pups, suggesting very early regulation of Oxt signaling. This work highlights how the interactive role of Oxt signaling and behavioral context throughout development can be derailed by drug abuse during pregnancy.

OXYTOCINERGIC REGULATION OF ENDOGENOUS AS WELL AS DRUG-INDUCED MOOD. Broadbear, J.H.; Mak, P.; Beringer, K. School of Psychology and Psychiatry, Monash University, Clayton, VIC 3800, Australia. The interconnections between the serotonergic and oxytocinergic systems in the brain suggest that changes in oxytocin levels from either natural or drug-induced stimuli may lead to measureable changes in mood. In this series of studies, we evaluated the effects of oxytocin and vasopressin receptor ligands in several models of animal behaviour. Our first aim was to investigate whether stimulation of oxytocin and vasopressin receptors, via central or systemic drug administration, would produce behavioral changes indicative of anti-depressant or anxiolytic activity. Our second aim was to examine whether oxytocin receptor activation was implicated in the effects experienced using the popular party drug, MDMA (ecstasy). Carbetocin, an oxytocin analogue, had anti-depressant actions in the forced swim test following systemic and central administration. These effects were blocked by the oxytocin and vasopressin 1A receptor antagonist, atosiban. Carbetocin also had anxiolytic effects in the elevated plus maze, but only after central administration. Systemic administration of desmopressin, a vasopressin analog, was anxiogenic; its effects were blocked by atosiban which on its own produced robust anxiolytic behavioural changes. MDMAs drug effects were evaluated using a drug discrimination paradigm. Carbetocin partially substituted for MDMA, while atosiban interfered with MDMA discrimination, suggesting that oxytocin receptor

activation was an important component of the interoceptive cues that some rats had learned to associate with MDMA treatment. The results of these and other preclinical studies provide compelling evidence that oxytocin, as well as its closely related counterpart vasopressin, may provide alternative therapeutic targets for the treatment of anxiety and depression. Regulation of mood via the use of drugs such as MDMA, with its pronounced serotonergic effects, is also likely to recruit oxytocin to produce its effects.

PREFRONTAL OXYTOCIN MEDIATES DRUG AND SOCIAL REWARD INTERACTION. Wang, Z.; Young, K.A. Florida State University, Tallahassee, FL. Prairie voles (Microtus ochrogaster) are socially monogamous rodents that form pair bonds after mating. This behavior is mediated by dopamine (DA) and oxytocin (OT) neurotransmission in mesocorticolimbic brain regions, including the nucleus accumbens (NAcc) and prefrontal cortex (PFC). Similarly, the rewarding effects of drugs of abuse are also mediated by these neurotransmitter systems. Our recent studies in the prairie vole have demonstrated that exposure to the psychostimulant, amphetamine (AMPH), impairs mating-induced pair bonding; pair-bonding experience decreases the rewarding properties of AMPH; and such behavioral interactions are regulated by NAcc DA via a receptor-specific mechanism. In a most recent study in female prairie voles, we found that an AMPH treatment paradigm known to inhibit pair bonding decreased oxytocin receptor (OTR) density in the PFC. As PFC OTR activation is essential for pair bonding, decreased OT neurotransmission may mediate the AMPH-impairment of pair bonding. This notion is supported by our data showing that intra-PFC OT infusions restored mating-induced pair bonding in AMPH-treated voles. AMPH treatment also decreased DA D2-type (D2R), but not D1-type (D1R), receptor density and increased extracellular levels of DA in the NAcc. Both of these changes increase the likelihood of NAcc D1R activation, which inhibits pair bond formation. Interestingly, intra-PFC OT infusion tended to decrease NAcc DA activity, suggesting that PFC OT may interact with NAcc DA to restore pair bonding in AMPH-treated voles. Collectively, these data demonstrate that alterations in OT and DA neurotransmission underlie the AMPH-impairment of pair bonding and suggest that it may be worthwhile to pursue pharmacotherapies targeting central OT to restore prosocial behaviors in the addicted. (Supported by NIDAR01-19627, NIDAK02-23048, & NIMHR01-58616 to ZW and NIDAF31-25570 to KY).

A CONDITIONAL KNOCKOUT MOUSE LINE OF THE OXYTOCIN RECEPTOR: FINDINGS RELATING TO SOCIAL RELATIONS AND LEARNING. Pagani, J.H. & Young, W.S. SNGE/NIMH/HHS, Bethesda, MD 20892 USA. Our understanding of oxytocin (Oxt) has moved beyond a role in lactation and parturition to centrally mediated effects on anxiety, social and reproductive behaviors, and learning and memory. Oxt and Oxt receptor (Oxtr) knockout (KO) mice have contributed to the work outlining the Oxt systems influence on many of these behaviors. In our attempts to understand Oxts role in specific circuitry, we have created mice with loxP sites flanking the gene for the Oxtr (Oxtr flox/flox). When crossed with mice expressing Cre recombinase under control of cell or region specific promoters, very selective inactivation of the Oxtr is achieved. We have created a line with Oxtr loss specific to the forebrain by crossing Oxtr flox/flox with a transgenic line expressing Cre under the Camk2a promoter. These KO mice (Oxtr FB/FB) develop normally until post-natal day 21, at which point the Oxtr begins to disappear. The result is a pattern of behavioral phenotype that is unlike wildtype or total Oxtr (/) KO mice. OxtrFB/FB mice have normal maternal behavior but still have pup mortality rates higher than wildtype mice. Oxtr/ and OxtrFB/FB have social recognition deficits, but those of the OxtrFB/FB may reveal a more profound intrastrain recognition failure. Furthermore, unlike the Oxtr/, OxtrFB/FB mice show a deficit in contextual and auditory fear conditioning. This learning deficit is coupled with a reduction in vasopressin 1a receptors in the central nucleus of the amygdala, something also not seen in Oxtr/. By creating receptor specific lesions with defined spatial and temporal properties, we learn more about Oxts critical functions across the brain and lifespan. The NIMH Intramural Research Program (Z01-MH-002498-22) supported this research.

OXYTOCIN AS A REGULATOR OF ADDICTION: A NEURODEVELOPMENTAL PERSPECTIVE. Buisman-Pijlman, F.T.A. 1; Tops, M. 2 1) Lecturer, Pharmacology and Psychiatry. University of Adelaide, Australia; 2) Assistant Professor, Centre for Child and Family Studies, University of Leiden, Netherlands. Oxytocin is more than a neuropeptide involved in childbirth and bonding. It has an important role in facilitating social relationships and can directly influence rewarding effects of social relations and drugs of abuse. This paper will discuss whether oxytocin plays a role in individual differences in sensitivity to addiction from a neurodevelopmental perspective. Early life-events and parenting can influence the developing oxytocin systems. The oxytocin system is a modulator of the HPA-axis and of the dopamine and immune systems. These systems are all important, even vital, in different phases of addiction. Adverse early life-events or insecure attachment might have long-term effects on alcohol and drug use by reducing the protective effect of oxytocin. We showed that oxytocin is involved in social awareness and stress habituation: oxytocin increases trust in novel social contexts, allowing for habituation of stress responses. Alcohol and drugs are often used to cope in such situations. Interestingly, the oxytocin response to novelty will counter-regulate itself: by facilitating familiarization to social contexts, oxytocin decreases novelty responses that would trigger its own release. The balance between the rewarding properties of drugs and social relations can also affect drug use. Strong social relations have been shown to delay initiation of drug use. Recent studies show rewarding properties of social relations in social animals, mediated via a direct interaction between the dopamine and oxytocin system. Special social relations could be rewarding in itself and therefore balance the need for drug reward. However, how rewarding social

relations are depends on social experiences. Supported by University of Adelaide (FBP) and Veni grant by NWO (451-07-013) (MT).

BREAKING THE LOOP: PRECLINICAL AND EARLY CLINICAL EVIDENCE FOR OXYTOCIN AS A TREATMENT FOR DRUG ADDICTION. McGregor, I. School of Psychology, University of Sydney, Sydney, New South Wales, Australia. There is accumulating evidence for an interaction between the neural substrates of affiliation and those of drug reward, and particularly for a role for oxytocin systems in modulating acute and long-term drug effects. In rats and mice, oxytocin administration can prevent development of tolerance to ethanol and opiates, the induction of stereotyped, hyperactive behavior by stimulants, and the withdrawal symptoms associated with sudden abstinence from drugs and alcohol. Additionally, stimulation of endogenous oxytocin systems is a key effect of prosocial party drugs such as MDMA (Ecstasy) and GHB (Fantasy). Brain oxytocin systems are highly plastic and drugs of abuse cause long-term changes in markers of oxytocin function that can be linked to enduring deficits in social behavior that may parallel the social disintegration seen in persons with drug problems. Very recent preclinical studies have illustrated a remarkable ability of exogenously delivered oxytocin to inhibit stimulant and alcohol self-administration, to modulate associated drug-induced changes in dopamine and glutamate release, and to prevent stress and priming-induced relapse to drug seeking. In summary, oxytocin has fascinating potential to reverse the corrosive effects of long-term drugs abuse on social behavior and to perhaps inoculate people against future vulnerability to addictive disorders. The results of clinical studies examining intranasal oxytocin in humans with drug use disorders are ongoing and results are eagerly awaited. Supported by grants from the ARC and NHMRC

8:00-10:00 **Poster Session 1:** ***Brain and Behavior***

1. ROLE OF VENTRAL SUBICULUM IN CONTEXT-INDUCED REINSTATEMENT OF HEROIN SEEKING. Bossert JM1; Eichenbaum, H1; Marchant NJ1; Wang HL2; Morales M2; Shaham Y1 Behavioral Neuroscience Branch1, Cellular Neurobiology Research Branch2, IRP/NIDA/NIH/DHHS. In humans, exposure to contexts previously associated with heroin use can provoke relapse. In rats, exposure to heroin-paired contexts after extinction of drug-reinforced responding in different contexts reinstates heroin seeking. This reinstatement is attenuated by inhibition of glutamate or dopamine transmission in nucleus accumbens shell, or inactivation of ventral medial prefrontal cortex (vmPFC). More recently, we assessed whether the glutamatergic projection from vmPFC to accumbens shell is activated during context-induced reinstatement. To accomplish this, we combined the marker of neuronal activity, Fos, with the retrograde tracer Fluoro-Gold (FG) and found that context-induced reinstatement was associated with increased Fos expression in vmPFC neurons, including those projecting to accumbens shell. Another brain site that sends glutamatergic projections to accumbens shell is the ventral subiculum. Therefore, in the current study we examined whether this brain area also contributes to context-induced reinstatement of heroin seeking. Rats were trained to self-administer heroin for 12 days; drug infusions were paired with a discrete tone-light cue. Lever-pressing was subsequently extinguished in a non-drug-associated context in the presence of the discrete cue. Rats were then tested in the heroin- or extinction-associated contexts under extinction conditions. Bilateral injections of muscimol+baclofen into ventral subiculum decreased context-induced reinstatement of heroin seeking. Using the same anatomical procedure as described above, we are currently exploring whether exposure to heroin contexts previously paired with heroin intake activate the glutamatergic projections from ventral subiculum to accumbens shell.

2. THE COGNITIVE EFFECTS OF OVARIECTOMY TRANSITIONS FROM DETRIMENTAL TO BENEFICIAL WITH AGE Acosta, J.I.; Engler, E.B.; Talboom,J.S.; and Bimonte-Nelson, H.A. Department of Psychology, Arizona State University, Tempe, AZ 85287 Arizona Alzheimers Consortium It is well established that cognitive decline occurs with aging, and hormone loss may exacerbate this decline. Recent evidence from our laboratory suggests that in rats, the cognitive effects of hormone loss depend on the age of ovariectomy (Ovx). For example, in one study we found that Ovx in young female rats was detrimental to spatial working memory (WM) performance (Bimonte and Denenberg, 1999), and in another study Ovx in aged female rats facilitated spatial WM performance (Bimonte-Nelson et al., 2003). However, the effects of Ovx at multiple timepoints during aging has not yet been methodically addressed in one study. Here, we test the hypothesis that the effects of Ovx on cognition would transition from beneficial to detrimental based on our previous findings. We used a between-subjects design to test spatial WM and reference memory (RM), on the water radial arm maze (WRAM), in ovary-intact Sham or Ovx rats at 5, 12, 18, and 20 months old. At the end of behavioral testing, serum was collected and levels of LH, FSH, estradiol, and progesterone were measured. Results demonstrated that for the later testing block (days 11-12) of the WRAM, 12 month old Ovx animals made more WM errors relative to Sham animals, as trials progressed and WM load increased. However, at 18 months of age, the WM detriment after Ovx was reversed, with 18 month old Ovx animals making less WM memory errors on two orthogonal measures relative to 18 month old sham animals. On the trial with the highest working memory load, 12 month old Ovx animals exhibiting impaired performance and 18 month old Ovx animals exhibiting enhanced performance relative to Sham age groups. At 18 months, Ovx also

enhanced RM performance on the WRAM relative to Sham. Collectively, the data support a transition of Ovx from detrimental at 12 months, to beneficial, at 18 months of age. There were distinct patterns of hormone change across age for LH, FSH, progesterone, and estradiol.

3. DIFFERENTIAL CONTRIBUTION OF MESOHABENULAR AND MESOACCUMBENS DOPAMINE NEUROTRANSMISSION TO BRAIN STIMULATION REWARD. Duchesne, V.; Boye, S.M. Department of Psychiatry, University of Montreal, Quebec, Canada. The contribution of mesoaccumbens dopamine neurotransmission to reward and reinforcement has been the focus of many years of study. Other terminal sites have received comparatively less research attention, but may be potentially important. One of these sites is the lateral habenula, a medially-located structure that receives dopaminergic innervation from ventral tegmental area dopamine cells. Very little is known about the contribution of this mesohabenular pathway to reward in general and to brain stimulation reward in particular. The goal of this study was to begin to understand the contribution of the mesohabenular dopamine pathway to reward function. To this end, we employed intracranial self-stimulation of the posterior mesencephalon, a brain region that supports robust responding and is highly sensitive to changes in dopamine neurotransmission. Male Sprague-Dawley rats were implanted with bilateral cannulae in the lateral habenula and a monopolar stimulation electrode in the posterior mesencephalon, in and around the dorsal raphe nucleus. Using the curve-shift paradigm, we measured the reward-enhancing effect of intra-habenular infusions of amphetamine (10-40 g) or vehicle. Control rats received amphetamine (or vehicle) infusions into nucleus accumbens core or shell subregions (1-20 g). Our findings show that regardless of concentration, intra-habenular amphetamine does not alter brain stimulation reward. As expected, infusions into the nucleus accumbens enhanced the rewarding effectiveness of the stimulation, as previously shown by others. Our findings suggest that dopaminergic neurotransmission within the lateral habenula does not contribute significantly to the function of the circuitry that mediates the rewarding effect of electrical brain stimulation.

4. D1 RECEPTORS IN THE NUCLEUS ACCUMBENS SHELL REGULATE THE EXPRESSION OF CONTEXTUAL FEAR CONDITIONING AND ACTIVITY OF THE ANTERIOR CINGULATE CORTEX IN RATS. Albrechet-Souza, L; Carvalho, MC; Brando, ML. Department of Psychobiology, University of Sao Paulo, Ribeirao Preto, Brazil. Although the nucleus accumbens (NAc) and dopamine-related circuits are best known for their roles in appetitive motivation, consistent data have implicated both in some forms of aversive-related processes, including fear conditioning. The NAc, however, is an anatomically heterogeneous structure divided into two subregionsthe medioventral shell (NAcSh) and dorsolateral core (NAcC)characterized by distinct connectional, neurochemical, and regulatory properties. In the present study, we initially investigated the involvement of the NAcSh and NAcC in the expression of contextual and cued conditioned fear. In addition to the freezing response, Fos protein expression was measured in the brains of rats conditioned to a context (i.e., a light or tone previously paired with footshock). The three conditioned stimuli were able to increase the freezing response. Nonetheless, in contrast to the animals exposed to explicit cues, rats subjected to contextual fear presented a significant increase in Fos protein expression in the NAcSh and NAcC. We then examined the effects of the D1- and D2-like receptor agonists and antagonists SKF38393, SCH23390, quinpirole, and sulpiride injected bilaterally into the NAcSh on the expression of contextual fear. SKF38393, quinpirole, and sulpiride induced no behavioral changes, but the D1-like receptor antagonist SCH23390 increased the freezing response and reduced Fos protein expression in the anterior cingulate cortex. These findings suggest the involvement of the NAc in the expression of contextual fear memories and indicate the selective role of NAcSh D1-like receptors and the anterior cingulate cortex in this process.

5. MUSCARINIC M4 POSITIVE ALLOSTERIC MODULATION OF CIRCADIAN ACTIVITY RHYTHMS. Gannon, R.; Millan, M.J. MUSCARINIC M4 POSITIVE ALLOSTERIC MODULATION OF CIRCADIAN ACTIVITY RHYTHMS aGannon, R.L.; bMillan, M.J. aDepartment of Biology, Valdosta State University, Valdosta, Georgia USA bCNS Unit, Institut de Recherches Servier, Paris, France. Entrainment of circadian rhythms to the light-dark cycle is essential for restorative sleep, and abnormal sleep timing is implicated in CNS disorders like depression, schizophrenia and Alzheimers disease. Since positive allosteric modulators of muscarinic M4 receptors are candidates for treatment of mood and cognitive deficits of CNS disorders, it is important to evaluate their circadian actions, a question addressed employing hamsters, a model organism for studying activity rhythms. Systemic administration of the muscarinic receptor agonist oxotremorine (0.01 - 0.04 mg/kg) inhibited light-induced phase delays and advances of hamster circadian wheel running rhythms. The M4 positive allosteric modulator, LY2033298 (10 - 40 mg/kg) had no effect on light-induced phase shifts when administered alone, yet significantly enhanced (at 20 mg/kg) the inhibitory influence of oxotremorine on light-induced phase delays. In addition, the muscarinic receptor antagonist, scopolamine, which was without effect on light-induced phase shifts when administered alone (0.001-0.1 mg/kg) antagonized (at 0.1 mg/kg) the inhibitory effect of oxotremorine and LY2033298 on light-induced phase delays. These results are the first to demonstrate that systemically-applied

muscarinic receptor agonists modulate circadian activity rhythms, and they also reveal a specific role for M4 receptors.

6. DOES FETAL HANDEDNESS REFLECTS THE FUNCTIONAL MATURITY OF ITS BRAIN. Hepper, P.; Dornan, J.; Lynch, C.; Wells, D. Fetal Behaviour Research Centre, Psychology, Queens University, Belfast. The link between handedness and brain function remains elusive. Here we relate the prenatal development of handedness to performance on an habituation task, an indicator of information processing, at 36 weeks gestation. Left and right arm movements were recorded for 60 minutes at 3 weekly intervals from 24 to 36 weeks gestation in 156 fetuses. Laterality was assessed at each age by the determining its direction and strength. The development of laterality was calculated as a change score between the strength exhibited at 36 and 24 weeks. The number of stimulus presentations to habituate was recorded. 18 fetuses exhibited more left arm movements, 130 more right arm movements and 8 no consistent pattern. Across gestation 130 fetuses exhibited a decrease in the strength of laterality, 26 became more lateralised. There was no correlation between the direction ($p>0.05$) or strength ($p>0.05$) of laterality and habituation performance. There was a significant correlation between the change in the strength of laterality and habituation ($p<0.05$). The greater the decrease in the strength of handedness the fewer stimuli were required to habituate (indicating more efficient information processing). The results suggest a link between the development of handedness and the brains ability to process information. We speculate that this is mediated by a greater functional integration between the two hemispheres. The study suggests that a greater understanding of fetal neurobehavioural development may elucidate the link(s) between brain function and laterality.

7. DEVELOPMENT OF A LABORATORY PARADIGM THAT ELICITS CHECKING UPON ACTIVATION OF SECURITY MOTIVATION. Hinds, A1; Van Ameringen1, M; Schmidt, L2; Woody, E3; Szechtman, H1. 1Dept. of Psychiatry & Behavioural Neurosciences; 2; Dept. of Psychology, Neurosci. & Behaviour, McMaster Univ., Hamilton, ON, Canada; 3Dept. of Psychology, Univ. of Waterloo, Waterloo, ON, Canada. An evolved special motivational system the Security Motivation System (SMS) is proposed to manage detection, and response to, the risk from potential dangers (Szechtman & Woody, 2004). Because the environment is not able to supply a signal for the absence of potential (as opposed to imminent) danger, the signal for termination of the SMS is proposed to come from performance of precautionary behaviours such as washing or checking. Previous work by Hinds et al (2010; 2012) tested this hypothesis using a paradigm in which stimuli suggesting potential harm from contamination were effective in producing a state of SMS activation, a state which returned to baseline only after engagement in corrective hand washing. We sought to determine if similar results could be seen with exposure to checking-related threats. In a preliminary test of such a checking paradigm, participants (N=40) were told they would be directly responsible for the success of a novel medication classification system by acting as a beta tester for the program. After exposure to potential threat (the possibility of failure in the critical task) or a neutral control situation, checking for task success was either permitted or delayed; checking was later permitted for as long as desired for all participants. Rhythmical sinus arrhythmia (RSA) and subjective ratings were measured to monitor the state of activation and deactivation produced by exposure to potential threat, and by checking. Exposure to potential threat did indeed produce SMS activation, and no such activation was evident in the control (no threat) condition. Engagement in corrective checking behavior for 90 seconds produced a deactivation of RSA to baseline, while RSA remained elevated for those in the delayed check condition (results approaching significance). Continuation of this paradigm will provide further evidence for the role of the SMS in checking-related threats; significant results would support the hypothesis that the SMS is similarly sensitive to checking threat detection and corrective behavior as has been previously determined for contamination based threats. This research was supported by operating grants from the Canadian Institutes of Health Research (CIHR MOP-74553 and CIHR MOP-64424). ALH was supported by a Frederick Banting and Charles Best Canada Graduate Scholarship (CIHR GSD-104525).

8. EVALUATING NEUROPSYCHOLOGICAL PERFORMANCE AMONG KHAT USERS. Ismail A.A.;1 El-Setouhy, M.;2 El Sansoy, R.;2 Rohlman, D.S.3 1Community and Family Medicine Department, Faculty of Medicine, Jazan University, Jizan, Saudi Arabia, 2Substance Abuse Research Center (SARC), Jazan University, Jizan, Saudi Arabia, 3Center for Research on Occupational and Environmental Toxicology (CROET), Oregon Health and Sciences University (OHSU), Portland, OR 97239, USA. The cultivation and consumption of the stimulant leaf Khat is widespread in several countries of East Africa and the Arabian Peninsula. Most of the effect of chewing khat is thought to come from cathinone and cathine which are structurally related to amphetamine. The central nervous activity of cathinone is qualitatively and quantitatively similar to that of amphetamine. However studies on behavioral and cognitive problems following khat use in humans is not extensive as several of the available studies have been done only in the context of observational and single-case studies. The aim of the study was to test neuropsychological functions among khat chewers. A sample of 65 adult male khat chewers were recruited from Jazan region in south-west Saudi Arabia, a matched control group on age, and educational level was also tested. A structured questionnaire about the socioeconomic background; medical and occupational history;

education; chewing khat habit and its frequency, other habits associated with chewing, e.g. smoking, tea, coffee, or soft drinks drinking. Neurobehavioral performance of both groups were assessed using the Behavioral Assessment and Research System (BARS), it includes tests to assess the memory, attention, sustained attention, motor speed and coordination, information processing speed, and visuomotor functions. The preliminary results of the study showed that khat chewers demonstrated deficits in the most of the assessed neurobehavioral functions. There are many factors contribute to the deficits in neurobehavioral performance among khat chewers e.g. duration and amount of chewed khat, age of the chewers.

9. TEMPORAL INVOLVEMENT OF THE PERIRHINAL CORTEX IN CROSSMODAL OBJECT RECOGNITION. Jacklin, D.L.; Potvin, A.; Winters, B.D. psychology, Univ. Guelph, Guelph, ON. Canada. Object representations that integrate information from multiple sensory modalities likely provide optimal information for such processes as the production of object-appropriate behaviour. We have recently developed a novel version of the spontaneous object recognition paradigm that allows us to investigate crossmodal object recognition (CMOR) in rats. In fact, we have recently shown that the perirhinal cortex (PRh) is critically involved in spontaneous tactile-to-visual CMOR. In the current study, we assessed the role of PRh in the formation of multisensory object representations. Male rats were tested in a modified version of the CMOR paradigm, in which the retention delay between the tactile sample phase and the visual choice phase was increased to 3 hours. This increased mnemonic demand abolished the ability of rats to perform the CMOR task. However, providing rats with a brief (10-sec) multimodal pre-exposure to the sample object 24 hours prior to the tactile sample phase rescued their CMOR performance using the 3-hour delay. Moreover, this multimodal pre-exposure was insufficient as a sample session, as rats receiving this pre-exposure were unable to recognize the object in a visual choice phase 27 hours later if the tactile sample phase was omitted. Additionally, by utilizing an immunohistochemical stain for the immediate early gene c-fos, we show that cells in PRh but not the hippocampus are activated following repeated multimodal pre-exposure to objects. Finally, we demonstrate that PRh is critically involved in the pro-mnemonic effects of multimodal pre-exposure, as transient inactivation of PRh via local infusions of lidocaine before or after pre-exposure or prior to the tactile sample phase, abolished the facilitatory effects of the pre-exposure session. These results extend previous findings implicating PRh in object representational functions and suggest an important role for PRh in the formation of complex associations between multisensory object features.

10. DISPLAY AND SEARCH DYNAMICS IN MULTI-ATTRIBUTE CHOICE. Vanessa Janowski[1], Erik Madsen[2], Martijn Willemsen[3], Eric Johnson[4], Antonio Rangel[1]. [1]California Institute of Technology, Pasadena, CA; [2]Stanford Graduate School of Business, Palo Alto, CA; [3]Eindhoven University of Technology, Eindhoven, The Netherlands; [4]Columbia Business School, New York, NY. Consumer choices are a crucial component of everyday decisions. When entering a store to make a purchase, consumers are confronted with shelves full of items and must quickly parse and select among a variety of options. Understanding the details of this decision-making process is therefore essential for developing models of choice behavior. We hypothesized that (1) while display configuration would have a significant impact on search, (2) search patterns would impact choice through value integration. We tested these hypotheses using a two-item, two-attribute choice task to determine how decision-making processes are modified by the introduction of multiple discrete attributes for each item. Subjects were presented with pairs of posters, each of a different design and size, and asked to choose the more desirable one. Attributes of each choice were arranged in two visual conditions: designs on top, and sizes on top. Mouselab was used to gather detailed search-process data. Choices were then compared to prior value measures to construct psychometric choice curves. We found striking differences in search patterns depending on the condition, which subsequently impacted choice through differential weighting and integration of the attributes. Our results have important implications for product attribute emphasis and placement.

11. OXYTOCIN SYNTHESIS IN THE HYPOTHALAMUS ARE INFLUENCED BY FASTING AND REFEEDING IN THE OXYTOCIN-MONOMERIC RED FLUORESCENT PROTEIN 1 TRANSGENIC RATS. Katoh, A. ; Ishikura, T.; Yoshimura, M.; Ohkubo, J.; Onaka, T.; Suzuki, H.; Ueta, Y. Department of Physiology and Otorhynolaryngology, School of Medicine, University of Occupational and Environmental Health, 807-8555, Japan Department of Physiology, Jichi Medical School, 329-0498, Japan. We have generated oxytocin (OXT)-monomeric red fluorescent protein 1 (mRFP1) transgenic rats that express the OXT-mRFP1 fusion gene in the hypothalamus and the posterior pituitary. The mRFP1 fluorescence was observed in the supraoptic nucleus (SON), the paraventricular nucleus (PVN), the internal layer of the median eminence (ME) and the posterior pituitary. Our previous study demonstrated that salt loading for 5 days caused a marked increase in the expression of the mRFP1 gene in the hypothalamus and that the response of the OXT-mRFP1 transgene to chronic salt loading was greatly exaggerated in comparison with that of the OXT gene in the SON and the PVN (Katoh et al., Endocrinology 2011). The present study demonstrated that fasting for 2 days caused a marked increase of mRFP1 fluorescence in the SON, the PVN and the ME, and after fasting for 2 days, refeeding for 2 days returned the mRFP1 fluorescence on

the same extent as control levels. These results suggest that OXT may be involved in the regulation of feeding and metabolic status in rats.

12. NATURAL ELEMENTS IN ENRICHED ENVIRONMENTS ENHANCE EMOTIONAL RESILIENCE IN MALE LONG EVANS RATS. 1Kaufman, C.; 1Brown, M.; 1Tschirhart, M.; 1Rzucidlo, A.; 1Hyer, M.; 2Bardi, M.; 1Lambert, K.; Dept of Psychology, 1Randolph-Macon College, Ashland VA USA 23005; Dept of Psychology, 2Marshall University, Huntington WV USA 25755. Enriched environments are beneficial to neurobiological development; specifically, rodents exposed to complex, rather than standard laboratory, environments exhibit evidence of neuroplasticity and enhanced cognitive performance (Diamond, 1988). In the current study, the nature of elements placed in the complex environment was investigated. Accordingly, rats (n=8) were housed in a natural environment characterized by stimuli such as dirt and rocks; an artificial environment characterized by plastic toys and synthetic nesting materials, a natural/artificial environment characterized by a combination of artificial and natural stimuli or a laboratory standard environment characterized by no enrichment stimuli. Following exposure to emotional and cognitive behavioral tasks including a cricket hunting task, novel object preference task and forced swim task, brains were processed for glial fibrillary acidic protein (GFAP)-, neuronal nuclei (NeuN)-, and brain derived neurotrophic factor (BDNF)-immunoreactivity (ir). Baseline and stress fecal samples were collected to assess corticosterone (CORT) and dehydroepiandrosterone (DHEA). Natural environment animals exhibited shorter diving latencies and increased diving frequencies in the second forced swim task, along with higher DHEA/CORT ratios, and higher GFAP-ir in the hippocampus. Type of environmental enrichment did not influence levels of BDNF-ir in the CA1, CA3, and dentate gyrus of the hippocampus; however, natural environment animals exhibited higher levels of NeuN-ir in the retrosplenial cortex, an area involved in spatial memory and other cognitive functions. These results suggest that, in addition to enhancing behavioral and endocrinological variables associated with resilience, exposure to natural stimuli alters plasticity in brain areas associated with cortical processing and learning.

13. EXPERIENCE-BASED PREFERENCE FOR DRIED-BONITO DASHI (A TRADITIONAL JAPANESE FISH STOCK). Kondoh, T.; Matsunaga, T. AJINOMOTO Integrative Research for Advanced Dieting, Graduate School of Agriculture, Kyoto University, Kyoto 606-8502, Japan. The dried-bonito dashi is a traditional Japanese fish stock that improves the palatability of various dishes, possibly via enhancement of umami taste. Here we investigated sensory and physiological mechanisms involved in preferences for dried-bonito dashi using 48-h two-bottle choice tests in rats. We found that preference for dashi was suppressed by chronic exposure to high fat or high sucrose diets. However, past experience/learning associated with dashi ingestion was the most important factor overcoming the influences of diet exposure. In particular, repeated exposure to dashi solutions eliminated the influences of high fat/sucrose diets on dashi preference. In descending concentration series, preference for dashi increased 100-fold compared to those obtained from ascending series. These results suggest that chemosensation (taste and smell) as well as postingestive signals regulate preference for dashi solutions in addition to the macronutrient composition of currently consumed foods.

14. THE ROLE OF DORSAL AND VENTRAL HIPPOCAMPUS IN THE ACQUISITION, STRENGTHENING AND EXPRESSION OF OLFACTORY FEAR CONDITIONING IN RATS. Kroon, J.A.V.; Carobrez, A.P. Departamento de Farmacologia. UFSC, Florianopolis, Brazil. The association between an odor and an aversive event is an effective model to study the neurobiology of associative fear memories. Several studies revealed differential contributions for the dorsal and ventral portions of hippocampus (HPC) in cognition and emotion processes. The present work was outlined to evaluate the role of NMDA receptors in the ventral and dorsal HPC on the generation, strengthening and expression of aversive memories of rats submitted to the Olfactory Fear Conditioning (OFC) paradigm. The acquisition phase occurred in a conditioning chamber where subjects received 5-footshock-pairings associated with amyl acetate odor (CS; conditioned stimulus). The expression of conditioned emotional responses (CER) occurred in an odor box where the CS was exposed. Male Wistar rats bilaterally implanted with guide cannulae aimed at the ventral (HPCv) or the dorsal (HPCd) HPC were injected with NMDA receptor antagonist (AP5 6 or 24nmol) or NMDA receptor agonist (NMDA100 or 200pmol) or PBS before/after the conditioning or pre-CS test session. In Experiment 1, AP5 into the HPCd, pre-conditioning session, reduced the CER toward CS when compared to the PBS-group. In Experiment 2, AP5 either into the HPCd or the HPCv, pre-CS test, reduced CER toward CS. In experiment 3, NMDA into the HPCd, immediately after a weak training paradigm (1footshock+odor), promoted OFC, while PBS or NMDA-only (no-shock) failed. These results suggest that the acquisition and strengthening of fear memory requires the participation of HPCd NMDA receptors. Moreover, the expression of fear requires the activation of NMDA receptors from both HPCd and HPCv.

15. A COMPUTATIONAL MODEL OF FEAR CONDITIONING IN ANIMALS AND HUMANS: IMPLICATIONS FOR PTSD. Moustafa, A.1,2, Gilbertson, M.W.3,4; Orr, S. P.4,5; Servatius, R. J.2,6,7; Myers, C.E 2,7,8. 1 School of Psychology, University of Western Sydney, NSW, Australia,2 Department of Veterans Affairs, New Jersey Health Care System, East Orange, NJ, 3 Manchester VA Medical Center, Manchester, NH.,4 Harvard Medical School, Boston, MA, 5 Massachusetts General Hospital, Boston, MA, 6 Stress & Motivated Behavior Institute, New Jersey Medical School, 7 Graduate School of Biomedical Sciences, University of Medicine and Dentistry of New Jersey, Newark, NJ, 8 Department of Psychology, Rutgers University, Newark, NJ. Fear conditioning involves establishing learned responses to an aversive stimulus. It is commonly measured in terms of physiological changes such as heart rate and skin conductance that are associated with fear. Empirical research has shown that the amygdala, hippocampus, and ventromedial prefrontal cortex are involved in fear conditioning; however, the functional contribution of each brain area and the nature of their interactions are not yet clearly understood. Here, we present a computational model that assumes that the basolateral amygdala participates in fear acquisition, the ventromedial prefrontal cortex in the formation of extinction memory, and the hippocampus in the representation of contextual information. In our model, hippocampal input to both the basolateral amygdala and ventromedial prefrontal cortex is essential for contextual modulation of acquisition and extinction. Each brain area is simulated using a layer of nodes and learning is modeled so as to occur differently in different simulated brain areas. The amygdala and ventromedial prefrontal cortex modules in our model are trained using the temporal difference (TD) learning algorithm, while the hippocampus module is trained using Hebbian learning (coupled with k-winner-take-all competition). This model successfully simulates various aspects of fear conditioning in animals, including acquisition, extinction, reacquisition, renewal, and the context specificity effects. Consistent with studies on lesioned animals (as well as animal models of PTSD), our model shows that damage to the ventromedial prefrontal cortex impairs fear extinction, while damage to the hippocampus impairs extinction in a different context. Second, we also present data from an extended model that additionally simulates the (a) role of dorsal anterior cingulate cortex in fear acquisition, and (b) generation of skin conductance responses in human subjects and individuals with PTSD.

16. THE ROLE OF NEURONAL NITRIC OXIDE IN THE LONG-TERM MEMORY TO OLFACTORY FEAR LEARNING. Pavesi, E.; Heldt, S.A.; Fletcher, M.L. Dept of Anatomy and Neurobiology. University of Tennessee Health Science Center. Memphis-TN 38163 USA. In rodents, the neural mechanisms involved in odor learning are important for social interaction, feeding behavior and protect to threatening situation. Experience-induced changes associated with odor learning are mediated by a number signaling molecules including nitric oxide (NO) which is predominantly synthesized by neuronal nitric oxide synthase (nNOS) in the brain. In the current study, we investigated the role of nNOS in the acquisition and retention of conditioned olfactory fear. In our protocol, mice received 6 training trials each consisting of an odor-CS co-terminating with the shock-US. One and 7 days after training, fear to the odor-CS was assessed in a different context using the conditioned freezing paradigm. Mice lacking the nNOS (nNOS knock-out) showed reduced fear to the odor-CS both 24h and 7-days after training when compared to wild-type mice. Pre-training systemic injections of the NO donor, Molsidomine, rescued fear retention 7-days after training in nNOS knock-out mice. In wild-type mice, pre-training systemic injections of L-NAME, a non-specific nNOS blocker, disrupted odor-CS fear retention in a dose-dependent manner. Neither wild-type mice receiving L-NAME nor nNOS knock-out mice showed any deficits in novel odor recognition or odor habituation, suggesting intact short-term olfactory memory .These results suggest nNOS signaling is necessary for normal retention of odor conditioned fear. In contrast, nNOS signaling may not be necessary odor perception or short-memory olfactory learning.

17. SOCIETAL IMPACT OF DIETARY PHYTOESTROGEN AND LEARNED BEHAVIOR IN ANIMAL MODELS AND COLLEGE UNDERGRADUATES: PERSONALITIY AND PHYSIOLOGICAL ANXIOLYTIC REACTIONS. Sanstrum, B.J., Totton, R.T. Depart. of Psychology and Neuroscience. University of Evansville, Evansville, Indiana 47722 USA. Phytoestrogens are plant-derived estrogens present in a variety of plant products. Isoflavones are the most common phytoestrogens and they can be found in soybeans and fermenting (Price & Fenwick, 1985). Isoflavones are heterocyclic phenols that are similar in structure to human steroidal estrogen (Messina, 1994). They are capable of having both estrogenic and anti-estrogenic effects on physiology and the endocrine system (Adlercreutz, Hockersteadt, Bannwart, Bloigu, Hamalainen, Fotsis, & Ollus, 1987). Evidence in rats suggests that the amount of phytoestrogen intake can alter anxiolytic behavioral responses into adulthood (Sanstrum, B.J., Totton, R.R., & Becker, L.A., 2011). Asian cultures consume far more phytoestrogens and are more empathic then individuals of Western culture (Okazaki, Sumie, 2010). Undergraduates from varying cultural backgrounds were measured on social, emotional opinions, dietary habits, as well as physiological galvanic skin responses. It was noted that foreign exchange students and those with special diets (vegans and vegetarians) have higher levels of societal guilt, lower anxiety levels, and lower aggression than the native typical diet population. This shows effects of diet between differing cultures and later components of adult behavior.

18. A NEW TASKTO STUDY EXECUTIVE CONTROL IN MICE. Scheggia, D.1; Bebensee, A.2; Weinberger, D.2; Papaleo, F1,2. 1Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genova, Italy. 2Clinical Brain Disorders Branch; National Institute of Mental Health, NIH, Bethesda, MD, USA. Similarly to the analogous regions of the PFC in human and monkey, rodent medial prefrontal cortex (mPFC) has been shown to mediate the ability to shift an attentional set. In human, these PFC-dependent functions can be investigated using the Intradimensional/Extradimensional (ID/ED) and Wisconsin Card Sorting (WCST) tests which have proven clinical relevance for several neuropsychiatric diseases. These tasks have been successfully adapted for rodents in the Attentional Set-Shifting Task digging version (ASST). Despite its unquestionable validity, the ASST presents practical limitations due to its manual-based testing procedure. We created a novel semi-automated behavioral apparatus that avoids the problems linked with the manual version of the ASST and closely mimics the task used in primates. Our apparatus is a reward-based operant box equipped with nose-poke holes that allows manipulating four dimensions (olfactory, tactile, visual and position - left or right). Firstly, we validated the task using C57BL/6J male mice. The results show that these mice were able to develop an attentional set for a specific dimension, as they needed more time and trials to reach the criterion to solve the extradimensional shifting (EDS) compared to the other stages. This task is specifically linked to dopamine in the PFC and catechol-O-methyl transferase (COMT) activity. Thus we used COMT mutant mice to study the effects of genetic variations resulting in relatively low COMT activity, and by inference increased dopamine, on attentional shifting abilities. In particular, we found that the COMT+/- and -/- male mice performed better than their wild-type littermates at the EDS. These results indicate this is a promising, efficient new tool for studying attentional set-shifting abilities and PFC-dependent functions in mice.

19. BEHAVIORAL INHIBITION TRAIT AFFECTS FEEDBACK-BASED LEARNING WITH AN AVOIDANCE OPTION. Sheynin, J.1,2; Shikari, S.3; Ostovich, J.3; Gluck, M.A.4; Moustafa, A.A.5; Servatius, R.J.1,2,6; Myers, C. E.1,2,6. 1Graduate School of Biomedical Sciences, Univ. of Medicine and Dentistry of NJ, Newark, NJ 07103; 2Stress & Motivated Behavior Institute, NJ Medical School, Newark, NJ; 3Honors College, Rutgers Univ., Newark, NJ; 4Center for Molecular and Behavioral Neuroscience, Rutgers Univ., Newark, NJ; 5School of Psychology, Univ. of Western Sydney, Australia; 6Dept. of Veterans Affairs, NJ Health Care System, East Orange, NJ. Avoidance is a core feature of anxiety disorders, including post-traumatic stress disorder (PTSD). The tendency to avoid may represent a risk factor for anxiety disorders. Although avoidance learning has been studied extensively in animal models, such research in human subjects is lacking. Here, we administered personality scales, including those to assess behaviorally inhibited (BI) temperament, a risk factor for anxiety disorders, to college students. We have also modified a computer-based task for probabilistic learning in which subjects predict an outcome and either increment or decrement points depending on cues (BÃ³di et al., 2009), to allow subjects to skip trials (eliminating forced choice). In one experimental condition, no feedback was provided on skipped trials; in a second condition, feedback regarding the correct choice was provided on skipped trials. Results show that BI affects learning when an option to avoid exists. Furthermore, results suggest that subjects with high BI change their avoidance behavior in response to manipulations with the feedback provided by the task. This work was supported by NSF/NIH Collaborative Research in Computational Neuroscience (CRCNS) Program, NIAAA (R01 AA018737) and SMBI.

20. BRAIN SPECIFIC DELETION OF THE CREATINE TRANSPORTER (CRT) LEADS TO SPATIAL LEARNING AND MEMORY DEFICITS WITHOUT REDUCTIONS IN BODY WEIGHT Matthew R. Skelton, Emily R. Hautman, Michael T. Williams and Charles V. Vorhees Division of Neurology, Cincinnati Childrens Research Foundation and Department of Pediatrics, University of Cincinnati College of Medicine. In humans, loss of the creatine transporter (CrT) gene leads to intellectual disability, loss of speech, increased seizure risk, and sometimes autistic-like features. In order to develop a mouse model of CrT deficiency, exons 2-4 of the CrT were flanked with loxP sites. In a previous study, ubiquitous knockout mice were created from this line and show learning and memory deficits, suggesting that this mouse is an excellent model of the disease. However, there were some motor performance deficits observed in the CrT-/y mice and they were significantly smaller than WT. In order to determine if the deficits observed were due to motor deficits, brain-specific CrT knockout (bKO) mice were generated using the nestin-cre expressing mouse. CrT(flox/y) mice served as controls. Cr levels were reduced in the brain of bKO mice. In the Morris water maze, bKO mice showed and increase latency and path length to find the hidden platform in two phases of the maze (acquisition and reversal). bKO mice showed an increase in average distance during probe trials during both phases . There were no differences in swim speed observed during MWM testing. bKO mice did not show a preference in novel object recognition, performing at chance levels. The results of this study show that the learning and memory deficits observed in ubiquitous CrT-/y mice are attributable to the loss of Cr in the brain and not the periphery. In addition, it shows that CrT expression is required in the CNS, as the CrT is expressed in the cells of the blood brain barrier.

21. PARAVENTRICULAR OXYTOCIN REGULATES SOCIAL-MEDIATION OF THE STRESS RESPONSE IN FEMALE PRAIRIE VOLES. Smith, A.S.; Wang, Z. Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL 32306 USA. Stressful life events promote homeostatic imbalance, via the hypothalamic-pituitary-adrenal (HPA) axis, and can be deleterious to mental health. Social support from an intimate partner can ameliorate such effects, yet the neuroendocrine mechanism is unknown. The prairie vole (Microtus ochrogaster) is a monogamous rodent, forming long-term pair bonds that affect HPA axis activity and mediating hormones. Recently, we evaluated the effects of social support on the behavioral, physiological, and neuroendocrine response in pair-bonded female prairie voles to 1 hr immobilization stress. In Experiment 1, immobilized females recovered alone or with their male partner for 30-min. Social support attenuated the stress-induced increases in corticosterone (CORT) and anxiety-like behaviors in an elevated plus maze (EPM) test. In Experiment 2, oxytocin, vasopressin, and corticotrophin-releasing hormones (CRH) content and receptor densities were assessed in brain tissue punches from females in Experiment 1. Oxytocin, but not vasopressin or CRH, content in the paraventricular nucleus (PVN) was significantly decreased after 30-min of social support. In Experiment 3, microdialysis samples from the PVN were collected from females to monitor oxytocin release during immobilization stress and recovery. While oxytocin was released in all immobilized females, only females recovering with their partner, but not alone, had elevated oxytocin during recovery. In Experiment 4, we did pharmacological manipulation of oxytocin in the PVN, via site-specific administration of oxytocin or a selective oxytocin receptor antagonist (OTA) at varying doses. Intra-PVN oxytocin injections reduced CORT levels and EPM anxiety-like behavior in immobilized females recovering alone. In addition, the anxiolytic effects of recovering with the social partner were no longer apparent after intra-PVN OTA injections. Together, our data demonstrate that oxytocin has anxiolytic effects and regulates the socially-derived reduction in the biobehavioral stress response. (Supported by NSF Graduate Research Fellowship, APF Graduate Student Scholarship, and NIMHF31-095464 to AS and NIMHR01-058616 and NIDAK02-23048 to ZW).

22. DOES PROTEIN SYNTHESIS INHIBITOR (ANISOMYCIN) MODULATES STEP-DOWN INHIBITORY AVOIDANCE IN MICE? 1Canto-de-Souza, L.; 2Mattioli, R. 1Faculdade de Filosofia, Cincias e Letras de Ribeiro Preto, FFCLRP-USP;2Departamento de Fisioterapia, CCBS-UFSCar. Several studies using inhibitory avoidance models have demonstrated the importance of limbic structures as the hippocampus on emotional memory. On the other hand, there are few studies assessing the involvement of this limbic structure on the emotional memory of mice exposed to the step-down inhibitory avoidance. Given to that, our goal was to investigate the role of the dorsal hippocampus, through bilaterally microinfusions of anisomycin (ANI-40g; a protein synthesis inhibitor), on the modulation of emotional memory in mice subjected to the step-down model. The experiment consisted of two sessions: Training (footshock; 0.5mA/10sec) and Test (24h later; without footshock). For this purpose, 15 male Swiss mice, weighing from 25 and 35g were assigned into two groups: control (n=7), animals that were treated with vehicle into the dorsal hippocampus 30 min before Training and ANI (n=8), animals that were treated with ANI into the dorsal hippocampus 30 min before Training. The step-down latency increased in both groups on the Test day, and no statistical differences were observed between groups at Training and Test day. Based on our results, we suggest that the dorsal hippocampus of mice is not involved on the acquisition/consolidation of the emotional memory in the step-down inhibitory avoidance model. Moreover, we cannot exclude the hypothesis that the dose of ANI (40 g) microinjected did not promote sufficient protein synthesis inhibition.

23. WHEN THE GOING GETS TOUGH, DO FATHERS MATTER? AN INVESTIGATION OF FAMILY STRUCTURE AND RESILIENCE IN A BIPARENTAL (PEROMYSCUS CALIFORNICUS) AND UNIPARENTAL (PEROMYSCUS MANICULATUS) MOUSE SPECIES. 1Tschirhart, M.; 1Kaufman, C., 1Brown, M.; 1Rzucidlo, A.; 1Hyer, M.; 2Bardi, M.; 1Lambert, K. Dept of Psychology, 1Randolph-Macon College, Ashland VA USA 23005; Dept of Psychology, 2Marshall University, Huntington WV USA 25755. Parental support is vital to the development of offspring; however, in approximately 95% of mammalian species, the female is the sole caregiver. Of interest in the current study was the behavioral and neurobiological responses of mothers housed with paternal mice (intact families) compared to females with no male present (single mother families) in biparental and uniparental mice (Peromyscus californicus and Peromyscus maniculatus, respectively). Both species were divided into intact families (n=9) and single mother families (n= 8) and exposed to two parental challenge tasks: the pup-rescue test and the pup-restraint test. In the rescue task, a pup was placed into an open cup centered in an open field apparatus. In the pup-restraint task, pups were placed in an enclosed wire mesh container; in both tasks, mice were videotaped and response latencies and interaction durations between the parent(s) and pup were recorded. Fecal samples were collected from the mothers to determine the levels of dehydroepiandrosterone (DHEA) and corticosterone (CORT) during baseline and stress conditions. Maternal brains were subsequently processed to quantify oxytocin- and vasopressin-immunoreactivity (ir) in the paraventricular nucleus of the hypothalamus. Results from both tasks indicated that californicus females from intact families were more responsive to pups than their single mother counterparts, an effect not observed in the uniparental maniculatus females. Further, DHEA/

CORT ratios were significantly higher in single mothers of both species. Neural quantification results indicated higher oxytocin-ir levels in the maniculatus females than found in californicus females, with no effect in vasopressin-ir. In sum, this research suggests that, in biparental species exposed to distressed pups, the presence of the father facilitates maternal-pup responsiveness.

24. EFFECTS OF NOCICEPTIVE STIMULATION ON FOS EXPRESSION AND BEHAVIOR IN MICE. Yoichi Ueta, Toru Ishikura, Takanori Matsuura, Mitsuhiro Yoshimura, Jun-ichi Ohkubo and *Hideo Ohnishi Department of Physiology and *Orthopedics, School of Medicine, University of Occupational and Environmental Health, 807-8555 JAPAN.Although the formalin test is widely used as a model of persistent pain, the primary afferent fiber types that underlie the cellular and behavioral responses to formalin injection are remarkably limited. Transient receptor potential protein vanilloid (TRPV) 1 and TRPV4 mainly exist in a sensory nerve, and they are well known as ion channels that are activated by nociceptive stimulation. In the present study, we investigated Fos protein by immunohistochemistry in the dorsal horn of the spinal cord (L4) and in the paraventricular nucleus (PVN) of the hypothalamus and also investigated nocifensive behavior during phase I and II after subcutaneous (s.c.) injection of formalin (0.5%) or saline in left hind paw of TRPV1 and TRPV4 knockout mice in comparison with wild type mice. The number of Fos-expressing neurons in laminae I-II of the dorsal horn (L4) in TRPV1 knockout mice was reduced but not significant difference compared to that of TRPV4 knockout mice and wild type mice after s.c. injection of formalin. The number of Fos-expressing neurons in the PVN was significantly reduced compared to that of the TRPV4 knockout mice and wild type mice after s.c. injection of formalin. On the other hand, nocifensive behavior during phase I was remarkably reduced in the TRPV1 and TRPV4 knockout mice, and nocifensive behavior during phase II was significantly reduced in the TRPV1 knockout mice but not TRPV4 knockout mice. Our result suggested that both TRPV1- and TRPV4-expressing neurons were activated directly after s.c. injection of formalin and TRPV1-expressing neurons were also activated by inflammation secondary after s.c. injection of formalin.

