International Behavioral Neuroscience Society

Program/Abstracts

June 19-23, 2002
Capri, Italy

Abstracts of the International Behavioral Neuroscience Society, Volume 11, June 2002

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Dear Fellow Behavioral Neuroscientists,

Welcome to the Eleventh Annual Meeting of the International Behavioral Neuroscience Society. On behalf of the Officers, Council, and membership of IBNS, I want to convey our pleasure that you are joining us this year in beautiful Capri. Our colleagues from Italy that served on the Local Organizing Committee, under the very capable leadership of Professor Adolfo Sadile, have arranged the excellent conference facilities. We thank our host country, Italy, for the warm hospitality in hosting our international scientific conference.

A very special thanks is due to Martin Sarter and his Program Committee. They have succeeded in putting together an exciting and diverse program. We have excellent keynote speakers and six special symposia representing a wide breadth of areas within behavioral neuroscience. Once again, Marianne Van Wagner, IBNS Executive Coordinator, has done a magnificent job in effectively handling the myriad of issues related to running our annual meeting.

While I hope to see you at many of the interesting sessions, there are several features of the program that I do want to call to your attention. First, this year, we will have a special symposium (Friday, 4:15-6:25) in which our thirteen student travel award winners will make brief oral presentations. I urge you to attend and give support to the future leaders of our society. Second, I hope that you can attend the IBNS Business Meeting (Friday, 6:00-7:00). It is during this meeting that discussions emerge about future meeting venues and other society business. It is a terrific opportunity to express your opinions about your society. Third, I call your attention to the Myers Lifetime Achievement Award presentation - just prior to the banquet. This year the society will honor Dr. Robert Isaacson. Finally, I hope to see all of you at the banquet on Saturday evening (8:00 - 10:00 pm). In addition to presenting the student travel awards, we will honor Dr. Gaetano DiChiara for his many years of distinguished research in behavioral neuroscience.

If you have not yet become a member of IBNS, you are cordially invited to sign up at the registration desk here at the Congres or after the meeting through the IBNS website (www. ibnshomepage.org). We hope to welcome you again to future IBNS meetings.

In closing, it has indeed been an honor to serve as your IBNS President this year. Our society is strong and is growing - moreover, it occupies a critical niche in the neuroscientific community. I look forward to welcoming each of you to our Eleventh Annual Meeting.

John P. Bruno
IBNS President

We are pleased to announce the recipients of the IBNS Travel Awards for the 2002 meeting in Capri, Italy. 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 AWARD WINNERS

(listed by category and alphabetically)

Dr. Walter Adriani, *Istituto Superiore Di Sanita, ITALY*

Ms. Nicole Cameron, *Boston University, USA*

Ms. Elissa J. Chesler, *University of Illinois, USA*

Dr. Elena Choleris, *The Rockefeller University, USA*

Ms. Suzanne A. Henry, *University of California at San Diego, USA*

Ms. Lisa Jackson, *University of Michigan, USA*

Ms. Anna Lee, *Dalhousie University, CANADA*

Ms. Miranda Lim, *Emory University, USA*

Ms. Sara Morley-Fletcher, *Univ. De Lille 1, FRANCE*

Ms. Jennifer J. Quinn, *UCLA, USA*

Ms. Victoria Risbrough, *University of California at San Diego, USA*

Ms. Daniela Ruedi-Bettschen, *Swiss Federal Institute of Technology, Zurich, SWITZERLAND*

Mr. Holger Russig, *ETH, Zurich, SWITZERLAND*

SPONSORS

The IBNS would like to express our gratitude to the following organizations who have given financial support to the 11th International Behavioral Neuroscience Society Conference. This financial support enabled many students to attend the conference and also allowed recruitment of excellent special symposium speakers. *(Listed alphabetically.)*

Ministry Education University and Research (MIUR)

National Institute of Mental Health

Second University of Naples

University of Naples "Federico II"

EXHIBITORS

The IBNS would like to express our gratitude to the following exhibitors and publishers that are attending or have books and materials on display, and/or have given special support to the 11th International Behavioral Neuroscience Society Conference:

Annual Reviews

Blackwell Publishing, Ltd.

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The IBNS was formed to encourage research and education in the field of behavioral neuroscience. In support of this goal, members contributed over $1500 towards the student travel awards for the Capri meeting.

MEMBER CONTRIBUTIONS OVER $500

Jacqueline Crawley

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ACKNOWLEDGMENTS

The International Behavioral Neuroscience Society would like to acknowledge and thank its Corporate Sponsors for their continued financial support.

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

PROGRAM COMMITTEE:

Martin Sarter (Chair); Tim Moran, (Co-Chair); Christopher Engeland (Student); Linda Spear; Betty Zimmerberg; Steve Dunnett; Mark Geyer; Joseph Huston; Alain Gratton; Markus Heilig.

LOCAL ORGANIZING COMMITTEE:

Adolfo Sadile (Chair) – Naples, Enrico Alleva – Rome, Lucio Annunziato – Naples, Gaetano Di Chiara – Cagliari, Antonio Giuditta – Naples, Giovanni Laviola – Rome, Stefano Puglisi Allegra - Rome, Tommaso Russo – Naples.

EDUCATION AND TRAINING COMMITTEE:

Mark Kristal (Chair), John Rosecrans (Co-Chair), Anders Agmo, C. Robert Almli, Deborah Colbern, Kyle Frantz, Laura Ricceri, Jeanne Wehner.

SCIENTIFIC PROGRAM

KEYNOTE SPEAKERS

- **John Crabbe**, Oregon Health Sciences University: Behavioral genomics: Abused drugs as model system
- **Gaetano DiChiara**, University of Cagliari, Cagliari, Italy: Neurobiology of addiction
- **Edward Stricker**, University of Pittsburgh, Pittsburgh, USA: The biological bases of thirst: An integration of excitatory and inhibitory signals

PRESIDENTIAL ADDRESS

John P. Bruno, Ohio State University, Columbus, OH, USA: The basal forebrain cortical cholinergic system: Its role in attentional processing and contribution to neuropsychiatric disorders

SPECIAL SYMPOSIA

- **The Role of the Immune System in Behavior: New Frontiers.** : Adrian Dunn, Louisiana State University Health Sciences Center, Shreveport, LA, USA; Susan Larson, Concordia College, Moorhead, MN, USA.

- **Cannabinoid receptor genetics, signaling and behavior.** *Organizer*: Emmanuel Onaivi, William Paterson University, Wayne, NJ, USA.

- **Valid models of alcohol dependence x functional genomics = novel drug targets for treatment of alcoholism?** *Organizer*: Markus Heilig, Karolinska Institute, Huddinge, Sweden.

- **Stress effects on limbic function and behavior.** *Organizer*: Robert Adamec, Memorial University of Newfoundland, St. John's, Canada.

- **Analyzing neonatal behavior to understand brain development: human and animal data**. *Organizers*: Gemma Calamandrei, Italian National Health Institute, Rome, Italy; Laura Ricceri, Italian National Health Institute, Rome, Italy.

- **Hormones, behavior and the neural circuits that guide them.** *Organizers*: Jennifer Swann, Lehigh University, Bethlehem, PA, USA; Anne Murphy, University of Maryland School of Medicine, Baltimore, MD, USA.

SATELLITES

- **A tribute to Paul MacLean: The neurobiological relevance of social behavior.** *Organizer*: Kelly G. Lambert, Randolph-Macon College, Ashland VA, USA.

- **Molecular and behavioral phenotypes in animal models of Alzheimer's disease.** *Organizers*: Lucio Annunziato, University of Naples, Naples, Italy; Tommaso Russo, University of Naples, Naples, Italy.

- **Brain development, sex differences and stress: Implications for psychopathology.** *Organizers*: Giovanni Laviola, Italian National Institute of Health, Rome, Italy; Susan Andersen, Harvard Medical School, Boston, MA, USA.

NOTE: All presentations, meetings, satellites, posters will be held in the **Sala Le Ginestre** (Le Ginestre Room) unless otherwise noted.
Presenting authors are indicated by **bold** type.

Wednesday, June 19:

8:30–10:00 **Registration -** Le Ginestre Reception Desk

8:00–12:00 **Satellite. A tribute to Paul MacLean: The neurobiological relevance of social behavior.** *Organizer*: Kelly G. Lambert, Randolph-Macon College, Ashland VA, USA

- Kelly G. Lambert, Randolph-Macon College, Ashland, VA, USA
  Conversations with Paul MacLean: Reflections on his career and advice for behavioral neuroscientists
- Sue Carter, University of Illinois at Chicago, Chicago, IL, USA
  The neuroendocrinology of monogamy
- Craig Kinsley, University of Richmond, Richmond VA, USA
  From the triune to the dyad: The importance of mother/infant bi-directional interactions
- Courtney DeVries, Ohio State University, Columbus, OH, USA
  The effects of stress and social contact on experimental stroke outcome
- Robert Gerlai, Eli Lilly, Indianapolis, IN, USA
  Autism: Animal models and the need for drug development
- Stephen Porges, University of Illinois at Chicago, Chicago, IL, USA
  The polyvagal theory: Phylogenetic substrates of the social nervous system
- Detlev Ploog, Max Planck Institute for Psychiatry, Munich, Germany
  The place of the triune brain in psychiatry
- Israel Lederhendler, NIMH, Bethesda, MD, USA
  New directions for social neuroscience

1:00-5:00 **Satellite. Molecular and behavioral phenotypes in animal models of Alzheimer's disease.** *Organizers*: Lucio Annunziato, University of Naples, Naples, Italy; Tommaso Russo, University of Naples, Naples, Italy.

- M. Jucker, University of Basel, Basel, Switzerland
  Cerebral amyloidosis: Mechanism, therapy, transgenic mice
- N. Zambrano, University of Naples, Naples, Italy
  Gene KO in Caenorabditis elegans as a model for the study of the function of APP.Fe 65 complex
- L. D'Adamio, Albert Einstein College of Medicine, Bronx, NY, USA
  Molecular machinery involved in the pathogenesis of Alzheimer's disease
- M. Racchi, University of Pavia, Pavia, Italy
  Receptor and signal transduction regulation of APP metabolism

- M. Cataldi, University of Napoli, Napoli, Italy
  Ionic homeostasis in Alzheimer's disease
- A. Mohammed, Karolinska Institute, Sweden
  Environmental influences on brain neurotrophins and behavior
- H.P. Lipp, T. Wolfer, University of Zurich, Zurich, Switzerland
  Tracing the behavioral profile of mouse mutants

5:00-7:00 **Student Forum:** CAREER OPTIONS IN BEHAVIORAL NEUROSCIENCE
Organizer: Chris Engeland, Univ. of Western Ontario, London, Ontario, Canada
Panelists:

Joanne Berger-Sweeney, Wellesley College, Wellesley, MA, USA
Robert Gerlai, Lilly Research Labs, Indianapolis, IN, USA
Mark A. Geyer, University of California at San Diego, La Jolla, CA, USA
Sandra Kelly, University of South Carolina, Columbia, SC, USA

7:00-9:00 **Registration**
Exhibitors Display

7:15-7:30 **Welcome:** John P. Bruno

7:30-8:30 **Keynote Speaker**: **Gaetano DiChiara**, University of Cagliari, Cagliari, Italy
NEUROBIOLOGY OF DRUG ADDICTION

8:30-10:30 **Reception**

Thursday, June 20:

8:00-10:00 **Registration/Exhibitors Display**

8:30-10:30 **Symposium I: The Role of the Immune System in Behavior: New Frontiers**
Organizers: Adrian Dunn, Louisiana State University Health Sciences Center, Shreveport, LA, USA; Susan Larson, Concordia College, Moorhead, MN, USA

8:30-9:00 **Goebel, M.**, Exton, M.S.; Schedlowski, M.
CONDITIONING IN THE RAT: AN IN VIVO MODEL TO INVESTIGATE THE MOLECULAR MECHANISMS AND CLINICAL IMPLICATIONS OF BRAIN-IMMUNE COMMUNICATION.

9:00-9:30 **Kent, S.**; Sell, K.M.; Dedda, K.; Crowe, S.F.
COGNITIVE EFFECTS OF IMMUNE ACTIVATION

9:30-10:00 **Larson, S.J.**
MOTIVATIONAL EFFECTS OF IMMUNE SYSTEM ACTIVATION

10:00-10:30 **Sakic, B.**
CYTOKINE-INDUCED CHANGES IN BEHAVIOR IN SYSTEMIC AUTOIMMUNE DISEASE

10:30-11:00 Refreshment Break/Exhibitors Display

11:00-12:00 **Keynote Speaker: Edward Stricker**, Univ. of Pittsburgh, Pittsburgh, PA, USA
THE BIOLOGICAL BASES OF THIRST: AN INTEGRATION OF EXCITATORY AND INHIBITORY SIGNALS

12:00-2:00 **Council Meeting**

2:00-4:00 **Oral Session 1: Neurobiology of addiction and related issues**
Chairperson: Mark A. Geyer

2:00-2:15 **Jones, B.C.**; Wheeler, D.S.; Beard, J.L.; Grigson P.S.
IRON DEFICIENCY DELAYS COCAINE SELF-ADMINISTRATION IN RATS

2:15-2:30 **Markou, A.**; Skjei, K.L.; Bruijnzeel, A.; Cryan, J.F.
THE ANTIDEPRESSANT BUPROPION INCREASED BRAIN REWARD FUNCTION AND REVERSED NICOTINE WITHDRAWAL

2:30-2:45 **McGregor, I.S.**; Morley, K.C.; Hunt, G.E.; Li, K.; Duffield, H.
MODULATION OF THE LONG TERM NEUROTOXICITY OF MDMA ("ECSTASY") BY THC IN RATS

2:45-3:00 **Chirwa, S.**; Reasor, J.; Onaivi, E.S.
ALTERED EXPRESSION OF DA1, DA2 mRNA AND OF LONG-TERM POTENTIATION (LTP) IN RATS SENSITIZED TO METHAMPHETAMINE (METH)

3:00-3:15 **Schrott, L.M.**; Sparber, S.B.
PRENATAL OPIATE AND QUASI-OPIATE WITHDRAWAL ACTIVATES THE EMBRYONIC HPA AXIS

3:15-3:30 **Macrì, S.**; Laviola, G.
EFFECTS OF EARLY MATERNAL DEPRIVATION AND CANNABINOID EXPOSURE IN ADOLESCENT MICE OF BOTH SEXES

3:30-3:45 Gardell, L.R.; **Porreca, F.**
REPEATED SPINAL WIN55,212-2 ELICITS ABNORMAL PAIN AND ANTINOCICEPTIVE TOLERANCE

3:45-4:00 **Hohmann, A.G.**; Neely, M.H.; Suplita, R.L.; Farthing, J.; Nackley, A.G.; Holmes, P.V.; Crystal, J.D.
NONOPIOID STRESS-INDUCED ANALGESIA IS MEDIATED BY AN ENDOCANNABINOID MECHANISM

