International Behavioral Neuroscience Society

Santa Fe, New Mexico
Land of Enchantment

Program/Abstracts

Annual Meeting
June 1-5, 2005

Abstracts of the International Behavioral Neuroscience Society, Volume 14, June 2005

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USA ..... Robert Gerlai
..... Christine Hohmann
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CONTENTS

Dear Colleagues,

Welcome to the 14th annual meeting of the International Behavioral Neuroscience Society. We have a fabulous program including a variety of papers, talks, symposia, and satellites. The presentations cover almost every field in our discipline, and attendees will represent an array of scientific approaches and countries of origin. The people and the research presented at this meeting offer an opportunity for cross-disciplinary interaction, for learning and for dissemination of findings in a beautiful setting in the "land of enchantment".

It is especially important to extend our thanks to Gary Coover, who has chaired the Program Committee for two years. The diligence of Gary and the Program Committee has woven together the various threads of a wonderful scientific program. As always, we are extremely grateful to Marianne Van Wagner whose amazing energy maintains the many core activities of IBNS, especially those necessary for our annual meeting. There are many others to thank, including all of you who plan to attend, whose involvement promises to make this a successful meeting.

We are especially fortunate that this year's meeting with be held in historic Santa Fe, New Mexico. This year's organizing committee, chaired by Bob Blanchard, selected a wonderful venue for the 2005 meeting. Like some of you, this is my first visit to Santa Fe. However, a little internet homework (www.visitsantafe.com; www.santafe.org) leaves no doubt that we are in for an exciting cultural experience. Hopefully, many of you will find an opportunity to extend your visit to explore the wonders of this historical region.

It is my pleasure to welcome each of you to IBNS 2005 to what is promised to be an unforgettable meeting.

My warmest wishes,

Sue Carter
President IBNS

We are pleased to announce the recipients of the IBNS Travel Awards for the 2005 meeting in Santa Fe, New Mexico. These awards will be presented at the Conference Banquet on Saturday evening. Award winners will receive a cash award, certificate, and waiver of registration and banquet fees. Congratulations to all.

TRAVEL AWARDS

(listed by category and alphabetically)

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

Postdoctoral

Angela Grippo, *University of Illinois at Chicago, USA*

Sreenivasulu Naidu Pattipati, *Univ. Institute of Pharmaceutical Sciences, INDIA*

Graduate

Sarah Boudreau, *Dalhousie University, CANADA*

Andrea Kudwa, *University of Virginia, USA*

Denise Leblanc-Duchin, *Univ. of New Brunswick, Saint John Campus, CANADA*

Lauren Levy, *Yale University, USA*

Vicente Martinez, *University of Michigan, USA*

Melanie Paquette, *Arizona State University, USA*

Marisa J. Rubinow, *University of Illinois, USA*

Masafumi Takatsuna, *Toyama University, JAPAN*

Kandy Velazquez, *University of Puerto Rico, USA*

Amy Zmarowski, *The Ohio State University, USA*

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

The IBNS would like to express our gratitude to the following organization who has given financial support to the 14th International Behavioral Neuroscience Society Conference. This financial support enabled many students to attend the conference and also allowed recruitment of excellent special symposium speakers.

National Institute of Mental Health

CORPORATE SPONSORS

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

Elsevier Science, Inc.

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EXHIBITORS

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

Clever Sys. Inc.

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IBNS 2006 - CALL FOR PROPOSALS

The next annual IBNS meeting will be held on May 23-28, 2006, at the Fairmont Chateau Whistler Resort in Whistler, British Columbia, Canada. Symposium and satellite proposals may be submitted directly to the IBNS Central Office by email at ibns@ibnshomepage.org with a copy to the 2006 Program Chairperson, Andrew Holmes, at holmesan@mail.nih.gov. Proposals should include the title of the satellite/symposium, list of speakers, titles of the speakers' presentations and the chairperson(s).

ACKNOWLEDGMENTS

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

PROGRAM COMMITTEE:

Gary Coover (Chairperson); Andrew Holmes (Co-Chair); Jacques Abraini; Caroline Blanchard; Marcus Brandao; Jacqueline Crawley; Marcus Heilig; Athina Markou; Emmanuel Onaivi; Klaus-Peter Ossenkopp; Paul Rushing; Tori Schaefer (Student).

LOCAL ORGANIZING COMMITTEE:

Robert Blanchard (Chairperson); Moore Arnold; Isadora Bielsky; Caroline Blanchard.

EDUCATION AND TRAINING COMMITTEE:

Robert Gerlai (Chairperson); Robert Adamec (Co-Chair); Kyle Frantz; Francisco Gonzalez-Lima; Vickie Risbrough (Student); Susan Powell; Martin Sarter; Pascual Gargiulo.

SCIENTIFIC PROGRAM

KEYNOTE SPEAKERS

Larry Cahill, Ph.D., University of California, Irvine.
Sex and Hemisphere Influences on Brain Mechanisms of Emotional Memory

Robert Dantzer, D.V.M., Ph.D, CNRS-INRA, University of Bordeaux, France.
Cytokines and Sickness Behavior: An Integrated Perspective

PRESIDENTIAL ADDRESS

C. Sue Carter, The University of Illinois at Chicago.
Epigenetic Perspectives On Monogamy: Insights From Prairie Voles

SPECIAL SYMPOSIA

- **How would you model the behavioral symptoms of autism in rodents?** *Chairs:* Jacqueline N. Crawley, National Institute of Mental Health, Bethesda, MD, and Stephen W. Porges, University of Illinois at Chicago, Chicago, IL, USA.

- **Integrative function of the hypothalamus in autonomic, endocrine responses to stress and behavioral changes.** *Chair:* Yoichi Ueta, University of Occupational and Environmental Health, Japan.

- **Modeling different facets of disease - steps toward exploration of endophenotypes in psychiatry.** *Chairs:* Haim Einat, University of Minnesota-Duluth, MN, USA, and Henry Szechtman, McMaster University, Hamilton, Ontario, Canada.

- **New insights in ventral striatal organization and physiology: Perspectives for the behavioral sciences.** *Chair:* Jacques H. Abraini, Universite de Caen, Caen, France.

- **The paradox of acute stress effects on memory: Contrasting views, competing approaches, & compatible findings.** *Chair:* James C. Woodson, University of Tampa, Tampa, Florida.

SATELLITE

Ultrasonic vocalization in rodents. Behavioural and neural determinants of call production. *Organizer:* Stefan M. Brudzynski.

8:45 **Stefan M. Brudzynski** (Brock University)
Opening Remarks

9:00 **Robert and Caroline Blanchard** (University of Hawaii)
The Environmental and Pharmacological Control of Ultrasonic Alarm Cries in the Laboratory Rat

9:25 **Klaus Miczek** (Tufts University)
Maternal Separation Distress: Serotonergic Mechanisms and Thermoregulation in Rodents

9:50 **Susan Brunelli** (New York State Psychiatric Institute)
Selective Breedig for Infant Ultrasonic Vocalizations: Lifespan Effects

10:15 Refreshment Break (20 min)

10:35 **Harry Shair** (New York State Psychiatric Institute)
Physiological Mechanisms Underlying a Socially-Mediated Separation Response

11:00 **Thoms H. Brown** (Yale University)
Using Rat Ultrasonic Vocalizations to Explore the Mnemonic Functions of Perirhinal Cortex

11:25 **Jeff Burgdorf and Jaak Panksepp** (Bowling Green State University)
Neurobiology of 50-kHz ultrasonic vocalizations

11:50 **Stefan M. Brudzynski** (Brock University)
Function of the Mesolimbic Cholinergic System in the Production of Alarm Calls in Rats

12:15 General Discussion

12:30 Adjourn

WORKSHOPS

NIH Grant Workshop:

"NIH 101", **Paul A. Rushing**, National Institute of Diabetes and Digestive and Kidney Diseases. Much of the biomedical research in the United States is supported by the National Institutes of Health (NIH). This brief "NIH 101" workshop will provide information on all aspects of the grant process from submission to funding. A special emphasis will be placed on peer review. In addition, the presentation will be followed by a question and answer period.

Student Workshop:

Student career development symposium: Selecting the right postdoctoral fellowship and getting the first position in academia or industry. Chair: **Robert Gerlai**, Department of Psychology, University of Toronto at Mississauga, Mississauga, Ontario, Canada. The symposium is intended for the student who is thinking about the direction of his or her future career and will discuss numerous principal and practical aspects of making an informed decision.

NOTE: Oral presentations from Wednesday until Saturday noon will be held in the MESA Ballroom, Section B&C. From Saturday noon until 6:30 p.m. the oral presentations will be held in the Ortiz Ballroom. All exhibits, registration and food breaks will be held in MESA Ballroom, Section A. The satellite will be held in the Aspen Room. The reception will be held in the Chamisa Courtyard. Both poster sessions will be held in the Ortiz Ballroom.

Presenting authors are indicated by **bold** type.

Wednesday, June 1:

8:00-12:00 Exhibitor Setup. ***Mesa Ballroom A***

8:45-12:30 **Satellite Symposium: Ultrasonic vocalization in rodents. Behavioural and neural determinants of call production.** *Organizer:* **Stefan Brudzynski**, Brock University. ***Aspen Room***

9:00-14:00 Meeting Registration – *(Note: Even if you have preregistered, please use this time to pick up your receipts, name badges, programs and pay dues.)* ***Mesa Ballroom A***

12:00- Exhibits will be open from Wednesday noon through Saturday afternoon. ***Mesa Ballroom A***

13:30-14:00 Welcoming Remarks and Exhibitor Introduction: **C. Sue Carter,** IBNS President, University of Illinois at Chicago. ***Mesa Ballroom B&C***

14:00-14:30 **2004 Marjorie A. Myers Lifetime Achievement Award: Laszlo Lenard**, Pecs University Medical School. Central regulation of feeding.

14:30-15:24 **Oral Session 1: Chemistry of Behavior.** *Chair*: **Iain McGregor**, University of Sydney. ***Mesa Ballroom B&C***

14:30-14:48 M5 MUSCARINIC GENE FACILITATES DOPAMINE REWARD FUNCTION IN RATS. **Yeomans, J.S.**; Steidl, S.; Wang, H.

14:48-15:06 GROUP I AND GROUP III METABOTROPIC GLUTAMATE RECEPTORS OPPOSE EACH OTHER IN THE CONTROL OF LOCOMOTOR RESPONSES PRODUCED BY D1-LIKE AND/OR D2-LIKE RECEPTORS. **David, H.N.**; Chevallier, K.; Abraini, J.H.

15:06-15:24 ACUTE EFFECTS OF 3,4-METHYLENEDIOXYMETHAMPHETA-MINE (MDMA) ON STRIATAL SINGLE-UNIT ACTIVITY AND BEHAVIOR IN

FREELY MOVING RATS: DIFFERENTIAL ROLES FOR 5-HT2A AND 5-HT2C/2B RECEPTORS**. Ball, K.T.**; Rebec, G.V.

15:24-15:55 **Refreshment Break/Exhibitors Display.** ***Mesa Ballroom A***

15:55-16:13 NEONATAL EXPOSURE TO 3,4-METHLYNEDIOXYMETHAM-PHETAMINE ALTERS NMDA RECEPTOR AND ASSOCIATED PROTEINS IN ADULT RATS. **Skelton, M.R.**; Williams, M.T.; Vorhees, C.V.

16:13-16:31 MECHANISMS UNDERLYING MDMA FACILITATION OF SOCIAL INTERACTION IN THE RAT. **McGregor, I.**; Thompson, M.; Morley. K.; Arnold, J.; Hunt, G.

16:31-16:49 MDMA - ALCOHOL INTERACTIONS: EFFECTS ON ACTIVITY AND THERMOREGULATION. **Jones, B.C.**; Cassel, J-C., Koenig, J.; Jeltsch, H.

17:00-18:00 **Keynote Speaker: Larry Cahill**, Ph.D., University of California, Irvine. Sex and Hemisphere Influences on Brain Mechanisms of Emotional Memory

18:00-19:00 **Margarita Fiesta Reception.** Join us in welcoming our exhibitors and invited guests with complimentary margaritas and Mexican beer. Traditional New Mexican hors d'oeuvres will also be served. Mariachis will provide the entertainment. ***Chamisa Courtyard***

Thursday, June 2:

7:15-8:15 **New Mexican Continental Breakfast/Exhibitors Display.** ***Mesa Ballroom A***

8:15-10:15 **Student Travel Award Slide Blitz. Chair: Robert Gerlai,** University of Toronto at Mississauga. ***Mesa Ballroom B&C***

10:15-10:30 **Break/Exhibitors Display.** ***Mesa Ballroom A***

10:30-11:42 **Oral Session 2: Aversive Behavior.** *Chair*: **Robert Blanchard**, University of Hawaii. ***Mesa Ballroom B&C***

10:30-10:48 NORADRENALINE TRANSMISSION WITHIN THE BED NUCLEUS OF THE STRIA TERMINALIS IS CRITICAL FOR FEAR BEHAVIOR INDUCED BY TMT-EXPOSURE. **Fendt, M.**

10:48-11:06 VOCALIZATION-RELATED INPUT INTO THE PERIAQUEDUCTAL GRAY OF THE MIDBRAIN IN THE SQUIRREL MONKEY. **Juergens, U.**; Dujardin, E.

11:06-11:24 SOCIAL APPROACH-AVOIDANCE TEST IN F-344 RATS: PHARMACOLOGICAL VALIDATION. **Nicolas, L.B.**; Prinssen, E.P.

11:24-11:42 PROBLEMS IN THE MODELING OF AGGRESSIVE BEHAVIOR. **Blanchard, R.**; Yang, M.K.; Litvin, Y.

11:45-13:15 **Council Meeting.** ***Aspen Room***

13:15-15:15 **Student Workshop:** *Student career development symposium: Selecting the right postdoctoral fellowship and getting the first position in academia or industry.* Chair: **Robert Gerlai**, Department of Psychology, University of Toronto at Mississauga, Mississauga, Ontario, Canada. The symposium is intended for the student who is thinking about the direction of his or her future career and will discuss numerous principal and practical aspects of making an informed decision.

15:15-17:15 **2005 Marjorie A. Myers Lifetime Achievement Award:** *Jacqueline N. Crawley.* **Symposium 1: How would you model the behavioral symptoms of autism in rodents?** *Chairs:* **Jacqueline N. Crawley,** National Institute of Mental Health, Bethesda, MD, and **Stephen W. Porges,** University of Illinois at Chicago, Chicago, IL, USA.

15:15-15:45 BEHAVIORAL TASKS TO MODEL THE CORE SYMPTOMS OF AUTISM IN MICE. **Crawley, J. N.**

15:45-16:15 MODELING AUTISM BEHAVIORAL DEFICITS IN THE LABORATORY RAT. **Walker, B.R.**

16:15-16:45 BEHAVIORAL GENETICS OF SOCIAL AND REVERSAL TRAITS IN INBRED STRAINS OF MICE. **Bolivar, V.**; Walters, S.; Santiago, A.; Phoenix, J.; Flaherty, L.

16:45-17:15 CLINICAL SYMPTOMS AND POTENTIAL TREATMENTS FOR AUTISM; HOW ANIMAL MODELS CAN HELP. **Porges, S.W.**

17:30-19:30 **Poster Session 1. (Refreshments)** ***Ortiz Ballroom***

Genetic and Chemistry of Learning and Performance

1. *Withdrawn*.
2. *Withdrawn*.
3. AUGMENTATION OF ATTENTIONAL PERFORMANCE-ASSOCIATED INCREASES IN PREFRONTAL ACETYLCHOLINE RELEASE DURING BASAL FOREBRAIN NMDA RECEPTOR BLOCKADE-INDUCED IMPAIRMENTS IN PERFORMANCE. **Kozak R.**; Bruno J.P.; Sarter M.
4. TWO BEHAVIORAL TASKS REVEAL MOTOR AND LEARNING DEFICITS IN THE YAC72 MOUSE MODEL OF HUNTINGTON'S DISEASE. **Lawhorn, C.**; Smith, D.M.; Brown, L.L.
5. ENVIROMENTAL ENRICHMENT ENHANCES LEARNING AND MEMORY AND HIPPOCAMPAL EXPRESSION OF NEUROGRANIN AND OTHER SIGNALING MOLECULES. **Huang, F.L.**; Huang, K.P.; Wu, J.F.

Fear and Anxiety

6. IMPROVED PREDICTIVE VALIDITY OF THE MARBLE BURYING TEST FOR ANXIETY BY SIMULTANEOUS MEASUREMENTS OF LOCOMOTOR ACTIVITY. **Nicolas, L.B.**; Kolb, Y.; Prinssen, E.P.

7. GALANIN GAL-R2 RECEPTOR NULL MUTANT MICE EXHIBIT AN ANXIOGENIC-LIKE PHENOTYPE ON TESTS OF ANXIETY-LIKE BEHAVIOR. **Bailey, K**.; Pavlova, M.; Hohmann, J.; Zeng, H.; Crawley, J.
8. INVOLVEMENT OF TRANSMITTERS IN THE ANXIOLYTIC ACTION OF UROCORTIN 2 IN MICE. **Telegdy, G.**; Adamik, A.
9. BEHAVIORAL PROFILE OF RATS FOLLOWING CRF-MEDIATED STRESSORS. **Sajdyk, T.**; Fitz, S.; Merrill, C.; Conroy, S.; Chambers, R.; Shekhar, A.
10. REPEATED ADMINISTRATION OF NEUROPEPTIDE Y IN THE BASOLATERAL NUCLEUS OF THE AMYGDALA ELICITS LONG-TERM ANXIOLYTIC-LIKE RESPONSES. **Sajdyk, T.**; Fitz, S.; Rainnie, D.; Shekhar, A.
11. SODIUM LACTATE INDUCED PANIC-LIKE PHYSIOLOGICAL RESPONSES CORRELATE WITH CELLULAR RESPONSES IN SPECIFIC SUBREGIONS OF THE DORSOMEDIAL HYPOTHALAMUS OF RATS. Johnson, P.; **Fitz, S.**; Keim, S.; Lowry, C.; Shekhar, A.

Development & Individual Differences

12. EFFECT OF NEONATAL NOVELTY EXPOSURE ON SOCIAL COMPETITION. **Akers, K.G.**; Tang, A.C.
13. TIMING AND AMOUNT OF EARLY EXPERIENCE AFFECTS PARENTAL CARE IN PRAIRIE VOLES. **Boone, E.M.**; Lewis-Reese, A.; Carter, C.S.; Bales, K.L.
14. PATERNAL RESPONSIVITY IN BIPARENTAL (PEROMYSCUS CALIFORNICUS) AND NONPARENTAL (PEROMYSCUS MANICULATAS) MICE. **Everette, A.**; Tu, K.; Love, G.; McNamara, I.; Kinsley, C.H.; Lambert, K.G.
15. EFFECTS OF NEONATAL NOVELTY EXPOSURE ON ANOXIA-INDUCED PATHOLOGICAL BEHAVIOR IN THE CONTEXT OF ENVIRONMENTAL AND SOCIAL NOVELTY. **Nakazawa, M**.; Tang, A.C.
16. COPING STRATEGIES IN LONG-EVANS MALE RATS: INNATE VS. ACQUIRED CHARACTERISTICS. **Tu, K.**; Everette, A.; Love, G.; McNamara, I.; Banks, M.; Kinsley C.; Lambert, K.G.
17. *Withdrawn*.
18. EARLY DEPRIVATION AND MATERNAL SEPARATION HAVE DIFFERING EFECTS ON JUVENILE PLAY AND COMMUNICATIVE BEHAVIORS IN RATS. **Zimmerberg, B.**; Sageser, K.A.

Social Behavior

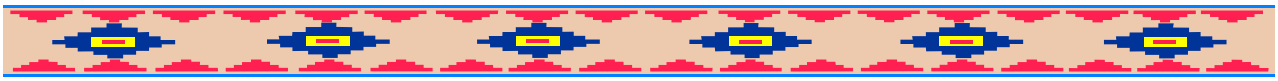
19. THE EXPRESSION OF COCAINE AND AMPHETAMINE REGULATED TRANSCRIPT PEPTIDE (CART) IN THE SOCIALLY DEFEATED MALE LONG EVANS RAT. **Pulliam, J.V.K.**; Plotsky, P.M.
20. SOCIAL ENVIRONMENT REGULATES THE HPA AXIS AND CELLULAR PROLIFERATION IN THE PRAIRIE VOLE. **Ruscio, M.G.**; Sweeny, T.; Suppatkul, P.; Hazelton, J.; Carter, C.S.
21. BEHAVIORAL EFFECTS RESULTING FROM THE DISRUPTION OF GLIAL FUNCTIONING IN THE BASOLATERAL AMYGDALA. **Gaskins, D.**; Lee, Y.; Shekhar, A.
22. DEFICITS IN BEHAVIORAL RESPONSES TO FAMILIAR STIMULI MEDIATED BY THE BASOLATERAL NUCLEUS OF THE AMYGDALA. Truitt, W.; Sajdyk, T.; Fitz, S.D.; **Dietrich, A.**; Shekhar, A.

23. EFFECTS OF ZIPRASIDONE AND D-CYCLOSERINE TREATMENT ON THE BEHAVIORAL DEFICITS IN RATS WITH DISRUPTED BASOLATERAL AMYGDALA FUNCTION. Sajdyk, T.; **Fitz, S.**; McDougle, C.; Shekhar, A.
24. FLAVOR PAIRING BIASES OUTCOMES IN A SOCIAL FOOD PREFERENCE TASK. **Walker, E.M.**; Desir N.; Hohmann, C.F.

Chemistry of Behavior

25. EFFECTS OF 5-METHOXY-DIISOPROPYLTRYPTAMINE ON HORMONE AND NEUROTRANSMITTER LEVELS IN THE ADULT RAT. **Schaefer, T.L.**; Herring, N.R.; McCrea, A.E.; Lipton, J.W.; Campbell, N.G.; Vorhees, C.V.; Williams, M.T.
26. BEHAVIORAL EFFECTS OF 5-METHOXY-N,N-DIISOPROPYLTRYP-TAMINE (FOXY) IN ADULT RATS. **Herring, N.R.**; Schaefer, T.L.; McCrea, A.E.; Vorhees, C.V.; Williams, M.T.
27. EFFECTS OF SHORT-TERM REM SLEEP DEPRIVATION ON THE EXPRESSIONS OF THE HYPOTHALAMIC NEUROPEPTIDES GENES IN RATS. **Fujihara, H.**; Sei, H.; Morita, Y.; Ueta, Y.
28. ENKEPHALIN REGULATES INCREASES IN CONSTITUTIVELY ACTIVE MU RECEPTORS DURING OPIATE WITHDRAWAL. **Shoblock, J.**; Maidment, N.
29. THE EFFECTS OF KETAMINE ON THE EXPRESSION OF NMDA NR2B RECEPTOR SUBUNITS. **Hoxha, N.**; Mickley G.A.
30. GENE DELETION OF THE GLUTAMATE GLUR1 RECEPTOR CAUSES HYPER-REACTIVITY TO NOVELTY AND SENSORIMOTOR GATING DEFICITS IN MICE. **Wiedholz, L.**; Holmes, A.
31. GROUP II, BUT NOT GROUP I, MGLURS IN THE RAT NUCLEUS ACCUMBENS CONTRIBUTE TO CONDITIONED LOCOMOTION ELICITED BY AMPHETAMINE-ASSOCIATED ENVIRONMENTAL CUES. Kim, W.Y.; **Kim, J.-H.**; Vezina, P.
32. THE ANABOLIC STEROID NANDROLONE BUT NOT 17á-METHYLTESTOSTERONE INDUCES CONDITIONED PLACE PREFERENCE IN ADULT MICE. **Rundle-Gonzalez, V.**; Garcia-Sosa, R.; Ayala-Baez, C.; Gandia-Cruz, G.; Jorge, J.C.
33. EFFECTS OF AN ANABOLIC STEROID ON GABA IMMUNOREACTIVITY IN REWARD AND ANXIETY BRAIN CENTERS. **Arriaga-Gonzalez, D.**; Rundle-Gonzalez, V.; Barreto-Estrada, J.L.; Jorge, J.C.
34. FURTHER STUDIES OF ESTRADIOL AND INTAKE OF PALATABLE INGESTA. **Reid, L.D.**; Boswell, K.J.; Klein, L.A.; Caffalette, C.A.; Schlosburg, J.E.; Stitt, K.T.; Reid, M.L.
35. PLASTIC FUNCTION OF GLUCOSE INCREASED IN THE BRAIN DURING. **Oomura, Y.**; Aou, S.; Hori, N.; Fukunaga, H.; Sasaki, K.
36. ELEVATED BLOOD GLUCOSE LEVELS IN SUGAR-DEPENDENT RATS. **Murphy, H.M.**; Wideman, C.H.
37. EFFECTS OF THE ENVIRONMENT EXPOSURE ON BEHAVIORAL SENSITIZATION INDUCED BY REPEATED ADMINISTRATION OF COCAINE. **Araujo, N.P.**; Carrara-Nascimento, P.F.; Fukushiro, D.F.; Rodrigues, M.S.D.; Oliveira-Lima, A.J.; Frussa-Filho, R.
38. THE EFFECTS OF METHAMPHETAMINE AND COCAINE ON RATS' Y-MAZE PERFORMANCE USING DIRECTIONAL VS. VISUAL CUES. **Klipec, W.D.**; Brackney, R.J.; Sounhein, K.; Mejia, R.; Dolezal, A.
39. INTERLEUKIN-1 AND ENDOTOXIN EFFECTS IN BEHAVIORAL TESTS FOR DEPRESSION AND ANXIETY. **Dunn, A.J.**; Swiergiel, A.H.

40. THE ROLE OF THE STRIATUM ON THE EFFECTS OF MODAFINIL. **Giordano, M.**; Mendoza-Trejo, M.; Mena-Segovia, J.
41. D3 RECEPTOR DOES NOT MEDIATE DA ANTAGONIST INHIBITION OF MK-801 HYPERACTIVITY. **Joyce, J.N.**; Iarkov, A.V.
42. EFFECTS OF 7-OH-DPAT, A D3 RECEPTOR AGONIST, ON PAIN MODULATION, IN THE RAT. Casarrubea, M.; Sorbera, F.; Saia, V.; Greco, P.; **Crescimanno, G.**



Friday, June 3:

7:30-8:30 **Traditional Continental Breakfast/Exhibitors Display.** ***Mesa Ballroom A***

8:30-10:30 **Symposium 2: Integrative function of the hypothalamus in autonomic, endocrine responses to stress and behavioral changes.** *Chair:* **Yoichi Ueta**, Univ. of Occupational and Environmental Health, Japan. ***Mesa Ballroom B&C***

8:30-9:00 OREXIN/HYPOCRETIN AND NEUROMEDIN U AS A STRESS MEDIATOR IN THE HYPOTHALAMUS. **Ueta, Y.**

9:00-9:30 CLOCK GENE MUTATION AND AUTONOMIC AND ENDOCRINE CHANGES. **Sei, H.**; Oishi, K.; Ishida, N.

9:30-10:00 AUTONOMIC AND CARDIOVASCULAR RESPONSES TO GRAVITATIONAL STRESS. **Morita, H.**; Gotoh, M.T.; Matsuda, T.; Tanaka, K.

10:00-10:30 HYPOCRETIN/OREXIN DEFICIENT NARCOLEPSY AS A DISEASE MODEL TO STUDY THE HYPOTHALAMIC FUNCTION IN HEALTH AND DISEASE. **Nishino, S.**

10:30-10:45 **Break/Exhibitors Display.**

10:45-11:45 **Presidental Lecture:** EPIGENETIC PERSPECTIVES ON MONOGAMY: INSIGHTS FROM PRAIRIE VOLES. **C. Sue Carter**, The University of Illinois at Chicago.

11:45-13:45 **Free time.**

13:45-15:45 **Symposium 3: Modeling different facets of disease toward endophenotypes in psychiatry.** *Chairs:* **Haim Einat,** University of Minnesota-Duluth, Duluth, MN, USA and **Henry Szechtman,** McMaster University, Hamilton, Ontario, Canada. ***Mesa Ballroom B&C***

13:45-14:15 ANIMAL MODELS FOR BIPOLAR DISORDER – NEW UNDERSTANDING AND NEW POSSIBILITIES. **Einat, H.**

14:15-14:45 COMPULSIVE CHECKING AND ITS ROOTS IN NORMAL BEHAVIOR: TOWARD AN ANIMAL MODEL OF OCD. **Szechtman, H.**; Woody, E.Z.; Eilam, D.

14:45-5:15 COMPULSIVE RITUALS IN ANIMALS AND HUMANS: APPLICATION OF A NEW CONCEPT IN THE STUDY OF OBSESSIVE-COMPULSIVE DISORDER (OCD). **Eilam, D.**

5:15-5:45 AN IMMUNO-PRECIPITATED NEURODEVELOPMENTAL ANIMAL MODEL OF SCHIZOPHRENIA IN MICE. **Feldon, J.**; Meyer, U.; Yee, B.

15:45-16:15 **Refreshment Break/Exhibitors Display**

16:15-17:27 **Oral Session 3: Animal Models.** *Chair*: **Richard Paylor**, Dept. of Molecular and Human Genetics, Baylor College of Medicine. ***Mesa Ballroom B&C***

16:15-16:33 MODELING AUTISM-RELATED BEHAVIORS IN THE FMR1 KNOCKOUT MOUSE MODEL OF FRAGILE X SYNDROME. Spencer, C.M.; Alekseyenko, O.; Serysheva, E.; Yuva-Paylor, L.; **Paylor, R.**

16:33-16:51 CONDITIONED FEAR IN CONGENITALLY HELPLESS RATS: EXTINCTION DEFICIT, TREATMENT, AND IMPLICATIONS FOR POST-TRAUMATIC STRESS DISORDER. **Shumake, J.**; Barrett, D.; Wrubel, K.M.; Johnson, S.E.; Gonzalez-Lima, F.

16:51-17:09 AUTISM-RELATED BEHAVIORS IN A NEW X-LINKED TRANSGENIC MOUSE. **Spencer, C.M.**; Yuva-Paylor, L.; Schuster, G.; Shope, C.; Noebels, J.; Brownell, W.; Overbeek, P.; Paylor, R.

17:09-17:27 SECRETIN RECEPTOR DEFICIENT MICE EXHIBIT AUTISTIC PHENOTYPES. **Nishijima, I.**; Givens, B.; Paylor, R.; Bradley, A.

17:30-19:30 **Poster Session 2. (Refreshments)** ***Ortiz Ballroom***

Fragile X Syndrome and Autism

43. A DEVELOPMENTAL APPROACH TO UNDERSTANDING FRAGILE X SYNDROME: THE INFLUENCE OF ENVIRONMENTAL AND GENETIC FACTORS ON BEHAVIOR PROBLEMS IN PATIENTS WITH FRAGILE X SYNDROME. **Akbarzadeh, M.**; Akbarzadeh, R.; Akbarzadeh, R.
44. ADVANCES IN RESEARCH ON THE FRAGILE X SYNDROME: ANALYZING GENE – BRAIN – BEHAVIOR RELATIONSHIPS IN NEURODEVELOP-MENTAL EFFECTS. **Akbarzadeh, R.**; Akbarzadeh, R.; Akbarzadeh, M.

45. SUPPRESSION OF TWO MAJOR FRAGILE X SYNDROME MOUSE MODEL PHENOTYPES BY THE MGLUR5 ANTAGONIST MPEP. Yan, Q.J.; Rammal, M.; **Bauchwitz, R.P.**
46. ALTERED RESPONSE TO SOUND AND ENVIRONMENT IN CUED/CONTEXUAL FEAR CONDITIONING IN A MOUSE MODEL FOR AUTISM. Desir, N; Walker, E.M.; **Hodges, A.B.**; Blue, M.E.; Hohmann, C.F.
47. EFFECTS OF TEST AND GENETIC BACKGROUND ON ANXIETY-RELATED BEHAVIORS IN THE FMR1 KNOCKOUT MOUSE MODEL OF FRAGILE X SYNDROME. **Spencer, C.M.**; Alekseyenko, O.; Serysheva, E.; Yuva-Paylor, L.; Paylor, R.
48. GABRB3 GENE KNOCKOUT MICE: A MODEL OF AUTISM SPECTRUM DISORDER? **DeLorey, T.M.**; Hashemi, E.; Sahbaie, P.; Homanics, G.