25. NEUROMODULATION OF PHOSPHOLIPASE C IN THE BASOLATERAL AMYGDALA CONTROLS FEAR MEMORY CONSOLIDATION. Young, M.B.; Ouyang, M.; Thomas, S.A. Depts. of Neuroscience and Pharmacology. The University of Pennsylvania, Philadelphia, PA, 19104. Long-term memory storage requires that learning-induced changes in neural networks are stabilized by intracellular signaling and protein synthesis in the hours after learning a process called consolidation. Extreme fear is hypothesized to cause abnormally powerful consolidation and lead to the recurrent intrusive fear memories in post-traumatic stress disorder (PTSD). Therefore, pharmacologically inhibiting consolidation could effectively prevent PTSD. We present a new molecular model of fear memory consolidation that depends on phospholipase C (PLC) as a point of convergence for a range of neuromodulatory receptors believed to be unnecessary for consolidation. In mice, the basolateral amygdala (BLA) undergoes a transient increase in PLCs second-messenger inositol-1,4,5-trisphosphate soon after auditory Pavlovian fear conditioning. Pharmacologically increasing PLC activity in the BLA after training enhances fear memory 24 hours later, whereas inhibiting PLC had the opposite effect. Consolidation and PLC activity in the BLA are both enhanced by activating either β2-adrenergic or D5-dopaminergic receptors there. However, both receptors must be blocked together to inhibit consolidation or PLC activity. Further investigation revealed inclusion of the M1 muscarinic receptor in this relationship. These data indicate that a range of neuromodulatory receptors redundantly activate PLC to ensure reliable consolidation of memory for a frightening experience. This redundant relationship could explain the ineffectiveness of treating PTSD by inhibiting neuromodulatory systems individually.

26. VISUAL ABILITIES AND SOCIAL INTERACTION OF MANTA RAYS WITH THE LARGEST BRAIN OF FISHES AND THE POSSIBLE UNDERLYING NEUROLOGICAL STRUCTURES. Ari, C. University of South Florida, Byrd Alzheimer`s Institute, Department of Molecular Medicine, Tampa, FL 33613 USA. Devil rays in the family Mobulidae have been recently reported to possess the largest brain of all fish, while no scientific data is available on why this large brain was necessary to be developed or how is it utilized. Some previous studies debate on whether larger brains can be connected to better cognitive abilities, or the brain weight to body weight ratio is a better indicator of intelligence in the animal kingdom. While devil rays have higher values in both these parameters, the present study was intended to reveal a connection between unique features of their brain by gross morphological and histological studies and their behavior by studying both captive and wild individuals. Behavioral studies conducted at the Atlantis Aquarium, Bahamas and the Lisbon Aquarium, Portugal show that giant manta rays have very good visual abilities, in spite of the fact that they live in plankton rich environment with bad visibility, which finding is supported by their highly developed visual center, the tectum opticum. Observations on captive and wild animals showed sophisticated social life (courtship, cleaning stations, feeding aggregations, welcoming of new individuals) in parallel to their enlarged forebrain and central nucleus. Histological studies show that their glial cell to neurons ratio is much higher than in mammals, which functional role is yet unknown. Understanding more the sensory and cognitive abilities of the fishes with the largest brain could help us answer how evolution forms brain structures in response to behavioral adaptations from underwater environmental pressures.

27. NEONATAL EFFECT OF TWO PHYTO-OESTROGENS ON MALE RAT PARTNER PREFERENCE. Morales-Otal A., Ferreira-Nuño A., Olayo-Lortia J., Fernandez-Soto C., and Tarrag-Castellanos R. Dpto. Biologa de la Reproduccin. Universidad Autonoma Metropolitana Iztapalapa. Mexico D.F. 09340. otal@xanum.uam.mx. Soy and alfalfa-derived products contain isoflavones and coumestans that mimic the actions of oestrogens and may exert adverse effects on male reproduction. To study the effects of two phyto-oestrogens (coumestrol and genistein) on reproductive behavior, groups of male rats (n = 10), were injected daily from day 1 to 5 after birth with the following compounds dissolved in 10 l Olive Oil as vehicle: Coumestrol (COUM, 150 g), Genistein (GEN, 150 g), 17-beta estradiol (E2, 1 g) and the vehicle (VEH, 10 l). Also a fifth group of Intact rats (INT, n = X), was included. When adults (age: 7 mo) partner preference was assessed in a Multiple Partner Choice Arena made with 6 cylinders put it together in circle fashion, with a small entrance directed to the central compartment. One of the next tethered stimulus animals was introduced in each cylinder: sexually expert male (SEM), castrated male (CASM), receptive female (RECF) and ovariectomized female (OVXF) and 2 cylinders were left empty. First, each experimental male was placed in the center of this arena during a 5 min Non-Contact Test (NCT: entrances closed with a wire mesh) and the partner preference was determined evaluating the time the male spent in front of each entry. Immediately, each male was tested during 20 times in a 1 min Contact Test (CT: without wire mesh), allowing the male enter in the preferred cylinder. The partner preference was determined by assessing the frequency with which each option was chosen by the male. In the NCT, the significant preference for the RECF against the SEM, observed in the INT, VEH and GEN groups of males, disappear in the COUM group. In the CT, the significant preference for the RECF was observed only in INT and GEN groups of males. As in both tests estrogen change the preference for the SEM in the E2 group, COUM had an estrogenic effect and GEN had an antiestrogenic effect on the Partner Preference.

28. NEURAL BASIS OF MATERNAL LOVE. Kikuchi, Y.; Noriuchi, M. Dept. of Cognitive Neuroscience. Div. of Frontier Health Science. Graduate School of Tokyo Metropolitan University. 7-2-10 Higashi-ogu, Arakawa, Tokyo, Japan. Background: Maternal love, which may be the core of maternal behavior, is essential for the mother-infant attachment relationship and is important for the infant's development and mental health. However, little has been known about these neural mechanisms in human mothers. We examined patterns of maternal brain activation in response to infant cues using video clips. Methods: We performed functional magnetic resonance imaging (fMRI) measurements while 13 mothers viewed video clips, with no sound, of their own infant and other infants of approximately 16 months of age who demonstrated two different attachment behaviors (smiling at the infant's mother and crying for her). After the fMRI scan, the mother was asked to rate her feelings (happy, motherly, joyful, warm, love, excited, anxious, etc.) on a five-point scale while watching each video clip. Results: We found that a limited number of the mother's brain areas were specifically involved in recognition of the mother's own infant, namely orbitofrontal cortex (OFC), periaqueductal gray, anterior insula, and dorsal and ventrolateral parts of putamen. The magnitude of the activation in response to viewing the mother's own infant versus other infants in the left OFC was positively correlated with the intensity of joyful ($R = .626$, $p = .022$) and happy ($R = .635$, $p = .020$), while that in the right OFC was positively correlated with the intensity of anxious ($R = .611$, $p = .027$) reported by the mother while viewing video clips of her own infant. Conclusions: Our results showed the highly elaborate neural mechanism mediating maternal love.

29. MATERNAL BRAIN RESPONSES TO INFANT'S CRYING. Noriuchi, M.; Kikuchi, Y. Dept. of Cognitive Neuroscience. Div. of Frontier Health Science. Graduate School of Tokyo Metropolitan University. 7-2-10 Higashi-ogu, Arakawa, Tokyo, Japan. Background: The neural system mediating maternal behavior of the mother who should protect her infant is a biologically essential mechanism for preservation of the human species. Here, we investigated the neural brain responses of mother by viewing the situation of her own infant in distress, by using fMRI. Methods: We performed functional magnetic resonance imaging (fMRI) measurements while 13 mothers viewed infantsf video clips, with no sound (see the methods of gNEURAL BASIS OF MATERNAL LOVEh in the abstracts). We compared the mother's brain responses for her own infant's crying with those for his/her smiling. Results: We found the strong and specific mother's brain response for the mother's own infant's distress. The differential neural activation pattern was found in the dorsal region of OFC, caudate nucleus, right inferior frontal gyrus, dorsomedial prefrontal cortex (PFC), anterior cingulate, posterior cingulate, thalamus, substantia nigra, posterior superior temporal sulcus (STS), and PFC. In addition, the activity level of the left STS or right STS was positively correlated with the intensity of love ($R = .624$, $p = .023$) or excited feeling ($R = .598$, $p = .031$), respectively. Conclusions: Our findings that a mother responds stronger to cry than smiling of her own infant seem to be biologically meaningful in terms of adaptation to specific demands associated with successful infant care.

30. EFFECT OF LITHIUM ON THE BEHAVIORAL DISINHIBITION INDUCED BY THE LESION OF MEDIAN RAPHE NUCLEUS AREA Pezzato, F.A. (1,2); Novais, D.B.(2); Silveira, D.T.L.(2); Olivato, S.(2); Garcia-Mijares, M.(1); Hoshino, K.(2)/ 1 Sao Paulo University, Brazil; 2 Saao Paulo State University, Brazil. Aim: to study the effect of chronic lithium treatment on the hyperactivity induced by the electrolytic lesion of the Median Raphe Nucleus (MRN). It was hypothesized that the behavioral disinhibition produced by that lesion may be associated to manic manifestations. Methods/Results: 20 Wistar male rats (90 days, 350g) were submitted to the electrolytic lesion of MRNs area and 20 were sham-lesioned and served as controls. After recovery, baseline locomotor activity was evaluated for 15 minutes using an automatic activity chamber (Med Associates/ENV-515). Next, half of the animals of both groups received lithium treatment (47.5 mg/kg, twice a day, i.p.) for 10 days, whereas the remaining animals were treated with saline under the same schedule. After treatments, locomotor activity was reevaluated. Baseline evaluation showed hyperactivity development in MRN lesioned groups, but not in sham-lesioned controls. Lithium treatment significantly reduced the locomotor activity in lesioned rats. No significant change was observed in the values displayed by the lesioned group treated with saline. Sham-lesioned groups maintained their low level of activity after lithium and saline treatments. Conclusion: obtained data support the hypothesis that the lesion of MRNs area induced behavioral manifestations similar to those observed in manic episodes and suggest the need for further researches about its validity as an animal model of mania. Source of research support: CNPq.

31. INCREASED HEDONIC BEHAVIOR IN RATS SUBMMITED TO THE ELECTROLYTIC LESION OF MEDIAN RAPHE NUCLEUS AREA Pezzato, F.A. (1,2); Horta Junior, J.A.C.(2); Mijares, M.G.(1); Hoshino, K.(2)/1 So Paulo University , Brazil; 2 Sao Paulo State University, Brazil. The Median Raphe Nucleus (MRN) lesion induces behavioral alterations that suggest face validity to manic disorder: hyperactivity, impulsivity, sexual facilitation, reduced sleep time, increased aggression and fewer submissions in home-intruder tests. This hypothesis was strengthened by the demonstration that lithium chronic treatment significantly decreases the hyperactivity induced by this lesion. The present research aimed to investigate if the MRN lesion alters the frequency of responses on a simple schedule of reinforcement and positive reinforcement value. Thirty Wistar male rats (90 days, 350g) were MRNs area electrolytic lesioned (L, n=10), sham-lesioned (S, n=10) or non-operated (C, n=10). After recovery they were tested in double bars (active/control) conditioning chambers under Fixed Ratio (FR2/4 days) and Progressive Ratio (PR/3 days) schedules for 10% sucrose solution consequence (0,02ml) under food restriction. Obtained data showed that L group response rates - only in active bar - were significantly higher than the two other groups in all FR2 days. However there were no significantly differences in Break Points (BP) accomplished in PR sessions between groups. The obtained data add evidences to consider the participation of MRN in mania`s etiology, since elation - operationalized as increases in behavioral rates for appetitive consequences (hedonic behavior) - is considered a central symptom of manic disorder. Null differences in BP may be explained by changes in sensibility to consequence`s immediacy, but still need further investigation. Sources of research support: CNPq

32. NEUROPEPTIDES AND HORMONE RECEPTOR CHANGES FOLLOWING PARENTAL EXPERIENCE IN MONGOLIAN GERBILS. Anna Phan1, Virginia Roberts1, R Abadilla2, Jessica A Mong3, Elena Choleris1, Mertice M Clark2, 1Psychology, University of Guelph, 2Psychology, Neuroscience and Behaviour, McMaster University, 3Pharmacology and Experimental Therapeutics, University of Maryland. Mongolian gerbils (Meriones unguiculatus) live in small family units and both males and females contribute to raising their pups. In other rodent species, oxytocin (OT), vasopressin (AVP), estrogen, progesterone and androgen receptors (ERα, PR, AR, respectively) are involved in a variety of sexually dimorphic social behaviors, as well as parental behaviors. We investigated the effect of sex, and sexual and parental experience in the expression of these neuropeptides and receptors. 19 experienced males (which had mated and raised pups), 36 virgin males and 6 female gerbils were tested for various social behaviors. Separate sections of brain tissue were immunostained for OT, AVP, ERα, PR or AR and analyzed using ImageJ. Sex differences: There were no sex differences in OT staining, but females had higher levels of AVP and ERα staining than males, while PR staining was higher in males than females in almost all brain nuclei analyzed. AR staining is currently being quantified. Differences between virgin and experienced males: OT and AVP staining was higher in experienced males compared to virgin males. Conversely, ERα staining in several brain nuclei was higher in virgin males compared to experienced males, but there was no difference in PR expression between these groups. Overall, neuropeptide and endocrine systems appear to undergo large changes following the experience of mating, raising pups and/or aging in male Mongolian gerbils. Funded by NSERC.

33. THE NATURE OF HIPPOCAMPAL INVOLVEMENT IN ESTROGEN-MEDIATED LEARNING ENHANCEMENT. Phan A, Suschkov S, Pecchioli N, Seguin L, Winters BD, Choleris E. Dept of Psychology, University of Guelph, ON, Canada. Previously, we reported systemic administration of physiological doses of 17β-estradiol rapidly (within 40min) enhanced learning (object placement, object recognition, social recognition), likely via action at ERα (Phan et al., 2011). Estrogen also rapidly increased dendritic spine density in the CA1 hippocampus, suggesting a site of action of estradiol rapid effects on learning. Therefore, bilateral microinjections of

17β-estradiol (25nM, 50nM, and 100nM) into the hippocampus of young adult ovariectomized female CD1 mice were performed 15min prior to testing in object placement, object recognition and social recognition paradigms. We found that intrahippocampal 50nM of 17β-estradiol improved performance on all 3 learning paradigms. Thus, the hippocampus seems capable of mediating 17β-estradiols rapid facilitatory effects on social and object recognition as well as object location learning. The results with the object placement paradigm are consistent with the established involvement of the hippocampus in spatial and contextual learning. However, its role in object and social recognition is unclear. Lesions of the hippocampus do not consistently impair object or social recognition. One possibility is that the hippocampus is not necessary for, but may facilitate, social and object recognition by providing spatial contextual information. Therefore, we tested the effects of intrahippocampal infusions of 17β-estradiol on object or social recognition when mice were tested in a Y-apparatus, which minimizes spatial and contextual cues. In the Y-apparatus intrahippocampal 17β-estradiol improved object recognition, but not social recognition. Therefore, while estradiol action in the hippocampus may directly facilitate learning and memory about objects, it may only indirectly facilitate social recognition, by providing contextual information. Funded by NSERC.

34. DEFENSIVE AGGREGATION (HUDDLING) IN LABORATORY RATS IN RESPONSE TO PREDATOR ODORS: GENERAL CHARACTERISTICS AND NEURAL CORRELATES. Bowen, M.T.; Kevin, R.; Kendig, M.D.; McGregor, I.S. School of Psychology, University of Sydney, NSW 2006 Australia. Rats show characteristic defensive responses to predator odors, such as hiding, avoidance, risk assessment, and inhibition of non-defensive behaviors. While these species-typical responses have been extensively examined in individual rats in the laboratory, the response of groups of rats has rarely been studied. In a series of recent experiments we have found that groups of 4 Wistar rats exposed to a ball of cat fur in a large test arena show pronounced defensive aggregation (huddling), spending long periods in tight clumps of 3 or 4 rats at maximal distance from the odor source. Group size is an important determinant of huddling, with groups of four, but not two, familiar rats huddling. Many groups were found to consist of 1-2 active responders that approach the cat odor source more readily, and 2-3 passive responders who spend nearly all of their time huddling. The traits of these individuals remain remarkably stable over repeated trials with cat fur although coping style in the cat odor paradigm did not necessarily predict coping style on other models of anxiety. Fos immunohistochemistry showed that, compared to rats exposed to cat odor alone, those exposed to cat fur in a group had: less activation in the lateral amygdala, LPO, medial caudoputamen, dorsomedial PAG and lateral habenula; and more activation in the mitral cell layer of the AOB. Compared to rats with more passive coping styles, those with more active coping styles had: less activation in the lateral AON, accumbens shell, ventrolateral septum and barrel cortex; and more activation in the mitral cell layer of the AOB. Finally, blockade of vasopressin V1a receptors by administration of the V1a receptor antagonist SR 49059 (1 mg/kg IP) interfered with defensive aggregation, suggesting that, as in songbirds and zebrafish, V1a receptor stimulation plays an important role in defensive aggregation in rats.

35. AROMATASE INHIBITION IN THE ZEBRA FINCH HIPPOCAMPUS DECREASES ACQUISITION AND PERFORMANCE IN A SPATIAL MEMORY TASK. David J. Bailey[1] & Colin J. Saldanha[2,3] [1]Biology, St. Norbert College, De Pere, WI Departments of [2]Biology and [3]Psychology, American University, Washington D.C. Songbirds are excellent models for determining the neural substrates of learning and memory. While much attention is focused on the development of procedural memory systems, such as song learning and production in passerines, birds also acquire robust episodic-like memories, including hippocampus (HP)-dependent spatial memories. The vertebrate brain synthesizes estrogens (specifically, 17-estradiol (E_2)) via the enzyme aromatase located in neuronal somata and presynaptic boutons. This synaptic, not somal, aromatase is especially high in the zebra finch HP. Surprisingly, another source of E_2 in the songbird brain results from injury, as reactive glia around areas of damage express aromatase 24 hr after disruption of the neuropil. Whether this injury-induced aromatase is functionally (learning and memory) significant remains to be tested. We hypothesized that local inhibition of the constitutive, presynaptic aromatase would disrupt learning and memory performance in a spatial task, and that the up-regulation of glial aromatase in the HP would enhance these behaviors. Birds with the aromatase inhibitor 1,4,6-androstatriene-3,17-dione (ATD) placed bilaterally onto the HP took more trials to acquire the task and made more mistakes than controls following a retention interval. Importantly, performance in ATD birds was similar to birds whose HP was lesioned. Aromatase induced by sham HP lesions did not have an effect in this task. We believe these data are among the first to suggest a physiological role for constitutive, presynaptic aromatization in any vertebrate. Supported by NIH grant NS042767 (CJS)

36. EMBRACING COMPLEXITY: TIME SERIES, LONG-RANGE CORRELATIONS, AND DIMENSIONAL SCALING AS ALTERNATIVE BEHAVIORAL ASSESSMENTS IN BEHAVIORAL NEUROSCIENCE. Bardi, M1, Lambert, KG2. 1Psychology Department, Marshall University, Huntington, WV -2Department of Psychology, Randolph-Macon College, Ashland, VA. Detailed analyses of behavioral responses are not often utilized in neurobiological research. When behavioral responses have been investigated, dependent variables such as latency,

duration, and frequency of behaviors have been reported. These general measures lack the sensitivity to detect relevant trends, especially when interactions exist among multiple rapidly changing variables. The common and widespread use of averaged measures taken at specific time intervals is useful for collecting snap-shots summaries of behavior, but they fail to disentangle more subtle variations. Also, when multiple measures are collected in the same study, it is common practice to investigate the relationship between each single behavioral measure and the set of neuroendocrine measures assessed, assuming a de facto very unlikely independence among the observed behaviors. Behavioral time series analysis during a variety of experimental conditions, though they may appear erratic, often reveals precise spectra. In other words, such analyses generate characteristics that could better represent the neuroendocrine status of the animals. To illustrate these points, a comparative analysis of specific data sets from our laboratories will be presented. Long-range correlation in biological systems is also informative because it serves as an organizing principle for highly complex, nonlinear processes and it avoids restricting the functional response of an organism to highly periodic behavior. Theoretical issues related to the use of traditional behavioral measures, such as the ceiling effect for latency, will also be discussed. Thus, comparisons between traditional and non-traditional assessments of behavior reveal a striking difference in the overall conclusions and interpretation of the exact same studies.

37. FUNCTIONAL ANTAGONISM BETWEEN EMISSION OF 50 kHz AND 22 kHz ULTRASONIC VOCALIZATIONS. Silkstone, M.; Brudzynski, S.M. Depts of Psychology and Biology, Brock University, St. Catharines, ON, L2S 3A1, Canada. Emission of 50 kHz vocalizations is driven by release of dopamine or injection of dopamine agonists, while emission of 22 kHz vocalizations is initiated by release of acetylcholine or injection of carbachol to specific forebrain regions. Productions of these vocalizations are mutually exclusive in both pharmacological and natural conditions. In the present study we are proposing a model explaining this phenomenon and rebound responses occasionally observed. Experiments were performed on 44 Long-Evans rats chronically cannulated in the anterior hypothalamic-preoptic area or in the lateral septum. Intracerebral injection of carbachol (1 μg) produced long lasting emission of 22 kHz vocalizations from both of these structures. Rats produced approximately 20 calls/min during the first 4 min of the response. During the decaying phase of the response, occasional emission of single 50 kHz was observed over the next 6 min. In total, however, there were 15 times more emitted 22 kHz calls than 50 kHz calls. This late, occasional emission of single 50 kHz calls is interpreted as a rebound effect. The 50 kHz calls appeared always during the decreasing phase of the carbachol-induced response or after 22 kHz seized to be produced. After the initial 4 min of exclusive production of 22 kHz calls after injection, the ratio of 22 kHz : 50 kHz was significantly decreasing from 20-40 times more 22 kHz than 50 kHz calls to approximately 4-5 times more of these calls toward the end of the response. The results are explained by functional antagonism between emission of 22 kHz and 50 kHz vocalizations. Supported by NSERC of Canada.

38. ADOLESCENT STRESS HORMONE EXPOSURE AFFECTS HIPPOCAMPAL NEUROGENESIS IN MALE AND FEMALE RATS. Brummelte S.; Duarte-Guterman P.; Crozier T.M.; Lieblich S.E.; Galea L.A.M. Dept. of Psychology, University of British Columbia. Chronic stress or elevated levels of glucocorticoids are known to cause sexually dimorphic changes in behaviour and brain morphology. Stress decreases hippocampal neurogenesis in adult males, but in females, chronic stress studies are equivocal with either no change, an increase or a decrease in neurogenesis. We have found that adolescence stress decreases adult neurogenesis in females, but not in males. Prolonged exposure to high levels of the stress hormone corticosterone (CORT: the major glucocorticoid in rodents) on the other hand reduces hippocampal cell proliferation and survival in both adult male and female rodents. Thus, the current study was conducted to investigate the effects of chronic CORT exposure during adolescence on hippocampal neurogenesis to better understand the contribution of high stress hormone levels during adolescence. For this, 30 day old male and female rats received a daily s.c. injection of either a high (40mg/kg) or low (10mg/kg) dose of CORT, or vehicle (sesame oil) for 14 days. Animals received an i.p. injection of BrdU (50mg/kg) prior to the start of treatment and were sacrificed either 24 hours after the last injection (adolescence) or in adulthood. Results reveal that both doses of CORT cause a significant interruption of weight gain in males and females. The high dose decreased brain weights in adolescence and adulthood in males and females, but brain/body ratios were only affected in males. Based on previous results we hypothesize that we will see a suppression in hippocampal cell proliferation and survival, but to different degrees in males and females. These results underline the different sensitivities of males and females to glucocorticoid exposure, particularly during a vulnerable time of development.

39. SWIM STRESS-INDUCED ANALGESIA AND ITS EFFECTS ON SCRATCHING BEHAVIOR IN RATS Jessica M. Spradley, Mirela Iodi Carstens, E. Carstens Neurobiology, Physiology & Behavior, Univ. Calif., Davis Many acute stressors induce analgesia, but effects on itch are poorly understood. We addressed this using a rat model that distinguishes between itch and pain behaviors. Male rats were subjected to 3 swim stress conditions: no stress (NS, 22C for 2 min), opioid-dependent low stress (LS, 12C, 3 min), or opioid-independent high stress (HS, 10C, 5 min), as verified by pretreatment with naltrexone (14 mg/kg ip) using the tail flick assay. We then tested

effects of these stress conditions on itch and pain using a cheek model. The pruritogen serotonin (5-HT, 1%/10 l) elicits hindlimb scratching but few forelimb wipes, whereas the algogen allyl isothiocyanate (AITC, 10%/ l) elicits forelimb wipes but little hindlimb scratch bouts, directed to the site of cheek microinjection. AITC-evoked forelimb wiping was suppressed under LS and HS conditions. 5-HT-evoked hindlimb scratching was suppressed under the HS condition only. 5-HT-evoked scratching was also suppressed by a combination of cold exposure and shaking, suggesting that thermal and psychological stressors contributed to analgesia. Curiously, 5-HT-evoked wiping was enhanced under the NS condition, as well as by exercise (wheel running), suggesting a pronociceptive effect of motor activity. Thus, pain-related behavior is suppressed by both opioid-dependent (LS) and -independent (HS) stressors, while itch-related scratching behavior was only suppressed under the opioid-independent HS swim condition and may be enhanced by exercise. Future studies identifying the mechanism by which high stress attenuates both itch and pain will be beneficial in developing novel treatments for both of these conditions.

40. NEURAL CORRELATES OF ANXIETY VULNERABILITY: AN ASSESSMENT OF ASSOCIATIVE LEARNING, TEMPERAMENT, AND CEREBELLAR REACTIVITY TO NOVEL SOCIAL STIMULI. M.D. Caulfield1,2 J.D. McAuley1,3 D.C. Zhu3,4 and R.J. Servatius1,2,5 1Stress & Motivated Behavior Institute, NJMS, 2Graduate School of Biomedical Sciences, UMDNJ, 3Department of Psychology, Michigan State University, 4Department of Radiology, Michigan State University, 5Department of Veterans Affairs, NJHCS, East Orange, New Jersey 07019. Behavioral inhibition is a risk factor for anxiety disorders typified by extreme withdrawal when facing novel social and nonsocial challenges. Here, we assess the relationship between scales measuring risk for anxiety disorders, associative learning and cerebellar activity. 150 college students were given a battery of sociobehavioral measures before undergoing delay eyeblink conditioning. Significant interactions of acquisition and the Adult Measure of Behavioural Inhibition ($F(8,736)=5.324$, $p<.05$), and both scales of the STAI (Trait: $F(8,728)=3.280$, $p<.05$,; State: $F(8,728)=5.580$, $p<.05$) indicate facilitated eyeblink acquisition in the at-risk group. Thus far, a subset (n=9) have participated in a follow-up imaging study. Participants are familiarized to 96 faces and scenes on day one and then scanned on day two while making Old/New behavioral responses to the familiar stimuli and 96 new faces and scenes. A within-group ANOVA, voxel based $p<.005$, whole brain corrected $p<.019$, resulted in a significant cluster (familiar face > non-familiar face) at Lobule VII, Crus II used for subsequent ROI analyses. Comparisons of BOLD % signal change in this area revealed larger correlations with eyeblink acquisition when viewing faces ($r=.57$, n=9) than scenes ($r=.26$, n=9). Behavioral data during fMRI revealed no significant differences of corrected recognition (d) between face and scene stimuli, $t(8)=.079$, $p=.939$. Recruitment for this project is ongoing with the intention of comparing cerebellar activity of high and low scoring groups on measures of anxiety vulnerability. Supported by the GSBS, Foundation of UMDNJ and the SMBI.

41. GENETICALLY-INFLUENCED DEFICITS IN INHIBITORY CONTROL ARE ASSOCIATED WITH PROPENSITY FOR ADDICTION-RELATED BEHAVIORS IN MICE Cervantes, M.C., Jentsch, J.D. Semel Institute for Neuroscience and Human Behavior, University of California at Los Angeles, Los Angeles CA 90095. While initial studies attributed inhibitory control deficits to drug use, recent work shows that impulsive traits can predict addiction susceptibility. As we have determined that impulsivity in a reversal learning task is heritable, we now aimed to test whether genetically-determined differences in this phenotype predicts propensity for addiction-related behaviors; specifically, if strains with poor impulse control engage in high levels of cocaine self-administration (SA) and have difficulty in extinguishing this behavior. BxD mice from strains exhibiting either good or poor reversal ability were tested for cocaine SA under FR1, FR2, and FR5 schedules and for drug-seeking behavior under extinction. Psychomotor effects were also assessed after IP cocaine administration. Overall, mice from impulsive strains exhibited faster and higher rates of cocaine SA during acquisition. While these higher rates were maintained in subsequent SA phases, along with an overall slower decrease in drug-seeking responses during extinction, more complex differences in behavioral trajectories were identified between strains. Impulsive strains also exhibited larger locomotor responses to cocaine at higher doses. In summary, strains with a phenotype of poor inhibitory control over impulsive responses show an increased sensitivity to the psychomotor, reinforcing, and conditioning effects of cocaine. These data suggest that genetically-influenced deficits in this form of impulsivity are predisposing factors for susceptibility to substance abuse.

42. DIFFERENTIAL EFFECTS OF PRE- AND POST-ACQUISITION ADMINISTRATION OF AN ESTROGEN RECEPTOR BETA AGONIST ON THE SOCIAL TRANSMISSION OF FOOD PREFERENCES. Clipperton-Allen, A.E.1,2; Flaxey, I.1; Foucault, J.N.1; Rush, S.T.1; Webster, H.K.1; Nediu-Mihalache, C.1; Choleris, E.1 1Dept Psychology, University of Guelph, ON, Canada 2Now at Dept Neuroscience, Scripps Florida, Jupiter, FL, U.S.A Estrogens are gonadal hormones that bind to two intranuclear receptors, alpha ($ER\alpha$) and beta ($ER\beta$), and can modulate numerous behaviours, including the social transmission of food preferences paradigm (STFP). In this task, a demonstrator animal eats of one of two distinctively flavoured but otherwise identical foods. After interacting with the demonstrator for 30 minutes, an observer animal is given an 8 hour choice between the two flavoured foods, one

of which the demonstrator had eaten. We have previously shown that when treated prior to learning a socially acquired food preference, mice given an ERα agonist show no preference for the demonstrators food, while mice receiving and ERβ agonist show a socially acquired food preference for twice as long as vehicle controls (Clipperton et al., 2008), suggesting ER facilitation of the STFP. However, it is unclear how ERβ is involved in three phases of memory: acquisition, consolidation or retrieval of this memory. Hence, mice were administered ERβ agonist DPN (0.025, 0.05, 0.1 mg/kg) immediately, or 24h, following the interaction with the demonstrator. When tested 48h after treatment, mice that received any dose of DPN immediately after the social interaction failed to show a preference for the demonstrated food, while results of the 24h post-acquisition administration are more varied. Feeding behaviour per se was not affected by drug treatment. These results suggest that ER activation can impair the consolidation of a socially acquired memory. Conversely, the pre-acquisition facilitation of social learning we found previously may be due to ER effects on dominance-related behavior during the social interaction. Funded by NSERC.

43. STRESS FACILITATES PREDATOR FEAR MEMORY CONSOLIDATION AND INDUCES EXTINCTION-RESISTANT FEAR IN A TIME-DEPENDENT MANNER. Corley M.J.; Takahashi, L.K. Psychology Dept. Univ. of Hawaii, Honolulu, HI, 96822, USA. Previous studies reported that exposure to stress prior to fear conditioning enhances conditioned fear behavior. However, it remains to be determined whether stress facilitates the consolidation of fear conditioning in a time-dependent manner and whether an enhanced consolidated fear memory becomes resistant to extinction. To address this issue, we first exposed rats to a unique auditory fear conditioning training procedure by pairing auditory clicks (CS) with a cloth containing the predator odor of a cat (US). Rats were then exposed to acute footshock stress (0.8 mA) at post-training intervals of 0, 1, 3, 9, and 24 hr. During the next 5 days, rats were placed in a runway apparatus containing a small hide box and tested for fear extinction to the auditory CS. Results showed that rats exposed to footshock stress 0, 1, or 3 hr after auditory fear conditioning exhibited significantly higher levels of freezing throughout extinction than their respective no shock controls and rats exposed to footshock 9 and 24 hr after fear conditioning. These results suggest that exposure to stress within 3 hr after auditory fear conditioning plays an important role in facilitating the consolidation of a conditioned fear memory that becomes resistant to extinction. In summary, our study highlights a limited time-dependent effect of stress on enhancing the consolidation of an emotional memory that becomes resistant to extinction. The results have implications for eventually determining how stress-induced enhancement of fear memory consolidation produces extinction resistant fear, which is a hallmark of posttraumatic stress disorder.

44. ROLE OF THE NORADRENERGIC SYSTEM IN THE REACQUISITION OF HEROIN-SEEKING IN RATS. Cummins, E; Boughner, E; Grant, J; Ricchetti, A; Kwiatkowski, D; Leri, F. Psychology, Univ. Guelph, Guelph, ON, Canada. We investigated the role of the noradrenergic system on reacquisition of heroin seeking using the conditioned place preference in male SpragueDawley rats. To accomplish this, we used a reacquisition procedure involving: place conditioning (1 mg/kg heroin and vehicle; 4 pairings each over 8 days), test of conditioning (drug-free; 1 day), extinction (vehicle and vehicle; 4 pairings each over 8 days), test of extinction (drug-free; 1 day), reconditioning (1 mg/kg heroin and vehicle; single pairing with each over 2 days) and test of reconditioning (drug-free; 1 day). Animals were injected with clonidine, an alpha 2-receptor agonist, either immediately (vehicle, 10, 40 or 100 ug/kg SC; n=15, 13, 12 and 14 respectively) or 4h (vehicle, 10 or 40 ug/kg; n=3, 12, 12) following reconditioning, with the goal of interfering with the consolidation of information acquired during reconditioning and hence block reacquisition. At the end of the experiment, to verify the action of systemically administered clonidine, animals were tested for locomotion activity immediately following injections of the same doses (latin square design). It was found that 10 and 40 ug/kg of clonidine administered either immediately or 4h post-reconditioning, significantly blocked the reacquisition of heroin CPP, while the 100 ug/kg dose had no effect. However, similar to the lower doses, heroin reacquisition was blocked when the highest clonidine dose was co-administered with idazoxan (0.5 or 5 mg/kg IP), an alpha 2-receptor antagonist, immediately following reconditioning. Further, while all clonidine doses decreased spontaneous locomotion, this effect was dose dependently reversed when animals also received idazoxan. These data suggest that reacquisition of drug-cue associations involves a memory process sensitive to manipulations of the noradrenergic system. Follow up studies will investigate the effects of systemic clonidine injections on the expression of heroin reacquisition, as well as infusions aimed at the locus coeruleus.

45. RAPID EFFECTS OF ESTROGEN RECEPTOR AGONISTS ON SOCIAL TRANSMISSION OF FOOD PREFERENCES IN FEMALE MICE. Ervin, K.; Friesen, J.; Gallagher, N.; Roussel, V.; Zicherman, J.; Clipperton Allen, A.; Phan, A.; Choleris, E. Dept. of Psychology. University of Guelph, Guelph, ON N1G 2W1 Canada. The social transmission of food preferences (STFP) is a specifically social learning paradigm in which an animal exhibits a preference for a novel food based on olfactory cues provided by a conspecific. Estrogens can modulate performance on this task. In mice, estrogen receptor alpha (ER-alpha) agonists eliminate the preference for the demonstrated food, whereas estrogen receptor beta (ER-beta) agonists prolong the preference (Clipperton et al.,

2008). In these studies, STFP was assessed 48 hours after drug administration. This time scale points at long-term effects of estrogen. Estrogens are also known to have behavioural effects within minutes of treatment. On this rapid time scale, ER-alpha agonists improve social recognition and increase dendritic spine density in the hippocampus, while ER-beta agonists impair social recognition (Phan et al., 2011). Whether social learning would also be affected in a similarly rapid time scale is currently unknown. We therefore administered 17beta-estradiol, the ER-alpha agonist propyl pyrazole triol (PPT), and the ER-beta agonist diarylpropionitrile (DPN) to ovariectomized observer mice 15 minutes prior to brief social exposure to a recently fed demonstrator mouse. We used a modified STFP paradigm that allowed us to examine the effect on the acquisition phase of STFP, with specific attention to the first hour of testing for possible rapid effects. Results show that within this first hour, 17beta-estradiol improves performance. These results extend the rapid effects of estrogens to a social learning paradigm and shows that estrogenic effects on learning of socially acquired information can be much more rapid than previously thought.

46. NUTRRHYTHM-DEPENDENT EVALUATION OF THE EFFECT OF HIGH-FAT DIET ON LEARNING AND MEMORY IN MICE. Horie, S.1; Nakamura, S.1; Oishi, K.2 1Kagawa Nutrition University, Saitama 350-0288, Japan. 2National Institute of Advanced Industrial Science and Technology, Ibaraki 305-8566, Japan. Nutrrhythm is a coined term from the nutrition and the biological rhythm, and we realize that a study of food-dependent effect on circadian clock could serve understanding various physiological and pathological phenomena including the field of brain neuroscience. In this study, we examined the effect of a high-fat diet on learning and memory functions in male and female clock-mutant mice (clock) comparing it to wild mice (wild). Clock and wild mice were divided into high-fat (24% fat) diet group and control (5% fat) diet group under the condition of feeding by free access (ad lib) or restricted day-time access to chow through 6 to 40 weeks, and then evaluated those effects on learning and memory with passive avoidance test (PAT) and the Morris Water Maze (MWM). In the results, not only male and female clock mice fed on the control diet, but also wild female mice fed on the high-fat diet were impaired the retention for PAT. Although no functional differences were seen between the male mice allowed to eat control and the high-fat diets ad lib, the mice eating the high-fat diet at day-time only resulted in reduction in the value of MWM, even in younger mice. Our data suggesting that female mouse is more susceptible to high-fat diet which may cause to impair the learning function and that entrainment of the peripheral circadian rhythm including gene expression of clock, which is directly affected by feeding, is essential for maintenance of learning and memory functions in mice.

47. THE COGNITIVE OVERRIDE OF ANXIETY IS ACCOMPLISHED BY SOCIAL FAMILIARITY AND IS MEDIATED BY THE MEDIAL PREFRONTAL CORTEX. Lungwitz, E.A.; Sanghani, S.; Harvey, B.; Bah, A.; Dietrich, A.; Truitt, W.A. In rats, social familiarity can alleviate anxiety-like behavior observed in the social interaction test. We propose that a neural circuit that includes the medial Prefrontal Cortex (mPFC) and Basolateral Amygdala (BLA), in which the mPFC processes social cues of familiarity and suppresses BLA outputs that lead to anxiety-like behavior, regulate this social familiarity effect. To investigate the effect of social familiarity on anxiety, we developed the Social Interaction-Habituation (SI-h) paradigm, consisting of a 5 min social interaction test repeated daily with the experimental rat exposed to the same partner rat on each test day. As the experimental rat becomes familiar with the partner rat, a significant increase in SI time is observed by day 5 compared to day 1, producing a SI-familiarity effect (SI-f). This SI-f effect is dependent on the presence of an anxiogenic stimulus (bright light), and familiarity to a partner rat. No increases in SI times were observed in rats when the SI-h test was performed under dark conditions or when exposed to novel partners on days 1-5. After establishing SI-f, exposure to a novel partner significantly reduces SI times, suggesting the SI-f effect is a result of recognition of the familiar partner rat. Re-exposure to the original partner in a new environment produces an enhanced SI-f effect; SI time significantly increases from day 1 to day 3. Bilateral inhibition of the mPFC with a GABAA agonist blocks the anxiolytic SI-f effect. Exposure to the same partner 24 hours following mPFC inhibition, SI times increase significantly higher than day 1. These data indicate that the mPFC activity is necessary for expression of the SI-f effect.

48. KETAMINE BLOCKS LATENT INHIBITION OF A CONDITIONED TASTE AVERSION IN FETAL RATS. Mickley, G.A.; Hoxha, Z.; DiSorbo, A.; Wilson, G.N.; Remus, J.; Biesan, O.; Ketchesin, K.; Ramos, L.; Luchsinger, J.; Prodan, S.; Rogers, M.; & Hoxha, N. The Neuroscience Program, Baldwin-Wallace College, Berea, OH 44017 USA. Conditioned taste aversions (CTAs) may be acquired when an animal consumes a novel taste (Conditioned Stimulus = CS) and then experiences the symptoms of poisoning (Unconditioned Stimulus = US). When later re-exposed to the CS, the animal will avoid the taste or reduce consummatory oral-facial movements. In the current study we sought to determine if a CTA could be diminished by non-reinforced pre-exposure to a CS in fetal rats (i.e., latent inhibition; LI). We injected E18 pregnant Sprague-Dawley rats with 100% allicin (the taste component of garlic which crosses the placental barrier; i.p.) or an equal volume of physiological saline. On this day some of the pregnant dams also received the N-Methyl-D-Aspartate (NMDA)-receptor blocking drug ketamine (100mg/kg, i.p.). Later (E19), the pregnant dams received a second injection of the CS, allicin (i.p.) followed by either LiCl (81

mg/kg, i.p.; the US) or a saline. Finally, on E21 pups received oral lavage with 10l, 0.1% allicin and observations of ingestive orofacial motor responses (mouthing and licking) were recorded. If allicin had been paired with LiCl in utero, E21 fetuses exhibited a conditioned suppression of orofacial movements, indicative of an aversion to this taste. Pre-exposure to the garlic taste on E18 produced a latent inhibition of this CTA. Ketamine significantly disrupted the formation of both the CTA and LI. Our data provide the first demonstration that fetal rats can acquire a LI. Moreover, NMDA receptor blockade in E18 fetuses impairs the acquisition of these gustatory memories. Supported by NSF Award: 9514799

49. SEXY PREDATORS; A TWO PRONGED MANIPULATION OF VASOPRESSIN-SOCIAL SYSTEM DRIVES TOXOPLASMA INDUCED BEHAVIOR CHANGES. Hari Dass, S.A.; Vyas, A. School of Biological Sciences, Nanyang Technological University, Singapore 637551. Parasites can act as puppeteers manipulating behavior of their host for their benefit. Toxoplamsa rats system is one such example that is tractable for studying defensive and social behaviors. Infected male rats display a remarkable alteration in defensive behavior; they are attracted to their feline predators. This enables it masterfully hitch a ride into its only definitive host, the feline gut. We are investigating the mechanism underlying this manipulation; specifically focusing on the vasopressin-social system in the medial amygdala. Vasopressin is involved in social affiliation in the extended amygdala. Its promotor contains two androgen sensitive methylation sites. Cat odor stimulated brains were labeled for AVP-ir and cFOS-ir neurons. We studied the MEA which governs both defense (posteroventral medial amydgala;MEApv) and affiliation (posterodorsal medial amygdala; MEApd). Infected males showed a higher proportion of colabelled neuron; cat odor was activating the affiliative zones here. These changes in behavior arent transient, implying a long lasting robust proximate mechanism. Epigenetic regulation is an ideal candidate. Infection decreased methylation at both the androgen dependent sites in the MEApd .Correspondingly we observed a 12 fold boost in AVP mRNA levels here. Testosterone, in addition to mediating AVP promotor methylation, also influences defensive behavior; castrated males are more fearful than intact controls. Infected males showed an uncharacteristic; infection decreases sexual display, increase in testicular T. We have elucidated a two pronged proximate mechanism acting via the vasopressin- social system in the MEApd of infected males; an atypical cat odor induced activation and epigenetic driven boost in AVP. These could be driven by a common mediator; Testosterone. Together these result in infected male rats perceiving an affiliatory cue when exposed to cat odor hence the attraction.

50. EFFECTS OF ADOLESCENT SOCIAL DEFEAT ON COGNITION AND PREFRONTAL CORTEX DOPAMINE FUNCTION. Novick, A.M.; Forster, G.L.; Watt, M.J. Division of Basic Biomedical Sciences, Sanford School of Medicine, University of South Dakota, Vermillion SD 57069 USA. Bullying victimization during adolescence is associated with an increased incidence of psychiatric disorders characterized by deficits in executive function. These often manifest as impairments in working memory, the ability to utilize and maintain task-relevant information. We have shown that adolescent male rats exposed to social defeat stress, a model of human bullying, develop persistent reductions in prefrontal cortex dopamine (PFC DA) activity. Given the known role of PFC DA in mediating executive function, we hypothesized that PFC DA hypofunction caused by adolescent social defeat would result in decreased working memory in early adulthood. Rats were exposed daily to repeated social defeat from postnatal day (P) 35-39, with age-matched controls placed into empty cages for the duration of each defeat trial. At P56, subjects were trained in one of two working memory tasks. Compared to controls, rats defeated in adolescence exhibited impaired performance both in the delayed win-shift task when a 5 min delay was used, and in the delayed alternating T-maze test with a 90 s delay. To further investigate mechanisms underlying altered PFC DA activity and related behaviors following adolescent defeat, quantitative autoradiography was used to identify potential differences in markers of DA function. Previously defeated rats showed upregulation of the DA transporter, which may contribute to decreased DA availability within the PFC and subsequent deficits in working memory. Combined, findings suggest that cognitive deficits associated with bullying victimization may be a direct result of psychosocial stress-induced insult to the developing adolescent PFC DA system. Support: NIH P20 RR15567, NIDA RO1 DA019921, and USD Joseph F. and Margaret P. Nelson Grant.

51. TOXIN-INDUCED GUSTATORY CONDITIONING IN RATS: THE EFFECTS OF ORAL INGESTION OF LOW LEVELS OF A TOXIN (LITHIUM CHLORIDE) ON DRINKING BEHAVIORS. Good, A.N.; Kavaliers, M.; Ossenkopp, K.-P., Dept. of Psychology, Graduate Neuroscience Program, University of Western Ontario, London, Ontario, Canada N6A 5C2. In nature, foraging animals must decide which foods will maximize nutrients and minimize toxin ingestion. When an organism ingests a novel flavor and subsequently becomes ill within minutes to hours, it will learn to avoid this flavor in the future. In the laboratory the toxin lithium chloride (LiCl) has been shown to produce robust conditioned taste avoidances (CTA). The current study examined the effects of orally ingesting low levels of LiCl (in a palatable 0.3 M sucrose solution) on drinking behavior in rats using a lickometer. In an acquisition phase (5 consecutive days, 20 min sessions) rats were presented with a solution contained 0.3 M sucrose + 0.12 M salt. The salt component of the solution consisted of NaCl, LiCl, or a combination of both. Four

different low concentrations of LiCl were examined (0.005, 0.01, 0.015, 0.02 M). In addition a 0.12 M NaCl negative control group and a 0.12 M LiCl positive control group were included. In an extinction phase (5 days, 20 min sessions) all rats were presented with 0.3 M sucrose + 0.12 M NaCl. Volume intake, number of licks, and licking pattern microstructure variables were recorded for each session. Rats drinking 0.12 M LiCl exhibited very low levels of consumption. Rats drinking sucrose with low levels of LiCl (0.005 0.02 M), showed significant dose dependent linear reductions in volume intake and lick totals. Lick cluster size varied significantly across doses in a non-linear fashion. Present results show that rats adjust their drinking behavior in a dose-dependent manner, to maximize calorie intake and minimize toxin ingestion.

52. ACUTE RESTRAINT DIFFERENTLY ALTERS DEFENSIVE RESPONSES AND FOS IMMUNOREACTIVITY IN THE RAT BRAIN. Andrade, JS; Abrao, RO; Cespedes, IC; Garcia, MC; Nascimento, JOG; Spadari-Bratfisch, RC; Melo, LL; da Silva, RB; Viana, MB. Dept. of Biosciences. Federal University of Sao Paulo (UNIFESP), Santos, SP 11060001 Brazil. Results from a previous study shows that rats exposed to acute restraint display anxiogenic-like behavior, evidenced by facilitation of avoidance responses in the elevated T-maze (ETM) model of anxiety. In contrast, escape responses were unaltered by stress exposure. Since ETM avoidance and escape tasks seem to activate distinct sets of brain structures, it is possible that the differences observed with acute restraint are due to particularities in the neurobiological mechanisms which modulate these responses. In the present study, analysis of fos protein immunoreactivity (fos-ir) was used to map areas activated by exposure of male Wistar rats to restraint stress (30 min) previously (30 min) to the ETM. Corticosterone levels were also measured in stressed and non-stressed animals. Confirming previous observations restraint facilitated avoidance performance, an anxiogenic result, while leaving escape unaltered. Performance of avoidance task increased fos-ir in the frontal cortex, intermediate lateral septum, anterior hypothalamus and dorsal raphe nucleus. In contrast, performance of escape increased fos-ir in the basolateral amygdala, ventromedial hypothalamus, dorsolateral periaqueductal gray and locus coeruleus. Both behavioral tasks also increased fos-ir in the dorsomedial hypothalamus. Restriction significantly raised corticosterone levels. Additionally after restriction, fos-ir was predominantly seen in the dorsal raphe of animals submitted to the avoidance task. This data confirms that different sets of brain structures are activated by ETM avoidance and escape tasks and suggests that acute restraint differently alters ETM behavior and the pattern of fos activation in the brain.