4:00-6:00 **Exhibitors Display**

4:00-6:00 **Poster Session I:**
TOPICS: *INGESTION, MOTIVATION, HORMONES AND BEHAVIOR, LEARNING AND MEMORY*

1. **Davidowa, H.**; Plagemann, A.
HYPOTHALAMIC ARCUATE NEURONS OF HYPERPHAGIC OVERWEIGHT RATS ARE NOT INHIBITED BY INSULIN

2. **Meguid, M.**; Xu, Y.; Ohinata, K.; Marx, W.; Tada, T.; Chen, C.; Quinn, R.; Inui, A.
GHRELIN IN GASTRIC BYPASS MODEL

3. **Lukáts, B.**; Papp, Sz.; Karádi, Z.
NEW CONSTITUENTS OF THE CENTRAL GLUCOSE-MONITORING NETWORK: CHEMOSENSORY NEURONS IN THE NUCLEUS ACCUMBENS OF THE RAT

4. Withdrawn.

5. **Martin, J.**; Bradham, K.; Fleming, E.; Farmer-Dougan, V.; Wallrich, L.; Dean, M.
EFFECTS OF D1 AND D2 AGONISTS ON MATCHING IN AN OPEN FORAGING PARADIGM

6. **Fekete, É.**; Bagi, É.E.; Coy, D.H.; Toth, K.; Lénárd, L.
ELIMINATION OF FEEDING SUPPRESSION EFFECT OF GASTRIN SING PEPTIDE (GRP) BY SELECTIVE GRP RECEPTOR ANTAGONIST IN THE RAT AMYGDALA

7. **Bagi, É. E.**; Fekete, É.; Bányai, D.; Lénárd, L.
RECEPTORIAL FUNCTIONS IN THE REGULATION OF ANGIOTENSIN II AND III INDUCED DRINKING IN THE ZONA INCERTA OF RATS

8. **Viggiano, A.**; Mancone, A.; Catone, L.; Montella, R. C.; De Luca B.
OREXIN A INCREASES EXTRACELLULAR GABA IN THE VENTROMEDIAL HYPOTHALAMUS

9. **Rau, V.**; Grijalva, C. V.
THE ROLE OF CRH IN ACTIVITY STRESS

10. **Moles, A.**; Rizzi, R.; D'Amato, F.R.
EFFECTS OF POSTNATAL MATERNAL CHRONIC EXPOSURE TO THE ODOR OF A NAIVE MALE ON OFFSPRING'S DOPAMINERGIC FUNCTION, BODY WEIGHT AND FEEDING IN MICE

11. Withdrawn.

12. Reid, M.L.; Boswell, K.J.; Fitch, J.V.; Gentile, B.M.; **Reid, L.D.**
INTAKES OF SACCHARIN SOLUTIONS, INCLUDING AN ALCOHOLIC BEVERAGE, AMONG FEMALE RATS TREATED WITH ESTRADIOL VALERATE

13. **Coy, R.T.**; Kanarek, R.B.
CHRONIC SUCROSE REDUCES THE ANTAGONISTIC EFFECT OF β - FUNALTREXAMINE ON MORPHINE-INDUCED ANTINOCICEPTION IN BOTH FEMALE AND MALE RATS

14. **Yamamoto, R.T.**; Coy, R.T.; Vitale, M.A.; Kanarek, R.B.
THE DEVELOPMENT OF CONDITIONED PLACE PREFERENCE, FOR FENTANYL IS ENHANCED BY EITHER ACCESS TO CHRONIC SUCROSE SOLUTION OR PERIPHERAL GLUCOSE ADMINISTRATION

15. **Bassareo, V.**; De Luca M.A.; Di Chiara, G.
DIFFERENTIAL RESPONSIVENESS OF SHELL/CORE/PREFRONTAL DOPAMINE TRANSMISSION TO MOTIVATIONAL STIMULI

16. **Smriga, M.**; Kondoh, T.; Torii, K.
EARLY DEFICIENCY OF AN ESSENTIAL AMINO ACID LYSINE IS RECOGNIZED BY THE VENTROMEDIAL/LATERAL HYPOTHALAMUS

17. **Albrecht, D.**; Walther, T.; Hellner, K.
ANGIOTENSIN-(1-7) ENHANCES HIGH FREQUENCY INDUCED LTP IN THE LATERAL AMYGDALA OF MICE

18. **Aksoy, A.**; Ozuak, T.; Ademoglu, A.; Saybasili, H.; Demiralp, T.; Canbeyli, R.
EFFECT OF INTRASEPTAL COLCHICINE ON MORRIS WATER MAZE PERFORMANCE

19. **Scattoni, M.L.**; Ricceri, L.; Calamandrei, G.
NEONATALLY 192 IgG SAPORIN LESIONED PUPS: EFFECTS ON LOCOMOTION AND OBJECT EXPLORATION FOLLOWING A GABAa AGONIST ON POSTNATAL DAY 18.

20. **Bennett, J.C.**
ESTROGEN REGULATION OF STRATEGY USE IN A CUE-ENRICHED T-MAZE

21. **Adamik, A.**; Telegdy, G.
EFFECTS OF PITUITARY ADENYLATE CYCLASE POLYPEPTIDE (PACAP) ON EXTINCTION OF ACTIVE AVOIDANCE LEARNING IN RATS: INVOLVEMENT OF TRANSMITTERS

22. **Gasbarri, A.**; Pompili A.; Pacitti C.; Cicirata F.C.
ROLE OF THE PONTOCEREBELLAR PATHWAY IN MOTOR SKILLS AND MOTOR LEARNING IN THE RAT

23. Dere, E.; De Souza-Silva, M.; Frisch, C.; Teubner, B.; Willecke, K.; **Huston, J.**
CONNEXIN30 GENE-INACTIVATION IN MICE IMPAIRS MOTOR-COORDINATION, DECREASES EXPLORATORY ACTIVITY AND INDUCES AMNESIA FOR SPATIALLY DISPLACED OBJECTS

24. Kart, E.; **Huston, J.P.**; de Souza Silva, M.A.
DISTINCT PATTERNS OF ACH RELEASE IN THE FRONTAL CORTEX, AMYGDALA AND HIPPOCAMPUS IN RESPONSE TO NK-1 ANTAGONIST SR140333 - A MICRODIALYSIS STUDY IN THE ANAESTHETIZED RAT.

25. **Topic, B.**; Jocham, G.; Schulz, D.; De Souza Silva, M.A.; Huston, J.P.
NEUROCHEMICAL AND BEHAVIORAL CONCOMITANTS OF EXTINCTION OF WATER MAZE ESCAPE BEHAVIOR IN OLD AND ADULT RATS

26. **Hale, M.**; Crowe, S.
THE EFFECTS OF SELECTIVE DOPAMINE AGONISTS ON PASSIVE AVOIDANCE LEARNING IN THE DAY-OLD-CHICK

27. **Ricceri, L.**; Moles, A.; Scattoni, M.L.; Calamandrei, G.
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28. **Ricceri, L.**; Markina, N.; Valanzano, A.; Puopolo, M.; Calamandrei, G.
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30. **Van Vleet, T.**; Corwin, J.; Reep, R.; Heldt, S.
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31. **Ottani, A.**; Zaffe, D.; Botticelli, A.R.; Bertolini, A.
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32. **Berry, A.**; Chiarotti, F.; Alleva, E.; Cirulli, F.
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36. **Lehmann, M.L.**; Sable, G.M.; Erskine, M.S.
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37. **Carey, P.S.**; Erskine, M.S.; Cameron, N.
NORADRENERGIC LESIONS CAUSED BY ANTI-DOPAMINE-β-HYDROXYLASE SAPORIN INFUSIONS IN THE MEDIAL AMYGDALA

38. **Razzoli, M.**; Polidori, M.; Valsecchi, P.
BEHAVIORAL AND PHYSIOLOGICAL CORRELATES OF SOCIAL BONDS IN MONGOLIAN GERBILS

39. Withdrawn.

40. **Turi, A.L.**; Ellingsen, E.; Larsson, K.; Agmo, A.
A FEMALE COOLIDGE EFFECT

41. **Johns, J.**; Lubin, D.; Elliott, J.; Black, M.; Joyer, P.; Lomas, L.; Middleton, C.
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44. Pryce, C.; Dettling, A.; **Feldon, J.**
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45. **Palanza, P.**; Howdeshell, K.; Parmigiani, S.; vom Saal, F.S.
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46. **Domínguez, R.**; Cruz-Morales, S.E.; Carvalho, M.C.
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47. **Portillo, W.**; Basañez, E.; Paredes, R.G.
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48. Meurisse, M.; Gonzalez, A.; Delsol, G.; **Poindron, P.**; Lévy, F.
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49. **Weiss, I.C.**; Lesslauer, A.; Knobloch, M.; Mansuy, I.M.
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50. **Grammatikopoulos, G.**; Pignatelli, M.; Ruocco, L.A.; Sadile, A.G.
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51. Jiménez Vasquez, P.A.; Salmi, P.; Ahlenius, S.; **Mathé, A.A.**
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53. **Miller, S.**; Cook, M.; Murphy, M.; Merritt, J.; Mason P.
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54. **Lehmann-Masten, V.**; Ralph-Williams, R.; Otero-Corchon, V.; Low, M.J.; Geyer, M.A.
D1 DOPAMINE RECEPTORS REGULATE PREPULSE INHIBITION OF STARTLE IN C57BL/6 MICE

55. **Russig, H.**; Durrer, A.; Murphy C.A.; Feldon, J.
EFFECTS OF AMPHETAMINE WITHDRAWAL ON THE MORRIS WATER MAZE TASK

56. **Ferguson, S.A.**; Cada, A.M.
HYPERACTIVITY EXHIBITED BY SPONTANEOUSLY HYPERTENSIVE RATS (SHR) DIFFERS WITH APPARATUS AND ACTIVITY TYPE

57. **Viggiano, D.**; Ruocco, L.A.; Rimoli G.; Melisi D.; De Caprariis P.; Annunziato L.; Sadile A.G.
PERIPHERAL ADMINISTRATION OF GLYCOSILATED DOPAMINE MODULATES THE ACTIVITY AND FUNCTION OF CENTRAL DOPAMINE SYSTEMS IN MICE AND RATS

58. **Malatynska, E.**; Rapp, R.; Crites, G.
DOMINANT BEHAVIOR MEASURED IN A COMPETITION TEST AS A MODEL OF MANIA

59. **Rinaldi, A.**; Mandillo, S.; Oliverio, A.; Mele, A.
SPATIAL LEARNING IS SELECTIVELY IMPAIRED BY REPEATED ADMINISTRATION OF AMPHETAMINE AND MK-801: A POSSIBLE MOUSE MODEL OF COGNITIVE DEFICITS

60. López, L.; Aller, M.A.; Arias, J.; González-Pardo, H.; Begega, A.; **Conejo, N.**; Miranda, R.; Arias, J.L.
CIRCADIAN RHYTHM AND CYTOCHROME OXIDASE ACTIVITY OF THE SUPRACHIASMATIC NUCLEUS IN TWO EXPERIMENTAL MODELS OF HEPATIC INSUFFICIENCY

61. **Conejo, N.M.**; González-Pardo, H.; Vallejo, G.; Arias, J.L.
SEX DIFFERENCES IN BRAIN OXIDATIVE METABOLISM AFTER SPATIAL LEARNING

62. **Telegdy, G.**; Adamik, A.
INVOLVEMENT OF DIFFERENT RECEPTORS IN PACAP 38-INDUCED OPEN-FIELD ACTIVITY IN RATS

63. **Durand, E.**; Dauger, S.; Vardon, G.; Gressens, P.; Gaultier, C.; de Schonen, S.; Gallego, J.
CLASSICAL CONDITIONING OF BREATHING PATTERN IN TWO-DAY-OLD MICE

64. **Creson, T.**; Rasch, E.; Monaco, P.; Woodruff, M.
DOSE-RESPONSE EFFECTS OF CHRONIC LITHIUM TREATMENT ON SPATIAL MEMORY IN THE BLACK MOLLY FISH

65. **Corona-Morales, A.A.**; Castell, A.; Hernández-Peñaloza, A.; Roldán-Roldán, G; Zhang, L.
EFFECTS OF LEVODOPA TREATMENT WITH ANTIOXIDANTS ON ADRENAL CHOMAFFIN CELL TRANSPLANTS USING RAT MODEL FOR PARKINSON DISEASE

66. **Puopolo, M.**; Venerosi Pesciolini, A.; Valanzano, A.; Chiarotti, F.; Calamandrei, G.; Ricceri, L.
STATISTICAL METHODS FOR THE ANALYSIS OF THE BEHAVIOURAL SEQUENCES

67. **Abílio, V.C.**; Carvalho, R.C.; Ribeiro, R. de A.; Frussa-Filho, R.
SPONTANEOUSLY HYPERTENSIVE RATS DO NOT PRESENT AGING-INDUCED OROFACIAL DYSKINESIA: A POSSIBLE PROTECTIVE EFFECT OF CATALASE

68. Álvarez, E.; Gómez, A.; **Rodríguez, F.**; González, J.A.; González-Pardo, H.; Arias, J.L.; Salas, C.
EFFECTS OF CLASSICAL CONDITIONING ON CYTOCHROME OXIDASE ACTIVITY IN THE CEREBELLUM OF GOLDFISH

Friday, June 21:

8:00-10:00 **Registration/Exhibitors Display**

8:00-9:00 **Oral Session 2: Behavioral endocrinology**
Chairperson: Paolo Preziosis

8:00-8:15 **Klein, S.L.**; Wisneiwski, A.B.; Marson, A.L.; Glass, G.E.; Gearhart, J.P.
PERINATAL EXPOSURE TO PHYTOESTROGENS ALTERS ENDOCRINE-IMMUNE INTERACTIONS IN MALE RATS

8:15-8:30 Fortis, A.; Bonet, Y.; Cruz, N.; Barreto, J.; Rivera, J.C.; Corretjer, G.; **Jorge, J.C.**
NEUROSTEROID EXPOSURE DURING NEONATAL DEVELOPMENT PRODUCES SEX-SPECIFIC EFFECTS ON ANXIETY-RELATED BEHAVIORS IN THE ADULT RAT

8:30-8:45 **Hohmann, C.F.**; Karikari, P.D.; Lipscomb, D.
NEONATAL TEMPERATURE/SEPARATION STRESS ALTERS EXPLORATORY BEHAVIOR IN MALE BALB/CBYJ MICE

8:45-9:00 **Carere, C.**; Groothuis, T.T.G.; Möstl, E.; Koolhaas J.M.
ADRENAL RESPONSE INDUCED BY SOCIAL STRESS IN A TERRITORIAL BIRD SELECTED FOR DIFFERENT COPING STYLES

9:00-10:00 **Presidential Lecture: John P. Bruno**, Ohio State Univ., Columbus, OH, USA
THE BASAL FOREBRAIN CORTICAL CHOLINERGIC SYSTEM: ITS ROLE IN ATTENTIONAL PROCESSING AND CONTRIBUTION TO NEUROPSYCHIATRIC DISORDERS

10:00-10:15 **Refreshment Break/Exhibitors Display**

10:15-12:15 **Symposium II**: **Cannabinoid receptor genetics, signaling and behavior**
Organizer: Emmanuel Onaivi, William Paterson University, Wayne, NJ, USA

10:15-10:35 **Hampson, R.**; Deadwyler, S.
EFFECTS OF CANNABINOIDS ON MEMORY, OR "WHERE DID I PARK MY CAR?"