Other Nervous System Disorders and Models

49. EFFECT OF CURCUMIN ON 3-NITORPROPIONIC ACID-INDUCED MODEL OF HUNTINGTON'S DISEASE. †**Pattipati, S.N.**; Kumar, P.; Kumar, A.
50. A COPPER AND CHOLESTEROL DIET DISRUPTS LEARNED IRRELEVANCE IN RABBIT EYEBLINK CONDITIONING: AN ANIMAL MODEL FOR ALZHEIMER'S DISEASE. **Walker, A.G.**; McKinney, C.J.; Allen, M.T.
51. DELAYED ACQUISITION OF A VISUAL DISCRIMINATION IN RATS CHRONICALLY INFUSED WITH SOLUBLE AMYLOID BETA PEPTIDE. **Arnold, H.M.**; Brenneman, D.E.; Yohrling, G.J.
52. NICOTINE SENSITIZATION IN A RODENT MODEL OF PSYCHOSIS: A COMPARISON OF ADULT AND ADOLESCENT RATS. **Perna, M.**; Smith, K.; Handy, C; Brown, R.
53. NEONATAL QUINPIROLE TREATMENT PRODUCES DEFICITS IN PREPULSE INHIBITION IN RATS. **Maple, A.**; Smith, K.; Thacker, S.; Perna, M.; Brown, R.
54. OLFACTION IMPAIRMENTS IN MICE OVEREXPRESSING HUMAN WILDTYPE ALPHA-SYNUCLEIN. **Fleming, S.**; Schallert, T.; Levine, M.; Masliah, E.; Chesselet, M.
55. NEUROPSYCHOLOGICAL FUNCTIONING OF A FAMILY WITH MITOCHONDRIAL CYTOPATHY. **Sullivan, K.D.**; Neargarder, S.; Carvalho, J.
56. A FUNCTIONAL GENOMICS RESOURCE FOR NEUROSCIENTISTS: THE NIH NEUROGENOMICS PROJECT. **Yates, J.**; Siepka, S. ; Shimomura, K,; Li, Y.; Hong, H.K.; Simpson, E.; Mohn, A.; Caron, M.G.; Kandel, E.; Kibbe, W.A.; Hohman, M.M.; Levine, J.E.; Mullins, R.; Redei, E.; Sheffield, V.; Turek, F.H.; Vitaterna, M.H.; Pinto, L.H.; Takahashi, J.S.

Stress

57. CHILDHOOD ABUSE AND REGIONAL BRAIN DEVELOPMENT: EVIDENCE FOR SENSITIVE PERIODS. **Teicher, M.H.**; Andersen S.L.; Tomoda, A.; Vincow, E.; Valente, E.; Polcari, A.
58. EFFECTS OF ENERGY- REPRODUCTION- AND STRESS-RELATED SIGNALS ON THE PERFORMANCE OF VISUAL CATEGORICAL DISCRIMINATION OF FOOD AND SEX IN RHESUS MONKEYS. **Inoue, T.**; Takara, S.; Mizuno M.; Aou, S.
59. MODULATION OF MOTOR FUNCTION BY STRESS: A NOVEL CONCEPT OF THE EFFECTS OF STRESS ON BEHAVIOR. **Metz, G.A.**; Jadavji, N.M.

60. GENETIC MODULATION OF EARLY LIFE TRAUMA AND NEGLECT IN MICE. **Millstein, R.A.**; Boyce-Rustay, J.M.; Izquierdo, A.; Wiedholz, L.; Holmes, A.
61. CARDIAC REGULATION AT REST AND FOLLOWING STRESS IN FEMALE PRAIRIE VOLES: PRELIMINARY FINDINGS. †**Grippo, A.J.**; Carter, C.S.; Porges, S.W.

Drugs and Behavior

62. CAFFEINE'S ROLE IN CONDITIONING PREFERENCE AND PALATABILITY SHIFTS. †**Boudreau, S.**; LoLordo, V.
63. A NOVEL METHOD OF ORAL ADMINISTRATION OF METHYLPHENIDATE TO RATS REVEALS POST-DRUG MEMORY IMPAIRMENT. †**LeBlanc-Duchin, D.**; Taukulis, H.K.; Chuhan, Y.; Batra, N.
64. ESTABLISHING BEHAVIORAL PARADIGMS FOR THE EFFECTS OF PRENATAL COCAINE EXPOSURE IN RABBITS. **Thompson, B.L.**; Stanwood, G.D.; Levitt, P.
65. EVALUATION OF AMPHETAMINE WITHDRAWAL-INDUCED ANHEDONIA USING A LICKING MICROSTRUCTURE ANALYSIS. **Baird, J.P.**; Molchen, W.A.; Marks, G.
66. OREXIN-1 RECEPTORS MEDIATE FOOD AND WATER INTAKE RELATED EFFECTS OF OREXIN-A IN THE BED NUCLEUS OF STRIA TERMINALIS. **Lenard, L.**; Hangodi, O.; Bagi, E.; Urban, B.; Fekete, E.; Toth, K.
67. EFFECT OF PERCHLORATE ADMINISTRATION AND ETHANOL CONSUMPTION ON THYROID HORMONE AND BRAIN CATECHOLAMINE CONCENTRATIONS IN THE RAT. James, N.; Williams, H.; **McMillen, B.**

Neurochemical Basis of Behavior

68. EFFECTS OF OREXINS/HYPOCRETINS ON INTRACELLULAR CALCIUM IN NEURONS OF THE MEDIAL PREOPTIC AREA IN RATS. †**Takatsuna, M.**; Watanabe, K.; Nakajima, K.; Oomura, Y.; Wayner, M.J.; Sasaki, K.
69. SENSITIZED ATTENTIONAL PERFORMANCE AND FOS-IMMUNOREACTIVE CHOLINERGIC NEURONS IN THE BASAL FOREBRAIN. †**Martinez, V.**; Parikh, V.; Sarter, M.
70. DIFFERENTIAL SENSITIVITY OF AMPHETAMINE-EVOKED ROTATIONAL BEHAVIOR TO DOPAMINE SYNTHESIS BLOCKADE EARLY AFTER UNILATERAL NIGROSTRIATAL OR CORTICAL DAMAGE. †**Paquette, M.A.**; Hutchings, J.E.; Marsh, S.T.; Castañeda, E.
71. MODULATION OF CORTICAL ACETYLCHOLINE RELEASE VIA GLUTAMATERGIC AND D1 INTERACTIONS IN THE NUCLEUS ACCUMBENS. †**Zmarowski, A.**; Sarter, M.; Bruno, J.P.
72. A TESTOSTERONE METABOLITE IS REWARDING TO FEMALE RATS. †**Velazquez, K.**; Ramos, D.; Lorenzini, I.; Jessica Marrero, J.; Maldonado-Vlaar, C.; Jorge, J.

Sexual Differentiation

73. PERINATAL ACTIVATION OF ESTROGEN RECEPTOR â DEFEMINIZES THE DISPLAY OF SEXUAL BEHAVIOR. †**Kudwa, A.E.**; Gatewood, J.D.; Michopoulos, V.J.; Rissman, E.F.

74. SPINE DENSITY IN THE RAT BASOLATERAL AMYGDALA IS SEXUALLY DIMORPHIC. †**Rubinow, M.J.**; Juraska, J.M.
75. NON-TOXIC DOSES OF ENDOCRINE DISRUPTERS IMPAIR SEXUAL DIFFERENTIATION OF BEHAVIORS AND ENHANCE DEPRESSIVE BEHAVIOR IN RATS. **Aou, S.**; Fujimoto, T.; Kubo, K.
76. FLUOXETINE EXPOSURE DURING NEONATAL DEVELOPMENT ALTERS ACCESORY OLFACTORY BULB MORPHOLOGY ACCORDING TO SEX. **Melendez, D.**; Lugo, N.; Jorge, J.C.
77. EFFECTS OF ENVIRONMENTAL ENRICHMENT ON SPATIAL AND NON-SPATIAL MEMORY IN MALE AND FEMALE MICE THROUGHOUT THE LIFESPAN. †**Levy, L.J.**; Lambert, T.J.; Frick, K.M.

Physiology of Learning

78. THE MEDIAL THALAMUS IS CRUCIAL FOR WATER MAZE BEHAVIORAL STRATEGIES BUT IS NOT REQUIRED FOR SPATIAL PLACE MEMORY. **Cain, D.P.**; Boon, F.; Corcoran, M.E.
79. MEMORY DEFICITS IN NEONATAL AND JUVENILE RATS FOLLOWING CHRONIC STRESS. **Hoxha, Z.**, Mickley, G.A
80. SLEEP DISRUPTION IMPAIRS HIPPOCAMPAL RAT DENTATE GRANULE CELL LTP IN VIVO. **Wayner, M.J.**; Mery, L.R.; Marks, C.A.
81. THE RAT P300 ERP TO SIGNALED OCCURRENCE AND OMISSION OF EXPECTED REINFORCERS FOLLOWING EXTENDED TRAINING. **Klipec, W.D.**; Schneider, B.; Stanley, K.; Brackney, R. J.; Schwabe, J; Young, B.
82. THE DEVELOPMENT OF THE RAT P300 ERP DURING BACKWARD CHAINING. Stanley, K.; **Klipec, W.D.**; Lem, K.
83. ERP EVIDENCE FROM DYNAMIC DISSOCIATION OF TEMPRAL STORAGE AND REHEARSAL OF CHINESE CHARACTERS. **Wang,Y.W.**; Lin, C.D.; Zhang, W.X.
84. EFFECT OF EMOTIONAL CONTENT ON DECLARATIVE MEMORY: AN EVENT RELATED POTENTIAL STUDY. **Gasbarri, A.**; Arnone, B.; Pompili, A.; Marchetti, A.; Pacitti, F.; Saad Calil, S.; Pacitti, C.; Tavares, M.C.; Tomaz, C.

Saturday, June 4:

7:30-8:30 **Health Nut Continental Breakfast/Exhibitors Display.** ***Mesa Ballroom A***

8:30-10:30 **Symposium 4: New insights in ventral striatal organization and physiology: perspectives for the behavioral sciences.** *Chair:* **Jacques H. Abraini,** Université de Caen. ***Mesa Ballroom B&C***

8:30-9:00 GLUTAMATE-DOPAMINE INTERACTIONS IN THE NUCLEUS ACCUMBENS: EFFECTS ON CORTICAL ACh RELEASE AND ATTENTIONAL PROCESSING. **Bruno, J. P.**; Sarter, M.; Neigh, G.; Zmarowski, A.

9:00-9:30 DOPAMINERGIC MODULATION OF GLUTAMATERGIC RESPONSES IN THE NUCLEUS ACCUMBENS. **O'Donnell, P.**; Brady, A.M.; Benoit-Marand, M.

9:30-10:00 BEHAVIORAL ELECTROPHYSIOLOGY OF THE MOTIVE CIRCUIT. **Rebec, G.V.**; Wood, D.A

10:00-10:30 GLUTAMATE MODULATION OF DOPAMINERGIC MOTOR RESPONSES IN THE NUCLEUS ACCUMBENS: TOWARDS AN EXTENDED MODEL OF STRIATAL ORGANIZATION AND MOTOR FUNCTION. **Abraini, J.H.**; David, H.N.

10:30-10:45 **Break/Exhibitors Display.** ***Mesa Ballroom A***

10:45-11:45 **Keynote Speaker:** **Robert Dantzer**, D.V.M., Ph.D, CNRS-INRA, University of Bordeaux, France. Cytokines and Sickness Behavior: An Integrated Perspective. ***Mesa Ballroom B&C***

12:45-14:15 **NIH Grant Workshop:** "NIH 101", **Paul A. Rushing**, National Institute of Diabetes and Digestive and Kidney Diseases. Much of the biomedical research in the United States is supported by the National Institutes of Health (NIH). This brief "NIH 101" workshop will provide information on all aspects of the grant process from submission to funding. A special emphasis will be placed on peer review. In addition, the presentation will be followed by a question and answer period. ***Ortiz Ballroom***

14:15-15:15 **Business Meeting – open to all IBNS members.** Members are strongly encouraged to attend and participate. ***Ortiz Ballroom***

15:15-17:15 **Symposium 5: The paradox of acute stress effects on memory: Contrasting views, competing approaches and compatible findings.** *Chair:* **James C. Woodson,** University of Tampa, Tampa, Florida. ***Ortiz Ballroom***

15:15-15:45 STRESS PRODUCES TASK- AND MEMORY SPECIFIC SPATIAL MEMORY IMPAIRMENTS: CORRELATIONS WITH MOLECULAR, ULTRASTRUCTURAL, AND HORMONAL FACTORS. **Woodson, J.**

15:45-16:15 MECHANISMS OF AMYGDALA MODULATION OF HIPPOCAMPAL PLASTICITY. **Akirav, I.**; Richter-Levin, G.

16:15-16:45 FEMALES UNDER STRESS: WHY THEY KEEP CHANGING THEIR MINDS. **Shors, T.J.**

16:45-17:15 OPPOSING EFFECTS OF GLUCOCORTICOIDS ON MEMORY CONSOLIDATION AND MEMORY RETRIEVAL. **Roozendaal, B.**

17:15-17:30 **Break.**

17:30-18:24 **Oral Session 4: Plasticity.** *Chair*: **Robert Adamec**, Memorial University. ***Ortiz Ballroom***

17:30-17:48 FROM 'LOOPING' TO 'HOME BASE': HOW PRE-EXPLORATION PROGRESSIVELY BECOMES ANCORED TO THE OPEN-FIELD. Avni, R.; Zadicario, P.; Roitburd, A.; **Eilam D.**

17:48-18:06 HOW LEARNING LIKE ARE NEUROPLASTIC MECHANISMS OF LASTING CHANGE IN ANXIETY INDUCED BY SEVERE STRESS? **Adamec, R.**; Blundell, J.; Strasser, K.

18:06-18:24 A BEHAVIORAL HOMEOSTASIS THEORY OF THE EVOLUTIONARY SIGNIFICANCE OF HABITUATION AND SENSITIZATION. **Eisenstein, E.M.**; Eisenstein, D.; Smith, J.C.; Clark, K.B.

19:00- **Banquet and Presentation of Awards.** ***Mesa Ballroom A, B & C***
New Mexican Dinner Buffet and cash bar

Wednesday, June 1:

14:30-15:24 Oral Session 1: Chemistry of Behavior. Mesa Ballroom B&C

M5 MUSCARINIC GENE FACILITATES DOPAMINE REWARD FUNCTION IN RATS. Yeomans, J.S.; Steidl, S.; Wang, H. Mesopontine cholinergic neurons provide the main excitatory input to dopamine neurons from the brain stem. Removal of the M5 muscarinic receptor inhibits brain-stimulation reward in rats, and morphine reward in mice. Dopamine release in the nucleus accumbens is activated by mesopontine stimulation, but the prolonged release from 10-60 minutes is lost in M5 knockout mice (Forster et al., 2001). Here, we add the M5 muscarinic receptor gene to neurons in the ventral tegmental area of adult rats by means of a new in vivo electroporation method. Gene expression measured by GFP post mortem increased in a halo around the electrode from 1-4 days after electroporation. Brain-stimulation reward frequency thresholds were measured for 14 days after electroporation. Rats showed improved sensitivity to the reward stimulation from 2-14 days after anodal electroporation, and less so after cathodal electroporation. Control plasmids had no effect except reduced sensitivity on the first few days after electroporation, suggesting a small lesion effect. Therefore, adding the M5 muscarinic gene to dopamine cell groups can facilitate dopamine reward sensitivity.

GROUP I AND GROUP III METABOTROPIC GLUTAMATE RECEPTORS OPPOSE EACH OTHER IN THE CONTROL OF LOCOMOTOR RESPONSES PRODUCED BY D1-LIKE AND/OR D2-LIKE RECEPTORS. David, H.N.; Chevallier, K.; Abraini, J.H. UMR CNRS 6185, CYCERON, University of Caen, BP 5229, Caen cedex, France There is strong evidence for the existence of functional interactions between metabotropic glutamatergic (mGlu) receptors and dopaminergic neurotransmission in the rat nucleus accumbens. We studied the effects of activation or blockade of group I mGlu receptors or group III receptors on the locomotor responses induced by administration of a D1-like- and/or D2-like receptor agonist in the rat nucleus accumbens. Our findings demonstrated that stimulation of group III mGlu receptors opposes the behavioral responses induced by D1-like receptor activation, but favors those induced by activation of D2-like receptors, and further indicated that group I and group III mGlu receptors oppose each other in the control of dopaminergic neurotransmission in the nucleus accumbens.

ACUTE EFFECTS OF 3,4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA) ON STRIATAL SINGLE-UNIT ACTIVITY AND BEHAVIOR IN FREELY MOVING RATS: DIFFERENTIAL ROLES FOR 5-HT_{2A} AND 5-$HT_{2C/2B}$ RECEPTORS. Ball, K.T.; Rebec, G.V. Program in Neural Science, Dept. of Psychology, Indiana University, Bloomington, IN 47405 USA. Like amphetamine, a locomotor-activating dose of 3,4-methylenedioxymethamphetamine (MDMA) predominantly excites striatal single-unit activity in freely moving rats. Although both D_1- and D_2-like dopamine (DA) receptors play important roles in this effect, MDMA, unlike amphetamine, strongly increases both DA and serotonin (5-HT) transmission. To investigate the 5-HT receptor mechanisms underlying the striatal effects of MDMA, we recorded the activity of >200 single units in the striatum of awake, unrestrained rats in response to acute MDMA administration (5 mg/kg) combined with the selective blockade of either 5-HT_{2A} or 5-$HT_{2C/B}$ receptors. Prior administration of SR-46349B (a 5-HT_{2A} antagonist; 0.5 mg/kg) blocked nearly all MDMA-induced striatal excitations, which paralleled its significant attenuation of MDMA-induced locomotor activation. Conversely, prior administration of SB-206553 (a 5-$HT_{2C/B}$ antagonist; 2.0 mg/kg) had no effect on the amount of MDMA-induced locomotor activation or the distribution of single-unit responses to MDMA. However, a coefficient-of-variation analysis indicated significantly less variability in the magnitude of both MDMA-induced neuronal excitations and inhibitions in rats that were pre-treated with SB-206553 compared to vehicle. Analysis of concurrent single-unit activity and behavior confirmed that MDMA-induced striatal activation was not merely due to behavioral feedback, indicating a primary action of MDMA. These results support and extend our previous findings by showing that 5-HT_{2A} and 5-$HT_{2C/B}$ receptors differentially regulate the expression of MDMA-induced behavioral and striatal neuronal responses, either directly or through the modulation of DA transmission.

NEONATAL EXPOSURE TO 3,4-METHLYNEDIOXYMETHAMPHETAMINE ALTERS NMDA RECEPTOR AND ASSOCIATED PROTEINS IN ADULT RATS Skelton, M.R.; Williams, M.T.; and Vorhees, C.V. Div. of Neurology, Cincinnati Children's Res. Found. Cincinnati, OH 45229. USA. Exposure to MDMA from postnatal (P) day 11-20, a period of hippocampal development analogous to late third trimester human development, causes learning and memory deficits when the animals are tested in adulthood. In order to identify possible mechanisms responsible for the learning and memory deficits, the hippocampi of adult rats treated from P11-20 with either MDMA or saline were hybridized to Affymetrix microarrays containing approximately 8,800 genes. 48 genes were

significantly up-regulated in MDMA treated animals and 5 genes were significantly down-regulated. Twenty-four genes were selected for real-time RT-PCR analysis, of which 8 were verified to be altered in the rat hippocampus. To examine when the expression changes in the hippocampus of MDMA treated animals began, we examined MDMA treated animals on P12 and P21 using RT/RT-PCR for the 8 genes that were altered at P60. Two of the 8 selected genes were up-regulated on P12, and only 1 gene was altered on P21. CAPON, a scaffolding protein that appears to inhibit the interaction of PSD-95 and nNOS, showed the greatest fold change in both the gene chip and RT/RT-PCR assays in the adult hippocampus and was further investigated using immunohistochemistry. Along with CAPON, nNOS, PSD-95, and NR1α were also examined. While no changes were seen in levels of CAPON proteins in the dentate gyrus or CA1-CA3 regions of the hippocampus, nNOS, PSD-95 and NR1α all showed increases in protein levels throughout the hippocampus, suggesting that developmental MDMA exposure alters NMDA receptor function in adult animals.

MECHANISMS UNDERLYING MDMA FACILITATION OF SOCIAL INTERACTION IN THE RAT McGregor, I.; Thompson, M.; Morley. K.; Arnold, J.; Hunt, G. A widely reported positive effect of the drug MDMA ("Ecstasy") in humans is a strong feeling of love and closeness towards others. Despite widespread research into MDMA there is a lack of understanding of this pro-social effect. The current study examined the pharmacological and neural basis of this phenomenon using a social interaction task with rats. In the first experiment, male Wistar rats were pre-treated with either the 5HT1A receptor antagonist, WAY 100635 (1 mg/kg), the 5-HT2B/2C receptor antagonist, SB 206553 (2 mg/kg), the 5-HT1B receptor antagonist GR 55562 (1 mg/kg), the 5-HT2A receptor antagonist ketanserin (1 mg/kg), or the selective serotonin reuptake inhibitor fluoxetine (10mg/kg). Twenty minutes later they were given MDMA (5 mg/kg) or vehicle. They were then tested in the social interaction test. MDMA significantly increased the duration of time that rats spent engaged in social interaction. Pre-treatment with WAY 100635 or fluoxetine prevented MDMA-induced increases in social interaction while GR 55562 and ketanserin were ineffective. This suggests the importance of 5-HT1A receptors in the MDMA social effect. In a second study using c-fos immunohistochemistry, rats were given MDMA (5 mg/kg) or vehicle and either kept is isolation or permitted to engage in social interaction for 1 h prior to perfusion. Results showed that MDMA increased Fos expression in a number of sites, including the caudate-putamen, nucleus accumbens, median preoptic region, medial amygdala and ventral tegmental area. When rats were permitted to engage in social interaction, MDMA-induced Fos expression in the medial amygdala and nucleus accumbens was enhanced. These data suggests that MDMA, perhaps acting through 5-HT1A receptors and the nucleus accumbens and amygdala, is able to increase the rewarding efficacy of social interaction. Supported by the National Health and Medical Research Council of Australia.

MDMA - ALCOHOL INTERACTIONS: EFFECTS ON ACTIVITY AND THERMOREGULATION. Jones, B.C., Dept. of Biobehavioral Health, Penn State University, University Park, PA 16802, Cassel, J-C.; Koenig, J.; Jeltsch, H. Laboratoire de Neurosciences Comportementales et Cognitives, Université Louis Pasteur, 67000 Strasbourg, France. 3,4 methylenedioxymethamphetamine (MDMA or ecstasy) is a popular club drug often used in combination with ethanol. In this study, we investigated the acute effects of MDMA and ethanol singly and in combination on spontaneous activity and body temperature of rats. For four consecutive days, male Long-Evans rats were treated daily with 10 mg/kg MDMA with or without 1.5 g/kg ethanol. MDMA increased spontaneous activity 11-fold and this increase was potentiated by ethanol to more than 17-fold on all days. Moreover, ethanol inhibited the MDMA-induced hyperthermia, on the first but not on subsequent treatment days, suggesting short-term tolerance to ethanol. These observations suggest that combined ethanol-MDMA may induce effects on activity and thermoregulation that involve separate mechanisms. Our results have important implications as to understanding the potential health risks of polydrug use combining ecstasy and ethanol. Supported in part by USPHS Grants NS 35088 and AG 21190 and by a Tobacco Settlement grant from the State of Pennsylvania. BCJ was supported as Professeur Invité by ULP.

17:00 - 18:00 Keynote Speaker: Larry Cahill. Mesa Ballroom B&C

SEX AND HEMISPHERE INFLUENCES ON BRAIN MECHANISMS OF EMOTIONAL MEMORY. Cahill, L. A large and compelling body of evidence from animal research indicates that the amygdala interacts with stress hormones released during and after an emotionally arousing event to modulate consolidation of memory for that event. Evidence involving human subjects further supports this view. However, in recent years human subject research has also revealed unexpected influences of both subject sex and cerebral hemisphere on these brain mechanisms. This lecture will highlight these recent developments in our evolving understanding of how the brain stores memory for emotional events.

Thursday, June 2:

10:30-11:42 Oral Session 2: Aversive Behavior. Mesa Ballroom B&C

NORADRENALINE TRANSMISSION WITHIN THE BED NUCLEUS OF THE STRIA TERMINALIS IS CRITICAL FOR FEAR BEHAVIOR INDUCED BY TMT-EXPOSURE. Fendt, M. Animal Physiology, University of Tubingen, Tubingen, Germany. The bed nucleus of the stria terminalis (BNST) is involved in the mediation of fear behavior in rats. A previous study of our laboratory demonstrated that temporary inactivation of the BNST blocks fear behavior induced by exposure to trimethylthiazoline (TMT), a component of fox odor. The present study investigates whether noradrenaline release within the BNST is critical for TMT-induced fear behavior. First, we demonstrated that the ventral BNST is that part of the BNST which receives the densest noradrenaline innervation. Second, using in vivo microdialysis we showed that noradrenaline release within the BNST is strongly increased during TMT exposure, and that this increase can be blocked by local infusions of the alpha2-receptor blocker clonidine. Third, using intracerebral injections, we showed that clonidine injections into the ventral BNST, but not into neighboring brain sites, completely blocked TMT-induced potentiation of freezing behavior. The present data clearly show that the noradrenergic innervation of the ventral BNST is important for the full expression of behavioral signs of fear to the predator odor TMT.

VOCALIZATION-RELATED INPUT INTO THE PERIAQUEDUCTAL GRAY OF THE MIDBRAIN IN THE SQUIRREL MONKEY. Juergens, U.; Dujardin, E. German Primate Center, Goettingen, Germany. The aim of the present study was to find out whether there are differences in the afferent connections of periaqueductal gray sites producing different vocalizations when electrically stimulated. The experiments were carried out in six squirrel monkeys (Saimiri sciureus). Three call types were investigated: clucking, a short-distance contact call; cackling, a social mobbing call; and shrieking, a call uttered during fighting. In a self-stimulation test in which the animals received the opportunity to switch on and off the vocalization-inducing PAG stimulation themselves, it was found that clucking is accompanied by neutral emotional states, cackling is accompanied by slightly aversive emotional states, while shrieking is accompanied by highly aversive emotional states. In order to clarify the input into the vocalization-eliciting sites, we injected wheat germ agglutinin-conjugated horseradish peroxidase (WGA-HRP) into these sites and scanned the brain for retrogradely labeled nerve cells. It turned out that there was an almost complete overlap of the afferent projections to the different vocalization-eliciting PAG sites. The projections, however, showed marked quantitative differences. In the posterior hypothalamus, for instance, the number of retrogradely labeled neurons correlated with the degree of aversiveness of the vocalization elicited from the injection site (highest for shrieking, lowest for clucking). In the nucleus accumbens and preoptic region, in contrast, the number of retrogradely labeled neurons were the higher the less aversive the vocalization site was (highest for clucking, lowest for shrieking). It is concluded that the posterior hypothalamus is involved in the vocal expression of aversive emotional states, while the nucleus accumbens and preoptic region are involved in the vocal expression of hedonic emotional states.

SOCIAL APPROACH-AVOIDANCE TEST IN F-344 RATS: PHARMACOLOGICAL VALIDATION. Nicolas, L.B. ; Prinssen, E.P. PRBD-N, F. Hoffmann-La Roche, CH-4070, Basel, Switzerland. To better understand anxiety disorders with comorbid social anxiety states as well as to identify new treatments it is important to develop pre-clinical testing procedures involving social components of anxiety. We modified and automated the Social Approach-Avoidance (SAA) test recently developed by Haller and Bakos (Physiol Behav, 2002). The apparatus consists of a small non-social compartment connected to a larger social compartment by a sliding door. The social compartment contains a large stimulus rat confined in a sub-chamber delimited by a perforated transparent wall. In F-344 rats that show spontaneous high avoidance of the social compartment, chlordiazepoxide and the benzodiazepine receptor inverse agonist, RO 19 4603, dose-dependently increased and decreased the time spent in the social compartment, respectively. Single treatment with the SSRI fluoxetine (1-30 mg/kg, p.o.) had no significant effect on the SAA behavior. Similarly, after 12-days administration (3, 10 mg/kg, p.o., once daily), fluoxetine did not affect behavior. In contrast, after a prolongation of the treatment up to 22-days in the same animals, 10 mg/kg fluoxetine induced a significant increase in the time spent in the social compartment. However, it should be noted that the avoidance in vehicle-treated animals at day 22 was significantly higher than that observed in vehicle animals tested either acutely or on day 12. These results suggest that the modified SAA is not only sensitive to rapidly acting anxiolytics but also to slowly acting compounds

PROBLEMS IN THE MODELING OF AGGRESSIVE BEHAVIOR. Robert J. Blanchard, Mu K Yang, Yoav Litvin Department of Psychology, University of Hawaii. A major impediment in the study of offensive aggressive behavior in rodents is the perception that biting is injurious and must therefore be limited or controlled by the experimenter. Data will be presented demonstrating that for encounters among mice, fewer than 4% of bites observed by trained observers actually produces skin lesions in the bitten animal. Parallel results for rats and

hamster lead to similar conclusions. Observed bites, involving mouth/jaw movements of one animal against the pelage of another, and accompanied by vocalizations of the latter, are appropriately classified as "pinch-vocalizations". We suggest that the term "bite" be reserved for actions resulting in lesions. The distinction between lesion-producing bites and pinches, with or without vocalization is also important to an analysis of inhibited bites, such as those of females on males.

15:15-17:15 Symposium 1: How would you model the behavioral symptoms of autism in rodents? Mesa Ballroom B&C

BEHAVIORAL TASKS TO MODEL THE CORE SYMPTOMS OF AUTISM IN MICE. Jacqueline N. Crawley, Ph.D., Chief, Laboratory of Behavioral Neuroscience, Intramural Research Program, National Institute of Mental Health, Bethesda, MD 20892-1375, and STAART Project Investigator, Neurodevelopmental Disorders Research Center, University of North Carolina, Chapel Hill, NC 27599, USA. Autism is a highly heritable neurodevelopmental disorder. Mice with mutations in candidate genes for autism represent a critical research tool for testing hypotheses about the causes of autism. Behavioral neuroscientists have a unique opportunity to contribute to this growing research field. New rodent tasks are needed to approximate the defining symptoms of autism: 1) deficits in appropriate reciprocal social interactions, 2) impaired social communication, and 3) high levels of repetitive behaviors and restricted interests. We modeled the core deficit in social interaction with a new automated three-chambered apparatus for quantitating social approach behaviors in mice. Sociability scores were similar with automated and observer-scored methods, in juveniles and adults, in males and females, and with repeated use of the same individuals (Moy et al. Genes, Brain and Behavior 2004; Nadler et al. Genes, Brain and Behavior 2004). First results show high levels of social approach and preference for social novelty in C57BL/6J, C57L/J, DBA/2J, FVB/NJ, C3H/HeJ, and B6129PF2/J mice, while A/J, BALB/cByJ, and BTBRT+tf/J strains displayed unusually low levels of social approach (Moy et al. Society for Neuroscience 2004). Resistance to change in routine is being modeled by training mice to form a spatial position habit for a food reinforcer in a T-maze, or for the escape platform in the Morris water maze, and then changing the location of the reinforcer. In addition, comprehensive behavioral phenotyping is conducted to rule out artifacts and detect traits relevant to associated symptoms of autism, including anxiety, mental retardation, and idiosyncratic hypersensitivity to sensory stimuli. Identification of genes underlying social interaction, social communication, and resistance to change in mice may inform the search for human genes linked to autism. Supported by STAART U54 MH66418 and the NIMH Intramural Research Program

MODELING AUTISM BEHAVIORAL DEFICITS IN THE LABORATORY RAT. Walker, B.R., Laboratory of Integrative Systems Neuroscience, Department of Psychology, Georgetown University, Washington, DC 20057 USA. Autism is most commonly characterized by deficits in social interaction and communication, environmental awareness, as well as demonstrating obsessional mannerisms, behavioral inflexibility, and a higher incident rate of epileptic seizures throughout childhood. Many brain alterations have been suggested as being responsible for these core symptoms, including reductions in Purkinje cells in the cerebellum and alterations of specific neurotransmitter systems within the forebrain. In order to test whether specific brain lesions lead to behavioral deficits, we measured social preferences to novel social interactions in adult laboratory rats via an automated 3-chambered apparatus before and after selective removal of ACh neurons within the forebrain or Purkinje cells within the cerebellum. Our results demonstrate strong preferences for novel social interactions in the control condition. These preferences are reduced after selective ACh lesions, but not after Purkinje cell loss. Further, we examined environmental exploration by recording the frequency of nose-poking behavior per minute of exploring an automated activity chamber. Rats with Purkinje cell loss demonstrated a reduction in environmental exploration, while rats with ACh lesions maintained control levels of exploration frequency. Additionally, in an attempt to test the hypothesis that procedures shown to be anticonvulsant for resistant seizures (Walker et al., Epilepsia 1999) will reduce these social and exploratory deficits, due to the overlap in brain structures for both seizures and autism, we inhibited the neural axis of the vagus nerve within the nucleus tractus solitarius (NTS) in the brainstem. Increasing GABAergic transmission within the NTS ameliorated the deficits seen in social preferences and environmental exploration. Knowledge of the specific anatomical alterations seen in autism will not only allow us to correlate behavioral alterations and potential gene candidates for the etiology of autism, but also may suggest potential future treatment options. *Supported by Cure Autism Now Foundation Georgetown University*

BEHAVIORAL GENETICS OF SOCIAL AND REVERSAL TRAITS IN INBRED STRAINS OF MICE. Bolivar, V.; Walters, S.; Santiago, A.; Phoenix, J.; Flaherty, L. Genomics Institute, Wadsworth Center, Troy, NY 12180 USA. Autism is a pervasive developmental disorder, generally defined by social deficits, communication difficulties, restlessness and distraction, cognitive inflexibility, and repetitive movements. We recently developed a set of behavioral assays for mice that reflect some characteristics of this disorder. As inefficiency of social interaction is a hallmark of autism, we are analyzing social interactions between pairs of mice. We are examining cognitive inflexibility with extinction of fear conditioning and Morris water maze (changing platform position)

assays. Finally, we are evaluating motor behavior (e.g., hyperactivity, stereotypic movements) during exploration of a novel environment. In this way we can evaluate social, cognitive, and motor behaviors in mice and determine if they have similar properties to those seen in autistics. We have found that inbred strains display behavioral abnormalities that may make them useful as models for some aspects of autism. BTBR T+ tf/J mice spend very little time engaged in social interactions and display poor extinction of fear conditioning behavior. 129P2/OlaHsd mice have difficulty "learning" new platform positions in the water maze. Finally, several strains, including BTBR T+ tf/J and FVB/NJ, display more stereotypic movements in a novel environment than other strains. Our preliminary results indicate that there are behavioral abnormalities in inbred strains of mice that resemble some of the altered behaviors found in autistics. Indeed, these strains may provide a useful avenue for the pursuit of genes or biochemical pathways underlying this complex disorder. Supported by NIH grants to VB & LF.