53. AN EXAMINATION OF PREDISPOSED COPING STRATEGIES AND NEUROBIOLOGICAL RESPONSES IN MALE RATS EXPOSED TO VARIOUS PROBLEM-SOLVING TASKS 1Brown, M.; 1Kaufman, C.; 1Tschirhart, M.; 1Rzucidlo, A.; 1Hyer, M.; 2Bardi, M.; 3de Silva, I.; 1Lambert, K. Dept. of Psychology, 1Randolph-Macon College, Ashland VA USA 23005; Dept. of Psychology, 2Marshall University, Huntington WV USA; Dept. of Psychology, 3University of Richmond, Richmond VA USA. Stress is a common denominator among many mental illnesses (e.g., depression and anxiety disorders). Effective coping strategies allow individuals to adapt and respond appropriately to unpredictable environments, providing a buffer against the detrimental effects of stress on the brain and body. Accordingly, the current study examined interactions among coping styles, neurobiological indicators of emotional resilience and performance in novel challenging tasks. The coping styles of 24 male Long-Evans rats were assessed using the back-test (Hawley, 2010) and were subsequently categorized as passive, active, or variable copers (n=8). All rats were subsequently exposed to three tasks with varying problem solving requirements, a swim escape task, a digging task, and a novelty suppression feeding task. Corticosterone (CORT) and dehydroepiandrosterone (DHEA) were assessed in fecal samples collected at baseline and after the swim task. Subsequently, brains were processed for neuropeptide Y (NPY) and brain derived neurotrophic factor (BDNF) immunoreactivity, both associated with resilience, in relevant brain areas. In the problem solving digging task the variable copers exhibited more exploratory behavior; however, no additional significant effects were observed in the feeding and diving-escape tasks. Variable copers also exhibited the greatest change in CORT and DHEA responses ($p<0.004$ in both cases) from baseline to stress in the swim task and less BDNF immunoreactivity in the dentate gyrus ($p<0.05$). A multiple dimensional scaling analysis indicated that the variable copers were characterized by more reactive CORT and DHEA responses whereas the more consistent passive and active copers were characterized by longer latencies to respond in the various tasks. Confirming prior research in our lab assessing coping strategies, variable copers exhibited evidence of more adaptive responses (e.g., higher DHEA levels and bolder responses).

54. NEURONAL ACTIVATION PATTERNS ASSOCIATED WITH HYPER-EMOTIONAL AGGRESSION IN RATS SOCIALLY ISOLATED FROM WEANING. Tulogdi, A.; Toth, M.; Biro, L.; Soros, P.; Haller, J. Department of Behavioral Neuroscience, Institute of Experimental Medicine, Budapest, Hungary. Post-weaning social isolation in rats is believed to model symptoms of early social neglect-induced externalizing problems including aggression-related problems. We showed earlier that rats reared in social isolation were hyper-aroused during aggressive contacts, delivered substantially more attacks that were poorly signaled and were preferentially

aimed at vulnerable body parts of opponents (head, throat and belly). Here we studied the neural background of this type of aggression by assessing the expression of the activation marker c-Fos in 22 brain areas of male Wistar rats submitted to resident-intruder conflicts. Post-weaning social isolation readily produced the behavioral alterations noticed earlier. Social isolation significantly increased the activation of brain areas that are known to directly or indirectly control inter-male aggression. Particularly, the medial and lateral orbitofrontal cortices, anterior cingular cortex, bed nucleus of the stria terminalis, medial and basolateral amygdala, hypothalamic attack area, hypothalamic paraventricular nucleus and locus coeruleus showed increased activation. This contrasts our earlier findings obtained in rats with experimentally induced hypoarousal, where abnormal attack patterns were associated with over-activated central amygdala, lateral hypothalamus, and ventrolateral periaqueductal gray that are believed to control predatory attacks. We have seen no similar activation patterns in rats socially isolated from weaning. Taken together, these findings suggest that despite some phenotypic similarities, the neuronal background of hypo and hyperarousal-associated abnormal forms of aggression are markedly different. While the neuronal activation patterns induced by normal rivalry and hypoarousal-driven aggression are qualitative different, hyperarousal-associated aggression appears to be an exaggerated form of rivalry aggression.

55. NPAS4 REGULATES A TRANSCRIPTIONAL PROGRAM IN CA3 REQUIRED FOR CONTEXTUAL MEMORY FORMATION. Ramamoorthi, K; Fropf, R; Belfort, GM; Fitzmaurice, HL; McKinney, RM; Neve, RL; Otto, T; Lin, Y. McGovern Institute for Brain Research, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA. The rapid encoding of contextual memory requires the CA3 region of the hippocampus, but the necessary genetic pathways remain unclear. We found that the activity-dependent transcription factor Npas4 regulates a transcriptional program in CA3 that is required for contextual memory formation. Npas4 was specifically expressed in CA3 after contextual learning. Global knockout or selective deletion of Npas4 in CA3 both resulted in impaired contextual memory, and restoration of Npas4 in CA3 was sufficient to reverse the deficit in global knockout mice. By recruiting RNA polymerase II to promoters and enhancers of target genes, Npas4 regulates a learning-specific transcriptional program in CA3 that includes many well-known activity-regulated genes, which suggests that Npas4 is a critical regulator of activity-regulated gene programs and is central to memory formation.

56. NEURONAL ENSEMBLES IN CA1 AND MPFC DIFFERENTIALLY REPRESENT RECENT AND REMOTE CONTEXTUAL FEAR MEMORIES. Zelikowsky, M.; Fanselow, M.S. Caltech, Pasadena, CA. The ability to recognize contexts and the significant events that occur within them is vital to the survival of any species. Contextual fear conditioning provides an excellent model of this ability, as it requires an animal to form a contextual representation and associate that representation with an aversive event. Activity within the brain regions implicated in contextual fear can be assessed using catFISH (cellular compartment analysis of temporal activity using fluorescence in situ hybridization), which provides a visualization of the neuronal populations involved in two, temporally distinct events as indexed by Arc mRNA expression (Guzowski et al., 1999). Classically, the dorsal hippocampus (DH) has been implicated as a key structure in contextual processing (Fanselow, 2000; 2010) and is thought to initially provide the detailed contextual representation underlying contextual fear conditioning (Wiltgen et al., 2010). Meanwhile, recent findings suggest a possible role for the medial prefrontal cortex (mPFC) in contextual fear, with an emphasis on the mPFC in the permanent storage of long-term memories (Quinn et al., 2008; Frankland et al., 2004; Goshen et al. 2011). We investigated the behavior of neuronal ensembles in the CA1 region of the DH, the basolateral amygdala (BLA), and the mPFC (both infralimbic (IL) and prelimbic (PL) subregions) following contextual fear conditioning and testing one or thirty days later (recent vs. remote memory test), in the same context or in a novel context (generalization test). We found that recently acquired memories were context-specific and recruited neuronal populations in CA1 and mPFC that showed a profile of Arc induciton consistent with a role for contextual encoding. In contrast, when contextual fear memories transferred from a recent to remote state, Arc expression in CA1 persisted but failed to exhibit context-specificity, suggesting that the detailed contextual representation encoded in CA1 following recently acquired memories may fade with time.

Thursday, June 7, 2012

9:00-10:00 **Presidential Lecture:** *Behavioral Neuroscience: A View from Down Under*
Stephen Kent, La Trobe University; **Iain McGregor**, University of Sydney

Behavioral Neuroscience: A View from Down Under**.** Kent, S. School of Psychological Science, La Trobe University. Melbourne (Bundoora), VIC 3086 Australia. McGregor, I.S. School of Psychology, University of Sydney, Sydney, New South Wales, Australia. Following a special request by the current IBNS president, this talk will provide a light-hearted view of current behavioural neuroscience research in Australia. After exploding a few erroneous beliefs about Australia that are commonly held by Americans and Europeans we will provide a brief history of Australian neuroscience and of the strong links between IBNS and Australian researchers over time. We will meander into a discussion of various strange Australian animals (e.g. koalas, quolls and numbats) and their unusual behaviours, and also focus on some of the unusual behaviours of Australian people (playing footy, drinking piss and chasing sheilas). More seriously we will also discuss the current Australian academic and scientific context (e.g., specific challenges, leading universities and research centres and their rankings). The current work occurring in leading institutions and outstanding researchers will be highlighted. Both speakers will also provide a brief summary of their ongoing work examining the behavioural and physiological effects of caloric restriction (SK) and animal models of defensive behaviour and translational studies of drug addiction (ISM). The opportunities available for overseas graduate students, postdocs and faculty in Australia will be highlighted. We will conclude with the uncontroversial message that "Australia is the best bloody country in the world mate".

10:30-12:30 **Symposium:** Plasticity in the maternal brain: Effects of stress, drugs and medication.
Chair: **Jodi Pawluski**

MATERNAL CORTICOSTERONE: DIFFERENCES IN PRE- VERSUS POST-PARTUM EXPOSURE IN THE DAM AND HER OFFSPRING. Galea, L.A.M., Brummelte, S. Univ British Columbia. Postpartum depression (PPD) affects 15% of women and very few women with PPD seek treatment. Women with untreated PPD have impaired cognitive ability, marital difficulties, and are more likely to abuse their children. Children of untreated PPD mothers have an increased risk to develop depression and have impaired cognitive, motor and social development. Steroid hormones play a significant role in depression. During pregnancy and postpartum, levels of steroid hormones fluctuate dramatically and may contribute to the etiology of PPD. Furthermore stress is cited as a precipitating event leading to depression. The hippocampus is involved in depression and maintains the ability to produce new neurons in adulthood. Adult neurogenesis in the hippocampus may be reduced in depressed patients and is modulated by both sex and steroid hormones. We examined the effects of maternal corticosterone during gestation or the postpartum on behavioural and neural markers of depression in the dam and her offspring. High CORT during gestation and the postpartum reduced hippocampal cell proliferation in the dam but only high CORT postpartum resulted in depressive-like behaviours in the dam. Further, offspring of dams exposed to high maternal CORT in utero showed more depressive-like behavior, while offspring exposed to high maternal CORT postpartum exhibited more anxiety-like behavior. High CORT during gestation or postpartum altered basal and stress levels of CORT differently in adult offspring. Together these studies suggest differential effects of gestational versus postpartum high maternal CORT on the dam and her offspring.

EFFECT OF GESTATIONAL STRESS AND SSRI MEDICATION USE ON HIPPOCAMPAL NEUROGENESIS IN THE MOTHER. Pawluski, J.L. School of Mental Health and Neuroscience, Maastricht University, The Netherlands, 4559 ER. The incidence of stress and stress-related disorders, such as Postpartum Depression, with the transition to motherhood is estimated to be 20%. Selective serotonin reuptake inhibitor medications (SSRI) are currently the antidepressant of choice to treat ante- and post-partum depression. However, little is know about the effects of these medications on the maternal brain and behavior. Therefore the present study investigated how a commonly used SSRI, fluoxetine, affects neurobehavioral outcomes in the mother using a model of maternal adversity. To do this, gestationally stressed and non-stressed Sprague-Dawley rat dams were treated with either fluoxetine (5mg/kg/day) or vehicle. Dams were divided into 4 groups: 1) Control + Vehicle, 2) Control + Fluoxetine, 3) Stress + Vehicle, 4) Stress + Fluoxetine. Fluoxetine or vehicle was administered to the dam during the postpartum period via osmotic minipump implants (Alzet) for 28 days. Results show effects of chronic fluoxetine treatment on maternal care of pups, corticosterone and corticosteroid binding globulin levels as well as anxiety-related behavior. However, these effects were most prominent in dams that were not subject to gestational stress. In addition, fluoxetine treatment to gestationally stressed dams increased hippocampal neurogenesis. This research provides important information on how SSRIs may act on the physiology, behavior, and neural plasticity of the mother. Although this is a first step in investigating the role of antidepressant treatment on the mother, much more work is needed before we can understand and improve the efficacy of these medications to treat mood disorders in pregnant and postpartum women.

EFFECTS OF GESTATIONAL COCAINE ON SPINE DENSITY IN PREGNANT RAT DAMS. **Luine, V.**; Frankfurt, M. Hunter College of CUNY, New York, NY. Several laboratories have shown that cocaine administration is associated with increased dendritic spine density in different brain areas including the prefrontal cortex (PFC) and nucleus accumbens (NAc). The majority of these studies have been done in males, and the effects of cocaine on spine density in adult female rats is poorly described. In addition, although many studies have explored effects of gestational cocaine, they are limited to effects in the pups, rather than the dams. As part of our ongoing studies of parity influences on neural and behavioral function, we examined the effects of 30mg/kg of cocaine, given on gestational days (GD) 8 to 20, on spine density in brain areas of the dams within 24 h of parturition. For comparison, cocaine was given at the same dose and for the same duration to adult, virgin females. Overall, dams appeared more sensitive to cocaine since more areas were affected and larger changes were seen in dams. Cocaine increased apical and basal PFC spine density by 15% in dams but did not affect virgins. Changes were higher in basal CA1 of dams, 14% increase, vs 8% increase in virgins. Moreover, in the medial preoptic area, which is critical for maternal behavior, cocaine decreased spine density in dams but increased it in virgins. Cocaine induced changes in dams were similar in magnitude to effects seen in pups treated from GD8 to GD20 and analyzed at adulthood. These results show that pregnancy enhances cocaine dependent neural changes and adversely affects brain areas involved in maternal behavior. The responses of dams maybe related to high levels of estrogens present during gestation.

MOTHERHOOD AND AGING: THE EFFECTS OF DIFFERENT ESTROGENS ON HIPPOCAMPAL NEUROGENESIS AND COGNITION IN MIDDLE-AGED FEMALES. Cindy Barha; Stephanie Lieblich; Carmen Chow; Liisa Galea. Department of Psychology, University of British Columbia. Estradiol is the more common estrogen in young women, while estrone is more common in older women. The most commonly prescribed hormone replacement therapy (HRT) consists primarily of estrone, and does not have as many cognitive enhancing benefits as HRTs that consist primarily of estradiol. We have shown that different estrogens promote cell proliferation in the hippocampus and influence hippocampus-dependent memory in young female rats. We examined the effects of acute and chronic treatment with different estrogens (17β-estradiol, 17α-estradiol, estrone) on hippocampus-dependent memory and neurogenesis, and whether these effects were dependent on previous reproductive experience (pregnancy and mothering) in middle-aged female rats. Acute treatment with all three estrogens increased cell proliferation in middle-aged multiparous female rats but had no effect in middle-aged virgin female rats. Chronic treatment with these estrogens differentially influenced spatial working and reference memory in multiparous and virgin females. Importantly, ovariectomy impaired reference memory in multiparous rats compared to virgin rats. Therefore, the effects of estrogens on learning and memory in middle-aged females are dependent on previous reproductive experience. Findings from this study advance our understanding of how different estrogens mediate cognition in older rats, and may ultimately lead to the development and tailoring of new therapeutic advances in the treatment of symptoms associated with menopause in women.

2:00-4:00 **Oral Session 1:** Psychiatry and Cognition

DIFFERENCES IN FEEDBACK-BASED LEARNING AND PREFRONTAL DOPAMINE UTILIZATION ARE ASSOCIATED WITH VARIATION IN THE DRD4 GENE Groman S.M., Feiler K., Seu E., Woods J.A., and Jentsch J.D. Dept. of Psychology, UCLA The dopamine (DA) D4 receptor (DRD4) gene contains polymorphisms in human and non-human animals, and variation in the number of exon III tandem repeats has been linked to risk for attention deficit/hyperactive disorder and addictions. However, little is known about the functional consequence(s) of this polymorphism on brain chemistry and putative behavioral endophenotypes. To address this, the current study examined the behavioral and biochemical impact of this functional polymorphism in vervet monkeys that carried either a rare (or common) variant similar in structure to that found in humans. Fourteen male monkeys (N=7 monkeys that carried at least one of the rare alleles (DRD4.5), N=7 monkeys that were homozygous for the common allele (DRD4.6)) were trained to acquire, retain and reverse 3-choice discrimination problems. After completing the behavioral assessment, levels of DA and related metabolites in brain homogenates were measured ex vivo with high-pressure liquid chromatography. Carriers of the DRD4.5 allele required more trials to acquire a stimulus-outcome association than those homozygous for the DRD4.6 allele. An analysis of response patterns revealed that these differences were due DRD4.5 carriers having lower sensitivity to positive feedback. Ex vivo measurements found elevated levels of DA utilization in prefrontal regions of DRD4.5 allele carriers. These data provide evidence of the functional impact the DRD4 VNTR has on behavioral and biochemical processes thought to underlie risk for psychiatric disorders and provide a framework for interpreting the phenotypic abnormalities that associate with this polymorphism.

MEASUREMENT OF A SCHIZOPHRENIA ENDOPHENOTPE IN A RODENT MODEL: MISMATCH NEGATIVITY (MMN) TO FREQUENCY DEVIANTS. Hodgson, D.M.; Harms, L.; Nakamura, T.; Fulham, W.R.; Todd, J.; Schall. U.; Michie, P.T. Centre for Translational Neuroscience & Mental Health Research, University of Newcastle, Callaghan. NSW, 2308, Australia. We have previously reported MMN-like responses in epidural recordings to high but not low frequency deviants from awake rats that appear to meet stringent criteria for deviance detection as opposed to differential adaptation of neuronal responses(Nakamura et al.,2011,Frontiers in Psychology, 367). Here we report data from an improved design that

replicates some but not all aspects of the previous findings. Responses were recorded during 4 separate sequences in 9 awake Wistar rats a low (6636 Hz)and a high (8137 Hz) frequency deviant oddball sequence (deviant probability 12.5%), and two control sequences consisting of 8 different frequencies (12.5% probability) with the two deviants of the oddball sequences positioned in the middle of the range. Three components were measured, N22, P37 and a late negative displacement (ND) from 60-100ms. N22 amplitude was larger to deviants than standards in oddball sequences and to the same sounds in control sequences. P37 effects were similar to N22 - larger to oddball deviants for both frequencies. For the late ND, the deviant negative displacement was significant for high frequency stimuli only. Except for P37 which was smaller to deviants in our earlier report, these results confirm our previous findings that it is possible to measure a human equivalent of the MMN, an endophenotype for schizophrenia, in rodents.

IMPAIRED ATTENTION OF DOPAMINE TRANSPORTER (DAT) KNOCKDOWN (KD) MICE IN A CONTINUOUS PERFORMANCE TEST: SIMILARITIES TO PATIENTS WITH BIPOLAR DISORDER (BD). van Enkhuizen, J.1,2; Geyer, M.A.1,3; Young, J.W.1. 1UCSD, La Jolla, CA, USA; 2Utrecht University, Utrecht, Netherlands; 3VA, VISN 22, La Jolla, CA, USA. Impaired attention is apparent in several neuropsychiatric disorders including BD. The continuous performance test (CPT) is widely used to assess attention in humans using target and non-target stimuli. We have described DAT KD mice as a model of BD. To further validate this model, we trained wildtype (WT; n=28) and DAT KD (n=31) mice in the 5-choice serial reaction time task (5CSRTT) and the 5-choice CPT (5C)-CPT. We hypothesized that DAT KD mice would be hyper-responsive in the 5CSRTT but exhibit impaired response control in the 5C-CPT. For the 5CSRTT, mice were trained to holepoke when a stimulus (target) appeared in 1 of 5 locations. The 5C-CPT included non-target stimuli with 5 locations illuminated, requiring inhibition from responding. During initial training in the 5CSRTT, DAT KD mice made more premature responses compared with WT mice ($F(1,57)=25.7$, $p<0.001$), although levels normalized over time. Once stable in the 5CSRTT, DAT KD mice omitted fewer trials than WT mice ($F(1,57)=7.0$, $p<0.05$). When in the 5C-CPT however (requiring the inhibition of responding), omission levels of DAT KD mice became comparable to WT mice but the former responded more often to non-target stimuli ($T=-2.2$, $p<0.05$). With training, WT and DAT KD mice improved their response inhibition to non-target stimuli, but the difference between the two genotypes remained. Mice with reduced DAT expression exhibited hyper-responding in the 5CSRTT as measured by increased premature responses and fewer omissions. When discriminated responding was required by introducing non-target stimuli however, DAT KD mice exhibited difficulty inhibiting from responding while their omissions normalized. Thus, DAT KD mice exhibit impaired attention consistent with BD patients.

SUBSECOND MESOLIMBIC DOPAMINE RELEASE PREDICTS THE AVOIDANCE OF PUNISHMENT Erik B. Oleson, Ronny N. Gentry and Joseph F. Cheer Department of Anatomy and Neurobiology. University of Maryland School of Medicine. Baltimore, MD 21201 USA. The mesolimbic dopamine system is generally considered to be a reward pathway. In support of this theory â€“ when animals are presented with conditioned cues predicting reward availability, midbrain dopamine neurons fire in high frequency bursts. This pattern of neural activity results in subsecond dopamine release events in terminal fields such as the nucleus accumbens, which are thought to promote reward seeking. A number of studies, however, also implicate the mesolimbic dopamine system in behavior requiring the avoidance of punishment. To assess the role of dopamine during the avoidance of punishment, we measured accumbal dopamine concentrations in near real-time using fast-scan cyclic voltammetry while well-trained rats responded in an operant signaled shock avoidance task. In this procedure, a stimulus light was presented as a warning signal while a response lever extended 2s prior to the delivery of recurring foot shocks (0.5s shock every 2s). A lever response at any time within the session produced a 20s safety period signaled by a tone. This design allowed us to assess dopamine signaling during warning signal presentation, safety periods and two distinct behavioral responses (avoidance and escape). We found that dopamine release encodes warning signal presentation and predicts when animals will successfully avoid punishment. Our data, demonstrating that dopamine indiscriminately processes motivationally salient stimuli, supports a growing consensus that the mesolimbic dopamine system is more than merely a reward pathway. Rather, subsecond dopamine signaling might facilitate behavioral orientation in a manner that promotes behavioral adaptation and survival.

DISTINCT NEURAL SUBSTRATES FOR REINFORCEMENT AND PUNISHMENT IN THE STRIATUM. Kravitz, AV; Tye, LD; Kreitzer, AC. Gladstone Institute of Neurological Disease, San Francisco, CA 94158 USA. Reinforcement and punishment are fundamental processes that shape animal learning. Reinforcement maintains or increases, while punishment decreases, the future probability of specific behavior. While the striatum is implicated in both reinforcement and punishment, the specific roles of the two populations of striatal projection neurons are not well understood. We tested the hypothesis that D1-expressing direct pathway medium spiny neurons (dMSNs) mediate reinforcement, while D2-expressing indirect pathway neurons (iMSNs) mediate punishment. We targeted the expression of channelrhodopsin-2 (ChR2) to dMSNs or iMSNs in separate groups of mice, and trained them on an operant task in which they could self-administer laser stimulation to activate each pathway. Within the first 30-minute training session, nave mice that expressed ChR2 in dMSNs exhibited a significant bias towards the laser-paired trigger whereas mice that expressed ChR2 in iMSNs mice exhibited a significant bias away from the laser-paired trigger. This indicates that activation of direct pathway dMSNs is sufficient for reinforcement, while

activation of indirect pathway iMSNs is sufficient for punishment. Our results support our hypothesis, and indicate that these neural populations could be targeted independently to address specific dysfunctions in reinforcement or punishment associated with psychiatric disorders.

MEDIAL SEPTAL-DIAGONAL BAND (MSDB) AND HIPPOCAMPAL INVOLVEMENT IN THE CLASSICALLY CONDITIONED EYEBLINK RESPONSE. Roland, J.J.1; Gluck, M.A.2; Myers, C.1,3; Pang, K.C.H.1,3; Servatius, R.J.1,3; 1SMBI-NJMS, Newark; 2CMBN, Rutgers University, Newark, NJ; 3DVA Medical Center, East Orange, NJ. Human and animal studies have demonstrated that while the hippocampus is not essential for the acquisition of the delay classically conditioned eyeblink response (CCER), total MSDB damage retards learning. Both systemic and intraseptal, but not intrahippocampal, scopolamine retards delay CCER and studies have shown that the effects of intraseptal scopolamine on learning are mediated by the GABAergic system. Therefore, total MSDB lesion and scopolamine disruption of delay CCER learning may be due to effects on the MSDB GABAergic system. In this experiment, the effect of GABAergic MSDB lesions on the acquisition and extinction of delay CCER was examined. Male Sprague-Dawley rats received a GABAergic MSDB lesion (GAT1-Saporin) or sham surgery. Training consisted of delay eyeblink conditioning (500ms tone CS with 10ms periorbital stimulation US) on two consecutive days with 100 trials per day and an average intertrial interval of 30s. On the third day, animals received 40 CS-US paired trials immediately followed by 60 CS-alone extinction trials. Initially, GABAergic lesioned animals displayed impaired acquisition but eventually reached the same asymptotic performance as sham animals. There was also no difference in extinction rate between groups. In the future, we will examine whether MSDB GABAergic lesions affect a CCER task that is hippocampal-dependent (e.g. long-delay) to further assess MSDB-hippocampal involvement in the acquisition and extinction of eyeblink conditioning. Supported by NIH T32-NS051157, NIH R01-NS044373 and the SMBI.

NPAS4 REGULATES A TRANSCRIPTIONAL PROGRAM IN CA3 REQUIRED FOR CONTEXTUAL MEMORY FORMATION. Ramamoorthi, K; Fropf, R; Belfort, GM; Fitzmaurice, HL; McKinney, RM; Neve, RL; Otto, T; Lin, Y. McGovern Institute for Brain Research, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA. The rapid encoding of contextual memory requires the CA3 region of the hippocampus, but the necessary genetic pathways remain unclear. We found that the activity-dependent transcription factor Npas4 regulates a transcriptional program in CA3 that is required for contextual memory formation. Npas4 was specifically expressed in CA3 after contextual learning. Global knockout or selective deletion of Npas4 in CA3 both resulted in impaired contextual memory, and restoration of Npas4 in CA3 was sufficient to reverse the deficit in global knockout mice. By recruiting RNA polymerase II to promoters and enhancers of target genes, Npas4 regulates a learning-specific transcriptional program in CA3 that includes many well-known activity-regulated genes, which suggests that Npas4 is a critical regulator of activity-regulated gene programs and is central to memory formation.

ON MAKING ZEBRAFISH SAD AND ANXIOUS: DEVELOPING NOVEL AQUATIC MODELS OF AFFECTIVE DISORDERS. Kyzar, E.; Roth, A.; Gaikwad, S.; Green, J.; Collins, C.; El-Ounsi, M.; Davis, A.; Pham, M.; Stewart, A.M.; Cachat, J.; Zukowska, Z.; Kalueff, A.V. Dept. of Pharmacology and Neuroscience Program, Tulane University Medical School, New Orleans, LA 70112; Dept. of Integrative Biology and Physiology, University of Minnesota Medical School, Minneapolis, MN 55455, USA. Zebrafish (Danio rerio) are a promising translational animal model with significant physiological homology to humans. Zebrafish are ideal for high-throughput biopsychiatry research due to their low cost, ease of maintenance/genetic manipulations, and robust behavioral responses to various psychotropic drugs. Here, we present innovative high-throughput strategies recently developed in our laboratory for the thorough dissection of zebrafish affective phenotypes. First, we developed and successfully applied 3D mapping of fish exploratory behavior for the analysis of swimming patterns in response to a wide range of anxiolytic and anxiogenic treatments, using the novel tank test (a zebrafish version of rodent open field paradigm) and shoaling tests. We also present novel evidence that depression, in addition to anxiety, can also be modeled in zebrafish. Using reserpine (agent that efficiently depletes brain monoamines, causing depression in humans and rodents), we have examined the acute and long-term alterations in zebrafish behavior and physiology in several paradigms, including the novel tank, open field, lightdark box, social preference and shoaling tests. While reserpine did not evoke overt behavioral effects in these tests acutely, it markedly affected activity after chronic treatment, with robust hypolocomotion resembling motor retardation observed in depression-like states. Collectively, our results suggest that zebrafish are highly sensitive to drugs modulating anxiety and depression-like states, generally paralleling rodent and clinical phenotypes, and strongly supporting the utility of zebrafish models to study a growing spectrum of affective disorders.

2:00-4:00 **Oral Session 2:** Stress and the Environment

APPEASING PHEROMONE MEDIATES SOCIAL BUFFERING OF CONDITIONED FEAR RESPONSES. Kiyokawa, Y.; Takahashi, Y.; Takeuchi, Y.; Mori, Y. Laboratory of Veterinary Ethology, 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 found in male rats that the presence of a conspecific mitigates conditioned fear responses to an auditory conditioned stimulus (CS). Furthermore, we have shown that the social buffering was mediated by signals perceived by the main olfactory system of the subject. Based on these findings, we hypothesized that the olfactory signals from a conspecific is sufficient for the social buffering of conditioned fear responses. To assess this issue, we prepared a clean test box and a scented test box in which a conspecific rat had been kept for three hours to leave scent. Then, fear-conditioned subjects were re-exposed to the CS in one of these two boxes. When the subjects were tested in the clean box, they showed conditioned fear responses with increased Fos expression in the paraventricular nucleus (PVN) and amygdala. In contrast, the olfactory signal from a conspecific blocked conditioned fear responses and increment of Fos expression in the PVN and amygdala. These subjects also showed increased Fos expression in the posterior part of the anterior olfactory nucleus that is a putative linkage site between the main olfactory system and amygdala during the social buffering. These results suggest an existence of appeasing pheromone that mediates social buffering of conditioned fear responses.

BEHAVIOURAL CHANGES OF MALE MICE PERINATALLY EXPOSED TO FLUOXETINE. Kiryanova, V.; Smith, V.M.; Antle, M.C.; Dyck, R.H. Department of Psychology. University of Calgary, Calgary, Alberta, Canada. Fluoxetine (Flx) is the antidepressant most commonly used by pregnant women. Flx can cross the placenta, potentially affecting the fetus by changing neurodevelopmental processes, thereby affecting the expression of behaviours in adulthood. We examined the effects of perinatal Flx exposure on behaviour and circadian rhythms of mice as adults. Dams were treated with Flx from embryonic day 15 to postnatal day 12, and the behaviour of the male offspring was assessed at 6-8 weeks of age. We found that perinatal Flx exposure leads to increased aggression, improved spatial memory, and decreased anxiety. The circadian system was also affected, as Flx treated mice had shorter free running periods, larger phase advances to light during the late subjective night, and smaller phase advances to daytime administration of the serotonin 1A/7 agonist 8-OH-DPAT. Our results suggest that while perinatal exposure to Flx may have long-term effects on neural functioning, these effects are not necessarily detrimental.

NEONATAL PROGRAMMING OF THE AUTONOMIC NERVOUS SYSTEM BY IMMUNOLOGICAL CHALLENGE: IMPLICATIONS FOR ANXIETY. Sominsky, L. 1; Fuller, A.E. 1; Bondarenko, E. 2; Ong, L.K. 3; Clark, V.R. 4; Bobrovskaya, L. 5; Dunkley, P. 3; Nalivaiko, E. 2; Hodgson, D.M. 1. 1.Laboratory of Neuroimmunology, 2.School of Biomedical Sciences and Pharmacy, 3.Medical Biochemistry, The University of Newcastle, Australia. ;4.Human Biology, Brown University, USA; 5.School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia. Neonatal exposure to lipopolysaccharide (LPS) in rats results in persistent changes to the HPA axis and increased anxiety-like behaviours in adulthood. Neonatal immune challenge also alters sympathetic nervous system (SNS) activity, indicated by increased tyrosine hydroxylase (TH) phosphorylation in neonatal adrenals. In the current study, the impact of neonatal LPS exposure on autonomic nervous system (ANS) functioning and its role in anxiety were explored. Autonomic arousal was assessed by the measurement of respiratory rate, using whole-body plethysmography. Wistar rats were treated with either LPS (0.05 mg/kg, i.p.) or saline on postnatal days (PNDs) 3 and 5. The efficacy of treatment was assessed in a subgroup of animals via analysis of TH in the adrenals and plasma corticosterone at 4h, 24h and 48h following treatment on PND5. In adulthood (PND85) respiratory responses to acoustic and light stimuli were recorded in neonatally-treated rats. Animals were placed for one hour in a transparent plexiglass cylinder receiving a constant flow of compressed air, with a piezoelectric sensor attached for assessment of motor activity. Blood was collected at the end of the procedure, to assess plasma corticosterone. Animals were left undisturbed for one week following the respiratory study, after which anxiety-like behaviours were assessed on the elevated plus maze (EPM) and holeboard, and adrenals were collected for the TH analysis. LPS exposure resulted in increased and sustained TH phosphorylation and activity on PND5 ($p<.001$) and increased TH phosphorylation in adulthood ($p<.05$). Elevated plasma corticosterone levels in LPS-treated males were observed on PND5 and in adulthood ($p<.05$). LPS-treated animals had significantly increased respiratory responses to acoustic (80db) and light stimuli($p<.05$). These animals also exhibited increased anxiety-like behaviours ($p<.05$). These data indicate that neonatal immune challenge produces long-term alterations not only to the HPA axis, but also the ANS, and is associated with increased anxiety-like behaviours. Importantly, augmented respiratory responses in LPS-treated animals validate the respiratory rate as a sensitive index of ANS activity and correspond to human data indicating that respiratory dysregulation is characteristic of anxiety and panic disorders.

INDIVIDUALLY VENTILATED CAGE SYSTEMS: A NOVEL HOUSING TYPE CAUSING PROBLEMS FOR MOUSE MODEL RESEARCH. Logge W.[1], Kingham J.[2] and Karl T.[1] [1]Neuroscience Research Australia, Randwick, Australia [2]Garvan Institute of Medical Research, Darlinghurst, Australia. Over recent years, the use of individually ventilated cage (IVC) rack systems in laboratory mouse facilities has increased. Compared to conventional housing, these IVC rack systems provide a very different environment, as cage structures are limited as is external acoustic and olfactory stimulation. The frequency of stressful cage changes is also reduced. Importantly, studies so far have concentrated on the evaluation of behavioural effects of IVC rack systems on wild type-like (WT) mice. Here we present the first data on how different cage systems (IVC versus traditional) impact on the behavioural phenotype of a mouse mutant for the schizophrenia candidate

gene neuregulin 1 (Nrg1 HET mice). Male and female Nrg1 HET mice and their WT littermates (all on pure C57BL/6J background) were bred and raised until postnatal day 90 in either IVC or traditional cage systems. Mice (N = 12/cohort) were then tested in a comprehensive test battery for locomotion, exploration, anxiety, social interaction, cognition and sensorimotor gating. IVC systems suppressed the hyper-locomotive phenotype typical for Nrg1 HET mice kept in traditional cage systems. Furthermore, impairments in fear-associated contextual learning of Nrg1 hypomorphs were modified by IVC housing and sensorimotor gating deficits of Nrg1 HET mice were absent when animals were kept in IVC. Finally, mice in IVC appeared less sensitive to the locomotor-stimulating effects of an acute challenge with 0.25 mg MK-801. Some of the behavioural effects described showed sex-specific characteristics.
Our data reveal for the first time the significant impact of IVC systems on genetic mouse models for brain disorders. Thus, researchers have to consider the breeding and housing conditions of their test cohorts carefully and consider housing condition differences, when comparing data across institutions.

EXERCISE PROTECTS AGAINST APOPTOSIS INDUCED BY CHRONIC RESTRAINT STRESS. Gerecke, K.M., Kolobova, A. and Allen, S. Rhodes College, Dept. of Psychology and Neuroscience Program, Memphis, TN. Chronic restraint stress has been shown to cause deleterious effects on neurons due to the chronic elevation of glucocorticoids (GCs), particularly because GCs make neurons vulnerable to other toxic insults such as oxidative stress and inflammation. Exercise has been shown to protect against this oxidative stress in several models; therefore, we investigated the neuroprotective effects of exercise against the deleterious effects of chronic psychological stress. Mice were kept in either sedentary (standard housing) or exercise (cages with one running wheel per mouse) housing conditions. Chronic psychological stress was induced using chronic restraint stress for 2 hours per day for 14 consecutive days. To assessed neurotoxicity, astrocytosis and expression of the apoptotic protein Bax was quantified 1 and 24 hours following the last stress. Exercise significantly increased the expression of GFAP labeled astrocytes in the hippocampus at 24 hours, suggesting enhanced cellular activity in that region. In addition, expression of Bax was significantly greater in the cortex of sedentary stressed animals at the 1 hour time point; however, stressed mice that had exercised were completely protected, as Bax expression was not significantly greater than controls in those animals. The observed enhanced Bax expression was transient, as there were no differences in expression at the 24 hr time point. Thus, stress acutely increases Bax expression in the cortex. There were no significant changes in Bax expression in the hippocampus at either time point. The expression of markers for oxidative stress is also being assessed. These data indicate that exercise upregulates the adaptive glial response, and protects against chronic psychological stress induced neurotoxicity.

ANXIOGENIC-LIKE EFFECTS INDUCED BY CRF RECEPTOR ACTIVATION WITHIN THE AMYGDALA IN MICE. 1,2Cipriano, A.C., 2Gomes, K.S., 1,2Nunes-de-Souza, R.L. 1Joint Graduate Program in Physiological Sciences UFSCar/UNESP, 2Lab. Pharmacology, School of Pharmaceutical Sciences, Sao Paulo State University, UNESP, Brazil. It is well-known that the amygdala (Amy) plays an important role in the modulation of aversively motivated behavior. This study investigated the effects of pharmacological manipulations of the corticotropin-releasing factor type 1 and type 2 receptors (CRFr1 and CRFr2) on anxiety-like behavior in mice exposed to the elevated plus maze (EPM). Male Swiss mice (n= 5-9/group) received bilateral intra-Amy injections of vehicle, CRF (37.5 or 75pmol/0.1l), CP376395 (1.5 nmol/0.1l), a CRFr1 antagonist, or antisauvagine-30 (1 or 3nmol/0.1l), a CRFr2 antagonist, and 10 min later they were individually placed in the EPM, where the anxiety indices (% open-arm entries and time: %OE and %OT) and locomotor activity (closed arm entries: CE) were recorded during a 5-min session. One-way ANOVA followed by Duncan test revealed that intra-Amy CRF 37.5 and 75 pmol reduced both %OE ($F_{2,21} = 5.11$, $p < 0.02$) and %OT ($F_{2,21} = 3.70$, $p < 0.05$) when compared to the saline control group. Furthermore, CRF 75 pmol increased CE ($F_{2,21} = 4.80$, $p < 0.02$). Intra-Amy injection of the CRFr1 antagonist alone significantly increased %OT ($t(12) = -2.85$, $p < 0.01$) and reduced CE ($t(12) = 2.48$, $p < 0.03$). No effects were observed with intra-Amy antisauvagine-30 on behavior (higher $F_{2,17}$ value = 0.47, $p > 0.60$). Taken together, these results suggest that CRFr1 (but not CRFr2) located within the amygdala plays an important role in the mediation of defensive behavior in mice exposed to the EPM. Financial support: Fapesp, CNPq, PADC/FCF/UNESP

GENETIC ANALYSIS OF CHRONIC MILD STRESS IN MICE. Jones, B. C.1; Lu, L.2; Williams, R. W.2: Cavigelli, S.A.1; Mormede, P.3 1Department of Biobehavioral Health, Penn State University, University Park PA 16802, USA, 2Department of Anatomy and Neurobiolgy, UTHSC, Memphis, TN 38163, USA, 3INRA-Laboratoire de Genetique Cellulaire, 31326 Castanet-Tolosan, FRANCE.There have been repeated efforts to detect and analyze individual differences in stress-related alcohol consumption in animal models. Results have been mixed for reasons that may involve genetic heterogeneity in responses to stress and ethanol, as well as heterogeneity of stressors themselves. Here we have tested the effects of chronic mild stress (CMS) on voluntary ethanol consumption across members of a diverse panel of BXD strains. CMS is a procedure that subjects animals to perturbations in housing, light cycle, social, and exposure to predator-associated stimuli over several weeks. We recently tested the effects of CMS across a family of 15 BXD recombinant inbred strains of mice to evaluate their utility to study the genetic and environmental sources of individual differences in stress-related alcohol consumption and acute stress response. Females from the fifteen strains were subjected to 7 weeks of CMS with alcohol consumption measured before CMS, during the last week of CMS, and during the week following CMS. After post-CMS

alcohol intake measurement and thirty minutes prior to sacrifice, all animals were subjected to 15 min of physical restraint to assess stress response. At sacrifice, blood, thymus, adrenal glands, and the hippocampus were harvested. Thymus and adrenal weights were recorded, and serum was assayed for corticosterone. We find significant genetic variation in all measures. Preliminary quantitative trait locus analysis detected distinct patterns of linkage and several suggestive loci for alcohol consumption and other measures. We found a significant QTL for corticosterone response to acute restraint following CMS. The candidate gene identified is Atxn1. Atxn1 is cis-regulated and its expression in hippocampus correlates r=0.79 with corticosterone response to acute stress (CMS minus control).

WHAT BETWEEN OBSESSIVE-COMPULSIVE (OCD) RITUALS, SPORT RITUALS, AND DAILY MOTOR TASKS? A POSSIBLE ADAPTIVE VALUE FOR SEEMINGLY UNNECESSARY ACTS. Eilam, D.; Keren, H.; Mort, J.; Weiss, O. Dept. of Zoology, Tel-Aviv University, ISRAEL. Repetitive behaviors are common in daily life, constituting a seemingly non-functional component, manifested in excess in sport or compulsive rituals. The similarities and differences among various types of repetitive behavior remain unclear. Here we compared several daily motor tasks (donning a shirt, making coffee, etc.) with obsessive-compulsive disorder (OCD) rituals and sport rituals during basketball free-throws and weightlifiting. Commonality of performance of each act was used as a proxy for functionality: the more individuals perform a specific act, the stronger the inference that this act is functional and relevant to the task at hand. Conversely, the less common the act, the less functional it was for that task. We found that tasks and rituals comprise functional acts performed by all subjects, and non-functional acts performed by only few subjects. Each task or ritual comprised three sections: a pragmatic component (body), which was preceded by a non-pragmatic component (head) and was also followed by a non-pragmatic component (tail). We suggest that seemingly non-functional acts have an adaptive value, with the head serving as a preparatory phase and the tail serving as a confirmatory phase. In sport rituals with definite end and high stakes, the head was long and the tail absent. In everyday tasks, the head and tail were relatively short, whereas OCD rituals featured a relatively long tail. These comparisons revealed that compulsive pathologic rituals share the same structural components with daily tasks but not with sport rituals, suggesting that normal and OCD rituals could develop on different grounds. Moreover, the non-functional content of the tail in OCD, we claim that incompleteness in OCD does not seem to be a product of perfectionism, but more reasonable a result of an over-activation of security motivation or precautionary system.

8:00-10:00 **Poster Session 2:** Pharmacology

57. THE ENDOCANNABINOID SYSTEM CRITICALLY MODULATES THE EXPRESSION OF SOCIAL BEHAVIORS IN ADULT MALE MICE. Pietropaolo S.[1]*, Le Maire V.1*, Bellocchio L.[2], Crusio W.E.[1], Marsicano G.[2] [1]Institut de Neurosciences Cognitives et Intégratives d'Aquitaine, Univ. Bordeaux and CNRS UMR 5287, 33405 Talence, France; [2]Endocannabinoids and Neuroadaptation Group, NeuroCentre Magendie, U862 INSERM, 33077 Bordeaux, France. The endocannabinoid system (ECS) is an important modulator of neuronal functions in the mammalian brain, critically regulating the expression of several behaviors. Recent lines of evidence have suggested a role of the ECS in the control of social behaviors in rodents and humans, although the precise mechanisms involved have not been identified yet. Here, we have combined genetic and pharmacological approaches to assess whether the ECS indeed mediates the expression of adult social behaviors in male laboratory mice. The results clearly showed the involvement of the main endocannabinoid receptor, i.e., CB1, in the control of social investigation and sexual behavior. Furthermore, the behavioral analysis of conditional CB1-KO mice in specific neuronal populations contributed to disentangle the brain mechanisms underlying the complexity of adult social interactions. *Contributed equally.

58. RELATIVELY BRIEF EXPOSURE TO AN ENRICHED ENVIRONMENT EFFECTIVELY BLOCKS SUCROSE SEEKING AND REDUCES SUCROSE SELF-ADMINISTRATION IN RATS. Grimm J.W.; Weber R.; Barnes J.; Koerber J.; Dorsey K.; Deuse L.; Glueck E.; Collins S.; North K. Department of Psychology and Program in Behavioral Neuroscience. Western Washington University. Environmental enrichment dramatically reduces drug and sucrose seeking in rats. In a previous study we reported that 1 month of environmental enrichment (large cage, toys, and social cohorts) effectively blocked cue-induced sucrose seeking. In the present study, we examined whether overnight (22h) enrichment would be as effective. We also examined whether social enrichment (housing with a conspecific only) might account for the environmental enrichment effect. Rats self-administered 10% sucrose (.4 mL/delivery) in daily 2-h sessions wherein each sucrose delivery was accompanied by a tone+light cue. Sucrose seeking was measured after either 1 or 30 days of forced abstinence in a session identical to training but no sucrose was delivered with the cue. In the 22 h preceding, rats either remained singly-housed (control), were housed with another rat in a double-wide cage (social enrichment), or were housed with 2 other rats plus toys in a large habitat (environmental enrichment). Both enrichment conditions markedly reduced sucrose seeking after 1 day of forced abstinence. Sucrose consumption was also reduced in a next-day test. Both enrichment conditions also reduced sucrose seeking when administered after 1 month of forced abstinence, but environmental enrichment was approximately two and a half times as effective as social enrichment. Self-administration in a next-day test was

reduced only in the environmentally-enriched rats. These are the first results we are aware of indicating that a relatively brief exposure to environmental enrichment can nearly abolish sucrose seeking and decrease sucrose self-administration. Social enrichment does not completely account for this effect. Preliminary results with pretreatment of rats immediately prior to enrichment with the corticosterone antagonist mifepristone (20 mg/kg IP) indicate that HPA activation is not responsible for the effects of either social or environmental enrichment.

59. CHRONIC TREATMENT WITH FLUOXETINE IMPAIRS THE FACILITATORY EFFECT PRODUCED BY 5-HT2C RECEPTOR ACTIVATION WITHIN THE DORSAL PERIAQUEDUCTAL GRAY (DPAG) ON ELEVATED PLUS MAZE (EPM)-INDUCED ANTINOCICEPTION IN MICE. 1,4Baptista, D.; 2,4Nunes-de-Souza, R.L.; 1,3,4Canto-de-Souza, A. Dept Psychology-Psycobiology group/UFSCar, Pharmacol, FCF/Unesp/Araraquara, 3Graduate Program in Psychology/UFSCar/So Carlos, 4Joint Graduate Program in Physiological Sciences UFSCar/UNESP, Brazil. This study investigated the effects of chronic treatment with fluoxetine combined with intra-dPAG injection of MK-212 (6-chloro-2-(1-piperazinyl)pyrazine hydrochloride), a preferential 5-HT2C receptor agonist on the EPM open arm confinement-induced antinociception (OAA) in mice. Male Swiss mice (30-35g), (7-10/group) received subcutaneous injection of fluoxetine (5.0 mg/kg) for 21 consecutive days. At 21 day, they were injected with MK-212 (0.63 nmol/0.1l) into the dPAG and then received an intraperitoneal injection of 0.6% acetic acid (nociceptive stimulus). After that, each mouse was confined to either open arm (OA) or enclosed arm (EA) of the EPM for 5 minutes, when the number of writhes was recorded. Three-way ANOVA revealed significant effects only for place of confinement factor [$F(1,85) = 100.21$, $P<0.05$], treatment factor [$F(2,85)= 3.13$, $P<0.05$], place of confinement x pretreatment x treatment interaction [$F(2,85)= 7.97$, $P<0.05$]. Post hoc comparisons (Duncans test) revealed that OA-confined animals showed lower number of writhes than EA group, an effect that was increased by intra-dPAG MK-212 [saline + Vehicle saline + MK-212, $P<0.05$]. Fluoxetine prevented the effects of MK-212 on OAA [Fluoxetine + Vehicle Fluoxetine + MK-212, $P>0.05$]. Chronic treatment with fluoxetine impaired the enhancement of OAA observed in animals receiving intra-dPAG MK-212. Considering that fluoxetine also acts as a 5-HT2C receptor antagonist (Proc. Natl. Acad. Sci., 1997), it is likely that serotonin plays a role facilitating OAA at this receptor subtype within the dPAG in mice. FINANCIAL SUPPORT: UFSCar, FAPESP (2009/17938-6).

60. DIMINISHED NICOTINE BEHAVIORAL SENSITIZATION IN GHRELIN RECEPTOR NULL RATS. Wellman, P.J.; Clifford, P.S.; Rodriguez, J.A. Dept . of Psychology. Texas A&M University, College Station, TX 77843 USA. Ghrelin receptors (GHR-Rs) located on dopamine neurons within the ventral tegmental area modulate the behavioral and reinforcing actions of psychostimulants as well as ethanol. Pharmacological antagonism of GHR-Rs diminishes the development of locomotor sensitization to cocaine as well as to nicotine. Ablation of the GHR-R in rats has been accomplished using N-ethyl-N-nitrosourea (ENU)-driven target-selected mutagenesis (Till et al., 2007; Zan et al., 2003). GHR-R null rats do not overeat in response to systemic injection (i.p.: 15 nmol) of GHR and importantly, these rats exhibit diminished induction of locomotor sensitization (relative to WT rats) to daily injection of cocaine (Clifford et al., 2011). In the present study, we examine the development of locomotor sensitization to daily administration of nicotine (0.4 mg/kg, i.p. per day for 10 days) in wild type (WT) rats and GHR-R null rats (obtained from Transposagen Biopharmaceuticals, Lexington, KY) and we further studied the behavioral phenotype of these rats when fed a high-fat diet. Daily administration of nicotine induced a robust locomotor sensitization in WT rats but was significantly attenuated in GHR-R null rats. Additionally, GHR-R null rats ate significantly fewer calories per day than did WT rats during a 10 day access period to a 33% high-fat diet. These results confirm our earlier observations that nicotine sensitization requires functional GHR-Rs and provide further evidence that ablation of GHR-R function diminishes daily food intake.

61. SOCIAL CONTEXT ENHANCES INITIAL REINFORCING EFFECTS OF NICOTINE. Peartree, N.A.; Chandler, K. N.; Goenagga, J.; Whillock, C. L.; Neisewander, J.L. School of Life Sciences, Arizona State University, Tempe AZ 85287 USA. Research suggests that the more positive the first drug experience, the more likely addiction will develop. Since smoking is initiated in a social setting, it is surprising how little is known about social context effects on acquisition of nicotine self-administration. We examined this issue using conjoined self-administration chambers that had a removable shared wall. Initially, 58 day-old male rats received 2, 30-min habituation sessions/day over 2 consecutive days without levers present. For one of the daily sessions, the wall separating the 2 self-administration chambers was solid, black Plexiglas and for the other session the wall contained wire mesh that allowed limited social contact between rats in their respective chambers. Rats were assigned to training conditions with either the solid or the mesh partition in place throughout 22 subsequent 2-h daily training sessions. Sessions began with presentation of a retractable lever and thereafter each response resulted in simultaneous delivery of nicotine (0.015 mg/kg, IV) and lever retraction for a 20-sec time out. The results demonstrated that during the first session, rats in the social group had higher nicotine intake than the isolated group, but this effect did not persist beyond the first session. The findings suggest that a social context may enhance the initial reinforcing effects of nicotine. Since the

hedonic experience of the initial drug exposure is related to the vulnerability to subsequent addiction, these findings have important implications for substance use disorders.