10:35-10:55 **Gardner, E.L.**
NEUROBIOLOGICAL BASIS FOR THE ADDICTIVE POTENTIAL OF CANNABINOIDS

10:55-11:15 **Gorelick, D.**; Heishman, S.; Preston, K.; Nelson, R.; Moolchan, E.; Frank, R.; Huestis, M.
BLOCKADE OF EFFECTS OF SMOKED MARIJUANA IN HUMANS BY THE CB1-SELECTIVE CANNABINOID RECEPTOR ANTAGONIST SR141716

11:15-11:35 **Makriyannis, A.**
THE ENDOCANNABINOID SYSTEM AS A NOVEL TARGET IN DRUG DISCOVERY

11:35-11:55 **Onaivi, E.**; Ishiguro, H.; Zang, P.; Akinshola, B.; Hall, F.; Leonard, C.; Lin, Z.; Darmani, N.; Hanus, L.; Hope, B.; Uhl, G.
ENDOCANNABINOID GENETICS AND BEHAVIOR

11:55-12:15 **Giuffrida, A.**; Piomelli, D.
ENDOCANNABINOID MODULATION OF MOTOR FUNCTIONS

12:15-2:00 **Free Time**

2:00-4:00 **Symposium III: Valid models of alcohol dependence x functional genomics = novel drug targets for treatment of alcoholism?**
Organizer: Markus Heilig, Karolinska Institute, Huddinge, Sweden

2:00-2:20 **Spanagel, R.**
THE ALCOHOL DEPRIVATION EFFECT AS A MODEL OF ALCOHOL RELAPSE

2:20-2:40 **Hyytia, P.**; Koistinen, M.; Ojanen, S.; Tuomainen, P.; Kiianmaa, K.
GENETIC SELECTION AND OPIOID SENSITIZATION IN MODELS OF ALCOHOL PREFERENCE

2:40-3:00 **Wolffgramm, J.**; Heyne, A.
PROGRESSION TO LOSS OF CONTROL IN LONG TERM VOLUNTARY ETHANOL INTAKE IN RATS

3:00-3:20 **Ciccocioppo, R.**; Massi, M.; Liu X.; Weiss, F.
STRESS AND CUE-INDUCED REINSTATEMENT OF ALCOHOL SEEKING BEHAVIOR AS A MODEL FOR RELAPSE

3:20-3:40 **Rimondini, R.**; Sommer, W.; Arlinde, C.; Heilig, M.
PROLONGED ETHANOL PREFERENCE FOLLOWING REPEATED CYCLES OF ETHANOL VAPOUR EXPOSURE

3:40-4:00 **Heilig, M.**; Arlinde, C.; Rimondini, R.; Sommer, W.
FUNCTIONAL GENOMICS FOR TARGET GENE IDENTIFICATION IN ANIMAL MODELS WITH GENETICALLY AND ENVIRONMENTALLY INDUCED ETHANOL PREFERENCE

4:00-4:15 **Break/Exhibitors Display**

4:15-6:25 **Student Travel Award Winners' Symposium**
Chairperson: Martin Sarter
(Slide-Blitz style--maximum 5 slides/speaker; 8 min talk and 2 questions)

4:15-4:25 **Choleris, E.**; Forder, J.P.; Kavaliers, M.; Ossenkopp, K.-P.
THE DOPAMINE D2 RECEPTOR ANTAGONIST RACLOPRIDE BLOCKS SOCIAL LEARNING OF FOOD PREFERENCES IN MALE AND FEMALE RATS

4:25-4:35 **Lee, A.W.**; Kalynchuk, L.
EFFECT OF POSTNATAL HANDLING ON THE EMOTIONAL BEHAVIOR OF ADULT AMYGDALA-KINDLED RATS

4:35-4:45 **Adriani, W.**; Caprioli, A.; Laviola, G.
AN ANIMAL MODEL OF ADHD: EVIDENCE OF INATTENTIVE AND IMPULSIVE SUBPOPULATIONS IN THE ADOLESCENT SHR STRAIN

4:45-4:55 **Chesler, E.J.**; Wilson, S.G.; Lariviere, W.R.; Rodriguez-Zas, S.L.; Mogil, J.S.
COMPUTATIONAL APPROACH TO IDENTIFICATION OF LABORATORY FACTORS THAT INFLUENCE GENETIC STUDIES OF PAIN BEHAVIOR

4:55-5:05 **Quinn, J.J.**; Ma, Q.D.; Tinsley, M.R.; Fanselow, M.S.
ROLE OF THE DORSAL HIPPOCAMPUS IN THE ACQUISITION AND EXPRESSION OF DISCRIMINATION REVERSAL IN AUDITORY FEAR CONDITIONING

5:05-5:15 **Lim, M**.; Sharer, C.; Insel, T.; Zohar, N.; Hoffman, G.; Young, L.
IMMUNOHISTOCHEMICAL LOCALIZATION OF THE VASOPRESSIN V1A RECEPTOR IN THE MONOGAMOUS PRAIRIE VOLE BRAIN

5:15-5:25 **Risbrough, V.**; Geyer, M.
PHARMACOLOGY OF FEAR POTENTIATED STARTLE IN MICE

5:25-5:35 **Jackson, L.R.**; Becker, J.B.
ESTROGEN ENHANCES DEVELOPMENT OF BEHAVIORAL SENSITIZATION TO COCAINE AND DOPAMINE

5:35-5:45 **Morley-Fletcher, S.**; Darnaudery, M.; Mocaer, E.; Maccari, S.
EFFECTS OF A CHRONIC TREATMENT WITH IMIPRAMINE IN PRENATALLY STRESSED RATS

5:45-5:55 **Rüedi-Bettschen, D.**; Feldon, J.; Pryce, C.R.
EARLY DEPRIVATION LEADS TO REDUCED MOTIVATION AND INCREASED BEHAVIOURAL DESPAIR IN THE ADULT RAT

5:55-6:05 **Henry, S.A.**; Geyer, M.A.; Large, C.H.
THE ABILITY OF LAMOTRIGINE TO REVERSE KETAMINE BUT NOT AMPHETAMINE-INDUCED PPI DEFICITS IN MICE

6:05-6:15 **Russig, H.**; Murphy C.A.; Feldon, J.
WITHDRAWAL FROM REPEATED AMPHETAMINE ADMINISTRATION, A MODEL OF SCHIZOPHRENIA?

6:15-6:25 **Cameron, N.**; Erskine, M.S.
FOS EXPRESSION IN THE FOREBRAIN AFTER MATING IS ALTERED BY ADRENALECTOMY.

6:30-8:30 **Exhibitors Display**

6:30-8:30 **Poster Session II**
TOPICS: *BEHAVIORAL TOXICOLOGY, NEUROIMMUNOLOGY, ADDICTION, LEARNING AND MEMORY, STRESS AND ANXIETY, KINDLING, BEHAVIORAL GENETICS*

69. **Colín-Barenque, L.**; Avila-Costa, M.R.; Fortoul, T.; Rugerio-Vargas, C.; Borgonio-Pérez, G.; Pasos, F.; Rivas-Arancibia, S.
CYTOLOGICAL AND ULTRASTRUCTURAL CHANGES OF OLFACTORY MUCOSA AND BULB INDUCED BY OZONE EXPOSURE

70. **Pereyra-Muñoz, N.**; Acosta-Vázquez, F.; Rodríguez-Martínez, E., Rugerio-Vargas, C.; Borgonio-Pérez, G.; Rivas-Arancibia, S.
TAURINE EFFECTS ON PROGRESSIVE ASTROCYTE DAMAGE IN HIPPOCAMPUS CAUSED BY OXIDATIVE STRESS

71. **Rodríguez-Martínez, E.**; Acosta-Vázquez, F.; Juárez-Meavepeña, M.; Borgonio-Pérez, G.; Pereyra-Muñoz, N.; Rivas-Arancibia, S.
ANTIOXIDANT EFFECT OF TAURINE ON OXIDATIVE DAMAGE IN HIPPOCAMPUS CAUSED BY 3-NP ADMINISTRATION IN RATS

72. **González-Rivas, S.**; Sánchez-Vega, R.; Acosta-Vázquez, F.; Rugerio-Vargas, C.; Quintana-Rojas, Y.; Borgonio-Perez, G.; Rivas-Arancibia, S.
OXIDATIVE CHANGES IN HIPPOCAMPUS CAUSED BY OZONE EXPOSURE MODIFY SHORT-TERM MEMORY IN RATS

73. **Juárez-Meavepeña, M.**; Acosta-Vázquez, F.; Pineda-Solis, K.; Rivas-Arancibia, S.
BEHAVIORAL AND GLIAL CHANGES IN STRIATUM, INDUCED BY 3-NITROPROPIONIC ACID TREATMENT IN RAT

74. **Berlanga Taylor, A.**; Acosta-Vázquez F.; Rugerio-Vargas, C.; Fernández-Barocio, F.; Durán-Vázquez, A.; Borgonio-Pérez, G.; Rivas-Arancibia, S.
EFFECTS OF TAURINE ON OXIDATIVE STRESS CAUSED BY FRONTAL CORTEX LESION

75. **Dorado-Martínez, C.**; Borgonio-Pérez, G.; Rivas-Arancibia, S.
GROOMING BEHAVIOR ALTERATIONS IN RATS CAUSED BY PROLONGED OZONE EXPOSURE

76. **Valencia-Reyes, R.**; Rugerio-Vargas, C.; Rodríguez-Mata, V.; Dorado-Martínez, C.; Borgonio-Pérez, G.; Rivas-Arancibia, S.
A PROGRESSIVE DAMAGE IN HIPPOCAMPUS CAUSED BY CHRONIC OZONE EXPOSURE IN RATS.

77. **Ballok, D.A.**; Sakic, B.
THE ROLE OF PRO-INFLAMMATORY CYTOKINES IN THE ETIOLOGY OF AUTOIMMUNITY-INDUCED NEURODEGENERATION AND BEHAVIORAL DYSFUNCTION

78. **Genedani, S.**; Saltini, S.; Filaferro, M.;Ottani, A.; Benelli, A.
EFFECTS OF INTERLEUKIN-2 ON MALE SEXUAL BEHAVIOR IN MICE

79. **Franklin, A.E.**; Engeland, C.G.; Kavaliers, M; Ossenkopp, K.-P.
HYPOACTIVITY AND BEHAVIORAL TOLERANCE TO LIPOPOLYSACCHARIDE ARE DIFFERENTIALLY EXPRESSED ACROSS THE LIGHT AND DARK PERIODS IN MALE AND FEMALE RATS

80. **Hennessy, M.B.**; Deak, T.; Schiml-Webb, P.A.; Schwartz, K.; Stewart, H.; Wilson, S.E.
SIMILARITIES IN THE BEHAVIORAL RESPONSES OF PREWEANING GUINEA PIGS TO CRF, LPS, AND ISOLATION: DO STRESS-INDUCED SICKNESS BEHAVIORS CONTRIBUTE TO THE RESPONSE TO MATERNAL SEPARATION?

81. Saber, A.J.; **Engeland, C.G.**; Ossenkopp, K.-P.; Kavaliers, M.;Cain, D.P.
THE EFFECTS OF CHRONIC LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION ON LOCOMOTOR ACTIVITY AND WATER MAZE PERFORMANCE IN RATS

82. **David, H.N.**; Abraini, J.H.
FUNCTIONAL INTERACTIONS BETWEEN GROUP III METABOTROPIC RECEPTORS AND DOPAMINE RECEPTORS IN THE RAT NUCLEUS ACCUMBENS

83. **David, H.N.**; Abraini, J.H.
BLOCKADE OF NMDA RECEPTORS BY THE LAUGHING GAS NITROUS OXIDE AND XENON PREVENT AMPHETAMINE SENSITIZATION

84. **Morley-Fletcher, S.**; Puopolo, M.; Macri, S.; Gentili, S.; Macchia, T.; Laviola, G.
BEHAVIOURAL AND PHARMACOKINETIC PROFILE FOLLOWING MDMA ("ECSTASY") ADMINISTRATION IN ADOLESCENT RATS: INFLUENCE OF PRENATAL STRESS

85. Viggiano, D.; Vallone, D.; **Sadile, A.G.**
THE NAPLES HIGH-AND LOW EXCITABILITY RATS: SELECTIVE BREEDING, BEHAVIORAL PROFILE, BRAIN MORPHOMETRY AND MOLECULAR BIOLOGY

86. **Carroll, M.E.**; Morgan, A.D.; Roth, M.E.; Cosgrove, K.P.; Lynch, W.D.
ESTROGEN, WHEEL-RUNNING AND INBRED SACCHARIN PREFERENCE: PREDICTORS OF ACCELERATED DRUG SELF-ADMINISTRATION IN RATS

87. **Walker, B.**; Ettenberg, A.
CENTRALLY ADMINISTERED ETHANOL PRODUCES PLACE PREFERENCES AND POTENTIATES OPIATE REWARD

88. Akinshola, B.; Fryar, E.; Taylor, R.; **Onaivi, E.**
DIFFERENTIAL SENSITIVITIES OF ENDOCANNABINOIDS AND VANILLOIDS

89. **Pert, A.**; Sundstrom, J.; Hall, S.
THE ROLE OF DOPAMINE AND GLUTAMATE IN THE EXTINCTION OF COCAINE INDUCED CONDITIONED INCREASES IN LOCOMOTOR ACTIVITY

90. **Silva, R.H.**; Abilio, V.C.; Frussa-Filho, R.
EFFECTS OF TACRINE ON MEMORY AND ANXIETY OF MICE TESTED IN THE PLUS-MAZE DISCRIMINATIVE AVOIDANCE TASK

91. **Silva, R.H.**; Kameda, S.R.; Araújo, N.P.; Frussa-Filho, R.
EFFECTS OF ETHANOL ON MEMORY AND ANXIETY OF MICE TESTED IN THE PLUS-MAZE DISCRIMINATIVE AVOIDANCE TASK

92. Ciccocioppo, R.; **Fedeli, A.**; Economidou, D.; Massi, M.
INHIBITION OF ETHANOL SELF-ADMINISTRATION AND RELAPSE BY NOCICEPTIN/OP4 RECEPTOR SYSTEM STIMULATION

93. **Glasper, E**.; Paul, G.; Brundin, P.
IMPROVING TRANSPLANT SURVIVAL FOR PARKINSON'S DISEASE: AN EXPLORATION OF A DIFFERENTIATED HUMAN DOPAMINERGIC CELL LINE

94. **Venderova K.**; Ruzicka E.; Visnovsky P.
EFFECT OF CANNABIS ON PARKINSON'S DISEASE SYMPTOMS: QUESTIONNAIRE-BASED STUDY

95. **Sobrian, S.K.**; Ressman, K.; Marr, L.
EFFECTS OF PRENATAL COCAINE AND/OR NICOTINE ON INDICES ON MENTAL ILLNESS IN ELDERLY RATS

96. **Chotro, M.G.**; Arias, C.
INCREASED ALCOHOL INTAKE AFTER PRENATAL ALCOHOL EXPOSURE IN THE RAT: A CONDITIONED RESPONSE?