CLINICAL SYMPTOMS AND POTENTIAL TREATMENTS FOR AUTISM: HOW ANIMAL MODELS CAN HELP. Porges, S.W., Brain-Body Center, Department of Psychiatry, University of Illinois at Chicago, IL 60612 USA. The vagus as a "system" provides a rich organizing principle to investigate several of the behavioral, psychological, and physiological features associated with a diagnosis of autism. The Polyvagal Theory proposes a hierarchy of autonomic states, which foster different adaptive behavioral strategies (i.e., social engagement, fight-flight, freeze) that are phylogenetically ordered. The most recent phylogenetic system links the myelinated vagus to structures involved in social engagement (i.e., the muscles of the face and head). The Polyvagal Theory describes this integrated system as the Social Engagement System. Observations of the behavioral and physiological responses of autistic individuals suggest that they have great difficulties in recruiting the neural circuit that regulates the Social Engagement System. It appears that autism is associated with autonomic states that remove the individual from direct social contact by supporting the adaptive defensive strategies of mobilization (i.e., fight-flight) or immobilization (i.e., shut-down). Behaviorally, the retraction of the neural regulation of the Social Engagement System would be expressed as reduced tone and regulation of the muscles of the face and head. The functional consequence of this retraction would limit facial expressions and head gestures, result in difficulties in extracting human voice from background sounds, and produce aprosodic speech. These profound deficits in social engagement behavior form a core characteristic of autism. This presentation focuses on several questions related to the value of animal models in understanding autistic behaviors. For example, how well do animal models of social behavior capture the deficits in social engagement behavior and autonomic regulation that form a core characteristic of autism?

17:30-19:30 Poster Session 1. (Refreshments) Ortiz Ballroom

Genetic and Chemistry of Learning and Performance

1. *Withdrawn*.
2. *Withdrawn*.
3. AUGMENTATION OF ATTENTIONAL PERFORMANCE-ASSOCIATED INCREASES IN PREFRONTAL ACETYLCHOLINE RELEASE DURING BASAL FOREBRAIN NMDA RECEPTOR BLOCKADE-INDUCED IMPAIRMENTS IN PERFORMANCE. Kozak[1] R.; Bruno[2] J.P.; Sarter[1] M. [1]Department of Psychology, University of Michigan, Ann Arbor, MI and [2]Departments of Psychology and Neuroscience, Ohio State University, Columbus, OH. Previous research demonstrated that attentional performance depends on the integrity of the cortical cholinergic input system and that such performance is associated with increases in cortical acetylcholine (ACh) release. Furthermore, blockade of basal forebrain (BF) NMDA receptors impaired attentional performance and, in non-performing animals, attenuated increases in cortical ACh release. The present experiment tested the hypothesis that the attentional impairments produced by bilateral BF infusions of the NMDA receptor antagonist DL-2- amino- 5-phosphonovaleric acid (APV) are associated with attenuated increases in performance-associated ACh release. Rats were trained in a sustained attention task and equipped with three guide cannula for the bilateral infusion of the NMDA receptor antagonist APV (0, 3, 20 nmol) and for the insertion of a dialysis probe into the medial prefrontal cortex (mPFC). APV or vehicle was infused remotely into the BF of task-performing and dialyzed rats, following completion of the first of five 8-min blocks of trials. During the first block of trials, attentional performance was associated with a 140% increase in prefrontal ACh efflux. Subsequent BF infusions of vehicle did not affect this increase. Infusions of APV decreased the animals' ability to detect signals and augmented the increases in ACh efflux observed prior to infusions. These data indicate a dissociation between levels of attentional performance and increases in mPFC ACh release. Augmentation of performance–associated increases in mPFC cholinergic transmission is hypothesized to mediate the increased demands on attentional 'effort' that are required to maintain performance under challenging conditions. *Supported by PHS Grants NS37026, MH01072, and MH57436*.

4. TWO BEHAVIORAL TASKS REVEAL MOTOR AND LEARNING DEFICITS IN THE YAC72 MOUSE MODEL OF HUNTINGTON'S DISEASE. C. Lawhorn, D.M. Smith, and L.L. Brown. Albert Einstein College of Medicine, Bronx, NY. While, Huntington's disease (HD) mouse models provide us with important tools for investigation, thorough and replicable phenotypic characterization is necessary to fully understand its relevance to the human disease. We used mice with yeast artificial chromosomes containing 72 CAG repeats (YAC72), as a model for studying the relationship between the neuropathology and behavioral symptoms of HD. To determine quantifiable behavioral deficits in this model we used a novel and challenging sensorimotor coordination task called the wire maneuver task, and an accelerating rotarod. At 7 months old, YAC72 mice (n=7) showed no difference on the wire maneuver task compared to age matched controls (n=13). As we have previously reported,13 month old YAC72 mice showed a performance deficit on the wire maneuver task. This deficit was replicated in a second group of 13 month old mutants (n=12) compared to age matched controls (n=10) with a 50% decrease in performance (Controls: 50 ± 10 seconds; YAC72: 25 ± 8 seconds). In addition, we tested 13 month old YAC72 mice and controls on two rotarod tasks. On an accelerating rotarod, control mice showed an improvement in their performance on the rod over 3 days of training. However, 13 month old YAC72 mice did not show a significant improvement across 3 days. Interestingly, wire maneuver scores were positively correlated with day 1 performance on the accelerating rotarod irrespective of genotype ($r=.75$, $p<.001$). On a constant speed rotarod YAC72 mice did not differ from controls at 9, 18 and 36 RPM. This is the first study of YAC72 mutant mice to a show (1) a replicable behavioral deficit on a challenging sensorimotor coordination task, and (2) a motor skill learning learning deficit using the rotarod. Furthermore, these data suggest that more challenging behavioral tasks are necessary to detect deficits in the YAC72 mouse model of HD.

Fear and Anxiety

5. ENVIROMENTAL ENRICHMENT ENHANCES LEARNING AND MEMORY AND HIPPOCAMPAL EXPRESSION OF NEUROGRANIN AND OTHER SIGNALING MOLECULES Huang, F.L.; Huang, K.P.; Wu, J.F. NICHD, NIH, Bethesda, MD 20892, USA Environmental enrichment is known to enhance hippocampal neurogenesis and cognitive functions. The underlying molecular mechanisms, however, are not fully understood. Several protein kinases, including CaMKII, PKC, PKA and ERK, and their substrates are known to involve in the processes of learning and memory. We have been investigating the role of neurogranin (Ng), a specific PKC substrate, in such processes. Ng is abundantly expressed in hippocampus, cortex and amygdala, brain regions that are important for memory formation. Ng binds CaM in a Ca2+-sensitive manner and regulates neuronal Ca2+ and CaM concentrations. Using Ng knockout mice, we showed previously that Ng-/- mice exhibited severe deficits in LTP and spatial memory. These mice, as compared to +/+, respond poorly upon treatments of hippocampal slices with PMA, forskolin and NMDA in the activation of CaMKII, PKC, PKA, ERK and CREB. Most importantly, the performance scores of Morris water maze are positively correlated to hippocampal Ng levels of +/+ and +/- mice. In the present study, mice of different genetic background were housed in regular home cages (control) or more spacious cages with twice a week changes of toys (enrich) for at least three weeks. In Morris water maze, the enriched +/+ and +/- mice performed significantly better than their corresponding control, while the enriched -/- mice show only minimal improvement. Enriched +/+ and +/- mice also showed enhanced LTP following HFS, but not that of -/- mice. Immunoblot analysis, however, showed that enriched mice of all three groups have elevated hippocampal levels of CaMKII and CREB, but not ERK. Interestingly, enrichment results in a greater increase in hippocampal Ng levels in +/+ mice than those of +/- mice. These results suggest that Ng regulates neuronal Ca2+ and CaM-dependent enzymes involved in memory formation. During environmental enrichment, these Ng-regulated reactions were further facilitated and led to improved cognitive functions.
6. IMPROVED PREDICTIVE VALIDITY OF THE MARBLE BURYING TEST FOR ANXIETY BY SIMULTANEOUS MEASUREMENTS OF LOCOMOTOR ACTIVITY. Nicolas, L.B.; Kolb, Y.; Prinssen, E.P. PRBD-N, F. Hoffmann-La Roche, CH-4070, Basel, Switzerland. Over the last decades, the suppression of spontaneous burying of glass marbles by mice has been used as an index of anxiolytic drug action. I.e., in the marble burying test (MBT), acute administration of benzodiazepines and different classes of antidepressants inhibit marble burying. However, non-anxiolytic compounds such as antipsychotics also reduce marble burying thus raising the question about the predictive validity of this procedure for anxiety. In addition, it has been suggested that marbles do not function as aversive stimuli. In the present study, we used a videotracking system to measure locomotor activity (LA) in the MBT and also, as a control condition, to measure spontaneous locomotor activity (SLA) in test-boxes without sawdust or marbles. We examined 6 compounds of different classes in C57BL/6 mice. Whereas all 6 compounds decreased MB, 4 different profiles could be distinguished: (1)

Diazepam and MTEP did not affect LA in the MBT; (2) Paroxetine decreased LA in the MBT, but not SLA; (3) Haloperidol and yohimbine decreased both LA in the MBT and SLA; (4) Amphetamine showed a complete different profile by increasing LA in the MBT. Finally, we showed that C57BL/6 mice avoided glass marbles when the latter were placed on one half of the test box, suggesting the anxiogenic-like nature of the marbles. These data suggest that, under our current test conditions, the selective inhibition of marble burying has predictive validity for anxiety.

7. GALANIN GAL-R2 RECEPTOR NULL MUTANT MICE EXHIBIT AN ANXIOGENIC-LIKE PHENOTYPE ON TESTS OF ANXIETY-LIKE BEHAVIOR. Bailey, K ; Pavlova, M ; Hohmann, J ; Zeng, H ; Crawley, J Laboratory of Behavioral Neuroscience, NIMH, Bethesda MD Nura Inc. Seattle WA The neuropeptide galanin is co-localized in neurons containing serotonin and norepinephrine. Excess endogenous galanin and exogenously administered (ICV) galanin have been implicated in cognitive, affective and anxiety-like behaviors in mice and rats. Three G-protein coupled galanin receptor subtypes are known: GAL-R1, GAL-R2, AND GAL-R3. GAL-R1 receptor null mutant mice demonstrate anxiety-like behavior, specific to the elevated plus-maze test, suggesting an anxiolytic-like effect of galanin at this receptor for this stress-inducing test (Holmes et al., 2003). A newly generated line of GAL-R2 null mutant mice provides a means for exploring the role of this receptor subtype in anxiety. We first confirmed that there were no significant effects of genotype on measures of general health (i.e. reflexes, empty cage behavior), rotarod performance, or thermal sensitivity in the hotplate analgesia test. We then utilized three anxiety-related behavioral tests (elevated plus-maze, light/dark exploration, and open field activity) to further assess this phenotype. GAL-R2 null mutant mice demonstrated less time in the open arms and fewer open arm entries in the elevated plus-maze, along with no significant genotype difference in total entries, consistent with an anxiogenic-like phenotype. These findings, in conjunction with previous results, suggest an expanded role for galanin receptor subtypes in mediating anxiety-like behaviors.

8. INVOLVEMENT OF TRANSMITTERS IN THE ANXIOLYTIC ACTION OF UROCORTIN 2 IN MICE. Telegdy, G., and Adamik, A. Department of Pathophysiology, University of Szeged, Hungary. Urocortin 2 (UC 2) is a nem member of the corticotropin-releasing factor peptide family. UC 2 positiv neurones were found in the hypothalamus, amygdala and nucleus tractus solitarii etc. The UC 2 is an endogenous ligand for CRF-2 receptor. It has been suggested that UC 2 might play a role in food intake, stress-related behavior and anxiolytic action. The UC 2 was tested for anxiolytic action in an elevated plus maze. For detecting the possible involve-ment of neurotransmitters, the mice were pretreated with receptor blockers. The following receptor blockers were used: haloperidol, phenoxybenzamine, propranolol, atropine, methysergide, bicuculline and nitro-l-arginine for blocking the nitric oxide production. The peptides were administered into the lateral brain ventricle, the receptor blockers were used intraperitoneally. UC 2 administered into the lateral brain ventricle elicited a dose dependent bell-shaped action. The most effective dose was 1.0 ug. For further testing the 1.o ug was used. All receptor blocker used in a dose, which themselves had no action in the test, could attenuate or block the anxiolytic action of UC 2. The results suggest that in the anxiolytic action of UC 2 D1/D2, alpha- and beta-adrenergic, cholinergic, serotonergic, GABA-ergic transmitters and nitric oxides are involved.

9. BEHAVIORAL PROFILE OF RATS FOLLOWING CRF-MEDIATED STRESSORS. Sajdyk, T.; Fitz, S.; Merrill, C.; Conroy, S.; Chambers, R.; Shekhar, A. Dept. of Psychiatry, Indiana Univ. Sch. Med., Indianapolis, IN 46202 USA. Corticotrophin-releasing factor (CRF) is a key neuropeptide involved in generating the biological response to stressful stimuli. Currently, there are two receptor subtypes identified, CRF1 and CRF2. It appears that the CRF1 receptor is critical for mediating stress responses, while the role for the CRF2 receptor is not as clear. In the present study male Wistar rats were exposed to two different types of stressors, restraint stress (general) and predator odor (specific) and then assessed for behavioral responses in the social interaction (SI) test, the elevated-plus maze (EPM)and the locomotor activity chamber (AC). Subsequently, a second group of animals were tested and half were treated with saline and half with a selective CRF1 antagonist to determine 1) which responses were mediated by the CRF1 receptor subtype; and 2) if there was a difference between the types of stressors and the role of CRF1 receptors. Our results indicate that behavioral responses to restraint and predator odor stress are pharmacologically similar in that both are blocked by pretreatment of a CRF1 receptor antagonist. In contrast, the behavioral profile of the three administered tests is not identical and thus it appears that the type of stressful stimulus is important in determining the overall response. Research supported by NIMH grant K01 01869-01.

10. REPEATED ADMINISTRATION OF NEUROPEPTIDE Y IN THE BASOLATERAL NUCLEUS OF THE AMYGDALA ELICITS LONG-TERM ANXIOLYTIC-LIKE RESPONSES. Sajdyk, T.; Fitz, S.;Rainnie, D.; Shekhar, A. Dept. of Psychiatry, Indiana Univ. Sch. Med., Indianapolis, IN 46202 USA. Anxiety is a normal emotional response to perceived adverse conditions and helps the organism to survive and negotiate through stressful stimuli. Thus, like any other homeostatic response, there

needs to be appropriate mechanisms in place for both generation and termination of the response. Neuropeptide Y (NPY) is one of the key neuromodulators of the anxiolytic responses within the brain, particularly the amygdala. Our past studies show that repeated activation of CRF receptors in the BLA leads to LTP-like responses that coincide with long-term anxiogenic-like behaviors in the SI test and that pretreatment with NPY will prevent the development of the persistent anxiety state. In addition, we have shown that administration of NPY alone into the basolateral nucleus of the amygdala (BLA) will produce anxiolytic-like behaviors in the social interaction (SI). Results from electrophysiology studies indicate that neurons in the BLA can exhibit both long-term potentiation (LTP) and long-term depression (LTD), thus, the purpose the of this study was to determine if repeated activation of the NPY system in the BLA could elicit long-term anxiolytic-like behaviors. Male Wistar rats administered daily injections of NPY into the BLA for 5 days showed significant anxiolytic responses in SI following testing on day 5 and continued to do so without further treatment for an additional two weeks. These findings suggest that repeated stimulation of the NPY system may induce a form of plasticity in the BLA which results in the persistent expression of anxiolytic-like social behaviors. Research supported by NIMH grant K01 01869-01.

11. SODIUM LACTATE INDUCED PANIC-LIKE PHYSIOLOGICAL RESPONSES CORRELATE WITH CELLULAR RESPONSES IN SPECIFIC SUBREGIONS OF THE DORSOMEDIAL HYPOTHALAMUS OF RATS. Johnson, P; Fitz, S; Keim, S; Lowry, C; Shekhar, A. Dept. of Psychiatry, Indiana University, Indianapolis, IN 46223,U.S.A., H.W. L.I.N.E., University of Bristol, Bristol, U.K. Patients with panic disorder are susceptible to panic attacks following intravenous (i.v.) sodium lactate infusions. Although the neural pathways mediating lactate-induced panic are not well defined, disruption of GABAergic activity in the dorsomedial hypothalamus (DMH) produces anxious (measured by social interaction time) and panic-prone (increased likelihood of panic-like physiological responses following sodium lactate infusions) rats. Here we attempted to determine which subregion of the DMH, after inhibition of GABA synthesis, produces panic-like responses after i.v. lactate infusions in panic-prone rats. To measure cellular responses we examined c-Fos immunoreactive (ir) cells in the DMH following lactate infusions in panic-prone and control rats. Rats were made panic prone by locally inhibiting GABA synthesis in the DMH with infusions of L-allylglycine (L-AG: a GABA synthesis inhibitor). Five days later, rats were i.v. infused with lactate or saline. L-AG infused rats had decreased GABA-immunostaining in the DMH, which correlated with anxiety-related behavior. Subregional analysis of c-Fos responses in the DMH revealed that specifically the dorsal hypothalamic area (DA) had significant increases in numbers of c-Fos-ir cells in panic prone rats displaying panic-like responses (i.e, tachycardia and hypertension) after sodium lactate infusions. The c-Fos responses in the DA also correlated with heart rate responses. Previous studies (Samuel et al., 2004) have demonstrated that neurons in the DA are particularly implicated in bicuculline methiodide (GABAA receptor antagonist) induced tachycardia. The c-Fos responses in the DA also appear to be critical for sodium lactate induced tachycardia in panic-prone rats (Supported by RO1s MH 52619 & MH 065702).

Development & Individual Differences

12. EFFECT OF NEONATAL NOVELTY EXPOSURE ON SOCIAL COMPETITION. K.G. Akers; A.C. Tang. Department of Psychology, University of New Mexico, Albuquerque, NM, 87131, U.S.A. We investigated, among male Long Evans hooded rats, whether neonatal novelty exposure, an early life stimulation procedure, affects adult ability to compete for access to a desired but limited food resource in the presence of a conspecific. During the first 3 weeks of life, half of each litter was exposed to a novel environment (Novel) for 3 min daily while the other half remained in the home environment (Home). Twelve months later, these rats were trained for six days to obtain chocolate rewards in the absence of a conspecific. Upon reaching asymptotic performance, they were tested in the presence of a conspecific for their ability to compete for exclusive access to chocolate, indexed by number of wins. We found that in the absence of a motivational difference, indexed by latencies to reach the chocolate rewards on the last day of training, Novel rats had a greater number of wins than Home rats during this competition. This suggests that very brief and transient early life environmental manipulations can create persistent individual differences during adulthood in the ability to compete for limited resources. This enhanced ability was paralleled by a greater attention to cues signaling the availability of chocolate rewards, indexed by a higher orientation score among Novel rats in comparison to Home rats. These results suggest that the long-lasting effect of neonatal novelty exposure on adult competitive ability may be mediated via an attenuated distractibility in novel social situations.
13. TIMING AND AMOUNT OF EARLY EXPERIENCE AFFECTS PARENTAL CARE IN PRAIRIE VOLES. Boone, E.M.; Lewis-Reese, A.; Carter, C.S.; Bales, K.L. Brain Body Center, Department of

Psychiatry. University of Illinois at Chicago, Chicago, IL 60612 USA. Decades of clinical and basic research support a relationship between early life experiences and future life events. In human, non-human primate and rodent studies, nurturing received during the neonatal period influences not only the ability to cope with future life stress but also the exhibition of future parental and other social behaviors. In this study, we used the socially-monogamous prairie vole (Microtus ochrogaster) to examine the effect that timing and differential amounts of early life manipulation (MAN) would have on spontaneous parental behavior. Prairie voles were subjected to brief neonatal manipulation (being picked up either on postnatal day 1 (MAN1), 7 (MAN7), 1-7 (MAN1-7) or no handling (MAN0, cage changing in which families were transferred in a cup) and then tested for juvenile parental behaviors at approximately 21-24 days of age. On day of testing, animals received a 10-min parental care test in which infant-directed behavior was scored. Preliminary results suggest that timing and amount of early postnatal handling significantly affects future demonstration and quality of parental care. MAN1 voles displayed greater frequency and duration of licking and grooming toward unfamiliar stimulus pups (PND1-3) compared to all other groups. MAN1 animals also displayed greater amounts of general contact with the pups than all other groups. This study supports the hypothesis that even mild changes in the neonatal experience, possibly mediated by parental stimulation, can lead to long-term developmental consequences for behavior. This research was supported by National Alliance for Autism Research and NIH PO1 HD 38490 to CSC, NRSA F32 HD 08702 and NSF #0437523 to KLB, and American Psychological Association/DPN to EMB.

14. PATERNAL RESPONSIVITY IN BIPARENTAL (*PEROMYSCUS CALIFORNICUS*) AND NONPARENTAL (*PEROMYSCUS MANICULATAS*) MICE. Everette, A.; Tu, K.; Love, G.; [1]McNamara, I.; [1] Kinsley, C.H.; Lambert, K.G. Dept. of Psychology, Randolph-Macon College, Ashland, VA USA 23005; [1]Dept. of Psychology, University of Richmond, VA USA 23173. An abundance of research has documented the changes that occur in female rodents as they transform from virgin to maternal females (Numan & Insel, 2003). Although rare, certain male mammals also exhibit parental responses toward their offspring (Cantoni & Brown, 1997; Gubernick & Nelson, 1989). The genus *Peromyscus* provides a valuable model for behavioral and neurobiological studies of male parental care because, although possessing genetic similarities, different *Peromyscus* species show immense differences in paternal responsiveness (Bester-Meredith et al., 1999). Extending previous findings in our laboratory suggesting that primiparous female rats exhibit enhanced foraging and reduced emotionality, the current study investigated the effect of paternal experience on foraging and emotionality in biparental (*p. californicus*) and nonparental (*p. maniculatas*) mice. Additionally, males with and without paternal experience were exposed to an alien conspecific pup so that their behavioral and brain responsiveness could be assessed. Results suggest that the biparental fathers (*p. californicus*) displayed more efficient foraging, lower emotionality, and faster and more efficient parental care in the Paternal Behavioral Test than their *p. maniculatas* counterparts. Focusing on brain activity, preliminary results suggest that, upon being exposed to an alien conspecific pup, *p. californicus* exhibited a trend toward less fos immunoreactvity in the Bed Nucleus of the Stria Terminalis (known to be involved in anxiety) than *p. maniculatas* males. We are currently exploring responsiveness in additional relevant brain areas such as the medial preoptic area, amygdala, and the cingulate cortex. These results confirm that *p. californicus* and *p. maniculatas* comparisons provide a valuable model to assess critical brain areas necessary for care and nurturing of offspring.

15. EFFECTS OF NEONATAL NOVELTY EXPOSURE ON ANOXIA-INDUCED PATHOLOGICAL BEHAVIOR IN THE CONTEXT OF ENVIRONMENTAL AND SOCIAL NOVELTY. Nakazawa, M; Tang, A.C. Department of Psychology, The University of New Mexico, Albuquerque, NM 87131 USA We investigated in an animal model of neonatal anoxia whether effects of oxygen deprivation on emotional reactivity and social interaction can be reversed by neonatal novelty exposure, a behavioral method involving daily 3-min away from the home cage for the first three weeks of life. Male neonates were exposed to either 100% N2 gas (Anoxia) or room air (Control) for 25 min on postnatal day 1. Within each of the two treatment conditions, one half of the neonates were further individually exposed to relatively novel non-home cages for 3 min daily during postnatal days 2-21 while the other half remained in the home cage. Emotional reactivity to environmental novelty was evaluated on postnatal day 25 in an open field during four 20-sec trials and dyadic social interactions with an unfamiliar conspecific on postnatal days 100-101 in four 5-min sessions. The open-field experiment showed that among Home rats, ambulatory activity significantly differed between the Anoxia and Control rats, and among the Novel rats, these differences were eliminated. In contrast, the social-interaction experiment revealed that Anoxia rats showed higher frequency of biting than the Control rats during social interactions particularly during the initial sessions, but neonatal novelty exposure did not have any significant effect on this Anoxia-induced aggression. These contrast findings indicate that brief neonatal exposures to environmental novelty may reverse some but not all behavioral expressions of neonatal trauma. They further suggest the hypothesis that in comparison to physical environmental

novelty, social novelty may be a more potent elicitor of pathological behavior, which may be more difficult to counteract.

16. COPING STRATEGIES IN LONG-EVANS MALE RATS: INNATE VS. ACQUIRED CHARACTERISTICS. Tu, K., Everette, A., Love, G., [1]McNamara, I., [1]Banks, M., [1]Kinsley C., Lambert, K.G., Dept. of Psychology, Randolph-Macon College, Ashland, VA USA 23005; [1]Dept. of Psychology, University of Richmond, VA USA 23173. Research suggests that an animal's behavioral coping strategy influences the intensity of the stress response. In Experiment 1, after establishing a profile of innate coping strategies (i.e., passive, variable, active) in 30 juvenile male rats (after Schouten et al., 1997), responses in additional stressful situations were subsequently assessed in several ecologically relevant stress paradigms (e.g., predator odor exposure). Results indicated that passive response strategies, in the passive group, persisted across several stress challenges; whereas, in some tests, the variable responders were more active than the active responders—suggesting a possible advantage for the variable responders. Plasma corticosterone assessments revealed no significant differences among groups (although passive animals had 30% higher levels than variable animals). In Experiment 2, we examined the degree to which experience with positive consequences following directed behavioral effort might alter an animal's active coping, or persistence, in a novel-challenging situation. Sixteen young adult male rats were divided into two groups, a worker group that had to dig in mounds of bedding for Froot Loops© rewards each day for five weeks and a control group that was simply presented with the rewards in the same environment, regardless of expended effort. Following training, animals were exposed to a novel stimulus containing an inaccessible food reward and the worker rats persisted longer in their attempts to obtain the food in this novel situation. All rats were subsequently exposed to a novel stimulus and sacrificed one hour later; results indicated no differences in c-fos immunoreactivity in the nucleus accumbens, paraventricular nucleus of the hypothalamus, or the anterior cingulate cortex (related to reward, stress responsivity, and problem solving, respectively). In sum, the findings suggest that (1): behavioral coping strategies exhibited early in an animal's life generalize to other stressful situations as the animal ages, and (2): in some cases, coping strategies appear to be plastic, emphasizing the potential value of behavioral therapy.

17. *Withdrawn*.

18. EARLY DEPRIVATION AND MATERNAL SEPARATION HAVE DIFFERING EFECTS ON JUVENILE PLAY AND COMMUNICATIVE BEHAVIORS IN RATS. Zimmerberg, B.; Sageser, K.A. Department of Psychology and Neuroscience Program. Williams College, Williamstown, MA 01267 USA. Studying the persistent consequences of neonatal stress in rodents may elucidate environmental influences on developing psychopathology. We previously found that isolation stress reduces ultrasonic vocalizations in neonatal rats; these vocalizations are used for communication as well as reflecting affective state. We examined the effects of early stress on the development of play and communicative behaviors, using two models of early stress: Early Deprivation (ED) in which pups are isolated individually and the dam is left with a subset of pups in the home cage, and Maternal Separation (MS) in which the litter is separated as a group and the dam placed in a novel cage. Maternal behavior upon reunion was observed in both conditions as well as in undisturbed control litters. Subjects experiencing either ED or MS for 3 hr per day for the first two weeks of life were observed for play behavior and vocalizations at one month of age. In a follow-up experiment, ED was used for either the first or second week of life. Both ED and MS disturbed maternal behavior, but more so in the MS condition. ED increased factors of play such as attacking and boxing while MS decreased them compared to controls. ED during Week One alone caused even greater increments in play compared to controls, but ED during Week Two alone had the opposite effects. Twelve distinct categories of vocalizations were detected, and ED significantly reduced the occurrence of several categories during play bouts. These results indicated that early stress has an effect on juvenile play behaviors and vocalizations during play, but these effects varied with the paradigm and the timing of isolation.

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19. THE EXPRESSION OF COCAINE AND AMPHETAMINE REGULATED TRANSCRIPT PEPTIDE (CART) IN THE SOCIALLY DEFEATED MALE LONG EVANS RAT John V. K. Pulliam, Paul M. Plotsky Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta GA, USA 30332 Exposure to extreme stressors may either enhance or reduce the hypothalamic-pituitary-adrenal and behavioral responses to subsequent stressors. These effects can also be observed at the central level via alterations in the number of neurons positive for the immediate early gene, cFos-ir. Recently, CART peptide (CART) has been implicated to have a role in anxiogenic behavior in rodents. The effects of an ethologically relevant psychological stressor can be assessed in

rats using social defeat. The aims of this study were to: (1) characterize anxiety and/or depressive-like behaviors following social defeat and (2) To characterize the expression pattern of CART in the in the brain of socially defeated male Long Evans rats. In experiment (1) all rats were assessed for anxiety and depressive-like behaviors during subsequent days following the defeat. In experiment (2), one hour after the separation from the resident male all rats were euthanized, perfused and had brains removed. Behavioral analysis indicates that defeated rats displayed anxiety-like and not depressive-like behavior when compared to controls which received a cage transfer. Immunohistochemical analysis for c-Fos and CART in brain regions of animals detected increases in c-Fos in regions of the central and medial amygdala, paraventricular nucleus of the hypothalamus and the central gray area. Increases in co-labeled neurons for c-Fos and CART were observed in the medial amygdala and dorsal raphae. (Supported by Emory Conte Center MH58922, American Psychological Association Minority Fellowship Program NIH # 5, T32, MH18882 & The Center for Behavioral Neuroscience (NSF agreement #IBN-9876754), Atlanta GA USA,).