62. EFFECTS OF KETOGENIC DIET ON MOTOR PERFORMANCE AND BEHAVIOR IN MOUSE MODELS OF ALZHEIMER'S DISEASE. Dominic D'Agostino, Milene Brownlow, Leif Benner, Marcia N. Gordon, Dave Morgan. Byrd Alzheimer's Institute and Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa FL, USA. Interest is emerging in the involvement of dietary manipulations and their pharmacological outcomes in neurodegenerative diseases. Recent studies suggest that Alzheimer's disease (AD) patients display an energy imbalance with brain hypometabolism and/or mitochondrial deficits. Ketogenic diets (KD), widely investigated in the treatment and prevention of seizures, have been suggested to bypass metabolic deficits present in AD brains by providing ketone bodies as an alternative fuel. We investigated the effects of a ketogenic diet on two mouse models of AD. Five-month-old APP/PS1 and Tg4510 mice were kept on either a KD or a control (NIH-31) diet for 3 months, and then submitted to a battery of behavioral tests. Body weight and food intake were monitored throughout the study; blood was collected at 4 weeks and at the end of the study for ketone and glucose assessments. Both APP/PS1 and Tg4510 mice weigh less than nontransgenic mice, despite an increased food intake. Interestingly, the ketogenic diet did not affect these differences in body weight or food consumption. We found that both mouse models of AD presented hyperactivity, compared to nontransgenic, age-matched controls, and that this effect was not prevented by KD. This was measured by both open field and y-maze tests. Mice kept on KD performed significantly better on an endurance trial in the rotarod compared to mice on the control diet. Only a genotype effect was observed in the radial arm water maze test with no significant differences between diets. Brain tissue was collected at the end of behavioral testing and analysis of amyloid, tau and microglial markers are ongoing. This initial data suggests that the metabolic rate of the transgenic mice is considerably greater than the nontransgenic mice and that ketogenic diet may play an important role in motor performance in mice. *Research Supported by: IIRG-10-174448*

63. DEVELOPMENT, TESTING AND THERAPEUTIC APPLICATIONS OF KETONE ESTERS (KE) FOR CNS OXYGEN TOXICITY (CNS-OT); I.E., HYPERBARIC OXYGEN (HBO2)-INDUCED SEIZURES. Dominic D'Agostino[1], Raffaele Pilla[1], Heather Held[1], Carol Landon[1],Csilla Ari[2], Patrick Arnold[3], Jay B Dean[1]. [1]University of South Florida, Tampa, FL, [2]Byrd Alzheimer's Institute, Tampa, FL, [3]Savind Inc, Seymour, IL. We previously described the effect of KEs, non-ionized and pH-neutral precursors of ketone bodies, in delaying seizures in rats breathing HBO at 5 ATA. We hypothesize that oral administration of specific KEs (esters of acetoacetate) will cause a rapid and sustained ketosis that confers neuroprotection against CNS-OT in rats. Male rats (n = 53) were implanted with radio-transmitters to measure diaphragmatic electromyogram (dEMG), ECG and EEG. > 7 days post-surgery, rats were fasted for 12h and administered intragastrically with 1 of 2 KEs (10g/kg), including *R,S*-1,3-butanediol acetoacetate monoester (mKE) or *R,S*-1,3-butanediol acetoacetate diester (dKE) and placed into a hyperbaric chamber and pressurized to 5 ATA oxygen. Latency to seizure (LS) was measured from the beginning of maximum level of HBO until the onset of increased EEG activity and/or tonic-clonic twitches. Blood was drawn from 18 animals and levels of glucose, pH, pO2, pCO2, beta-hydroxybutyrate, acetoacetate and acetone were analyzed. KEs caused a rapid and sustained ketosis and delayed LS by ~227% (mKE) and ~574% (dKE) compared to control (water). In conclusion, KEs mimic the mild therapeutic ketosis produced by ketogenic diets and confer a significant neuroprotective effect by delaying seizures associated with CNS-OT. Supported by Office of Naval Research (ONR) grant #N0000140910244

64. THE USE OF AGOMELATINA IN DRUG ADDICTED PATIENTS WITH PSYCHIATRICS DISORDERS. Pieri, M.C.; Comaschi, A.C. Dept of Mental Health and Drug Dependence Bologna East, Bologna, Italy. Agomelatine is an antidepressant drug that has a melatoninergic agonist action on receptors MT1 and MT2, and an antagonistic action on receptor 5HT/20. Agomelatine has no interactions with the reuptake of monoamines and has no affinity for alpha or beta-adrenergic, histaminergic, cholinergic, dopaminergic and benzodiazepine receptors. We have selected, from the total number of patients treated for heroin, cocaine, alcohol dependence at the SerT East Bologna, a group of 28 patients. We observed this group during a period of 6 months using Ham A, Ham D, VAS for craving substances, VAS for sleep, Quality of Life and the number of hours of sleep and sleep quality. Agomelatine is the first; in a class of melatoninergic drugs that could be very important in the treatment of sleep disorder, anxiety and mood in patients, in particular, with dependence heroin in opioid agonist treatment but also in other dependence. Patients improve the quality of their life and increase the number of hours slept and we can see a decrease in heroin, cocaine and alcohol use.

65. THE EFFECTS OF THE AGONIST THERAPY IN ANXIOUS-DEPRESSED POSITIVE HCV DRUG-ABUSERS TREATED WITH IFN THERAPY. Pieri, M.C.; Comaschi, A.C. Dept of Mental Health and Drug Dependence Bologna East, Bologna, Italy. Addiction presents in three stages: social use, regulated relapse, and compulsive relapse. The abuse of drugs as well as stressful events are able to activate CREB determining an increase in the gene transcription of dynorphins with the consequent increase in the activity of the kappa receptors-mediated. The important general clinical objectives in addiction are: 1) to induce a stable abstinence condition; 2) to prevent or to treat co-morbid conditions; 3) to promote and maintain a global Quality of Life and satisfactory state of health. Buprenorphine, in base to k-receptor antagonism, modify the emotional disregulation, that often appears with depressive symptoms, dysphoria and anxiety as soon as after the use of the first dose of opioids. The block of k receptors allows to buprenorphine to decrease these effects. The normalisation of the stress axis induced by buprenorphine contributes to its stabilizing action on the psycho-physical effect. HCV decreases the mood and a re-balancing with agonist drugs improves also the quality of life. We choose, in the group of patients treated in east drug addiction unit with agonist of opioid and HCV hepatitis, 44 patients: 30 patients taking buprenorphine (68%); 14 patients taking methadone (32%). We divided the patients into 3 subgroups: 1) Patients taking buprenorphine and SSRI (escitalopram); 2) Patients taking methadone and SSRI (escitalopram); and 3) Patients taking buprenorphine. The occupation is an important factor for the success of the treatment. All three subgroups successfully ended the treatment with INF keeping the depression under control only with buprenorphine or in association with SSRI.

66. CB1-RECEPTOR LIGAND PRE-TREATMENT INFLUENCES BEHAVIORAL EFFECTS INDUCED BY REPEATED COCAINE ADMINISTRATIONS IN MARMOSET MONKEYS. Cagni, P.; Netto, G.C.M.; Jesus, A.G.L.; Barros, M. Primate Center and Dept. of Pharmaceutical Sciences, University of Brasilia, DF 70910-900 Brazil. In spite of existing evidence for the involvement of the endocannabinoid system in drug addiction, its precise role in cocaine dependence has yet to be fully established, particularly in non-human primate models. Thus, we analyzed the influence of CB1-receptor ligand pre-treatment on the behavioral effects induced by repeated cocaine administrations in marmoset monkeys (Callithrix penicillata). Each subject was submitted in an open-field apparatus to six 15-min test trials and then two 15-min withdrawal trials, all held 48-h apart. On each test trial, marmosets (n=5/group) were pre-treated with either the CB1-receptor agonist WIN 55-212,2 (0 or 1 mg/kg, ip) or the antagonist AM 251 (0 or 2 mg/kg, ip), followed by a cocaine (5 mg/kg, ip) or saline (ip) injection. Repeated cocaine administrations, compared to saline controls, significantly increased vigilance-related behaviors (scan, glance) by the 3rd trial, while locomotion (distance traveled, number of sections crossed, travel speed) remained unaltered throughout. Pre-treatment with the CB1-receptor antagonist had no effect on its own, yet it immediately potentiated cocaine-induced hypervigilance, with locomotion also remaining constant. On the other hand, pre-treatment with the CB1-receptor agonist induced a significant increase in vigilance, yet had no effect on locomotion or cocaine-induced hypervigilance. Immediate cessation of cocaine and/or CB1-receptor ligand injections rapidly reversed all effects previously detected. Therefore, CB1-receptors seem to modulate the behavioral effects induced by repeatedly-administered cocaine in marmoset monkeys. Supported by CNPq and CAPES.

67. THE ATYPICAL ANTIPSYCHOTIC DRUG ARIPIPRAZOLE ENHANCES COGNITION AFTER EXPERIMENTAL TRAUMATIC BRAIN INJURY. Phelps, T.I.; Cheng, J.P.; Kline, A.E.; Physical Medicine & Rehabilitation, Safar Center for Resuscitation Research, Center for Neuroscience, Center for the Neural Basis of Cognition, and Psychology, University of Pittsburgh, Pittsburgh, PA 15213 Background and aims: Antipsychotic drugs (APDs) are routinely administered after traumatic brain injury (TBI) to reduce agitation and aggression. However, APDs with dopamine2 (D2) receptor antagonist properties (e.g., haloperidol and risperidone) impede cognitive recovery after TBI. Therefore, evaluation of APDs with different mechanisms of action is warranted. Aripiprazole (ARIP) exhibits 5-HT1A and D2 receptor agonist activity, but not D2 antagonism. Studies from our laboratory have shown that pharmacological agents with these properties enhance outcome after TBI. Thus, the aim of the study was to test the hypothesis that ARIP will enhance motor and cognitive performance after TBI. Methods: Adult male rats were anesthetized and received either a cortical impact (2.8 mm depth) or sham injury and then received either ARIP (0.1, 0.5, or 1.0 mg/kg; i.p) or saline VEHicle beginning 24 hours after injury and once daily for 19 days. Motor (beam-balance/walk) and cognitive (Morris water maze) performance was assessed on post-operative days 1-5 and 14-19, respectively. Results: The Sham groups did not differ from one another and thus the data were pooled. No motor differences were revealed among the TBI+VEH and TBI+ARIP groups [$p>0.05$]. No cognitive differences were revealed among the TBI+VEH and the TBI+ARIP (0.5 and 1.0 mg/kg) groups [$p=0.94$ and $p=0.43$]. In contrast, the TBI+ARIP (0.1 mg/kg) group performed better in the water maze vs. the TBI+VEH group [$p=0.0036$] and did not differ from the SHAM controls [$p>0.05$]. Conclusions: No deleterious effects on behavioral outcome were observed with ARIP after TBI. Furthermore, the lower dose of ARIP facilitated spatial learning. The findings support our hypothesis and suggest that 1) ARIP may be a safer alternative for alleviating behavioral disturbances in TBI patients, and 2) may be effective in improving cognitive function. Future studies will explore specific mechanism(s) mediating the beneficial effects of ARIP on recovery after TBI.

68. ELECTROACUPUNCTURE AT JOKSAMNI AND PUNGNYUNG ACUPOINTS ALLEVIATES POLOXAMER 407-INDUCED HYPERLIPIDEMIA THROUGH THE REGULATION OF SREBP-2 EXPRESSION IN RATS. Jinhee Park[1,2], Bombi Lee[1], Chang Shik Yin[1], Insop Shim[1,2], Hye-Jung Lee[1,2], and Dae-Hyun Hahm[1,2*]
[1]*Acupuncture and Meridian Science Research Center, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea.* [2]The Graduate School of Basic Science of Oriental Medicine, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea. The purpose of this study was to examine whether the electoracupuncture stimulation affects the levels of serum lipids such as total cholesterol (TC) and triglyceride (TG) and high-density lipoprotein-cholesterol (HDL-C), and the expression levels of several target proteins in the lipid metabolism such as sterol regulatory element-binding protein-2 (SREBP-2), 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, and low-density lipoprotein receptor (LDLr) in the rats. Intraperitoneal injection of poloxamer 407 (P-407) at dose of 400 mg/kg was performed to induce the experimental acute hyperlipidemia (hypercholesterolemia and hypertriglyceridemia) which lasted more than 72 hour. The electroacupuncture stimulation for 10 min each treatment (2Hz, 0.6mA) was bilaterally performed at both Joksamni (ST36) and Pungnyung (ST40) acupoints totally 3 times with 12 hr-interval starting 30 min before the P-407 injection. Serum levels of TC, TG and HDL-C, and antherogenic index (A.I.) were examined using enzymatic assay kits, and the expression levels of SREBP-2, HMG-CoA reductase and LDLr mRNAs in the liver tissues were analyzed using RT-PCR. While serum lipid levels and the expression levels of TC, TG, SREBP-2, HMG-CoA reductase and LDL-r mRNAs were markedly elevated by P-407 injection, and HDL-C level was decreased. The electroacupuncture stimulation at two acupoints significantly inhibited P-407-elicited changes of these indicators. However the same stimulation at a non-acupoint, located on the base of the tail, did not show inhibition of these changes. These findings demonstrated that the electroacupuncture stimulation showed a significant lipid and protein-lowering activities against P-407-induced hyperlipidemia in the rats, and accordingly might be applicable for preventing hyperlipidemia as an adjunctive therapy (This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MEST) (R11-2005-014)).

69. INHIBITORY EFFECT OF IXERIS DENTATE ON DEVELOPMENT AND EXPRESSION OF BEHAVIORAL LOCOMOTOR SENSTIZATION TO NICOTINE IN RATS Park J.H.1,2; Lee, B.1; Shim, I.1,2; Lee, H.1,2; Hahm, D.H.1,2. 1Acupuncture and Meridian Science Research Center, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea, 2The Graduate School of Basic Science of Oriental Medicine, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea. The aim of this study was to investigate the effects of Ixeris dentate (IXD) extract on the development and expression of nicotine-induced locomotor sensitization in rats and underlying neuronal activation reflected by c-Fos expression in brain tissue. Rats were pretreated with IXD (50 or 100 mg/kg, i.p.) 30 min before a daily injection of nicotine (0.4 mg/kg, i.p.) during an 8-day development phase and then challenged with nicotine (0.4 mg/kg) after a 6-day withdrawal period. Locomoter activity was analyzed daily during the development phase (days 1-8), once after the withdrawal period (day 15) and once on the final day (day 22). In another set of experiments, the same IXD doses were administered once 30 min before nicotine challenge following a 6-day withdrawal period. Daily IXD treatment during the development phase was not effective in blocking nicotine-induced locomotor sensitization in rats. However, a single IXD treatment after the development and withdrawal periods of nicotine sensitization significantly alleviated sensitized locomotor behavior on day 15. These behavioral results were coincident with significant inhibition of nicotine-induced c-Fos expression by IXD treatment in the nucleus accumbens. Taken together, these results indicated that IXD extract pretreatment significantly blocked the expression (i.e., the continuation of addictive behavior), but not the development (i.e., initial neuroadaptation) of nicotine-induced locomotor sensitization in rats. Thus, IXD might be useful in developing new therapies to treat nicotine addiction despite its limited effect on early neuroadaptation during nicotine-dependence (This research was supported by the National Research Foundation of Korea Grant funded by the Korean Government (MEST)(2010-0003678) and the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MEST) (R11-2005-014)).

70. CRF2 RECEPTORS MEDIATE ANXIETY STATES DURING AMPHETAMINE WITHDRAWAL. Jamie L. Scholl, Emily D. Reinbold, Kathryn M. Oliver, Michael J. Watt & Gina L. Forster. Neuroscience Group, Division of Basic Biomedical Sciences, Sanford School of Medicine, University of South Dakota, Vermillion, SD, USA. Increased anxiety-like behaviors are commonly exhibited by rats and humans experiencing withdrawal from psychostimulants. Previous studies have shown that corticotropin-releasing factor (CRF) type 2 receptors are increased in the serotonergic dorsal raphe nucleus (dRN) during amphetamine withdrawal. These experiments determined whether CRF2 receptors in the dRN mediate anxiety states during amphetamine withdrawal. Adult male rats were treated with either amphetamine (2.5 mg/kg, ip) or saline, or were unhandled in their home cages prior to testing. Following 2 weeks withdrawal, rats were infused with 2g ASV-30 or vehicle into the lateral ventricle (icv.) or into the dRN, 20 minutes prior to behavioral testing in the elevated plus maze (EPM). Amphetamine pre-treatment increased anxiety-like behavior in the EPM, which was reversed by both icv. and dRN ASV-30 treatment.

Ventricular, but not dRN, ASV-30 infusion increased anxiety-like behavior in rats pre-treated with saline. To explore this further, western blots were used to measure CRF1 and CRF2 receptor levels in several brain regions that mediate anxiety-like behavior. Saline pre-treatment reduced CRF1 receptor expression in the lateral septum (LS), and both saline and amphetamine pre-treatment reduced CRF1 expression in the central nucleus of the amygdala. There were no treatment effects on CRF2 receptor expression in any of the amygdala and septal regions tested. These results suggest that CRF2 receptor antagonism of saline pre-treated rats unmasked the reduction in LS CRF1 receptors to increase anxiety states. Overall, results show that central CRF2 receptor antagonism reduces anxiety states during amphetamine withdrawal, likely mediated through the dRN. Supported by: NIH NIDA R01 DA019921

71. ETHANOL DOSE GENERALIZATION CURVES FOLLOWING MULTIPLE DISCRIMINATION TRAINING CONDITIONS IN ADOLESCENT AND ADULT RATS. Anderson, RI; Spear, LP. Binghamton University, Binghamton NY 13905. The present study assessed ethanol (EtOH) dose generalization curves in adolescent and adult male Sprague-Dawley rats following training in a conditioned approach discrimination procedure previously only used in adults. One of 3 doses of EtOH (0.75, 1 and 1.25 g/kg, ip) at 2 time points (5 or 30 min post-injection) served as a positive occasion setter for reward delivery following 15-s presentations of two cue lights located on either side of a reward delivery area. Following 10 days of acquisition (2 trials/day) beginning at postnatal day (P) 28 or 70, cycles of maintenance and test sessions were conducted for 15 days. Duration of head entries into the reward delivery area was measured during each 15-s cue presentation and expressed as an elevation score over total head entry duration during the preceding 15 s. For adolescents, the 1.0 g/kg training dose yielded a generalization curve, with the 0.5-1.25 g/kg testing doses eliciting responding higher than saline. The other two training doses did not produce differential responding to the test doses from saline. Adults were differentially responsive to the test doses depending on training dose. Animals trained at 0.75 g/kg responded more for 0.5 and 0.75 than saline, whereas those trained at 1.0 demonstrated increased responding relative to saline at 0.5, 0.75, 1.0 and 1.25. Adults trained with 1.25 g/kg responded more than saline to doses of 0.75 up to the highest test dose of 1.5 g/kg. Despite meeting training criteria at all 3 doses, adolescents may have failed to exhibit differential responding at test after the lower and higher training doses in part due to the emergence of EtOH tolerance and/or toxicity.

72. ADOLESCENT CB1 RECEPTOR AGONISM, BUT NOT ANTAGONISM, ENHANCES ADULT MALE SEXUAL PERFORMANCE. Gorzalka, B.; Lee, T.-Y.T. Dept. of Psychology, University of British Columbia, Vancouver, BC V6T 1Z4 Canada. An extensive literature documents the frequently adverse effects of cannabinoids on adult male reproductive behavior in many species, including humans. However, very little is known about whether adolescent cannabinoid exposure affects male reproductive processes in the long term. Previous work in our laboratory has shown that both CB1 receptor agonism and antagonism during adolescence induces long term neural and behavioral changes in adulthood related to stress reactivity and emotionality. Given that cannabinoids have powerful effects on neuroendocrine regulation, we examined whether adolescent treatment with the CB1 receptor agonist, HU-210, or the CB1 receptor antagonist, AM-251, would influence sexual activity in adulthood. Male rats received escalating doses of HU-210 (0.025, 0.05, and 0.1 mg/kg for 4 days each) or 1 mg/kg AM-251 daily from post-natal days 35-46 and were then left undisturbed. On postnatal day 70, blood samples were collected and males began sexual training at 75 days of age with estrogen/progesterone primed female rats. During training, males were exposed to a sexually receptive female rat twice a week for three consecutive weeks, during which sexual behaviors were scored. Throughout the repeated exposures to female rats, all males progressively increased their sexual proficiency as revealed by significant increases in ejaculations and significant reductions in latencies to engage in sexual activity from the initial sessions to the final session. Surprisingly, males which had received HU-210 during adolescence exhibited enhanced sexual performance as revealed by more ejaculations in fewer sessions with a primed female, and ultimately greater sexual activity across all six sessions than what was seen in the vehicle treated males. On the other hand, adult male sexual behavior was unaffected by AM-251 treatment during adolescence, relative to control males. Moreover, males administered HU-210 during adolescence also exhibited a strong trend to having elevated levels of basal testosterone at day 70, while not demonstrating any difference in testicular weight. Thus, against expectations, adolescent CB1 receptor agonist exposure enhanced male sexual performance in adulthood while adolescent antagonist exposure did not.

73. THE ROLE OF THE BASOLATERAL AMYGDALA IN CONDITIONED CUE-INDUCED ALTERATIONS IN ALCOHOL-SEEKING G.A. Deehan Jr.; S. R. Hauser; E.A. Engleman; Z-M. Ding; W.J. McBride; Z.A. Rodd. Indiana University School of Medicine, Dept. of Psychiatry, Indianapolis IN, 46202. Exposure to stimuli (conditioned cues) previously associated with drug availability can elicit drug-seeking behaviors thereby increasing the likelihood of drug relapse. Conditioned cues can be positively (CS+) or negatively (CS-) associated with the availability of a reinforcer and neurobiological data indicate that presentation of a CS+, associated with alcohol (EtOH) access, increased c-Fos+ neurons in the basolateral amygdala (BLA). Therefore, the current experiments examined the effects of the pharmacological silencing of the BLA (GABA agents) on conditioned cue-induced

EtOH-seeking and the effect of conditioned cue presentation on glutamate (GLU) levels in the BLA. Alcohol-preferring (P) rats were trained to self-administer EtOH in an operant chamber in which a CS+ or CS- signaled the availability or absence of EtOH respectively. A CS0 was presented in neutral environment with no association to EtOH access. Pharmacological silencing of the BLA was effective at blocking the ability of the CS+ to enhance EtOH-seeking, but failed to prevent the expression of EtOH-seeking or the ability of the CS- to reduce EtOH-seeking. Microdialysis data indicated that presentation of the CS- decreased, while presentation of the CS+ increased, GLU levels in the BLA. The CS0 did not significantly alter GLU levels in the BLA. Overall, the data suggest that the BLA can mediate the effects of conditioned cues on drug-seeking, but not the expression of drug-seeking, and that alterations in GLU signaling in the BLA may represent an underlying neurological mechanism contributing to drug craving and relapse.

74. THE GALANIN-3 RECEPTOR ANTAGONIST, SNAP 37889, REDUCES BREAKPOINT AND CUE-INDUCED RELAPSE TO ETHANOL IN ALCOHOL-PREFERRING RATS Belinda L. Ash1, Sammi Tsegay2, Spencer J. Williams2, Andrew J. Lawrence3,4 & Elvan Djouma1 1Department of Human Biosciences, Faculty of Health Sciences, La Trobe University, Bundoora, Victoria, Australia 2Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne, Parkville, Victoria, Australia 3Florey Neuroscience Institutes, Parkville, Victoria, Australia 4Melbourne Brain Centre, University of Melbourne, Parkville, Victoria, Australia The galanin-3 receptor (GALR3) subtype has been identified as having a role in addiction. We have previously shown that the selective GALR3 antagonist, SNAP 37889, reduces voluntary alcohol consumption in the iP (alcohol-preferring) rat. Therefore, the present study firstly aimed to investigate the effect of GALR3 blockade on the breakpoint at which rats cease responding for ethanol. Secondly, the potential of GALR3 as a therapeutic target in the prevention of relapse was investigated in response to drug related cues. iP rats were trained to lever press for water and a 10% (v/v) ethanol solution. Rewards were delivered on a progressive ratio schedule where the response requirement increased by one additional lever press to receive each subsequent reward. Once a base level breakpoint was established, rats were pre-treated with SNAP 37889 (30mg/kg, i.p.) or vehicle prior to the operant session and the breakpoint for this session was recorded. The same cohort of rats was then used to investigate the effect of SNAP 37889 on cue-induced re-instatement for ethanol. Following a lengthy period of extinction, cues that had previously been associated with the delivery of alcohol were re-introduced in to the chambers for a single re-instatement session. Rats were pre-treated with SNAP 37889 (30mg/kg, i.p.) or vehicle prior to this session and the number of rewards made during the operant session was recorded. Administration of SNAP 37889 (30 mg/kg, i.p.) prior to the progressive ratio operant session significantly reduced the breakpoint for ethanol. SNAP 37889 was also found to successfully reduce cue-induced re-instatement when compared with the extinction sessions and vehicle treatment group. Collectively, results from the current study provide further evidence that GALR3 antagonism reduces the motivational drive to consume alcohol and suggests that GALR3 may be implicated in cue-induced relapse of drug-seeking behaviour.

75. CAN THE COMBINATION OF MORPHINE AND THE NON-OPIOID ANALGESIC FLUPIRTINE, REDUCE MORPHINE'S ABUSE POTENTIAL? Elkman, L.; Goodchild, C.S.; Kolosov A.; Broadbear, J.H. School of Psychology and Psychiatry, Monash University, Clayton, VIC 3800, Australia. Morphine is an opioid drug used widely in the treatment of severe pain. Although it is effective for treating many pain states, its analgesic benefits are coupled with addictive properties that make it liable to abuse. A promising approach for improving the utility and reducing the abuse liability of opioids is to combine a lower opioid dose with non-opioid analgesics, thus maintaining an optimal level of analgesia with reduced adverse effects. Our aim was to assess whether the reinforcing effects of morphine differ when morphine and flupirtine when given alone and in combination. 80 male Wistar rats were evaluated using Conditioned Place Preference (CPP), in which they learned to associate one distinctive environment with the effects experienced following drug treatment, and another environment with the absence of the drug. The doses of morphine and flupirtine chosen for evaluation are known to be efficacious in producing analgesia in rat chronic pain models. The results showed that intraperitoneally administered morphine produced CPP at two doses (4 and 8mg/kg). Flupirtine (10 and 20mg/kg) did not cause significant CPP, suggesting that the non-opioid has a low abuse potential. Drug co-administration (2mg/kg morphine+ 10mg/kg flupirtine and 4mg/kg morphine + 20mg/kg flupirtine) did not result in CPP, suggesting that the addition of flupirtine reduced morphine CPP. This study provides preliminary evidence that combining low-dose morphine with flupirtine, at doses which have potent analgesic effects, may confer less abuse potential than the use of similarly analgesic doses of morphine alone. The development and utilization of combination analgesics containing flupirtine and low-dose morphine may be an effective strategy for reducing the potential for opioid abuse.

76. DEVELOPMENT OF A DISCRETE TRIALS TASK TO ASSESS SEROTONERGIC MODULATION ON INTERVAL TIMING IN MICE. **Halberstadt, AL;** Young, JW; Geyer, MA. University of California San Diego, La Jolla, CA. The perception of time is essential for survival and is required for the precise organization of sequences of activity as well as the anticipation of behavioral outcomes and future events. One form of temporal perception is interval timing, which refers to the discrimination of durations, typically in the seconds to minutes range. A variety of reports indicate that schizophrenia is associated with timing deficits, and it has been proposed that impaired temporal processing is a core deficit of schizophrenia that contributes to cognitive dysfunction, hallucinations, and inappropriate behavior. There is also evidence that the serotonergic system, which is believed to play a role in the neuropathology of schizophrenia, regulates temporal perception and timing behavior. Unfortunately, very little is known about the neural substrate(s) that are involved in serotonergic modulation of timing. We have developed a discrete trials interval timing task in mice that can be used to elucidate the neural and receptor mechanisms underlying the modulation of interval timing by both endogenous serotonin and hallucinogenic drugs. In the discrete trials task, a lamp is illuminated for a variable duration, and then two levers are presented. Responding on lever A is reinforced if the stimulus duration is shorter than 6.5 s, and responding on lever B is reinforced if the stimulus duration is longer than 6.5 s. C57BL/6J mice were trained to discriminate between short (2.5 and 5.0 s) and long (8 and 10.5 s) stimulus durations, and then challenged with a wider range of test stimuli (2.5, 3.75, 5.0, 6.5, 8.0, 9.25, and 10.5 s). We also examined whether the 5-HT2A/2C agonist 2,5-dimethoxy-4-iodoamphetamine (DOI), a serotonergic hallucinogen, alters performance of the task. We found that mice can learn to reliably discriminate between the short and long duration training stimuli, responding on the correct lever >80% of the time for the two extreme stimulus durations (2.5 and 10.5 s). Challenge studies demonstrated that the proportion lever B responding increased with the stimulus duration, and showed that administration of DOI (0.25-1 mg/kg, IP) altered interval timing. Our goal is to use this behavioral paradigm to investigate the regulation of interval timing by the serotonergic system, and to determine the neural site(s) involved in this effect. It is possible that the disruption of temporal perception induced by hallucinogens could be developed as an animal model relevant to schizophrenia, potentially facilitating the development of novel agents with antipsychotic activity.

77. THE EFFECTS OF GENE KNOCKOUT OF CADHERIN 13 (CDH13) ON NICOTINE CONSUMPTION Hall, F.S.; Arnold, E.R.; Deshmukh, A.A.; Perona, M.T.G.; Drgonova, J.1; Ranscht, B.; Uhl, G.R. Molec. Neurobiol. Branch, NIDA-IRP, Baltimore, MD, USA; Sanford-Burnham Med. Res. Inst., La Jolla, CA, USA The gene for the cell adhesion molecule Cadherin 13 (CDH13) has been repeatedly associated with drug addiction in genome wide association studies (GWAS). More recently GWAS have also associated CDH13 with both nicotine cessation and attention deficit hyperactivity disorder (ADHD). Nicotine use is especially high, nearly twice that in the general population in individuals with a diagnosis of ADHD, and even higher in individuals with schizophrenia. This suggests the possibility that the associations of CDH13 with nicotine addiction, nicotine cessation and ADHD may share a common basis. To assess the potential role of CDH13 in nicotine addiction, nicotine consumption was examined in CDH13 KO (+/+, +/- and -/-) mice using a home-cage two-bottle test. Mice were presented with a bottle containing nicotine solution (5, 10, 20, 40, 80 mg/L, concentration increased every 2 days) and a bottle containing water. In +/+ mice high nicotine concentrations were aversive, so that with increasing concentrations preference for nicotine solutions was reduced and consumption (mg/kg/day) leveled off. CDH13 -/- mice were resistant to these effects so that more nicotine was consumed compared to +/+ mice at high nicotine concentrations. One of the consequences of such a reduction in nicotine aversiveness at high concentrations might be to expand the range of tolerable concentrations. Such a circumstance has been suggested for some other genes associated with nicotine addiction. This may make self-medication more likely, such as appears to be the case for nicotine use in ADHD and schizophrenia. Thus, further studies are underway to examine behavioral phenotypes associated with cognitive impairments observed in ADHD and schizophrenia. (Support: NIDA-IRP)

78. THE EFFECT OF COCAINE ON ROTOROD PERFORMANCE IN MALE AND FEMALE C57BL/6J MICE. Heyser, C.J.; Vishnevetsky, D.; Berten, S. Franklin & Marshall College, Dept of Psychology, Lancaster, PA 17604. Surprisingly, there is little research examining the effect of cocaine on motor learning. Given that changes in motor performance can confound behavioral assays of learning and memory a direct assessment of cocaine on motor learning seems warranted. The present study was conducted to examine the effect of cocaine exposure on motor learning using an accelerating rotorod test. Adult male and female C57BL/6J mice were given 3 trials per day, with a 30 sec intertrial interval. In the first phase of the experiment, mice were given an injection of either saline or cocaine (10 mg/kg, i.p.) 10 min prior to the start of each days testing for 5 consecutive days. In the second phase, half the animals continued to receive saline or cocaine prior to testing, while the other half were switched from saline to cocaine or from cocaine to saline (an A-B crossover design) and then tested for an additional 5 days. The latency to fall was recorded for each trial. There were no differences between saline- or cocaine-treated mice on the first day of testing. All mice exhibited motor learning as evidenced by an increased latency to fall across days. Animals that received cocaine injections exhibited significantly longer latencies to fall on days 2 5 compared to

those mice receiving saline. This enhanced performance was lost when cocaine-injected animals were switched to saline on day 6. The pattern of results was similar for male and female mice. It is hypothesized that the performance enhancing effects of cocaine are the due to increased stamina and/or psychomotor stimulation and not the result of increased motor learning as increased performance was lost when the drug was discontinued.

79. *IN VIVO* CHARACTERISATION OF SOC-1: A NOVEL PROSOCIAL COMPOUND. Hicks, C.[1]; Bowen, M.T.[1]; Ramos, L.[1]; Jorgensen, W.[2]; Kassiou, M.[2]; Hunt, G.E.[3]; McGregor, I.S.[1]. [1]School of Psychology, Brennan MacCallum Building, University of Sydney, Sydney, N.S.W. 2006, Australia; [2]Brain and Mind Research Institute, University of Sydney; [3]Discipline of Psychiatry, Sydney Medical School, University of Sydney, Concord Hospital, Concord, N.S.W. 2139, Australia. Psychiatric disorders (e.g. autism) may benefit through the development of compounds that act to stimulate social behaviour. Accordingly, our drug discovery program is focused on compounds that modulate brain oxytocin, vasopressin and neurosteroid systems to facilitate social behaviour in rodents. SOC-1 evolved from our program producing non-peptide compounds that interact with brain oxytocin receptors. SOC-1 (5 mg/kg, IP) caused similar brain Fos expression to the non-peptide oxytocin agonist/vasopressin antagonist WAY 267,464 (100 mg/kg, IP) and oxytocin itself (1 mg/kg, IP), with pronounced expression in the supraoptic and paraventricular hypothalamic nuclei, lateral parabrachial nucleus and nucleus of the solitary tract, and greater activation in the lateral septal nucleus and medial preoptic area. In the 'classic' social interaction test, SOC-1 (5 mg/kg) increased the time rats spent lying adjacent to a novel conspecific. The same dose also increased the time rats spent interacting with a caged live rat, relative to a caged dummy rat, in a social preference paradigm. These prosocial effects appeared to be independent of a general anxiolytic effect as SOC-1 failed to affect behaviour on the elevated plus-maze. Biotelemetry studies in rats showed that SOC-1 (5 mg/kg) had a strong hypothermic effect, similar to oxytocin (1 mg/kg), but unlike oxytocin did not cause reductions in heart rate. SOC-1 also reversed the hyperthermia seen during acute social interaction. Pretreatment with an oxytocin receptor antagonist (Pfizer Compound 25, 10 mg/kg, IP), vasopressin 1a receptor antagonist (SR 49059, 10 mg/kg, IP) or a benzodiazepine antagonist (flumazenil, 10 mg/kg, IP) did not prevent the hypothermic effects of SOC-1. Ongoing receptor binding studies suggest that SOC-1 actually has low affinity for oxytocin and vasopressin receptors and may therefore be acting on an upstream target to indirectly modulate these systems. Overall, SOC-1 is a novel prosocial compound with an oxytocin-like profile of brain activation and body temperature. It represents a novel research tool for examining in vivo the mechanisms and neural circuitry underlying social behaviour.

80. SHORT-TERM AND ENDURING BEHAVIORAL EFFECTS OF CHRONIC RISPERIDONE IN THE ADOLESCENT AND ADULT RAT Karanges, E.; Caminer, A.; McGregor, I.S. School of Psychology, The University of Sydney, Australia. Second-generation antipsychotics are frequently prescribed to adolescents, yet their safety has not been convincingly demonstrated in this population. Atypical antipsychotics act on neurotransmitter systems undergoing development during adolescence; hence the long-term consequences of these treatment practices are of particular concern. Here we investigated the immediate and long-term behavioral effects of chronic (28-day) risperidone (RISP) administration during rat adolescence or adulthood. Female Sprague-Dawley rats were treated concurrently with RISP (2.5 mg/kg/day in drinking water) and a high-fat diet during adolescence (P28-56) or early adulthood (P66-94). Rats were examined for on-drug changes in weight, blood glucose, anxiety-like behavior (open field (OF), social interaction), locomotor activity, and cognition (novel object recognition/location (NOR/NOL)). This test battery was repeated 6-8 weeks after drug cessation to explore lasting effects of prior drug exposure. Behavioral inhibition was examined in a task requiring rats to perform a 3s nose poke for 2% sucrose solution. Performance was assessed in cued (poke exceeding 3s is signaled with a tone) and uncued (unsignaled) probe sessions. During drug administration, RISP treatment was associated with decreased OF exploration in adolescent rats only; while NOR/NOL deficits were apparent only in treated adults. Locomotor activity, social interaction and object investigation were reduced in both RISP-treated cohorts. A trend to increased blood glucose was observed in treated rats despite no change in body weight. RISP cessation normalized on-drug changes in anxiety, locomotor activity, cognition and blood glucose. However, reductions in social interaction persisted. Moreover, rats treated with RISP during adolescence, but not adulthood, performed more nose pokes of insufficient duration during the uncued probe session, indicating possible impairments in time estimation and/or impulsivity. Consequently, ongoing work is assessing the effects of chronic exposure to RISP during adolescence on the maturation of the dopamine system and higher cortical areas.

81. ANALYSIS BY AUTORADIOGRAPHY FOLLOWING MEPHEDRONE (4-METHYLMETHCATHINONE) INDUCED SELF ADMINISTRATION BEHAVIOUR IN ADOLESCENT RATS. Craig P. Motbey1, Emily Karanges1, Nadine Apetz1, Paul D. Callaghan2, Kelly Clemens3, Jennifer Cornish3, Iain S. McGregor1. Mephedrone (4-methylmethcathinone, MMC) is a novel recreational drug that has rapidly increased in popularity in recent years. In this study, we compared MMC-driven self-administration behaviour in male adolescent Sprague-Dawley rats with the well-characterised stimulant methamphetamine (METH). A variety of doses and schedules

were used in order to develop dose-response curves for both fixed- and progressive-ratio reward schedules before a final stage of maximum-dosage drug access. During this final period, MMC rats self-administered a mean of 31.3 mg/kg/day MMC, while METH rats self-administered a mean of 4 mg/kg/day METH. Three days after the completion of dosing, brains were analysed using OX-42 immunohistochemistry and FluoroJade-C fluorescence microscopy. In addition, autoradiographic analyses measured potential changes in levels of serotonin and dopamine transporters (SERT, DAT) as well as the inflammation marker TSPO. MMC was found to promote extremely vigorous self administration behaviour. Mean response levels for MMC under progressive ratio testing more than doubled those found for METH, with the most strongly responding animals continuing to work for MMC until the response/reward ratio passed 400. To the best of the authors knowledge, this rate of responding exceeds that found with any other drug of abuse. Under an FR1 schedule, peak responding for MMC was found at a dose of 0.1 mg/kg/infusion, while the highest response rate for METH was found at a dose of 0.01 mg/kg/infusion. During the progressive ratio test, MMC responding peaked at 1 mg/kg/infusion while the METH response was greatest at 0.3 mg/kg/infusion. All treatment groups tolerated dosage without mortality or apparent morbidity, although MMC animals gained less weight relative to other groups. No significant changes were observed on any of the neurological measures conducted. Although MMC does not appear to easily induce neurotoxicity, these findings suggest that MMC has an extremely high potential for inducing uncontrolled use and addiction. 1School of Psychology, University of Sydney 2Australian Nuclear Science and Technology Organisation 3Department of Psychology, Macquarie University

82. PROGESTERONE DECREASES COCAINE CHOICE IN FEMALE RATS. Kippin, TE, Kerstetter, KA, Carr AE, Lee JI, Togal VL. University of California, Santa Barbara, CA. Sex differences in cocaine dependence indicate that women relative to men exhibit a more severe addiction prolife. In animal experiments, female rats exhibit higher operant responding for cocaine reinforcement relative to males which varies across the estrous cycle and can be modulated by estrogen and progesterone. Recently, we have shown that female rats will choose cocaine reinforcement over food reinforcement more frequently than will males and that this difference is estrogen dependent. In the present study, we extend our analysis by examining the impact of progesterone on the choice between cocaine and food reinforcement in intact female rats. Intact female Sprague-Dawley rats were trained on a FI:20s schedule to respond on distinct levers for food (2 x 45 mg pellets) or cocaine (1.0 mg/kg IV) during separate daily sessions and then were allowed to choose between the two reinforcers on 25 trials per daily sessions. Throughout training and testing one group of females received daily progesterone (0.5 mg) and another received vehicle (0.1 ml of peanut oil). All rats acquired operant responding for both food and for cocaine at approximately equivalent rates. During choice tests, females treated with vehicle exhibited a preference for cocaine over food (selecting cocaine on > 80% of choice trials) whereas, females treated with progesterone exhibited a preference for food over cocaine. These data replicate our previous finding that females exhibit a high preference for cocaine over food reinforcement and, further, indicate that progesterone can suppress cocaine choice in females. However, it remains unclear as to whether these effects are due to the genomic effects of progesterone or to the neuromodualtory effects of progesterone metabolites. Supported by NIDA (1R01DA027525).

83. THE ROLE OF MIDBRAIN DOPAMINE IN PREDICTIVE FEAR LEARNING. Li, S.; McNally, G.P. School of Psychology. University of New South Wales, Sydney, NSW 2052 Australia. The firing of midbrain dopamine neurons during appetitive learning tasks conforms to the assumptions of associative learning theories. Some dopamine neurons also respond to aversive USs and CSs predictive of such USs. However, the role of dopamine in predictive fear learning, and its relationship to amygdala mechanisms for fear learning, remains unclear. Here we studied the role of dopamine in predictive fear learning using blocking designs and assessing fear via conditioned freezing and conditioned suppression. Blocking involved training rats to fear conditioned stimulus (CS) A in Stage I via pairings with shock. In Stage II, rats received pairings of CSA+CSB and shock. Blocking was shown by less fear to CSB than a control group that received Stage II, but not Stage I, training. Whilst microinjections of the D2 antagonist sulpiride into the VTA prior to Stage II conditioning prevented blocking using freezing as a measure of fear, they failed to do so when fear was assessed via conditioned suppression. Intra-VTA microinjections of the kappa opioid receptor antagonist nor-BNI also failed to prevent blocking as assessed via conditioned suppression. Additional experiments studying the effects of dopamine receptor antagonism in terminal regions, namely the amygdala, nucleus accumbens and prefrontal cortex will be reported.

84. CONTEXT-INDUCED RELAPSE TO ALCOHOL SEEKING AFTER PUNISHMENT IN A RAT MODEL. Marchant, N. J.; Khuc, T. N.; Bonci, A.; Shaham, Y. Behavioral Neuroscience Research Branch, NIDA, Baltimore, MD, USA. Rationale and objective: Many studies have demonstrated context-induced reinstatement of alcohol seeking after its suppression by extinction of the alcohol-reinforced responding. However, it is unknown whether contexts can provoke relapse to alcohol seeking that is suppressed by punishment. This is an important question because abstinence in humans typically occurs because of the increasing negative consequences associated with

excessive alcohol use. Methods: Two groups of alcohol-preferring P rats were given 12 24-hr sessions of home cage intermittent access to 20% ethanol. Next, they were trained every other day in 2-h sessions to self-administer 20% ethanol (0.1 ml/reward delivery) in one context (context A); the final reinforcement schedule was VI30. Subsequently, all rats continued to self-administer alcohol in the punishment context (context B). For one group, 50% of alcohol deliveries were punished by footshock (0.4-0.9 mA, 0.5-s) for 3-7 sessions until alcohol-reinforced responding less than 20 responses; the other group received no shocks. All rats were then tested for alcohol seeking in 30-min extinction tests in both contexts. Results: We found that alcohol seeking recovered on test in context A. In contrast, alcohol seeking remained suppressed on test in context B. Interestingly, responding in context A on test did not differ between groups Punished and Unpunished. Conclusions: Our data indicate that the effect of punishment on alcohol seeking is context specific. We propose that the punishment-context relapse model can be used to explore mechanisms of relapse after conditions that more closely mimic abstinence promotion in humans.

85. COMBINATIONS OF SKF 38393 WITH MEMANTINE DO NOT HAVE AN ADDITIVE EFFECT TO REDUCE THE VOLITIONAL CONSUMPTION OF ETHANOL BY THE MYERS MHEP RAT. McMillen, B. A.; Lommatzsch, C.L.; Sayonh, M.J.; Williams, H.L. Brody School of Medicine, Greenville, NC. Dopamine- and cAMP-regulated neuronal phosphoprotein (DARPP-32) is an important protein phosphatase-1 inhibitor in neurons that express the PPP1R1B gene. Stimulation of the dopamine D1 receptor to increase intraneuronal levels of cAMP increases PKA activity, lead to phosphorylation of DARPP-32 at the threonine 34 and 75 positions and activate the protein. If intracellular Ca2+ is increased, then PP2B, or calcineurin, activity increases and the phosphates will be removed. This balance of phosphorylation control suggests that a D1 receptor agonist and a NMDA glutamate receptor antagonist should have additive or synergistic actions to increase activated DARPP-32 and consequent behavioral effects. This hypothesis was tested in a volitional consumption of ethanol model. Male Myers mHEP rats (N=9, F33 generation) were screened for high consumption of ethanol solutions, 3% to 30% (v/v) over 10 days, and the concentration that resulted in the greatest consumption with a proportion of ethanol solution to tap water closest to 0.5 chosen as the fixed concentration for each rat. A 3-day baseline period was followed by 3-days of twice daily injections of drug or vehicle and then a 3-day post-treatment period. Consumption of fluids and food along with body weight were measured daily. Vehicle, the D1 agonist SKF 38393, the non-competitive NMDA receptor antagonist memantine, or their combination were injected 2 hr before and after lights out. During treatment with 5.0 mg/kg SKF, consumption of ethanol declined by 27.3% and during 10 mg/kg memantine treatment by 39.8%. When the two drugs were combined, consumption declined by 48.2% and the proportion declined by 17%. However, the consumption of food also declined by 36.6%. The latter result indicates that an anorexic action rather than an effect specifically for ethanol occurred. The lack of additivity and specificity suggests that the hypothesis may not be correct. The interaction of these different receptor systems with intraneuronal signaling and behaviors needs to be studied further.

86. DEVELOPMENTAL FLUOXETINE EXPOSURE, BUT NOT PRENATAL STRESS, DEMASCULINIZES SEXUAL BEHAVIOR IN MALES, BUT HAS NO EFFECT ON SEXUAL BEHAVIOR IN FEMALES. Rayen I.; Charlier T.D.; Balthazart J.; Steinbusch H.W.M.; Pawluski J.L. School for Mental Health and Neuroscience, Maastricht University, Universiteitssingel 50, 6229 ER Maastricht, The Netherlands; University of Lige, GIGA-Neurosciences, 1 avenue de l'Hpital (Bat. B36), B-4000 Lige, Belgium; EURON, European Graduate School for Neuroscience.Depression during pregnancy and postpartum is a significant health problem and affects up to 20% of women. While selective serotonin reuptake inhibitor (SSRIs) medications are commonly used for treatment of maternal depression, the combined effect of maternal depression and perinatal SSRI exposure on offspring development is poorly investigated. Here, our aim was to determine the role of exposure to fluoxetine during development on sexual behavior in offspring using a rodent model of maternal adversity. To do this, gestationally stressed and non-stressed Sprague-Dawley rat dams were chronically treated throughout lactation with either fluoxetine (5mg/kg/day) or vehicle beginning on postnatal day 1 (P1). Four groups of male and female offspring were obtained: 1) prenatal stress + fluoxetine, 2) prenatal stress + vehicle, 3) fluoxetine alone, and 4) vehicle alone. In Experiment 1, we assessed ano-genital (AG) distance in juvenile male and female offspring. In Experiment 2, adult male and female offspring were tested to assess the effect of developmental fluoxetine exposure and prenatal stress on sexual behavior. Maternal fluoxetine exposure significantly decreased AG distance in juvenile male offspring, regardless of prenatal stress. In adult male offspring, maternal fluoxetine treatment, regardless of exposure to prenatal stress, significantly increased the latency to first intromission, decreased the number of intromissions and tended to increase the latency to the first ejaculation. In adult female offspring, preliminary results show that prenatal stress, regardless of maternal fluoxetine treatment, significantly increased the female lordosis response to a male mount and decreased the number of rejections by the female. These results provide important evidence for the long-term impact of maternal adversity and maternal fluoxetine use on the development of fundamental physiological systems in male and female offspring. Further work will investigate the neurobiological plasticity underlying these behavioral effects.

87. EFFECTS OF SHORT-TERM TREATMENT WITH LOW DOSE OF FLUOXETINE ON THE EXTRACELLULAR LEVELS OF SEROTONIN IN THE PERIAQUEDUCTAL GRAY MATTER OF FEMALE RATS IN LATE DIESTRUS. Santos JM; Carvalho MC; Lovick TA; Brandao ML. During late diestrus (LD) in female rats, the rapid fall in brain allopregnanolone (ALLO) concentration triggers for neuronal changes that lead to increased excitability of the periaqueductal gray matter (PAG). In males, it has been showed that fluoxetine (FLX), a well-known SSRI, can enhance the brain content of ALLO at low doses by a mechanism independent from 5-HT reuptake inhibition. Behavioral experiments have showed that short-term treatment with FLX (1.75 mg/kg) prevented the development of stress-induced hyperalgesia and the decrease in threshold for evoking fear-like responses in the PAG of female rats in LD. In this study we have investigated whether short-term administration of low dose of FLX affects 5-HT efflux in the PAG, measured by in-vivo microdialysis coupled to HPLC. Female Wistar rats were treated with 2 i.p. injections of saline or FLX (1.75 mg/kg FLX1.75 - or 10 mg/kg FLX10). The first injection was given around 6 pm in the day previous to the experiment when rats were in early diestrus phase of the cycle. The second one was given during microdialysis next day (around 11 am) when they were in LD. The results indicate that treatment with FLX 1.75 did not change 5-HT release in the PAG whereas treatment with FLX10 decreased the extracellular levels of 5-HT. Although preliminary, these results suggest that the effects of low dose of FLX on behavior take place by a mechanism independent from serotonergic system. FLX might slows the kinetics of the rapid fall in ALLO by raising its concentration during LD, thus removing the trigger for the neuronal changes that lead to increased excitability of the PAG.