97. **Tammimäki, A.**; Gäddnäs, H.; Ahtee, L.
EFFECT OF CHRONIC NICOTINE ADMINISTRATION ON ACCUMBAL DOPAMINERGIC TRANSMISSION IN MICE

98. **Costanzi, M.**; Pavone, F.; D'Amato, F.R.; Castellano, C.; Cestari, V.
INTERACTION BETWEEN MK-801 AND MORPHINE IN DIFFERENT BEHAVIOURS

99. Allen, K.V.; Mallet, P.E.; Singh, M.; **McGregor, I.S.**
REGIONAL DIFFERENCES IN NALOXONE MODULATION OF THC–INDUCED C-FOS EXPRESSION IN RATS.

100. **Harris, A.**; Brier-Bauder, G.; Vasserman, E.; Gewirtz, J.
ACOUSTIC STARTLE AS A MEASURE OF SPONTANEOUS AND PRECIPITATED MORPHINE WITHDRAWAL IN RATS

101. Thompson, A.C.; Sallaj, A.S.; Acheson, A.; Martin, L.B.E.; Martin, T.; **Kristal, M.B.**
BUPRENORPHINE FALLS SHORT AS A POSTOPERATIVE ANALGESIC IN RODENTS

102. **Kanarek, R.B.**; Mathes, W.F.
CHRONIC EXERCISE ATTENUATES THE PAIN RELIEVING PROPERTIES OF NICOTINE IN FEMALE RATS

103. Borghi, V.; Nalepa, I.; Kowalska, M.; Przewlocka, B.; Vetulani, J.; **Pavone, F.**
CONTRIBUTION OF CENTRAL ALPHA1-ADRENOCEPTORS TO FORMALIN-PAIN MODULATION IN MICE

104. **Ossenkopp, K.-P.**; Anderson, S.; Engeland, C. G.; Kavaliers, M.
INFLUENCE OF SEX AND BREEDING STATUS ON THE BEHAVIOR OF MEADOW VOLES IN THE AUTOMATED DIGISCAN LIGHT-DARK ANXIETY TEST

105. Anderson, S.; Engeland, C. G.; Kavaliers, M.; **Ossenkopp, K.-P.**
EFFECTS OF A BRIEF EXPOSURE TO FOX ODOR ON ANXIETY AND LOCOMOTOR ACTIVITY LEVELS IN THE LIGHT-DARK TEST IN MALE AND FEMALE MEADOW VOLES

106. Campbell, T.; Lin, S.; DeVries, C.; **Lambert, K.**
AN EXPLORATION OF COPING STRATEGY CONSISTENCIES IN MALE AND FEMALE RATS EXPOSED TO MULTIPLE STRESSORS

107. **Lointier, L.**; Roy, V.; Chapillon, P.
POSTNATAL HANDLING HAS POSITIVE EFFECTS ON ANXIETY DURING PREGNANCY IN RATS

108. **Lin, S.**; Campbell, T.; DeVries, C.; Lambert, K.G.
EFFECTS OF CHRONIC STRESS AND SOCIAL CONTACT ON HIPPOCAMPAL APOPTOSIS AND STRESS RESPONSIVITY IN PEROMYSCUS CALIFORNICUS

109. **Kentner, A.C.**; Baker, S.; Konkle, A.T.M.; Fouriezos, G.; Bielajew, C.
BRAIN-STIMULATION REWARD AS A BEHAVIOURAL MEASURE OF CHRONIC MILD STRESS IN FEMALE RATS

110. **Baker, S.L.**; Kentner, A.C.; Konkle, A.T.M.; Bielajew, C.
INVESTIGATING THE EFFECTS OF CHRONIC MILD STRESS ON SUCROSE PREFERENCE IN TWO FEMALE RAT STRAINS

111. **Lee, S.**; Jahng. J.W.; Kim, D.G.
5-HT1A RECEPTOR ACTIVITY AT A STRESSFUL EVENT MODIFIES LATER BEHAVIOR ALTERED BY THE STRESSFUL EXPERIENCE

112. **McFarlane, H.**; Henry, S.; Dewey, T.; Cornwell, C.
BEHAVIORAL AND NEURAL EVIDENCE OF SOCIAL STRESS AND SOCIAL SUPPORT IN CONTROL CAGE MATES OF DSP-4 TREATED RATS

113. **Coover, G.D.**; Trivedi, M.; Heldt, S.A.
HIPPOCAMPAL ASPIRATION DECREASES OPEN ARM AVOIDANCE IN TWO RAT STRAINS AND BOTH PLUS- AND T-MAZE TESTS OF ANXIETY

114. **Kavaliers, M.**; Choleris, E.; Colwell, D.
SOCIAL LEARNING OF NATURAL FEAR RESPONSES IN DEER MICE: ROLES OF KINSHIP AND FAMILIARITY

115. **Brudzynski, S.M.**
FIFTY-kHz CALLS INDUCED BY A DIRECT ACTIVATION OF THE DOPAMINERGIC SYSTEM IN THE RAT BRAIN

116. Macedo, C.E.; Castilho, V.; **Brandao, M.L.**
DUAL 5-HT MECHANISMS IN BASOLATERAL AND CENTRAL NUCLEI OF AMYGDALA IN THE REGULATION OF THE DEFENSIVE BEHAVIOR INDUCED BY ELECTRICAL STIMULATION OF THE INFERIOR COLLICULUS

117. Stearns, N.A.; **Floerke-Nashner, L.**; Berger-Sweeney, J.
BEHAVIORAL CHARACTERIZATION OF MECP2 MUTANT MICE - A RETT SYNDROME MODEL

118. Heldt, S.A.; Gouilland, A.M.; **Matuszewich, L.**
FEAR POTENTIATED STARTLE IS MAINTAINED IN CHRONICALLY STRESSED RATS

119. **Darnaudéry, M.**; Del-Favero, F.; Maccari, S.
EFFECTS OF RESTRAINT STRESS DURING PREGNANCY ON COPING STRATEGIES IN LACTATING DAMS

120. **Teicher, M.H.**; LeBlanc, C.; Andersen, S.L.
REGIONAL-SPECIFIC CHANGES IN CATECHOLAMINE INNERVATION FOLLOWING MATERNAL SEPARATION

121. **Andersen, S.L.**; Thompson, A.; Teicher, M.H.
MATERNAL SEPARATION DOES NOT ALTER STRIATAL RESPONSIVENESS

122. **Blanchard, D.C.**; Blanchard, R.J.
TMT AND CAT FECES FAIL TO SUPPORT CONDITIONING OF DEFENSIVE BEHAVIORS

123. **Teixeira Silva, F.**; Bordini, G.; Leite, J.R.
PSYCHOLOGICAL AND PHYSIOLOGICAL REACTIONS TO ANXIETY INDUCED BY THE STROOP COLOR-WORD TEST IN HEALTHY VOLUNTEERS – EFFECTS OF DIAZEPAM

124. **Saltini, S.**; Genedani, S.; Benelli, A.; Filaferro, M.; Ottani, A.; Bertolini, A.
INFLUENCE OF SAMe ON THE BRAIN POLYAMINE LEVELS AND NMDA RECEPTOR EXPRESSION IN AN ANIMAL MODEL OF DEPRESSION

125. **Cruz-Morales, S.**; Saldívar, N.; Gómez-Romero, J.; González-López, M.
EFFECTS OF MIDAZOLAM IN THE ELEVATED T-MAZE

126. Withdrawn.

127. Withdrawn.

128. **Rossi III, J.**; McInturf, S.; McDougle, F.; Ritchie, G.D.; Bekkedal, M.Y.V.
IN VITRO TISSUE SLICE INDICATORS OF NEUROBEHAVIORAL COMPETENCE

129. **Tagliaferro, P.**; Ramos, A.J.; López-Costa, J.J.; Brusco, A.
PARACHLOROAMPHETAMINE TREATMENT INDUCES ALTERATIONS ON THE NITRIC OXIDE SYSTEM

130. González-Sánchez, H.; **Roldán, G.**
SELECTIVE BLOCKADE OF NEURAL NITRIC OXIDE SYNTHASE (nNOS) INTO THE NEOSTRIATUM IMPAIRS CONSOLIDATION AND RETRIEVAL OF INHIBITORY AVOIDANCE LEARNING

131. **Radovic, A**; Wittkopp, P.J.; Long, A.D.; Drapeau, M.D.
THE BEHAVIOR GENE YELLOW IS DOWNSTREAM OF FRUITLESS IN THE DROSOPHILA DEVELOPING BRAIN

132. **Viggiano D.**; Ruocco L.A.; Gallo A.; Zambrano N.; Russo T.; Sadile A.G.
DISSOCIATION OF SPATIAL AND NON-SPATIAL BEHAVIORAL COMPONENTS IN TRANSGENIC MICE OVEREXPRESSING A MUTANT FORM OF THE FE65 PROTEIN

133. **Branchi, I.**; Santucci, D.; Puopolo, M.; Alleva, E.
ANALYSIS OF BEHAVIOURAL ITEMS TEMPORALLY RELATED WITH ULTRASONIC VOCALISATIONS IN THE INFANT MOUSE (MUS MUSCULUS)

134. **Santucci, D.**; Francia, N.; Aloe, L.; Alleva, E.
CHARACTERISATION OF MOTION SICKNESS IN THE MOUSE

135. **Powell, S.B.**; Paulus, M.P.; Geyer, M.A.
MODULATION OF APPROACH-AVOIDANCE BEHAVIOR IN A NOVEL OBJECT EXPLORATION PARADIGM IN MICE

136. **Adriani, W.**; Laviola, G.
INCREASED IMPULSIVITY AND LOW AMPHETAMINE-INDUCED REWARD AS RISK FACTORS FOR DRUG ABUSE DURING ADOLESCENCE

137. **Diana, G.**; Pieri, M.; Valentini G.
DO CB1 AGONISTS AFFECT LONG-TERM POTENTIATION?

Saturday, June 22:

8:00-10:00 **Registration/Exhibitors Display**

8:30-10:30 **Symposium IV: Stress effects on limbic function and behavior**
Organizer: Robert Adamec, Memorial University of Newfoundland, St. John's, Canada

8:30-8:50 **Adamec, R.**; Blundell, J.
NEUROPLASTICITY IN LIMBIC CIRCUITS IN RESPONSE TO SEVERE STRESS

8:50-9:10 **Blanchard, R.J.**; Blanchard, D.C.
SOCIAL STRESS OF AGONISTIC INTERACTION: THE VISIBLE BURROW SYSTEM

9:10-9:30 **Cahill, L.**
HEMISPHERIC, SEX-RELATED LATERALITY IN AMYGDALA INVOLVEMENT IN THE STORAGE OF MEMORY FOR EMOTIONALLY AROUSING EVENTS

9:30-9:50 **Haller, J.**
ENDOCRINE BACKGROUND AND ENDOCRINE RESPONSIVENESS IN BEHAVIORAL AND BRAIN RESPONSES TO STRESS

9:50-10:10 **Merali, Z.**; Khan, S.; Michaud, D.; Anisman, H.
STRESS, ANXIETY AND LIMBIC CRH

10:10-10:30 **Roozendaal, B.**; McGaugh, J.L.
STRESS, STRESS HORMONES AND MEMORIES FOR EMOTIONAL EVENTS, LIMBIC SYSTEM INVOLVEMENT

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

10:45-12:00 **Oral Session 3: Models of disorders and neuroplasticity**
Chairperson: Joseph P. Huston

10:45-11:00 **Espejo, E. Fdez.**; Caraballo, I.; El Banoua, F.; Flores, J.A.
CANNABINOID CB1 ANTAGONISTS AMELIORATE FUNCTIONAL DEFICITS IN PARKINSONIAN RATS AFTER INTENSE BUT NOT MODERATE NIGRAL DEGENERATION

11:00-11:15 **Sarter, M.**; Bruno, J.P.; Burk, J.A.; Herzog, C.D.; Nowak, K.A.
AGING OF THE BASAL FOREBRAIN CORTICOPETAL CHOLINERGIC SYSTEM: INTERACTIONS BETWEEN THE EFFECTS OF AGE AND PRIOR LOSS OF CORTICAL CHOLINERGIC INPUTS ON CORTICAL ACH EFFLUX AND ATTENTIONAL PERFORMANCE

11:15-11:30 **Pletnikov, M.**; Dietz, D.; Vogel, M.; Moran, T.H.; Carbone, K.
DIFFERENTIAL AUTISM-LIKE NEURODEVELOPMENTAL DAMAGE IN "VULNERABLE" FISHER344 RATS AND "RESISTANT" LEWIS RATS

11:30-11:45 **Gonzalez-Lima, F.**; Jones, D.
BRAIN IMAGING OF PAVLOVIAN DIFFERENTIAL INHIBITION OF BEHAVIOR

11:45-12:00 Eyman, M.; Mandile, P.; **Crispino, M.**; Giuditta, A.
SYNAPTIC PROTEIN SYNTHESIS: MODULATION BY TRAINING

12:00-2:00 **Free Time**

2:00-4:05 **Symposium V: Analyzing neonatal behavior to understand brain development: human and animal data**
Organizers: Gemma Calamandrei, Italian National Health Institute, Rome, Italy.
Laura Ricceri, Italian National Health Institute, Rome, Italy.

2:00-2:25 **Monk, C.**; Fifer, W.P.; Tseng A.; Anderson, K.
NEUROBEHAVIORAL DEVELOPMENT OF HUMAN PERINATE

2:25-2:50 **Cioni, G.**
ONTOGENY OF EARLY MOTOR BEHAVIOR PATTERNS AND BRAIN DAMAGE

2:50-3:15 **De Schonen, S.**; Sangrigoli, S.; Turati, C.
VISUAL COGNITION: CORTICAL FUNCTIONAL SPECIALIZATION AND POSTLESIONAL PLASTICITY IN INFANCY

3:15-3:40 **Calamandrei, G.**; Ricceri, L.; Puopolo, M.
ANIMAL MODELS OF EARLY BRAIN DAMAGE: A BATTERY OF TESTS FOR NEONATAL ANALYSIS OF BEHAVIOR AND RELATED STATISTICAL ISSUES.