20. SOCIAL ENVIRONMENT REGULATES THE HPA AXIS AND CELLULAR PROLIFERATION IN THE PRAIRIE VOLE. Ruscio, M.G.; Sweeny, T.; Suppatkul, P.; Hazelton, J.; Carter, C.S. Brain Body Center, Dept. of Psychiatry, University of Illinois, Chicago 60612 USA. Recent studies establish a causal link between environmental conditions and neurogenesis in certain vertebrate species. We examine the relationship between social environment, hypothalamic-pituitary-adrenal (HPA) axis and cellular proliferation in the prairie vole. The prairie vole is a rodent species that displays a number of highly affiliative behaviors including biparental care, alloparental care and pair bonding. These behaviors are closely tied to a variety of neuroendocrine mechanisms. Following weaning at 21 days of age, subjects were maintained in one of three housing conditions for four days: social isolation, paired with a same sex sibling, or paired with a same sex stranger. On the third day of housing animals were injected with BrdU to label newly divided cells. Brain sections were stained for BrdU and alternate sections were double labeled with the neuronal marker, TuJ1. Labeled cells were counted in areas associated with affiliative behaviors including the medial amygdala (MeA), cortical amygdala (CoA) and dentate gyrus (DG). Additionally, corticotropin releasing hormone immunoreactivity (CRH-ir) in the paraventricular nucleus (PVN) and basal circulating corticosterone (CORT) were measured. Socially isolated animals had greater CRH-ir density in the PVN and higher basal circulating CORT. Preliminary data show that CORT is negatively correlated with cellular proliferation in the MeA. Social isolation resulted in reduction of cellular proliferation in the MeA. Double label confirms that a portion of BrdU-labeled cells in the MeA are neurons. Supported by NIH PO1 HD38490, IRUL 322 and NAAR.

21. BEHAVIORAL EFFECTS RESULTING FROM THE DISRUPTION OF GLIAL FUNCTIONING IN THE BASOLATERAL AMYGDALA. D.L. Gaskins, Y. Lee & A. Shekhar. Dept. of Psychiatry, Indiana Univ. School of Med., Indianapolis, IN 46122 Neuroimaging studies and postmortem studies have shown a reduction in the population of glia in areas implicated in mood disorder such as the basolateral amygdala (BLA). Further, many lines of evidence implicate a role for glutamate in mood disorders and this reduction in glia can affect the glutamatergic sytem a number of ways. One possibility is that reduced glial function can result in inadequate glutamate transport, which potentially leads to elevated glutamate. Considering that glia are critical for normal neuronal function and have a key role in regulation of the glutamatergic system, it is hypothesized that compromised glia/neuronal communication may underlie the pathophysiology of mood disorders. To disrupt this communication we first injected a racemic mixture of the glia toxin, alpha-aminoadipate (a-AA), into the BLA of Wistar rats. A single injection resulted in a significant decrease in social interaction (SI) on day 2 (D2) post injection with normalization occurring by day 7. Following multiple injections of a-AA, the animals showed a decrease in SI which was sustained beyond post injection D2. In the second experiment we chronically blocked the glial specific glutamate transporters, GLAST and GLT-1, by infusing the glutamate transport blocker, L-trans-Pyrrolidine-2,4-dicarboxylic acid (PDC) into the BLA. We see a significant decrease in SI scores during infusion with the animals normalizing within 2 weeks after infusion is stopped. An interesting speculation is that this behavior change is due to an imbalance of glutamate and GABA caused by loss of glial integrity. We believe that the more we learn of glia's role in neuronal communication the more we will understand psychopathology. (Supported by NIMH grant R01 MH52619; DLG is supported by the Scottish Rites scholarship)

22. DEFICITS IN BEHAVIORAL RESPONSES TO FAMILIAR STIMULI MEDIATED BY THE BASOLATERAL NUCLEUS OF THE AMYGDALA Truitt, W.;Sajdyk T.J.; Fitz S.D.; Dietrich, A.; Shekhar A.; Dept. of Psychiatry, Indiana Univ. Sch. Med., Indianapolis, IN 46202. Acute stimulation of the corticotrophin releasing factor (CRF) receptors in the basolateral amygdala (BLA) of rats elicits avoidance of social interactions and can be reversed with pretreatment of Neuropeptide Y (NPY). Given the role of the amygdala in social cognition, we hypothesized that over-stimulation of the BLA with CRF or ablation of NPY containing interneurons would not only elicit a deficit in social behavior,

but also during interactions with familiar stimuli. The effects of 3(5) daily injections of the CRF receptor agonist urocortin (Ucn; 6 and 100 fmoles/100 nl per side), lesions of NPY-containing neurons or vehicle into the BLA of rats on responses in the social interaction test (SI) and familiar/novel stimulus exploration test (EXP) were examined. When the BLA was repeatedly stimulated with the high dose of Ucn (100 fmoles) or NPY neurons were ablated, the rats became permanently avoidant in SI even when the same partner was utilized (i.e., not ameliorated by familiarity as in the 'anxious rats'). In the EXP paradigm, the rats injected with Ucn (100 fmoles) showed significantly reduced exploration of novel stimuli and had no preference for a familiar object, suggesting disruption of normal attachment behaviors. Thus, based on the above features of 'face validity,' it is suggested that the BLA disrupted rats provide a putative model of behavioral deficits in psychiatric disorders.

23. EFFECTS OF ZIPRASIDONE AND D-CYCLOSERINE TREATMENT ON THE BEHAVIORAL DEFICITS IN RATS WITH DISRUPTED BASOLATERAL AMYGDALA FUNCTION. Sajdyk, T.; Fitz, S.; McDougle, C.; Shekhar, A. Dept. of Psychiatry, Indiana Univ. Sch. Med., Indianapolis, IN 46202 USA. In previous studies, we have demonstrated that over-stimulation of the basolateral amygdala (BLA) with corticotrophin releasing factor (CRF) receptor agonists reduces social behaviors and interactions with familiar stimuli traits similar to some symptoms seen in syndromes such as schizophrenia and autism. In the present study, we tested the effects of treatment with the novel atypical antipsychotic ziprasidone, as well as D-cycloserine, an agonist at the glycine site of the glutamate N-methyl-D-aspartate receptor, on the social behaviors as well as the aggressive responses observed. Rats were implanted with bilateral injection cannulae into the BLA and the effects of 3 daily injections of the CRF receptor agonist urocortin (Ucn; 100 fmoles/100 nl per side) into the BLA on responses in the social interaction test (SI), and conspecific aggression test (AGR) were recorded. The rats were next treated with vehicle, ziprasidone (1 & 5 mg/kg i.p.) or D-cycloserine (10 & 30 mg/kg i.p.) and retested in the above behavioral paradigms. Ziprasidone treatment resulted in a dose-dependent improvement in only aggressive responses, while D-cycloserine treatment significantly improved aggression and the impaired social interaction responses. Thus, the BLA disrupted rats appear to provide a putative model for some of the behavioral symptoms observed in psychiatric disorders such as schizophrenia and autism. Research supported by NIMH grant K01 01869-01.

24. FLAVOR PAIRING BIASES OUTCOMES IN A SOCIAL FOOD PREFERENCE TASK. Walker, E.M., Desir N. and Hohmann, C.F. Dept. Biology, Morgan State University, Baltimore, MD, USA. The social food preference task (SFPT), designed to assess acquisition of flavor preference via animal-to-animal interaction, is well suited to evaluate non-spatial learning and memory in mice of both sexes. A demonstrator is trained to consume flavored chow (cued food) and subsequently is placed within a small wire cage into an approx. 12" x 30" enclosure. An observer is added to the enclosure and interacts with the demonstrator though the wire. The observer is removed after 20 min. and given a choice of cued [c] vs. a different, non-cued [nc] flavor; retesting occurs 24h later with the same c/nc flavors. Food consumption is measured as indicator of learning. Three cohorts [CO] of Balb/CbyJ mice, at five months postnatal, were tested. The food pairings were: CO1: cued (c)-garlic/ (nc)-nutmeg; CO2: c-thyme / nc-nutmeg CO3: c-caraway / nc-dill. All flavors had individually been tested in mice of the same strain and resulted in comparable amounts of food consumed. Our studies were designed to compare male and female observers with neonatal bilateral injections of a) 5, 7 DHT (5µg/µl) and b) saline into the medial forebrain bundle to normal age matched controls. In both CO1 and CO2, controls showed preferences of c over nc food. In CO1 5,7-DHT injected mice showed significantly more consumption of c vs. nc food, compared to controls, but in CO2, consumption of c vs. nc was significantly impaired in 5,7-DHT mice. In contrast, in CO3, all groups ate more nc then c food although differences in c/nc food consumed were more reliably present in control mice. These data strongly suggest, that flavor pairing biases the outcome of food preference in this task. U54 MH066417-01A1 and 1G12RR17581.

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25. EFFECTS OF 5-METHOXY-DIISOPROPYLTRYPTAMINE ON HORMONE AND NEUROTRANSMITTER LEVELS IN THE ADULT RAT Schaefer, TL; Herring, NR; McCrea, AE; Lipton, JW; Campbell, NG; Vorhees, CV; Williams, MT Cincinnati Children¡¯s Res Found., Univ of Cinci College of Medicine, Cincinnati, OH, and Sinclair Com. College, Dayton OH A new drug of abuse, 5-methoxy-diisopropyltryptamine (5-Meo-DIPT or Foxy), is gaining popularity, is sometimes substituted for MDMA, and very little is known about its effects. Human users have experienced auditory and visual hallucinations, seizures, and limb paralysis while under the influence 5-Meo-DIPT. In the current study we have investigated the effects of 1 day of 5-Meo-DIPT administration on temperature, neurotransmitter, and hormone levels in the adult rat. Animals received either 10 or 20

mg/kg 5-Meo-DIPT, or saline (SAL) vehicle once every two hours for a total of 4 subcutaneous injections. Animals were decapitated 72 hours following the last dose and tissues were harvested. We chose the 72 hour time point because we know substituted amphetamines produce neurotoxicity at this time point. Animals that received 5-Meo-DIPT had significantly decreased body temperatures during dosing in a room with an ambient temperature of 23¢ªC and demonstrated seizure-like behavior that was confirmed by EEG. 5-Meo-DIPT administration caused an increase in adrenal weights and a trend for a decrease in thymus weights. These changes were accompanied by elevated corticosterone levels in the 5-Meo-DIPT group compared to SAL. There was a trend for norepinepherine to be decreased in the hippocampus, striatum, hypothalamus and prefrontal cortex and the ratio of 5-HIAA/5-HT was increased in the striatum and prefrontal cortex. These data demonstrate that 5-Meo-DIPT has a different profile than MDMA and warrants investigation.

26. BEHAVIORAL EFFECTS OF 5-METHOXY-N,N-DIISOPROPYLTRYPTAMINE (FOXY) IN ADULT RATS Herring N.R., Schaefer T.L., McCrea A.E., Vorhees C.V., Williams M.T. Neurology, Cincinnati Children's Res. Found. Cincinnati, OH USA. 5-Methoxy-n,n-diisopropyltryptamine (Foxy) was placed on emergency schedule 1 status by the DEA in April 2003 and permanently scheduled in September 2004. Foxy has been reported to induce auditory, visual, and tactile hallucinations in humans and has been sold as MDMA or used in conjunction with MDMA. Structurally, the compound resembles serotonin; however no data exist describing the physiological and/or behavioral effects of Foxy in an animal model. In this study we examined the behavioral effects of Foxy. Adult male Sprague-Dawley rats (n=12/treatment) were administered Foxy (20 mg/kg) or SAL, 4 times s.c. on a single day at 2 h intervals and body temperatures were recorded. Hypothermia and seizure-like behavior were observed in the Foxy treated animals. Behavior testing began one week following the dosing regimen in various behavioral paradigms including locomotion, marble burying, Cincinnati water maze (CWM), Morris water maze (MWM), and novel object recognition (NOR). Foxy treated animals demonstrated hypoactivity in the locomotor testing. These animals also demonstrated an increased time to attend to objects during NOR, but remembered them as well as saline-treated animals. In the CWM, the Foxy treated animals returned to the start position fewer times on the first day of learning and more times on some of the subsequent days. There was also a trend for increased errors during CWM learning. No deficits were observed in marble burying or MWM compared to SAL controls. These data are the first to show that Foxy can induce long-term changes in behavior and physiology following a single day of drug administration.

27. EFFECTS OF SHORT-TERM REM SLEEP DEPRIVATION ON THE EXPRESSIONS OF THE HYPOTHALAMIC NEUROPEPTIDES GENES IN RATS. Fujihara, H. 1, Sei, H. 2, Morita, Y. 2 and Ueta, Y. 1 1Department of Physiology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, 807-8555, Japan; 2Department of Integrative Physiology, Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima 770-8503, Japan. REM sleep is well discussed to be associated with higher brain functions. The hypothalamus has many neuropeptides and is one of the important regions to regulate sleep. We examined the effects of short-term REM sleep deprivation (RSD) on the gene expressions of galanin, galanin like peptide (GALP), arginine vasopressin (AVP), oxytocin (OXT) and orexins/hypocretins in the rat hypothalamus, using in situ hybridization histochemistry. The galanin mRNA levels in the preoptic area was significantly increased by RSD for 6 hours. The mRNA levels of corticotrophin-releasing factor in the paraventricular nucleus (PVN), AVP and OXT in the supraoptic nucleus and the PVN, and orexins in the lateral hypothalamic areas were not significantly changed by RSD. In addition, GALP mRNA level in the arcuate nucleus did not change after sleep deprivation. These results suggest that short-term RSD may not induce the activation of the hypothalamo-pituitary adrenal axis, and that the expression of the galanin gene in the hypothalamus reacts more readily against the RSD in comparison to other hypothalamic neuropeptides such as AVP, OXT and orexins.

28. ENKEPHALIN REGULATES INCREASES IN CONSTITUTIVELY ACTIVE MU RECEPTORS DURING OPIATE WITHDRAWAL J. Shoblock, N. Maidment. Dept. of Psychiatry and Biobehavioral Science, UCLA, Los Angeles CA. We previously showed that 20h morphine (M) pretreatment, given to increase constitutive mu receptors (mu*), enhances the conditioned place aversion (CPA) produced by naloxone (NAL), an inverse agonist, but not 6beta-NAL, a neutral antagonist. To further test this, the ability of NAL to produce CPA in the absence of agonist was examined using enkephalin-/- mice (ENK) given 20h M pretreatment. NAL did not produce CPA. Since mu* produced by M has been shown to be short lived in vitro, we hypothesized that enkephalin release during M withdrawal was responsible for the increase in mu* previously observed in WT. Therefore, the ability of NAL to produce jumping was measured in WT and ENK mice at different time points after M. Jumping peaked 2h after M treatment. NAL's ability to produce jumping continued to diminish at 4.5h in the ENK mice but increased in WT mice. Next, the ability of NAL to produce CPA in the ENK mice 2h after M treatment, during peak levels of mu*, was determined.

NAL, but not 6beta-NAL, produced CPA. These data are in agreement with the hypothesis that NAL acts as an inverse agonist to produce physical and psychological withdrawal, and that compensatory increases in enkephalin during M withdrawal produce increases in mu*.

29. THE EFFECTS OF KETAMINE ON THE EXPRESSION OF NMDA NR2B RECEPTOR SUBUNITS. Hoxha, N.; Mickley, G.A. Department of Biology and The Neuroscience Program. Baldwin - Wallace College, Berea, OH 44107 USA. Ketamine, a potent noncompetitive NMDA receptor antagonist has shown to impair learning and memory in a conditioned taste aversion (CTA) paradigm in adults and neonatal rats. However, in fetal rats ketamine was reported to produce paradoxical effects: ketamine given on embryonic day 18 (E18) enhances memory, whereas, administration of the antagonist on E19 blocks memory of the CTA. Objective of the present study was to characterize the expression of NMDA NR2B receptor subunits in the hippocampus and gustatory neocortex (GNC) in E18 and E19 fetal rats since, over-expression of NR2B subunits has shown to correlate with enhanced learning and memory. Pregnant dams at either E18 or E19 were injected with ketamine (100mg/kg, i.p.) or saline, and after 2, 4, or 24 hours, the hippocampus collected was homogenized and examined for NR2B subunit expression by western blot analysis. Expression of NR2B subunits in GNC were assessed 24 hours after ketamine injection. Two hours after ketamine, levels of NR2B subunits in hippocampus of E18 and E19 fetal rats were unchanged compared to the saline controls. However, after 4 and 24 hours of ketamine treatment the E19 group showed reduced levels of NR2B subunits; but, in E18 group the levels of NR2B subunits were unchanged. Ketamine after 24 hours produced increased levels of NMDA NR2B subunits in GNC in E18 pups; however, no change was observed in E19 group. In conclusion, these age-dependent changes in how ketamine influences NMDA receptor populations should encourage future studies aimed at confirming the role of NR2B subunits in the production of “ketamine paradox”. Supported by: Edith Robinson Grant and Thomas Surrar Fund.

30. GENE DELETION OF THE GLUTAMATE GLUR1 RECEPTOR CAUSES HYPER-REACTIVITY TO NOVELTY AND SENSORIMOTOR GATING DEFICITS IN MICE Lisa Wiedholz and Andrew Holmes Section on Behavioral Science and Genetics, Laboratory for Integrative Neuroscience, NIAAA-DICBR, NIH, Bethesda, MD Dysfunction of glutamatergic neurotransmission is increasingly implicated in the etiology of various neuropsychiatric diseases, such as mood disorders and schizophrenia. Glutamatergic neurotransmission is mediated via a diverse class of receptors (kainate, metabotropic, NMDA, AMPA). However, recent evidence suggests a specific role for the AMPA GluR1 subtype in the pathophysiology and treatment of disorders characterized by mood disturbances and manic behaviors; bipolar disorder (BP) and attention deficit hyperactivity disorder (ADHD). In the present study, we further studied the role of GluR1 via phenotypic analysis of GluR1 knockout (KO) mice. Behavioral responses were assessed in a range of test environments that differed in the magnitude of the approach-avoid conflict generated: novel object test, open field, elevated plus-maze, dark-light emergence test, home cage. Sensorimotor gating, which is impaired in BP and ADHD, was tested via prepulse inhibition of startle (PPI). Results showed that relative to wild type (WT) littermates, GluR1 KO mice exhibited marked locomotor hyperactivity in high-conflict environments, such as the open field and the elevated plus-maze, but little or no phenotypic differences in low-conflict environments, such as the emergence test. These data indicate a highly specific behavioral abnormality in GluR1 KO in response to conflict that that may be relevance to clinical observations of symptom-provocation in BP and ADHD by situations that evoke emotional arousal. Providing another potential parallel with these disorders, GluR1 KO mice showed clear deficits in PPI. Ongoing studies assess whether hyper-reactivity and PPI abnormalities in GluR1 KO mice are reversible by clinically efficacious treatments for BP (valproate) and ADHD (methylphenidate). Supported by the NIAAA-DICBR.

31. GROUP II, BUT NOT GROUP I, MGLURS IN THE RAT NUCLEUS ACCUMBENS CONTRIBUTE TO CONDITIONED LOCOMOTION ELICITED BY AMPHETAMINE-ASSOCIATED ENVIRONMENTAL CUES. Kim, W.Y.[1]; Kim, J.-H.[1]; Vezina, P.[2]; [1] Dept. of Physiology and Brain Korea 21 Project for Medical Science, Yonsei University Medical Center, Seoul, South Korea; [2] Dept. of Psychiatry, University of Chicago, Chicago, IL 60637, USA. The exclusive pairing of psychomotor stimulants like amphetamine (AMPH) with one set of environmental stimuli leads to the formation of conditioned associations between the two. Metabotropic glutamate receptors (mGluRs) are abundantly expressed in the nucleus accumbens (NAcc) and known to regulate the locomotor activity produced by these drugs in this site. This study assessed the contribution of mGluRs in the NAcc to the generation of AMPH-induced conditioned locomotion. Rats were administered injections of AMPH (1.0 mg/kg, IP) or saline in each of five 3-day blocks as follows. Rats received either AMPH or saline paired with the locomotor activity boxes on day 1 of each block, saline in their home cages on day 2 and no injections on day3. One week after the last injection, rats were injected with saline and placed in the locomotor activity boxes for a test for conditioned locomotion. AMPH-

paired rats showed increased locomotor activity compared to saline-paired rats. Interestingly, the conditioned locomotion exhibited by the AMPH-paired rats was dose-dependently blocked when microinjections into the NAcc of the group II mGluR antagonist, EGLU (0.5, 5 nmole/side), were made 10 min prior to the test. Microinjecting the group I mGluR antagonist, AIDA (0.5, 5 nmole/side), was without effect. These results suggest that NAcc group II mGluRs may play a role in the expression of conditioned behavioral effects associated with psychomotor stimulants. Supported by the Neurobiology Research Program from the Korea Ministry of Science and Technology (J.-H. Kim).

32. THE ANABOLIC STEROID NANDROLONE BUT NOT 17á-METHYLTESTOSTERONE INDUCES CONDITIONED PLACE PREFERENCE IN ADULT MICE. Rundle-Gonzalez, V[1#]; García-Sosa, R[1#]; Ayala-Báez, C[1]; Gandía-Cruz, G[2]; Jorge, JC[3] Department of Biology[1] and Honors Program[#] , Río Piedras Campus, Department of Biology[2], Arecibo Campus, Department of Anatomy[3], Medical Sciences Campus, University of Puerto Rico, San Juan - Puerto Rico. Anabolic androgenic steroids (AAS) are often misused by adolescents and athletes. In this study, adult C57Bl/6 male mice were systemically exposed to AAS, 17á-methyltestosterone (17á-meT) or nandrolone. Control animals received vehicle injections (0.9% NaCl + 30% cyclodextrin). In order to determine the hedonic or aversive properties of each drug, the conditioned place preference (CPP) test was employed. Rearing and locomotor activity were also monitored. Nandrolone shifted place preference and increased rearing activity ($p \leq 0.001$) but did not modify locomotion. In contrast, animals treated with 17á-meT did not show significant behavioral differences. Our data suggest that AAS effects on behavior are structure-specific. Support provided by the MBRS-RISE Program at MSC-UPR (GM61838) to VRG, RGS, and GGC. Study funded by NIH-COBRE (RR15565), a Young Investigator Award (NIH-BRIN, RR16470), and the RCMI Program at MSC-UPR (G12RR03051) to JCJ.

33. EFFECTS OF AN ANABOLIC STEROID ON GABA IMMUNOREACTIVITY IN REWARD AND ANXIETY BRAIN CENTERS. Arriaga-Gonzalez, D.1; Rundle-Gonzalez, V.2; Barreto-Estrada, J.L.1; Jorge, J.C.3. 1 Department of Sciences, Mathematics and Technology-Universidad del Este-Carolina, P.R., 2 Department of Biology-University of Puerto Rico, R¨ªo Piedras Campus, 3 Department of Anatomy-University of Puerto Rico, Medical Sciences Campus Anabolic androgenic steroids (AAS) have been misused by athletes and a growing number of adolescents and females. In this study, we have investigated the basic neural mechanisms of chronic exposure of AAS on ¦Ã-aminobutyric acid immunoreactivity (GABA-ir) in discrete brain regions of C57Bl/6 mice. The AAS, 17¦Á-methyltestosterone (17¦Á-meT; 7.5 mg/kg) or saline were administered for a two-week period through an osmotic pump. Brain sections were obtained through the levels of the nucleus accumbens (NAc), the basolateral amygdala (BLA), and the ventral tegmental area (VTA). Brain sections were stained for GABA by immunohistochemistry methods. Whereas no changes in GABA-ir were detected in the NAc, statistical analysis revealed significant gender x treatment interactions in the VTA ($p < 0.007$) and the BLA ($p < 0.05$). Our data shows region-specific and sex-specific changes in GABA-ir cells, suggesting that the GABAergic system may influence reward processes and anxiety after AAS exposure according to sex. Supported by MBRS-Rise Program at UNE (1R25-GM066250-01A1) and at MSC-UPR (GM61838) to A-GD, R-GV and B-EJ, NIH-COBRE (RR15565), a Young Investigator Award (NIH-BRIN, RR16470), and the RCMI Program at MSC-UPR (G12RR03051) to JCJ.

34. FURTHER STUDIES OF ESTRADIOL AND INTAKE OF PALATABLE INGESTA. Reid, L.D.; Boswell, K.J.; Klein, L.A.; Caffalette, C.A.; Schlosburg, J.E.; Stitt, K.T.; Reid, M.L. At recent meetings of the IBNS, we have presented data supporting the conclusion that, under certain circumstances, large doses of estradiol can enhance female rats' intakes of alcoholic beverages, a saccharin solution, and chocolate cake mix batter. Those same doses that enhance intakes of certain ingesta do not enhance intakes of other ingesta, e.g., a bittersweet saccharin solution and ordinary laboratory food. In an effort to better define the class of ingesta that will be taken more avidly subsequent to treatment with estradiol, we gave female rats either injections of estradiol valerate (EV at doses of 0.19, .38 or 0.75 mg/kg) or placebo and then provided them with the opportunity to take a combination of fat and sugar as well as their ordinary food and water. Females receiving EV took more fat and sugar than those receiving placebos, but the increment in amount was not so large or consistent to meet standards for statistical significance. The females receiving EV, however, gained weight at a more rapid rate than the placebo controls. The conclusion is that estradiol could induce effects that increase the risk of obesity.

35. PLASTIC FUNCTION OF GLUCOSE INCREASED IN THE BRAIN DURING FOOD INTAKE. Y. Oomura[1)], S. Aou[2)], N Hori[1)], H Fukunaga[3)] and K Sasaki[4)] Dept. Physiol. Fac. Med. Kyushu Univ. Fukuoka[1)], Dept. Brain Sci. Kyushu Inst. Tech., Kitakyushu[2)], Dept Pharmacol. Fac. Pharm. Tohoku Univ. Sendai[3)], Dept. Bio-inf. Fac. Eng. Toyama Univ. Toyama[4)] The glucose (G) concentration in CSF is 2-3 mM and increases twice during food intake. When G was injected into the hippocampus to turn to 7 mM, spatial learning and memory were facilitated. To make clear this, neurophysiological measurement using hippocampal slice preparations were carried out. The G concentration in perfusate

was changed from 3.5 to 7 mM for 15 min and returned to 3.5 mM. The CA1 synaptic potentials produced by Schaffer collateral stimuli were augmented, started from 3-4 min after the change to 7mM G This augmentation continued for 40 min even after returning to 3.5 mM G. This was like a long-term potentiation (LTP) without a tetanic stimulation. LTP produced by tetanic stimulation (100 Hz, 1 s) just after returning to 3.5 mM G was significantly facilitated, while only short-term potentiation was produced in 3.5 mM G. Presynaptic transmitter release measured by paired pulse facilitation method and postsynaptic response to NMDA applied at the apical dendrites were also facilitated by 7 mM G. The membrane potential and input resistance were a little changed by 7 mM G. The phosphorylation of presynaptic synapsin I-3 and of postsynaptic CaMkII of CA1 neurons were facilitated by 7 mM G. These evidences indicate that food intake is necessary not only for keeping body homeostasis but also reforcing the higher brain plasticity.

36. ELEVATED BLOOD GLUCOSE LEVELS IN SUGAR-DEPENDENT RATS. Murphy, H.M.; Wideman, C.H. Neuroscience Program, John Carroll University, Cleveland, OH 44118 USA. Research has suggested that sugar has an effect on the release of brain opioids and dopamine in the mesolimbic system similar to that observed with drugs of addiction. Although food is generally beneficial, excessive sugar intake provides additional calories that may result in obesity and altered physiological conditions. The purpose of this study was to develop sugar dependence in the rat, observe withdrawal when the sugar was removed, and initiate relapse when the sugar was reinstated. In addition, levels of blood glucose were measured in sugar-dependent versus control rats. For four weeks, experimental and control Long-Evans rats were provided with daily access to food for 12 hours during the dark phase of a 12hr/12hr light/dark cycle. During weeks 2 and 4, experimental animals had 12-hour access to a 25% glucose solution in addition to food. Glucose intake was measured for experimental animals and body weight, food intake, and water intake were recorded daily for all animals throughout the experiment. At the conclusion of the experiment, animals were sacrificed and blood glucose levels were measured. Experimental animals markedly increased their glucose intake during the first four days of week two, and maintained a peak level for the remainder of the week. During week 4, there was an immediate return to high glucose intake on the first day and the animals maintained this level for the rest of the week. Blood glucose levels were significantly higher in experimental compared to control animals at the conclusion of the experiment. During week 3, when no sugar was present, experimental animals exhibited withdrawal symptoms and, with the reintroduction of sugar in week 4, the animals showed immediate relapse.

37. EFFECTS OF THE ENVIRONMENT EXPOSURE ON BEHAVIORAL SENSITIZATION INDUCED BY REPEATED ADMINISTRATION OF COCAINE Araujo, N.P.; Carrara-Nascimento, P.F.; Fukushiro, D.F.; Rodrigues, M.S.D.; Oliveira-Lima, A.J.; Frussa-Filho, R. Department of Pharmacology, UNIFESP, SP, Brazil. e-mail: nilza.farm@epm.br Introduction- Behavioral sensitization (BS) is characterized by a progressive increase of a behavior as a result of repeated administration of a drug, such as cocaine. The stimulating properties of cocaine are a model for the rewarding effects of cocaine in humans and it has been proposed that drug craving is closely related to sensitization. Objective- Our aim was to verify the possible involvement of the environment conditioning on the sensitization to the locomotor stimulating effect induced by repeated administration of cocaine (COC). Methods- Habituation: all animals were habituated to the open-field arena before the begining of drug treatments. Female mice were then distributed in 5 groups of 14 animals each: SAL-SAL, SAL-EXP-SAL, SAL-EXP-COC, SAL-COC and COC-EXP-SAL. All the animals were treated with 10 mg/kg cocaine, i.p., and/or saline every other day, for 15 days. The animals of the group COC-EXP-SAL received an injection of cocaine 30 minutes before a 5- minute exposure to the open field apparatus followed by another injection of saline 30 min later. Animals of the SAL-EXP-COC received the saline injection 30 minutes before a 5- minute exposure to the open field apparatus followed by an injection of cocaine 30 min later. The animals of the SAL-EXP-SAL received the saline injection 30 minutes before a 5- minute exposure to the open field apparatus followed by another injection of saline 30 min later. Finally, the animals of the SAL-SAL and SAL-COC groups received the respective injections of saline and /or cocaine but were not exposed to the open field apparatus. On day 17, all the animals were challenged with COC 10 mg/kg (test session). Thirty minutes later, locomotion frequency was quantified in the open field for 5 minutes. Results- On the test session, sensitization was observed for the groups SAL-EXP-COC and COC-EXP-SAL but not for the SAL-C0C group. Conclusion- These results suggest that although environmental stimuli are critical to the development of BS, the conditioning between the environment and the stimulant effect of cocaine is not. (Supported by CNPq)

38. THE EFFECTS OF METHAMPHETAMINE AND COCAINE ON RATS' Y-MAZE PERFORMANCE USING DIRECTIONAL VS. VISUAL CUES. Klipec, W.D.; Brackney, R.J.; Sounhein, K.; Mejia, R.; Dolezal, A. Department of Psychology, Drake University, Des Moines, IA 50311, USA. Two experiments in our laboratory have demonstrated that across a wide range of doses,

amphetamine but not cocaine (COC) disrupts the discrimination performance of rats running toward the lighted arm of a Y-Maze. In these experiments we noticed that rats in the amphetamine group were repeatedly running in the same direction (e.g., always left) rather than toward the lighted arm. Since amphetamine increases stereotypic behavior we hypothesized that the disruption of performance in the amphetamine group was due to perseverative responding in one direction. To test this hypothesis rats were trained on a directional cue that would be compatible with perseverative responding. One group of rats (n=8) was trained to run to the right arm (R) for water reinforcement while a second group of rats (n=8) was trained to run to the left arm (L). After reaching a 90% correct stability criterion, the rats were tested with an ascending and descending series of either methamphetamine (0.56 to 2.0 mg/kg) or COC (3.0 to 20 mg/kg) counterbalanced across groups, with saline and no injection days interspersed. With the exception of the 20 mg/kg COC dose, neither METH nor COC produced a significant increase in errors for rats in the R Group. The L Group, showed a significant increase in errors for METH at 0.56, 1.0 and 2.0 mg/kg and COC at the 10 and 20 mg/kg doses. The results were surprising in that METH did not result in perseverative errors and that it selectively effected rats trained to run left. We are currently investigating the handedness of the rats to determine if that accounts for the selective effect on left trained rats.