88. DEVELOPMENTAL METHAMPHETAMINE EXPOSURE ALTERS NEUROTRANSMITTER SYSTEMS: POTENTIAL NEUROBIOLOGICAL MECHANISMS OF LEARNING AND MEMORY DEFICITS IN RATS. Schaefer, T.L.; Graham, D.L.; Amos-Kroohs, R.M.; Braun, A.A.; Grace, C.E.; Skelton, M.R.; Williams, M.T.; and Vorhees, C.V. Cincinnati Childrens Research Foundation, Cincinnati, OH 45229 USA. Prenatal exposure to the highly addictive psychostimulant methamphetamine (MA) has been shown to cause learning and memory deficits in children and neonatal rats (model of 2nd-3rd trimester brain exposure). This problem may be increasing since the proportion of pregnant women seeking treatment for MA abuse is rising. It was 8% in 1994 and rose to 24% in 2006, the latest data available. Little is known about the pathophysiology induced by developmental MA exposure. We previously demonstrated neurotransmitter and cytoarchitectural changes after neonatal MA exposure, including decreases in dorsostriatal D2 receptor binding and PKA activity (a modulator of the D1 receptor), reductions in entorhinal cortex and striatal 5-HT levels, and decreased dendritic length and spine densities in the nucleus accumbens and hippocampus. However, the functional contribution of such changes to behavioral responses is unknown. Rats were treated from postnatal days 11-20 (stage that approximates third trimester human development) with MA or saline and assessed as adults using locomotor activity as a readout following pharmacological challenge with dopamine, 5-HT, or glutamate agonists or antagonists. Exposure to MA early in life resulted in exaggerated adult locomotor hyperactivity in response to the dopamine D1 agonist SKF-82958 at multiple doses, under-responsiveness to higher but not lower doses of the D2 agonist quinpirole, and a marked under-responsiveness to the activating effect of the NMDA receptor antagonist, MK-801. No change in response was seen following challenge with the 5-HT releaser p-chloroamphetamine, or the 5-HT2/3 receptor agonist, quipazine. These are the first data to show that P11-20 MA exposure induces long lasting alterations to the functional expression of dopamine D1, D2, and glutamate NMDA receptors and may provide clues to future studies to determine if these same receptors are involved in the learning and memory deficits induced by early MA exposure. (Supported by NIH grants DA006733 and T32 ES07051)

89. DOES PRENATAL METHAMPHETAMINE EXPOSURE INDUCE CROSS-SENSITIZATION TO OTHER DRUGS IN ADULT MALE RATS? Slamberova R; Pometlova M; Schutova B; Hruba L; Deykun K. Charles University in Prague, Third Faculty of Medicine, Department of Normal, Pathological and Clinical Physiology, Prague, Czech Republic. Our recent studies demonstated that prenatal methamphetamine MA exposure makes adult rats more sensitive to acute injection of the same drug. Other studies show that abuse of one drug may increase sensitivity to abuse of another drug (cross-sensitization). The aim of the present study was to examine the cross-sensitization between prenatal MA exposure and challenge dose of other drugs. Rat mothers received a daily injection of MA (5 mg/kg) or saline throughout the gestation period. Adult male offspring were divided to groups with challenge dose of the tested drug; (1) the same drug as prenatally (MA), (2) drugs with similar mechanism of action (amphetamine, cocaine and MDMA), and (3) drugs with different mechanism of action (morphine and cannabinoids). Behavior in unknown environment was examined in Laboras, and active drug-seeking behavior in the Conditioned place preference (CPP). In the Laboras, prenatal MA exposure induced sensitization and cross-sensitization only after administration of MA and amphetamine challenge dose, while animals with cocaine and morphine challenge displayed rather tolerance. The active drug-seeking behavior in the CPP was induced by MA and morphine regardless of prenatal drug exposure and by cocaine in controls but not in prenatally MA-exposed rats. While control rats after amphetamine challenge dose did not show drug-seeking behavior, the increase was

apparent in prenatally MA-exposed rats suggesting cross-sensitization. MDMA and cannabinoids did not induce drug-seeking behavior or even decreased it. Thus, our data demonstrate that there are cross-effects between prenatal MA exposure and the challenge dose of other drug in adulthood, however, prenatally MA-exposed rats do not display higher drug-seeking behavior (with exception of amphetamine challenge) as we expected. Supported by: GACR 305/09/0126, 264706/SVV/2012, CSM 110

90. NOREPINEPHRINE ANTAGONISM IN THE EXTENDED AMYGDALA REDUCES THE APPROACH-AVOIDANCE BEHAVIOR OF RATS RUNNING AN ALLEY FOR IV COCAINE. Wenzel,J.M.;Su,Z.-I.; Haber,Z.M.;Ettenberg, A. Dept. of Psychological and Brain Sciences. University of California Santa Barbara, Santa Barbara, CA 93106 USA. Cocaine self-administration is known to produce both positive/euphoric and negative/anxiogenic effects. While the rewarding effects of cocaine have been well-documented, the neurobiology underlying its anxiogenic effects remain unclear. Our laboratory has developed a self-administration runway paradigm to investigate cocaine's dual effects within the same trial. Rats trained to run a straight alley for IV cocaine reinforcement develop a unique approach-avoidance behavior over trials not seen with other drug or natural rewards. Subjects rapidly approach the goal, but then stop, turn, and retreat back towards the start box. These retreats stem from the association of the goal with both the positive (approach) and negative (avoidance) effects of cocaine. Previous work from our lab has identified a role for regions within the extended amygdala (the central nucleus of the amygdala/CeA and the bed nucleus of the stria terminalis/BNST) in the development of retreats. Given that norepinephrine (NE) signaling in the extended amygdala has been implicated in anxiety states during drug withdrawal and stress-induced reinstatement of cocaine-seeking, the current project sought to explore the role of NE within the CeA and BNST in cocaine's anxiogenic effects. Rats received single daily runway trials for IV cocaine following bilateral intra-BNST or intra-CeA administration of one of two doses of an equal mixture of β1 and β2 NE antagonists (betaxolol + ICI-118,551; 0.5g or 1g/0.5l/side) or nanopure water vehicle. While vehicle-treated rats developed retreats over trials, NE antagonism within either the CeA or BNST dose-dependently attenuated the development of retreat behavior. These data suggest that NE signaling in regions of the extended amygdala contributes to cocaine's anxiogenic properties.

91. GIT1 IS ASSOCIATED WITH ADHD. Won, H. Mah, W. Kim, E. Department of Biological Sciences, KAIST, Daejeon, South Korea. Attention deficit hyperactivity disorder (ADHD) is a psychiatric disorder with high prevalence. However, mechanisms underlying ADHD are still unclear. Here I report a novel ADHD associted gene G proteincoupled receptor kinaseinteracting protein-1 (GIT1): an intronic single-nucleotide polymorphism in GIT1 shows a strong association with ADHD susceptibility in humans. GIT1 knockout mice also show ADHD-like phenotypes such as hyperactivity, enhanced electroencephalogram theta rhythms and impaired learning and memory. Hyperactivity learning impairment, and elevated theta rhythms in GIT1 knockout mice are ameliorated by amphetamine, psychostimulants commonly used to treat ADHD. In the hippocampus of GIT1 knockout mice,neuronal excitation-inhibition balance in postsynaptic neurons was disrupted toward excitation. Our study identifies a previously unknown involvement of GIT1 in ADHD and suggests a novel mechanism for ADHD pathogenesis.

92. ADOLESCENTS ARE AT GREATER RISK FOR COCAINE ADDICTION THAN ADULTS. Wong, WC; Bamman MT; Ford KA; McCutcheon JM; Marinelli M. Cellular and Molecular Pharmacology, Chicago Medical School, IL, USA. In humans, adolescence is a period of heightened propensity to develop cocaine addiction. We used preclinical models to examine the nature of this observation, and the neurobiological mechanisms involved. Adolescent (postnatal day 42) and adult (~postnatal day 88) rats were compared for cocaine addiction liability according to DSM-IV criteria, using intravenous self-administration. Relative to adult rats, adolescents took cocaine more readily, escalated cocaine intake, and worked harder for cocaine. This was associated with elevated activity of midbrain dopamine neurons, as measured with in vivo extracellular recordings. The next question to ask is: are adolescents more likely to remain addicted to cocaine compared with adults? We tested how punishment (electric footshock) associated with drug intake affects drug use. Cocaine intake was suppressed for both ages on the day of punishment. However, on the next day, adolescents resumed cocaine taking whereas adults did not. Next, we tested the long-term consequence of drug use by examining relapse in response to different stressors. Relapse was far more pronounced if onset of cocaine use occurred during adolescence vs. adulthood. Our research is the first to offer scientific evidence that when all opportunities to take drugs are equal, adolescents are more prone to cocaine addiction compared with adults. Importantly, adolescents do not refrain from taking cocaine after punishment and they are more likely to relapse in response to stress later on in life. These results have broad implications for the attempts to steer adolescents away from drug use using punishments as well as for preventing relapse.

93. ADOLESCENTS ARE INSENSITIVE TO PUNISHMENT-INDUCED SUPPRESSION OF COCAINE SELF-ADMINISTRATION. Cellular and Molecular Pharmacology, Chicago Medical School, IL, USA. Wong, WC; Lamoureux, L; Bamman MT; Marinelli M. In humans, adolescence is a period of heightened propensity to develop cocaine addiction. One hallmark of addiction is continuation of drug use despite adverse consequences. We tested the sensitivity of adolescents vs. adults to punishment associated with cocaine. Adolescent and adult rats were trained to self-administer cocaine. Punishment in the form of a electric footshock paired with cocaine infusions was administered at various phases of drug use. When footshock was administered upon initial exposure to cocaine, none of the adult rats learned self-administration of cocaine, whereas majority of adolescents did. When electric footshock was administered aAfter acquisition of cocaine self-administration was established, cocaine intake was suppressed for all ages on the day of punishment. However, the next days adolescents resumed cocaine taking whereas adults did not. In addition, adolescents showed shorter latency than adults in returning to cocaine taking. When footshock was administered to aged rats with adolescent- or adult-history of cocaine self-administration, responses to punishment were similar across ages. These results indicate that punishment produces long-term suppression of cocaine taking in adults, but not in adolescents. Such Insensitivity insensitivity of adolescents to following punishment associated with cocaine may contribute to the high susceptibility of drug addiction during adolescence. Furthermore, these findings have implications for methods used for drug cessation; our data suggests that punishment is not an effective means for drug cessation during adolescence, and prompts to explored other means to more effectively manage adolescent addiction.

94. THE MULTIPLE PARTNER CHOICE ARENA SATISFIES THE CONSTRUCT VALIDITY OF AN ANIMAL MODEL TO STUDY PREMETURE EJACULATION. Ferreira-Nuño, A.; Olayo-Lortia, J.; Cruz-Benites, A.; Velazquez-Moctezuma, J.; Morales-Otal, A. Dpto. Biologia de la Reproducción. Universidad Autónoma Metropolitana - Iztapalapa. México D.F. 09340. fena@xanum.uam.mx. Premature ejaculation (PE) is a frequent male sexual complaint. According to Waldinger (2005), this sexual disorder is mediated mainly by disturbances of serotonergic neurotransmission and certain serotonin (5-HT) receptors. In the actual animal model (AM) to study PE, once the male sexual behavior (MSB) of a rat is obtained in a Standard Arena (SA, a closed cylinder), the male receives a chronic administration of a drug to test later if the treatment could prolong their ejaculation latency. This AM satisfies the construct and predictive validity criteria, but not the face validity, because the male rat do not behaves as PE from the beginning. Recently we develop a new AM to study PE: the Multiple Partner Choice Arena (MPCA) made with four acrylic cylinders placed together in a cross fashion and each with a small hole in the bottom directed to the central area. A sexually expert male rat is placed in each cylinder and a receptive female located in the central area is allowed choose the male who wants to copulate with. Under the competitive conditions imposed by the MPCA all the males behave as PE, satisfying the face validity criteria of an AM. To demonstrate if the MPCA also satisfies the construct validity of an AM, 0.1mg/kg of WAY 100635 (a 5-HT1A receptor antagonist) in 0.03 ml of saline was administered during 15 consecutive days to 14 male rats (WAY Group) while the CONTROL group (CON Group, n =14) only received the saline. During days 1, 8 and 15 of the treatment MSB was registered in the SA in half of the males of each group and the other half was tested in the MPCA. The chronic administration of WAY 100635 could abolish the PE behavior as significant reductions in mount, intromission and ejaculation latencies and intromission frequency observed in the CON group tested in the MPCA disappear in the WAY Group. Then MPCA could satisfy the construct criteria of an animal model.

95. TRANSIENT CRF OVEREXPRESSION IN THE FOREBRAIN DURING EARLY LIFE INCREASES STARTLE REACTIVITY AND ANXIETY IN ADULTHOOD. Gresack, J.E.; Toth, M.; Gross, M.; Vicentini, E.; Mangiarini, L.; Mansuy, I.M.; Merlo-Pich, E.; Risbrough, V.B. UCSD, San Diego, CA. Transient CRF overexpression in the forebrain during early life increases startle reactivity and anxiety in adulthood JE Gresack1,5, M Toth1*, M Gross4, E Vicentini2, L Mangiarini2, IM Mansuy3, E Merlo-Pich2, and VB Risbrough1,4 1UCSD; 2GSK; 3 SFIT; 4VAH; 5Rockefeller University The corticotropin releasing factor (CRF) pathway coordinates behavioral and neuroendocrine respones to stress. Increased CRF concentrations have been associated with depression, childhood trauma and posttraumtic stress disorder (PTSD) and genetic variance in CRF receptors is linked to altered risk for these disorders. To test the hypothesis that increased CRF neurotransmission increases the risk of development of PTSD symptoms, we compared three animal models of CRF hypersignaling: (1) mice with lifetime CRF overexpression (CRFOE) to model a heritable increase of CRF, (2) mice in which CRFOE is induced only during development to model early life stress or (3) only during adulthood to model adult onset stress. To induce CRFOE we used a double mutant mouse line that shows forebrain-specific CRF over-expression that can be controlled by doxycycline administration in food at discrete developmental stages. We examined fear conditioning, behavioral activity, anxiety and startle reactivity at adulthood. Mice exposed to CRFOE during early development showed normal fear conditioning and behavioral activity, but showed increased anxiety, startle potentiation, and reduced prepulse inhibition. Suprisingly, mice with lifetime CRFOE exhibited a similar pattern of startle but no anxiety-like behavior. In contrast, mice with adult-onset CRFOE showed none of the phenotypic changes observed in the

developmental or lifetime CRFOE models. These data suggest that CRFOE is sufficient to induce robust alterations in anxiety-like traits, especially during developmental stages.

96. ENDURING EFFECTS OF METHYLPHENIDATE: THE ROLE PLAYED BY ROUTE OF DRUG ADMINISTRATION. Bigney, E.; Taukulis, H. Dept. of Psychology. The University of New Brunswick, Saint John, Canada. Methylphenidate (MPD; Ritalin) is a psychostimulant used to treat attention deficit/hyperactivity disorder. In rodents, chronic treatment with MPD via intraperitoneal (IP) injection during adolescence results in both neurochemical and behavioral indices of depression during adulthood; however, in clinical practice, MPD is administered orally. Drug effects can vary widely depending on mode of administration, and therefore it is necessary to determine if oral treatment with MPD also enhances modeled depression. Experiment 1 investigated blood plasma levels of MPD following both oral and IP administration to male Sprague-Dawley rats. The quantitative plasma results demonstrated that 2 mg/kg IP and 5 mg/kg oral MPD resulted in equivalent and clinically relevant levels of systemic MPD. Experiment 2 investigated the enduring effects of both IP and oral chronic MPD on two of the hallmark symptoms of depression (anhedonia and behavioral despair) and a measure of anxiety. The current study showed that in the sucrose preference test and the forced swim test (measures of anhedonia and behavioral despair, respectively), MPD resulted in an increase in depressive-like behaviours, independent of mode of administration. MPD effects on anxiety (as measured by the elevated-plus maze) were dependent upon mode of administration. IP administration of MPD resulted in a significant increase in anxiety, whereas oral administration of MPD had no effect on anxiety levels. The results of this study indicated that different mode of administrations can alter research findings, resulting in vastly different conclusions.

97. EARLY ADOLESCENT IMPULSIVITY PREDICTS LATE ADOLESCENT BINGE IN FEMALE RATS McClure JR, Richardson HN Department of Psychology, Neuroscience & Behavior Program, University of Massachusetts Amherst, Amherst, MA 01003. Impulsivity is a behavioral trait that has been implicated in a number of disorders ranging from attention deicit hyperactivity disorder to addiction. While animal models have provided useful insights to these human conditions, inconsistent patterns of results remain. Between-study inconsistencies in the relationship between impulsivity and addiction may stem from the fact that some studies focus only on one sex of model organism, or from diferences in the route and rate of delivery of the addictive substance. The current study uses a recently established test of impulsive choice to assess impulsivity during early adolescence in male and female rats. The rats are then allowed to self-administer sweetened alcohol (10% v/v) in a voluntary two-week binge during late adolescence. Our data suggest that early adolescent impulsivity may predict late adolescent alcohol consumption selectively in females, while male consumption seems independent of impulsivity score. Preliminary results also suggest that alcohol consumption may also have sex-dependent efects on adult impulsivity. Together these data highlight the importance of accounting for diferent patterns between the sexes in studies of addiction. By accounting for such diferences we may strengthen our ability to detect general trends, while also allowing for a sex-dependent understanding of addiction which may inform treatment methods for human addiction.

98. EFFECTS OF DIFFERENT HALLUCINOGENIC NMDA ANTAGONISTS AND XYLAZINE ON FEAR EXTINCTION. Eimeira Padilla, John DeMis, Dong-Oh Seo, DeAnna Adkins and Marie H. Monfils. Department of Psychology, The University of Texas at Austin, USA.Ketamine and phencyclidine (PCP) are NMDA antagonists with hallucinogenic properties. Recently, ketamine has been used to treat patients with treatment-resistant depression (Ibrahim et al., 2011, Messer et al., 2010). However, peritrauma ketamine administration can also produce sustained posttraumatic stress symptoms following a traumatic experience (Schnenberg et. al., 2005, Winter and Irle 2004). Given the high co-morbidity of depression and anxiety-related disorders (DeVane et al., 2005), administration of ketamine may exacerbate trauma-linked memories. The present study examines the long-term effects of NMDA antagonists on the extinction of traumatic memories. In animals and humans, ketamine is usually given in combination with a sedative (e.g. xylazine in animals) for anesthesia. Thus, we examined the long-term effects of ketamine plus xylazine, ketamine alone, xylazine or PCP alone on later fear extinction in rats. Rats were fear conditioned by pairing a tone with a footshock. One day after fear conditioning, they received systemic injections of ketamine plus xylazine, ketamine, PCP, xylazine or vehicle. The rats then received an extinction session either 1-day or 1-week following drug injection. Ketamine plus xylazine impaired fear extinction (i.e. more freezing behavior) compared to vehicle in the 1-day and 1-week extinction groups. Ketamine alone impaired fear extinction in the 1-day extinction group. There were no effects of PCP or xylazine alone on fear extinction. The current study provides evidence that a single injection of ketamine impairs fear extinction 24 hours later and a long-term impairment is observed with the addition of xylazine, a potent sedative. The goal of ongoing studies is to identify the behavioral and neural mechanisms underlying short-term and long-term retrieval and extinction of fear memories that have been reinforced with ketamine.

99. ACUTE PROSOCIAL EFFECTS OF PERIPHERALLY ADMINISTERED OXYTOCIN IN RATS: REVERSAL BY THE V1A ANTAGONIST SR49059. Linnet Ramos, Callum Hicks, Richard Kevin, Iain S. McGregor. University of Sydney, Australia. The neuropeptide oxytocin (OT) is renowned for its role in regulating social behaviour and social cognition in mammals including humans. It has often been thought that peripherally injected OT does not permeate the blood brain barrier (BBB) in adequate quantities to alter behavior. For this reason, human studies usually give OT intranasally, while animal studies typically involve intracranial administration of OT2. However recent studies from our laboratory suggests reasonable penetration of the BBB by intraperitoneal (IP) injections of OT3 and it was therefore of interest to examine possible prosocial effects arising from this. Male Long Evan rats received IP injections of OT (0.1, 0.5 and 1.0 mg/kg) and saline in a counterbalanced order with 2 washout days between treatments. After injection they were placed in a testing chamber with an unfamiliar conspecific given the same drug treatment. Testing continued for 30 min at an ambient temperature of 23˚C. Rats given the 0.5 mg/kg OT dose displayed a profound increase in adjacent lying behaviour (somewhat akin to cuddling) and a decrease in rearing relative to the other treatments. In a further study, pre-treatment with the non-peptide, centrally active, vasopressin 1A receptor (V1A) antagonist SR49059 (1 mg/kg) prevented the increased adjacent lying caused by OT (0.5 mg/kg). As OT has substantial affinity for V1A receptors, this suggests that the prosocial effects of OT may be VIA mediated. Ongoing experiments are assessing the effects of centrally active OT antagonist drugs on these prosocial effects of OT. Overall our results show for the first time that peripherally delivered OT can stimulate social behaviour in rodents and that this effect may be, somewhat surprisingly, mediated by vasopressin receptors.

100. INCREASE IN THE SENSITIVITY OF NICOTINE WITHIN THE POSTERIOR VENTRAL TEGMENTAL AREA PRODUCED BY CHRONIC ETHANOL CONSUMPTION Hauser S; Deehan G; Toalston J; Truitt W; McBride W; Rodd Z Department of Psychiatry; Indiana University: School of Medicine There is evidence for a genetic association between alcoholism and nicotine dependence. Ethanol (EtOH) drinking has been shown to increase the sensitivity of the pVTA to the reinforcing effects of EtOH. There is also evidence that prior exposure to nicotine can increase the sensitivity of the pVTA to the stimulating actions of EtOH. The current study examined the effects of chronic EtOH consumption on the self-administration of nicotine directly into the pVTA. Adult alcohol-preferring (P) rats were allowed to consume water only or 15% EtOh and water for 10 consecutive weeks. Following a two week EtOH abstinence period, rats were tested in standard 2-lever operant chambers (active and inactive) for the self-administration of nicotine directly into the pVTA. Rats were randomly assigned to one of four groups that self-infused (FR1 schedule) artificial CSF (aCSF), or 1, 3, or 10 M nicotine (nicotine tartrate) in a volume of 100 nl/infusion for sessions 1-4; only aCSF for sessions 5 and 6; and the original infusate for sessions 7. EtOH nave P rats failed to self-administer either 1 or 3 M nicotine, but did self-administer 10 M nicotine (25 + 4 infusions/session). In contrast, P rats that chronically consumed EtOH self-administered all concentrations of nicotine (e.g., 33 + 6 infusions/session for 1 M nicotine) into the pVTA. In addition, P rats with chronic EtOH experienced received more self-infusions of 10 M nicotine than nave P rats (44 + 5 vs 25 + 4 infusions/session). The current data indicate that chronic EtOH consumption increased the reinforcing properties of nicotine within the pVTA, and suggest that cross-sensitization can occur to the reinforcing effects of EtOH and nicotine in this region, which can persist in the absence of EtOH. AA019366, AA07611

101. FUCOIDAN AMELIORATES SCOPOLAMINE-INDUCED NEURONAL IMPAIRMENT AND MEMORY DYSFUNCTION IN RATS VIA ACTIVATION OF CHOLINERGIC SYSTEM AND REGULATION OF CREB AND BDNF EXPRESSION. Sur, B.J.1,2; Lee, B.2; Kwon, S.1,2; Shim, I.1,2; Yin, CS1,2; Lee, H.1,2; Hahm, D.H.1,2*. 1The Graduate School of Basic Science of Oriental Medicine, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea, 2Acupuncture & Meridian Science Research Center, College of Oriental Medicine, Kyung Hee University, Seoul, Republic of Korea. The purpose of this study was to examine whether fucoidan (FCN) improves memory defects caused by administration of scopolamine (SCO) to the rat. The effects of FCN on the acetylcholinergic system as well as the expression of cAMP-response element-binding protein (CREB) and brain-derived neurotrophic factor (BDNF) mRNAs in the hippocampus were also investigated. Male rats were administered daily doses for 14 days of FCN (10, 20, and 50 mg/kg, i.p.) 30 min before scopolamine injection (2 mg/kg, i.p.). Daily administration of FCN improved memory impairment as measured by the passive avoidance test (PAT) and reduced the escape latency for finding the platform in the Morris water maze (MWM) test. Administration of FCN significantly alleviated memory-associated decreases in cholinergic immunoreactivity and restored the expression level of BDNF and CREB mRNAs in the hippocampus. Additionally, FCN significantly decreased the expression of pro-inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor- (TNF-) mRNAs in the hippocampus. These results demonstrated that FCN has significant neuroprotective effects against neuronal impairment and memory dysfunction caused by scopolamine in rats. Thus, these findings suggest that FCN might be useful as a therapeutic agent for improving cognitive functioning via stimulating cholinergic enzyme activities and regulating CREB and BDNF expression in the brain (This research was supported by the National Research Foundation of Korea Grant funded by the Korean Government (MEST)(2010-0003678) and the

Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MEST) (R11-2005-014)).

102. THE INVOLVEMENT OF KAPPA OPIOD RECEPTORS IN THE DSL STRIATUM AND PDSM STRIATUM DURING HABITUAL AND GOAL DIRECTED COCAINE SEEKING. Wang, Y; Zapata, A; Minney, V; Shippenberg, T; Integrative Neuroscience Branch, NIDA IRP, Baltimore, MD 21224. In this study, Long Evans rats were trained under a seeking/taking chained schedule of intravenous cocaine self-administration. An outcome devaluation method is implemented to determine whether cocaine seeking behavior is goal-directed or habitual by devaluing the outcome of the drug seeking link (the drug taking response) via extinction. Characterization experiments indicated that cocaine seeking was goal-directed after limited experience but became habitual after extensive training. Furthermore, transient inactivation of the pDSM striatum by local lidocaine infusion blocked goal-directed cocaine seeking while inactivation of the DSL striatum blocked habitual responding. To determine the involvement of KORs in goal-directed and habitual cocaine seeking, Norbinaltorphimine, a kappa-opiod receptor antagonist, locally microinjected into the pDSM striatum in animals with a short training history, did not alter goal directed cocaine seeking compared to the control group. Conversely, local infusions of Norbinaltorphimine into the DSL striatum in well-trained animals was able to block habitual cocaine seeking behavior. These studies provide direct evidence that KORs in the DSL striatum play a critical role in regulating established habitual cocaine seeking behavior and contribute to our understanding of the neural circuitry involved in goal-directed and habitual cocaine seeking.

103. RESILIENCE TO EARLY LIFE STRESS IN FEMALE PRAIRIE VOLES (MICROTUS OCHROGASTER): POTENTIAL MODERATION BY OXYTOCIN RECEPTORS. Barrett, C.E.; Modi, M.;Young, L.J. Ctr. Transl. Soc. Neurosci. Yerkes Primate Ctr. Emory Univ., Atlanta, GA, 30329, USA. We examined effects of stress during the postnatal period on adult attachment in the highly social, monogamous prairie vole. Between PND1-14 litters underwent daily 3hr social isolations, and adult offspring were assessed for partner preference formation. Neonatally isolated females did not display a partner preference after 48 hrs of cohabitation while controls did ($F_{1,18}=5.33, p=0.033$). To explore the neural mechanisms underlying this disruption in females, we quantified oxytocin receptor (OTR) density in the nucleus accumbens (NAcc), which is critical for partner preference formation. Early social isolation did not alter NAcc OTR expression. However, isolated females with low levels of NAcc OTR did not display a preference for their mated partner, while those with high OTR densities did ($F_{1,16}=8.11, p=0.012$). In isolated females, but not controls, time spent huddling with the partner correlated strongly with oxytocin receptor binding in the nucleus accumbens ($R=0.66, R^2=0.43, p<0.05$). This potential gene by environment interaction suggests that females with low OTR levels in the NAcc may have a heightened susceptibility to disruptions in social development. We also present findings that postnatal treatment during the first week of life with an MC4 receptor agonist, which activates oxytocin neurons, enhances adult social bonding in female voles ($F_{1,32}=4.87, p=0.035$). The role of oxytocin in the neonatal environment may be critical in the development of social neural circuits. Future studies will examine the potential of neonatal oxytocin enhancements in buffering against adverse early events.

104. EFFECTS OF A DYSFUNCTIONAL BRAIN SEROTONERGIC SYSTEM ON SOCIAL BEHAVIORS IN MALE PET-1 KNOCKOUT MICE Can, A.1; Piantadosi, S.C.1; Gould, T.D. 1,2 1.Department of Psychiatry, University of Maryland School of Medicine, Baltimore MD. 2.Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore MD. Serotonin has largely inhibitory control over sexual behaviors. Studies using pharmacological manipulations of serotonin in the rodent brain indicated that higher levels of serotonergic activity are associated with diminished performance and some motivational aspects of the male sexual behavior. While pharmacological agents, such as para-chlorophenylalanine, deplete the brain from its serotonin, they also have effect on other monoamines. This makes it difficult to draw conclusions about the specific role of serotonin on male sexual behavior. However, recently, it had been found that male mice with a genetically induced complete lack of brain serotonin lost their preference for females over males in targeting their sexually motivated behaviors. The Pet-1 gene codes for a transcription factor necessary for the normal development of brain serotonergic system. We tested Pet-1 knockout male mice for social and related behaviors. Our results indicate that Pet-1 knockout male mice spent significantly less time engaging in grooming and other social behaviors toward male intruders compared to wildtype mice, but did not differ in terms of aggression. Pet-1 knockout males also manifested more episodes of sexually specific mounting behavior toward male intruders and they also spent more time in engaging mounting behavior. While the majority of serotonergic neurons are missing in the Pet-1 knockout mouse brain, a specific subpopulation of them remains intact. The remaining serotonergic neurons innervate brain areas such as the basolateral amygdala and the paraventricular nucleus of the hypothalamus. Our findings indicate that serotonergic innervation of these areas is likely to be not associated with male sexual preference, even though compensatory activity from other areas is still possible. Pet-1 knockout males also loose the sexually dimorphic

serotonergic innervation of the ventrolateral part of the ventromedial nucleus of the hypothalamus, suggesting the possibility that serotonergic activity in this region plays an important role in male sexual preference.

105. INESCAPABLE TAIL SHOCK AND COLD SWIM STRESS INTERACT TO ELEVATE TPH2 MRNA EXPRESSION IN AN ANXIETY-RELATED SUBSET OF SEROTONERGIC NEURONS. 1Donner, N.C.; 2Kubala, K.H.; 3Drugan, R.C.; 2Maier, S.F.; 1Lowry, C.A. Depts. of 1Integrative Physiology, 2Psychology & 1,2Center for Neuroscience, University of Colorado Boulder, Boulder, CO, USA. 3Dept. of Psychology, University of New Hampshire, NH, USA. The effects of stressful stimuli on the expression of tryptophan hydroxylase 2 (tph2) mRNA expression are controversial. The tph2 gene encodes the rate-limiting enzyme for serotonin synthesis. Here, we studied the effects of inescapable tail shock (IS; 100 5 s, 1.0 mA shocks with random intervals), cold swim stress (SWIM; 10 min, 15 C), or the succession of IS and SWIM on tph2 mRNA expression in the dorsal raphe nucleus (DR), using in situ hybridization histochemistry. Adult male rats served as home cage controls (HC, n=8), or were exposed to IS (n=8) or SWIM (n=8), and were killed 4 h after the start of either stressor. Another group of rats was exposed to IS on day 1, and either HC (n=8) or SWIM (n=8) on day 2, with all rats being killed 4 h after the start of SWIM. IS, but not SWIM, was sufficient to increase tph2 expression selectively in the anxiety-related dorso-caudal DR (cDRD). Furthermore, IS on day 1 sensitized rats to SWIM-induced increases of tph2 expression in the cDRD and to increases in the ratio of plasma interleukin-6 to interleukin-10 on day 2. Compared to HC-SWIM control rats, the IS-SWIM group also displayed increased immobility and decreased climbing behavior in the SWIM test. Our results indicate that stressor type and severity are crucial factors in regulating tph2 expression, and that IS creates a neuronal, immunological, and behavioral vulnerability to a succeeding stressor.

106. PLATELET Platelet Serotonin Function and its Relationship to Adolescent Suicidal Ideation and Histories of Suicide Attempts. Dougherty, D.M.; Mathias, C.M.; Hill-Kapturczak, N.; Tian, P. Y.; Javors, M. Dept. of Psychiatry. UT Health Science Center, San Antonio, TX 78229 USA. The serotonin (5-HT) neurotransmitter system has been related to suicide in postmortem studies, but there are public health motivations to assess its function among living individuals. We have completed two studies examining platelet serotonin transporter (SERT) function among individuals expressing suicidal ideation and having histories of attempts. Study 1, SERT function was compared among three adolescent groups: controls (n=95), and patients expressing high (n=37) or low (n=45) levels of suicidal ideation. In Study 2, SERT function among controls (N=95) was compared to psychiatric patients with (n=35) or without (n=79) histories of suicide attempts. Three kinetic parameters of SERT function were assessed in fresh blood platelets: the maximum velocity of serotonin uptake (Vmax), the equilibrium constant (Km), and SERT uptake potential (Vmax/Km). We found: in Study 1 that those with high suicidal ideation had a significantly higher Km, and lower uptake potential (Vmax /Km), than patients with low suicidal ideation or healthy controls. Both the patient groups in this study had lower Vmax than healthy controls; and in Study 2 that Vmax and SERT uptake potential (Vmax / Km) were significantly higher in the healthy control and non-attempter groups than the attempter group. Km was lower in the control and non-attempter groups versus the attempter group. Collectively, these studies suggest that current thoughts of suicide and histories of previous attempts are associated with disruptions in the serotonin neurotransmitter system. These findings indicate that the measure of platelet SERT uptake potential (Vmax / Km) may be a clinically useful biological marker.

107. DOPAMINE MANIPULATIONS IN THE ORBITOFRONTAL CORTEX MODULATE REVERSAL LEARNING DEFICITS OF SPONTANEOUSLY HYPERTENSIVE RATS IN AN ATTENTIONAL SET-SHIFTING TASK. Li, J.-S.; Cheng, J.-T. Dept. of Psychology. National Chung Cheng University, Taiwan. Numerous studies suggest that dysfunctions of prefrontal cortex can impair inhibitory controls of patients with attention deficit/hyperactivity disorder (ADHD), resulting in their impulsive behaviors. Furthermore, rats with lesions in the orbitofrontal cortex show deficits in the reversal learning of attentional set-shifting task (ASST), a behavioral test frequently used in human studies to asses the inhibition system. However, the role of orbitofrontal dopamine system in the mechanism responsible for the dysfunctions of inhibitory controls in ADHD patients and animal models remains unknown. In the present study, we manipulated orbitofrontal dopamine activities of spontaneously hypertensive rats, a widely used ADHD animal model, through intra-peritoneal injection of methylphenidate (MPH) and central infusion of haloperidol, and observed performances of animals in ASST. The results show that juvenile SHRs learned slower than Wistar controls in the first and second reversal learnings of ASST. The deficits could be removed by intra-peritoneal injections of MPH. Furthermore, central infusions of haloperidol in the orbitofrontal cortex blocked the effects of MPH. In conclusion, dopamine manipulations in orbitofrontal cortex can modulate deficits of reversal learning in SHRs, suggesting a possible involvement of the orbitofrontal dopamine system in the pathology of ADHD.

108. G PROTEIN-COUPLED RECEPTOR KINASE 6 DEFICIENCY AND MOUSE MODELS OF PARKINSON'S DISEASE. Manago', F.; Espinoza, S.; Salahpour, A.; Sotnikova, T.D.; Caron, M.G.; Premont, R.T.; Gainetdinov, R.R. 1. Neuroscience and Brain Technologies Department, Istituto Italiano di Tecnologia, Genova, Italy. 2. Pharmacology and Toxicology Department, University of Toronto, Toronto (ON), Canada. 3. Cell Biology Department, Duke University, Durham (NC), USA. 4. Department of Medicine, Duke University, Durham (NC), USA. GRKs belongs to a family of seven serine/threonine kinases that phosphorilate GPCR activated by an agonist leading to rapid desensitization. Phosphorylation of GPCRs by GRKs and recruitment of arrestin proteins could also promote novel G-protein-independent signaling events. It has been reported that animal models of PD and PD patients have an increased levels of G Protein-Coupled Receptor Kinase 6 (GRK6) in the striatum. A study on GRK6-KO mice has revealed an enhanced coupling of striatal D2-like dopamine receptors and reduced D2 receptor desensitization in absence of GRK6. Furthermore, it has been shown that 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 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. To further clarify the role of GRK6-mediated regulation in β-Arrestin2/AKT/GSK3β and MAPK signaling we analyzed the pattern of phosphorylation of AKT/GSK3β and ERK1/2. The results demonstrated that GRK6 deficiency in animal models of PD leads to a reduction in cataleptic behavior, potentiate the effect L-DOPA induced and induces a reduction of the rotational behavior and AIMs. This may suggest that future pharmacological approaches to regulate GRK6 activity could be effective in reducing L-DOPA side-effects.

109. EXERCISE DOES NOT PROTECT AGAINST EXPERIMENTAL PARKINSONISM IN MICE DEFICIENT IN BDNF. Gerecke, K; Jiao, Y; Pagala, V; Pani, A; Smeyne, R. Rhodes College and St. Jude Childrens Research Hospital, Memphis, TN. Exercise has been shown to be potently neuroprotective, including in the MPTP model of Parkinsons disease (PD). To determine the critical duration of exercise necessary for DA neuroprotection, sedentary mice were compared to mice that ran for either 1, 2 or 3 months prior to treatment with saline or MPTP. Sedentary mice, and mice allowed to run unrestricted for 1 or 2 months, lost significant numbers of SN DA neurons following MPTP; however, 3 months of exercise provided complete protection. To determine the critical intensity of exercise, mice ran for 3 months but were restricted to 1/3 or 2/3 of the daily distance of the full running group. Restricted groups lost significant numbers of DA neurons due to MPTP toxicity; however, the 2/3 group demonstrated partial protection. Analyses of DA and its metabolites DOPAC and HVA show that exercise also functionally protects neurons from MPTP neurotoxicity. A possible mechanism for protection may be via BDNF. To test this, DA neuronal loss due to acute MPTP administration in BDNF+/- and Wt mice was compared. Exercised BDNF+/- mice lost a significant number of DA neurons in the SN such that they were not significantly different from sedentary mice administered MPTP. Proteomic analysis of SN and STR tissues indicates that exercise induces changes in proteins related to energy regulation, cellular metabolism, the cytoskeleton, and intracellular signaling events in Wt and BDNF+/- mice; however, exercised BDNF+/- mice did not show increased expression of energy metabolism proteins. Thus, exercised-induced DA neuroprotection is abolished in mice deficient in BDNF in experimental parkinsonism. This suggests that both exercise and BDNF may represent useful targets for prevention of PD.

110. DISTINCT NEURAL SUBSTRATES FOR REINFORCEMENT AND PUNISHMENT IN THE STRIATUM. Kravitz, AV; Tye, LD; Kreitzer, AC. Gladstone Institute of Neurological Disease, San Francisco, CA 94158 USA. Reinforcement and punishment are fundamental processes that shape animal learning. Reinforcement maintains or increases, while punishment decreases, the future probability of specific behavior. While the striatum is implicated in both reinforcement and punishment, the specific roles of the two populations of striatal projection neurons are not well understood. We tested the hypothesis that D1-expressing direct pathway medium spiny neurons (dMSNs) mediate reinforcement, while D2-expressing indirect pathway neurons (iMSNs) mediate punishment. We targeted the expression of channelrhodopsin-2 (ChR2) to dMSNs or iMSNs in separate groups of mice, and trained them on an operant task in which they could self-administer laser stimulation to activate each pathway. Within the first 30-minute training session, nave mice that expressed ChR2 in dMSNs exhibited a significant bias towards the laser-paired trigger whereas mice that expressed ChR2 in iMSNs mice exhibited a significant bias away from the laser-paired trigger. This indicates that activation of direct pathway dMSNs is sufficient for reinforcement, while activation of indirect pathway iMSNs is sufficient for punishment. Our results support our hypothesis, and indicate that these neural populations could be targeted independently to address specific dysfunctions in reinforcement or punishment associated with psychiatric disorders.

111. SUBSECOND MESOLIMBIC DOPAMINE RELEASE PREDICTS THE AVOIDANCE OF PUNISHMENT Erik B. Oleson, Ronny N. Gentry and Joseph F. Cheer Department of Anatomy and Neurobiology. University of Maryland School of Medicine. Baltimore, MD 21201 USA. The mesolimbic dopamine system is generally considered to be a reward pathway. In support of this theory â€“ when animals are presented with conditioned cues predicting reward availability, midbrain dopamine neurons fire in high frequency bursts. This pattern of neural activity results in subsecond dopamine release events in terminal fields such as the nucleus accumbens, which are thought to promote reward seeking. A number of studies, however, also implicate the mesolimbic dopamine system in behavior requiring the avoidance of punishment. To assess the role of dopamine during the avoidance of punishment, we measured accumbal dopamine concentrations in near real-time using fast-scan cyclic voltammetry while well-trained rats responded in an operant signaled shock avoidance task. In this procedure, a stimulus light was presented as a warning signal while a response lever extended 2s prior to the delivery of recurring foot shocks (0.5s shock every 2s). A lever response at any time within the session produced a 20s safety period signaled by a tone. This design allowed us to assess dopamine signaling during warning signal presentation, safety periods and two distinct behavioral responses (avoidance and escape). We found that dopamine release encodes warning signal presentation and predicts when animals will successfully avoid punishment. Our data, demonstrating that dopamine indiscriminately processes motivationally salient stimuli, supports a growing consensus that the mesolimbic dopamine system is more than merely a reward pathway. Rather, subsecond dopamine signaling might facilitate behavioral orientation in a manner that promotes behavioral adaptation and survival.

112. STRUCTURAL NEUROANATOMY CORRELATES WITH FUNCTIONAL MOTOR-RELATED NETWORKS IN STROKE PATIENTS. Sook-Lei Liew, Kathleen Garrison, Justin Haldar,Carolee Winstein,Hanna Damasio & Lisa Aziz-Zadeh. University of Southern California. Stroke is the leading cause of disability in adults, often resulting in lasting motor impairments that hinder ones ability to engage in meaningful activities. Recent rehabilitation efforts have focused on ways to activate damaged motor regions through action observation, by engaging the putative human mirror neuron system (MNS), a neural network comprised of premotor and parietal motor-related regions that are active both during the execution of an action and the observation of the same or similar actions. However, it is unclear how individual differences in the underlying structural anatomy of the post-stroke brain may influence functional activity in these motor-related brain regions, and how these measures may correlate with behavioral motor outcomes. We scanned 12 participants with chronic stroke resulting in moderate-to-severe upper limb hemiparesis and obtained high-resolution structural MRIs, diffusion-weighted imaging, functional MRI while participants observed grasp actions, and behavioral scores from standardized motor assessments. Relationships between this battery of measures demonstrate several promising findings: 1) functional plasticity of the MNS when observing actions performed by the counterpart to the paretic limb correlate with structural measures of lesion volume and 2) with general cortical atrophy, and 3) structural plasticity of motor-related white matter tracts with functional activation patterns. Altogether these findings suggest specific measures of functional and structural plasticity that hold promise as biomarkers for improved motor recovery and indicators of who might respond best to different types of therapy. Such information provides a foundation for developing individualized treatments that harness each patients specific profile of structural and functional plasticity post-stroke for maximal rehabilitation benefits.

Friday, June 8, 2012

9:00-10:00 **Keynote: David M. Diamond**, University of South Florida

A NOVEL PERSPECTIVE ON THE INVOLVEMENT OF THE HIPPOCAMPUS IN FLASHBULB AND TRAUMATIC MEMORIES. David M. Diamond, Research and Development Service, Tampa Veterans Hospital, Departments of Psychology, Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL 33620 USA. It is well-known that the hippocampus is necessary for the formation of new memories. However, research on rodents and humans indicates that in times of stress hippocampal functioning is impaired. This finding has been interpreted to indicate that there is an absence of hippocampal involvement in the formation of traumatic memories. I will incorporate findings from rodent and human studies to provide an alternative interpretation of the literature. I will suggest that traumatic experiences produce a relatively brief and intense activation of amygdala-hippocampal circuitry, with a concomitant suppression of neocortical functioning, which helps to explain the unique and fragmentary nature of traumatic memories. This perspective on how stress affects the hippocampus, amygdala and neocortex is potentially relevant toward understanding how traumatic experiences generate long-lasting intrusive memories which are highly resistant to extinction.

10:30-12:30 **Symposium:** Use of Optogenetics in Behavioral Neuroscience. Chair: **Peter Shiromani**, Ralph H. Johnson VA and the Medical University of South Carolina, Charleston

SHINING LIGHT ON WAKEFULNESS AND AROUSAL USING OPTOGENETICS. Carter, M.E.; de Lecea, L**.** Stanford University, Stanford, CA. The recent development of light-activated optogenetic probes allows for the identification and manipulation of specific neural populations and their connections in freely moving animals with unprecedented spatial and temporal precision. The relative low-cost and easy set-up of this technology has enabled many neuroscientists to add optogenetics to their repertoire of tools to study the brain. This presentation will illustrate the universal utility and methodology of applying optogenetics to questions in behavioral neuroscience by highlighting our recent research on the neural basis of sleep and wakefulness. We recently used multiple optogenetic probes to study hypocretin (Hcrt)-expressing neurons in the hypothalamus and noradrenergic locus coeruleus (LC) neurons in the brainstem, both in isolation and in combination. We found that both structures play a causal role in sleep-to-wake transitions and the maintenance of wakefulness. Furthermore, we used a variety of optogenetic techniques to demonstrate that the LC is necessary and sufficient for acute Hcrt-mediated promotion of wakefulness. These results demonstrate how optogenetics can be used both at the neuronal and circuit level to address fundamental questions about the brain and behavior.

DISSECTING ADDICTION CIRCUITRY WITH OPTOGENETICS. Moorman D.E.; Vazey E.M.; Aston-Jones G. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29425. The neural circuitry underlying motivation for both natural and drug rewards is distributed across brain regions and diverse neuronal phenotypes. Optogenetics allows manipulation of specific neuronal circuits involved in reward and drug seeking with exquisite spatial and temporal precision. By using cell-type-specific promoters, specific classes of neurons can be probed, even in phenotypically-heterogeneous neuronal regions. Here we will present our recent work investigating how optogenetic manipulation of neurons in multiple brain regions influences reward- and drug-seeking. We will first describe results from electrophysiological studies of addiction-related neural circuitry, demonstrating how data previously obtained using electrical stimulation can be refined with optogenetics to unambiguously characterize neuronal relationships across brain regions (e.g., the projection from the prefrontal cortex to the ventral tegmental area). We will next focus on studies investigating the roles of interconnected areas such as the lateral hypothalamic hypocretin/orexin system and subregions of the prefrontal cortex in regulating behavior during reward- and drug-seeking tasks. Additionally, we will emphasize the relative ease and low cost with which optogenetics can be incorporated into most behavioral testing environment, making the use of this technique accessible to all behavioral neuroscientists. Acknowledgements: Dr. Priyattam J. Shiromani and Dr. Luis de Lecea generously contributed the hypocretin/orexin channelrhodopsin-2 construct. Funding provided by PHS grants R37-DA 06214, P50-DA015369, R01-MH092868, and R21-DA032005.

SEEING IS BREATHING. Feldman, J.L.,Dept of Neurobiology, UCLA, Los Angeles, CA 90095-1763. I will describe two projects that exploit optogenetics/advanced optics to study mechanisms underlying the generation of the rhythm of breathing. 1) We (and others) have established that the preBtzinger Complex is the critical kernel for normal breathing at rest, when inspiration is active and expiration is passive. We hypothesized a second oscillator for breathing, called the retrotrapezoid nucleus/parafacial respiratory group (RTN/pFRG), generated active expiration. We transfected RTN/pFRG neurons in adult rats with channelrhodopsin. By activating these neurons we can rapidly transform a resting breathing pattern with passive expiration into one with active expiration (Pagliardini S, Janczewski WA, Tan W, Dickson CT , Deisseroth K, Feldman JL (2011) Active expiration induced by excitation of ventral medulla in adult anesthetized rats. J. Neurosci. 31(8):28952905.). 2) A medullary slice from neonatal rodents containing the preBtzinger Complex can generate an inspiratory-related rhythm. Using holographic photolysis of caged glutamate, we can target and excite 1-10 inspiratory neurons with considerable

temporal precision. Stimulation of 3-9 neurons can trigger an inspiratory burst (Kam K, Worrell JW, Ventalon C, Emiliani V, Feldman JL. Holographic photostimulation of 4-9 neurons triggers inspiratory burst generation in the neural circuit controlling mammalian respiratory rhythm in vitro. Program No. 386.18. 2011 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2011. Online). I will discuss this technique and the interpretation of these data.

SLEEP INDUCTION BY OPTOGENETIC INHIBITION OF HYPOCRETIN NEURONS: IMPLICATIONS FOR INSOMNIA. Kilduff, T.S. Center for Neuroscience, SRI International, Menlo Park, CA 94025 USA. Hypocretin/orexin (Hcrt) neurons have a crucial role in the regulation of sleep and wakefulness. To help determine how these neurons promote wakefulness, we collaborated with the lab of Dr. Akihiro Yamanaka at the National Institute of Physiological Sciences (Okazaki, Japan) who generated transgenic mice in which Hcrt neurons expressed the light-activated chloride pump, halorhodopsin. Slice patch clamp recordings of Hcrt/halorhodopsin neurons demonstrated that photic illumination reduced Hcrt neuron discharge. Acute silencing of Hcrt neurons in vivo induced synchronization of the electroencephalogram (EEG) and reduction in amplitude of the electromyogram (EMG) that is characteristic of slow wave sleep (SWS). Although the discharge of dorsal raphe (DR) serotonergic neurons was reduced during acute Hcrt neuron photoinhibition, DR neurons exhibited normal discharge rates in mice lacking Hcrt neurons. Thus, although usually highly dependent on Hcrt neuronal activity, serotonergic DR neuronal activity can be regulated appropriately in the chronic absence of Hcrt input. Together, these results demonstrate that acute inhibition of Hcrt neurons results in EEG synchronization and reduction of EMG amplitude characteristic of SWS and in reduced firing rate of neurons in an efferent projection site thought to be involved in arousal state regulation. Since these effects were time-of-day dependent, activation of Hcrt neurons appears to be necessary for wakefulness during the light period when homeostatic sleep drive is at the highest level (Supported by NIH R01NS057464).

2:00-3:35 **Symposium:** BRAIN HEALTH: THE ESSENTIAL NATURE OF OMEGA-3 FATTY ACIDS. Chairs: **Corina O. Bondi** and **Michael J. Weiser**

DOCOSAHEXAENOIC ACID (DHA) IS ESSENTIAL FOR NEURAL DEVELOPMENT: A BEHAVIORAL PERSPECTIVE. Weiser, M.J.; Salem, N.; Dahms, I. DSM Nutritional Products LLC, Columbia, MD, 21045, USA. Docosahexaenoic acid is a 22-carbon fatty acid containing six double bonds, a most unusual structure, found at high concentrations in membrane aminophospholipids in the brain and retina. Dietary deprivation of omega-3 fatty acid sources in the pregnant female leads to a deficiency of DHA in the nervous system of her offspring. This loss of brain DHA leads to losses in brain function as best measured by behavioral means. For example, increases in escape latency in the Morris Water maze occur which can be subsequently reversed when a single nutrient (alpha-linolenic acid) is again added to the rat diet. This conclusively demonstrated that this loss in brain function is a result of the loss of this single compound in the brain. Stress can exacerbate the behavioral deficits associated with brain DHA loss as observed in the elevated plus maze. A failure to acquire a set learning paradigm was observed in an olfactory based, two odor discrimination task. Studies indicate that this was not due to a sensory or motivational loss but an emotional or executive function change and a change in cognitive capability is suggested.