3:40-4:05 **Zimmerberg, B.**; Rosenthal, A.J.; Davidson, A.L.
ULTRASOUNDS IN RODENTS: EARLY MARKERS OF ALTERATION IN CNS DEVELOPMENT

4:05-5:00 **Break/Exhibitors Display**

5:00-6:00 **Keynote Speaker: John C. Crabbe**, Oregon Health Sciences University, Portland, OR, USA
BEHAVIORAL GENOMICS: ABUSED DRUGS AS A MODEL SYSTEM

6:00-7:00 **Business Meeting**
Exhibitors Display

7:00-7:30 **Marjorie A. Myers Lifetime Achievement Award in Behavioral Neuroscience**
Robert L. Isaacson, Binghamton University, Binghamton, NY, USA
THE FUTURE: NEW IDEAS AND NEW WORDS

8:00-10:00 **Banquet (La Palma Hotel)**
Presentation of Travel Awards
Recognition of Local Scientist: Gaetano DiChiara

Sunday, June 23:

8:00-10:00 **Symposium VI: Hormones, behavior and the neural circuits that guide them**
Organizers: Jennifer Swann, Lehigh University, Bethlehem, PA, USA; Anne Murphy, University of Maryland School of Medicine, Baltimore, MD, USA

8:00-8:25 **Murphy, A.**
NEURAL CIRCUITS UNDERLYING MALE REPRODUCTIVE BEHAVIOR

8:25-8:50 **Berkley, K.J.**
HOW DO CHANGES ASSOCIATED WITH REPRODUCTIVE STATUS CONTRIBUTE TO OUR UNDERSTANDING OF SEX DIFFERENCES IN PAIN?

8:50-9:15 **Young, L.**
NEUROENDOCRINE REGULATION OF SOCIAL ATTACHMENT IN THE MALE PRAIRIE VOLE

9:15-9:35 **Schneider, J. E.**
NEURAL CIRCUITS THAT LINK ENERGY BALANCE TO REPRODUCTIVE SUCCESS

9:35-10:00 **Swann, J.M.**; Wang, J.; Govek, E.K.
NEUROANATOMICAL EVIDENCE FOR THE ORGANIZATIONAL AND ACTIVATIONAL EFFECTS OF GONADAL STEROIDS

10:00-10:15 **Refreshment Break**

10:15-12:15 **Oral Session 4: Feeding and body weight regulation**
Chairperson: Timothy H. Moran

10:15-10:30 **Monda, M.**; Viggiano, A.; Salemme, M.; De Luca, B.
A PARADOXICAL EFFECT OF OREXIN A: THE HYPOPHAGIA

10:30-10:45 **Dunn, A.J.**; Swiergiel, A.H.
THE MECHANISM OF INTERLEUKIN-1-INDUCED HYPOPHAGIA CHANGES OVER TIME

10:45-11:00 **Rushing, P.A.**; Seeley, R. J.; Lutz, T. A.; Woods, S. C.
REPEATED DAILY ADMINISTRATION OF SALMON CALCITONIN REDUCES THE LEVEL OF DEFENDED BODY WEIGHT IN RATS

11:00-11:15 **Holmes, A.**; Yang, R.J.; Tolliver, T.J.; Huang, S.; Li, Q.; Ren-Patteson, R.F.; Saavedra, M.C.; Murphy, D.L.; Crawley, J.N.
ANALYSIS OF ADULT-ONSET OBESITY AND FEEDING BEHAVIOR IN 5-HT TRANSPORTER-DEFICIENT MICE

11:15-11:30 **Lenard, L.**; Fekete, E.; Bagi, E.; Coy, D.H.
ELEVATION OF BLOOD GLUCOSE LEVEL BY GASTRIN RELEASING PEPTIDE (GRP) MICROINJECTION INTO THE RAT AMYGDALA AND ITS ELIMINATION BY SELECTIVE GRP RECEPTOR ANTAGONIST

11:30-11:45 **Oomura, Y.**; Li, X.L.; Aou, S.; Hori, N.; Armstrong, D.L.; Wayner, M.J.
AN ESSENTIAL ROLE FOR LEPTIN IN HIPPOCAMPAL SYNAPTIC PLASTICITY

11:45-12:00 **Lutz, T.**; Riediger, T.; Zünd, D.; Barth, S.; Scharrer, E.
A DECREASE IN THE EXPRESSION OF OREXIGENIC NEUROPEPTIDES IN THE LATERAL HYPOTHALAMUS MAY CONTRIBUTE TO THE ANORECTIC ACTION OF AMYLIN

12:00 Adjourn.

1:00-5:00 **Satellite. Brain development, sex differences and stress: Implications for psychopathology.** *Organizers*: Giovanni Laviola, Italian National Institute of Health, Rome, Italy; Susan Andersen, Harvard Medical School, Boston, MA, USA.

1:00-1:25 Susan Andersen (Boston, USA): Age-related changes in the brain as mechanism for psychopathology.

1:25-1:55 Stefania Maccari (Lille, FR): Influence of prenatal stress and psychopathology: Implications of glucocorticoid hormones.

1:55-2:25 Judith Stern (New Brunswick, USA): Stress and maternal responsiveness: A mother's point of view.

2:25-2:55 Dario Maestripieri (Chicago, USA): Develpmental consequences of infant abuse in rhesus monkeys.

2:55-3:05 Coffee Break

3:05-3:30 Giovanni Laviola (Roma, Italy): Adolescence and psychobiological risk factors for vulnerability to psychostimulants.

3:30-4:00 Keith Matthews (Dundee, UK): Periodic neonatal maternal separation: Effects on adult responses to appetitive stimuli.

4:00-4:30 Francesca Cirulli (Roma, Italy): Early maternal separation and NGF expression in the developing rat brain.

4:30-5:00 Martin H. Teicher (Boston, USA): Effects of child maltreatment: Clinical findings and implications.

Wednesday, June 19

7:30-8:30 Keynote Speaker: Gaetano DiChiara

NEUROBIOLOGY OF DRUG ADDICTION, Di Chiara, G. Dept. Toxicology, Univ. Cagliari, Cagliari, Italy. Drug addiction can be conceptualized as a disturbance of motivated behavior related to responding for drug reinforcers. This notion is consistent with the operational definition of dependence by DSM IIIR and IV where items 3-5 (persistent desire and unsuccessful attempts to quit; use of drugs in larger amounts and for longer period than intended; continued use in the face of medical, familiar or social problems) express the strong control by drugs over the subject's behavior while items 6 and 7 (important social, familiar and recreational activities given up or reduced because of drug-seeking; expenditure of a great deal of time and activity in relation to drugs) reflect the focusing of behavior on drugs at the expense of non-drug reinforcers. Clinical accounts indicate that conditioned stimuli acquired through pavlovian association with the drug itself play a major role in the maintenance and relapse of drug-seeking .Thus ,the motivational disorder of drug addiction can be understood as the result of an excessive impact exerted by drug-related incentives on instrumental responding for drugs .This abnormality has been explained by Incentive –Sensitization (Robinson and Berridge) and by Appetitive Dependence theories (Koob and Le Moal) as the result of non-associative mechanisms acting at the stage of the expression of incentive motivation or of responding. We instead propose that the motivational disturbance of drug addiction takes place at the stage of acquisition i.e. of pavlovian incentive learning . Drugs share with conventional reinforcers the property of stimulating dopamine transmission in the accumbens shell but this effect is not subjected to habituation upon repeated drug exposure as instead is the case of conventional reinforcers. The repetitive, non-decremental stimulation of DA transmission induced by drugs in the shell abnormally strengthens stimulus-drug associations. Thus, stimuli contingent upon drug reward acquire powerful incentive properties after a relatively limited number of predictive associations with the drug and, once acquired, become particularly resistant to extinction. By this mechanism stimuli conditioned to drugs by pavlovian association acquire excessive incentive value, thus abnormally facilitating behavior instrumental to the self-administration of the drug to which they have been conditioned .Under these conditions, response non-contingent occurrence of drug-conditioned cues or contexts facilitates or even reinstates drug self-administration (transfer from pavlovian to instrumental responding).

Thursday, June 20

8:30-10:30 Symposium I: The Role of the Immune System in Behavior: New Frontiers

CONDITIONING IN THE RAT: AN IN VIVO MODEL TO INVESTIGATE THE MOLECULAR MECHANISMS AND CLINICAL IMPLICATIONS OF BRAIN-IMMUNE COMMUNICATION. Goebel, M.; Exton, M.S.; Schedlowski, M. Department of Medical Psychology, University Clinic of Essen, Germany. A wealth of in vitro and in vivo evidence has described both close anatomical interaction and functional bi-directional communication between the immune and central nervous systems (CNS). These data have provided a framework for understanding the physiological mechanisms whereby behavioral factors may impact immune-related disease. An understanding of this interaction, however, as well as verification of the biological relevance of communication among these systems, requires in vivo animal modeling. The development of psychoneuroimmunological models in the laboratory rat has played a key role in advancing the understanding of the influence of behavior on immune status. One such paradigm is the behavioral conditioning of immune function in the rat. This elegant model is characterized by the ability to examine simultaneously both afferent and efferent brain-immune communication. Specifically, the role of peripheral cytokines in signaling the brain, as well as their anatomical and cellular targets in the CNS, can be identified. On the other hand, the neural and humoral pathways whereby the CNS influences the function and distribution of peripheral immunocytes can be demonstrated, together with the target hormone receptors on immunocompetent cells. Finally, the in vivo biological relevance of brain-immune communication is revealed by behavioral conditioning, demonstrating that behavioral processes can modify clinically relevant conditions such as heart allograft survival. Behavioral conditioning thereby provides an excellent example of the utility of in vivo laboratory rat models in psychoneuroimmunology research. Such paradigms not only provide a more complete knowledge of CNS-immune system interaction, but are the platform for determining potential clinical information of this information.

COGNITIVE EFFECTS OF IMMUNE ACTIVATION. Kent, S.; Sell, K.M.; Dedda, K.; Crowe, S.F. School of Psychological Science. La Trobe University, Bundoora, VIC 3086 Australia. Infection and inflammation are usually accompanied by profound physiological and behavioural changes (e.g., fever, loss of appetite) due to the actions of the pro-inflammatory cytokines. Recent evidence suggests that cognitive deficits are also associated with immune activation. We have investigated the effects of lipopolysaccharide (LPS), the active fragment of Gram-negative bacterial cell wall, and polyinosinic: polycyctidylic acid (poly I:C), a synthetic double stranded viral RNA, on the memory processes of day-old chicks trained on a single-trial passive avoidance task. Results have been interpreted in terms of the Gibbs and Ng (1977) three-stage model of memory, to determine the point at which memory processing becomes impaired. Dose-response studies were conducted with both compounds and the optimal dose tested at several administration times. These results were used to test for retention at 5, 10, 20, 40, 60, and 90 min following training. LPS resulted in deficits in memory processing evident by 20 min post-training, whereas poly I:C resulted in deficits at 40 min post-training. These results demonstrate an inhibitory effect of immune activation on memory processing at the transition point from short-term memory to intermediate-term memory (ITM) in the case of LPS and the transition between ITM (A) and ITM (B) for poly I:C. These findings suggest a possible role for

sodium pump activity and ATP synthesis, which are necessary for retention of the task beyond 20 min post-training. We have recently demonstrated that LPS suppresses brain Na+/K+-ATPase activity both before and after training on the passive avoidance task compared to saline-treated and untreated/untrained controls. Further, both LPS and poly I:C induced fever and LPS increased plasma corticosterone.

MOTIVATIONAL EFFECTS OF IMMUNE ACTIVATION. Susan J. Larson, Dept. of Psychology. Concordia College, Moorhead, MN 56562. It is well known that immune system activity induces changes in behavior such as decreased food intake, decreased exploratory behavior, increased sleep, impaired cognitive functioning and lack of interest in pleasurable stimuli. These changes are mediated by pro-inflammatory cytokines and cytokines, most notably interleukin-1ß (IL-1ß), produce the same profile of behavior change as infection and inflammation. Although, in general, immune activity produces decreases in behavior, studies have shown that behavior change depends upon testing conditions. For instance, reduced food intake induced by treatments such IL-1ß is less apparent in food-restricted organisms than in free feeding organisms. Studies of this nature, demonstrating differential effects of immune activation depending upon environmental contingencies and physiological states, support the hypothesis that the behavioral effects of immune activation depend upon motivation. For example, in as much as food-restriction increases motivation for food, it appears that motivation mediates the effect of IL-1ß on feeding-related behavior. During this presentation, the role of motivation in immune-induced behavior change will be discussed and evidence supporting a motivational analysis will be presented. The value, as well as potential limitations, of using a motivational approach to synthesize and understand immune-induced behavior change will be considered.

CYTOKINE-INDUCED CHANGES IN BEHAVIOR IN SYSTEMIC AUTOIMMUNE DISEASE. Sakic, B. **:** Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton Ontario L8N 3Z5, Canada. Development of the systemic autoimmune disease lupus erythematosus is characterized by changes in affective behavior and emotional reactivity. In particular, depression and anxiety of unknown etiology coincide with serological manifestations of inflammation, such as hyperproduction of pro-inflammatory cytokines. To elucidate the role of immune factors in the etiology of autoimmunity-induced behavioral dysfunction we have been examining the behavior and brain morphology of lupus-prone MRL-lpr mice. Similarly to humans, these animals show changes in motivated and ingestive behaviors at the time when serum levels of interleukin-6 and interferon-gamma start to increase, but well before other manifestations of the disease are apparent. The series of our recent experiments suggest that proinflammatory cytokines have multiple roles in the etiology of aberrant behavior. They may include activation of the pituitary-adrenal system, stimulation of the nervus vagus, and expression of cell adhesion molecules on endothelial cells of the blood-brain barrier at the onset of the disease. However, it is possible that at an advanced stage of the lupus-like disease some cytokines induce neurotoxicity when present in the cerebrospinal fluid. The above results will be discussed in relationship to the etiology of neuropsychiatric lupus and immune theory of mental disorders, such as major depression, schizophrenia, and Alzheimer's disease.

11:00-12:00 Keynote Speaker: Edward Stricker

THE BIOLOGICAL BASES OF THIRST: AN INTEGRATION OF EXCITATORY AND INHIBITORY SIGNALS. Stricker, E.M. Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260 USA. It is generally recognized that three signals can stimulate thirst independently. One signal is elicited by an increase in osmolality of systemic body fluids (detected by cerebral osmoreceptors), while a second is elicited by a decrease in plasma volume (detected by cardiac baroreceptors). The third signal is mediated by an increase in blood levels of the peptide hormone angiotensin II (detected by angiotensin II receptors in the subfornical organ), as might be elicited by a decrease in arterial blood pressure. In addition to these excitatory signals, there also are two signals that can inhibit thirst: one derived from a decrease in osmolality of systemic body fluid (presumably detected by cerebral osmoreceptors), and the other derived from an increase in arterial blood pressure (detected by arterial baroreceptors). Recent experiments indicate that two more signals should be added to this mix of stimuli in rats; one is excitatory and the other is inhibitory, and both are mediated by peripheral osmoreceptors in response to the composition of fluid leaving the stomach. Thus, gastric NaCl loads, in addition to increasing systemic plasma osmolality, have the more rapid effect of stimulating thirst via visceral osmoreceptors. The induced water intake has two effects: a rapid one, acting on the putative visceral osmoreceptors to inhibit drinking, and a slow one, when absorbed water lowers systemic plasma osmolality and affects the cerebral osmoreceptors. The point here is that signals from putative visceral receptors promote osmoregulation by allowing rats to respond promptly to the composition of ingested fluid, well before the time required for absorption of that fluid into the systemic circulation. We presume that the amount of water consumed by thirsty rats is determined by the relative strengths of these excitatory and inhibitory signals, perhaps acting together with other inhibitory signals stimulated by associated gastric distension.