39. INTERLEUKIN-1 AND ENDOTOXIN EFFECTS IN BEHAVIORAL TESTS FOR DEPRESSION AND ANXIETY. Dunn, A.J.; Swiergiel, A.H. Dept. Pharmacol., Toxicol. & Neurosci., LSU. Hlth Sci Center, Shreveport, LA 71103 USA It has been hypothesized that cytokines (especially interleukin-1, IL-1) may cause depression. We tested various doses of IL-1beta and endotoxin (LPS) in behavioral tests considered to assess depression and anxiety in mice: the tail suspension test (TST), the Porsolt forced swim test (FST), the elevated plus-maze (EPM), and in an open field (OF). IL-1 injected into male CD-1 mice 90 min earlier induced dose-dependent increases in the immobility time in the TST and the floating time in the FST, effects considered to reflect depression. The effects of IL-1 in the TST and FST were statistically significant only at doses of 300 and 1000 ng (not 100 ng), but all three doses decreased line crossings and rears in the OF, and depressed food intake and body weight. 1 and 5 mcg doses of LPS ip increased immobility in the TST and floating in the FST, but the same doses strongly depressed locomotor activity and body weight. All three doses of IL-1 injected 1 h previously significantly decreased open arm entries and the time spent on the open arms in the EPM, effects considered to reflect anxiety. However, entries to all arms were reduced, indicating an overall decrease in locomotor activity. These results indicate that both IL-1 and LPS can induce depression-like effects in the TST and the FST, and anxiety-like effects in the EPM. However, the doses necessary to induce these changes reduced feeding and locomotor activity. Thus the effects observed in the FST, TST and EPM could be attributed to a general reduction in activity. These results do not provide strong support for an IL-1 hypothesis of depression or anxiety, although we cannot exclude roles for IL-1.

40. THE ROLE OF THE STRIATUM ON THE EFFECTS OF MODAFINIL. Giordano M, Mendoza-Trejo M.S, Mena-Segovia J. Dept. of Behavioral and Cognitive Neurobiology, Institute for Neurobiology, Campus UNAM-Juriquilla, Querétaro, México 76230. The striatum may play a significant role in mediating cortical activation required for behavioral arousal, and this function may be independent from the motor function classically associated with the basal ganglia. We have observed that striatal dopaminergic stimulation leads to an increase both in locomotor activity and in wakefulness, plus increased Fos expression in the pedunculopontine nucleus, while others have observed increased Fos expression in the cerebral cortex. Modafinil, a recently discovered wake-improving substance induces prolonged wakefulness in a number of species, apparently without inducing locomotor stimulation. The underlying mechanisms of the effects of modafinil remain unknown, particularly with regard to the brain targets involved in its wake-promoting effects, although it has been found that systemic modafinil increases striatal extracellular dopamine. The purpose of this experiment was to determine if the striatum is involved in the wake-promoting effects of modafinil. To that effect an initial group of male Sprague-Dawley animals underwent stereotaxic surgery in order to implant bilateral cannulae to the anterodorsal striatum, a second group was implanted with cannulae, and electrodes for EEG recordings. At the end of the behavioral experiment, these animals received unilateral (1 ?l) instrastriatal injections of modafinil and were processed for immunochemistry against Fos. The results obtained so far indicate that instrastriatal administration of modafinil (0.5, 1, 10 and 50 mM) does not increase locomotor activity. We thank Cephalon for providing Modafinil, this work was supported by IN225305-3 from DGAPA-UNAM.

41. D3 RECEPTOR DOES NOT MEDIATE DA ANTAGONIST INHIBITION OF MK-801 HYPERACTIVITY . Joyce, J.N.; Iarkov, A.V. Parkinson's Disease Res Ctr, Sun Health Res Inst, Sun City, AZ 85351 USA Sokoloff and associates (Neuropharmacology 45, 174-181) reported that hyperactivity induced by MK-801 in mice is dependent on stimulation of D3 receptors. To examine this further, we measured MK-801 induced hyperactivity in WT and D3 KO mice, as well as the interaction with D3 selective antagonists. We studied the effect of saline-stimulated and MK-801-

stimulated locomotor activity in WT and D3 KO mice administered the D3 antagonists S33084 and U99194A. Mice were administered saline or one of 4 drug/doses (dissolved in saline): S33084 (1.0 mg/kg, s.c.), U199194A (0.1 mg/kg I.P.), or U199194A (0.01 mg/kg I.P.), administered at 1 ml/100 g body weight. Activity was measured for 30 mins, then the second drug injection, saline or MK801 (0.12 mg/kg I.P) was made and returned to the open field for an additional 55 mins. D3 KO mice showed a small but significantly higher level of activity in the 1st 30 mins (saline) compared to WT mice. Activity declined during the next 55 mins to saline, and in response to MK-801 there was a 5-fold increase in activity in both D3 KO and WT mice. There was a nonsignificantly greater locomotor response to MK-801 in D3 KO mice compared to WT mice. The D3 selective antagonist S33084 and both doses of U99194A suppressed the locomotor activity response to MK-801, and to an equal extent in D3 KO and WT mice. D3 KO mice showed a significantly higher level of rearing in the 1st 30 mins (saline) compared to WT mice. Rearing declined during the next 55 mins to saline, and was significantly attenuated in response to MK-801. In response to S33084 and the higher dose of U99194A D3 KO mice retained the significantly higher level of rearing in the 1st 30 mins compared to WT mice, and attenuated the inhibitory effect of MK-801. We don't find evidence for a role of the D3 receptor in MK-801 induced hyperactivity.

42. EFFECTS OF 7-OH-DPAT, A D3 RECEPTOR AGONIST, ON PAIN MODULATION, IN THE RAT. Casarrubea, M.; Sorbera, F.; Saia, V.; Greco, P.; Crescimanno, G. Dept. of Experimental Medicine, Human Physiology Section, University of Palermo, Italy. Previous studies have implicated dopamine receptors in nociception. Interestingly, within D2 receptor family, D3 receptors are expressed in brain regions likely involved in the processing of painful information. Aim of the present research was to investigate whether a D3 receptor agonist could influence specific parameters of the response to painful stimuli. Experiments were performed in adult male Wistar rats weighing 220-250 g. Five groups were used: four groups were administered 7-OH-DPAT (0.5, 1, 2, 4 mg/kg I.P.), a D3 agonist, and a control one was administered saline. Animals were tested on a hot plate apparatus maintained at the constant temperature of 54 + 0.5 °C. As soon as rats showed the first sign of pain they were removed from the plate. Each animal was tested 5, 10, 20 and 30 minutes after injection. Responses were recorded by means of a digital videocamera and analysed frame by frame by a video recorder. Latency of the first reaction to pain (i.e. paw licking, lifting, flinching-slapping of the paws)was calculated and compared among the different groups. Following 7-OH-DPAT, a significant and dose-dependent increase of the first response latency occurred: e.g. latency varied from about 980 ms (control) to 2500 ms (4 mg/kg of drug). Results show that administration of a D3 receptor agonist induces a delayed response to noxius stimuli without motor impairment. It is possible to hypothesize a key role of this receptor population in sensorimotor integration mechanisms linked to pain modulation.

Friday, June 3:

8:30-10:30 Symposium 2: Integrative function of the hypothalamus in autonomic, endocrine responses to stress and behavioral changes. Mesa Ballroom B&C

OREXIN/HYPOCRETIN AND NEUROMEDIN U AS A STRESS MEDIATOR IN THE HYPOTHALAMUS. Ueta, Y. Dept. of Physiology, Sch. Med., Univ. Occup. Environ. Health, Kitakyushu 807-8555 Japan. Orexin-A, -B/hypocretin-1, -2 and neuromedin U (NMU) were identified as endogenous ligands of the orphan G-protein coupled receptors. Their receptors, orexin type 2 receptor and NMU type 2 receptor are abundantly expressed in the paraventricular nucleus (PVN) of the hypothalamus in rats. The parvocellular division of the PVN is well known to contain CRH-producing neurons that project their axons to the median eminence. The PVN neurons also project their axons to the pre-ganglionic autonomic neurons in the brainstem and spinal cord. Thus, the PVN is one of the important sites to integrate the endocrine and autonomic responses to various stressors. Intracerebroventricular (Icv) administration of orexin-A and NMU caused activation of CRH-producing neurons in the PVN in rats. Icv administration of orexin-A and NMU also stimulated secretion of ACTH into the systemic circulation in rats. Icv administration of orexins stimulates feeding behavior, while icv administration of NMU inhibits food intake in rats. Food deprivation causes marked increase of prepro-orexin mRNA levels in the lateral hypothalamic area, but decrease of NMU mRNA levels in the arcuate nucleus. It is interesting that both the orexigenic and the anorexigenic peptides activate hypothalamo-pituitary adrenal axis in rats.

CLOCK GENE MUTATION AND AUTONOMIC AND ENDOCRINE CHANGES. Sei, H.; Oishi, H.; Ishida, N. Department of Integrative Physiology, The University of Tokushima Graduate School, Tokushima 770-8503, Japan. Clock Cell Biology, National Institute of Advanced Industrial Science and Technology, IMCB 6-5, 1-1-1 Higashi, Tsukuba, 305-8566, Japan. Circadian rhythm is an endogenous rhythm controlled by a master oscillator in the supra-chiasmatic nucleus of hypothalamus. Recent developments in our understanding of the genetic mechanisms of circadian system have led to a transcriptional feedback loop contains both positive and negative components. In order to clarify the role of Clock gene, which is one of the main positive components, we recorded blood pressure (BP) and heart rate (HR) in the Clock mutant mice on Jcl:ICR background (Clockj) and wild-type mice (WT) using telemetry system (TA11PA-C20; DSI). BP in the Clockj was significantly higher than WT during the light period. HR in the Clockj was significantly lower than WT during the dark period. Daily mean of BP in the Clockj was significantly higher, and that of HR was significantly lower in comparison to WT. We hypothesized that Clockj has some impairment of water balance controlled by adreno-cortical hormones. After aderenalectomy, the amplitude of BP and HR lost the significant difference between the Clockj and WT, although the acrophase did not change. It is possible that the altered function of adrenal gland, which is caused by the lack of normal Clock gene, may induce non-dipping circadian profile of BP and HR.

AUTONOMIC AND CARDIOVASCULAR RESPONSES TO GRAVITATIONAL STRESS. Morita, H.; Gotoh, M.T.; Matsuda, T.; Tanaka, K. Dept. of Physiology, Gifu University School of Medicine, Gifu 501-1194, Japan. To examine role of the vestibular and baroreflex system in maintaining arterial pressure (AP) during gravitational stress, 4 groups of conscious rats, which were either intact or had sinoaortic denervation (SAD), vestibular lesion (VL), or SAD+VD, were exposed to 3 G load with measuring AP and renal sympathetic nerve activity (RSNA). In rats in which neither reflex was functional (SAD+VL group), RSNA did not change, but the AP showed a significant decrease (-8 } 1 mmHg). In rats with a functional baroreflex, but no vestibulosympathetic reflex (VL group), the AP did not change and there was a slight increase in RSNA (+25 } 10 %). In rats with a functional vestibulosympathetic reflex, but no baroreflex (SAD groups), marked increases in AP and RSNA were observed (+31 } 6 mmHg and +87 } 10 %), suggesting that the vestibulosympathetic reflex causes an increase in AP in response to gravitational stress; these marked increases were significantly attenuated by the baroreflex in the intact group (+9 } 2 mmHg and +38 } 7 %). Furthermore, in rats with midcollicular transection, the AP change was minimal, indicating that output from the vestibular system project to the diencephalon, and activation of diencephalic nuclei is indispensable to the pressor response via the sympathetic nerve system. In conclusion, AP is controlled by the combination of the baroreflex and vestibulosympathetic reflex. The vestibulosympathetic reflex elicits a huge pressor response during gravitational stress, preventing hypotension due to blood redistribution. In intact rats, this AP increase is compensated by the baroreflex, resulting in only a slight increase in AP.

HYPOCRETIN DEFICIENT NARCOLEPSY AS A DISEASE MODEL TO STUDY THE HYPOTHALAMIC FUNCTION IN HEALTH AND DISEASE. Nishino, S. Center for Narcolepsy, Stanford University School of Medicine, CA 94304 USA. Using forward (i.e., positional cloning) and reverse genetics (i.e., mouse gene knockout), genes (i.e., prepro-hypocretin/orexin and hypocretin/orexin receptor genes) involved in the pathogenesis of narcolepsy in animals has been recently identified. Human narcolepsy is a chronic sleep disorder affecting 1:2000

individuals. The disease is characterized by excessive daytime sleepiness and abnormal manifestations of REM sleep, such as cataplexy, sleep paralysis and hypnagogic hallucinations. Narcolepsy is also associated with obesity, a high incidence of type II diabetes, and autonomic neuroendcrine abnormalities. Narcolepsy in humans is tightly associated with human leukocyte antigen (HLA) DR2 and DQB1*0602. Contrary to findings in animals, mutations in hypocretin related-genes are extremely rare in humans, but hypocretin-ligand deficiency (possibly due to the acquired cell death of hypocretin containing neurons) is found in most narcolepsy-cataplexy cases. This discovery is likely to lead to the development of new diagnostic tests and treatments in human narcolepsy. Hypocretins/orexins are novel hypothalamic neuropetides discovered outside the sleep research field by searching endogenous ligands for orphan receptors and by subtractive PCR techniques. Hypocretins are also involved in various fundamental hypothalamic functions such as energy homeostasis and neuroendocrine functions. Thus, hypocretin-deficient narcolepsy now appears to be a more complex condition than a simple sleep disorder. The progress in narcolepsy research, along with pathophysiological aspects of hypocretin-deficient narcolepsy (with an emphasis on a link between arousal and other fundamental hypothalamic functions), will be discussed.

10:45-11:45 Presidental Lecture. Mesa Ballroom B&C

EPIGENETIC PERSPECTIVES ON MONOGAMY: INSIGHTS FROM PRAIRIE VOLES. C. Sue Carter, University of Illinois at Chicago. Studies of socially monogamous mammals, including prairie voles, have documented a neuroendocrine basis for positive behaviors, including social bonds and parental behavior. This work has implicated neuropeptide hormones, including oxytocin and the related peptide vasopressin, in the regulation of social interactions and reactivity to positive and negative experiences. Behavioral or hormonal experiences in early life, mediated in part by long-lasting changes in oxytocin and vasopressin or their receptors, can have life long consequences and may increase or decrease the capacity of an individual to form social bonds, show parental behavior and deal with the "stress of life." Knowledge of the plasticity of neuroendocrine systems also may help us understand individual differences in the vulnerability to mental disorders with a social component, such as autism. In the context of the peptide hormones that support social behaviors, we gain a different perspective on human concepts such as monogamy, social support and even "love".

13:15-15:15 Symposium 3: Modeling different facets of disease - steps toward exploration of endophenotypes in psychiatry. Mesa Ballroom B&C

ANIMAL MODELS FOR BIPOLAR DISORDER – NEW UNDERSTANDING AND NEW POSSIBILITIES. Einat, H. College of Pharmacy, Duluth. University of Minnesota, Duluth, MN 55812 USA. Models of bipolar disorder (BPD) are usually considered flawed because none includes all the main facets of BPD. However, the growing understanding that BPD may not be a single disorder but rather a collection of related subtypes and the current attempts to break down BPD into its component parts, study the biology of the component parts and come up with treatments for them, supports further development of models that may reflect different facets of the disease. Whereas depression models do take on some of the main symptoms of the disorder such as reduced activity, despair, unhedonia, sleep disturbances and others, traditionally, the commonly used models for mania emphasized only hyperactivity. It is now becoming more important to employ further models reflecting other components of mania such as increased risk taking, hedonistic behavior, aggression, reduced need for sleep and so on. Some such models are available but were previously used in different contexts. Other models should be developed. The better understanding of mechanisms involved in BPD and its treatment, combined with the increasing ability to pharmacologically and genetically target specific molecules permit us to try and develop models based on mechanistic hypotheses. For example, targeting PKC, ERK, BCL-2 or GSK, all have been demonstrated in-vitro to be relevant to the disorder, may be the source for more precise and better serving new models. New approaches to modeling hold much promise and are necessary for further attempts to delineate the underlying pathophysiology of this devastating illness, and for the development of novel, improved therapeutics.

COMPULSIVE CHECKING AND ITS ROOTS IN NORMAL BEHAVIOR: TOWARD AN ANIMAL MODEL OF OCD. [1]Szechtman, H; [2]Woody, EZ; [3]Eilam, D. [1]Dept Psychiatry & Behavioural Neurosciences, McMaster Univ; [2]Dept Psychology, Waterloo Univ; [3]Dept Zoology, Tel-Aviv Univ. The purview of psychiatry is mental life and behavior. Consequently, the discovery of mechanisms of psychiatric disorders will come only in the context of understanding the machinery of normal psychological functions. Hence, psychiatric animal models should elucidate the transition from normal to abnormal behavior. A preparation useful in this respect for obsessive-compulsive disorder (OCD) is the induction of compulsive checking in rats treated chronically with the dopamine agonist quinpirole. Such rats meet explicit ethological criteria for compulsive checking by showing a preoccupation with and an exaggerated hesitancy to leave one or two item(s) of interest; a ritual-like motor activity pattern; and, a dependence of checking behavior on environmental context. Quinpirole-treated rats direct their behavior at a likely

stimulus for checking activity - the home base, consistent with notion of OCD checking as exaggeration of normal checking regarding well-being and security. Expression of checking in quinpirole preparation is subject to external inhibitory control as for OCD checking and is partially attenuated by clomipramine, a drug used in treatment of OCD. We suggest that the development of perseverative compulsive checking in the quinpirole preparation is consistent with the security motivation theory of OCD (Szechtman and Woody, 2004) that posits a deficit in the shut-down satiety signal normally generated in the course of species-typical performance of security motivation-related behaviors such as checking.

COMPULSIVE RITUALS IN ANIMALS AND HUMANS: APPLICATION OF A NEW CONCEPT IN THE STUDY OF OBSESSIVE-COMPULSIVE DISORDER (OCD) David Eilam Department of Zoology, Tel-Aviv University, Ramat-Aviv 69 978 Israel This survey presents observations on the similarity in structure of motor rituals in animals in the wild, in captivity, in animal model of OCD, in normal humans, and in patients suffering from OCD. The content and form (sequential structure) of motor rituals is based on a core functional activity, which in normal behavior is the sole content of the motor action. In compulsive (abnormal) behavior, core activity is preceded and/or followed by additional chunks of the various components (movements) similar to those that construct the core activity. The similarity in components (movements) between core activity and appended chunks obscures the margin between the core activity and the compulsive ritual. This margin, however, becomes apparent when sequences of compulsive behavior are compared with stereotyped normal rituals. Thus, the sequential structure highlights the difference between the core activity (normal functional behavior) and the ritualized activity (malfunction).

DEVELOPING A MOUSE MODEL OF EARLY LIFE TRAUMA AND NEGLECT. Andrew Holmes, Ph.D. Section on Behavioral Science and Genetics, Laboratory for Integrative Neuroscience, NIAAA DICBR, NIH, Bethesda, MD. There is growing evidence of a link between childhood trauma, abnormal brain development and risk for emotional disorders. While there is evidence that genetic factors also affect risk for these disorders, the interplay between genes and early life stress remains poorly understood. The genetic malleability of the mouse makes it an excellent model system to study gene x early environment interactions shaping the development of brain systems mediating emotion. In the present study, we compared the effects of postnatal maternal separation (MS) on emotion-related phenotypes in 8 genetically-distinct inbred mouse strains: A/J/, 129P3/J, 129S1/SvlmJ, BALB/cJ, BALB/cByJ, C57BL/6J, DBA/2J, FVB/NJ. From postnatal days 0-13, pups were separated daily from the dam for either 3 h (MS) or 15 min (H15), or were undisturbed (facility reared, FR). Maternal care of pups was monitored at multiple time points relative to separation. At 8 weeks of age mice were tested for emotion-related behaviors using the novel open field, elevated plus-maze, acoustic startle, dark-light emergence, and forced swim tests. Preliminary results showed that MS altered adult anxiety-like behavior in a strain-dependent manner but, overall, MS did not produce major pervasive effects on emotional behavior. An important finding was that, across strains, MS caused a marked increase in maternal care upon reunion with pups that effectively compensated for the absence of care during separation. These data provide a basis for attempts to develop mouse models of genetic and neural factors underlying susceptibility and resilience to mental illness, with implications for understanding the childhood origins of affective disorders. Supported by the NIAAA-DICBR.

AN IMMUNO-PRECIPITATED NEURODEVELOPMENTAL ANIMAL MODEL OF SCHIZOPHRENIA IN MICE. Feldon, J; Meyer, U.; Yee, B. Laboratory of Behavioural Neurobiology, Swiss Federal Institute of Technology Zurich, Switzerland. feldon@behav.biol.ethz.ch. Epidemiological studies have indicated an association between maternal bacterial and viral infections during pregnancy and the higher incidence of schizophrenia in the resultant offspring post-pubescent. One hypothesis asserts that the reported epidemiological link is mediated by prenatal activation of the foetal immune system in response to the elevation of maternal cytokine level due to infection. Here, we report that pregnant mouse dams receiving a single exposure to the cytokine-releasing agent, polyinosinic-polycytidilic acid (PolyI:C; at 2.5, 5.0, or 10.0mg/kg) on gestation day 9 produced offspring that subsequently exhibited multiple schizophrenia-related behavioural deficits in adulthood, in comparison to offspring from vehicle injected or non-injected control dams. The efficacy of the PolyI:C challenge to induce cytokine response in naïve non-pregnant adult female mice and in foetal brain tissue when injected to pregnant mice were further ascertained in separate subjects: (i) a dose-dependent elevation of interleukin-10 was detected in the adult female mice at 1h and 6h post-injection, (ii) 12h following prenatal PolyI:C challenge, the foetal levels of interleukin-1β were elevated. The spectrum of abnormalities included impairments in explorative behaviour, prepulse inhibition, latent inhibition, the US-pre-exposure effect, spatial working memory; and enhancement in the locomotor response to systemic amphetamine (2.5mg/kg, i.p.) as well as in discrimination reversal learning. The neuropsychological parallelism between prenatal PolyI:C treatment in mice and psychosis in human demonstrated here leads us to conclude that prenatal PolyI:C treatment represents one of the most powerful environmental-developmental models of schizophrenia to date. The uniqueness of this model lies in its epidemiological and immunological relevance, and lends itself *sui generic* as a model ideally suited for the investigation of the neuropsychoimmunological mechanisms implicated in the aetiology and the disease process of schizophrenia within a developmental perspective.

MODELING AUTISM-RELATED BEHAVIORS IN THE FMR1 KNOCKOUT MOUSE MODEL OF FRAGILE X SYNDROME. Spencer, C.M.; Alekseyenko, O.; Serysheva, E.; Yuva-Paylor, L.; Paylor, R. Departments of Molecular and Human Genetics and Neuroscience, Baylor College of Medicine, Houston, TX 77030 USA. The loss of FMR1 gene function causes Fragile X syndrome (FXS), a common mental retardation syndrome. Many individuals with FXS exhibit behaviors similar to autistic individuals, such as hyperarousal, tactile defensiveness, gaze aversion, perseverative speech, and repetitive behaviors. Approximately 15-25% of individuals with FXS reach diagnostic criterion for autism. To better understand the role of FMR1 in autism-related behaviors, we analyzed anxiety-related and social behaviors in Fmr1 knockout (KO) mice. Our findings indicate that Fmr1 KO mice display abnormal social responses that may be considered consistent with 'social anxiety' and are influenced by experience with partners and test environment. Genetic background is also expected to be an important factor influencing autism-related behaviors. To address this issue, we analyzed behaviors in Fmr1 KO mice on different genetic backgrounds. Male Fmr1 KO and wildtype littermates from a pure C57BL/6J background and five F1 hybrid lines were generated. Mice were examined at 3-4 months of age for autism-related responses in a test battery that included marble-burying, partition test, and social interaction. Using this approach, we have observed that the effect of genotype on autism-related behavior differs depending upon genetic background and have identified more suitable models for the autism-related phenotype in FXS. Supported by FRAXA Research Foundation, the Baylor Fragile X Research Center and the Baylor MRDDRC.

CONDITIONED FEAR IN CONGENITALLY HELPLESS RATS: EXTINCTION DEFICIT, TREATMENT, AND IMPLICATIONS FOR POST-TRAUMATIC STRESS DISORDER. Shumake, J.; Barrett, D.; Wrubel, K.M.; Johnson, S.E.; Gonzalez-Lima, F. Institute for Neuroscience and Departments of Psychology, Pharmacology, and Toxicology, The University of Texas, Austin, Texas 78712 USA. Congenitally helpless rats, bred for susceptibility to learned helplessness, may model vulnerability to post-traumatic stress disorder (PTSD). One PTSD feature is the reduced ability to extinguish traumatic memories. We examined acquisition and extinction of conditioned fear in congenitally helpless rats and then tested the ability of methylene blue to improve extinction in these rats. Acquisition (4 tone-shock pairings) was followed by 2 days of extinction (30 tones/day) in a different context. Conditioned freezing was monitored throughout extinction and during probe trials one week later in both acquisition and extinction contexts. Congenitally helpless rats showed higher freezing to the fear-evoking tone and a dramatic extinction deficit. Congenitally helpless rats failed to show the gradual extinction curves seen in control subjects and continued to show greater tone-evoked fear one week after extinction training. Congenitally helpless rats were subsequently given 5 more days of extinction (4 tones/day), each session followed by 4 mg/kg methylene blue or saline. Rats treated with methylene blue or saline showed equivalent reductions in tone-evoked freezing in the extinction context, but the group treated with methylene blue showed substantially better extinction than the saline-treated group when the rats were probed in the acquisition context. In conclusion, the impaired ability to extinguish a traumatic memory in congenitally helpless rats supports the validity of this strain as a model for vulnerability to PTSD, and methylene blue shows potential utility for facilitating the extinction of conditioned fear in PTSD patients.

AUTISM-RELATED BEHAVIORS IN A NEW X-LINKED TRANSGENIC MOUSE. Spencer, C.M.[1]; Yuva-Paylor, L.[1]; Schuster, G.[2]; Shope, C.[3]; Noebels, J.[4, 5]; Brownell, W.[3, 5]; Overbeek, P.[2, 5]; Paylor, R.[1, 5] Depts of [1]Molecular & Human Genetics, [2]Cell Biology, [3]Otorhinolaryngology, [4]Neurology, and [5]Neuroscience, Baylor College of Medicine, Houston, TX 77030 USA. Autism is a developmental disorder characterized primarily by abnormal social behavior, communication deficits, and repetitive ritualistic behavior, with associated features such as hyperactivity, sensory hypersensitivity, cognitive rigidity and aggression. We report a new transgenic mouse generated by random insertional mutagenesis that exhibits several autism-related behaviors. Initial observations of home cage behavior indicated the development of aggression and repetitive circling behavior in 4-5-week old male mutant mice. Behavioral testing of mutant and wildtype littermates was performed at 17, 22, 28 and 45 days of age. Mutant males showed impaired pre-pulse inhibition (PPI) at all ages. Hyperactivity in mutant males was more pronounced at 45 days than at 22 days. Abnormal repetitive circling behavior was evident in mutant males at 45 days of age. Tests of auditory brainstem responses (ABR), swimming ability, righting and contact righting reflexes indicated normal auditory and vestibular function. There were no overt signs of brain pathology or EEG abnormalities. FISH analysis and physical mapping indicated a single site of transgene integration at the D-E1 region of chromosome X. Based on the behavioral phenotype (aggression, hyperactivity, impaired PPI and abnormal repetitive circling behavior that is not due to auditory or vestibular dysfunction), we propose that this new X-linked transgenic mouse may model relevant aspects of autism. Supported by the Baylor MRDDRC.

SECRETIN RECEPTOR DEFICIENT MICE EXHIBIT AUTISTIC PHENOTYPES. Nishijima, I.1; Givens, B.2; Paylor, R. 3; Bradley, A.4. 1Department of Pediatrics, 2Department of Psychology, The Ohio State University,

Columbus, OH; 3Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; 4The Welcome Trust Sanger Institute, Cambridge, UK. Secretin is a peptide hormone released from the duodenum to stimulate secretion of digestive juice by the pancreas. Secretin also functions as a neuropeptide hormone in the brain and exogenous administration has been reported to alleviate symptoms in some patients with autism. We have generated secretin receptor deficient mice to explore the relationship between secretin signaling in the brain and autistic-related phenotypes. Secretin receptor deficient mice were overtly normal and histological analysis reveals no distinct morphological abnormalities; however, synaptic plasticity (synaptic transmission and long term potentiation) in the hippocampus was impaired. Furthermore, secretin receptor deficient mice had an altered pattern of object exploration and recognition, and showed abnormal social behavior. These findings support the hypothesis that the secretin receptor system contributes to autistic-related phenotypes. These mice provide a new animal model to test potential therapeutic interventions.

17:30-19:30 Poster Session 2. (Refreshments) Ortiz Ballroom

Fragile X Syndrome and Autism

43. A DEVELOPMENTAL APPROACH TO UNDERSTANDING FRAGILE X SYNDROME: THE INFLUENCE OF ENVIRONMENTAL AND GENETIC FACTORS ON BEHAVIOR PROBLEMS IN PATIENTS WITH FRAGILE X SYNDROME.Marjaneh Akbarzadeh 1; Reza Akbarzadeh 2; Reyhaneh Akbarzadeh 1.Department of Psychology, Russian University of Economics and Culture, Moscow, Russia1, Mashhad University of Medical Sciences, Mashhad, Iran 2.INTRODUCTION: Fragile X syndrome (FXS) is a well-recognized cause of mental retardation and developmental delay, is associated with a particular profile of abnormalities of behavior, learning, language, and memory. AIMS AND METHOD: In this article, we summarize studies focused on to neuropsychological and neuropsychiatry approaches that have attempted to delineate the genetic and environmental factors influencing behavior problems and autistic symptoms in patient with (FXS). RESULTS: Fragile X syndrome is one of the world's leading hereditary causes of mental retardation .There is considerable variability in the behavioral and psychiatric problems and attributable to an identifiable genetic abnormality. The relative homogeneity of the neuropsychiatry phenotype in individuals with fragile X syndrome suggests that there are consistent central nervous system (CNS) abnormalities underlying the observed cognitive and behavioral abnormalities. The physical, cognitive and behavioral features of individuals with (FXS) depend on gender (females have two X chromosomes, one active and one inactive) and the molecular status of the mutation (permutation, full mutation or mosaic). Recent advances in molecular genetics, human brain imaging, and behavioral studies have started to unravel the complex pathways leading to the cognitive, psychiatric, and physical features that are unique to this syndrome. CONCLUSION: Fragile X syndrome is a relatively common form of inherited mental retardation, caused by loss of function of the FMR1 gene on the long arm of the X chromosome. The combinations of molecular genetics, neuroimaging, and behavioral research have advanced our understanding of the linkages between genetic variables, neurobiological measures, IQ, and behavior.
44. ADVANCES IN RESEARCH ON THE FRAGILE X SYNDROME: ANALYZING GENE – BRAIN –BEHAVIOR RELATIONSHIPS IN NEURODEVELOPMENTAL EFFECTS. Reyhaneh Akbarzadeh 1; Reza Akbarzadeh 2; Marjaneh Akbarzadeh 1. Department of Psychology, Russian University of Economics and Culture,Moscow, Russia1, Mashhad University of Medical Sciences, Mashhad, Iran 2. INTRODUCTION: Fragile X syndrome (FXS), caused by a single gene mutation on the X chromosome, offers a unique opportunity for investigation of gene- brain-behavior relationships. Neurobehavioral characteristics including social deficits with peers, social withdrawal, gaze aversion, inattention, hyperactivity, anxiety, depression, and autistic behavior. AIMS AND METHOD: In this paper, we review behavioral neurogenetics research by examining gene-brain-behavior relationships in patients with fragile X syndrome. RESULTS: Fragile X syndrome is a neurogenetic disorder that is the most common known heritable cause of neurodevelopmental disability. The converging approaches across these multilevel scientific domains indicate that fragile X, which arises from disruption of a single gene leading to the loss of a specific protein, is associated with a cascade of aberrations in neurodevelopment, resulting in a central nervous system that is suboptimal with respect to structure and function. In turn, structural and functional brain alterations lead to early disruption in emotion, cognition, and behavior in the child with fragile X syndrome. The observed correlations between biological markers and brain activation provide new evidence for links between gene expression and cognition. CONCLUSION: Fragile X syndrome, a single-gene disorder that has become a well-characterized model for studying neurodevelopmental dysfunction in childhood. Through better definition of the cognitive and behavioral phenotype, in combination with current progress in brain

imaging techniques and molecular studies should continue to hold exciting promise for fragile X syndrome and other neurodevelopmental disorders.