OMEGA 3 FATTY ACIDS: LIMITING DIETARY NUTRIENTS WITH CRITICAL ROLES IN BRAIN DEVELOPMENT. Innis S.M. Dept Paediatrics, Child and Family Research Institute, University of British Columbia, Vancouver, Canada. Docosahexaenoic acid (DHA) is a long chain omega 3 fatty acid essential in early development due to its role as a major component of neural membranes. Omega-3 fatty acids are sparsely distributed in foods, and DHA is naturally present only in animal tissues, with fish being the richest source. The shorter chain omega-3 alpha linolenic (ALA) is found in plants, but its distribution is also limited. Current evidence suggests ALA conversion to DHA is insufficient to meet brain DHA needs with typical western diets. The mothers DHA status in gestation and lactation determines the maternal-to-infant DHA transfer across the placenta and in breast milk. Selective DHA transfer does not protect the infant from low maternal DHA. Experimental studies show decreased DHA in the developing brain impairs neurogenesis, and alters neurotransmitters, behavior and learning. Whether omega-3 fatty acid insufficiency constrains neural development in infants, however, is a complex question due to the many variables impacting child development. We used a longitudinal intervention with 400 mg/d DHA or placebo from 16 wk gestation until delivery; in which case benefit of DHA can occur only if omega-3 fatty acid deficiency is present. DHA supplementation increased maternal DHA status by 35-40%. Using a risk reduction approach, infants in the placebo group were more likely to score in the lowest than highest quartile on the Bayley Scales III language subscale. Our studies show omega-3 fatty acids are limiting in many diets, DHA status is low, and provide evidence that poor fatty acid nutrition may limit childrens potential to reach their best developmental outcome. Funded by the Canadian Institutes of Health Research.

DIETARY DEFICIENCY IN OMEGA-3 FATTY ACIDS PRODUCES ALTERATIONS IN RAT BEHAVIOR AND BRAIN MARKERS OF MONOAMINERGIC INNERVATION. Bondi, C.O.; Tock, J.L.; Moghaddam, B. Dept. of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260 USA. The omega-3 (n-3) polyunsaturated fatty acids (PUFAs), such as docosahexaenoic acid (DHA), play an important role in normal brain structure and function. The current Western diet is deficient in n-3 PUFAs, and several findings in humans support the hypothesis of functional links between PUFA status, brain neurotransmission alterations and behavioral disorders. We investigated involvement of n-3 PUFAs in central nervous system function by assessing effects of dietary PUFA deficiency in a variety of behavioral tasks in consecutive generations of rats, as well as brain markers of monoaminergic innervation, such as tyrosine hydroxylase (TH) and vesicular monoamine transporter 2 (VMAT2). Behavioral testing during various stages of development included anxiety-like behavior, locomotor function, recognition memory and attentional set-shifting behavior in rats bred to a second generation on diets that were either deficient (DEF) or adequate (ADQ) in PUFAs. While the first generation of DEF rats rendered transient changes in behavior, the second generation offspring displayed increased anxiety-like behavior, hyperlocomotion, reduced recognition memory and impaired attentional set-shifting performance. Brain analyses revealed dramatic reductions in n-3 and compensatory increases in n-6 whole-brain fatty acid composition, as well as reduced VMAT2 and elevated TH protein expression in dorsal striatum. This generational n-3 PUFA deprived rat model may be useful for revealing the contribution of chronic dietary n-3 fatty acid deficiency to behavioral deficits relevant to psychiatric illnesses.

4:30-6:30 **Symposium:** AGGRESSION, NEUROMODULATION, AND SOCIAL ADAPTATION: LESSONS FROM MULTIPLE ANIMAL MODELS. Chairs: **Gary R. Ten Eyck** and **Cliff H. Summers**

SOCIAL ADAPTATION IN THE MOUSE. Blanchard, R.J.; Pearson, B.L. Dept. of Psychology. University of Hawaii, Manoa, Honolulu, HI 96822 USA. Social behaviors in the mouse involve a number of specific behavioral patterns. These include conspecific aggression and defense, parental and sexual behaviors and play fighting. In addition to these categories, each of which is associated with particular motivational states and functional outcomes, there is a more general category of social motivation not associated with particular functions. We are developing measures of such prosocial motives and the behaviors associated with them. Our tests include seminatural situations (the visible burrow system); situations in which direct contact with conspecifics cannot be avoided and social contact behaviors are analyzed (social proximity test); as well as tests aimed as assessing social motivations (social place preference conditioning). These tests are providing insights in the study of mouse models of autism.

THE NEUROENDOCRINOLOGY OF SEXUAL BEHAVIOR AND SEX CHANGE IN CORAL REEF FISHES. Godwin, J.; Slane, M.A. Dept of Biology and W.M. Keck Center for Behavioral Biology, North Carolina State University, Raleigh, NC 27695 USA. The study of sex differences has produced major insights into the organization of animal phenotypes and the regulatory mechanisms generating behavioral variation from similar genetic templates. Coral reef fishes display an extraordinary diversity of sexual expression including simultaneous hermaphroditism and functional, socially-controlled sex change. These systems provide powerful models for understanding gonadal and non-gonadal influences on behavioral and physiological variation. Our research using the Caribbean bluehead wrasse, Thalassoma bifasciatum, demonstrates a fully male sexual behavior phenotype can develop even in the absence of gonads, key influences of the neuropeptide arginine vasotocin on sexual and aggressive behavior, and a controlling role for estrogen biosynthesis in regulating female-to-male sex change. Current work is aimed at characterizing potential direct vasotocinergic and estrogenic influences on sexual function and sex change through the kisspeptin system.

CHOICES IN SOCIAL ADAPTATION TO AGGRESSION: NEUROMODULATORY MECHANISMS IN DECISION MAKING Cliff H. Summers1,2, Tangi R. Summers1,2, David H. Arendt1,2, Justin P. Smith1,2 and Russ E. Carpenter3; 1Department of Biology and 2Neuroscience Group, Basic Biomedical Sciences, Sanford School of Medicine, University of South Dakota, Vermillion, SD USA 3Department of Biological Sciences, Stanford University, Stanford, CA USA. A recently developed model of social decision making from our lab has a broad evolutionary scope. A wide range of vertebrate species, from Rainbow trout to rodents like mice, hamsters and rats utilize aggression to establish social hierarchy or territories, and the resulting interactions are an established and intense source of stress for both competitors. The model is designed to make use of this social stressor as a way to determine the neural mechanism involved during decision making under duress. Aggression from a much larger conspecific constitutes an unconditioned stimulus (after an auditory conditioned stimulus). This training includes an opportunity for the test animals to escape or remain submissively. The decision is simple but decisive, and the results are clear. In most species tested (trout, mice and rats) the population is divided between submissive animals and those that choose to escape. Specialized learning, neurochemical reactions, gene expression and behavior attend either choice. Learned escape is a 7 step process that includes spatial, social, and instrumental learning, and results in a rapid decline in latency to escape with each training day. Test animals that do not escape during training exhibit classically conditioned gene expression, hormonal and neurotransmitter responses, and behavior. Learning escape and submission involve changed expression of hippocampal brain-derived neurotrophic factor (BDNF), TrKB, and AMPA GluR1 subunit mRNAs. Treatment with the CRF1 receptor antagonist during training induces non-escaping animals to begin escaping. We

suggest that these social decisions during stressful conditions require environmentally mediated regulation of gene expression, activity dependent neuronal plasticity, modification of neural circuit signaling, and learning plus memory formation to produce adaptive behavioral responses.

AGGRESSION, DEFENSE, AND PATERNAL CARE IN THE INVASIVE PUERTO RICAN COQUÍ FROG, ELEUTHERODACTYLUS COQUI. Ten Eyck, G.R.; Calibuso, M.J. Dept. of Pharmaceutical Sciences, College of Pharmacy, University of Hawaii, Hilo, HI, USA. A novel animal model has been developed for studies in developmental, reproductive and social behaviors. The Puerto Rican coquí frog, Eleutherodactylus coqui, is a frog that has two very interesting evolutionarily derived characters, 1) paternal care - whereby paternal males brood and aggressively defend the developing eggs/embryos and hatched froglets 3-5 days following hatching, and 2) direct development - the free swimming, tadpole stage characterized by most frogs has been eliminated and frogs develop directly into the adult phenotype. Using this model we carried out investigations on the changes in the brain that occur during paternity and the effects of stress on paternal care. The stressor was a recording of a calling conspecific male, which is a natural stressor because other males (and females) eat the developing eggs and embryos. We investigated changes in behavior during stressful periods, if and how stress promotes offspring abandonment and the corresponding brain changes during paternity. Experiments were also carried out on territorial males and what neurochemical systems are involved in activating behavior during this time. Comparisons were made between aggressive behavior in territorial males and defensive behavior during paternal care. Investigations on reproductive behaviors are significant since the Puerto Rican coquí was recently introduced on the Island of Hawaii and its widespread distribution is a major environmental and economical concern.

4:30-6:30 **Symposium:** CONTEXTUAL CONTROL OVER FEAR BEHAVIORS: RECENT ADVANCES AND MOLECULAR MECHANISMS. Chair: **Gavan P. McNally**, University of New South Wales, Sydney, Australia

ELECTRICAL SYNAPTIC CONTROL OVER FEAR BEHAVIORS. Bissiere S. Department of Behavioural Neuroscience, Florey Neuroscience Institutes, University of Melbourne, VIC, Australia. Changes in behaviour following emotionally powerful experiences are mediated by longterm functional modifications in brain circuits. In particular, network activity among the amygdala, hippocampus and medial prefrontal cortex play a crucial role in the generation, maintenance and extinction of fear memories. In the last decade, key studies have demonstrated that such network activity can emerge from the synchronized firing of specific GABAergic interneuronal populations within these regions. In the adult mammalian brain, these interneurons are coupled via electrical synapses made of Cx36 proteins, typically referred to as gap junctions. As opposed to chemical synapses, gap junctions directly connect the membranes of neurons allowing for fast neurotransmission and for the bidirectional passage of ions, metabolites and second messengers. While our knowledge about electrical synapses has shed new light about their role in adult brain function, their contribution to fear learning and memory processes is only starting to be unravelled. Using a multidisciplinary approach in rats combining electrophysiology, imaging, molecular biology and fear conditioning, we recently identified a novel role for electrical synapses in both hippocampal and amygdala-dependent fear memories. These findings provide novel understanding about the functioning of the fear circuitry and may point towards new therapeutic avenues for anxiety disorders.

NEURONAL ENSEMBLES IN CA1 AND MPFC DIFFERENTIALLY REPRESENT RECENT AND REMOTE CONTEXTUAL FEAR MEMORIES. Zelikowsky, M.; Fanselow, M.S. Caltech, Pasadena, CA. The ability to recognize contexts and the significant events that occur within them is vital to the survival of any species. Contextual fear conditioning provides an excellent model of this ability, as it requires an animal to form a contextual representation and associate that representation with an aversive event. Activity within the brain regions implicated in contextual fear can be assessed using catFISH (cellular compartment analysis of temporal activity using fluorescence in situ hybridization), which provides a visualization of the neuronal populations involved in two, temporally distinct events as indexed by Arc mRNA expression (Guzowski et al., 1999). Classically, the dorsal hippocampus (DH) has been implicated as a key structure in contextual processing (Fanselow, 2000; 2010) and is thought to initially provide the detailed contextual representation underlying contextual fear conditioning (Wiltgen et al., 2010). Meanwhile, recent findings suggest a possible role for the medial prefrontal cortex (mPFC) in contextual fear, with an emphasis on the mPFC in the permanent storage of long-term memories (Quinn et al., 2008; Frankland et al., 2004; Goshen et al. 2011). We investigated the behavior of neuronal ensembles in the CA1 region of the DH, the basolateral amygdala (BLA), and the mPFC (both infralimbic (IL) and prelimbic (PL) subregions) following contextual fear conditioning and testing one or thirty days later (recent vs. remote memory test), in the same context or in a novel context (generalization test). We found that recently acquired memories were context-specific and recruited neuronal populations in CA1 and mPFC that showed a profile of Arc induciton consistent with a role for contextual encoding. In contrast, when contextual fear memories transferred from a recent to remote state, Arc expression in CA1 persisted but failed to exhibit context-specificity, suggesting that the detailed contextual representation encoded in CA1 following recently acquired memories may fade with time.

CONTEXTUAL INFLUENCE IN CONDITIONED FEAR IN JUVENILE RATS: FORGETTING VS. EXTINCTION. Kim, J.H. Florey Neuroscience Institutes, Parkville, Australia. The most common way of studying learned fear in the laboratory involves a Pavlovian conditioning procedure in which an initially neutral conditioned stimulus (CS) is presented with an aversive unconditioned stimulus (US). Subsequent presentations of the CS elicit a variety of fear behaviors. These fear responses can be spontaneously forgotten over time, at least due to changes in the context from where the memory is acquired. Alternatively, fear is also reduced by repeatedly presenting the CS without the US. This procedure is referred to as extinction. Extinction has attracted much attention over the past decade (for review, see Kim & Richardson, 2010), because understanding how fear is diminished is critically important to the development of effective treatments for various anxiety disorders. Similar to spontaneous forgetting, it is widely accepted that extinction memory is context-specific, at least in adult rats. That is, any changes in temporal, physical, or internal context from where extinction training has occurred can bring back the fear memory without any re-training (i.e., spontaneous recovery, renewal and reinstatement). However, I have collected substantial behavioral and neurobiological evidence that show fundamental differences in the extinction processes across development. Specifically, postnatal day (P) 17 rats (infant/juvenile), in contrast to P24 rats (pre-adolescent), fail to show spontaneous recovery, renewal or reinstatement following extinction of learned fear, suggesting that extinction is context-independent and is effectively erasure in P17 rats. These differences are accompanied by developmental differences in the neural circuitry underlying extinction, as indicated by immunohistochemistry and localized infusion studies. Interestingly, spontaneous forgetting in P17 rats appears to be sensitive to contextual influences, which suggests a double dissociation between forgetting and extinction across development. These findings suggest novel ways to explore treatments for anxiety disorders, and highlight that treatments should focus on the young population.

TRACES OF MEMORY: WHY RELEARNING FEAR FOLLOWING FORGETTING IS AN NMDAR-INDEPENDENT PROCESS. Li, S; Langton, J.M.; Richardson, R. School of Psychology, The University of New South Wales, Australia. NMDA receptors (NMDArs) are thought to be crucial for learning and memory. However, recent studies have shown that under certain circumstances learning can occur without the involvement of NMDArs, such as during reacquisition and re-extinction. That is, in contrast to initial acquisition and extinction, we have recently demonstrated that reacquisition and re-extinction can occur without the involvement of NMDArs. In addition, this transition is context-dependent. We have continued this line of investigation by examining whether reacquisition of fear following forgetting would be mediated by NMDArs. Unlike adult animals that are able to retain fear memories for almost their entire lifespan, infant rats exhibit substantial and spontaneous forgetting over several days. In this series of experiments, infant postnatal day (P) 17 rats were trained to fear a white-noise which was paired with a footshock; these animals exhibited complete forgetting after 2 weeks, as indicated by low levels of freezing to the white-noise. We then injected rats with either an NMDAr-antagonist (MK-801) or saline and retrained them to fear the same white-noise. The question of interest was whether reacquisition would be impaired by administration of MK-801. In the case that forgetting involves erasure of the memory trace, reacquisition (like initial acquisition) should be NMDAr-dependent, but if the original fear memory trace persists, reacquisition should be NMDAr-independent. Other factors that may influence NMDAr involvement in reacquisition such as stimulus-specificity (does it matter what stimulus is used at reacquisition?), context (how does a change temporal context affect reacquisition?), and early-life experiences (how does an aversive experience early in life affect reacquisition later in life?) are also discussed. The presentation will highlight the importance of further research into the role of NMDArs in learning and memory.

8:00-10:00 **Poster Session 3:** Disease Models

112. LOCAL OREXINERGIC ACTIVATION AND THE INFLUENCE ON THE FORCED SWIM TEST. Arendt D; Oliver K; Summers C. University of South Dakota, Vermillion, SD. Affective disorders are too often the result from stress overburdening behavioral and physiological coping mechanisms. Repeated laboratory and real world examples demonstrate that animal populations are heterogeneous with respect to their susceptibility to the negative effects of excessive stress. This study was designed to understand the underlying basis behind these variable stress coping abilities. Evidence suggests that the orexin (hypocretin) system is involved in anxiety and depression. While orexin projects to many of the brain regions associated with stress and depression, a number of studies on this neuropeptide have conflicting results with respect to anxious or depressive behaviors. The reason for this contradiction may be that most of these studies involve systemic effects rather than specific brain areas. Our experiments correlate depressive behavior, as measured by the forced swim test (FST), with site-specific orexinergic activation in mice. An often overlooked detail of the FST is that it is stressful. As such, it provides a means to monitor both coping behavior, and the physiological effects of a stressor. We found a greater orexinergic activation of the dorsomedial-perifornical hypothalamus in response to the FST despite there being a lack of relationship with overall duration of immobility. Some of the variation in FST behavior can be explained by the level of the peptide in regions where orexenergic neurons project. In the CA1, CA3 and dentate gyrus of the hippocampus there was a strong negative linear relationship between orexin A and the duration of immobility, lending some support to the idea of orexin A in the hippocampus producing an antidepressant effect. The impact of orexin signaling in the basolateral, medial and central nuclei of the amygdala on FST performance is more complex due to a U-shaped

function, where animals exhibiting both high and low immobility exhibit increased orexin A expression. Orexin in the thalamic paraventricular nucleus, an area densely innervated by orexin fibers in addition to being a convergence site for stress circuitry, surprisingly did not correlate with immobility. Some of the questions left unanswered from the site specific quantification of the orexin ligands may be better addressed once the gene expression of the two receptors is examined more closely. Preliminary data show a weak correlation between the type two orexin receptor transcript in the hippocampus and FST performance.

113. NEUREGULIN 1 AND REPEATED RESTRAINT STRESS INTERACT TO PROMOTE DEFICITS IN SENSORIMOTOR GATING AND GROWTH OF DENDRITIC SPINES IN ADOLESCENT MICE. Arnold, J.C a,b,c.; Chohan T.W.a,b; Boucher A.A.b; Karl, T.c,d; Bennett M.R.b a Department of Pharmacology, Bosch Institute, University of Sydney 2006, Australia;b Brain and Mind Research Institute, Camperdown 2050, Australia; c Schizophrenia Research Institute, Darlinghurst 2010, Australia; d Neuroscience Research Australia, Randwick 2031, Australia. Neuregulin 1 (NRG1) is a schizophrenia-susceptibility gene that may predispose to sensorimotor deficits and confer vulnerability to stress. Here we examined whether repeated stress in adolescence affects sensorimotor gating function as measured by prepulse inhibition of startle (PPI) in heterozygous Nrg1 mice (Nrg1 HET) compared to wild type (WT) mice. We also examined whether stress differentially affected dendritic spine morphology in these mice. Adolescent mice were subjected to 14 daily, 30 min restraint sessions or left in their homecages undisturbed. On days 1 and 14, immediately after stress exposure, animals were first tested in animal models of anxiety (the elevated plus maze and then light-dark test) before being assessed for changes in PPI. Adolescent Nrg1 HET mice were marginally more sensitive to acute stress than WT mice as measured in animal models of anxiety, however both genotypes habituated to stress-induced modulation of anxiety-related behaviour by the final day of testing. While acute restraint stress did not affect PPI in either genotype, Nrg1 HET mice repeatedly exposed to restraint stress displayed PPI deficits that were not observed in non-stressed Nrg1 HET mice or stressed WT mice. Repeated stress increased the growth of dendritic spines in the prefrontal cortex of WT mice, an effect absent in Nrg1 HET mice. These results demonstrate that Nrg1 modulates neurobehavioural responses to repeated stress at a vulnerable period of neurodevelopment.

114. WHAT DRIVES A FISH TO DIVE? Motivation and defensive behavior in zebrafish R. Blaser and K. Goldsteinholm, University of San Diego The diving response exhibited by zebrafish upon exposure to a novel environment is one of the most common behavioral tests used with zebrafish. Although both the diving response and scototaxis are used as a measure of anxiety, the defensive behavioral repertoire of zebrafish is quite complex and not yet well understood. We report here the results of a series of experiments aimed at better understanding the defensive behavior of zebrafish, using the black/white test and a depth preference test. Using a visual-cliff type apparatus, we have determined that avoidance of the surface, and not approach to the substrate, motivates the diving response. Similarly, behavior in the black/white test appears to be motivated by avoidance of the white chamber rather than approach to the black chamber. In both tests, subjects exhibit immobility only in the preferred location (deep or dark location) if the choice is available. However, confinement to deep/shallow conditions produces different patterns of behavior than confinement to black/white conditions. Depth preference appears to be more sensitive to stressors or stimuli external to the test, while black/white preference may measure primarily the behavioral response to the test stimuli. Combined with previous experiments presenting the effects of drugs on behavior in the tests, we argue that the tests measure dissociable mechanisms of behavior.

115. DISTINCT NEUROBEHAVIOURAL PROFILE OF P2X7-/- MICE: IMPLICATIONS FOR MANIA, ANXIETY AND AGGRESSION. Boucher, A.A.; Todd, S.; Bennett, M.; Kassiou, M.; Arnold, J.C. Brain and Mind Research Institute and Department of Pharmacology, The University of Sydney, Australia. The P2X7 receptor is implicated in the pathogenesis of mood disorders such as depression and bipolar disorder and P2X7 knockout (P2X7-/-) mice show resilience in animal model of depression. Here we aim to examine whether P2X7-/- mice display altered social anxiety, obsessive-compulsive behaviour and aggression as measured in the social interaction, marble burying and resident-intruder tests respectively. P2X7-/- and WT mice were tested in the social interaction test and marble burying test at 4, 6, and 8 weeks of age. A separate cohort of P2X7-/- and WT mice were then examined in the resident-intruder test of aggression. The neural substrates underlying any differential aggressivity in P2X7-/- mice was also investigated using c-Fos immunohistochemistry. P2X7-/- mice showed longer latency to social interaction and decreased locomotor activity compared to WT mice at 4 weeks but not at 6 or 8 weeks, suggestive of impaired novelty seeking in P2X7-/- mice. P2X7-/- mice showed decreased levels of marble burying over weeks of testing which was most pronounced at 8 weeks of age. In the resident-intruder test P2X7-/- mice showed decreased time per aggressive incident and were significantly less likely to show severely aggressive behavior compared to WT mice. The medial orbitofrontal cortex showed greater c-Fos activation in P2X7-/- residents but not in WT mice. Furthermore, severely aggressive P2X7-/- mice showed increased c-Fos expression in the ventrolateral septum compared to WT mice. P2X7 receptor antagonists may therefore be potentially beneficial in the treatment of

multiple psychiatric disorders such as obsessive-compulsive disorders, those involving altered novelty seeking (e.g. mania and addiction) and aggression.

116. EFFECTS OF MATERNAL SEPARATION ON SOCIAL INTERACTION. Diehl, L.A.; Henriques, T.P.; Corra, C.N.; Lucion, A.B; Dalmaz, C. Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil. The tactile stimulation from the mother during the first week of life appears to have an important role in establishing stable behavioral phenotypes on the offspring. The study of social behavior is critical for understanding the neurobiological basis for psychiatric disorders specifically affecting this behavior. Our objective was to analyze the effects of maternal separation (MS) on social behaviors of adult rats. Male and female Wistar rats were submitted (or not) to repeated MS (3h/day) during postnatal days 1-10. At 70 days of age, the animals were submitted to social interaction test which lasted 20 min. The test apparatus consisted of 2 clear boxes (A and B) connected to a third (neutral). With the connecting doors closed, two adult rats from the same experimental group (regarding sex, MS or not) were placed into boxes A and B, one in each box. Each rat remained confined to its own box, without access to the neutral box, for 24 h. The doors to compartments were opened allowing both rats the exploration of all three compartments. It was observed: number and duration of attacks, boxing, biting; time spent in non-social behavior; and time spent in active social interaction (sniffing, mounting or crawling under or over the other rat). Two-way ANOVA test showed differences on social behaviors. Total sniffing: MS and sex effects, MS males had decreased scores; non-social behaviors: MS had increased scores; lateral attack: MS and sex effects, MS males had increased scores; frontal attack: MS and sex effects, MS males had decreased scores; boxing: MS and sex effects, MS and females had decreased scores. Considering the development of rodents, stressful events that happen in the early stages of life can affect neural systems and behavior. MS during the neonatal period may adversely affect the establishment of social relationships in adult life.

117. IMPAIRED CONTEXT DISCRIMINATION AND NMDA RECEPTOR EXPRESSION AND FUNCTION IN THE DENTATE GYRUS OF A MOUSE MODEL OF FRAGILE X SYNDROME. Eadie, B.1,2; Cushman, J.3; Majaess, N.2; Bostrom, C.2; Kannangara, T.2; Fanselow, M.3; Christie, B.2. 1.MD/PhD Program, University of British Columbia, Vancouver, BC, Canada. 2.Division of Medical Sciences, University of Victoria, Victoria, BC, Canada. 3.Department of Psychology, University of California, Los Angeles, CA, USA. Fragile X syndrome (FXS) is the most common form of inherited intellectual disability. This X-linked disorder is caused by the transcriptional repression of a single gene, Fmr1. The loss of Fmr1 transcription prevents the production of Fragile X mental retardation protein (FMRP), which in turn disrupts the expression of a variety of key synaptic proteins. A clear link between synaptic dysfunction and behavioral impairment has been elusive despite the fact that several animal models of FXS have been generated. Here we report that Fmr1 knockout mice exhibit impaired bidirectional NMDAR (N-methyl-D-aspartate receptor)-dependent synaptic plasticity, NMDAR subunit expression and NMDAR-mediated currents in the dentate gyrus (DG) of the hippocampus. Interestingly, mice lacking the Fmr1 gene show impaired performance in a context discrimination task that normally requires functional NMDARs in the DG. These data indicate that loss of FMRP results in significant NMDAR dysfunction in the DG and associated impairments in behavior.

118. PRENATAL EXPOSURE TO PROPIONIC ACID PRODUCES DEVELOPMENTAL DELAY, HYPER-SENSITIVITY TO ACOUSTIC STARTLE, AND SOCIAL IMPAIRMENT IN ADOLESCENT RATS Foley, KA; MacFabe, DF; Kavaliers, M; Ossenkopp, K-P Dept Psychology, Neuroscience Graduate Program, Univ. of Western Ontario, London CAN Gastrointestinal (GI) system influences may contribute to the development of autism spectrum disorders (ASD) as a subset of patients exhibit GI symptoms, with abnormal bacterial flora present in the GI tract. Propionic acid (PPA) is a short chain fatty acid and an enteric bacterial fermentation product. PPA infusion (ICV) in adult rats produces behavioral (repetitive movements, impaired social interaction) and brain changes (neuroinflammation, oxidative stress) similar to those seen in ASD patients. This study extends the PPA model to developing rats. Long-Evans rats were injected once/day SC with PPA (500 mg/kg; G12-16), lipopolysaccharide (LPS, 50 μ/kg; G15-16) or phosphate buffered saline vehicle. Pups were monitored for developmental milestones and assessed in multiple behavioral paradigms in adolescence. Pups exposed to PPA or LPS prenatally displayed developmental delay. Hypersensitivity to acoustic startle, in the absence of prepulse inhibition deficits, was found in offspring and preliminary results suggest that female offspring of PPA-treated dams show significant social impairment, avoiding conspecific animals in an open-field. These results provide further support for the hypothesis that PPA and immune stimulation may be environmental factors contributing to the development of some forms of ASD.

119. CHEMOPROTECTIVE POTENTIAL OF COCCINIA INDICA AGAINST CYCLOPHOSPHAMIDE INDUCED OXIDATIVE STRESS AND GENOTOXICITY IN BONE MARROW Hirani K*, Nitharwal R#, Karchuli MS#, Patel H#, Ugale RR# *Sylvester Comprehensive Cancer Center, University of Miami Hospitals and Clinics, Miller School of Medicine, USA. #Division of Neuroscience, Department of Pharmacology, S.K.B.College of Pharmacy, Kamptee, Nagpur 440024, India. Although cyclophosphamide (CP), an alkylating agent is used in the treatment of cancer owing to its broad spectrum efficacy, its metabolites exhibits severe undesired toxicities in normal cells. The present study was aimed to investigate the chemoprotective potential of Coccinia indica against CP induced oxidative stress and genotoxocity in bone marrow. Animals were orally pre-treated with Coccinia indica extract (200, 400 mg/kg) for five consecutive days. On 5th day these animals were injected with CP (50 mg/kg i.p) and sacrificed after 24 hr. for the evaluation of oxidative stress, micronucleus formation and chromosomal aberrations. We found that the CP induced increase in the serum biomarker enzymes like alkaline phosphatase (ALP), alkaline aminotransferase (ALT) and aspartate aminotransferase (AST) were significantly reduced by Coccinia indica extract. We also found that the CP significantly increased malondialdehyde (MDA) and decreased catalase and glutathione (GSH) levels in brain and it was significantly reversed by Coccinia indica extract (400 mg/kg). Further, pre-treatment with Coccinia indica extract (200, 400, 600 mg/kg) significantly and dose dependently reduced micronuclei formation and incidence of aberrant cells. Thus, the present results indicate the chemoprotective potential of Coccinia indica extract against CP induced oxidative stress and genotoxicity in bone marrow.

120. IPOPOLYSACCHARIDE ALTERS HYPOTHALAMIC NEUROPEPTIDE EXPRESSION AND INDUCES A STATE OF NEGATIVE ENERGY BALANCE THROUGH THE CYCLO-OXYGENASE-2 DEPENDENT PRODUCTION OF PROSTAGLANDINS. Ganegala, H; Parkington, H; Hollis, J. Monash University, Melbourne, Australia**.** Lipopolysaccharide alters hypothalamic neuropeptide expression and induces a state of negative energy balance through the cyclo-oxygenase-2 dependent production of prostaglandins. Hasini Ganegala, Helena C. Parkington, Jacob H. Hollis Department of Physiology, Monash University, Melbourne, Victoria 3800, Australia. Inflammatory factors signal through hypothalamic neuropeptide systems to promote a state of negative energy balance, i.e. reductions in food intake and increases in energy expenditure. The primary hypothalamic neuropeptide systems that regulate energy balance include the pro-opiomelanocortin (POMC) neurons and neuropeptide Y (NPY) neurons of the arcuate nucleus. The present study has investigated in mice the acute effects of peripheral lipopolysaccharide (LPS, 100 μg/kg bw) with and without selective cyclo-oxygenase-2 (COX-2, 50 mg/kg/d) inhibition of prostaglandins on POMC, NPY and prostaglandin receptors 3 (EP3) and 4 (EP4) gene expression, as well as a number of measures of energy balance (food intake, respiratory exchange ratio, body temperature). LPS administration increased POMC and decreased NPY gene expression, increased the expression of EP3 and EP4, reduced food intake, decreased respiratory exchange ratio, and increased body temperature. COX-2 inhibition partially attenuated many of the effects of LPS, both in terms of POMC and NPY gene expression, as well as measures of energy balance. In a second series of experiments, central (icv) administration of prostaglandin E2 (PGE2, 100 nmol) increased the expression of the immediate early gene Fos within POMC neurons and also had much of the same effects on measures of energy balance as peripheral LPS administration. These studies will provide insight into potential therapeutics to counter the anorexia and cachexia suffered in chronic diseases such as cancer.

121. EXTENDED EXPOSURE TO NATURAL AND ARTIFICIAL ENRICHED ENVIRONMENTS: NEUROBIOLOGICAL AND BEHAVIORAL RESPONSES IN MALE LONG EVANS RATS. 1Hyer, M.; 1Rzucidlo, A.; 2de Silva, I.; 3Bardi, M.; 1Lambert, K. Dept. of Psychology, 1Randolph-Macon College, Ashland VA USA 23005; Dept. of Psychology, 2University of Richmond, VA USA; Dept. of Psychology, 3Marshall University, Huntington WV USA. Prior research in our laboratory suggests that exposure to natural, as opposed to artificial, stimuli in complex enriched environments differentially affects emotional responses. In the current study, effects of longer durations of varied types of enrichment were explored. Long-Evans male rats were randomly assigned to one of three environments [laboratory (L), artificial enriched (AE), or natural enriched (NE)] for sixteen weeks (n=10). Either artificial or natural objects intended for manipulation/exploration, hiding, digging or climbing comprised the enriched and naturalistic habitats. Subsequently, rats were exposed to four behavioral assessments; a problem-solving digging task, predator odor exposure, novel object exploratory task, and a diving escape task. Fecal samples were collected following habitat exposure for one month and analyzed for corticosterone (CORT) and dehydroepiandrosterone (DHEA). Animals were perfused following the dive-escape task and brains were processed for c-Fos, brain derived neurotrophic factor (BDNF), and neuropeptide Y (NPY) immunoreactivity (ir). BDNF and NPY ir were quantified in the dentate gyrus and bed nucleus of the stria terminalis, respectively. NE animals exhibited a longer latency to dig in the predator odor task than AE animals (p=.04); additionally, NE rats exhibited shorter freezing durations than the L and AE groups during the novel object task (p=.004). Focusing on brain data, NE animals exhibited decreased levels of fos-ir in the basolateral amygdala than the other groups (p=.01) and more fos-ir in the nucleus accumbens core than the L group (p=.05). No effects were observed in CORT or DHEA levels

or in other brain areas investigated. In sum, extended exposure to the NE habitats led to context specific fear responses; additionally, fos data suggest that the NE animals experienced less fear and more motivation during the water escape task. Thus, extended NE exposure may enhance emotional resilience in rodents.

122. BEHAVIORAL DISCREPANCY BETWEEN GIT1-/- AND GIT1+/- MICE. Jiseok Lee. Dept. of Biological Sciences. Korea Advanced Institute of Science and Technology, 373-1 Guseong-dong, Yuseong-gu, Daejeon 305-701, Republic of Korea. GIT1 is a multi-domain adaptor protein enriched in synapses. GIT1 is involved in diverse processes including receptor trafficking and cytoskeletal regulation. We generated Git1 mutant mice to study the function of GIT1 at behavior levels. We analyzed both Git1-/- and Git1+/-, and found that Git1-/- show increased locomotor activity in open field test, which is alleviated by amphetamine treatment. In contrast, Git1+/- showed locomotor activity comparable to wild-type, although the activity amount decreased near the end of open field session. When treated with amphetamine, Git1+/- showed increased locomotor activity, which is similar to typical response to psychostimulants in wild-type animals. Thus, Git1 mutant mice are one case of showing behavioral discrepancy between homozygous and heterozygous mutants.

123. INHIBITORY EFFECT OF PHELLODENDRI CORTEX ON LIPOPOLYSACCHARIDE-INDUCED MEMORY IMPAIRMENT IN RATS Lee, B.; Sur, B.J.; Shim, I.; Lee, H.; Hahm, D.H. Acupuncture and Meridian Science Research Center, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea. The purpose of this study was to examine whether Phellodendri cortex extract (PCE) could improve learning and memory impairments caused by lipopolysaccharide (LPS)-induced inflammation in the rat brain. The effect of PCE on modulating pro-inflammatory mediators in the hippocampus and its underlying mechanism were investigated. Injection of LPS into the lateral ventricle caused acute regional inflammation and subsequent deficits in spatial learning ability in the rats. Daily administration of PCE (50, 100, 200 mg/kg, i.p.) for 21 days markedly improved the LPS-induced learning and memory disabilities in the Morris water maze (MWM) and passive avoidance tests. It also significantly improved other LPS-induced sickness behavioral symptoms, such as locomotor impairment and body weight loss. PCE administration significantly decreased mRNA expression of pro-inflammatory mediators such as tumor necrosis factor- (TNF-), interleukin-1 (IL-1), and cyclooxygenase-2 (COX-2) in the hippocampus, as assessed by RT-PCR analysis and immunohistochemistry. Together, these findings suggest that PCE significantly attenuated LPS-induced spatial cognitive impairment through inhibiting the expression of pro-inflammatory mediators in the rat brains. These results suggested that PCE extract may be effective in preventing or slowing the development of neurological disorders, including Alzheimers disease, by improving cognitive and memory function due to its anti-inflammation activity in the brain (This research was supported by by the National Research Foundation of Korea Grant funded by the Korean Government (MEST)(2010-0003678)).

124. WHAT ARE WE ASSESSING IN JUVENILE PLAY BEHAVIOR? Lewter, L.; Hohmann, C.F. Department of Biology, Morgan State University, Baltimore MD. Play behavior has been used to test for sociability in juvenile rodents models for depression and schizophrenia. Our lab has used play behavior in a neonatal serotonin depletion model for autism spectrum disorder (ASD), as well as in a mouse model for neonatal stress effects. For the ASD model, three litters of AMC (n=15), vehicle injected (Veh) (n=12), and 5,7-DHT lesioned mice (n=10) that were tested in a Play Behavior Task adapted from Moy et al. Two weanlings, the test mouse and stranger mouse, are monitored for social interactions that include investigative and affiliative behavior, play soliciting (including pinning and wrestling) and non-social interactions such as exploratory and repetitive behaviors. We found decreased play behavior in 5,7-DHT lesioned mice, compared to both AMC and Veh, as well as decreased affiliative behavior compared to AMC. For the neonatal stress model, three litters of AMC (n=17) and four litters of stressed (STR) (n=14) and litter mate control (LMC) mice (n=12) were behaviorally tested in the same task. Here, we found decreased affiliative behavior in both STR and LMC mice, compared to AMC but an increase in play behavior. Thus, in the autism model, affiliative and play behavior trended into the same direction, while these two behaviors segregated in the neonatal stress model. This raises the question if affiliative and play behavior measure two substantially different types of social behavior. We are currently re-analyzing the different components of play behavior to see if pre-aggressive behaviors, such as pinning, may be more prevalent in the neonatal stress model. Supported by: SO6GM51771, U54MH066417 & 5R25GM058904.

125. GIT1 KNOCK-OUT MICE DISPLAY IMPAIRED HABITUATION AND ANXIOLYTIC BEHAVIORS. Mah, W.; Won, H.; Kim. E. Department of Biological Sciences. KAIST, Daejeon, South Korea. G protein-coupled receptor kinase interacting protein 1 (GIT1) is a multi-domain scaffolding protein and signaling adaptor, which is highly enriched at neuronal synapses and plays critical roles in synapse formation and maintenance. Recently a novel association between Attention Deficit/Hyperactivity Disorder (ADHD) and GIT1 gene has been revealed. In addition, GIT1 knock-out mutant mice (Git1−/−) show ADHD-like phenotype, which is ameliorated by treatment of psychostimulants, such as amphetamine and methylphenidate. Although the basic behavioral phenotypes were

characterized in previous study, further characterization is needed to fully understand the phenotypes of GIT1 knockout mice. Here, I show the impaired habituation and anxiolytic behavior in elevated plus maze of Git1-/- mice. These data suggest Git1-/- mice also have problems in cognition and anxiety emotions.

126. THE EFFECT OF EMBRYONIC ALCOHOL EXPOSURE ON SOCIAL BEHAVIOR AND NEUROCHEMISTRY IN TWO DIFFERENT ZEBRAFISH STRAINS. Mahabir, S.; Chatterjee, D.; Buske, C.; Gerlai, R. Dept. of Psychology, University of Toronto Mississauga, Mississauga, ON, CA. The biological mechanisms of social behaviour of vertebrates are complex and not well understood. Low concentrations of alcohol employed for a short period of time during early development of zebrafish caused no observable anatomical abnormalities, however, the exposed fish showed impaired social behaviour (i.e. reduced shoaling) at their adult age. Here we analyze the effect of embryonic alcohol exposure on the ontogenesis of shoaling (group forming) in two zebrafish strains, TU and AB. We expose the zebrafish to ethanol 24 hour post- fertilization for 2 hours using five concentrations, 0.00%, 0.25%, 0.50%, 0.75%, 1.00% (EtOH vol/vol %). We test shoaling behaviour of each group at 7, 23, 39, 55, 71 and 87 days post fertilization (dpf), a longitudinal analysis. We also analyze the levels of neurochemicals dopamine, DOPAC (the metabolite of dopamine), serotonin and 5HIAA (the metabolite of serotonin) from whole brain extracts of the treated fish at four time points: 15, 40, 70 and 102 dpf. We are currently completing the analyses but preliminary results have already revealed an intriguing strain effect: AB fish show a significantly more robust age-dependent increase compared to TU fish. Embryonic alcohol exposure induced changes in shoaling are also expected based upon two independent studies already published. We suggest that zebrafish may be successfully utilized to investigate the genetic underpinning of shoaling and we hope that once completed our analyses will reveal differences in alcohol responses between the strains and facilitate the identification of genes underlying naturally occurring variation in social behaviour and abnormal social behaviour associated with alcohol consumption as it happens in Fetal Alcohol Syndrome Spectrum Disorder cases.

127. ABNORMAL NEURONAL ACTIVATION IN RESPONSE TO NOVELTY AND SOCIAL INTERACTION IN BTBR T+tf/J MICE. Meyza, K.Z.; Pearson, B.L.; Pobbe, R.L.H.; Blanchard, D.C.; Blanchard, R.J. Pacific Biosciences Research Center and Department of Psychology, University of Hawaii at Manoa, Honolulu, HI 96822 USA. Autism spectrum disorders (ASD) are behaviorally characterized as impairments in social interaction and communication accompanied with repetitive behaviors. Since the genetics of the disorder is complex with as many as 100 contributing genes, the best way to find out what neuronal circuits are involved in formation of autistic phenotype, is to use animal models of ASD. Among them, the BTBR T+tf/J (BTBR) mice were shown to have the strongest face validity. We have compared the c-Fos protein expression in 23 brain areas of BTBR and highly social c57BL/6J (B6) mice after exposure to a novel arena or social interaction. We found that several nuclei, including cortical and central amygdala, CA3 field of the hippocampus, paraventricular and dorsomedial nucleus of the hypothalamus, ventral premammilary nucleus and the ventrolateral column of the periaqueductal grey react differently to these two types of stimuli in BTBR and B6 mice. The neuronal activation patterns observed in BTBR mice suggest that their social behavior impairments are related to stronger stress responsiveness of the HPA axis and that they find social interactions aversive and fear-evoking.

128. ELEVATED BRAIN HEPARAN SULFATES IN THE NEUROGENIC LATERAL VENTRICLE WALL OF MECP2 MUTANT MICE. Pearson, B.L.; Corley, M.J.; Blanchard, D.C., Blanchard R.J. Dept. of Psychology and Pacific Biosciences Research Center. University of Hawaii at Manoa, Honolulu, HI 96822 USA. Methyl CpG-binding protein 2 (MECP2) is an autism candidate gene and underlies most cases of Rett syndrome. Throughout development, MECP2 is expressed in an activity-dependent manner in neurons and regulates transcription of a variety genes implicated in psychiatric diseases. MeCP2 protein alters the expression of a variety of sulfotransferases and other extracellular matrix heparan sulfate (HS) glycosaminoglycan-regulating enzymes which, through growth factor sequestering and signaling, regulate neurogenesis, brain development and neuroplasticity. To determine if MeCP2 mutation affects the abundance of HS, dual channel immunohistochemistry and confocal microscopy were performed for HS and laminin, a basement membrane glycoprotein, in the lateral ventricle subependymal zone of adult male MeCP2 wild-type and truncated (MeCP2-308/Y) mutant mice. No genotype differences were noted in the number of HS- and laminin-immunoreactive puncta (fractones) in the subventricular zone. Likewise, no significant genotype effect was found for the average laminin immunoreactivity per fractone. However, there was a significant genotype difference in the mean level of HS-immunoreactivity; mutant (Y/-) mice displayed an elevation. Similarly, the ratio of HS to laminin was significantly increased in the mutants. Interestingly, these effects appeared to be isolated to bregma +1 but not in more posterior regions of the lateral ventricle, where mutant and wild-type siblings displayed comparable levels. This anatomical specificity might be relevant in light of noted disturbances in the forebrain and striatum in autism and Rett syndrome. These results converge on recent findings of HS disturbances in two other rodent models of autism and suggest that extracellular matrix regulatory

systems might underlie or contribute to altered neurodevelopmental trajectories in pervasive developmental disorders.

129. OXYTOCIN RECEPTOR AND MECP2(308/Y) KNOCKOUT MOUSE STRAINS DISPLAY ALTERED EXPRESSION OF AUTISM-RELATED SOCIAL BEHAVIORS. Pobbe, R.L.; Pearson, B.L.; Blanchard, D.C.; Blanchard, R.J.; Pacific Biosciences Research Center, University of Hawaii, Honolulu, HI 96822 USA; Department of Psychology, University of Hawaii, Honolulu, HI 96822 USA. The development of tasks measuring behaviors specific to the three major symptom categories of autism spectrum disorders (ASD) makes it possible to differentiate mouse models in terms of changes in these specific categories. Prior studies indicate that BTBR T+tf/J mice, the strain that has been evaluated most extensively, show autism-relevant changes in all three symptom categories; reciprocal social interactions; communication; and repetitive, ritualized behaviors. The present study was conducted to further analyze the expression of social behaviors of oxytocin receptor (Oxtr) and Mecp2(308/Y) wild-type (WT) and knockout (KO) mice, in comparison to the extensively described behavioral changes of BTBR mice, in a battery of tests specifically designed to provide information on behaviors that may show functional parallels to the core symptoms of ASD. Oxtr KO mice show robust decreases in reciprocal social interactions, and reduced levels of communication, but no changes in repetitive, ritualized behaviors; whereas Mecp2(308/Y) KO mice show a slight but consistent enhancement of social behavior and communication, and no changes in repetitive, ritualized behaviors. This data base strongly indicates that mouse models can sort the diagnostic symptoms of ASD, and suggests that biological and physiological analyses of these strains may be capable of providing differential information on the brain systems involved in particular symptoms of this group of disorders.

130. DEPRESSION & ANXIETY DIFFERENTIALLY PREDICT HPA REACTIVITY TO COUPLE CONFLICT. Powers, S.; Laurent, H.; Gunlicks-Stoessel, M.; Balaban, S.; Bent, E. Center for Research on Families, Dept. of Psychology, Neuroscience and Behavior Program. University of Massachusetts, Amherst MA 01003 USA; Univ. of Wyoming (Laurent); Univ. of Minnesota (Gunlicks-Stoessel). There is ample empirical evidence that stress in humans close relationships predicts increased depression and anxiety. Psychoneuroendocrine research has firmly established the association of depression and anxiety with dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. This study tested the extent to which patterns of HPA reactivity and recovery under conditions of conflict in close relationships were differentially predicted by older adolescents depression and anxiety. We examined adolescent dating couples salivary cortisol responses to a laboratory discussion of a heated and unresolved relationship conflict. One hundred and ninety-nine opposite-sex couples, 18 21 years old, provided seven salivary samples in anticipation of the conflict, during the conflict, and throughout an hour-long recovery period. Symptoms and clinical diagnoses were assessed through questionnaires and structured diagnostic interviews. Hierarchical linear modeling was used to model the entire trajectory of the HPA response as predicted by symptoms or diagnoses. Womens depression predicted attenuated cortisol levels during discussion, with a flatter response curve a pattern consistent with earlier and more chronic course of depression by young adulthood and higher likelihood of comorbid trauma symptoms. In contrast, mens depression and womens anxiety predicted higher, hyper-activated cortisol levels. Discussion will focus on the relevance of links between social stress and HPA functioning in human adolescent couples for animal models of depression and anxiety.

131. PRENATAL EXPOSURE TO BACTERIAL LPS LEADS TO LONG-LASTING PHYSIOLOGICAL CONSEQUENCES IN MALE OFFSPRING. Solati, J.; Asiaei, M. Department of Biology, Faculty of Science, Karaj Branch, Islamic Azad University, Karaj, Iran. Growing evidence suggests that early life events are critical determinants for disorders later in life. According to a comprehensive number of epidemiological/animal studies, exposure to lipopolysaccharide, causes alteration in pro-inflammatory cytokine levels, hypothalamicpituitaryadrenal functioning and the hormonal system which may contribute to behavioral and neurological injuries. In this study we investigated the effects of lipopolysaccharide administration on physiological parameters in pregnant dams and their male offspring aged 9 weeks. In gestational Day 10, pregnant mice were injected intrapritoneally with Salmonella enterica lipopolysaccharide to model prenatal exposure to infection. The following results were obtained for offspring from dams stressed during pregnancy: (a) reduced anxiety-related behavior in the elevated plus maze; (b) reduced food and water intake; (c) reduced body weight from birth up to postnatal Day 40. The observed data provide experimental evidence showing that prenatal stress can have complex and long-lasting physiological/behavioral consequences in offspring.

132. TAIL-PINCH-INDUCED EATING IS ASSOCIATED WITH EMOTIONALITY AND ACTIVATION OF HYPOTHALAMIC-PITUITARY-ADRENAL AXIS. Someya N1; Narikiyo K2; Masuda A3; Hata T1,4; Tsuneyoshi D1; Aou S1. 1Kyushu Institute of Technology, Kitakyushu; 2The University of Tokyo, Bunkyo-ku; 3RIKEN, Wako; 4Kyushu University, Fukuoka, Japan. It is known that mild stress induced by a tail-pinch facilitates eating in rats. However, the relationship between stress-induced eating and individual physiological and

psychological characteristics has not been elucidated. Thus we investigated whether tail-pinch-induced eating is associated with anxiety-like behavior and/or activation of hypothalamus-pituitary-adrenal (HPA) axis using male Sprague-Dawley rats (n=43). At 7 weeks of age, anxiety-like behavior was assessed on the elevated plus maze (EPM). At 8 weeks of age, tail-pinch-induced eating was observed in an experimental field as follows: After a 30-min habituation period, the tail-pinch was applied for 5 min, followed by a 30-min recovery period. Then blood was obtained from 19 of 43 rats. During the habituation and recovery periods, rats were allowed to access food ad libitum. During the recovery period, we observed sizeable inter-individual variability in the amount of food intake. Thus, we divided the rats into high-responder (HR) and low-responder (LR) groups (n=18 and n=25, respectively). The amount of food intake was significantly greater in HR than LR during the recovery but not during the habituation period. The percentage of time spent in the open arms in the EPM was significantly greater in LR than HR. In addition, plasma concentration of corticosterone was tended to be higher in LR (n=13) than HR (n=6). These results suggest that the rats showing higher anxiety consumed more food after mild stress without concomitant activation of HPA.