2:00-4:00 Oral Session 1: Neurobiology of addiction and related issues

IRON DEFICIENCY DELAYS COCAINE SELF-ADMINISTRATION IN RATS. Jones, B.C.; Wheeler, D.S.; Beard, J.L.; Grigson P.S. Nutritional Neuroscience Group. The Pennsylvania State University, University Park, PA 16802 USA. Iron deficiency impairs nigrostriatal and mesolimbic dopamine systems by causing decreased densities of D1 and D2 receptors and the dopamine transporter in the terminal fields, caudate-putamen and nucleus accumbens. Iron deficiency also causes related deficits in dopamine-related pharmacological indices, e.g., locomotor stimulation by cocaine and locomotor inhibition by raclopride. Based on this knowledge, we hypothesized that iron deficiency would have a major impact on cocaine self-administration. Male Sprague-Dawley rats were fed an iron-deficient diet starting in adolescence (day 21) and continuing throughout the experiment. At 53-55 days of age, all animals received surgically implanted jugular catheters. Approximately one week later, all animals were trained to lick empty water spouts for water and then iv cocaine, delivered by infusion pump at 0.33 mg/kg. During the course

of training, all animals acquired iv cocaine self administration, however the course of acquisition was significantly and profoundly slower for the iron deficient than control animals. When tested for responding on a progressive ratio of reinforcement, the control animals maintained a constant number of infusions, whereas the iron deficient animals' responding fell off sharply. When the dose of cocaine was decreased, control, but not iron deficient animals adjusted the amount administered by increased responding. When tested for sucrose reinforcement, the responding of iron deficient animals was indistinguishable from the responding of control animals. The outcome clearly shows that severe iron deficiency early in life can diminish the capacity of cocaine, but not sucrose to reinforce behavior. The question raised by this research thus, is whether iron deficiency alters hedonic-like responses only to dopamine-related behaviors.

THE ANTIDEPRESSANT BUPROPION INCREASED BRAIN REWARD FUNCTION AND REVERSED NICOTINE WITHDRAWAL. Athina Markou, Karen L. Skjei, Adrie Bruijnzeel and John F. Cryan. Department of Neuropharmacology, The Scripps Research Institute, 10550 North Torrey Pines Rd., CVN-7, La Jolla, CA 92037, U.S.A. Withdrawal from drugs of abuse results in deficits in brain reward function similar to those observed in major affective disorders. Bupropion is an atypical antidepressant whose mechanism of action involves potentiation of dopaminergic and noradrenergic neurotransmission. Further, bupropion is the only non-nicotine based therapy currently approved for smoking cessation. As the negative affective aspects of withdrawal are hypothezised to contribute to the tobacco smoking habit, the present studies assessed the effects of bupropion on brain reward function under baseline conditions and subsequent to withdrawal from chronic nicotine exposure in rats. Rats were prepared with electrodes in the lateral hypothalamus and their current-intensity thresholds were assessed as a measure of reward. Bupropion (10-60 mg/kg) dose-dependently lowered reward thresholds under baseline conditions indicating an increase in reward. In contrast, the tricyclic antidepresssant desipramine (2.5-10 mg/kg) elevated thresholds slightly. Rats withdrawn from chronic nicotine exposure exhibited an elevation in thresholds indicative of "diminished interest or pleasure" (i.e. anhedonia) in the rewarding stimuli. Administration of bupropion dose-dependently diminished this reward deficit, with a protracted effect at the highest dose tested. Finally, the effects of bupropion on the somatic signs of nicotine withdrawal were also assessed. These data demonstrate that bupropion's superior utility over other antidepressants as an aid to smoking cessation may be due to its ability to reverse the negative affective aspects of nicotine withdrawal.

MODULATION OF THE LONG TERM NEUROTOXICITY OF MDMA ("ECSTASY") BY THC IN RATS. McGregor I. S.; Morley, K.C.; Hunt, G.E.; Li, K.; Duffield, H. Departments of Psychology, Psychological Medicine and Pharmacology, University of Sydney, NSW 2006, Australia. MDMA ("Ecstasy") is a drug that is widely used around the world. There is increasing evidence that heavy use of the drug damages brain 5-HT systems and that this could lead to chronic emotional and cognitive problems. We have recently shown that male Wistar rats briefly exposed to MDMA (4 x 5 mg/kg i.p. over 4 hours on each of 2 days) show long term increases in anxiety-like behavior when assessed in the drug-free state three months after MDMA (Morley et al (2001) EJP, 433, 91-99). Human MDMA users frequently consume cannabis while under the influence of MDMA and in ongoing work we have examined whether this might modulate the long term neurotoxic effects of MDMA in rats. The main psychoactive constituent of cannabis delta-9-THC (4 x 2.5 mg/kg) reversed the acute hyperthermic effects of MDMA (4 x 5 mg/kg) on each of two days of administration, with rats given the MDMA/THC combination showing a robust hypothermia. One month later rats that had received the MDMA/THC combination were found to be marginally less anxious on the emergence test and social interaction tests than rats that had previously received MDMA alone. Neurochemical analysis (HPLC) at six weeks post drug showed that THC had attenuated the 5-HT depletion produced by MDMA in the striatum, amygdala and cortex. We hypothesise that by minimising the acute hyperthermic effects of MDMA, THC may partly protect against MDMA neurotoxicity and associated long term changes in mood and behaviour.

ALTERATIONS IN THE EXPRESSION OF DOPAMINE DA1 AND DA2 MRNA AND THE INDUCTION OF LONG-TERM POTENTIATION (LTP) IN RATS SENSITIZED TO METHAMPHETAMINE. Chirwa, S.; Reasor, J.; Onaivi, E.S. Dept. Anatomy and Physiology, Meharry Medical College, Nashville, TN 37208, and Biology, William Paterson University, Wayne, NJ 07470. We have begun to characterize methamphetamine induced alterations in gene expression and how this correlates with changes in cognitive functions. Thus, we randomly divided 30 Long Evans rats into 3 groups which were then treated with either 1 mg/kg (LOM), or 10mg/kg methamphetamine (HIM), or saline (SAL) every day for 90 days. Behavioral assessments were done during the chronic treatment, after which bioelectrical and molecular studies were conducted. Briefly, we found stereotypic and spontaneous locomotor activity were increased in both LOM and HIM rats relative to SAL animals. Further, methamphetamine caused dose-dependent increases in the expression of DA1 and DA2 mRNA for both dopamine DA1 and DA2 receptors. The mean increase in DA1 mRNA expression was 19.7% in the LOM group and 39.3% in the Him group, when compared to the SAL group. Similarly, DA2 mRNA expression increased by 36.4% in the LOM and 40% in the HIM group relative to the SAL group. Whereas synaptic transmission remained unaltered in all animal groups, the propensity to produce long-term potentiation (LTP; a cellular correlate of learning and memory) in the hippocampus was reduced as follows. Tetanic stimulation (100 Hz, 1 sec) reliably produced LTP in 5 of 5 hippocampal slices obtained from representative SAL rats. In contrast, only 2 of 6 slices obtained the LOM group exhibited LTP. None of the slices from the HIM group developed LTP. Presuming the effects of methamphetamine were mediated via increased release of dopamine, our result suggests that there may be a "threshold" beyond which excessive activation of the dopaminergic system, as probably occurs with chronic methamphetamine administration, results in antagonism of LTP expression. (Supported in part by NIH grants RR0303208 and MH 57067).

PRENATAL OPIATE AND QUASI-OPIATE WITHDRAWAL ACTIVATE THE EMBRYONIC HPA AXIS. Schrott, L.M.; Sparber, S.B. Dept. of Pharmacology, Univ. of Minnesota, Minneapolis, MN 55455 USA. Opiate withdrawal is associated with HPA axis activation postnatally, suggesting it may act functionally as a "stressor". To determine if the developing embryo also mounts an HPA axis response to withdrawal, we used a chicken model system where we directly measure behavioral and physiological indices of withdrawal. White Leghorn chick embryos were made opiate dependent via administration of N-l-alpha-noracetylmethadol (NLAAM) on embryonic day 4 (E4). Opiate withdrawal was precipitated via the antagonist naloxone (NX; 10 mg/kg egg) on E15 or E18. Trunk blood was obtained 30 min post-injection and sera corticosterone (CORT) measured via radioimmunoassay. NLAAM on its own had no effect on E15 or E18 CORT concentrations, nor did NX in the absence of opiates increase CORT. However, on both E15 and E18 there were significant increases in CORT in NLAAM + NX-treated embryos and this effect was dose-related on E18. Prior research found that isobutylmethylxanthine (IBMX) mimicked aspects of precipitated opiate withdrawal when administered to chick embryos. Thus, we determined if IBMX similarly activated the HPA axis on E18. IBMX on E18 (10 mg/kg egg) increased serum CORT in a time-dependent fashion and to a similar magnitude as that of NX-induced opiate withdrawal. These data indicate that while chronic opiate exposure was not sufficient to activate the developing HPA axis, true or quasi-opiate withdrawal did increase serum CORT. Thus, prenatal opiate withdrawal may be more deleterious to the developing organism than chronic opiate exposure itself, and may be an important mechanism for subsequent postnatal dysfunction. Supported, in part, by USPHS NIDA grants K01 DA00362 and R37 DA04979.

EFFECTS OF EARLY MATERNAL DEPRIVATION AND CANNABINOID EXPOSURE IN ADOLESCENT MICE OF BOTH SEXES. Macrì S., Laviola G., Behavioural Pathophysiology Section, Lab F.O.S. Istituto Superiore di Sanità, viale Regina Elena 299, I-00161 Roma, Italy. Human adolescents are reported to display elevated levels of sensation-novelty-seeking behaviour that also includes the use of a number of psychoactive agents. A self-medication hypothesis has also been suggested for adolescents' coping with stressful life events and age-dependent changes in mood concerns. In this frame, animal models provided evidence that early maternal deprivation has profound consequences on emotional and affective as well as physiological responses in adult rodents. Outbred CD-1 mice from both sexes, which underwent a single 24-hr episode of maternal deprivation (DEP) on postnatal day (pnd) 12, were administered the cannabinoid agonist WIN 55,212-2 (0, 0.5 or 2 mg/kg) for three days during adolescence (pnd 35-37). The analysis of mice response to this subchronic administration revealed an hypotermic effect, an elevation in pain threshold and a marked reduction in general locomotion. A tolerance to some drug effects was also shown. Upon drug administration, mice also underwent a socio-sexual interaction test (experimental mice encountering target stimuli of both sexes). A marked reduction in social sniffing and in the time spent in "social" climbing on a mate-containing grid was found in DEP male mice. Drug treatment interacted with maternal deprivation by producing a mixed profile. Main drug effects were limited to a reduction in self-grooming behaviour upon the high WIN dose. Data from the present experiment strongly suggest that early life experiences might reduce the ability to cope with social duties emerging with the onset of adolescence. Cannabinoid consumption, however, does not seem to help in recovering this situation.

REPEATED SPINAL WIN55,212-2 ELICITS ABNORMAL PAIN AND ANTINOCICEPTIVE TOLERANCE. L. Gardell; F. Porreca, Department of Pharmacology, University of Arizona HSC, Tucson, AZ 85724, USA. Sustained spinal opioids paradoxically produce pain which manifests as decreased antinociceptive potency (i.e., tolerance). Elevated levels of spinal dynorphin promote abnormal pain. These possibilities may also relate to other analgesic classes, such as cannabinoids. Sensory thresholds to non-noxious tactile and noxious heat were recorded. Spinal WIN55,212-2, but not WIN 55,212-3 (inactive enantiomer) or vehicle produced antinociception (52°C tail-flick test). Repeated i.t. WIN55,212-2, but not WIN55,212-3 or vehicle, also produced time-dependent tactile and thermal hypersensitivity accompanied by decreased spinal antinociception. WIN55,212-2, but not WIN55,212-3 or vehicle, significantly increased spinal dynorphin content on day 5. MK-801 or dynorphin antiserum reversed abnormal pain. Similarly, antinociceptive tolerance was blocked by MK-801 or dynorphin antiserum. The antinociceptive potency of WIN55,212-2 in non-tolerant mice was not altered by either MK-801 or antiserum to dynorphin. These results extend to the cannabinoid system, and perhaps by inference to other inhibitory GPCRs on primary afferents, the observation that prolonged exposure to an agonist can elicit abnormal pain. Such increased pain manifests as antinociceptive "tolerance" and manipulations that block pain also block "tolerance".

NONOPIOID STRESS-INDUCED ANALGESIA IS MEDIATED BY AN ENDOCANNABINOID MECHANISM. Hohmann, A.G.; Neely, M.H.; Suplita, R.L., Farthing, J.; Nackley, A.G.; Holmes, P.V.; Crystal, J.D. Biopsychology Program, Department of Psychology, The University of Georgia, Athens, GA, USA. A large body of literature indicates that environmental stressors activate an endogenous mechanism for suppressing pain that is insensitive to opioid antagonists. However, the mechanism underlying nonopioid stress-induced analgesia has remained a major gap in the knowledge base. The present studies were conducted to test the hypothesis that nonopioid stress-induced analgesia is mediated by a cannabinoid mechanism. Nonopioid stress-induced analgesia was induced in rats using brief, continuous footshock. SR141716A, a competitive antagonist for cannabinoid CB1 receptors, blocked nonopioid stress-induced analgesia, defined behaviorally in the tail-flick test. By contrast, the opioid antagonist naltrexone and the competitive antagonist for cannabinoid CB2 receptors, SR144528, failed to alter stress analgesia in this paradigm. Blocking reuptake of the endocannabinoid anandamide with AM404 potentiated nonopioid stress-induced analgesia. Acute administration of the prototypic classical cannabinoid **Δ** 9-tetrahydrocannabinol similarly enhanced stress analgesia. Stress analgesia was attenuated in rats rendered tolerant to the potent cannabinoid agonist WIN55,212-2 but not in rats rendered tolerant to morphine. These data are consistent with direct support for the hypothesis that environmental stressors release endocannabinoids, as demonstrated by high performance liquid chromatography mass spectrometry (HPLC/MS). Administration of SR141716A directly to the dorsal periaqueductal gray or rostral ventral medulla attenuated nonopioid stress analgesia, suggesting that a

descending cannabinoid modulatory system is activated by stress to produce adaptive changes in pain responsiveness. The present data demonstrate that nonopioid stress-induced analgesia proceeds through a CB1 mechanism and is mediated by endogenous cannabinoids. (Supported by DA14265 and UGARF).