45. SUPPRESSION OF TWO MAJOR FRAGILE X SYNDROME MOUSE MODEL PHENOTYPES BY THE MGLUR5 ANTAGONIST MPEP. Yan, QJ; Rammal, M; Bauchwitz,, RP. St. Luke's-Roosevelt Institute for Health Sciences, Columbia University, New York, NY, USA. Fragile X Syndrome is the most common form of inherited mental retardation worldwide. A Fragile X mouse model, fmr1tm1Cgr, with a disruption in the X-linked Fmr1 gene, has three substantial deficits observed in several strains 1) sensitivity to audiogenic seizures (AGS), 2) tendency to spend significantly more time in the center of an open field, and 3) enlarged testes. Alterations in metabotropic glutamate receptor group I signaling were previously identified in the fmr1tm1Cgr mouse. In this study, we examined the effect of MPEP, an antagonist of the group I metabotropic glutamate receptor mGluR5, on audiogenic seizures and open field activity of fmr1tm1Cgr mice. Genetic analysis revealed synergistic reactions between fmr1tm1Cgr and inbred AGS alleles. In addition, AGS sensitivity due to the fmr1tm1Cgr allele was restricted during development. Examination of phenotypes combining mGluR5 inhibition and Fmr1 mutation indicated that absence of FMRP may affect mGluR5 signaling through indirect as well as direct pathways. All strains of fmr1tm1Cgr mice tested, (FVB/NJ, C57BL/6J, and an F1 hybrid of the two), had a more excitable AGS pathway than wild type, and consequently required more MPEP to achieve seizure suppression. In open field tests, MPEP reduced fmr1tm1Cgr center field behavior to one indistinguishable from wild type. Therefore, modulation of mGluR5 signaling may allow amelioration of symptoms of Fragile X Syndrome.

46. ALTERED RESPONSE TO SOUND AND ENVIRONMENT IN CUED/CONTEXUAL FEAR CONDITIONING IN A MOUSE MODEL FOR AUTISM. Desir, N[1], Walker, E.M.[1], Hodges, A.B.[1], Blue, M.E.[2], and Hohmann, C.F.[1], Dept. of Biol., Morgan State Univ.[1], Kennedy Krieger Inst.[2], Baltimore, MD Autism is a developmental disorder effecting social interaction, language and sensory motor functions. Neuropathologies include age dependent changes in cranium size, brain volume and in forebrain serotonin [5-HT] innervation. In a mouse model of neonatal depletion of cortical 5-HT innervation, we previously observed impaired passive avoidance behavior and improved delayed non-matched to sample odor discrimination. Male lesioned mice showed decreased exploration in response to object displacement and object novelty. Here we investigate the effects of cued contextual fear conditioning (CCFC). On the day of birth, 5 μg/ml (0.06 μl) of the 5-HT neurotoxin 5, 7-dihydroxy-tryptamine (5, 7-DHT) was injected bilaterally into the medial forebrain bundle of Balb/CbyJ mice. Littermate controls were injected with equal amounts of saline. We used 18 5, 7- DHT, 16 saline injected and 28 normal littermates of both sexes, as adults, for CCFC according to Crawley (2000). A tone (800 Hz) was used as the conditioning stimulus (CS) paired with a footshock (UCS, 0.1 mv). Freezing was measured in two different environments distinguished by shape, texture and smell. At first exposure to the CS, male lesioned mice showed no freezing response while all others displayed various levels of freezing. After mice were trained to recognize the CS, lesioned animals of both sexes responded with significantly higher freezing rates. Lesioned animals of both sexes reacted with higher freezing rates to the novel environment. These data are consistent with observed neophobic behavior in this mouse model for autism and they suggest altered sensory perception. U54 MH066417-01A1, SO6 GM051971 and 1G12RR17581.

47. EFFECTS OF TEST AND GENETIC BACKGROUND ON ANXIETY-RELATED BEHAVIORS IN THE FMR1 KNOCKOUT MOUSE MODEL OF FRAGILE X SYNDROME. Spencer, C.M.; Alekseyenko, O.; Serysheva, E.; Yuva-Paylor, L.; Paylor, R. Departments of Molecular and Human Genetics and Neuroscience, Baylor College of Medicine, Houston, TX 77030 USA. Anxiety is a prominent behavioral problem in individuals with Fragile X syndrome (FXS), one of the most common inherited causes of mental retardation. Contrary to expectations based on the human phenotype, earlier studies examining behaviors in Fmr1 knockout (KO) mice found a decrease in anxiety-related responses in the open-field and light-dark tests. The unexpected nature of the results suggested the need to assess anxiety-like behavior in additional rodent tests of anxiety. Also, since mice of different strains are known to differ significantly in anxiety-like responses, genetic background is expected to be an important factor influencing these behaviors in Fmr1 KO mice. Male Fmr1 KO and wildtype littermates from a pure C57BL/6J background and five F1 hybrid lines were generated from female Fmr1 heterozygous mice on a pure C57BL/6J background bred with male Fmr1 wild-type mice of various background strains (A/J, DBA/2J, FVB/NJ, 129S1/SvImJ and CD-1). Mice were examined at 3-4 months of age for anxiety-related responses in several tests: open-field, light-dark, marble-burying, social interaction, mirrored chamber, elevated circle and stress-induced hyperthermia. We will present data showing that the effect of genotype on anxiety-like behavior differs depending upon genetic background and the behavioral test used. This approach has allowed us to identify better models for the anxiety phenotype in FXS. Supported by FRAXA Research Foundation, the Baylor Fragile X Research Center and the Baylor MRDDRC.

48. GABRB3 GENE KNOCKOUT MICE: A MODEL OF AUTISM SPECTRUM DISORDER? DeLorey, T.M.; Hashemi, E.; Sahbaie, P.; & Homanics, G. Molecular Research Institute, Mountain View, CA 94043. Autism spectrum disorder is defined by three fundamental core symptoms: 1) inappropriate social interactions; 2) poor communication skills; and 3) restrictive, repetitive (stereotypical) behaviors. Additional traits observed with high frequency in autistic individuals include: anxiety, cognitive impairment, epilepsy, motor deficits, aggression, sleep disturbances, idiosyncratic responses to sensory stimuli, attentional deficits, hyperactivity, and altered exploratory behavior. Human chromosomal region 15q11-13 has been implicated as being an autism susceptibility locus. An especially attractive candidate gene within this region is the GABRB3 gene, which encodes the ?$_3$ subunit of the $GABA_A$ receptor. This subunit is highly expressed during neurodevelopment and is widely distributed in the adult Central Nervous System. Mounting evidence has provided strong support for an association between the GABRB3 gene and autism spectrum disorder. Furthermore, mice lacking the GABRB3 gene exhibit cognitive impairment, epilepsy, motor deficits, sleep disturbances, abnormal responses to sensory stimuli and hyperactivity. This study further assessed GABRB3 knockout mice for social behaviors including interactions with unfamiliar mice, nest building and exploratory behaviors. The GABRB3 null mice were found to significantly differ from wildtype mice in each of these behaviors. These results, along with previous findings, support the GABRB3 knockout mouse as a model of autism spectrum disorder. Research funded by NIMH R01 MH065393-01.

Other Nervous System Disorders and Models

49. EFFECT OF CURCUMIN ON 3-NITORPROPIONIC ACID-INDUCED MODEL OF HUNTINGTON'S DISEASE. Pattipati. S.N.; Kumar, P.; Kumar,A. Neuropsychopharmacology Division, University Institute of Pharmaceutical Sciences Panjab University, Chandigarh-160014, India. Huntington's disease (HD) is a progressive neurodegenerative disorder characterized by involuntary abnormal choriform movements and progressive dementia. 3-nitropropionic acid (3-NP) is known to induce cellular energy deficit and oxidative stress related neurotoxicity via an irreversible inhibition of the mitochondrial enzyme succinate dehydrogenase (SDH) and has been widely used as an animal model of HD. The present study was designed to study the effect of curcumin a natural antioxidant on 3-NP-induced cognitive impairment and oxidative stress in rats. 3-NP was administered intraperitonially at a dose of 20mg/kg for four consecutive days. Curcumin (10-50 mg/kg) both alone and in combination with 3-N, were given for a period of 8 days, beginning 4 days before and continuing for 4 days after first injection of 3-NP. Memory impairment was assessed by using Morris water-maze and elevated plus maze paradigms. Locomotor activity was measured by actophotometer. Rats were scarified on eighth day immediately after behavioral measurements for estimation of SDH and oxidative stress parameters. 3-NP treatment caused a significant impairment in locomotor activity, memory and also induced a significant raise in lipid peroxidation, and decrease in reduced glutathione and SDH levels. Curcumin (10-50 mg/kg) significantly improved the cognitive performance and motor activity. Chronic curcumin treatment also significantly reversed 3-NP-induced SDH and glutathione depletion and lipid peroxidation. In conclusion the present study suggests that curcumin ameliorates 3-NP-induced cognitive deficits and oxidative stress and its potential use in the treatment of Huntington's disease.

50. A COPPER AND CHOLESTEROL DIET DISRUPTS LEARNED IRRELEVANCE IN RABBIT EYEBLINK CONDITIONING: AN ANIMAL MODEL FOR ALZHEIMER'S DISEASE Walker,A.G.; Mckinney,C.J.; Allen, M.T. Dept. of Psychology. University of Northern Colorado. Greeley, CO 80639 USA Sparks & Schreurs (2003) have shown a copper-cholesterol diet results in beta amyloid accumulation which disrupts trace eyeblink conditioning. In the current work, another eyeblink conditioning task, learned irrelevance (LIRR) was tested. LIRR is known to involve the major cortical input to the hippocampus, the entorhinal cortex, which is damaged early in the course of Alzheimer's disease. Twenty four male rabbits (Oryctolagus cunniculus) were used in this study. Over eight weeks, half received a cholesterol diet with distilled water and half received a copper-cholesterol diet (2% cholesterol diet and distilled water with a concentration of .12 ppm copper sulfate). Rabbits were pre-exposed with unpaired presentations of the tone and air puff (LIRR pre-exposure) or no stimuli presentations (SIT pre-exposure). All rabbits were then delay conditioned with tone-air puff trials. Cholesterol rabbits in the LIRR condition were significantly slower to exhibit CRs to the tone in delay conditioning than those in the SIT condition (i.e., exhibited LIRR). Copper-cholesterol rabbits did not exhibit LIRR. These behavioral results mimic the effects of entorhinal cortical lesions in rabbits. The role of metals such as copper and zinc in beta amyloid induced oxidative stress will be discussed along with possible therapies.

51. DELAYED ACQUISITION OF A VISUAL DISCRIMINATION IN RATS CHRONICALLY INFUSED WITH SOLUBLE AMYLOID BETA PEPTIDE. Arnold, H.M., Brenneman, D.E., & Yohrling, G.J. CNS Research, Johnson & Johnson Pharmaceutical Research and Development, Spring House, PA 19477 USA. Recent efforts in understanding the pathology of Alzheimer's disease (AD) have focused on the toxicity of soluble oligomers of amyloid beta (sAß) rather than on the later developing insoluble fibrils of Aß known to compose plaques. Previous studies have shown that sAß is toxic to neuronal cell lines, results in deficits in LTP in cortical slices, and disrupts behavioral performance when administered directly to the brain. We sought to determine whether chronic administration of human sAß (1-42) would result in impaired performance in a behavioral task requiring learning, memory, and inhibitory processes. Male Long-Evans rats underwent surgery to implant bilateral icv cannula attached to osmotic mini-pumps that delivered 1 mg/hemisphere/day of sAß for 32-33 days (~64mg total). Following surgery, rats were shaped to lever press and then trained on a simple visual discrimination; press the lever beneath an illuminated panel light. After 5 sessions nearly all animals were able to respond with >80% accuracy. Animals were then trained on the reversal of this task (press lever under the non-illuminated panel light). Training on the reversal was much more difficult than the initial task for all animals (>10 sessions). Notably, animals treated with sAß were delayed on acquisition of the task relative to vehicle infused rats. These data add to a growing body of literature implicating soluble forms of Aß in the learning and memory deficits associated with Alzheimer's disease.

52. NICOTINE SENSITIZATION IN A RODENT MODEL OF PSYCHOSIS: A COMPARISON OF ADULT AND ADOLESCENT RATS. Perna, M.K.; Smith, K.J.; Handy, C; Brown, R.W. Dept. of Psychology, East Tennessee State University, Johnson City, TN 37614 USA. Past data from this laboratory has demonstrated that neonatal quinpirole (dopamine D2 agonist) treatment produces long-term dopamine D2 receptor priming that persists into adulthood. There were two experiments in this study. In Experiment 1, the offspring of four male-female breeder pairs were administered one daily i.p. injection of quinpirole (1mg/kg) or saline from postnatal days 1-21 (P1-21) and raised to adolescence. Beginning on P29 the offspring of four male-female breeder pairs were habituated to a locomotor arena for three consecutive days. Beginning the next day, all animals were administered one i.p. injection of 0.5 mg/kg free base nicotine tartarate every other day for three weeks. Results showed that animals administered nicotine. D2-primed rats did not demonstrate the typical nicotine-induced hypoactivity early in training as controls administered nicotine, but demonstrated equivalent levels of sensitization as compared to controls administered nicotine. D2-primed rats given saline over the three week sensitization period also demonstrated a significant increase in activity compared to controls, but lower levels of activity compared to animals administered nicotine. In Experiment 2, a different group of Sprague-dawley rats were given the identical neonatal drug treatment as in Experiment 1 but raised to adulthood (P60). Both D2-primed and control animals administered nicotine demonstrated hypoactivity early in training, but D2-primed rats demonstrated significantly more robust sensitization than controls administered nicotine by the end of sensitization training. This appears to indicate a hyperactive dopaminergic system in these animals, which may be important to explaining why approximately 80% of the schizophrenic population smokes cigarettes. An investigation is currently underway in a collaborating laboratoratory to analyze changes in receptor binding through autoradiography.

53. NEONATAL QUINPIROLE TREATMENT PRODUCES DEFICITS IN PREPULSE INHIBITION IN RATS. Maple, A.M; Smith, K. J.; Thacker, S. K.; Perna, M. K.; Brown, R. W. East Tennessee State University, Department of Psychology, Johnson City, TN 37614 The objective of this study was to test the hypothesis that neonatal quinpirole treatment, which results in priming of the dopamine D2 receptor that persists throughout the animal's lifetime, also produces deficits in prepulse inhibition (PPI) compared to controls. Thirteen Male and female Sprague-dawley rats were neonatally treated with quinpirole (1mg/kg) or saline from postnatal days 1-21. Verification of D2 receptor priming was demonstrated at P65 through an acute injection of quinpirole (100 mg/kg) and yawning was observed for 1h. Yawning is a behavior mediated exclusively by the D2 receptor. Beginning the next day, all rats were administered two phases of PPI testing. In phase I, three different prepulse intensities were utilized and administered 100-ms before a 115 dB pulse. In phase II, two different prepulse auditory intesntities were utilized with three different interstimulus intervals (ISIs) between the prepulse and pulse. A probe trial was administered at the end of each phase in which a 100 mg/kg injection of quinpirole was given to all animals 15 min before PPI testing. Results showed a more robust difference in yawning between D2-primed rats and controls in females as compared to males, suggesting significant gender differences in the nature of D2 receptor priming. Regarding PPI, D2-primed rats demonstrated a significant deficit compared to controls across both phases of testing. In Phase II, females demonstrated a significant deficit compared to males depending on the ISI between the prepulse and pulse. Probe trial results revealed that stimulation of the D2 receptor in primed rats

produced deficits that appear to be related to both auditory intensity and ISI. This study demonstrates that D2 receptor priming that persists throughout the animal's lifetime results in PPI deficits, at least partially validating this D2-priming model as a model of schizophrenia.

54. OLFACTION IMPAIRMENTS IN MICE OVEREXPRESSING HUMAN WILDTYPE ALPHA-SYNUCLEIN. Sheila M. Fleming1, Timothy Schallert3, Michael S. Levine2, E. Masliah4 and Marie-Françoise Chesselet1 1Departments of Neurology and Neurobiology, 2The Mental Retardation Research Center, UCLA, Los Angeles, CA, 3Department of Psychology, The University of Texas at Austin,TX, and 4Department of Pathology, UCSD, San Diego, CA The protein a-synuclein is thought to be involved in presynaptic neuronal function and is a major component of Lewy bodies, the pathological hallmark of Parkinson's disease (PD). Although PD is primarily characterized by loss of nigrostriatal dopamine neurons leading to motor impairment, impairments in olfaction, gastrointestinal function, and anxiety/depression often accompany or precede motor symptoms. Transgenic mice overexpressing wild type human a-synuclein (ASO) exhibit anomalies in dopamine function and sensorimotor impairments. We recently tested separate groups of young (3-4 months) and old (9 months) ASO and wildtype mice on a novel olfactory test and the habituation/dishabituation test of olfaction. In both tests young ASO and wildtype mice could detect a novel odor introduced into their cage, however, older ASO mice had trouble distinguishing the novel odor and sniffed it significantly less than wildtype mice. These data suggest that ASO mice may develop impairments in olfaction as they age, making them a good model to study the early stages of PD.

55. NEUROPSYCHOLOGICAL FUNCTIONING OF A FAMILY WITH MITOCHONDRIAL CYTOPATHY. Sullivan, K.D.; Neargarder, S.; & Carvalho, J. Vision and Cognition Laboratory, Boston University, Boston, MA 02215 USA; Bridgewater State College, Psychology Department, Bridgewater, MA 02325 USA. The neuropsychological functioning of patients with mitochondrial cytopathies, disorders of the energy-producing organelles of the cells, has been largely unexamined in the literature. These mitochondrial defects often result in cell death and eventually the failure of whole systems, including the brain. There are currently over 40 known types of mitochondrial cytopathies, which vary greatly in their physiological and behavioral manifestations. Even individuals with identical genetic defects can vary in their symptoms due to the unique mixture and distribution of healthy and defective mitochondria found throughout the body. In the following project we had the opportunity to compare the neuropsychological profiles of a family (a 39 year old mother, her 17 year-old-son and 13 year-old-daughter) afflicted by the same mitochondrial cytopathy caused by the same genetic defect. Standardized tests of attention, executive function, verbal and visual memory, spatial construction, language, sensorimotor functioning, visual acuity, mood and activities of daily living were administered. For all three individuals, results revealed premorbid functioning to be in the average to superior range. Attentional variability in the performances was demonstrated both between and within participants with primary deficits shown in working memory and sequencing abilities. Relative strengths were noted in the realms of verbal comprehension and conceptual reasoning across all individuals. These neuropsychological profiles are suggestive of specific cerebral dysfunction, with a primary effect seen in the prefrontal regions of the brain independent of overall cognitive abilities. The implications of these results in understanding the neurobehavioral manifestations of mitochondrial disease and the relation between age of onset, genetic defect burden, postmitotic tissues and cognitive symptom severity are discussed.

56. A FUNCTIONAL GENOMICS RESOURCE FOR NEUROSCIENTISTS: THE NIH NEUROGENOMICS PROJECT. C. J. Yates1, S.M. Siepka1, K. Shimomura1, Y. Li1, H.K. Hong1,5, E. Simpson2, A. Mohn3, M.G. Caron3, E.R. Kandel2, W.A.Kibbe1, M.M. Hohman1, J.E. Levine1, R. Mullins4, E. Redei1, V. Sheffield4,5, F.W. Turek1, M.H. Vitaterna1, L.H. Pinto1, and J.S. Takahashi1,5. 1. Center for Functional Genomics, Northwestern University, Evanston, IL 60208; 2. Columbia University, New York, NY 10032; 3. Duke University Medical Center, Durham, NC, 27710; 4. University of Iowa College of Medicine, Iowa City, IA 52242; 5. Howard Hughes Medical Institute. Established by a cooperative agreement with the National Institutes of Health (NIH), The Neurogenomics Project is devoted to producing novel mutant mice useful as model systems for neuroscience research and to facilitate use of mouse genetic tools in understanding the nervous system and behavior. Chemical mutagenesis is used to induce mutations throughout the genome, and combined with phenotypic screens to detect mice with mutations of neuroscientific interest. A three-generation breeding scheme produces homozygotes, so that dominant and recessive mutations can be recovered. Screening assays focus on recovering mice with alterations in Circadian Rhythmicity, Learning and Memory, Responses to Psychostimulants, Responses to Stress, and Vision. Once heritability of the trait is confirmed, mutants are made widely available to the scientific community. It is hoped that these will provide new models for study, as well as aiding functional identification of new genes and pathways in neuroscience-relevant processes. More information about the ongoing screens, heritability testing, and mutant lines can be obtained at the Neurogenomics Project website at

http://www.genome.northwestern.edu/neuro. The Neurogenomics Project participates in the Neuromice.org consortium to distribute these mutant mouse lines. Information regarding available mutants, and orders for mutant mice can be placed through Neuromice.org at http://www.neuromice.org. Supported by NIH cooperative agreement U01 61915 from NIMH, NIDCD, NIA, NEI, NIDA, NIAAA, and NINDS.

Stress

57. CHILDHOOD ABUSE AND REGIONAL BRAIN DEVELOPMENT: EVIDENCE FOR SENSITIVE PERIODS. Teicher, M.H.; Andersen S.L.; Tomoda, A.; Vincow, E.; Valente, E.; Polcari, A. The brain is molded by experiences that occur throughout the lifespan. However, there are particular stages of development when experience exerts either a maximal (sensitive period) or essential (critical period) effect. For example, Hubel and Wiesel found that binocular deprivation maximally affected development of the visual cortex in cats if it occurred early in postnatal life, but had no impact after puberty. Little direct evidence exists for sensitive or critical periods in human brain development. Based on differential rates of maturation specific brain regions should have their own unique periods of sensitivity to the effects of early experiences such as stress. To ascertain if this is true in humans, the size of apriori selected target regions were measured from high-resolution volumetric MRI scans (1.5 T GE Echospeed) from 26 unmedicated collegiate females (18-22 years old) with a history of repeated childhood sexual abuse and 19 healthy sociodemographically comparable controls. Based on stepwise regression hippocampal volume was particularly sensitive to abuse that occurred at 4 years of age ($p<0.001$). In contrast, the midsaggital area of the rostral body of the corpus callosum was affected by abuse that occurred at age 9 ($p<0.05$), while grey matter volume of the prefrontal cortex was affected by abuse at age 15 ($p<0.02$). These findings provide the first evidence in humans that brain regions with different rates of maturation have unique windows of vulnerability to the effects of early traumatic stress. This study was supported by RO1 awards from the National Institute of Mental Health (MH-53636, MH-66222) and National Institute of Drug Abuse (DA-016934, DA-017846) to MHT.
58. EFFECTS OF ENERGY- REPRODUCTION- AND STRESS-RELATED SIGNALS ON THE PERFORMANCE OF VISUAL CATEGORICAL DISCRIMINATION OF FOOD AND SEX IN RHESUS MONKEYS. Inoue, T.; Takara, S.; Mizuno M.; Aou, S. Dept. of Brain Sci. and Eng. Kyushu Institute of Technology, Kitakyushu 808-0196 Japan. Visual cognitive functions are under the influence of different physiological and stress conditions. In this study we examined whether energy-, reproduction- and stress-related signals modulate the performance of visual categorical discrimination of food and sex in rhesus monkeys, *(Macaca mulatta)*. Task-related neuron activities were also investigated in the orbitofrontal cortex (OFC). Each trial of the task was started with a visual presentation of one of the following pictures: food vs. non-food, male Japanese monkey vs. female Japanese monkey. One set (5 pictures) of the 50 pictures for each category was randomly presented to the monkey. Simple figures and letters were also used as the control task. The visual performance was facilitated by fasting-induced endogenous substance, 2-buten-4-olide, but suppressed during menstrual period. Social stress such as confrontation of the rival monkeys disturbed the performance of visual discrimination. Neurons of the OFC mainly involved in discrimination of food/non-food and reward-related processing. The results suggest that visual discrimination of food or sex is under the influence of energy- and reproduction- and stress-related signals in different manner and OFC is the one of the possible candidate to integrate those information.
59. MODULATION OF MOTOR FUNCTION BY STRESS: A NOVEL CONCEPT OF THE EFFECTS OF STRESS ON BEHAVIOR. Metz, G.A.; Jadavji, N.M. Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, AB T1K 3M4, Canada. Stress and stress hormones can influence a variety of behavioral responses and nervous system functions. The consequences of stress and glucocorticoids on motor function, however, have not been characterized although the presence of glucocorticoid receptors in parts of the motor system has been documented. This study systematically investigated whether acute and chronic stress and elevated levels of glucocorticoids (corticosterone) affect motor performance in adult rats. The animals were trained in skilled reaching and skilled walking tasks. Groups of animals underwent either daily stress-inducing procedures (restraint stress or swimming in cold water) or manipulation of corticosterone levels by daily corticosterone supplements. While these treatments continued, animals were tested daily in skilled reaching and skilled walking tasks for a period of two weeks. Analysis of blood samples confirmed that both the stress-inducing procedures and corticosterone supplements increased circulating corticosterone levels at acute and chronic time points. The analysis of skilled movement performance showed that both acute and chronic stress and elevated corticosterone levels impaired movement accuracy and led to characteristic changes in movement patterns. These observations

propose a novel aspect of the effects of stress and stress hormones on behavior and motor system function. This research was supported by: Alberta Heritage Foundation for Medical Research, National Institutes of Health (NINDS).

60. GENETIC MODULATION OF EARLY LIFE TRAUMA AND NEGLECT IN MICE. Millstein, R.A.; Boyce-Rustay, J.M.; Izquierdo, A.; Wiedholz, L.; Holmes, A. Section on Behavioral Science and Genetics, Laboratory for Integrative Neuroscience, NIAAA DICBR, NIH, Bethesda, MD 20892 USA. There is growing evidence of a link between childhood trauma, abnormal brain development and risk for emotional disorders. While there is evidence that genetic factors also affect risk for these disorders, the interplay between genes and early life stress remains poorly understood. The genetic malleability of the mouse makes it an excellent model system to study gene x early environment interactions shaping the development of brain systems mediating emotion. In the present study, we compared the effects of postnatal maternal separation (MS) on emotion-related phenotypes in 8 genetically-distinct inbred mouse strains: A/J/, 129P3/J, 129S1/SvlmJ, BALB/cJ, BALB/cByJ, C57BL/6J, DBA/2J, FVB/NJ. From postnatal days 0-13, pups were separated daily from the dam for either 3 h (MS) or 15 min (H15), or were undisturbed (facility reared, FR). Maternal care of pups was monitored at multiple time points relative to separation. At 8 weeks of age mice were tested for emotion-related behaviors using the novel open field, elevated plus-maze, acoustic startle, dark-light emergence, and forced swim tests. Results showed strain-differences in baseline maternal care. Across strains, MS caused a marked increase in maternal care upon reunion with pups that effectively compensated for the absence of care during separation. Nonetheless, MS altered adult anxiety-like behavior (ALB), but not depression-related behavior, in a strain-dependent manner. Notably, MS increased ALB in DBA/2J relative to FR and H15, while MS failed to alter ALB in C57BL/6J. These strain differences provide a potential model for identifying genetic and neural factors underlying susceptibility and resilience to mental illness, with implications for understanding the childhood origins of affective disorders. Supported by the NIAAA-DICBR.

61. CARDIAC REGULATION AT REST AND FOLLOWING STRESS IN FEMALE PRAIRIE VOLES: PRELIMINARY FINDINGS. Grippo, A.J.; Carter, C.S.; Porges, S.W. Dept. of Psychiatry and Brain-Body Center, Univ. Illinois Chicago, Chicago, IL, 60612, USA. Prairie voles *(Microtus ochrogaster)* form social bonds similar to those seen in primates. Cardiovascular function has not been investigated in this species. We used radiotelemetry to study cardiac regulation in prairie voles at rest and following exposure to stress. 8 adult female prairie voles were implanted with radiotelemetry transmitters, and electrocardiographic (ECG) parameters were recorded continuously. Autonomic blockade was conducted with atenolol (8 mg/kg sc) and atropine (4 mg/kg sc). Animals were exposed to an acute stressor (opening cage and picking animal up), and ECG parameters were recorded 2 hr later. Baseline heart rate (HR) was 395 ± 13 bpm and HR variability (standard deviation of R-R intervals) was 16 ± 4 ms. HR was slightly reduced under ß-adrenergic receptor (sympathetic) blockade (363 ± 21 bpm) and increased under cholinergic receptor (vagal; 550 ± 25 bpm) and complete autonomic blockade (453 ± 25 bpm). HR variability was reduced under cholinergic (7 ± 2 ms) and complete blockade (9 ± 1 ms), and not altered during ß-adrenergic blockade. Exposure to the stressor led to an increase in HR (503 ± 23 bpm) and a slight decrease in HR variability (10 ± 1 ms). The findings suggest that cardiac regulation at rest is dominated by vagal tone, and this regulation is disrupted following exposure to acute stress. These results offer insight into cardiac and autonomic regulation in the prairie vole, and provide a foundation for studying neural control of cardiovascular function during manipulations of the social environment in this unique rodent species. *Supported by MH67446 (SWP) and MH073233 (AJG)*.

Drugs and Behavior

62. CAFFEINE'S ROLE IN CONDITIONING PREFERENCE AND PALATABILITY SHIFTS. Boudreau, S.E.; LoLordo, V.M.; Psychology Dept.; Dalhousie University, Halifax, NS Canada Caffeine is one of the most widely consumed psychoactive substances in the human population. Human data indicate both an increased wanting and liking for substances containing caffeine. In animals, two-bottle tests are considered measures of wanting, while taste reactivity tests (TRTs) are measures of liking. The TRT involves measuring appetitive and aversive orofacial reactions to an infused solution. The current study sought to further examine the role of caffeine in liking and wanting. Rats were implanted with intraoral cannula that allowed infusion of solution directly into the mouth. On CS+ trials grape or cherry Kool-Aid was mixed into a tap water solution with caffeine, and on CS- trials the other flavor was mixed with water alone, in a counterbalanced procedure. Rats were given thirteen days of training; six days with the CS+ solution, and seven days with the CS- solution. Experimental bottles were placed on the cages overnight, and removed the next morning in a single

alternation schedule. Following training, rats were given a TRT with each Kool-Aid-water solution. Each TRT consisted of placing the rat in the taste reactivity chamber and allowing him to sit quietly for five minutes connected to the infusion pump. The infusion pump was then turned on, and the rat's orofacial reactions were recorded. Immediately following the TRTs, all rats were given two overnight two-bottle preference tests. Both groups showed a preference for the CS+ in the two-bottle test, but there was no evidence from the TR data of an appetitive palatability shift towards the CS+. These data indicate that while the rats learned to want the Kool-Aid previously paired with caffeine more then the Kool-Aid paired with water, they did not learn to like it any more then the CS-.

63. A NOVEL METHOD OF ORAL ADMINISTRATION OF METHYLPHENIDATE TO RATS REVEALS POST-DRUG MEMORY IMPAIRMENT. LeBlanc-Duchin, D.; Taukulis, H.K.; Chuhan, Y.; Batra, N. University of New Brunswick, Saint John NB, CA. Most studies of methylphenidate hydrochloride in rodents utilize interperitoneal injection as the administration method. Delivered in this way, the drug arrives at the brain in a bolus that is subject to pharmacokinetics that differ in significant ways from those seen when the drug is administered orally (Gerasimov, 2000). It has been argued (Vitiello, 2001; Volkow and Insel, 2003) that, due to its greater clinical relevance, the oral mode of administration should be given more attention in animal studies. With many types of drugs, it is difficult to get rodents to ingest drugs unless they are forced, as with a relatively stressful gavage method. Recently, LeBlanc-Duchin and Taukulis (2004) reported a reliable and effective oral administration procedure for methylphenidate. Essentially, the drug is mixed with moistened, powdered rat chow and is delivered to the animals in their home cages. Food is restricted to certain times of the day, but the animals are not food deprived; indeed, they typically maintain or gain weight while on the regimen. The present study replicated this procedure and subsequently, after a drug washout period, tested the lasting effects of methylphenidate on the rats' ability to recognize familiar objects and their placement. The results indicated that the animals treated with methylphenidate for 20 days exhibited memory impairment relative to untreated controls. The efficacy of the novel drug delivery method was thereby confirmed.