133. MATERNAL SEPARATION AND POSTNATAL OXYTOCIN ADMINISTRATION ALTER SOCIAL RECOGNITION MEMORY IN ADOLESCENT FEMALE MICE. Thomas, N.R., Cornwell, C.A. Depts. of Psychology. SUNY-Cayuga Community College, Auburn, NY 13021 and Syracuse University, Syracuse, NY 13244. Maternal separation of infant rodents results in long term changes in physiology and behavior, but data regarding its effects on later social interactions are sparse. This study determined whether separating female infant mice from their mother, but not siblings, for 3 hours daily, on postnatal days (PND) 1-14, influences social recognition memory in adolescence (Experiment 1), and whether injecting the social neurohormone, oxytocin (1 mg/kg), on PND 1-14, influences adolescent social memory or social odor preferences in control and maternally separated (MS) female mice (Experiments 2 and 3). Short- and long-term social recognition, defined as decreased investigation of a previously encountered adolescent female, were tested on PND 49 and 50 using the habituation-dishabituation design. Odor preferences were examined on PND 48 in a two-choice test (social nest bedding vs. fresh shavings). In Experiment 1, compared to control mice, MS females showed diminished social recognition over a 10 min interval and no recognition over a 24 hr interval that separated exposures to a consistent female stimulus animal. MS females also showed impaired discrimination between a previously encountered and novel mouse during dishabituation trials. Postnatal oxytocin injections did not alter either social recognition or social odor preferences in control females in Experiment 2, but improved these measures in MS females in Experiment 3. MS-induced disruption of the ability of adolescent female mice to recognize and discriminate social cues may be linked to its effects on oxytocin system development.

134. VICARIOUS SOCIAL DEFEAT INDUCES DEPRESSION- AND ANXIETY-LIKE BEHAVIOR AND DYSREGULATES GENE EXPRESSION WITHIN THE VTA. 1Warren B.L., 1Alcantara L.F., 1Wright K.N., 2Vialou V., 1Iiguez S.D., 2Nestler E.J., 1Bolaos-Guzman C.A. 1Department of Psychology, Program in Neuroscience, Florida State University. 2Fishberg Department of Neuroscience, Mount Sinai School of Medicine. It is well known that exposure to severe stress increases the risk for developing mood disorders. However, less is known about the complex interactions between witnessing and experiencing traumatic events. This study assesses the effects of a novel social stressor that is insulated from the effects of physical stress. Briefly, an adult male C57BL/6J mouse was socially defeated (PS) by a larger more aggressive CD1-mouse, while a second male C57BL/6J mouse witnessed this interaction from an adjacent compartment (ES). Ten days of exposure to ES induced long-lasting deficits in a battery of behavioral assays designed to assess changes in mood. Specifically, ES exposure increases sensitivity to anxiety- and stress-eliciting situations both 24 h and 1 month after witnessing physical stress. Increases in levels of serum corticosterone, a steroid hormone signaling stress response, accompanied these behavioral deficits. Additionally, we used high throughput sequencing to measure changes in VTA transcription. Interestingly, we found that a number of transcripts were dysregulated following exposure to ES. Taken together, these data indicate that witnessing traumatic events is a potent stressor in adult male mice capable of inducing long-lasting neurobiological perturbations.

135. KAOLIN-INDUCED VENTRICULOMEGALY AT WEANING PRODUCES LONG-TERM LEARNING AND MEMORY DEFICITS IN RATS. Williams, M.T.; Lindquist, D.M.; McAllister, J.P. II; Mangano F.T.; Yuan, W.; Vorhees, C. V. Cincinnati Childrens Research Foundation and University of Cincinnati College of Medicine, Cincinnati, OH. Primary Childrens Medical Center and University of Utah, Salt Lake City, UT. Kaolin injection in the cisterna magna of rats produces a permanent barrier to CSF outflow and results in ventriculomegaly and increased intracranial pressure. If left untreated, long-term behavioral changes can occur. Previous research with kaolin induced ventriculomegaly (KIV) shows that neonatal administration has mixed effects on Morris water maze (MWM) performance and motoric performance, perhaps because the severity of the ventriculomegaly was not accounted for in those studies. In this experiment, Sprague Dawley rats were injected with kaolin or saline on

postnatal day (P)21. Evans ratios at the end of testing (P49-P50) were used to subdivide the kaolin injected animals into 4 groups. Locomotor ability and MWM were tested starting on P28 and again on P42. Kaolin injected rats weighed less than controls throughout testing. Differences in locomotor ability were not apparent until P42. In the MWM on P28 (122 cm diameter tank), all KIV groups had longer path lengths than controls, but comparable swim speeds. With the exception of the lowest Evans ratio kaolin group (0.4-0.5), probe trial performance was worse in the KIV groups relative to controls. On P42 in the MWM (240 cm diameter tank) only the highest Evans ratio kaolin group (0.7-0.82) showed deficits in the MWM compared with control animals. These high Evans ratio animals demonstrated no learning in the test relative to all other groups and were the only group to show no probe trial preference for the platforms location. The swim speeds during the MWM test were comparable among the groups, suggesting that motor deficits were not responsible for the learning deficits observed. These data suggest that ventriculomegaly during the initial stages affects learning and memory regardless of severity, and more severe enlargement leads to longer term learning and memory deficits.

136. FACILITATION OF PANIC-RELATED DEFENSIVE BEHAVIORS AFTER CORTICOTROPHIN-RELEASING FACTOR (CRF) INJECTION IN THE RAT DORSOLATERAL PERIAQUEDUCTAL GRAY. Zangrossi, H.; Sergio, T.O. School of Medicine of Ribeirao Preto, University of Sao Paulo, Brazil. The neuropeptide CRF has been consistently implicated in the pathophysiology of anxiety. Recent clinical evidence suggests that polymorphisms in CRF-1 receptor gene may be associated with panic. The dorsal periaqueductal gray matter (DPAG) in the midbrain contains high concentration of CRF1 and CRF2 receptors, and has been considered a key region controlling behavioral and autonomic reactions associated with panic. The aim of this study was to characterize the role of DPAG CRF-1 and CRF-2 receptors in the mediation of the escape reaction evoked by either the electrical stimulation of this midbrain area or the elevated T-maze. Based on pharmacological evidence, these responses have been related in terms of psychopathology to panic attack. Male Wistar rats were implanted with a guide-cannula or a chemitrode (a guide cannula plus an electrode) aimed at the DPAG. One-week later, they were intra-DPAG injected with ovine CRF (non-selective CRF1/2 receptor agonist), the CRF1 receptor antagonist antalarmin or the preferential CRF2 agonist urocortin, Tests in the DPAG stimulation model or elevated T-maze were performed 10 min later. The results showed that microinjection of CRF facilitated escape expression in both animal models, indicating a panicogenic-like effect. Intra-DPAG injection of antalarmin or urocortin 2 was without effect. When antalarmin was administered before CRF, it fully blocked the panicogenic effect caused by the neuropeptide. Therefore, facilitation of CRF1 receptor-mediated neurotransmission in the DPAG potentiates the expression of panic-related defensive responses and this mechanism may be of importance in the pathophysiology of panic disorder. Financial support: FAEPA and CNPq (Brazil).

137. MORPHOLOGICAL AND FUNCTIONAL DEFECTS OF NEUROTRANSMITTER AND NEUROTROPHIN RECEPTORS CAUSED BY EG5 MOTOR PROTEIN INHIBITION LEADING TO COGNITIVE IMPAIRMENT IN ALZHEIMER`S DISEASE. Csilla Ari[1,2], Sergiy I. Borysov[1,2,3,7], Timothy D. Boyd[1,2] , Jiashin Wu[5], Jaya Padmanabhan[1,2], and Huntington Potter[1,2,3,6,7] 1 USF Byrd Alzheimer's Institute; 2 Department of Molecular Medicine, College of Medicine; 3 Eric Pfeiffer Suncoast Alzheimer's Center; 4 School of Aging Studies, College of Behavioral and Community Sciences; 5 Department of Molecular Pharmacology and Physiology, College of Medicine; 6 Florida Alzheimer's Disease Research Center, University of South Florida, Tampa FL, 33613, USA; 7 Moffitt Cancer Center, 12902 Magnolia Drive MRC-PSY Tampa, FL 33612. Our objective was to test whether Aβ or mutant PS/APP-induced microtubule dysfunction reduces cell surface localization and function of neurotransmitter and neurotrophin receptors (including p75 or NMDA), therefore leading to cognitive deficits in neurodegenerative diseases. Previous work had shown that APP over-expression or Aβ treatment disrupts the cellular MT network and causes mis-localization of Low Density Lipoprotein Receptor (LDLR). Furthermore Aβ was found to directly bind to and inhibit certain microtubule-dependent kinesin motors, including Eg5, which are necessary for mitotic spindle structure and function and are also present in mature neurons. Polymorphisms linked to Eg5/KIF11 are shown to increase AD risk. Cultures were generated of cortical+hippocampal neurons from brains of E18 mice and of H4/H4APP cells. Immunolabelled cell surface receptors were quantified by laser scanning confocal microscope. Inhibition of Eg5 by Aβ or the specific Eg5 inhibitor, monastrol reduced transport of the NMDA and NGF/NTR (p75) receptors to the cell surface. Monastrol or Ab treatment of PC12 cells reduced their sensitivity to NGF stimulation. Furthermore, like Aβ, monastrol inhibited long term potentiation, a cellular model of NMDA-dependent learning and memory, and Eg5 activity was almost completely absent from brains of APP/PS mice, which also show LTP deficits. Results of behavioral studies of mice at 2 months and 7 months of age treated with monastrol or vehicle only will be compared to transgenic PS/APP mice. Impairment in working memory trials will also be discussed based on assessment by radial arm water maze test. These data imply that cognitive deficits in Alzheimer's disease and Downs syndrome may derive in part from inhibition of neuronal Eg5 by Aβ, resulting in impairment of neuronal function through neurotransmitter and neurotrophin receptor mislocalization.

138. BCL9 AND C9ORF5 ARE ASSOCIATED WITH NEGATIVE SYMPTOMS IN SCHIZOPHRENIA: META-ANALYSIS OF TWO GENOME-WIDE ASSOCIATION STUDIES. Chun Xu; Nagesh Aragam; Erika Cynthia Villla; Yolanda Posada; ChunXiang Mao; Cynthia Camarillo; Yu Mao; Michael A Escamilla; Ke-Sheng Wang. Texas Tech University Health Sciences Center, El Paso, TX. Objective: Schizophrenia is a chronic and debilitating psychiatric condition affecting slightly more than 1% of the population worldwide. While positive symptoms are ameliorated with pharmacologic treatment, negative symptoms appear to be more resistant to treatment. Schizophrenia has also been shown to be a multifactorial disorder with a high degree of hereditability (80%) based on family and twin studies. More than 1000 susceptibility genes have been suggested, but definitive biomarkers remain elusive. Increasing lines of evidence suggest intermediate phenotypes/endophenotypes are associated with causes of the disease and less genetically complex than the broader disease spectrum. Therefore, our overall objective was to try to identify genetic variants that are associated with the presence of negative symptoms in schizophrenia by analyzing two genome-wide association (GWA) data sets: The GAIN sample from the Molecular Genetics of Schizophrenia including 1172 European-American patients with schizophrenia and 1379 matched healthy controls, while the nonGAIN sample represents 1090 European-American patients with schizophrenia and 1316 matched healthy controls. Method: Amongst the 2262 patients with schizophrenia, 835 met the DSM-IV-TR criteria for negative symptoms. Logistic regression analyses of negative symptoms of schizophrenia were performed for both samples using PLINK. Results: We identified six single nucleotide polymorphism (SNPs) in three genes/loci strongly associated with the presence of negative symptoms in schizophrenia ($p < 6.22$ 10-6), which included three SNPs in BCL9 gene (rs583583 showed the strongest association at $p = 6.00$ 10-7, OR = 1.28), two SNPs in C9orf5 ($p < 1.32$ 10-6) and one SNP in ST3Gal1 gene ($p = 2.46$ 10-5). Interestingly, two of three disease-associated BCL9-SNPs are located at species-conserved regions which suggest functional importance in gene regulation. This gene is thought to be involved in neuroplasticity, cell survival, and neurogenesis. Conclusion: Our current results provide pilot evidence to support the use of negative symptoms as an intermediate phenotype to dissect the complex genetics of schizophrenia. This is the first report to observe an association of BCL9, C9orf5 and ST3Gal1 genes with negative symptoms in schizophrenia and highlights the potential use of these SNPs as specific genetic markers for negative symptoms. However, additional studies are warranted to examine the underlying mechanisms of these disease-associated SNPs in the three genes.

139. SEIZURE 6-LIKE GENE ASSOCIATED WITH BIPOLAR DISORDER I Chun Xu[a,*], Jerry Mullersman[b], Liang Wang[c], Brenda Bin Su[d], ChunXiang Mao[e], Yolanda Posada, Yu Mao, Michael A Escamilla[a], Ke-Sheng Wang[c* a] Texas Tech University Health Sciences Center, Paul L. Foster School of Medicine Departments of Psychiatry and Neurology and The Center of Excellence in Neuroscience, El Paso, Texas [b]Department of Pathology (JEM), James H. Quillen College of Medicine, East Tennessee State University, Johnson City, TN 37614, USA [c] Department of Biostatistics and Epidemiology, College of Public Health, East Tennessee State University, Johnson City, TN 37614, USA [d] College of Bioinformatics Science and Technology, Harbin Medical University, Harbin 150086, the People's Republic of China [e] Univeristy of Toronto. Objective: Although genetic factors have been implicated in the etiology of bipolar disorder (BD), no specific gene has been conclusively identified. Given the evidence from the previous reports on the gene gender interaction and BD-associated genes/loci on human chromosome 22q11-13, a candidate gene association approach was applied to study the involvement of the genes/loci located on 22q11-13 in the susceptibility to BD as well as exam sex-specific genetic association with BD. Method: All genotype data on 22q11-13 from 691 BD cases and 1081 matched controls using the Affymetrix Genome-wide human SNP Array 6.0 from European American population were selected from the publicly available data of Whole Genome Association Study of Bipolar Disorder Study Accession: phs000017.v3.p1. PLINK and HAPLOVIEW were used to conduct single nucleotide polymorphism (SNP) and haplotype analyses. Results: Significant differences in the distribution of the alleles for 16 SNPs of SEZ6L gene were observed between the female bipolar patients and healthy controls. Conclusions: The results obtained in the European American population, for the first time, suggest the SEZ6L genetic variants associated with the female BD patients and provide additional compelling evidence of genetic variation on 22q11-13 that influences BD risk. The present findings highlight the interaction between gene-gender as an important factor modifying BD susceptibility.

140. EXECUTIVE FUNCTIONS IN AGENESIS OF THE CORPUS CALLOSUM: WORKING MEMORY AND SUSTAINED ATTENTION IN BTBR MICE. Gregg, M.; Sample, H.; Neal, H.; Branson, N.; Martin, L.A. Dept. of Graduate Psychology. Azusa Pacific University, Azusa, CA 91702 USA. Agenesis of the corpus callosum (AgCC) is a disorder characterized by the congenital partial or complete absence of the corpus callosum. The BTBR T+tf/J (BTBR) inbred mouse strain has consistently been observed to have a complete absence of the corpus callosum as well as a variable reduction in the size of the hippocampal commissure. While much research has recently focused on the social deficits of the BTBR strain, research on its cognitive behavior has been limited. Based upon cumulative evidence from human patients, AgCC is thought to cause a generalized deficit in complex behavior while simple behaviors remain intact. In this research, we test the hypothesis that simple executive functions remain

intact in AgCC but deficits emerge as complexity increases. To this end, we compared working memory and attention between the BTBR strain and the C57BL/6J strain, a common inbred strain that is widely used as a control for research on the BTBR mouse. Working memory was assessed with the delayed matching-to-position task and attention was measured with the sustained attention task. Both of these tasks involve operant conditioning and require discrimination between learned associations. It was hypothesized that BTBR mice would perform similar to B6 controls in simple versions of these tasks, but would demonstrate a deficit in performance as task difficulties increased. Early results have shown that approximately 40% of the BTBR mice fail to make learned associations between lever-pressing and the food reward. Histological analysis is underway in order to determine if generalized learning deficits are related to reductions in the hippocampal commissure.

141. QUANTITATIVE ASSESSMENT OF SOCIAL MOTIVATION IN BTBR AND C57BL/6J MICE THROUGH NOVEL OPERANT CONDITIONING PARADIGMS. Wood, C.; Sample, H.; Neal, H.; Gregg, M.; Branson, N.; Martin, L.A. Dept. of Graduate Psychology. Azusa Pacific University, Azusa, CA 91702 USA. Research on mouse models will benefit from the development of novel assays of complex social behavior including social motivation. The goal of this research is to develop and validate new quantitative measures of social motivation for mouse models of autism and other disorders involving social deficits. To this end, two operant conditioning paradigms that allow a test mouse to control access to another mouse have been employed. In the first paradigm, the test mice were trained to press a lever for a social reward in the form of access to an unfamiliar stimulus mouse for 15 sec. The social reward was set on a progressive ratio schedule with a step size of three. The number of lever presses achieved in the final trial of a testing session (breakpoint) was used as an index of social motivation. In the second paradigm, motivation for a food reward was compared to a social reward. The mice were conditioned to associate one lever consistently with a food reward and another consistently with the same social reward described in the previous paradigm. Research has been carried out with the C57BL/6J mouse, a prosocial inbred mouse strain, and on the BTBR T + tf/J (BTBR) mouse, an inbred mouse strain with previously documented social deficits. In addition to these novel quantitative measures of social motivation, traditional assessments of social behavior were conducted through the use of the ANYMAZE video tracking system, including a version of the 3-chamber task. Preliminary results indicate a trend for the BTBR mice to have a reduced breakpoint compared to the C57BL/6J mice.

142. MATERNAL PROBIOTIC INTERVENTION PROTECTS AGAINST NEUROENDOCRINE AND IMMUNE DYSFUNCTIONS AND DISRUPTION OF GUT MICROFLORA BALANCE PROVOKED BY NEONATAL AND SUBSEQUENT ADULT STRESS IN WISTAR RATS. Barouei, J.; Hodgson, D.M. Laboratory of Neuroimmunology, the University of Newcastle, Newcastle, Australia. This study aimed to examine whether maternal probiotic intervention can act to alleviate HPA axis, immune and colonic dysfunctions induced by early life and subsequent adult stress in Wistar rats. Female breeders had free access to a drinking water supply with or without probiotic Bifidobacterium lactis Bb12 and Propionibacterium jensenii 702 added from 10 days before conception until weaning day (PND 22). Pups were subjected to neonatal maternal separation (NS) from PND 2 to 14 or left undisturbed. In adulthood, animals were exposed to restraint stress (RS) for 30 min per day (PND83-85) followed by 30 min isolation at PND 86, or were set aside as controls. Immediately blood samples were collected to assess plasma corticosterone and IgA levels. Faecal pellets were also analysed for the composition of gut microflora. Exposure to RS or NS+RS significantly increased plasma corticosterone levels and counts of fecal Bacteroides, and declined counts of bifidobacteria compared with the controls ($p \leq 0.05$). Maternal probiotic intake normalised corticosterone levels in males but not females and returned the numbers of both bacterial groups to the control levels. Significant decreases in plasma IgA levels were observed in NS and NS+RS females born to vehicle-treated mothers compared to the control ($p \leq 0.05$), whereas in probiotic subset, significant increases were noted in both males and females in these treatment conditions relative to their respective vehicle controls. Our findings suggest that maternal probiotic intake can protect against HPA axis and immune system dysfunctions and disrupted gut microflora provoked by early and/or later life stress. Underlying mechanisms however need to be further investigated.

143. NEONATAL LIPOPOLYSACCHARIDE EXPOSURE ALTERS NOCICEPTION Zouikr I.1, Tadros M.A.2, Callister R.J.2, Nakamura T.1, Beagley K.3 , Clifton V.4 and Hodgson D.M.1. 1.Laboratory of Neuroimmunology, 2.School of Biomedical Sciences & Pharmacy, University of Newcastle, Australia. 3.Institute of Health Biomedical Innovation, Queensland University of Technology, Australia. 4. School of Paediatrics and Reproductive Health, University of Adelaide, Australia. Neonatal exposure to the bacterial mimetic, lipopolysaccharide (LPS) produces long term psychobiological and neurobiological changes such as altered immune, endocrine and behavioural responses. Early exposure to LPS is known to alter pro-inflammatory cytokines which play a critical role in the modulation of pain. The aim of the current study was to determine the long-term impact of LPS neonatal exposure on nociception using the formalin test. Wistar rats were subjected to either LPS (salmonella enteriditis, 0.05mg/kg, ip) or saline (equivolume) on postnatal days (PND) 3 and 5. At PND13 and PND22, rats underwent a subcutaneous

injection of 0.8% and 1.1% formalin (respectively) into the plantar surface of the hindpaw. Subsequent behavioural assessment involved counting flinching and licking the injected paw for one hour post-injection. After behavioural testing, transverse spinal cord slices (300m thick) were prepared for whole-cell patch-clamp recording (KCH3SO4-based internal) from superficial dorsal horn (SDH) neurons. At PND13, rats subjected to LPS (n=16) displayed significantly more flinching responses compared to saline treated animals (n=13) at 5 min (p = .009) and 15 min (p = .03). Whole-cell patch-clamp recordings from SDH neurons revealed no differences in input resistance, capacitance or resting membrane potential between the two groups (n=18 and 17). The patterns of action potential discharge observed in response to sustained current injection did not differ between groups. At PND22, LPS-treated animals (n=6) displayed significantly higher licking responses at 5 min (p = .023) compared to saline-treated animals (n=7). Neonatal LPS exposure results in elevated behavioural responses to formalin at PND13 and PND22. This response is not accompanied by changes in selected intrinsic properties of SDH neurons at PND13. Ongoing analysis will determine the neural and immune mechanisms underlying the observed behavioural differences.

144. COMMUNICATION AND STEREOTYPED BEHAVIORS OF MICE EXPOSED TO MATERNAL IMMUNE ACTIVATION Defensor, E.B.; Jensen, A.L.; Miske, M.M.; Yamamoto, L.H.L.; Blanchard, D.C.; Blanchard, R.J. Pacific Biosciences Research Center and Department of Psychology, University of Hawaii, Honolulu, HI 96822 USA. Deficits in communication and the display of stereotyped and repetitive behaviors serve as two of the three diagnostic symptoms for autism. A strong genetic component for the disorder is indicated by the 4:1 male to female prevalence and the approximately 70% concordance rate for monozygotic twins. However, given that the concordance rate for autism in monozygotic twins is less than 100%, it is implied that there are also non-genetic causal mechanisms for the disorder. Clinical data from over 10,000 cases suggests that prenatal viral infection is a risk factor for autism. The current study assessed communication as well as stereotyped and repeated behaviors of mouse offspring exposed to maternal immune activation (MIA). Pregnant mouse dams were administered either 20 mg/kg of polyinosinic-polycytidylic acid (poly I:C), to mimic viral infection and immune activation, or phosphate-buffered saline (PBS), used as a vehicle control. Behavioral testing of male and female offspring began at PND 70. To test for communication, scent marking behavior and ultrasonic vocalizations (USVs) were measured. To test for stereotyped and repeated behaviors, a microanalysis of grooming behavior was performed. Results from the scent marking test showed that there were no differences between poly I:C and PBS males; however, poly I:C females deposited a lower percentage of total scent marks near a live stimulus mouse. USVs measured in social proximity showed that there was no difference in number of USVs emitted between the male PBS and male poly I:C groups; however, poly I:C females emitted less USVs than PBS females. Analysis of grooming patterns showed that poly I:C males displayed a strict pattern of rostral to caudal grooming transitions. In addition, Poly I:C females groomed for longer durations than PBS females. Taken together, these results suggest that MIA produces sex-dependent changes in communication and stereotyped behaviors.

145. SOCIAL BEHAVIOR OF MICE EXPOSED TO MATERNAL IMMUNE ACTIVATION. Jensen, A.L.; Defensor, E.B.; Yamamoto, L.H.L.; Miske, M.M.; Blanchard, D.C.; Blanchard, R.J. Pacific Biosciences Research Center and Department of Psychology, University of Hawaii, Honolulu, HI 96822 USA. Deficits in reciprocal social interactions serve as a core symptom of autism. Despite a strong genetic component, other non-genetic causal mechanisms have been proposed for the disorder. Prenatal viral infection, in particular, has been proposed as an underlying mechanism for the manifestation of autistic symptoms. The current study assessed the social behaviors of mouse offspring exposed to maternal immune activation (MIA). Pregnant dams were administered either 20 mg/kg of polyinosinic-polycytidylic acid (poly I:C), a synthetic double-stranded RNA which mimics viral infection, or phosphate-buffered saline (PBS) used as a vehicle control. Offspring were weaned at postnatal day (PND 21) and housed with same-sex littermates. Behavioral testing of male and female offspring began at PND 70. Mice were assessed in a 3-chamber test for social approach, in a social proximity test and in a semi-natural visible burrow system (VBS). In the 3-chamber test males in the poly I:C group failed to display a preference for the chamber containing a live mouse when compared to the empty chamber; whereas, the male PBS group did display a preference for the social side. The opposite effect occurred in females: the poly I:C group showed a preference for the social side; whereas, the PBS group did not. In the VBS, the poly I:C group showed moderate sex-dependent decreases in interactive behaviors, when compared to the PBS group. The poly I:C and PBS groups did not show differences in behaviors measured in the social proximity test for males or for females. Taken together, these data suggest that prenatal MIA differentially alters social behaviors in males and females.

146. DETERMINATION OF ANXIETY DIFFERENCES BETWEEN C57BL/6 N AND J MICE TO INVESTIGATE EMOTIONAL PERSEVERATION. Landrau1, S.; Rodríguez1, C.; Vilarchao1, J.; Sáez1, E.; Santos2, I.; López1, O.; Budet1, A.; Hernández1, G.; Peña De Ortíz2, S.; Méndez-Merced1, A.T. 1Universidad del Este, Escuela de Ciencias y Tecnología, Carolina, PR, USA 00984; 2Universidad de Puerto Rico, Departamento de Biología, Río Piedras, PR, USA 00931. We are interested in studying the behavioral and gene expression differences within brain

regions potentially related to emotional perseveration in two C57BL/6 mouse substrains. Emotional perseveration is defined as the resistance to extinguish a previously learned fear. In the Pavlovian tone fear conditioning paradigm, C57BL/6 J mice are able to extinguish previously acquired fears more efficiently than C57BL/6 N mice; i.e., N mice are poor fear extinguishers, compared to J mice. Such impairment constitutes a form of emotional perseveration, or continued execution of fear related behaviors, similar to what can be displayed in Post Traumatic Stress Disorders (PTSD) patients. However, it is not known whether these two subtrains differ in terms of innate anxiety, which have been proposed as a possible indicator of PTSD susceptibility in humans. 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) and Light/Dark Transition (LDT) paradigms. We also measured corticosterone blood levels of naïve and post-EPM tested N and J mice by correlated enzyme immunoassay (EIA; Correlated EIA, Assay Designs). We hypothesized that if innate anxiety is significantly higher in N mice in relation to J animals, they will have higher concentrations of bloodstream stress hormones, explore less and spend more time in the enclosed dark safe areas of the paradigms. Our EPM tests trials showed that N mice spend significantly more time in the open arms and have a greater number of open arm entries compared to J mice. Furthermore, J mice spend significantly more time in the hub (EPM center), groomed more and had a greater number of partial and complete entries to the closed arms compared to N mice (n=14). The LDT tests showed that both substrains had comparable number of entries and amount of time spend in either, light or dark chambers. Nevertheless, J mice had significantly more partial entries to the dark LDT side than N animals (n=16). No significant difference was found in corticosterone concentrations when compared either naïve or post-EPM tested N and J mice. Therefore, N impairment to extinguish previously learned fear in relation to J mice is not related to higher levels of pre-existing anxiety in relation to J mice. Our data suggests that N mice are curious, engaging in exploratory and risky behaviors, when compared to J mice. Furthermore, J mice displayed a cautious behavior, keeping close to or within the secure enclosed and/or dark areas of the paradigms, which parallel to the animal's burrow, when compared to N mice. *Supported by*: NIMH 1SC1MH086072, MHDBSBRN-NIH IP20MD003355, and URGREAT-MBRS-RISE 2R25GM066250-05A

147. GENETIC BASES OF DIFFERENCES RELATED TO EMOTIONAL PERSEVERATION IN MOUSE SUBSTRAINS. Sáez1, E.; Budet1, A.; Landrau1, S.; Hernández1, G; Peña de Ortíz2, S.; Méndez-Merced1, A.T. 1Universidad del Este, Escuela de Ciencias y Tecnología, Carolina,PR, USA 00984; 2Universidad de Puerto Rico, Departamento de Biología, Río Piedras, PR, USA 00931. We are interested in studying the cellular and molecular neurobiological bases for individual differences related to emotional perseveration. Emotional perseveration is defined as the resistance to extinguish a previously learned fear. We use two C57BL/6 mouse substrains, J versus N, as animal models. In the Pavlovian fear conditioning paradigm, a behavioral procedure used to study the brain mechanisms underlying the acquisition and storage of information about danger induced fear, J mice are able to extinguish previously acquired fears more efficiently than N mice. Such impairment constitutes a form of emotional perseveration. Since fear extinction is considered as a new learning we want to address gene expression substrain differences within brain regions associated to extinction of conditioned fear. We hypothesize that N (poor extinguishers) and J (good extinguishers) mice display significant differences in the modulation of genes related to learning and memory processes during fear extinction. For the present study we performed quantitative Real Time Polymerase Chain Reaction (qRT-PCR; TaqMan Master Mix and Gene Expression Assay, Applied Biosystems) for CREB, Nurr-1 and c-Fos genes within the amygdala and hippocampus brain regions. We ran four replicates of pooled (n=2) samples from naïve and 30 min to one hour post-extinction trained N and J mice. Quantifications of both target (CREB, Nurr1, c-Fos) and reference (β-actin) genes were done with the standard curve and comparative threshold, delta CT, methods (1.4 Sequence Detection 7300, Applied Biosystems). Statistical analyses were performed using Prism version 4.0 (Graph Pad Software. Inc.). One-way ANOVA and Bonferroni's multiple comparisons test were used to assess the differences in mean and standard error between particular group pairs. A *p* value of <0.05 is accepted as statistically significant. Our results showed that the relative levels of c-Fos mRNA within the amygdala of post-extinction trained N and J mice were significantly up-regulated when compared to naïve animals (N mice p value < 0.05; J mice p value < 0.001). In the hippocampus, the relative c-Fos and Nurr-1 mRNA levels were found to be significantly up-regulated in N post-extinction trained animals only (N_{Fos} p value < 0.05; N_{Nurr} p value < 0.001). In this investigation we have collected data supporting the notion that the two substrains of C57BL/6 mice, N and J, display differences in the modulation of genes related to tone/context fear extinction learning. Supported by: NIMH 1SC1MH086072, MHDBSBRN-NIH IP20MD003355, and URGREAT-MBRS-RISE 2R25GM066250-05A

148. PREDATOR EXPOSURE INDUCES INHIBITED EXPLORATORY BEHAVIOR AND INCREASED AVOIDANCE OF TRAUMA-ASSOCIATED CUES. M Toth1, M Gross2, R Adamec3, and VB Risbrough1,2 1Department of Psychiatry, University of California San Diego, USA; 2Veterans Affairs Center of Excellence for Stress and Mental Health; 3Department of Psychology Memorial University, St Johns, Canada Posttraumatic stress disorder (PTSD) is a chronic anxiety disorder precipitated by extreme traumatic experiences, showing persistant

recurrence of the trauma memory, avoidance of trauma-related cues, and hyperarousal. Exposure of rodents to feline predator stress was shown to induce enduring generalized anxiety, increased startle and reduced exploration. Here we conducted a study to determine if exposure to feline predator stress can also model avoidance of trauma-related cues. C57BL/6J mice were exposed to a feline predator for 10 min or handled. Twenty-one days later we examined their response to an open field arena containing a cylinder with soiled cat litter or clean bedding. Handled controls spent a significantly greater amount of time investigating the cylinder filled with soiled cat litter compared to a cylinder with clean bedding. In contrast, mice exposed to feline predator stress showed the opposite pattern of effects, exhibiting significantly reduced exploration of the predator-scented cylinder. Time spent exploring the cylinder with clean bedding was not different across handled control and stressed mice, suggesting changes in overall exploration was not a confounding factor. In addition, predator stressed mice exhibited reduced center exploration of the open field compared to handled controls. These data suggest that predator stress induces prolonged increases in generalized anxiety-like behavior as well increases in avoidance of trauma-related cues.

149. BEHAVIORAL AND NEUROCHEMICAL ANALYSIS OF HDC-KO MICE, A MODEL OF A GENETIC FORM OF TOURETTE SYNDROME Authors: *Baldan Ramsey, L. C. 1; Crowley, M. J. 1; Hughes, Z. A. 2; Gorczyca, R. 2; Ohtsu, H. 3; De Araujo I. 1,4; State, M. 1; Mayes, L. C. 1; Pittenger, C. 1 1Yale Univ., New Haven, CT; 2Pfizer, Inc., New London, CT; 3Tohoku Univ., Sendai, Japan; 4Pierce Institute, New Haven, CT. Tourette Syndrome (TS) is a neurodevelopmental disorder characterized by stereotyped motor and vocal tics. In a genetic study of a family with a high density of TS cases, the State laboratory identified a potentially causal mutation in the gene encoding the rate-limiting enzyme in the biosynthesis of histamine: histidine decarboxylase (HDC). We examined HDC knockout mice as an animal model of this rare Mendelian form of TS. We tested behavioral stereotypy in HDC knockout (KO) mice, heterozygotes (HET), and wild-type (WT) littermate controls after administration of amphetamine (AMPHET). 8.5 mg/kg AMPHET produced stereotypical behaviors in the KO, but very few in HET or WT mice during the day period. These findings were replicated during the dark (active) period, when histamine levels in WT mice are higher. The increased in stereotypies potentiated by AMPHET in the HDC-KO mice were attenuated in a dose-dependent manner by haloperidol. We found both HDC-KO and HET to have deficits in prepulse inhibition (PPI) during the day and night periods. The family with the mutation in the HDC gene also showed impairment in PPI. These phenotypes mirror aspects of TS and support the face and predictive validity of the animal model for this family. The model possesses inherent construct validity, since the KO recapitulates the functional disruption found in this TS family. Histamine inhibits midbrain dopamine neurons. We hypothesized that reduction in histamine in these animals would increase extracellular levels of dopamine in the striatum. The HDC-KO mice showed dysregulation in dopamine in the dark period, relative to the WT controls, as measured by in vivo microdialysis. HDC-KO mice also presented very low levels of histamine in the striatum. These experiments establish an exciting new model for future studies on the pathophysiology of TS.

150. TOP DOWN CONTROL OF SEROTONERGIC SYSTEMS IN DEPRESSIVE-LIKE BEHAVIORS. Challis, C; Boulden, J; Beck, S.G.; Berton, O. Department of Psychiatry. University of Pennsylvania, Philadelphia, PA 19104 USA. Imaging studies reveal prefrontal cortex (PFC) dysfunction in major depressive disorder (MDD) and experimental use of deep brain stimulation in this region has yielded promising therapeutic results. Further studies demonstrate an intact serotonin (5-HT) system is required for this effect, particularly that of the Dorsal Raphe Nucleus (DRN), which contains the largest number of 5-HT neurons. However, the DRN is neuronally heterogeneous and its circuitry relevant to MDD has not been fully characterized. Reports suggest that PFC-DRN pathways converge on GABA neurons in the DRN, and we believe these GABA neurons play a key role in mediating antidepressant response and stress resiliency. In this work we use viral-mediated fluorescent tracers, whole cell patch clamp electrophysiology and optogenetic techniques in population-specific Cre- driver mice to explore the function of local DRN circuitry, as well as projections from the PFC, in the social defeat model of depression. We found that PFC glutamatergic projections preferentially synapse on DRN GABA neurons and that these GABA neurons show a significant increase in neural activity compared to 5-HT neurons following bouts of defeat. There were also location-specific electrophysiological changes in 5-HT and GABA neurons throughout the extent of the DRN in mice that underwent defeat. Additionally, we generated burst firing and silenced tonic firing of DRN GABA neurons in mice that were injected with a conditional (Cre-dependent) Channelrhodopsin or Archaerhodopsin respectively. We are currently performing behavioral tests with these techniques in social defeat conditions. The observed changes in DRN GABAergic neurons suggests that this cellular population may play an important role in mediating 5- HT activity in mood disorders and that manipulation of these neurons may have therapeutic implications.

151. KLP-1 RESCUES PREPULSE INHIBITION DISRUPTIONS AND SOCIAL WITHDRAWAL INDUCED BY NMDA CHANNEL BLOCKERS: A POTENTIAL ANTIPSYCHOTIC. Chiou, L.-C.1; Lee, H.-J.1; Chen, H.-L.1 ; Chou, R.-F.1; Mouri, A.3; Huang, W.-J.2; and Nabeshima, T.3 1Grad. Inst. Pharmacology, Coll. Med., Natl Taiwan

Univ.; 2Grad. Inst. Pharmacognosy, Taipei Med. Univ., Taipei, TAIWAN; 3Grad. Sch. Pharmaceutical Sci., Meijo Univ., Nagoya, JAPAN. Previously, we found a patient with intractable motor tic disorder, a spectrum of Tourette syndrome (TS), was responsive to the ground leaf juice of a local herb, Clerodendrum inerme (CI). Her tics subsided 1 hour after taking CI. No hemo-, renal- or hepatic toxicity was found after 2 years follow-up. Here, we examined CI effects on animal behaviors mimicking TS, hyperlocomotion and sensorimotor gating deficits. The latter is also observed in schizophrenic patients and can be reflected by a disruption of prepulse inhibition of acoustic startle response (PPI) in animal models induced by methamphetamine (MA) and NMDA channel blockers (ketamine, MK-801 and phencyclidine (PCP)), based on hyper-dopaminergic and hypo-glutamatergic hypotheses, respectively. The ethanol extract of CI (10-300 mg/kg, i.p.) inhibited MA (2 mg/kg, i.p.)-induced hyperlocomotion and PPI disruptions induced by MA, ketamine (30 mg/kg, i.p.) and MK-801 (0.3 mg/kg, i.p.), but not spontaneous locomotor activity, rotarod performance and grip force. From CI ethanol extract, we found a purified compound, termed KLP-1 (10 mg/kg), was effective in rescuing PPI disruptions induced by MA, ketamine, MK-801 and PCP (10 mg/kg). KLP-1 also reinstated MA-disrupted PPI in mice knocked out of the risk gene of schizophrenia, neuregulin-1. These results suggest that CI ethanol extract and KLP-1 can relieve hyperlocomotion and improve sensorimotor gating deficits, supporting the therapeutic potential of CI in TS and schizophrenia. Interestingly, KLP-1 also significantly improved social withdrawal-like behaviors in mice chronically treated with PCP, which mimic negative symptoms of schizophrenic patients. This finding reinforces the potential benefit of KLP-1 in schizophrenia treatment since negative syndromes are poorly treated by currently available antipsychotics.

152. RESTRAINT STRESS RELIEVES DEPRESSION-LIKE BEHAVIOR AND INDUCES ADULT NEUROGENESIS VIA OREXIN 2 RECEPTORS IN MICE. Chiu, S.-Y.1, Teng, S.-F.2, Chang, L.-Y1 and Chiou, L.-C.1, 2 1Graduate Institute and 2Department of Pharmacology, College of Medicine, National Taiwan University, Taipei, TAIWAN. The orexin system consists of orexin A and B and orexin 1 (OX1) and 2 (OX2) receptors, has been reported to be associated with depression in both human and animal studies. Acute restraint stress can activate hypothalamic orexin neurons. Here, we examined if the orexin system activated by restraint stress plays a role in relieving a depressive behavior, immobility in the forced swimming test (FST), and adult neurogenesis in mice. Adult neurogenesis was measured by the number of cells double-immunolabeled by doublecortin (a neuronal marker) and BrdU (a cell proliferation marker) in the subgranular zone of the dente gyrus (DG). Mice subjecting to restraint stress for 30 min showed significantly shorter immobility time in the FST than un-restrained mice. Orexin A (1 nmol/0.5 ml/mouse, i.c.v.) reproduced the effect of restraint stress, i.e. reducing FST immobility time. Pretreatment with the OX2 (Compound 29, 30 mg/kg, i.p.), but not OXR1 (SB-334867, 15 mg/kg, i.p.), antagonist for 15 min significantly reversed the immobility time shortening in mice induced by restraint stress and i.c.v. orexin A. Both antagonists alone had no effect in the FST. Acute restraint stress for 30 min also increased the number of Brdu/doublecortin double-immunorective cells in the DG subgranular zone. This restraint stress-induced neurogenesis was prevented by Compound 29 (30 m/kg, i.p.). These results suggest that acute restraint stress results in activation of hypothalamic orexin neurons to release orexins which lead to an antidepressant-like effect and adult neurogenesis mediated through OX2 receptors.

153. GIT1+/- MICE DISPLAY DIFFERENT CELLULAR PHENOTYPES IN BRAIN FROM GIT1-/- MICE WHICH ARE AN ADHD MOUSE MODEL. Chung, C. Dept. of Biological Sciences. Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea. Inhibitory neuronal transmission is crucial for regulating firing rate and timing of excitatory neurons. Impairment of inhibitory neurons has been postulated to underlie the pathogenesis of neuropsychiatric disorders, such as autism, schizophrenia, bipolor disorder, and so on. Recently, association of GIT1 with attention deficit/hyperactivity disorder (ADHD) was suggested by human single nucleotide polymorphism (SNP) analysis and Git1 knockout (Git1-/-) mice study. In particular, substantial reduction in presynaptic input at Git1-/- inhibitory synapses was detected. The association of GIT1 heterozygosity in the human rs550818 SNP with enhanced ADHD susceptibility predicts that Git1 heterozygous (Git1+/-) mice might show ADHD-like phenotypes like Git1-/- mice. Thus, we investigated whether presynaptic input was reduced in Git1+/- mice with immunohistochemistry. Surprisingly, Git1+/- mice did not show any detectable reduction in inhibitory presynaptic input. This result indicates that Git1+/- mice display different cellular phenotypes in brain from Git1-/- mice which are a novel ADHD mouse model.

154. IMPLICATION OF THE TRANSCRIPTION FACTOR NPAS4 IN COGNITIVE AND SOCIAL FUNCTIONS. Coutellier L., Beraki S., Saw N.L., Shamloo M. Behavioral and Functional Neuroscience Laboratory, Stanford University School of Medicine, Stanford, CA 94305, USA. A deregulation of the excitatory-inhibitory balance has been associated with a variety of human neurological disorders such as schizophrenia or autism. Most scientific studies have focused on the molecular mechanisms underlying the regulation of excitatory synapses. However, less is known about the activity-dependent regulation of inhibitory synapses and its reference to nervous system disorders. Here we are studying the transcription factor Npas4, which has been shown to regulate the formation and

maintenance of inhibitory neurons. We first found that Npas4 is highly expressed in the brain and more specifically in the cortex and limbic system. Then, using a Npas4 knockout (KO) mouse line, we demonstrated the importance of Npas4 in social and cognitive functions: Npas4-KO animals showed social avoidance toward an unfamiliar conspecific and aggressivity toward their WT littermates. They also displayed impaired pre-pulse inhibition, indicative of sensorimotor gating deficits. Finally, we observed that mice lacking Npas4 have hippocampal-dependent memory impairments as tested in the novel object recognition test and a place-reversal learning task. Altogether, these results demonstrate the importance of the inhibitory pathways in the expression of social behavior and cognitive functions. Studying further the transcription factor Npas4 might help obtaining a better understanding of neurological diseases characterized by an imbalance between inhibition and excitation such as autism or schizophrenia.

155. NEONATAL EXPOSURE TO ANTIDEPRESSANT RESULTED IN ADULT DECREASE OF NEUROLIGIN 1 IN THE PREFRONTAL CORTEX IN RATS. Feng, P.; Zhang, J.; Akladious, A.; Hu, Y. Div. Pul, Critical Care and Sleep Med, Dept Medicine, Case Western Reserve University/Cleveland VA Med, Cleveland, OH. Neuroligins (NLGNs) are synaptic adhesion proteins (SAPs) that play a role in regulating synaptic excitability and the formation of synapses. Alterations of NLGNs are associated with learning and cognitive behavior and the pathology of autism. A whole-genome association study of depression showed a linkage between depression and NLGN1 gene expression on chromosome 3 (Lewis et al., 2010). It has been consistently demonstrated that neonatal exposure to an antidepressant, clomipramine (CLI), produces adult behavioral despair and depression pathology. Our question is whether neonatal exposure to CLI will also produce adult changes of behavior and SAPs in brain regions associated with the regulation of mood and cognitive functions. Male Long Evans Hooted rats were administered with either CLI or saline for two weeks started from 8 days of age. For treatment details, please see Feng et al., 2008. At 4 month of age, rats were tested for immobility and social interaction. The rats were then sacrificed under CO2 anesthesia, and brain tissue was dissected and processed for RNA extraction using the Trizol method. First-strand cDNA synthesis was generated from total RNA using random primers that contained M-MLV reverse transcriptase. NLGN1 and NLGN2 expression levels in the hippocampus, prefrontal cortex, frontal cortex, and parietal cortex were identified by relative quantitative RT-PCR performed by multiplexing corresponding primers. The relative values of NLGNs were calculated by dividing the signal obtained for NLGN by that of 18S. The expression level of NLGN1 but not NLGN2 significantly decreased (-53%, $p = 0.008$) in the prefrontal cortex in CLI rats compared with controls. However, the expression levels of both NLGN1 and NLGN2 significantly increased in the frontal cortex (NLGN1: $p = 0.03$; NLGN2: $p = 0.01$) and parietal cortex (NLGN1: $p = 0.08$; NLGN2: $p = 0.06$) in CLI rats compared with controls. The expression levels of NLGN1 and NLGN2 were not altered in the hippocampus. Because NLGN1 and NLGN2 have opposite effects in regulating synaptic excitability, simultaneous increases in NLGN1 and NLGN2 in the frontal cortex and parietal cortex suggest that the changes in these two regions are not specific. Thus, we conclude that NLGN1 alterations in the prefrontal cortex are involved in the pathology of depression.

156. CANNABINOIDS: CANNABINOIDS: A RISK FACTOR FOR A NEUREGULIN 1 MOUSE MODEL OF SCHIZOPHRENIA? Karl T.1, Long L.1, Boucher A.2, McGregor I.2, Huang X.-F.3 and Arnold J.2 1Neuroscience Research Australia, Randwick, Australia 2University of Sydney, Australia 3University of Wollongong, Australia. Heavy cannabis consumption, particularly during adolescence, appears associated with an increased risk of developing schizophrenia (SZ) in susceptible individuals. However, cannabis is a mixture of cannabinoids, including the psychotomimetic cannabinoid receptor 1 (CB1) agonist Δ9-tetrahydrocannabinol (THC) and the potentially antipsychotic-like cannabidiol (CBD). To clarify the role of cannabinoids in the development of SZ, we investigated the effects of chronic CB1 stimulation (i.e. THC and CP 55,940 treatment) in adolescent/ adult mice mutant for the SZ candidate gene neuregulin 1 (i.e. Nrg1 HET). We also characterized the impact of adult CBD exposure in these mice.Adolescent male Nrg1 HET mice and their wild type-like (WT) littermates received vehicle or THC (10 mg/kg i.p.; 21 days), whereas adult cohorts were treated with vehicle, CP 55,940 (0.4 mg/kg; 15 days) or CBD (1, 50, 100 mg/kg; 21 days). Mice (N = 10/cohort) were tested for SZ-related behaviours and accompanying changes to neuronal activity (i.e. Fos expression) or expression of SZ-relevant receptors.Adolescent mice were equally sensitive to the locomotor suppressant effects of THC. Neither treatment nor genotype had any impact on prepulse inhibition. THC impaired cognition and suppressed social interaction in WT mice. However, Nrg1 mutants developed behavioural tolerance to chronic CB1 stimulation more readily than WTs. Exposure to CBD attenuated the hyperlocomotor activity and prepulse inhibition deficit observed in vehicle-treated Nrg1 HETs. Behavioural changes were linked to altered neuronal activity and receptor expression. Nrg1 mutants appear less sensitive to effects of adolescent CB1 stimulation but more susceptible than WT mice in adulthood. Importantly, chronic CBD rescued partially some of the behavioural abnormalities of Nrg1 mice.

157. OXYTOCIN RECEPTOR KNOCKDOWN PRAIRIE VOLES DISPLAY SOCIAL DEFICITS AND PROVIDE NOVEL MODELS FOR THE SCREENING OF PHARMACOTHERAPEUTICS. Alaine C. Keebaugh[1], Catherine E. Barrett[1], Jasmine J. Jenkins[1,2] and Larry J. Young[1] [1]Center for Translational Social Neuroscience, Yerkes National Primate Research Center, Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA, USA. [2]Behavioral Research Advancements in Neuroscience (BRAIN) Fellow, Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA, USA. Studies have implicated oxytocin and its receptor (OXTR) in the modulation of social behaviors, and disruptions in this system have been linked to diseases of social deficits such as autism spectrum disorder (ASD). Recently, *Oxtr* knockout mice have been shown to model multiple components of the ASD phenotype and highlight the importance of detailed behavioral phenotyping with relevance to social cognition. We extend these studies by site-specifically manipulating *Oxtr* in the prairie vole, a social rodent with an unusual repertoire of social behaviors. Here, we use viral-mediated RNA interference (RNAi) to knockdown expression of *Oxtr* within the shell of the nucleus accumbens (NAcc) of prepubertal female prairie voles. This localized gene knockdown blocked the formation of a pair bond, and resulted in reduced spontaneous nurturing behavior and maternal care. Currently we are extending our behavioral phenotyping to explore the role of accumbal OXTR signaling in the occurrence ASD related behaviors such as stereotypy and communication. We are complementing these studies by testing the ability of pharmacotherapuetics to rescue pair bond formation. These results underscore the potential of using viral-mediated RNAi for the rapid production and testing of genetic disease models in this species and for identifying pharmacotherapeutics for diseases of social deficits such as ASD.