4:00-6:00 Poster Session I: Ingestion, Motivation, Hormones And Behavior, Learning And Memory

1. HYPOTHALAMIC ARCUATE NEURONS OF HYPERPHAGIC OVERWEIGHT RATS ARE NOT INHIBITED BY INSULIN. Davidowa, H.; Plagemann, A. Institute of Physiology; Institute of Experimental Endocrinology, Faculty of Medicine (Charité), Humboldt University Berlin, Tucholskystr. 2, D - 10117 Berlin, Germany. Arcuate neurons that produce neuropeptide Y to induce feeding are normally inhibited by insulin. We studied now the responses of arcuate neurons to insulin (Human recombinant insulin, 50 µl drops of 100 nM, further diluted about 50 times by the perfusion medium) in brain slices of male, overweight rats (5th to 12th week of age). These rats grew up until weaning in small litters of three pups per mother (SL) compared to 10 rats in control litters (CL). SL rats are persistingly hyperinsulinemic, hyperglycemic and hyperleptinemic. The body mass of SL rats ($n = 12$) was 70,5 g compared to 45,9 g (CL, $n = 12$) on day 21 ($p < 0.0001$) and remained greater during later life. The daily food intake was significantly greater ($p < 0.05$) than that of normal rats (measured from day 60 to 68 it was 36.3 g per SL rat compared to 32.4 g). There was a significant difference in the effect of insulin on arcuate neurons of SL rats compared to controls ($p < 0.01$). Whereas an inhibitory action of insulin significantly predominated in normal rats ($p < 0.0005$), arcuate neurons in SL were rarely suppressed, but more often activated. The peak of the distribution of interspike - intervals of arcuate activity was moved to shorter values in SL ($p < 0.05$). This altered response to the satiety signal insulin, possibly developed during the critical differentiation period in postnatally overnourished rats, might contribute to their persisting hyperphagia and overweight. All procedures were carried out in accordance with the guidelines for the care of animals. Supported by grant Da 275/2-1 from the DFG, Germany.

2. GHRELIN IN GASTRIC BYPASS MODEL. Meguid, M; Xu, Y; Ohinata, K.; Marx, W.; Tada, T.; Chen, C.; Quinn, R.; and Inui, A. Dept. Surgery, SUNY Upstate, Syracuse, NY 13210. Gastric bypass is routinely done in morbidly obese patients to reduce weight. The hypothesis tested was that gastric ghrelin contributes to reduction in food intake (FI) and weight loss. Obese Zuckers (400g) were divided into 3 groups (n=8/gp): Sham-surgery ad lib-food (Controls); Gastric Bypass (GB, 20% gastric pouch); and Sham-surgery Pair-Fed (PF). Rats were fasted for 24h then given (1 kcal/ml) ad lib for 4d, then chow for 14d (3.5 kcal/g). Daily®liquid Boost FI and body weight (BW) were measured and compared statistically. In the 3 groups, rate of weight gain for 1 wk before surgery was similar (ns). After surgery, there was a 5-6 d decrease in BW in Controls. Thereafter BW increased by was 8g/d ($p<0.05$) reaching ~500g at 20d, when rats were killed. In contrast GB/PF continued to decrease BW below starting weight for 14d ($p<0.05$), then increased BW (3g/d; ns) reaching ~400g by 20d.Controls normalized energy intake (EI) in 5d. After surgery EI in GB (and thus PF) were similar to Controls (ns) at 19d. Gastric ghrelin mRNA in GB was underexpressed. Serum ghrelin at 20d, was SE (p±0.08ng/ml, M±lower in GB (0.74<0.05ng/ml) or±0.05)) vs. PF (1.07 0.05ng/ml). Retroperitoneal and epididymal fat mass and FFA±Controls (0.97 decreased ($p<0.05$) vs. Controls. Triglycerides (TG) did not change. Necropsy: size of gastric pouch grew proportionately in Controls and was empty of food. Pouch in PF remained unchanged and was also empty. GB's pouch always contained food and was consistent with raised insulin and lower FFA. Gastric ghrelin was released in response to FI but diminished after GB; being an appetite stimulatory gastric peptide acting as neuropeptide in arcuate nucleus and VMN, an area of known neuroendocrine and autonomic regulation of metabolism.

3. NEW CONSTITUENTS OF THE CENTRAL GLUCOSE-MONITORING NETWORK: CHEMOSENSORY NEURONS IN THE NUCLEUS ACCUMBENS OF THE RAT. Lukáts, B.; Papp, Sz. and Karádi, Z. Institute of Physiology, Pécs University, Medical School, H-7643 Pécs, Hungary. The nucleus accumbens (NAcc), a key structure of the forebrain limbic circuitry, is known to be involved in several regulatory mechanisms. Its role in the central feeding control has also been demonstrated. Nevertheless, related functional characteristics of NAcc neurons, with particular emphasis on their endogenous and exogenous chemosensitivity, are yet to be defined. In the present experiments, therefore, extracellular single neuron activity of the NAcc of male Wistar rats was recorded by means of tungsten wire multibarreled glass microelectrodes during 1) microelectrophoretic administration of chemicals, and 2) gustatory stimulations. Appx. the fifth of all neurons tested were either of the glucose-sensitive (GS) or glucose-receptor (GR) type of cells. A great majority (~80%) of these glucose-monitoring (GM) neurons were found to be modulated by gustatory stimuli as well. A clear topographical distribution of the GM cells was found: GS units were predominant in the 'shell', whereas GR neurons in the 'core' division of NAcc. In both region, the prevailing sort of chemosensory cells proved to be broadly tuned across qualities of the gustatory stimulus array, while the other /minor/ type of GM neurons (i.e., GR in the 'shell' and GS in the 'core') displayed more specific responses, to one or two tastants only. In addition to the above, differential activity changes to various neuromodulators were also seen in these chemosensory cells. The present data provided evidence for the existence of GM neurons in the rodent NAcc. Our results, along with previous data, also revealed that these cells possess specific endogenous and exogenous chemosensitivity in integrative-associative processes of the central feeding control.

4. Withdrawn.

5. EFFECTS OF D1 AND D2 AGONISTS ON MATCHING IN AN OPEN FORAGING PARADIGM. Martin, J; Bradham, K; Fleming, E; Farmer-Dougan, V; Wallrich, L; Dean, M. Departments of Psychology and Biological Sciences. Illinois State University, Normal, IL 61790-4620 USA. The dopaminergic cells of the mesolimbic system play a role in orienting animals toward environmental stilmuli. This study uses an infrared activity chamber to observe foraging behaviors of rats during injections of D1 and D2 dopamine agonists. Rats were trained in high or low activity tasks. The high group had to exhibit greater than 10,000 cm movement in 20 minutes, while the low

group had to exhibit less than 1,500. D1 and D2 agonists were administered and several parameters were measured. Amount of activity, onset of activity, and location of path choice (for high activity group).

6. ELIMINATION OF FEEDING SUPPRESSION EFFECT OF GASTRIN RELEASING PEPTIDE (GRP) BY SELECTIVE GRP RECEPTOR ANTAGONIST IN THE RAT AMYGDALA. Fekete, É.[1]; Bagi, É.E.[1]; Coy, D.H.[2]; Tóth, K.[1]; Lénárd, L.[1] [1]Inst. of Physiol. and Neurophysiol. Res. Group of the HAS, Pécs Univ. Med. School, Pécs, H-7643, Hungary and [2]Peptide Res. Lab. Tulane Univ. Med. Center, New Orleans, LA 70112, USA. Gastrin releasing peptide (GRP) and neuromedin B (NMB) are involved in the mechanisms of satiety. It has been revealed that two receptor subtypes are present in the central part of the amygdaloid body (ACE), namely the GRP- and NMB-preferring receptors. In our experiments bilateral guide tubes were implanted into the ACE. Vehicle (0.4 ul of 0.15 M NaCl), GRP (25, 50, 100, 150 or 300 ng/site) or NMB (15, 30 or 60 ng/site) were microinjected bilaterally. Selective GRP receptor antagonist [D-Phe6]-BN-(6-13)-Methyl ester (BME, 125 or 250 ng/site) was also used alone or in combination with 150 ng GRP or 30 ng NMB. Liquid food intake was measured in every 5 min for 60 min. Fifty and 150 ng GRP significantly suppressed consumption for 10 min while 100 ng GRP caused food intake reduction for 25 min. The lowest and the highest doses of GRP were ineffective. Fifteen or 60 ng NMB decreased food intake for 5 min, 30 ng for 10 min, respectively. BME used alone did not modify feeding. Effect of GRP was completely blocked by prior application of 125 or 250 ng BME. Effect of NMB could not be prevented by 125 ng BME, however, 250 ng attenuated feeding suppression. Our results suggest that GRP-preferring receptors in the ACE play specific role in the mechanisms of satiety. (This work was supported by OTKA T 034489, ETT 354/2000, by the HAS and the Pécs University Medical School.)

7. RECEPTORIAL FUNCTIONS IN THE REGULATION OF ANGIOTENSIN II AND III INDUCED DRINKING IN THE ZONA INCERTA OF RATS. Bagi, É. E.; Fekete, É.; Bányai, D.; Lénárd, L. Institute of Physiology, and Neurophysiol. Res. Group of the HAS, Pécs Univ. Med. School, Pécs, H-7643, Hungary. In our experiments the effects of angiotensin II (AII) and III (AIII) microinjections into the zona incerta (ZI) have been studied on drinking. Also, the influence of angiotensin receptor blockers on angiotensin induced drinking were tested. 90ng losartan (Los), an AT1 antagonist or 200ng CGP 42112 (CGP), an AT2 antagonist were injected prior to 100ng AII or 200ng AIII treatments, all dissolved in 0.3µl vehicle (Veh), respectively. Rats were to drink 60 min a day, consequently. Measurements took place in every 5 min during 30 min and in the 60th min. The following combination of treatments were applied: AII or AIII injections for experimenting single agonist effects. Veh+AII, Los+AII or CGP+AII for testing antagonists effects on AII. Veh+AIII, Los+AIII or CGP+AIII for testing antagonists effects on AIII. Equal amounts of Veh were injected for rats served as control groups. The Los+Veh and the CGP+Veh injections were for testing the effects of separate receptorial blockade, without external angiotensin microinjections. Both AII and AIII increased water consumption of rats. This effect of AII could be blocked by Los, but not by CGP 42112. On the other hand, the effect of AIII could not be blocked by losartan, but by the CGP 42112. When only the AT1 receptor was blocked, animals drank significantly less than after the blocking of the AT2. As the effects of AII, AIII, Los and CGP have not been tested in the ZI, the finding that water intake increased after AII or AIII injections and it could be blocked only by either of the antagonists suggests that AT1 and AT2 receptors play partially different roles in the regulation of water intake. (This work was supported by OTKA T 034489, ETT 354/2000, HAS and by the Du-Pont Merck Chemical Co.)

8. OREXIN A INCREASES EXTRACELLULAR GABA IN THE VENTROMEDIAL HYPOTHALAMUS. Viggiano, A.; Mancone, A.; Catone, L.; Montella, R.C. and B. De Luca, Department of Experimental Medicine, Section of Human Physiology Second University of Naples, via Costantinopoli 16, 80138 Naples, Italy. _Orexin A is a hypothalamic neuropeptide which induces an increase in food intake when administered into the lateral ventricle. Since it is well known that the ventromedial hypothalamus (VMH) is involved in the feeding behavior also through GABAergic circuits, the aim of this experiment was to investigate the effect of an orexin A injection on the extracellular levels of GABA in the VMH. GABA levels in the VMH were evaluated in 6 rats by microdialysis and HPLC-electrochemical detection 15 min before and 15-30-45-60 min after an intracerebroventricular injection of orexin A. The same procedure was used in another group of 6 rats but saline was injected into the lateral ventricle as control. The results showed that extracellular GABA increased in the VMH after injection of orexin A. This finding suggests a possible mechanism by which orexin A should induce hyperphagia in the first hour after injection. Since it is already known that the inhibition of the VMH by injection of GABA cause an increase of food intake, it is possible that orexin A causes an in crease of food intake by increasing the release of GABA in the VMH.

9. THE ROLE OF CRH IN ACTIVITY STRESS. Rau, V.; Grijalva, C. V. Dept. of Psychology. University of California, Los Angeles, Los Angeles, CA 90095-1563 USA. Activity stress is an animal model that can be used to study conditions representative of human anorexia nervosa. In the paradigm, animals are given a short daily feeding period and access to a running wheel the remaining time. After continuous exposure to these conditions for a few days, animals decrease food consumption while dramatically increasing running. Body weight drops considerably, and death can ensue without experimenter intervention. The neurochemicals of the stress cascade have been implicated in this model. It has been previously shown that corticosterone and ACTH levels are elevated in animals exposed to activity stress. This study investigates the involvement of CRH in the paradigm. Young (30-45 days old) female Sprague-Dawley rats were used in the study. Animals were given a 5 day period to adapt to the running wheel cages to control for novelty stress effects. On day 6, animals were exposed to either activity stress or a control condition. In activity stress, animals were given a 90 minute feeding period and access to the wheel for the remaining 22.5 hours. The control conditions included (1) a 90 minute feeding period and no wheel access and (2) ad libitum food and wheel access. From day 6 onward, animals were given a daily injection of either a CRH antagonist or vehicle. Food intake, number of wheel revolutions, and body weight were monitored daily. The activity stress conditions produced decreased food intake, increased running, and a decline in body weight. CRH

antagonist administration helped to attenuate the symptoms of activity stress, further implicating the involvement of stress neurochemicals in the paradigm.

10. EFFECTS OF POSTNATAL MATERNAL CHRONIC EXPOSURE TO THE ODOR OF A NAÏVE MALE ON OFFSPRING'S DOPAMINERGIC FUNCTIONING, BODY WEIGHT AND FEEDING IN MICE. Moles, A.; Rizzi R.; D'Amato, F.R. Istituto di Psicobiologia e Psicofarmacologia, C.N.R., Rome, Italy. The aim of this study was to assess the effect of postnatal maternal exposure to the odor of a naïve male conspecific on: 1) behavioral sensitisation to apomorphine; 2) feeding behavior and body weight development in CD-1 mice. Once a day, from postnatal day (PND) 1 to PND 14 mothers of Mother Male Bedding group (M-MB) were exposed for 15 min to the soiled bedding of a novel isolated naïve male, whilst controls (CC) were left undisturbed. On PND 15, after administration of the dopaminergic agonist apomorphine (0.5 mg /Kg) the climbing score of M-MB pups was higher than controls. Litter body weight of M-MB and CC mice did not differ on PND1. On PND 28, the weaning day, both M-MB males and females were lighter than CC. On PND 50 M-MB males weighted still less in comparison to CC. While female mice caught up their controls and on PND 100 weighted more. After weaning (PND 35-40) both male and female M-MB consumed a greater amount of food than CC. As adults (PND 75-80), this effect was still detectable, although was statistically significant only for males. Our results are consistent with the hypothesis that postnatal disruption of mother-offspring relation altered dopaminergic functioning, regardless the sex of the pups and affected both feeding behavior and body weight development to different extent according to the sex of the animals.