64. ESTABLISHING BEHAVIORAL PARADIGMS FOR THE EFFECTS OF PRENATAL COCAINE EXPOSURE IN RABBITS. Thompson, B.L.; Stanwood, G.D.; Levitt, P. Dept. of Pharmacol. and Vanderbilt Kennedy Ctr. for Res. on Human Develop., Vanderbilt Univ., Nashville, TN, USA. Previous studies from our laboratory have demonstrated that prenatal exposure to cocaine results in permanent alterations in morphology and cellular functioning in dopamine rich areas of the developing brain. Circuitry in these areas is involved in executive function, attention, and reward. Recent clinical research has reported that children exposed to cocaine in utero exhibit behavioral abnormalities, including changes in attention and emotional reactivity. Previous research from our laboratory has shown that rabbits previously exposed to cocaine (3mg/kg i.v., bid) during embryonic days 16-25 displayed long-lasting tolerance to amphetamine as adolescents; in contrast, the mothers previously exposed to cocaine during pregnancy displayed sensitization to amphetamine months after cocaine exposure. These results suggest alterations in drug sensitivity and reactivity based on developmental stage of drug exposure. The current experiments were designed to use this animal model of prenatal cocaine exposure to replicate and further characterize behavioral changes, comparable to what has been shown in humans. We adapted several established rodent behavioral paradigms, and examined specific behaviors in the adolescent rabbits. We have now assessed locomotion, attention, conditioned place preference, and short term memory in adolescent rabbits. Our data suggest that prenatal cocaine disrupts behaviors mediated via dopamine rich brain regions, but does not cause a global disruption in behavior. Furthermore, these studies demonstrate feasible strategies for comprehensive behavioral analysis in rabbits.

65. EVALUATION OF AMPHETAMINE WITHDRAWAL-INDUCED ANHEDONIA USING A LICKING MICROSTRUCTURE ANALYSIS. Baird, J.P.; Molchen, W.A.; Marks, G. Dept. Psychology; Neuroscience Program, Amherst College, Amherst, MA 01002. Traditional one- and two-bottle preference tests have been used to characterize anhedonia in animal models of depression. However, inconsistent results have occasionally been obtained with these tests. We evaluated whether licking microstructure analysis could provide a fruitful alternative to measurement of anhedonia through ingestion. In addition to measuring intake, the temporal distribution of licking over the intake test is recorded with millisecond resolution to provide several measures including meal duration, ingestion rate, lick volume, and size and number of licking bursts. Adapting the protocol of Barr & Phillips (1999), 12 non-deprived male rats received an ascending series of 10 i.p. d-amphetamine (AMPH) injections (1 to 10 mg/kg) over 4 days. Rats ingested 0.12M sucrose daily in a lickometer for 4 days both before and during AMPH injections, and for 8 tests after AMPH withdrawal. AMPH withdrawal had no significant effect on intake over the test session. However, analysis of the first meal taken in the 2h test session indicated a marginally significant ($p=0.06$) decline in intake on the first withdrawal day. There was no effect of AMPH withdrawal on the initial rate of licking (first minute),

mean burst size, or lick volume. However, both the meal duration and number of bursts in the meal were significantly reduced (ps < 0.05), and the rate of ingestion was significantly increased ($p < 0.03$) on the first day after AMPH withdrawal. A control group of 8 rats with matching vehicle injections expressed no significant changes in licking or intake after vehicle withdrawal. Results suggest that licking microstructure analysis may provide a sensitive measure of anhedonia through ingestion, although additional tests are necessary.

66. OREXIN-1 RECEPTORS MEDIATE FOOD AND WATER INTAKE RELATED EFFECTS OF OREXIN-A IN THE BED NUCLEUS OF STRIA TERMINALIS. Lenard, L.; Hangodi, O.; Bagi, E.; Urban, B.; Fekete, E., Toth, K. Neurophysiology Research Group of the HAS and Institute of Physiology, Pecs University Medical School, Pecs, Hungary. In our previous experiments orexin-A (OXA) microinjections into the bed nucleus of stria terminalis (BST) evoked an increase in liquid food intake and water intake and these effects were dose dependent. Since in the BST high level of orexin-1 receptor (OX1R) mRNA was observed, in the present experiments the effect of selective OX1R antagonist SB 334867 was examined in male Wistar rats. 100 ng (0.26 nmol) SB 334867 (Tocris 1960) was applied alone or 15 min prior 500 ng (0.14 nmol) OXA (Sigma, 0-6012) microinjections. Drugs were dissolved in sterile saline and were microinjected bilaterally into the BST in 0.4 ml volume. Four different groups of rats were used: vehicle treated, OXA, antagonist treated and antagonist+OXA animals, respectively. Liquid food intake (MilkQuick, Nutricia) or water intake were studied in separate experiments. Without deprivation subjects could consume liquid food or water from 9 h to 12 h every day. After microinjections food or water intake were measured every 5 min for the first 30 min and at the 40th, 60th, 120th and 180th min, respectively. ANOVA analysis showed that OXA significantly enhanced liquid food consumption and increased water intake. Application of the antagonist alone did not modify intakes. Vehicle treated, antagonist treated or antagonist+OXA groups did not show any significant differences, neither in milk, nor in water ingestion. Our results show that OXA effects on milk ingestion and on water intake can be antagonized by SB334867 and that OXA effects in the BST are mediated by OX1Rs. This work was supported by OTKA C012, M036687 and by the HAS.

67. EFFECT OF PERCHLORATE ADMINISTRATION AND ETHANOL CONSUMPTION ON THYROID HORMONE AND BRAIN CATECHOLAMINE CONCENTRATIONS IN THE RAT. James, N. L.; Williams, H. L.; McMillen, B. A. Dept. of Pharmacol. & Toxicol., Brody Sch. of Medicine, East Carolina Univ., Greenville, NC 27834 USA. Exposure to perchlorate may adversely affect thyroid hormone production and the subsequent functioning of the thyroid gland. In addition, ethanol consumption can deleteriously affect thyroid functioning through a reduction in thyroid hormone concentrations. The present investigation served to assess the effects of concomitant administration of both environmental contaminants on thyroid hormone functioning. Subjects were female, Myers' high ethanol preferring [mHEP] rats and randomly assigned to one of four groups: (1) food and water ad lib (control) (2) food and 300 ppb perchlorate solution only (3) food, water, and 10% ethanol (4) food, 300 ppb perchlorate solution and 10% ethanol (v/v in 300 ppb perchlorate). Body weight, consumption of food, water, perchlorate, and ethanol were measured daily. Average perchlorate consumption was 0.03 mg/kg/rat/day and ethanol consumption was 6.9 g/kg/rat/day. After the 21-day treatment period, plasma T3 and T4 were measured with a RIA kit and brain area concentrations of norepinephrine (NE), dopamine (DA) and DOPAC were measured by HPLC-ECD. The T3 control concentration was 67.93 ± 2.04 ng/dl; the T4 concentration was 4.25 ± 0.80 ug/dl. No treatment differed significantly from these values. Concentrations of NE and DA were unaltered in prefrontal cortex and corpus striatum; dopamine was altered significantly in the hypothalamus. The data suggest that these levels of consumption by the rat have no effect on thyroid hormone levels and minimal effect on brain catecholamines. Whether or not higher levels of perchlorate will add to the effects of ethanol remains to be elucidated.

Neurochemical Basis of Behavior

68. EFFECTS OF OREXINS/HYPOCRETINS ON INTRACELLULAR CALCIUM IN NEURONS OF THE MEDIAL PREOPTIC AREA IN RATS. Takatsuna,M[1]. Watanabe,K[1]. Nakajima,K[1]. Oomura,Y[2]. Wayner,M.J[3] and Sasaki,K[1]. [1]Div.of Bio-Information Engineering, Fac. of Engineering, Toyama University.Toyama,930-8555,Japan; [2]Dept. of Integrative Physiology, Grad. Sch. of Medical Science, Kyushu University, Fukuoka 812-0054, Japan; [3]Dept. of Biology, The university of Texas at San Antonio, TX 78249-0662, U.S.A. Orexin-A (ORX-A) and orexin-B (ORX-B), also called hypocretin-1 and hypocretin-2, respectively, act upon orexin1 (OX1R) and orexin2 (OX2R) receptors, and are involved in the regulation of feeding, sleep-wakefulness and sexual behavior. In the hypothalamus, orexin neurons project to the medial preoptic area (MPOA), which plays an important role in the

regulation of sexual behavior and sleep-wake state in rats. Therefore, the effects of ORX-A and ORX-B on MPOA neurons were investigated using cytosolic Ca2+ concentration ([Ca2+]i) imaging study in brain slice preparations of male rats. When ORX-A and ORX-B were applied to MPOA neurons, ORX-A and ORX-B increased [Ca2+]i with greater responses for ORX-B. In the presence of SB-334876-A, a selective blocker of OX1R receptors, dose-response curves for ORX-A and ORX-B shifted to the right, but the shift was greater for ORX-A than for ORX-B. The results suggest that MPOA neurons have both OX1R and OX2R receptors, but OX2R receptors are more than OX1R receptors. ORX-A and ORX-B increased [Ca2+]i under artificial cerebrospinal fluid (ACSF) containing tetrodotoxin as well as normal ACSF, suggesting that orexins directly affect MPOA neurons, but not through synaptic transmissions. Increase of [Ca2+]i induced by ORX-B under normal ACSF disappeared completely in about 80% of neurons tested under ACSF containing N-methyl-D-glucamine (NMDG), but not Na+. [Ca2+]i increase induced by ORX-B under normal ACSF was also attenuated significantly under ACSF containing Ni2+ or staurosporin, a inhibitor of PKC activation. KB-R7943, an inhibitor of Na+/Ca2+ exchanger, and H-89, an PKA inhibitor, had no effect on the increase of [Ca2+]i induced by ORX-B. The present results suggest that in most of MPOA neurons, orexins increase [Ca2+]i via non-selective cation channels and Ni2+ sensitive voltage-dependent Ca2+ channels, and that some of Ni2+ sensitive voltage-dependent Ca2+ channels are PKC dependent. Therefore, orexins may participate in the regulation of sexual behavior and sleep-wake state through the activation of MPOA neurons.

69. SENSITIZED ATTENTIONAL PERFORMANCE AND FOS-IMMUNOREACTIVE CHOLINERGIC NEURONS IN THE BASAL FOREBRAIN. Martinez, V.; Parikh, V.; & Sarter, M. Dept of Psychology, Biopsychology Area. University of Michigan, Ann Arbor MI, 48109-1109 USA. The consequences of repeated exposure to psychostimulants have been hypothesized to model aspects of schizophrenia. The present experiment assessed the consequences of the administration of an escalating dosing regimen of amphetamine (AMPH) on attentional performance. Fos-immunoreactivity (Fos-IR) in selected regions of these rats' brains was examined in order to test the hypothesis that AMPH-sensitized attentional impairments are associated with increased recruitment of basal forebrain cholinergic neurons. Rats were trained in a sustained attention task and then treated with saline or in accordance with an escalating dosing regimen of AMPH (1-10 mg/kg). Performance was assessed during the pretreatment and withdrawal periods, and following the subsequent administration of AMPH-'challenges' (0.5, 1.0 mg/kg). Brain sections were double-immunostained to visualize Fos-IR and cholinergic neurons. Compared with the acute effects of AMPH, AMPH-'challenges', administered over 2 months after the pretreatment was initiated, resulted in significant impairments in attentional performance. In AMPH-pretreated and -challenged animals, an increased number of Fos-IR neurons was observed in the basal forebrain. The majority of these neurons were cholinergic. The evidence supports the hypothesis that abnormally regulated cortical cholinergic inputs represent an integral component of neuronal models of the attentional dysfunctions of schizophrenia.

70. DIFFERENTIAL SENSITIVITY OF AMPHETAMINE-EVOKED ROTATIONAL BEHAVIOR TO DOPAMINE SYNTHESIS BLOCKADE EARLY AFTER UNILATERAL NIGROSTRIATAL OR CORTICAL DAMAGE. Paquette, M.A.; Hutchings, J.E.; Marsh, S.T.; Castañeda, E. Department of Psychology, Arizona State University, Tempe, AZ 85287. Three transient phenomena have been observed after damage involving dopamine (DA) systems: 1) elevated spontaneous levels of striatal DA metabolites, 2) elevated amphetamine (AMPH)-induced DA overflow, and 3) AMPH-induced behaviors. We postulate a disruption in DA turnover and currently are exploring whether modified DA synthesis contributes to these phenomena. Rats sustained unilateral nigrostriatal DA depletion or hemidecortication. At 24 hr or 14 days later, they were pretreated with the tyrosine hydroxylase (TH) inhibitor alpha-methyl-para-tyrosine (a-MPT; 0, 10, 32, 56, or 100, or 320 mg/kg) and tested for AMPH-evoked rotational behavior (ARB, 1.5 mg AMPH/kg). In DA-depleted rats, a-MPT was ineffective in reducing ARB at 24 hr but dose-dependently attenuated ARB mediated by the intact hemisphere after two weeks. a-MPT dose-dependently blocked ARB in hemidecorticate rats at 24 hr. The insensitivity of ARB to a-MPT 24 hr after DA depletion suggests that mechanisms other than synthesis may be altered early after neurotoxin exposure, including nonspecific spillage of neurotransmitter from dying cells. Conversely, the sensitivity of ARB to a-MPT after hemidecortication suggests that synthesis modulates ARB after cortical damage. We are currently developing a neurological test battery to evaluate behavioral function after nigrostriatal or cortical damage. Future research will quantify accumulation of DA precursor after a-MPT to explore changes in synthesis following damage. The ultimate goal of this research is to develop and test emergency interventions for brain trauma that will promote compensatory mechanisms and prevent dysfunctional processes to achieve the best possible outcome.

71. MODULATION OF CORTICAL ACETYLCHOLINE RELEASE VIA GLUTAMATERGIC AND D1 INTERACTIONS IN THE NUCLEUS ACCUMBENS A.Zmarowski[1]; M.Sarter[2]; J.P.Bruno[1] 1.

Psychology, Ohio State Univ., Columbus, OH, USA 2. Psychology, Univ. of Michigan, Ann Arbor, MI, USA. The basal forebrain cortical cholinergic system (BFCS) is essential for attentional processing. The BFCS is regulated, in part, by the nucleus accumbens (NAC) and its GABAergic medium spiny projection neurons (MSN). The MSNs are sites of convergence of glutamatergic (Glu) inputs from the amygdala, hippocampus and prefrontal cortex (PFC), and dopaminergic (DA) inputs from ventral tegmentum. NAC NMDA receptors are positively modulated by D1 receptors. This experiment determined whether D1 modulation is evident in targets of the NAC such as the BFCS, and ultimately, in changes in cortical acetylcholine (ACh) release. We previously reported that NMDA administration into the NAC increases ACh efflux in PFC. Here we report that interactions between NAC NMDA and D1 ligands affect PFC ACh efflux. Intra-NAC perfusion of 150 or 250 μM NMDA similarly increased cortical ACh efflux (by 150%). Co-administration of the D1 antagonist SCH-23390 (150 μM) attenuated the increase observed following the moderate concentration of NMDA, but not following the higher concentration of NMDA. We then determined whether the D1 agonist SKF-81297 (200 μM) would potentiate the effects of a low concentration of NMDA (75 μM) that does not increase ACh when administered alone. Results indicate this is not the case. The antagonist data indicate that D1 receptor activation contributes to increases in cortical ACh following certain concentrations of NMDA. These studies provide a platform by which DA and Glu interactions in the NAC can influence activity of the BFCS, and may ultimately contribute to higher functions like attentional processing. *Support Contributed By: PHS grants MH57436, NS37026, MH06314 and MH01072.*

72. A TESTOSTERONE METABOLITE IS REWARDING TO FEMALE RATS Kandy T Velázquez1, Dinah Lee Ramos3, Ileana Lorenzini3#, Jessica Marrero3^, Carmen S. Maldonado-Vlaar3* and Juan Carlos Jorge2 Department of Physiology 1 and Department of Anatomy 2, Medical Sciences Campus, Department of Biology3, Rio Piedras Campus, University of Puerto Rico, San Juan, Puerto Rico 00931 Anabolic androgenic steroids have become a major class of drugs of abuse among a growing population of male and female adolescents. Although the rewarding and reinforcing properties of androgens have been demonstrated in male rodents, it is unknown whether these properties are apparent among females. In this study, evidence shows that the endogenous androgen metabolite 3aDIOL is rewarding and reinforcing in ovariectomized (OVX) females according to the conditioned place preference (CPP) and self-administration (SA) paradigms. Specifically, a significant enhancement of the preference to the drug compartment was found in 3a DIOL group of OVX females when compared to vehicle controls on the test day ($p<0.001$) in the CPP. In addition, group factor significant differences were found between OVX-DIOL vs. EB-DIOL ($p < 0.001$), EB-V ($p < 0.01$) and OVX-V ($p <0.05$). These effects were not seen in OVX females that received estrogen replacement therapy. With regard to SA, a significant difference was observed in treatment factor ($p<0.05$). Since 3aDIOL can be synthesized de novo in the brain, it is hypothesized that this neurosteroid can provide a permissive neurochemical environment that can modulate reward processes. Support provided by the MBRS-RISE Program at MSC-UPR (GM61838) to IL and JM. Study funded by the NIH-COBRE (RR15565) to CSM-V and JCJ.

Sexual Differentiation

73. PERINATAL ACTIVATION OF ESTROGEN RECEPTOR â DEFEMINIZES THE DISPLAY OF SEXUAL BEHAVIOR. Kudwa, A.E.; Gatewood, J.D.; Michopoulos, V.J.; Rissman, E.F. Dept. of Biochem. and Molec. Genetics, University of Virginia, Charlottesville, VA, 22903 USA. Developmental differences in circulating gonadal steroid concentrations contribute to sexual dimorphisms in brain and behavior. Neonatal testes produce androgens, thus, males are exposed to both testosterone and estradiol, whereas females are not exposed to high concentrations of either hormone until puberty. Estradiol activates two processes in male neonates; masculinization, the development of neural circuits required for male-type behaviors, and defeminization, the failure to develop the neural circuits required for the display of female-type behaviors. We tested the hypothesis that defeminization is regulated by estrogen KO) and wildtype (WT) mice wereβ knockout (ERβreceptor â (ERâ). Adult male ER castrated, treated with estradiol benzoate (EB) and progesterone (P) and tested for receptive behavior. Indicative of incomplete defeminization, ERâKO males showed significantly more lordosis than WT littermates. Testes-intact males did not differ in their male sexual behavior regardless of genotype. To extend these data to WT mice, females were treated on postnatal days 1-3 with DPN (ERâ-selective agonist), PPT (ERá-selective agonist), estradiol or DMSO. Adult mice were ovariectomized, treated with EB and P and tested for female sex behavior. Females receiving neonatal DPN or E showed less lordosis behavior than PPT- or DMSO-treated females. These results support our hypothesis that perinatal activation of ERâ can defeminize sexual behavior.

This novel aspect of ERâ function may lead to developments in our understanding of neural-based sexually dimorphic human behaviors.

74. SPINE DENSITY IN THE RAT BASOLATERAL AMYGDALA IS SEXUALLY DIMORPHIC. Rubinow, M.J.[1]; Juraska, J.M.[1-2] [1]Dept. of Psychology and [2]Neuroscience Program. The University of Illinois at Urbana-Champaign, Champaign, IL 61820 USA. In spite of the sex differences found to interact with stress in a variety of tasks, little research has examined the influence of sex on the anatomy of the Basolateral Amygdala, which is involved in cognitive behaviors with an emotional or stressful component. The influence of age on performance of tasks like the water maze can likewise interact with stress response. Here, we investigated spine density in Golgi-Cox stained neurons of the basolateral nucleus of the amygdala (BL) in young and old, male and female Long Evans hooded rats. We quantified spine density on non-terminal dendritic sections, 40-100 microns from the soma, of primary BL neurons. All tissue was coded to prevent experimenter bias. Young males had greater spine density than young females ($p = .017$). Age had no influence on spine density. Currently we are investigating dendritic complexity in the same subjects to determine whether age or sex influences dendrites, and by extension how both factors affect spine number. The present results together with the analysis of BL dendrites may help to elucidate the substrate of reported sex differences in human processing, and lab animal performance, of a variety of emotional or stress-related tasks. Supported by NSF IBN 01-36468

75. NON-TOXIC DOSES OF ENDOCRINE DISRUPTERS IMPAIR SEXUAL DIFFERENTIATION OF BEHAVIORS AND ENHANCE DEPRESSIVE BEHAVIOR IN RATS Aou, S.; Fujimoto, T.; Kubo, K. Dept. Brain Sci. and Eng., Kyushu Inst. Technol.1, Dept. Otorhinolaryngol., Kyushu Univ. We demonstrated that perinatal six weeks exposure to bisphenol A (BPA, 0.1ppm) and diethylstilbestrol (DES, 50ppb) impaired the sexual differentiation of the locus coeruleus and exploratory behaviors even though the dosage was below the tolerable daily intake level (TDI of BPA, 50μg/kg/day) (Kubo et al. 2003). In this study, we exposed 0.1ppm of BPA to mother rats just before or after delivery for one week, then examined its effects on sexual differentiation of exploratory behavior and emotional behaviors such as anxiety and depression. In the open field test, control females explored more frequently than males. This sex difference was not affected by neonatal BPA treatment but was abolished by prenatal treatment. The time spent in open arms in the elevated plus maze test decreased by neonatal or prenatal BPA treatment although sex difference was not clearly affected. In the forced swimming test, both prenatal and neonatal BPA exposures increased immobility time, an index of depressive behavior, in male rats and reduced immobility latency in both sexes. These findings suggest that prenatal BPA exposure is more effective to impair sexual differentiation of exploratory behavior but neonatal period is also important for development of emotional behavior.

76. FLUOXETINE EXPOSURE DURING NEONATAL DEVELOPMENT ALTERS ACCESORY OLFACTORY BULB MORPHOLOGY ACCORDING TO SEX. Melendez, D. 1; Lugo, N. 1,2; Jorge, J.C.2. Institute of Neurobiology1 and Department of Anatomy2, Medical Sciences Campus, University of Puerto Rico, San Juan- Puerto Rico 00936 Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) used widely employed in the management of affective disorders. This SSRI can also inhibit hydroxysteroid oxidoreductase, a key enzyme in the biosynthetic pathway for neurosteroid production. The aim of this study is to determine the effects of this SSRI in the neuroanatomical profile of mitral and granular cells of the accessory olfactory bulb (AOB). Neonatal rats were injected (s.c.) daily from postnatal (PN) day 1 to 14 with fluoxetine in sesame oil vehicle (1mg/kg at a volume of 0.01cc/2g body weight), while controls received vehicle injections alone. On PN 75, rats were decapitated, the brain was removed and post fixed. Coronal sections (16 microns) of the olfactory bulbs were made and stained with cresyl violet. The NIH Image Analysis Program was employed to measure cell body and cell layer areas. We found that neonatal exposure to fluoxetine induced a significant change in AOB mitral and granular cell morphology in males but not in females. Specifically, Two Way Anova analysis revealed treatment effects ($P < 0.001$), sex effects ($P < 0.001$), and treatment x sex interaction ($P < 0.001$). The average area of mitral cells was enlarged in males treated with fluoxetine from 74.095 to 99.175 μm2 ($p < 0.05$), whereas cell area for granular cells was enlarged from 21.410 to 30.295 μm2 ($p < 0.05$). With regard to cell layer area, we found that there was not a significant effect.These results show, for the first time, that fluoxetine exposure during neonatal development alters AOB morphology. Study funded by RCMI-MSC (G12 RR 03051) to JCJ, and NIH-COBRE I (RR15565) to NL and JCJ.

77. EFFECTS OF ENVIRONMENTAL ENRICHMENT ON SPATIAL AND NON-SPATIAL MEMORY IN MALE AND FEMALE MICE THROUGHOUT THE LIFESPAN. Levy, L.J; Lambert, T.J.; Frick, K.M. Dept. of Psychology. Yale Univ., New Haven, CT 06520 USA. Environmental enrichment has been shown to improve memory in young and aging male and female mice. However, no study has directly compared the efficacy of enrichment to improve various types of memory in both sexes throughout the lifespan. The present study examined young (3 months), middle-aged (15 months), and aged (21 months) male and female C57BL/6 mice to identify the types of memory that

are improved by enrichment and establish whether these improvements vary by age and sex. For four weeks before testing and throughout the testing period, half of the mice were housed in groups of 10 in large bins containing numerous toys, wheels, and objects which provided exercise and cognitive stimulation. The remaining mice were housed in groups of five in standard shoe-box cages without enriching objects. Spatial memory was tested using Morris water maze and water-escape motivated radial arm maze tasks. An object recognition task tested non-spatial memory. Results suggest that spatial memory in the Morris water maze became progressively worse with age in both males and females and enrichment improved spatial memory at all ages. In the radial arm maze, enrichment reduced reference memory errors similarly in males and females, but there was no effect of enrichment on working memory errors in either sex. Enrichment improved non-spatial memory in the object recognition task in aged males, but not aged females. The data suggest that enrichment benefits memory similarly in males and females, but is somewhat more beneficial in aged males than in aged females. Sponsored by the Claude D. Pepper Older Americans Independence Center at Yale University School of Medicine (#P30AG21342).

Physiology of Learning

78. THE MEDIAL THALAMUS IS CRUCIAL FOR WATER MAZE BEHAVIORAL STRATEGIES BUT IS NOT REQUIRED FOR SPATIAL PLACE MEMORY. Cain, D.P.; Boon,F.; Corcoran, M.E. Department of Psychology and Program in Neuroscience, U. Western Ontario, London, ON N6A 5B8 and Department of Anatomy and Cell Biology, U. Saskatchewan, Saskatoon, SK S7N 5A5, Canada. The role of the medial thalamus in acquiring the water maze task was studied using the radiofrequency (RF) lesion technique, which damages both cells and fibers of passage. For studying water maze acquisition it is essential to separate behavioral strategies acquisition (swimming, suppression of thigmotaxis, recognizing and using the hidden platform as a refuge) from learning spatial locations. The use of both naive and nonspatially pretrained groups allows strategies learning and spatial place learning to be studied separately (Morris, 1989). Therefore naive or nonspatially pretrained rats received an RF lesion of medial thalamus followed by a 10 day recovery period and spatial training. Naive RF-lesioned rats were severely impaired in behavioral strategies acquisition on all three days of training and thus failed to learn anything about the hidden platform location. Nonspatially pretrained RF-lesioned rats were indistinguishable from controls on all measures. Preliminary evidence from additional groups given injections of N-methyl-D-aspartate (NMDA) to remove medial thalamic cells but spare fibers of passage indicated a reliable but modest impairment in strategies acquisition by naive NMDA-lesioned rats, but no impairment in nonspatially pretrained NMDA-lesioned rats. These results suggest that the medial thalamus, particularly fibers of passage, is important for acquiring essential water maze behavioral strategies but is not required for normal spatial memory in rats that have command of the required behavioral strategies.

79. MEMORY DEFICITS IN NEONATAL AND JUVENILE RATS FOLLOWING CHRONIC STRESS Hoxha, Z., Mickley, G.A. Department of Psychology and The Neuroscience Program, Baldwin-Wallace College, Berea OH 44017 USA Exposure to chronic stressors produces negative physiological and psychological changes in organisms. Previous studies from this laboratory have measured memory deficits in children and adolescents exposed to traumatic events during the war in Kosovo. Results indicated that exposure to traumatic war experiences caused short term memory impairments when tested four years after the war (Hoxha, 2004). The current experiment attempts to further explore the relationship between chronic stress exposure in young animals and subsequent memory problems. Fifty-two male and female rats were divided in four groups that received the following treatments: (1) stressed as fetuses on E15-E18; (2) not stressed as fetuses (fetal controls); (3) stressed as juveniles on P16-P19; (4) not stressed as juveniles (juvenile controls). Stressed animals received two days of foot shock (0.05mV; three times per trial/ three trials a day) and two days of restraint stress (three trials a day for 20 min). Controls remained in their home cage during these periods. During P25-P27 all animals were tested in a water maze (five trials a day over 3 days) for spatial memory. All rats were sacrificed on P28 for histological analysis. Group differences in learning and memory were most prominent during the last 2 days of behavioral testing. On the second day of testing, rats stressed as fetuses took longer to find the hidden platform than did non-stressed controls. However, rats stressed as juveniles did not show this effect. On the final day of testing, both rats stressed as fetuses or juveniles performed more poorly than did their respective controls. Future analyses will consider the physiological substrates of these stress-induced behavioral deficits (not presented in the abstract).

80. SLEEP DISRUPTION IMPAIRS HIPPOCAMPAL RAT DENTATE GRANULE CELL LTP IN VIVO. Wayner, MJ; Mery, LR; Marks, CA. Department of Biology, The University of Texas at San Antonio, San Antonio, TX 78249 USA. Sleep frequently fragmented or disrupted for prolonged

periods can result in mood changes and impaired mental ability and performance. Sleep deprivation is defined as depriving a person or organism of sleep for various periods of fixed duration. Sleep disruption (SD) occurs when a person is awakened at any time when he/she would normally be sleeping. Because memory has been impaired after sleep disrutpion, several studies have been conducted recently to examine the changes in long term potentiation in hippocampal brain slices following various periods of sleep deprivation in rats. Results of the present study show clearly that LTP is also decreased following SD but to a greater extent than that observed following sleep deprivation. The purpose of the present study was to measure dentate granule cell LTP in anesthetized rats following 1,2, or 3 Day schedules of SD using a modified flower pot procedure. Results showed that a single disruption of 3 hours reduced LTP from a normal 38.7% to 7.6%; that endured for at least 14 hours; and 9 hours reduced it completely. Easy to handle animals became irritable, hyperactive, and aggresive following SD. Results are discussed in terms of stress related effects of SD and changes in synaptic plasticity.

81. THE RAT P300 ERP TO SIGNALED OCCURRENCE AND OMISSION OF EXPECTED REINFORCERS FOLLOWING EXTENDED TRAINING. Klipec, W.D.; Schneider, B.; Stanley, K.; Brackney, R. J.; Schwabe, J; and Young, B. Department of Psychology, Drake University, Des Moines, Iowa, USA. A series of experiments in our laboratory have shown that rat P300 ERP amplitude is an incremental function of conditioned stimulus proximity to primary reinforcement in simple behavioral chains, suggesting that the P300 is a correlate of the brain's response to conditioned reinforcers. The present experiment was designed to investigate the P300 response to stimuli correlated with reinforcement (S+) and non-reinforcement (S-). A 500 msec 2.5 KHz non-target stimulus was presented on an 8:1 ratio with a 500 msec 3.5KHz stimulus that predicted the insertion of a lever. Lever responses on VR-6 reinforcement schedule produced a 500 msec tone with a frequency of either 4.5 or 5.5 KHz on a random 50% schedule. One tone predicted the delivery of a 45 mg food pellet while the other predicted the non-delivery of the pellet. S+ and S- tones were counterbalanced across rats. The P300 ERP to the S+ and S- tones were analyzed across 60 days of training. The results showed the development of a P300 ERP to both tones with the amplitude increasing across first the 12 days and maintained across the entire experiment. While the latency of the P300 to S+ was initially greater than the latency to S-, both latencies declined and converged across the first 12 days and did not differ significantly through the remainder of the experiment. These results demonstrate that the P300 ERP extends to the recognition of conditioned aversive stimuli as well as conditioned positive reinforcers. The similarity and stability of both S+ and S- P300 ERPs suggest that the P300 may be independent from reward affect and more related to the informativeness of the stimuli.