158. SLEEPING IN CLASS: ARE STUDENT SCHEDULES PHYSIOLOGICALLY INHIBITING LEARNING? Baynard, M.; McEachron, D.L. School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA USA. Sleep is a biological imperative for normal cognitive functioning. Irregular schedules, sleep loss and lighting levels are known to effect human cognitive performance and emotional stability. While research has demonstrated that most Americans are habitually sleep restricted to less that 8 hours a night, little is known about the sleep patterns of college students, who experience high cognitive demands. This study uses actigraphy and ambient light exposure to determine the habitual sleep/wake patterns of college students. Initial investigations revealed that students bedtimes vary widely with little consistency across consecutive days. A majority of students were found to be sleep restricted to less than 7 hours of sleep a night on weekdays, with a significant number of waking bouts exceeding 24 hours. While students slept significantly longer on weekends than during weekdays, overall they averaged less than 8 hours of sleep a night on weekends during the study. Considerable variance among individuals was observed in this regard. While sleep efficiency did not significantly differ when comparing weekdays to weekends, the average time spent awake after the onset of sleep was significantly increased during the weekends. Students did not appear to find nap opportunities during their daily schedules to compensate for sleep loss or misplaced bedtimes, as actigraphy revealed no significant shorter sleep bouts during subjective days. Day time light exposure was shown to vary significantly by time, with trend toward increasing light exposure as the day progresses. The highest average lux per subject was observed from 12:00 - 14:00, well later than the average class start time, Students earliest waking hours, from 06:00 - 09:00, analysis revealed significantly reduced light levels, equivalent to the sleeping environment, despite student's schedules and activity measurements correlating this time period as active class time. Ongoing work using wrist actigraphy correlated with daily sleep diaries, and cognitive performance during a college term will explore the inter-individual differences between students sleep amounts, bedtimes and circadian placement and the effects on learning and neurobehavioral output.

159. ACTIVATION OF B1-ADRENERGIC RECEPTOR AS A POTENTIAL MEMORY ENHANCEMENT STRATEGY IN NEURO COGNITIVE DISORDERS. Saw N.L., Coutellier L., Shamloo, M. Behavioral and Functional Neuroscience Laboratory, Stanford University School of Medicine, Stanford, CA 94305, USA. Neurodegenerative diseases such as Alzheimers disease (AD) are characterized by severe cognitive deficits. Yet, the underlying mechanisms and causes of these symptoms remain elusive and reliable therapeutic strategies are still missing. My laboratory goal is to better understand the underlying mechanisms of the cognitive impairments observed in AD using experimental models of AD. We hypothesize that a disturbance in noradrenergic signaling could be responsible for these cognitive impairments. To test this hypothesis, we studied the Thy1-hAPP$^{Lond/Swe+}$ mouse line model of AD. Similarly to patient affected by AD, tyrosine hydroxylase immunohistochemistry reveals that the Thy1-hAPP$^{Lond/Swe+}$ mouse line is characterized by a neurodegeneration of the locus coeruleus, primary source of noradrenergic innervations to various cortical areas. Furthermore this line displays social recognition deficit and working memory deficits when compared to their wild-type littermates as tested in the 3-chamber social test and the Y-maze test. We found that a single injection of the 1- adrenoreceptor (1-ADR) partial agonist xamoterol can fully rescue the cognitive and social deficit observed in this model. In conclusion, the disturbances in the neurotransmission regulated by the 1ADR might be responsible for some of the cognitive deficits observed in AD and 1ADR could be a potential therapeutic target for AD.

160. HYPOCRETIN GENE TRANSFER IN MICE MODELS OF NARCOLEPSY Roda Konadhode, Dheeraj Pelluru, Carlos Blanco-Centurion, Meng Liu, and PJ. Shiromani. Ralph H. Johnson VA and Medical University of South Carolina, Charleston, SC 29401 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 and 2010 IBNS meetings we presented evidence that hypocretin gene transfer can ameliorate symptoms of narcolepsy in bona fide mice models of the disease. We now report that adeno-associated virus-mediated hypocretin gene delivery into the zona incerta, an elongated region in the subthalamus, effectively blocks cataplexy. Hypocretin gene delivery into the striatum, whose neurons regulate motor coordination, has no such effect indicating site-specificity of the effects. Cataplexy or sleep-wake levels are not changed when the hypocretin was molecularly targeted to be coexpressed in the melanin concentrating hormone (MCH) neurons in the zona incerta or lateral hypothalamus. In transgenic mice given the hypocretin gene detectable levels of hypocretin-1 are evident in the cerebrospinal fluid indicating release of the peptide from the surrogate neurons. The zona incerta neurons receive input from the amygdala and in turn project to the locus coeruleus indicating that the zona incerta is part of a circuit that stabilizes motor tone. Indeed, deep brain stimulation of the zona incerta controls tremors in Parkinsons disease. Our results indicate that these neurons might also be recruited to block the muscle paralysis in narcolepsy. This study demonstrates recruitment of surrogate neurons outside the hypothalamus to block cataplexy, one symptom of narcolepsy. Our long-term strategic intent is to selectively activate phenotype specific cells to block narcoleptic behavior in a site-specific manner. Supported by NIH and VA Research Service.

161. ANTI-INFLAMMATORY EFFECTS OF GLUCOSYLCERAMIDE IN LPS-INDUCED RAW 264.7 CELLS Park, J.1,2; Yeom, M.1; Kim, S.1,2; Kim, M.1; Han, J.J.3;Yin, C.S.1; Park, H.J.1,2; Lee, H.1,2; Hahm, D.H.1,2* 1Acupuncture and Meridian Science Research Center, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea. 2The Graduate School of Basic Science of Oriental Medicine, College of Oriental Medicine, Kyung Hee University, Seoul, 130-701, Republic of Korea. 3Glonet BU, Doosan Corporation, Suwon 443-270, Korea. Sphingolipids constitute a highly diverse and complex class of molecules and exhibit important physiological functions. Glucosylceramide (GlcCer) has been reported to improve the skin barrier function in dermatitis or aging mice models, but the effects and the mechanism of GlcCer in inflammation have not been fully characterized. The objective of this study was evaluate anti-inflammatory effect of GlcCer and inverstigate its mechanisms in a LPS-stimulated RAW 264.7 cells. GlcCer reduced the LPS-induced expression of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumour necrosis factoralpha (TNF-). In addition, GlcCer inhibited LPS-induced expression of prostaglandin E2 (PGE2) protein, as well as cyclooxygenase-2 (COX-2). Furthermore, GlcCer significantly attenuated the translocation of nuclear factor-kappa B (NF-kB) p65 to the nucleus by LPS. These results suggest that GlcCer may play significant anti-inflammatory properties on LPS-treated RAW 264.7 cells through the down-regulation of NF-kB/p65 mediated signaling pathway (This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MEST) (R11-2005-014)).

162. INVOLVEMENTS OF CORTICOTROPIN-RELEASING FACTOR, BUT NOT GLUCOCORTICOID IN THE RESTRAINT-INDUCED CONDITIONED PLACE PREFERENCE. Mei, Y.Y.; Li, J.S. Dept. of Psychology. National Chung-Cheng University, Taiwan, ROC. The conditioned place preference (CPP) is a widely used paradigm to examine reinforcing effects of drugs. Interestingly, a previous study showed that acute stress produced by restraint could also induce CPP. Although the modulating effects of stress on divers forms of learning are well known, the finding that a stressor can play a direct part in the reinforcement mechanism is quite a novelty. Little is known about the neural mechanisms. In the present study, Wistar rats were given agonist or antagonist of two critical stress hormones before the conditionings, and the influences on restraint-induced CPP were observed. Results show that peripheral applications of corticosterone (3mg/kg, 5mg/kg and 10mg/kg, s.c.) fail to induce CPP. The highest dose even induces conditioned place aversion. Furthermore, a glucocorticoid antagonist, mifepristone (10mg/kg, 40mg/kg and 100mg/kg, s.c.) fails to block the restraint-induced CPP. However, intracerebroventricular (ICV) injection of a selective corticotropin-releasing factor receptor 1 (CRFR1) antagonist antalarmin completely blocks the restraint-induced CPP. Furthermore, ICV application of the same drug without coupling with restraint reveals conditioned place aversion. In conclusion, activation of CRFR1 in CNS is necessary to form the restraint-induced CPP. Peripheral corticosterone, on the contrary, is not involved.

163. DIFFERENCES IN FEEDBACK-BASED LEARNING AND PREFRONTAL DOPAMINE UTILIZATION ARE ASSOCIATED WITH VARIATION IN THE DRD4 GENE Groman S.M., Feiler K., Seu E., Woods J.A., and Jentsch J.D. Dept. of Psychology, UCLA The dopamine (DA) D4 receptor (DRD4) gene contains polymorphisms in human and non-human animals, and variation in the number of exon III tandem repeats has been linked to risk for attention deficit/hyperactive disorder and addictions. However, little is known about the functional consequence(s) of this polymorphism on brain chemistry and putative behavioral endophenotypes. To address this, the current study examined the behavioral and biochemical impact of this functional polymorphism in vervet monkeys that carried either a rare (or common) variant similar in structure to that found in humans. Fourteen male monkeys (N=7 monkeys that carried at least one of the rare alleles (DRD4.5), N=7 monkeys that were homozygous for the common allele (DRD4.6)) were trained to acquire, retain and reverse 3-choice discrimination problems. After completing the behavioral assessment, levels of DA and related metabolites in brain homogenates were measured ex vivo with high-pressure liquid chromatography. Carriers of the DRD4.5 allele required more trials to acquire a stimulus-outcome association than those homozygous for the DRD4.6 allele. An analysis of response patterns revealed that these differences were due DRD4.5 carriers having lower sensitivity to positive feedback. Ex vivo measurements found elevated levels of DA utilization in prefrontal regions of DRD4.5 allele carriers. These data provide evidence of the functional impact the DRD4 VNTR has on behavioral and biochemical processes thought to underlie risk for psychiatric disorders and provide a framework for interpreting the phenotypic abnormalities that associate with this polymorphism.

164. SPATIAL LEARNING DEFICITS IN MOUSE MODELS OF CONGENITAL MUSCULAR DYSTROPHIES. Yu, M.; Liu, Y.; Bampoe, K.; Hu, H. Department of Neuroscience and Physiology, SUNY Upstate Medical University, NY, 13210 USA. Congenital muscular dystrophies with brain malformations are a group of diseases that exhibit overmigration of neurons in the cerebral cortex. They are caused by mutations in genes that are involved in protein O-mannosyl glycosylation such as POMT2 (encoding protein O-mannosyltransferase 2), POMGnT1 (protein O-mannose N-acetylglucosaminyltransferase 1), and LARGE (like-glycosyltransferase), which results in hypoglycosylation of \-dystroglycan, an extracellular matrix receptor. Hypoglycosylation of \-dystroglycan results in abolished interactions of \-dystroglycan with extracellular matrix molecules such as laminin and pikachurin. Mouse models of these congenital muscular dystrophies recapitulate neuronal migration defects and exhibit abnormal neuronal lamination in the hippocampus. To determine whether they exhibit learning and memory deficits, POMGnT1 knockout and brain specific POMT2 knockout mice were evaluated on Barnes maze. Latency to find the target hole was increased in both knockout mice over their respective littermate controls. When tested on an elevated plus maze, the knockout mice spent similar length of times in open and closed arms indicating they did not exhibit anxiety-like behavior. These results suggest that mouse models of congenital muscular dystrophies exhibit spatial learning deficits.

Saturday, June 9, 2012

9:00-10:00 **Bench-to-Bedside Lecture: David L. McKinzie**, Eli Lilly, Indianapolis, IN, USA

FROM BENCH TO CLINIC: DEVELOPMENT OF METABOTROPIC GLUTAMATE-2/3 RECEPTOR AGONISTS FOR THE TREATMENT OF SCHIZOPHRENIA. McKinzie, D.L. Lilly Discovery Research. Eli Lilly & Co., Indianapolis, IN 46285 USA. A growing and consistent literature indicates dysregulated glutamatergic neurotransmission in the pathophysiology of schizophrenia. Recent preclinical and clinical studies provide strong evidence that metabotropic glutamate-2/3 (mGlu2/3) receptor agonists have potential as a novel, non-dopaminergic approach to treat schizophrenia. In this presentation, the drug development history of mGlu2/3 receptor agonists will be overviewed. Early preclinical data indicated an ability of mGlu2/3 receptor agonists to block hyperglutamatergic states in models of psychosis and anxiety. The culmination of this work led to clinical proof-of-concept studies in psychiatric disorders. LY2140023 monohydrate, a prodrug of the mGlu2/3 receptor agonist LY404039, is currently in Phase III clinical development for the treatment of schizophrenia. The scientific rationale for this mechanism of action as an antipsychotic medication, drug development challenges, and current clinical findings will be discussed.

10:30-12:30 **Symposium:** THE PROMISE AND POTENTIAL PITFALLS OF TRANSLATIONAL RESEARCH. Chair: Eva Ihle, University of California, San Francisco, USA

RESEARCH IN TRANSLATION: TOWARD CLARITY IN COMMUNICATION BETWEEN BASIC AND CLINICAL SCIENCES. Ihle, E.C., Department of Psychiatry, University of California, San Francisco. San Francisco, CA 94143 USA. This presentation will attempt to put forward a balanced discussion about T1 (the transfer of basic-science knowledge to clinical application) translational research. Much attention has been focused on it, many researchers assert involvement in it, and many scientists struggle with constructing valid models for studies in humans or formulating hypotheses for studies in animal models with direct clinical application. At a time when new chapters in translational research are being promulgated it is important to appreciate the benefits of interdisciplinary approaches to discovery, as well as the limitations. This talk will present a brief commentary on the experiences of a physician-scientist who has worked both with small animal model systems to investigate different components of social behaviors, and with a clinic population of individuals with neurodevelopmental disorders who are recruited for genetics and neuroimaging studies. Among the conclusions reached from these experiences are: 1) Research in neurodevelopmental disorders is complicated by limitations in the specificity of criterion symptoms; 2) Biases in assessment of clinical populations can lead to a lack of clarity in features that are studied in the lab; and 3) Integrating the disciplines of psychiatry and neuroscience into a unified construct will contribute to a more complex, yet developed, understanding of the pathology underlying disorders that impair social interactions. Ultimately, psychiatric care will be advanced through basic research investigating the biomarkers and neural substrates that subserve social behaviors, but only when the language spoken by each discipline is interpretable by both.

TRANSLATIONAL RESEARCH: FINDING THE "SWEET SPOT." Blanchard, D.C. Pacific Biosciences Research Center, University of Hawaii, Manoa, 1993 East-West Road, Honolulu, HI 96822 USA. A focus on the degree to which behavioral and medical research should be directly aimed at understanding and alleviating human diseases has been steadily evolving over the past half century. For behavioral neuroscience, the present strong emphasis on this aspect of research reflects both the current political and economic climate, and, a genuine recognition that such research does have substantial potential for translation to human problems. The latter is a testimony to the many advancements in this area, providing both goals and models stemming from successful translational work. However, the assumption that a direct emphasis on solutions for complex and poorly understood neurobehavioral abnormalities is not only feasible but also efficient can also trump the basic research needed for an understanding of these conditions. Finding the sweet spot in which basic work can be applied to an understanding of disorder-relevant behavioral and biological conditions is a core component of research. I will discuss this in the context of improved symptom-modeling for animal models of autism.

MIND THE GAP: A REPORT CARD ON TRANSLATIONAL TREATMENT ATTEMPTS IN AUTISM AND NEURODEVELOPMENTAL DISORDERS. McCracken, J.T. Department of Psychiatry, University of California, Los Angeles, Los Angeles, CA 90024 USA. This presentation provides a status report on initial clinical results of promising translational treatment approaches for autism and other neurodevelopmental disorders. Three representative examples are presented: Fragile X Syndrome (FXS), neurofibromatosis 1 (NF1), and idiopathic autism (ASD). The success of identifying disrupted molecular pathways in model systems for these conditions has heightened enthusiasm for the identification of targeted, disease-modifying treatments for a broad range of conditions. These model systems have shown responsiveness to efforts to rescue the disorder phenotypes. But with respect to interventions for early-onset developmental disorders, the odds of successfully translating from preclinical to clinical systems are unclear at present. This presentation will review, from the perspective of a clinician-scientist, concerns about: 1) the interpretation of results from preclinical models, especially the challenges in determining the suitability of the model to capture core domains of the human disorder, and, 2) the conclusions

from initial targeted treatment trials in humans, given the complexity of the human phenotypes. The experience to date for targeted treatments in FXS, NF1, and ASD will be presented. This far, results suggest there are many challenges to identify treatments that will have true disorder-modifying impact. However, it is unclear whether these initial trials should be considered negative or failed trials. In keeping with the increasing specificity with which preclinical models are examined, translational treatment trials may also need to declare more limited endpoints, and identify more discrete biomarkers of treatment effects. Such considerations suggest several important research design issues for clinical trials. These include identification of more proximal clinical endpoints such as better and more specific cognitive endpoints, concerns about the effects of development on treatment outcomes, study duration, and need to determine adequate treatment effects on targeted pathways.

WHAT ARE THESE THINGS CALLED WORKING MEMORY: TRANSLATIONAL PITFALLS IN DEVELOPING PROCOGNITIVE TREATMENTS. Jared W. Young. Department of Psychiatry, University of California San Diego, La Jolla, CA, 92093-0804. Numerous psychiatric disorders present with cognitive dysfunction that correlates with poor functional outcome, hence procognitive treatments need to be developed. Working memory (WM) deficits are observed in the majority of psychiatric disorders. Thus, drugs require development that will improve WM in these patients. As a part of the drug discovery process, novel compounds are routinely tested in animal models. Despite claims however, attention is not always focused on ensuring that the cognitive domain affected in humans is the one being assessed in animals. Never has this been clearer than in the domain of WM where despite evidence, reviews, and opinion pieces, little attention from preclinical studies is placed on how WM is assessed in clinical populations. Despite this discrepancy, researchers still expect drug treatments devised in animal paradigms to be efficacious in human trials. Here we will present data on dopamine D2-family agonist induced improvement in WM span in mice that is consistent with humans, in contrast with the failure of D1-family receptor activation to improve WM span, despite it improving delay-dependent memory. The future for such research into treatments for WM dysfunction in patients will be discussed.

2:00-4:00 **Symposium:** NEW ANIMAL MODELS OF BIPOLAR DISORDER.
Chairs: **Francisco Gonzalez-Lima** and **Eimeira Padilla**

REDUCED DOPAMINE TRANSPORTER FUNCTION: A MODEL OF MANIA WITH CROSS-SPECIES TRANSLATIONAL VALIDITY. Jared W. Young, Jordy van Enkhuizen, and Mark A. Geyer, plus TRIPEC. Department of Psychiatry, University of California San Diego, La Jolla, CA, 92093-0804.
Manic state symptoms include overactivity, hypersexuality, irritability, and reduced need for sleep, with cognitive deficits recently linked to functional outcome. Current treatments of mania have arisen through serendipity or from other disorders with none approved for cognitive dysfunction. There is an urgent need to develop targeted therapeutics. Part of the drug discovery process is the assessment of therapeutics in animal models. Given the genetic linkage between DAT and mania, we have developed pharmacological and genetic animal models of mania based on reduced dopamine transporter (DAT) function. Reduced DAT function in mice results in altered exploration, hedonic-like behavior, risk-taking, and impaired attention consistent with patients with mania. Moreover, valproate remediates some of these behaviors while not affecting others, providing evidence for predictive validity of the model. Thus, advances in therapeutic treatment may depend on such models that: 1) utilizes genetic information for etiological validity; 2) demonstrates some pharmacological predictive validity; 3) recreates various aspects of mania in a test-battery; and 4) utilizes cross-species tests in which patients with BD exhibit such a specific pattern of abnormalities that are distinct from other psychiatric disorders.

MUTANT *POLG1* TRANSGENIC MICE AS A MODEL OF BIPOLAR DISORDER. Kubota-Sakashita, M.; Kasahara, T.; Kato, T. Lab for Molecular Dynamics of Mental Disorders, RIKEN Brain Science Institute, Saitama, 351-0198, Japan.
Bipolar disorder (BD) is mood disorder characterized by recurrent manic and depressive episodes. Based on the clinical findings in BD patients, we hypothesized that mitochondrial dysfunction in brain was involved in the pathophysiology of BD. To generate an animal model of BD, we focused on a hereditary mitochondrial disease, because it was sometimes comorbid with BD. The disease can be caused by mutations of mtDNA polymerase (polymerase γ; *POLG1*), which induce mtDNA mutations leading to the deletions. In the transgenic (Tg) mice that expressed mutant *Polg1* in a neuron-specific manner, we observed BD-like behavioral abnormalities. The Tg mice exhibited fluctuation in wheel-running activity and supressed by treatment of a mood stabilizer, lithium. The Tg mice showed hypoactivity lasting a couple of weeks and recovered spontaneously. This was associated with alteration of body temperature and increase of sucrose preference. The hypoactivity resembled depressive episode in BD patients. To identify mechanisms underlying the BD-like behavioral change, we evaluated two data sets of DNA microarray analysis. From the comparison between BD patients and control subjects, and the comparison between the Tg and wild-type mice, the expression level of *Ppif* that encodes cyclophilin D (CypD), a component of mitochondrial permeability transition pore (PTP), was down-regulated in both groups. This is of interest because PTP plays a role in Ca^{2+} homeostasis. Inhibitor of CypD ameliorated behavioral activity in Tg mice, suggesting therapeutic role of a CypD inhibitor. To develop the new treatment for BD, the Tg mice would be a useful tool as an animal model of BD.

FORCED DESYNCHRONIZATION AS A BEHAVIORAL MODEL OF BIPOLAR DISORDER Koike BDV; Ribeiro JM; Gonalves, BSB; Araujo JF Physiology Department; Universidade Federal do Rio Grande do Norte Based on evidences that circadian alterations on behavior are related to bipolar affective disorder we studied rats under forced desynchronization protocol to assess mania-like and depression-like behavior. Wistar rats submitted to a 22h (11:11) light-dark (LD) cycle show locomotor rhythm dissociation (forced desynchronization). In this protocol, animals present two rhythmic components of circadian motor activity: one synchronized by the LD cycle (T22h) and another in free running (T>24h). Animals were tested at coincidence activity phase (T22C) when the objective night is overlapped with biological night and at non-coincidence activity phase (T22NC) when the objective night is overlapped with biological day. The control group was under a 24h (12:12) LD cycle. The T22C rats have a locomotor activity increased when compared with controls, characterizing a hyperlocomotor behavior. We assessed the affective state of the animals through behavioral tests: open field (OF), elevated plus maze (EPM) and forced swimming test (FST) during T22C or T22NC. We found that rats at T22NC had an increased anxiety in OF and LCE tests compared with T22C and control group. The latency for immobility in the FST was longer for rats at T22C than for rats at T22NC. In the EEG analysis we observed an increase in SWS and decrease in REM sleep, both in T22C and T22NC compared with controls, but there were no differences in total amount between them. T22 groups presented different architectural sleep, with phase inversion in the T22NC. These results suggest that rats in T22C have a manic-like behavior and rats in T22NC have a depression-like behavior. Furthermore, our data indicate an apparent validation of forced desynchronization protocol as an animal model to bipolar disorder.

BIPOLAR-DEPRESSIVE BEHAVIOR IN HOLTZMAN RATS. Padilla, E.; Shumake, J.; Auchter, A.; Barrett, D.; Gonzalez-Lima, F. Departments of Psychology and Pharmacology, The University of Texas at Austin. Bipolar II disorder is characterized by novelty hyper-reactivity (hypomania) and depressive episodes. Learned helplessness is a model of depression in which pre-exposure to inescapable electric shock prevents learning a subsequent escape response. Holtzman rats are a commercially available strain that is highly susceptible to learned helplessness (Padilla et al. 2009). It is unknown which characteristics at baseline can predict helpless behavior after exposure to inescapable stress. We determined behavioral predictors of helplessness using the novel and familiar open-field tests, sucrose consumption, and passive harm-avoidance tasks before learned helplessness training and testing. Increased activity in a novel environment, but not general activity or habituation, predicted susceptibility to learned helplessness. Novelty reactivity was the best predictor of helplessness susceptibility. However, differences in other measures were not observed. A possible explanation is that Holtzman rats are exhibiting a bipolar phenotype, since novelty seeking is more characteristic of bipolar depression (Janowsky et al., 1999). Furthermore, elevated harm avoidance is characteristic of unipolar depression (Janowsky et al., 1999). In conclusion, a subpopulation of Holtzman rats showed a bipolar-like pattern in that they experience excessive behavioral activation in response to novelty followed by excessive behavioral inhibition in response to uncontrollable stress.

4:30-6:30 **Symposium:** THE ROLE OF NEUROINFLAMMATION IN THE ETIOLOGY OF AUTISM SPECTRUM DISORDERS (ASD). Chairs: **Christine F. Hohmann** and **Judy Van de Water**

NEUROINFLAMMATION AND NEUROIMMUNE ABNORMALITIES IN CHILDREN WITH ASD. Van de Water, J. and Ashwood, P. Departments of Internal Medicine and Medical Microbiology, University of California and UC Davis M.I.N.D. Institute, Davis, Davis, CA 95616 USA. Autism spectrum disorders (ASD) are characterized by impairment in social interactions, communication deficits, and restricted repetitive interests and behaviors. A potential role for immune dysfunction has been suggested in ASD. Significantly altered cytokine profiles in children with ASD have been reported and these findings suggest that ongoing inflammatory responses may be linked to disturbances in behavior. The characterization of immunological parameters in ASD has important implications for diagnosis, the designing and monitoring of therapeutic treatments of ASD, and may help to identify mechanisms that are important in the etiology of ASD in a subgroup of subjects. The biological impact of increased cytokines in ASD children and their association with more impaired behaviors is intriguing and warrants further consideration.

VALIDATING IMMUNE FINDINGS IN ANIMAL MODELS OF AUTISM. Ashwood, P.; Van de Water, J.. Department of Medical Microbiology and Immunology; Division of Rheumatology, Allergy and Clinical Immunology, University of California Davis, CA, USA. Autism is a clinically heterogeneous neurodevelopmental disorder that occurs in childhood. Autism is characterized by impairments in social interactions, verbal and non-verbal communication and the presence of restricted and repetitive stereotyped behaviors. There is strong evidence that point to immunological dysfunction in children with autism. Aberrant immune activity during critical periods of neurodevelopment could participate in the generation of neurological dysfunction and behavioral changes characteristic of autism. Recently, animal models of maternal immune activation (MIA) and the BTBR T+tf/J mouse strain are reported to have face validity for behavioral symptoms and neuropathology found in autism. However, little is known with regard to immune status in the BTBR mice or in offspring generated from MIA. To determine whether the same immune dysfunctions observed in humans are also exhibited in the MIA and BTBR models we investigated dynamic cellular immune responses in these models. We show increased responses following immune challenge characterized by pro-inflammatory cytokine production, findings reminiscent of those observed

in children with autism. Further studies to determine the role of immune dysfunction and its affect on behaviors and neuropathology in the BTBR and MIA models will help shed light on potential pathogenic mechanisms with importance to neurodevelopmental disorders including autism.

SEROTONIN AS POSSIBLE MODULATOR OF NEUROINFLAMMATION IN THE FOREBRAIN: STUDIES IN A MOUSE MODEL FOR ASD. Hohmann, C.F.; *Blue, M.E. Department of Biology, Morgan State University and the *Hugo W. Moser Research Institute at Kennedy Krieger, Inc., Baltimore, MD, USA. Abnormal serotonin homeostasis has frequently been implicated in the pathophysiology of autism. Our labs have developed a mouse model to test the role of the neurotransmitter serotonin in creating autism like changes in brain development and behavior. We have previously shown, that mice with neonatal forebrain depletions of serotonin display decreased social interest and increased anxiety, as adults. Here we provide evidence, that social deficits in these mice appear in infancy and persist though adolescence. We also show that, as in autism, the cortical volume in serotonin-depleted mice is transiently increased and the cortical cytoarchitecture displays signs of delayed maturation and altered plasticity. Alongside such early morphological changes, we have observed significant alterations in both pro- and anti-inflammatory cytokines in the serotonin-depleted cortex, which suggest a developmental delay in cytokine production. These data support the hypothesis that decreased serotonin, during critical stages of brain development, can modulate cytokine responses in the brain and therewith may alter brain development and behavior. Future studies will need to characterize the trajectory neuroinflammatory brain mechanisms, following serotonergic depletion. Supported by SO6GM51771 & U54MH066417.

PROGRAMMING INNATE IMMUNITY: IMPLICATIONS FOR NEURAL AND BEHAVIORAL DEVELOPMENT. Bilbo, S.D. Department of Psychology and Neuroscience, Duke University, Durham, NC 27708, USA. A wide variety of host (genetic), biological (e.g., infections), and environmental factors (e.g., pollutants & toxins) have been implicated in autism, yet its etiology remains unknown. The immune system is well characterized for its critical role in host defense. Far beyond this limited role however, there is mounting evidence for the vital role the immune system plays within the brain, in both normal, homeostatic processes (e.g., sleep, metabolism, memory), as well as in pathology, when the dysregulation of immune molecules may occur. This recognition is especially critical during brain development. Microglia and astrocytes, the primary immunocompetent cells of the CNS, are involved in every major aspect of brain development and function, including neurogenesis, synaptic formation and pruning. Cytokines such as tumor necrosis factor [TNF]α, interleukin [IL]-1β, and IL-6 are produced by glia within the developing and adult CNS, and are implicated in synaptic scaling, long-term potentiation, and neurogenesis. Importantly, cytokines are involved in both injury and repair, and the conditions underlying these distinct outcomes are under intense investigation and debate. Evidence from both animal and human studies implicates the immune system in a number of disorders with known or suspected developmental origins, including autism. This talk will focus on the evidence that infection during the perinatal period of life acts as a vulnerability factor for later-life alterations in cytokine production, and marked changes in cognitive and affective behaviors throughout the remainder of the lifespan, with a focus on the hypothesis that long-term changes in brain glial cell function may underlie such vulnerability.

9:00-11:00 **Symposium:** NEW INSIGHTS INTO THE NEUROBIOLOGY OF ADDICTION: NEUROCHEMICAL AND BEHAVIOURAL ADAPTATIONS TO LONG TERM DRUG EXPOSURE. Chairs: **Christian P. Müller** and **Tomasz Schneider**

PRENATAL NICOTINE EXPOSURE AND ADHD: CURRENT CONTROVERSIES AND ANIMAL MODELS. Tomasz Schneider; Dep. of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, UK. Although there seems to be overwhelming evidence for a deleterious effect of in utero exposure to tobacco smoking on behaviour and cognition later in life and on increased risk for childhood onset psychiatric disorders, it is difficult to separate these effects from other confounding environmental and genetic factors. For example, it has been recently suggested that common genetic vulnerability factors may exist for both maternal smoking and offspring attention deficit hyperactivity disorder (ADHD) that may explain the increased rate of ADHD among children of smokers. This talk will focus primarily on cognitive deficits found in rats prenatally exposed to nicotine and will discuss animal results in light of human epidemiological studies suggesting that the previously observed association between maternal smoking in pregnancy and ADHD might represent an inherited effect.

SHIFT OF DRUG CUE-INDUCED PHASIC DOPAMINE RELEASE FROM LIMBIC TO SENSORIMOTOR STRIATUM DURING THE PROGRESSION OF DRUG TAKING. Willuhn, I.; Everitt, B.J.; Phillips, P.E. Dept. of Psychiatry & Behavioral Sciences, Univ. of Washington, Seattle, WA, USA. Dept. of Exp. Psychology, Univ. of Cambridge, Cambridge, UK. Drug addiction is characterized by the loss of control over drug use. Dopamine neurotransmission in the ventromedial striatum (VMS) is implicated in the control of acute drug use, whereas the dorsolateral striatum (DLS) is thought to become increasingly involved during chronic abuse. Using a rat model of drug addiction, we show how phasic dopamine release in the VMS induced by drug-associated stimuli decreased with repeated drug intake over the course of weeks, whereas signaling in the DLS increased over time. Efficient action selection of cocaine self-administration behavior developed in parallel with DLS signaling and was reversed to an early performance level by blockade of dopamine receptors in the DLS. Furthermore, cue-induced phasic dopamine release in the DLS failed to develop after lesions of the VMS and was blunted in rats that were given extended access to cocaine. Our results demonstrate that phasic dopamine signaling in the striatum in response to drug cues is region specific, developing in the VMS then DLS sequentially. This shift of dopamine signaling from limbic to sensorimotor regions of the striatum requires intact VMS circuitry. Together, these data suggest that the recruitment of sensorimotor striatal circuitry for dopamine-mediated encoding of drug cues facilitates the prioritization of drug taking over other behaviors. Depletion of phasic dopamine signaling in the DLS after extended access may promote escalation of drug intake and, thus, may contribute to the loss of control over drug abuse observed in addicts.

A HISTORY OF EXTENDED ACCESS TO COCAINE PRODUCES ANOMALIES IN CORTICO-ACCUMBENS GLUTAMATE: IMPLICATIONS FOR ADDICTION THERAPY. Szumlinski, K.K. Dept. Psychological and Brain Sciences. University of California at Santa Barbara, Santa Barbara, CA, 93106-9660, USA. Anomalies in excitatory transmission within prefrontal cortex (PFC) are theorized to contribute to poor inhibitory control over behavior, behavioral inflexibility, as well as drug craving, in addiction. As Group I metabotropic glutamate receptors (mGluRs) are critical for drug reinforcement/reward, as well as drug-related learning, we examined for changes in the expression of mGluR1/5 within PFC subregions produced during protracted withdrawal from an extensive history of cocaine self-administration and then tested the functional relevance of observed changes for cocaine craving and extinction learning using behavioral pharmacological approaches. Immunoblotting was conducted on ventral PFC (vPFC) and dorsal PFC (dPFC) tissue derived from rats trained to self-administer cocaine (0.25 mg/infusion) during 10 daily 6-hr sessions that were subjected to a 2-hr test for cue-reinforced behavior, in the absence of any further cocaine/saline delivery, at either 3 or 30 days withdrawal. Control animals received daily 1-hr or 6-hr training to lever-press for saline, and were sacrificed also following cue testing. Follow-up behavioral studies examined the effects of intra-PFC infusions of mGluR1/5 antagonists or an mGluR1/5 agonist on cue-reinforced behavior and on the extinction of behavior with subsequent testing. Animals with a history of cocaine self-administration exhibited time-dependent: increases in cocaine craving and impairments in extinction learning. These behavioral phenomena were related to a time-dependent reduction in vPFC Group 1 mGluR expression. Mimicking this cocaine effect via intra-vPFC infusion of antagonists at 3 days withdrawal produced no acute effect on cue-reinforced behavior in either saline or cocaine self-administering animals, but impaired extinction learning manifested upon subsequent testing only in animals with cocaine experience. Stimulating mGluR1/5 via intra-vPFC infusions of an mGluR1/5 agonist at 30 days withdrawal also produced no acute effects on cocaine craving, but facilitated extinction learning as manifested on a subsequent test for craving in cocaine-experienced animals only. The present report provides in vivo validation of an important role for vPFC Group1 mGluRs in learning to suppress cocaine-seeking behavior during cocaine abstinence by showing that the site-directed pharmacological manipulation of both mGluR1 and mGluR5 function within the vPFC bi-directionally affects extinction learning in animals with an extensive history of cocaine self-administration. Taken altogether, these results support the hypothesis that a time-dependent reduction in vPFC Group I mGluR function is a neural adaptation

produced during withdrawal from an extensive history of cocaine self-administration that impairs the capacity of an addicted individual to learn new stimulus-response contingences during protracted drug abstinence. If relevant to humans, such findings implicate a progressive decrease in vPFC mGluR1/5 function during drug abstinence as a molecular cordon to recovery, which may be best overcome using receptor agonist treatment strategies.

CALMODULIN-DEPENDENT KINASES IN THE ACQUISITION AND EXPRESSION OF ADDICTION RELATED BEHAVIOUR IN MAN AND MICE. Müller, C.P. Psychiatric University Clinic, Friedrich-Alexander-University of Erlangen-Nuremberg, Erlangen 91054, Germany. Systematic use as well as addiction of psychoactive substances requires the establishment of multiple memory systems. It was shown that addiction and normal memories share a number of anatomical, morphological and molecular substrates. At glutamate receptive neurons, Ca2+/Calmodulin dependent kinases (CaMKs) are important substrates for the intracellular Ca2+ activation. They are involved in the regulation of the functional plasticity of the synapse. In particular CaMKs with an autophosphorylation molecular memory control receptor phosphorylation, transcription and LTP/LTD and are crucial for normal learning and memory. Here we discuss latest evidence for the involvement of various CaMKs in addiction related behaviours. Pharmacological as well as recent genetic approaches in animal models as well as in human samples show a crucial role for CaMKs in the establishment and expression of addiction related behaviours for various abused drugs. These findings suggest CaMKs as potential targets for prevention and/or treatment of drug addiction

11:30-1:30 **Symposium:** EXAMINING A LEARNING DIATHESIS MODEL FOR ANXIETY DISORDERS. Chairs: **Xilu Jiao** and **Kevin C.H. Pang**

LEARNING DIATHESIS AS A MODEL FOR THE ETIOLOGY OF ANXIETY DISORDERS. Servatius, R.J. Stress & Motivated Behavior Institute, New Jersey Medical School, UMDNJ & Department of Veterans Affairs, NJHCS, East Orange, New Jersey. Among anxiety disorders, posttraumatic stress disorder (PTSD) is defined by a particular experience extreme physical or psychological harm. In fact, the diagnosis of PTSD is unique among psychiatric disorders in that it is the only condition in which diagnostic criteria contain the presence of a presumptive etiology (i.e., a traumatic event), in addition to the more typical symptom constellation. As a result, much emphasis has been placed upon the primary role of trauma exposure itself in defining PTSD. However, closer examination of the relevant human and animal literature questions this basic assumption. Conceptually, the firm focus on traumatic exposure as primary to our understanding of PTSD is contradicted by the epidemiology of the disorder. The case will be presented that the fundamental process by which PTSD, and all anxiety disorders, develop is avoidance. Avoidance is acquired. Thus, an understanding the development, expression and persistence of avoidance should be the focus of models and discussion of etiology. It is the subtleties of avoidance not what is avoided, per se that defines PTSD. Supported by the SMBI.

ANIMAL MODELS OF ANXIETY VULNERABILITY: INFLUENCE OF RISK FACTORS ON AVOIDANCE LEARNING. Kevin Pang, Stress & Motivated Behavior Institute, New Jersey Medical School, UMDNJ and Department of Veterans Affairs, NJHCS, East Orange, NJ. Behaviorally inhibited temperament, smaller hippocampus, BDNF polymorphism and female sex are some identified risk factors for developing anxiety disorders. Using animal models, we seek to understand how these risk factors contribute to enhanced and persistent avoidance learning. We found that an animal model of behavioral inhibition, the Wistar-Kyoto (WKY) rat, acquires lever-press avoidance faster, to a greater extent and more persistently than outbred Sprague Dawley rats. A similar pattern emerges for classical conditioning of the eyeblink response, suggesting facilitated associative learning in behaviorally inhibited individuals. Sex differences in avoidance learning are seen in Sprague Dawley but not WKY rats; females Sprague Dawley rats learn avoidance faster than male Sprague Dawley rats. We will describe possible mechanisms underlying the enhanced avoidance learning in WKY rats and females. Supported by the VA BLR&D, NIH and SMBI.

NEUROBIOLOGY OF FASTER ACQUISITION AND PERSEVERATION IN ANIMALS. X. Jiao, SMBI & Neurobehavioral Research Laboratory, DVA-NJHCS, EO, NJ Although there is support for inhibited temperament as a risk factor, the translation of risk to actualized anxiety disorder is unclear. On the other hand, acquisition, expression and retention of avoidance may be the final common pathway to anxiety disorders. Examination of neural activation in anxiety related regions during avoidance acquisition and extinction provides important information to study the mechanism underlying avoidance and extinction behavior. Neuronal activation in prefrontal cortical regions and subcortical areas are associated with various aspects of anxiety and related diseases, such as post-traumatic stress disorder. Specifically, cortical-subcortical connection and inhibitory innervations within the micro circuitry of amygdala plays a pivotal role in avoidance and extinction. Our current work supports the hypothesis that similar brain structures involved in anxiety disorder are related to avoidance behavior. Supported by VA BLR&D, NIH and SMBI.

COMPUTATIONAL MODEL OF AVOIDANCE LEARNING: MECHANISMS OF BEHAVIORAL INHIBITION. Myers, C.E. Department of Veterans Affairs, NJ Health Care System, East Orange, NJ 07018; Dept. of Neurology and Neurosciences, NJ Medical School-UMDNJ, Newark, NJ. Pathological avoidance is a core symptom of post-traumatic stress disorder (PTSD) and other anxiety disorders. Studies with inbred Wistar-Kyoto (WKY) rats, a model of behavioral inhibition (BI), shows facilitated acquisition and delayed extinction of avoidance compared to outbred rats. Computational models of avoidance learning provide a testbed for understanding how learning mechanisms that differ between strains, and between individuals, could give rise to the observed behaviors. Here, we present a simple Q-learning model of leverpress avoidance. Parametric manipulations in the model, including manipulation of the inverse temperature parameter that governs the tradeoff between the tendency to explore new behaviors vs. exploit previously-successful behaviors, produce BI that captures many of the features of avoidance acquisition and extinction in WKY rats. Individual differences in avoidance learning among humans might similarly reflect variability in BI; consistent with this idea, emerging empirical data show altered avoidance learning in humans with high BI, as well as in veterans with PTSD-related avoidance symptoms. Supported by NSF/NIH Collaborative Research in Computational Neuroscience (CRCNS) Program and NIAAA (R01 AA018737).

BEHAVIORAL AND NEURAL MARKERS OF ANXIETY VULNERABILITY IN HUMANS. McAuley, J.D. Dept. of Psychology and Neuroscience Program. Michigan State University, East Lansing, MI 48824. Inhibited temperament, typified by withdrawal in the face of novel social and nonsocial challenges, is a risk factor for the development of anxiety disorders. Previous work has shown that individuals with higher scores on the adult and retrospective measures of behavioral inhibition (AMBI/RMBI) show faster acquisition of the classically conditioned eyeblink response than individuals with lower scores. This talk will report the results of a functional magnetic resonance imaging (fMRI) study that investigated (1) the functional and neuroanatomical correlates of behaviorally inhibited temperament, and (2) the relationship between behavioral inhibition, associated learning and the processing of social and non-social stimuli. The study was conducted in two phases. In the first phase, 150 participants (18-26 years of age) completed a battery of surveys that included the AMBI/RBMI measures of behavioral inhibition before undergoing delay-type eyeblink conditioning. In the second phase, a sample of participants from phase one returned to complete two days of testing. On day one, 48 neutral faces and 48 scenes were familiarized through a procedure involving six presentations of each stimulus. On day two, participants made old/new recognition judgments about familiarized and novel face and scene stimuli while undergoing fMRI. Of primary interest was the relationship between self-report measures of behavioral inhibition, acquisition rates in eyeblink conditioning and the temporal dynamics of the blood oxygen level dependent (BOLD) signal in response to processing familiarized and novel face and scene stimuli. Differential cerebellar activity was observed in the processing of familiar and novel faces, but not scenes. Moreover, acquisition rates in eyeblink conditioning, which is known to be cerebellar dependent, reliably predicted BOLD % signal change in response to viewing faces, but not scenes. Potential neuroanatomical correlates of behavioral inhibited temperament will also be considered.

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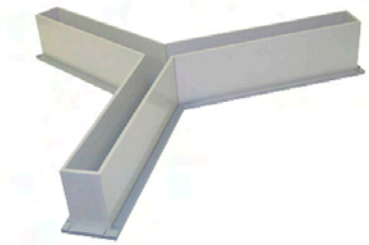

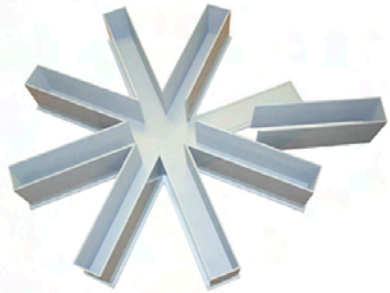

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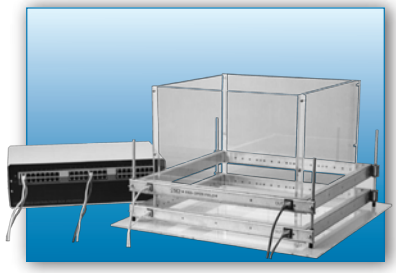

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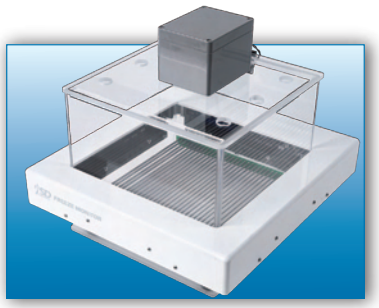

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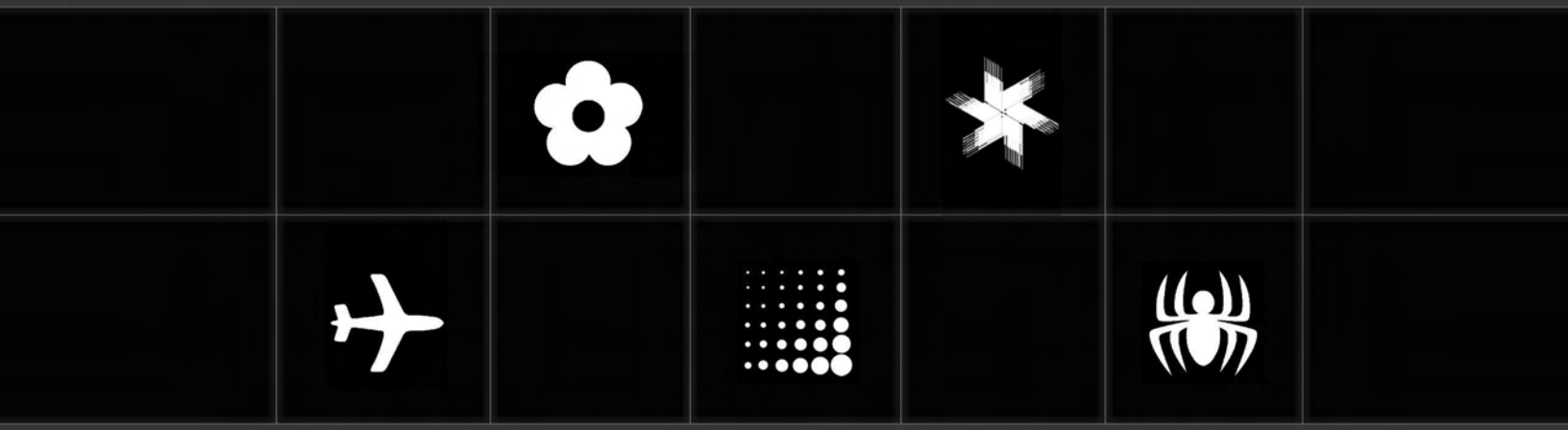

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2012 IBNS Schedule

		Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
		04-Jun	05-Jun	06-Jun	07-Jun	08-Jun	09-Jun	10-Jun
830	830			Welcome (8:45am-9:00am) Keauhou II	Exhibits, posters and breaks will			
900	900		Council Meeting (9:00am-Noon) Hualalai Room (next to Kai Restaurant)	Keynote-Leibowitz (9:00am-10:00am) Keauhou II	Presidential Lecture Kent-McGregor (9:00am-10:00am) Keauhou II	Keynote-Diamond (9:00am-10:00am) Keauhou II	Bench-to-Bedside Lecture-McKinzie (9:00am-10:00am) Keauhou II	Symposium-Mueller & Schneider (9:00am-11:00am) Keauhou II
930	930							
1000	1000			Coffee/Snack Break - Exhibits (10:00am-10:30am)	Coffee/Snack Break - Exhibits (10:00am-10:30am)	Coffee/Snack Break - Exhibits (10:00am-10:30am)	Coffee/Snack Break - Exhibits (10:00am-10:30am)	
1030	1030			Symposia-Walker (10:30am-12:30pm) Keauhou II	Symposium-Pawluski (10:30am-12:30pm) Keauhou II	Symposium-Shiromani (10:30am-12:30pm) Keauhou II	Symposium-Ihle (10:30am-12:30pm) Keauhou II	Coffee/Snack Break (11:00am-11:30am)
1100	1100							
1130	1130							Symposium-Jiao & Pang (11:30am-1:30pm) Keauhou II
1200	1200							
1230	1230			Mid-Day Break (12:30pm-2:00pm) on your own	Mid-Day Break Meet the Profs (12:30pm-2:00pm) Convention Center Lawn	Mid-Day Break Grant Workshop (12:30pm-2:00pm) Keauhou II	Mid-Day Break Meet the Profs (12:30pm-2:00pm) Convention Center Lawn	
100	1300		Student Social (1:00pm-3:00pm) Meet in Room 1329					
130	1330							
200	1400	Council Strategic Planning Meeting Open to IBNS Members (2:00pm-6:00pm) Hualalai Room (next to Kai Restaurant)		Symposium-Berger-Sweeney (2:00pm-4:00pm) Bayview Rooms	Oral Session 1 Psychiatry and Cognition (2:00pm-4:00pm) Keauhou BALLROOM	Symposium-Bondi & Weiser (2:00pm-4:00pm) Keauhou II	Symposium-Gonzales-Lima & Padilla (2:00pm-4:00pm) Keauhou II	
230	1430							
300	1500			Symposium-Papaleo (2:00-4:00) Keauhou II	Oral Session 2 Stress and the Environment (2:00pm-4:00pm) Keauhou II - Conv. Ctr.			
330	1530							
400	1600		Registration (4:00pm-6:00pm) Pool Terrace	Snack Break - Exhibits (4:00pm-4:30pm)	Snack Break - Exhibits (4:00pm-4:30pm)	Snack Break - Exhibits (4:00pm-4:30pm)	Snack Break - Exhibits (4:00pm-4:30pm)	
430	1630			Symposium-Buisman-Pijlman & Broadbear (4:30pm-7:00pm) Keauhou II	Student Slide Blitz (4:30pm-6:30pm) Keauhou II	Symposium-Ten Eyck & Summers (4:30pm-6:30pm) Bayview Rooms	Symposium-Hohmann & Van de Water (4:30pm-6:30pm) Keauhou II	
500	1700							
530	1730					Symposium-McNally (4:30pm-6:30pm) Keauhou II		
600	1800		Symposium-Lambert (6:00pm-8:00pm) Keauhou II					
630	1830	Optional Council Dinner (6:30pm-10:00pm) Sam Choy's Kai Lanai			Evening Break (6:30pm-8:00pm) on your own	Evening Break (6:30pm-8:00pm) on your own	Business Meeting (6:30pm-7:00pm) Keauhou II	
700	1900			Evening Break (7:00pm-8:00pm) on your own			(7:00-8:00) Luau dinner (7:30) Live Music starts (8:00-9:00) Cultural Show Hawaii Lawn	
730	1930							
800	2000		Welcome Reception Educational Talk Bayview Grounds Manta Ray viewing (8:00pm-10:00pm) Suites 1329 & 1425	Poster Session 1 Brain & Behavior (8:00pm-10:00pm) Keauhou I	Poster Session 2 Pharmacology (8:00pm-10:00pm) Keauhou I	Poster Session 3 Disease Models (8:00pm-10:00pm) Keauhou I	Dance with live band featuring LT Smooth (9:00-Midnight) Keauhou I	
830	2030							
900	2100							
930	2130							