82. THE DEVELOPMENT OF THE RAT P300 ERP DURING BACKWARD CHAINING. Stanley, K,; Klipec, W.D.; and Lem, K. Department of Psychology, Drake University, Des Moines, IA 50311 USA. Several experiments in our laboratory shown P300 amplitude to be a incremental function of proximity to conditioned reinforcers in simple behavioral chains. In this paradigm, one tone predicts lever insertion while a second tone signals the click of the food magazine. Since the P300 is consistently strongest to seeing the food pellet, and becomes progressively weaker to the click, pellet tone, and lever tones respectively, we concluded that the P300 is a function of the strength of the conditioned reinforcer. The present experiment was designed to further examine this hypothesis systematically by adding a second lever to the chain leading to food reinforcement. Rats were initially trained in a paradigm where lever insertion (LEV 1) was cued by a 4.5 KHz tone with a non-target (NT) 2.5 KHz tone presented on a variable time schedule at an 8:1 non-target to target ratio. Meeting criterion on a VR-6 schedule produced 5.5 KHz followed by the click of the pellet dispenser signaling delivery of the food pellet. After about seven weeks of training, a second lever (LEV 2) cued by a 3.5 KHz tone was introduced preceding LEV 1. LEV 2 responses, on a VR-6 schedule, produced the LEV 1 cue-sequence. This training continued for about 8 additional weeks. Contrary to what we expected, the P300 amplitude to the LEV 2 tone was consistently greater than the P300 to the LEV 1 tone. One explanation for this is that the LEV 1 cue represents redundant information about the sequence leading to food. LEV 2 is the most informative about the opportunity to engage in the entire sequence leading to food, compared to the NT. To test this we are introducing a third lever into the sequence to see if the greatest P300 amplitude shifts from LEV 2 to LEV 3.

83. ERP EVIDENCE FROM DYNAMIC DISSOCIATION OF TEMPRAL STORAGE AND REHEARSAL OF CHINESE CHARACTERS. Wang,Y.W.; Lin,C.D.; Zhang,W.X. Department of psychology, Shandong Normal University, Jinan 250014 China; Institute of Developmental Psychology, Beijing Normal University, Beijing 100875 China. Working memory (WM) is a system that is used for temporary storage and manipulation of information. For dissociate the brain areas involved in verbal storage and rehearsal, event-related brain potentials were measured when 14 normal young participants were performing 2-back task, 0-back task and rehearsal task of Chinese characters. The difference wave N430 appeared at the posterior of the scalp by subtraction of ERP in the rehearsal

task from that in 2-back task, which probably reflected the short-term storage and its time-course. The difference wave of sustained negative component (SNC) appeared at the anterior of the scalp by subtraction of ERP in 0-back task from that in 2-back task, which is a likely dynamic index of rehearsal processes. Frontal lobe and posterior areas of brain maybe govern the rehearsal and short-term storage, respectively. The dynamic division of both areas possibly is neural base of temporarily maintaining in verbal WM. Key words working memory, event-related potentials (ERPs), storage, Chinese character

84. EFFECT OF EMOTIONAL CONTENT ON DECLARATIVE MEMORY: AN EVENT RELATED POTENTIAL STUDY. (1) Gasbarri, A.; (1) Arnone, B.; (1) Pompili, A.; (1) Marchetti, A.; (1) Pacitti, F.; (2) Saad Calil, S.; (1) Pacitti, C.; (2) Tavares, M.C.; (2) Tomaz, C. (1) Dept. of Sciences and Biomedical Technologies. University of L'Aquila, 67100 L'Aquila, Italy. (2) Dept. of Physiological Sciences, Laboratory of Neurosciences and Behavior. University of Brasília, CEP 70910-900 Brasília, DF, Brazil. Several studies suggest that emotional arousal can promote memory storage. In this study we evaluated the effects of emotional content on declarative memory, utilizing an adaptation of two versions of the same story, with different arousing properties (neutral or emotional), which have been already employed in experiments involving the enhancing effects of emotions on memory retention. We used event related potentials to evaluate whether there is a sex-related hemispheric lateralization of electrical potentials elicited by the emotional content of a story. We compared left and right hemisphere P300 waves, recorded in P3 and P4 electrode sites, in response to emotional or neutral stimuli in men and women. In the left hemisphere, emotional stimuli elicited a stronger P300 in women, compared to men, as indexed by both amplitude and latency measures; moreover, the emotional content of the story elicited a stronger P300 in the right hemisphere in men than in women. The better memory for the arousal material may be related to the differential P300 at encoding. These data indicate that both sex and cerebral hemisphere constitute important, interacting influences on neural correlates of emotion, and of emotionally influenced memory.

8:30-10:30 Symposium 4: New insights in ventral striatal organization and physiology: Perspectives for the behavioral sciences. Mesa Ballroom B&C

GLUTAMATE-DOPAMINE INTERACTIONS IN THE NUCLEUS ACCUMBENS: EFFECTS ON CORTICAL ACh RELEASE AND ATTENTIONAL PROCESSING. Bruno, J.P.; Sarter, M.; Neigh, G.; Zmarowski, A. Depts. of Psychology and Neuroscience. The Ohio State University, Columbus, OH 43210 USA. Dysfunctions of attention have been demonstrated in a number of neuropsychiatric disorders and are postulated to contribute to the cognitive impairments that accompany these diseases. The basal forebrain cortical cholinergic system (BFCS) is a necessary component in a distributed neural system mediating attention. Our laboratory investigates the role of cortical cholinergic transmission in attention and the anatomical systems regulating the excitability of the BFCS. The nucleus accumbens (NAC)is a critical input to the basal forebrain, presumably conveying information about incentive salience that then guides attentional processing. Glutamate projections from cortex, hippocampus and amygdala converge on NAC projections to basal forebrain. These glutamate inputs are positively and negatively modulated by DA inputs from VTA. This talk will discuss the the relationship between transmitter modulation in the NAC and basal forebrain excitability. Such interactions provide a basis for incentive values and goals to direct subsequent attentional processing. Supported by MH63114, MH57436, and KO2 MH01072

DOPAMINERGIC MODULATION OF GLUTAMATERGIC RESPONSES IN THE NUCLEUS ACCUMBENS. O'Donnell, P., Brady, A.M., Benoit-Marand, M. Ctr. for Neuropharmacology & Neuroscience, Albany Medical College, Albany, NY 12208, USA The dopaminergic innervation of the nucleus accumbens (NA) is known to decrease the synaptic response of medium spiny neurons (MSN) to glutamatergic inputs from the prefrontal cortex. There has been some debate as to whether this modulation involved pre- vs. postsynaptic receptors and whether D1 or D2 receptors are involved. In vivo intracellular recordings from NA MSN revealed that PFC stimulation evoked synaptic responses that were attenuated by electrical stimulation of the ventral tegmental area; this attenuation was blocked by the D2 antagonist eticlopride, suggesting that endogenously released dopamine acts on D2 receptors to dampen weak prefrontal cortical inputs. In vitro whole cell patch-clamp recordings from NA neurons were conducted in parallel in slices obtained from adult (50-65 days old) rats Bath application of the D2 agonist quinpirole (5 μM) increased the number of spikes in response to intracellular current injection, indicating an increased excitability. EPSP evoked by cortical stimulation were increased by quinpirole in slices from adult, not prepubertal animals. Bath application of the GABA antagonist picrotoxin (50 μM) prevented the quinpirole effect on EPSP but not on excitability, revealing a quinpirole-induced decrease in EPSP amplitude. Moreover, quinpirole decreased FS excitability. It appears that the excitatory D2 effect on MSN was partially due to a GABA component involving fast-spiking interneurons. These results are consistent with the in vivo data, because the D2-mediated decrease in cortical synaptic responses is seen only during depolarizing events (up states), in which GABA responses are close to the reversal potential for chloride and are therefore weak. The data point out to a complex set of interactions between endogenous dopamine, glutamatergic synapses and GABA responses in the nucleus accumbens Supported by NIH grant MH60131 and Fondation Simone et Cino Del Duca

BEHAVIORAL ELECTROPHYSIOLOGY OF THE MOTIVE CIRCUIT. Rebec, G.V.; Wood, D.A. Program in Neural Science and Department of Psychology, Indiana University, Bloomington, IN 47405 USA. The nucleus accumbens (NAcc) integrates cortico-limbic input to modulate goal-directed behavior such as exploration of novel environments, responding for food or drug reward, and sex. To assess how NAcc neurons process motivational information, we used chronically implanted micro-wire electrodes to record the activity of >300 units in male rats performing a variety of goal-directed responses. When exposed to vaginal estrous, the animals showed vigorous approach responses accompanied by activation of NAcc neurons. The neuronal excitations, moreover, were more numerous and more pronounced in response to novel than familiar estrous. Further testing revealed that this neuronal difference is not secondary to motor activation but appears to reflect motivational state. In animals approaching a novel environment, both excitations and inhibitions were recorded in NAcc, although inhibitions dominated in NAcc shell. Thus, the pattern of neuronal firing depends on the nature of the motivational response. To assess stimulus-related information processing, separate animals were trained to perform an operant response (nose poke) for sucrose reward. Subsequent recording in well-trained animals revealed that although small populations of both core and shell units responded to task events such as the cue that signaled nose poke and the nose poke itself, most units were excited by sucrose delivery. During task performance, therefore, the NAcc appears to play a critical role in reward processing. Collectively, our results implicate the NAcc in both the expectation and delivery of reward. Supported by NIDA.

GLUTAMATE MODULATION OF DOPAMINERGIC MOTOR RESPONSES IN THE NUCLEUS ACCUMBENS: TOWARDS AN EXTENDED MODEL OF STRIATAL ORGANIZATION AND MOTOR FUNCTION. Abraini, J.H.; David, H.N. UMR 6185 Université de Caen - CNRS, Centre CYCERON, Boulevard Henri Becquerel, BP 5229, 14000 Caen cedex, France. The basal ganglia organization comprises a direct striato-nigral pathway, the neurons of which mainly expressed D1-like dopaminergic receptors, and a tri-synaptic indirect pathway that comprises a striato-pallidal link, which mainly expressed D2-like dopaminergic receptors, a pallido-subthalamic link, and a subthalamo-nigral link. Interactions between glutamatergic and dopaminergic neurotransmission in the striatum complex (that includes the caudate-putamen and the nucleus accumbens) are modelized by the current model of basal ganglia organization and motor function. Here, we review behavioral motor data obtained in rats that were given focally in the nucleus accumbens agonists and/or antagonists of the ionotropic glutamatergic (iGlu) receptors or the metabotropic glutamatergic (mGlu) receptors before focal administration of dopaminergic agonists allowing D1-like or D2-like receptor activation. Our results show that receptor-receptor interactions between glutamatergic and dopaminergic neurotransmission is not as simple as predicted by the current model of basal organization and motor function, which only considers glutamate and dopamine as neurotransmitters but does not take into account their different receptors. However, data analysis shows that functional interactions between glutamatergic and dopaminergic transmission depends on the type of receptors involved. For example, depending on the receptors involved, glutamate not only possesses an excitatory function, but also an inhibitory function. Finally, given our data, we conclude from a methodological point-of-view that behavioral studies on receptor function and involvement should include both aganists and antagonists investigations.

10:45-11:45 Keynote Speaker: Robert Dantzer. Mesa Ballroom B&C

CYTOKINES AND SICKNESS BEHAVIOR: AN INTEGRATED PERSPECTIVE. Dantzer, R. Integrative Neurobiology, Bordeaux, France, and Integrated Immunology and Behavior, University of Illinois at Urbana-Champaign. Proinflammatory cytokines are soluble mediators that are produced by activated innate immune cells for allowing coordination of the host immune response to pathogenic micro-organisms. These molecules have potent effects on brain functions resulting in the development of the subjective, behavioral, and physiological alterations that characterize an ill individual. They act as motivational signals to reorganize the organism's priorities in face of this particular threat represented by invading micro-organisms. Sickness behavior appears therefore to be a very important response of animals to their microbial environment. In terms of mechanisms, peripherally produced cytokines do not act directly on the brain. They induce the expression of the same cytokines in the brain by macrophage like cells and microglia. The peripheral immune message is transmitted to the brain via humoral and neural pathways, the relative importance of which depends on the end point. It is still unclear whether brain cytokines act directly on neurons or indirectly via alteration in glial cell functions. The production and action of cytokines in the brain are regulated by a number of molecules including anti-inflammatory cytokines, glucocorticoids, vasopressin, alpha-melanotropin and insulin-like growth factor-I. In vulnerable individuals, cytokines induce cognitive alterations and can precipitate the appearance of depressive like symptoms. This is partly due to the activating effects of cytokines on the indoleamine 2,3 dioxygenase enzyme that degrades tryptophan into kynurenine and quinolinic acid and decreases at the same time the bioavaibility of this aminoacid for the synthesis of serotonin. The understanding of the mechanisms of production and action of cytokines in the brain provides new avenues for the treatment of non specific symptoms of disease. (Supported by INRA, CNRS and NIH RO1-MH 71349).

15:15-17:15 Symposium 5: The paradox of acute stress effects on memory: Contrasting views, competing approaches, & compatible findings. Ortiz Ballroom

STRESS PRODUCES TASK- AND MEMORY SPECIFIC SPATIAL MEMORY IMPAIRMENTS: CORRELATIONS WITH MOLECULAR, ULTRASTRUCTURAL, AND HORMONAL FACTORS. Woodson, J.C., Department of Psychology, University of Tampa, Tampa, Florida, 33606, USA. The empirical study of the effects of acute stress on memory is directly applicable to understanding the consequences of traumatic events which happen to people, particularly people who develop post-traumatic stress disorder (PTSD). On one hand, memory for information central to their trauma is enhanced by stress while on the other hand, acute stress impairs memory for information peripheral to the stressful event. Commonly, recurring memories of the trauma lead to chronic stress accompanied by long-lasting cognitive impairments. Highlighting pre-clinical experiments, this presentation addresses a complex and controversial aspect of stress, specifically stress hormone-related effects on memory and brain functions at several levels. In the laboratory, spatial working memory impairments are caused by acute exposure to stressful events, including predator exposure or reexposure to a fear-avoidance conditioning context. In addition to non-linear correlations with stress hormone levels, working memory impairments are associated with brain region-specific fluctuations at the molecular and ultrastructural level. Observed changes include downregulation of neural cell adhesion molecule isoforms in hippocampus and PFC, and changes in dendritic spine

distribution in hippocampal CA1 neurons. Task-specific and brain region-specific analyses of the paradoxical effects of acute stress on memory will be presented.

MECHANISMS OF AMYGDALA MODULATION OF HIPPOCAMPAL PLASTICITY Akirav, I. (1,2); Richter-Levin, G. (2). (1) Neurobiology Dept., Weizmann Institute of Science, Rehovot 76100, Israel (2) The Brain and Behavior Research Center, Haifa University, Haifa 31905, Israel. Ample research has shown that the amygdala mediates the effects of stress on learning and memory. Specifically, it has been suggested that the basolateral amygdala (BLA) modulates the formation of emotionally-based memories in the hippocampus. We used long-term potentiation (LTP) and a spatial task to examine under which conditions the effects of stress or amygdala activation on hippocampal dependent memory change from improvement to impairment. We found that activating the BLA immediately before perforant path tetanization enhances hippocampal LTP, whereas stimulation in a spaced interval results in its suppression. This biphasic effect on hippocampal plasticity was found to be mediated by norepinephrine and corticosterone. Possibly, at the onset of an emotional event the stress hormones permissively mediate plasticity. However, their prolonged presence in the system may suppress the cognitive response to stress. Using the water maze spatial task, we manipulated the level of stress the animals experience by training in either cold water (moderate stress) or warm water (mild stress). Rats trained in cold water showed learning-specific activation of extra cellular-signal regulated kinase in the amygdala. The cold water trained animals performed better in the task and showed higher levels of corticosterone than animals trained in warm water. Injecting corticosterone to warm water trained rats improved their performance in the task whereas blocking corticosterone synthesis in cold water trained rats impaired their performance. Thus, under the conditions described, corticosterone was shown to be instrumental in the acquisition of the spatial learning task.

FEMALES UNDER STRESS: WHY THEY KEEP CHANGING THEIR MINDS. Tracey J. Shors, Ph.D., Dept. of Psychology and Center for Collaborative Neuroscience, Rutgers University, Piscataway, NJ 08854. Women are much more likely than men to experience depression and other stress-related disorders such as post-traumatic stress and generalized anxiety disorder. In previous studies, we have shown that female rats respond to stressful experience very differently than males. Specifically, exposure to an acute stressful event enhances associative learning in males but impairs the same type of learning in females (Wood and Shors, 1998, 2001, Shors et al. 1998, 2002, 2004). These opposite effects of stress on learning are mediated by differing hormonal substrates and associated with anatomical differences in the brain. The effects of stress in females also change across the lifespan. In the symposium I will focus on recent studies showing that learning in females is affected by stress differently in puberty than in adulthood (Hodes and Shors, 2005). I will also discuss the effects of stress on learning during pregnancy and post-partum, with an emphasis on post-partum. The effects of stress on learning during post-partum are suppressed and likewise suppressed in virgin females that act maternal in the presence of offspring (Leuner et al., 2005). Finally, I will discuss how these effects of stress on learning in females respond to controllability and to antidepressant treatment (Leuner et al., 2004). These findings have implications for understanding sex differences in human behavior and mental disorders such as unipolar depression and post-traumatic stress disorder (PTSD). [supported by NIMH (59970) to TJS]

OPPOSING EFFECTS OF GLUCOCORTICOIDS ON MEMORY CONSOLIDATION AND MEMORY RETRIEVAL. Roozendaal, B. Center for the Neurobiology of Learning and Memory, Dept. of Neurobiology and Behavior. University of California, Irvine, CA 92697 USA. Glucocorticoid hormones induce dose-dependent enhancement of the consolidation of newly acquired information. Findings from our laboratory indicate that the basolateral amygdala (BLA) is a critical component of the neural circuitry mediating glucocorticoid effects on memory consolidation. Lesions of the BLA or a beta-adrenoceptor antagonist infused into the BLA block the enhancing effects of posttraining systemic or intrahippocampal glucocorticoid administration on memory consolidation. These findings indicate that noradrenergic activity within the BLA is a co-requirement in enabling glucocorticoid effects on memory consolidation. These findings are consistent with recent evidence suggesting that glucocorticoids only modulate memory consolidation under emotionally arousing conditions that induce the release of norepinephrine in the BLA. In contrast, memory retrieval and working memory performance are impaired with high circulating levels of glucocorticoids. In recent experiments we found that glucocorticoid-induced impairment of these two memory functions also requires the integrity of the BLA and noradrenergic neurotransmission. As our findings indicate that BLA influences on other brain regions in regulating glucocorticoid effects on memory are not restricted to the consolidation of long-term memory but extend to memory retrieval and working memory, they provide compelling evidence that the BLA is part of an integrated network of cortical and subcortical brain regions engaged in regulating several, and often opposite, stress hormone effects on different aspects of memory function.

17:30-18:24 Oral Session 4: Plasticity. Ortiz Ballroom

FROM 'LOOPING' TO 'HOME BASE': HOW PRE-EXPLORATION PROGRESSIVELY BECOMES ANCHORED TO THE OPEN-FIELD. Avni R., Zadicario P., Roitburd A., and Eilam D. Dept. Zoology, Tel-Aviv University, Israel When introduced into a dark open field, rodents initially display a phase of pre-exploration of 'looping', moving continuously in circular paths at the center of the arena. These loops then spread all over the arena. Here we describe that in a 50 min exposure to a dark open field there is a progressive transition from the initial pre-exploratory phase of 'Looping' to exploration which is organized in relation to 'Home base'. This transition is characterized by three changes: 1) During 'Looping" the rodent spends equal time in the various zones of the arena, but with time, it increases its duration in one of the corners. 2) Nodes of loops that were first scattered over the entire arena, gradually amalgamate in corners and along the perimeter, and then converge to one corner as in 'home base' behavior. 3) Traveling distance gradually decreases to a level similar to the initial level in light. Thus, rodents in a dark open field gradually shift from an initial pre-exploratory 'Looping' phase that features a feeble coupling with the environment, to a phase of 'home base' behavior which is firmly anchored to the physical structure of the environment.

HOW LEARNING LIKE ARE NEUROPLASTIC MECHANISMS OF LASTING CHANGE IN ANXIETY INDUCED BY SEVERE STRESS? Adamec, R.; Blundell, J.; Strasser, K. Dept. of Psychology, Memorial University, St. John's, Newfoundland, A1B3X9, Canada. Unprotected predator stress lastingly increases anxiety and hyperarousal in rodents. Brain changes underlying behavioral changes involve in part NMDA receptor dependent LTP-like changes in hippocampo-amygdala and amygdalo-PAG transmission. NMDA dependent pCREB cascades are also implicated in initiation of limbic LTP. Consolidations of some stress induced behavioral changes appear protein synthesis dependent. However, repeated exposure to predator stress does not render reconsolidation of behavioral changes vulnerable to protein synthesis inhibition. Study of egr-1 mRNA expression induced by predator stress does not support the idea that mechanisms common to fear conditioning mediate changes in anxiety like behavior, at least in the amygdala.

A BEHAVIORAL HOMEOSTASIS THEORY OF THE EVOLUTIONARY SIGNIFICANCE OF HABITUATION AND SENSITIZATION. *Eisenstein,E.M.;Eisenstein,D.;**Smith,J.C.;Clark,K.B. *West Los Angeles VA Med.Ctr. **F.B.I., L.A., CA. Habituation may be viewed as a decremental behavioral change to iterative stimuli of little comparative relevance. It is generally observed from aneural protozoa to humans with great similarity. If habituation is interpreted as a way to filter out unimportant repetetive stimuli, then how should sensitization be interpreted? The 'behavioral homeostasis theory' views these two behaviors as opposing or antagonistic homeostatic processes which optimize an organism's ability to detect and assess the significance of current and future stimuli. Thus, organisms at a high level of 'alertness' (due primarily to changes in circadian biorhythms) prior to experiencing a new iterative stimulus will show a large initial response followed by a decrement (habituation) when the stimulus is of little significance. Conversely, the same organism at a low level of 'alertness' will show a small initial response followed by an increase in 'alertness' and a larger response to the next stimulus (sensitization) in order to receive enough information to assess its significance. The level of responsiveness achieved in both habituaters and sensitizers, as an asymptote is approached, is therefore a balance between being too 'alert' to an unimportant stimulus and consequently missing other significant stimuli and being too 'un-alert' and consequently missing a possible change in the relevance of the present iterative stimulus. Such behavioral homeostatic processes to optimize detection and assessment of constantly occurring external stimuli are critical for organism survival throughout phylogeny.

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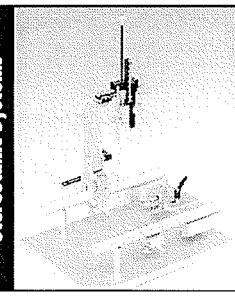

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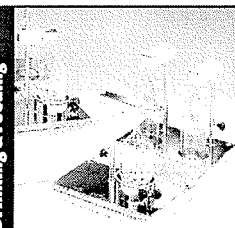

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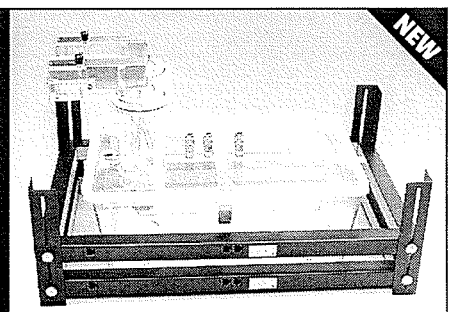

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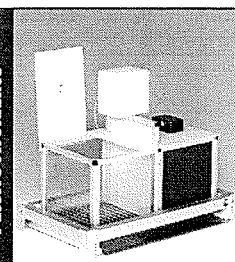

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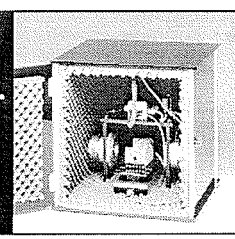

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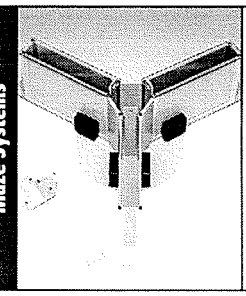

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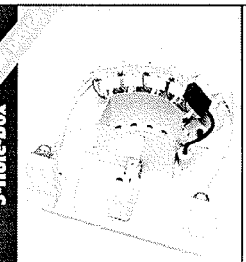

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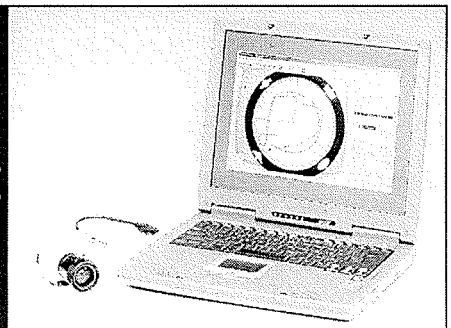

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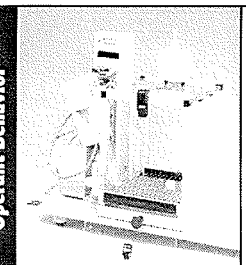

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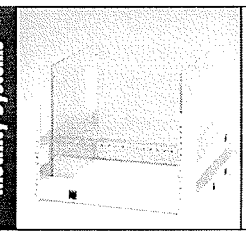

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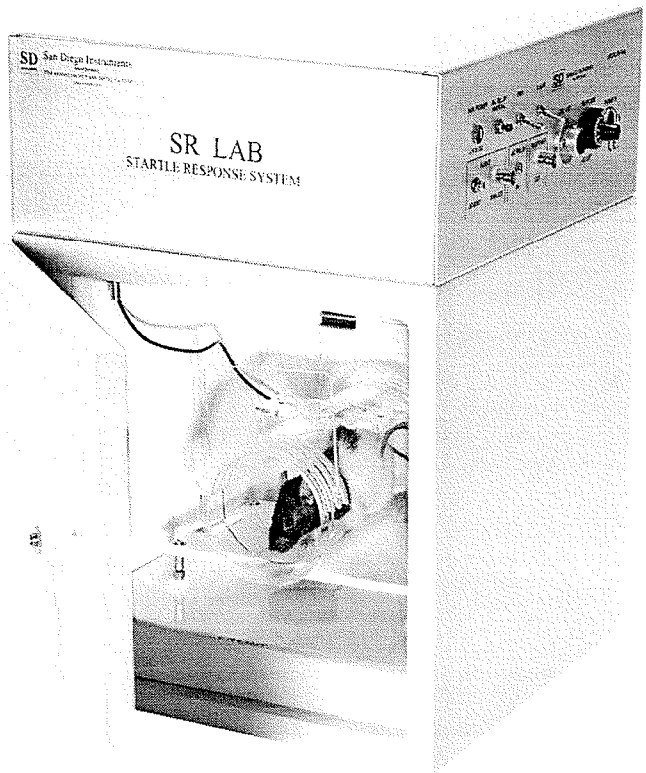

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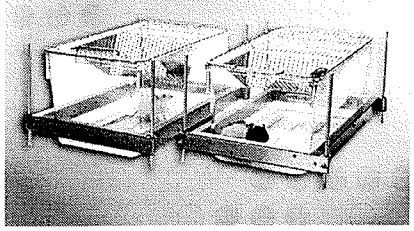

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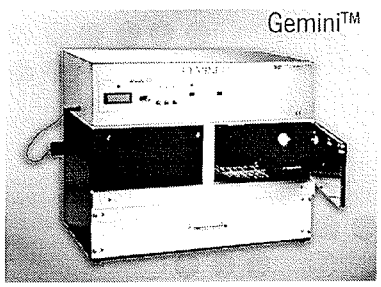

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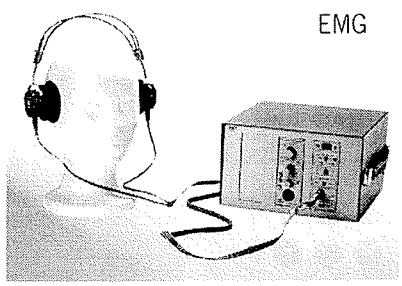

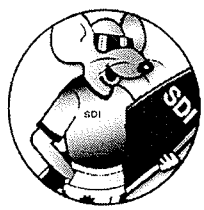

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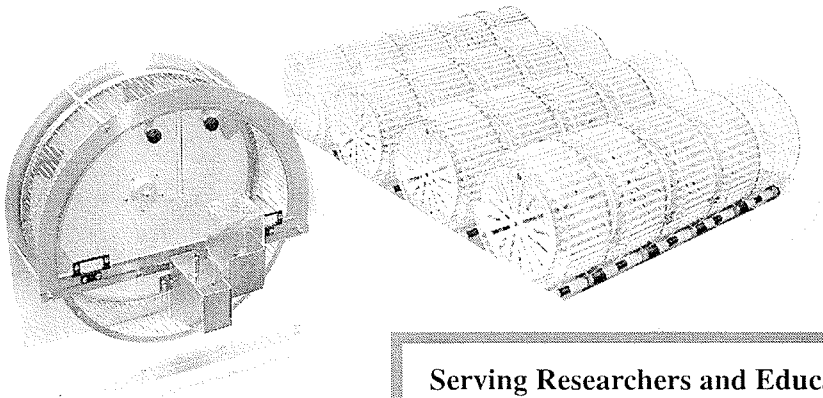

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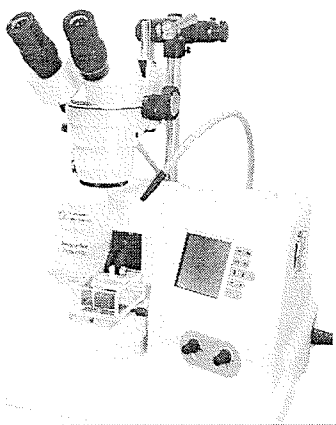

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IBNS PROGRAM (short version)

Wednesday, June 1:

8:00-12:00 Exhibitor Setup. *Mesa Ballroom A*
8:45-12:30 Satellite Symposium. *Aspen Room*
9:00-14:00 Meeting Registration. *Mesa Ballroom A*
13:30-14:00 Welcome and Exhibitor Introduction. *Mesa Ballroom B&C*
14:00-14:30 2004 Myers Award: Laszlo Lenard. *Mesa Ballroom B&C*
14:30-15:24 Oral Session 1: Chemistry of Behavior. *Mesa Ballroom B&C*
15:24-15:55 Refreshment Break/Exhibitors Display. *Mesa Ballroom A*
17:00 - 18:00 Keynote Speaker: Larry Cahill. *Mesa Ballroom B&C*
18:00-19:00 Margarita Fiesta Reception. *Chamisa Courtyard*

Thursday, June 2:

7:15-8:15 Continental Breakfast/Exhibitors Display. *Mesa Ballroom A*
8:15-10:15 Student Travel Award Slide Blitz. *Mesa Ballroom B&C*
10:15-10:30 Break/Exhibitors Display. *Mesa Ballroom A*
10:30-11:42 Oral Session 2: Aversive Behavior. *Mesa Ballroom B&C*
11:45-13:15 Council Meeting. *Aspen Room*
13:15-15:15 Student Workshop. *Mesa Ballroom B&C*
15:15-17:15 Symposium 1: Modeling behavioral symptoms of autism in rodents. *Mesa Ballroom B&C*
17:30-19:30 Poster Session 1. (Refreshments) *Ortiz Ballroom*

Friday, June 3:

7:30-8:30 Continental Breakfast/Exhibitors Display. *Mesa Ballroom A*
8:30-10:30 Symposium 2: Integrative function of the hypothalamus. *Mesa Ballroom B&C*
10:30-10:45 Break/Exhibitors Display. *Mesa Ballroom A*
10:45-11:45 Presidental Lecture. *Mesa Ballroom B&C*
13:15-15:15 Symposium 3: Modeling different facets of disease toward endophenotypes. *Mesa Ballroom B&C*
15:15-15:45 Refreshment Break/Exhibitors Display. *Mesa Ballroom A*
15:45-16:15 2005 Marjorie A. Myers Lifetime Achievement Award: Jacqueline N. Crawley. *Mesa Ballroom B&C*
16:15-17:27 Oral Session 3: Animal Models. *Mesa Ballroom B&C*
17:30-19:30 Poster Session 2. (Refreshments) *Ortiz Ballroom*

Saturday, June 4:

7:30-8:30 Continental Breakfast/Exhibitors Display. *Mesa Ballroom A*
8:30-10:30 Symposium 4: Ventral striatal organization and physiology. *Mesa Ballroom B&C*
10:30-10:45 Break/Exhibitors Display. *Mesa Ballroom A*
10:45-11:45 Keynote Speaker: Robert Dantzer. *Mesa Ballroom B&C*
12:45-14:15 NIH Grant Workshop. *Ortiz Ballroom*
14:15-15:15 Business Meeting – open to all IBNS members. *Ortiz Ballroom*
15:15-17:15 Symposium 5: Acute stress effects on memory. *Ortiz Ballroom*
17:30-18:24 Oral Session 4: Plasticity. *Ortiz Ballroom*
19:00- Banquet and Presentation of Awards. *Mesa Ballroom A, B & C*

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