11. Withdrawn.

12. INTAKES OF SACCHARIN SOLUTIONS, INCLUDING AN ALCOHOLIC BEVERAGE, AMONG FEMALE RATS TREATED WITH ESTRADIOL VALERATE. Reid, ML; Boswell, KJ.; Fitch JV.; Gentile BM.; Reid, LD. Lab. for Psychopharm., Siena College and Rensselaer Polytechnic Institute, Loudonville, NY 12211 USA. At last year's meeting, data were presented on the effects of a single injection of estradiol valerate (EV) on female rats' ingestion of alcoholic beverages, a saccharin and a sucrose solution. EV provides sustained release of estradiol (E) for weeks. While E is being released, intakes of an alcoholic beverage and a saccharin solution were markedly decreased, but intakes of a sucrose solution were not. After E's release, intakes of alcoholic beverages are increased. To get further information, we gave EV (2 mg) or placebos to female Sprague-Dawley rats. One pair was presented with a saccharin sweetened alcoholic beverage 15 days after the injection. Other pairs were provided either a .0625 or a 2% solution of saccharin (4 groups of 10 subjects each). EV reliably enhanced intakes of the alcoholic beverage, confirming previous findings. EV reliably reduced intakes of the more concentrated saccharin solution, but did not reliably affect the intake of the less concentrated one. The differences observed last year in sweet substance intakes were probably not due to post ingestive effects, but rather to effects related to saccharin's bitterness at higher concentrations, an effect not shared by sucrose solutions. Data on intakes of different saccharin solutions provide a context from which to address the issues of how EV can both decrease and then, subsequently, increase intakes of alcoholic beverages.

13. CHRONIC SUCROSE REDUCES THE ANTAGONISTIC EFFECT OF β-FUNALTREXAMINE ON MORPHINE-INDUCED ANTINOCICEPTION IN BOTH FEMALE AND MALE RATS. Coy, R. T.; Kanarek, R. B. Dept. of Psychology. Tufts University, Medford, MA 02155 USA. Chronic ingestion of a sweet-tasting sucrose solution enhances the pain relieving actions of morphine and other opioid agonists. These results taken in conjunction with other research investigating the effects of intake of palatable foods on the production and release of endogenous opioid peptides have led to the hypothesis that consumption of palatable foodstuffs stimulates the activity of the endogenous opioid system. To further assess this hypothesis, three studies determined if chronic intake of a palatable sucrose solution could block the antagonist effects of the μ-selective opioid antagonist β-Funaltrexamine (β-FNA) on morphine-induced antinociception. Male and female Long-Evans rats were provided with either chow and water, or chow, water and a 32% sucrose solution. In Experiment 1, after four weeks of adaptation to the dietary conditions, female rats received 0 or 10 mg/kg (sc) of β-FNA, while in Experiment 2, a different group of female rats received either 0, 5 or 20 mg/kg of β-FNA. To determine if there were sex differences in the effects of β-FNA, Experiment 3 replicated the first study with the exception that male rats were used. In all three experiments, six days after administration of β-FNA, rats were tested for morphine-induced antinociception using the hot water tail-withdrawal test. Morphine, administered using a cumulative dose regime (1.0, 3.0, 5.6, 10.0, 31.0 mg/kg sc), led to dose-dependent increases in tail-withdrawal latencies. β-FNA was less effective in blocking the antinociceptive actions of morphine in sucrose-fed rats than in rats fed only chow, regardless of sex. These results suggest that chronic intake of palatable foods leads to activation of the endogenous opioid system, thereby reducing the effects of irreversible μ-opioid antagonists

14. THE DEVELOPMENT OF CONDITIONED PLACE PREFERENCE, FOR FENTANYL IS ENHANCED BY EITHER ACCESS TO CHRONIC SUCROSE SOLUTION OR PERIPHERAL GLUCOSE ADMINISTRATION. Yamamoto, R. T., Coy, R. T., Vitale, M. A. & Kanarek, R. B. Dept. of Psychology. Tufts University, Medford, MA 02055 USA. Consumption of sweet substances alters the behavioral consequences of opiates. We utilized the conditioned place preference (CPP) paradigm to further investigate the abilities of sugars to alter the behavioral response of male rats to the μ - opioid agonist, fentanyl citrate. The first experiment looked at chronic oral consumption of a 32% sucrose solution, while the second explored the effects of bypassing the oral route of ingestion by administering glucose intraperitoneally. In experiment 1, chronic access to the sucrose solution enhanced the development of conditioned place preference for fentanyl at a dose of 0.016 mg/kg (sc) relative to rats that did not consume the sucrose solution. Additionally, rats in this experiment were assessed for fentanyl-induced antinociception using a cumulative dosing procedure in the tail-flick test. Rats that had consumed the sucrose

solution displayed significantly greater responses to fentanyl than those not consuming sucrose. In experiment 2, injection of a 560 mg/kg glucose solution into the peritoneal cavity of rats enhanced the development of CPP for a 0.04 mg/kg (sc) dose of fentanyl relative to rats that received sterile water or a 300 mg/kg ip injection of glucose and either saline, 0.016 or 0.04 mg/kg (sc) fentanyl. These results suggest that sugars have the ability to alter behavioral responses to opioid drugs through both oral and peripheral routes, suggesting that the response is not a function of simple taste hedonics, rather it is a result of the sugars enhancing the activation of the endogenous opioid system.

15. DIFFERENTIAL RESPONSIVENESS OF SHELL/CORE/PREFRONTAL DOPAMINE TRANSMISSION TO MOTIVATIONAL STIMULI. Bassareo V.; De Luca M. A.; Di Chiara G., Dept. of Toxicology, University of Cagliari & Centre for Neuropharmacology-CNR, Italy. The response of extracellular dopamine (DA) and its relationship to motivational valence (positive or negative) and novelty of motivational stimuli was investigated by brain microdialysis in the nucleus accumbens (NAc) shell and core and prefrontal cortex (PFCX) of undeprived rats. Stimuli were elicited by intraoral infusion of 20% sucrose, sucrose+chocolate, quinine and NaCl solutions, feeding of a palatable food (Fonzies) or smelling of a predator (red fox) urine. Sucrose elicited appetitive reactions and increased DA in the PFCX but not in the NAc shell. An unfamiliar appetitive taste such as that of sweet chocolate and Fonzies, increased DA in all three areas. Habituation of the stimulatory DA response to intraoral chocolate or to Fonzies feeding was observed in the NAc shell after a single pre-exposure to the same taste or food; no habituation was observed in the NAc core nor in the PFCX. Aversive taste stimuli (quinine, saturated NaCl soluitons) rapidly increased DA in the PFCX and in the NAc core and this response did not undergo one-trial habituation. In the NAc shell, instead, no effect (10 min exposure) or a delayed, transitory increase of DA (5 min exposure) sensitive to one-trial habituation was obtained in response to the aversive taste (quinine and saturated NaCl) or olfactory (red fox urine) stimuli. These observations indicate that DA responsiveness is an integrated function of the motivational valence and novelty of stimuli in the NAc shell and an expression of generic motivational value in the NAc core and PFCX.

16. EARLY DEFICIENCY OF AN ESSENTIAL AMINO ACID LYSINE IS RECOGNIZED BY THE VENTROMEDIAL/LATERAL HYPOTHALAMUS. Smriga, M.; Kondoh, T.; Torii, K. Ajinomoto Co., Central Res. Labs., Kawasaki, Japan. A risk of deficiency in the essential amino acid, L-Lysine (Lys) exists in developing regions where cereals supply the major proportion of energy, and also among the elderly in developed countries. Little is known about the physiological consequences of such a deficiency. Rats respond to a Lys-deficient diet with anorexia and an increase in taste preferences for a previously aversive Lys solution. These responses are initiated by metabolic and blood-born factors, including plasma Lys, activin A and the plastically-activated vagal Lys sensors and the neurons of the nucleus solitarus. The information reaches the brain and triggers a rapid recovery from the deficiency, as shown by a functional MRI. Presently, a dialysis probe was implanted into the ventromedial or lateral hypothalamus (VMH, LH) of freely behaving male rats. Online microdialysis measurement was done during the first 26 h (starting at 13:00) of Lys deficiency in rats that had free access to food and fluid. The dark phase was from 19:00 to 07:00. Rats were divided into 6 groups according to their food and fluid intakes. They were fed either normal or Lys deficient diet and provided with water, Glycine or Lys solution. In controls, VMH, but not LH, norepinephrine (NE) release changed diurnally, with the lowest levels measured at the onset of the dark phase. In Lys-deficient rats, the release was depressed from the early morning (10 h after a deficient diet was introduced), without any differences in food/fluid intakes, when compared to controls. Normal pattern of VMH NE was restored by the provision of Lys to deficient rats. Thus, VMH NE is specifically involved in the early integration of signals on Lys deficiency.

17. ANGIOTENSIN-(1-7) ENHANCES HIGH FREQUENCY INDUCED LTP IN THE LATERAL AMYGDALA OF MICE. Albrecht, D.; Walther, T.; Hellner, K. The amygdala is discussed in terms of its role in receiving afferent sensory input and in processing information related to hydromineral balance. Angiotensin acts on and through the amygdala to stimulate thirst and sodium appetite. In addition, the angiotensinergic system seems to play a role in cognition and learning mechanisms by acting on and through the amygdala. In previous experiments we have shown that angiotensin II blocks the induction of long term potentiation (LTP) evoked by a strong 100 Hz stimulation in the lateral amygdala of rats. The ability of angiotensin-converting enzyme (ACE) inhibitors to facilitate cognitive processes and to improve the emotional feeling in patients may be related not only to reduced availability of angiotensin II, but might be due to an increase in the level of Angiotensin-(1-7) (Ang-(1-7)). In this study we could demonstrate that Ang-(1-7) significantly enhanced the LTP recorded in brain slices of the lateral amygdala. It is also known that Ang-(1-7) binds at high concentrations at the type 1 and 2 angiotensin II receptors. The studies in AT1- and AT2-KO mice showed that the Ang-(1-7)-induced facilitation of LTP was mediated neither by AT1- nor by AT2-receptors. Therefore, angiotensin II and Ang-(1-7) have an opposite action on synaptic plasticity in the amygdala.

18. EFFECT OF INTRASEPTAL COLCHICINE ON MORRIS WATER MAZE PERFORMANCE. Ayla Aksoy; Tan Özuak*; Ahmet Ademoglu*; Hale Saybaþýlý*; Tamer Demiralp** and Resit Canbeyli. Psychobiology Laboratory and *Institute of Biomedical Engineering, Bogazici University and **Istanbul Medical School, University of Istanbul. Adult male Wistar rats injected in the medial septal area with colchicine (2 microgram in 1 microliter saline, n=8) or saline (n=8) were trained approximately 2 weeks later in Morris water maze (5 trials per day for 6 days) followed a week later by a one-day retraining session (5 trials). Intraseptal colchicine slowed but did not significantly alter water maze performance in the 6-day training period but impaired retraining a week later. Results indicate that the dose of colchicine used has a slow impact, possibly on hippocampal function, that impairs learning 3 to 4 weeks after intraseptal injection. In a parallel, ongoing study, adult male Wistar rats were implanted with electrodes in the dorsal CA1 in both hipocampi, frontal cortex and the frontal sinus and a cannula aimed at the medial septal area. Both spontaneous and auditory evoked electrophysiological activity were recorded before and

after rats received either colchicine (2 microgram in 1 microliter, n=7) or saline (n=6) intraseptally. Preliminary results indicate no significant electrophysiological effect of colchicine in the first 2 weeks after administration. (Supported by Bogazici University ARFON Grant 00R103 to AA, RC, TD and HS).

19. BEHAVIORAL RESPONSIVENESS TO A GABAa AGONIST IN PREWEANING RATS WITH SELECTIVE NEONATAL LESIONS OF THE CHOLINERGIC BASAL FOREBRAIN NEONATALLY 192 IgG SAPORIN LESIONED PUPS: EFFECTS ON LOCOMOTION AND OBJECT EXPLORATION FOLLOWING A GABAa AGONIST ON POSTNATAL DAY 18. Scattoni, M.L.; Ricceri,L.; Calamandrei, G. Section of Comparative Psychology, Lab. FOS. Istituto Superiore di Sanità, V.le Regina Elena 299, 00161 Rome, ITALY. We have previously shown that neonatal intracerebroventricular (icv) injections of the selective cholinergic immunotoxin 192 IgG-saporin on postnatal day (pnd) 7 induces learning impairments when they are tested before weaning (pnd 15) and a selective impairment in spatial discrimination in an open field with objects when tested as adults. In the present study we analyzed behavioral effects of neonatal cholinergic lesions (icv on pnd 7) on responsiveness to muscimol, a GABAa receptor agonist, on both spontaneous locomotor activity and object exploration. 192 IgG-saporin lesioned and sham rats were injected with muscimol (ip) on pnd 18 and tested in an modified open field test with objects. The high muscimol dose (0.1 mg/kg) decreased locomotor activity in control but not in saporine treated pups; this differential effect of muscimol was not evident in the initial session of the open field test, but emerged in the last 15min of the test when objects are placed in the arena. The same muscimol dose equally decreased object exploration in both control and cholinergic lesioned pups. The low muscimol dose (0.05 mg/kg) appear to increase reactivity to object displacement in cholinergic lesioned pups, leaving control spatial reactivity totally unaffected. Lesions effectiveness was confirmed by a marked reduction of choline acetyltransferase (ChAT) activity in hippocampus and neocortex. These data suggest that only in selective behavioral patterns, associated with locomotion and exploration of the environment, reactivity to a GABAergic agonist is altered following neonatal cholinergic lesions, probably because of a decrease of GABAa receptors in the medial septal nucleus.

20. ESTROGEN REGULATION OF STRATEGY USE IN A CUE-ENRICHED T-MAZE. Bennett, J.C. Dept. of Psychology. University of Washington, Seattle, WA 98195-1525 USA. Estrogen (E) has been identified as a natural regulator of neuroplasticity in the hippocampus (HPC), a structure involved in spatial navigation. There is strong evidence linking high E levels to increases in dendritic spine and synapse density in the adult, female, rat HPC. Attempts to correlate E levels with behavioral performance during spatial navigation tasks have been equivocal. High E both improves and impairs performance. This study tests the hypothesis that, rather than improve or impair performance during spatial navigation, E biases the HPC to solve a task using either a place (P) or response (R) strategy. Female rats (6-12 mo.) were trained to solve a t-maze in a cue-enriched environment by turning east or west to find a reward. Reward location was constant for each rat but varied between rats. All rats were then ovariectomized (OVX) and divided into groups: OVX (n = 7), OVX+LoE (n = 5), and OVX+HiE (n = 5). E was delivered via osmotic minipumps (LoE dose = 1ìg/day, HiE dose = 10 ìg/day). After recovery, rats were repeatedly probed for either a place (turning toward the familiar cue) or response (turning in the familiar direction) strategy. Mean strategy use differs significantly between groups [$F(2, 14) = 8.733$, MSE = .003]. Post-hoc testing reveals OVX+HiE rats differ significantly from both OVX+LoE and OVX rats (HSD = .3220, $p = .012$, and HSD = .3477, $p = .004$). OVX+HiE rats prefer a place strategy (P = 77%) while OVX+LoE and OVX rats prefer a response strategy (P = 44% and 42%). Accuracy does not differ between groups. High E appears to bias HPC structure to rely on cues to solve this spatial navigation task, whereas animals deprived of or given an ineffective dose of estrogen appear to solve this task relying on motor movement cues.

21. EFFECTS OF PITUITARY ADENYLATE CYCLASE POLYPEPTIDE (PACAP-38) ON EXTINCTION OF ACTIVE AVOIDANCE LEARNING IN RATS: INVOLVEMENT OF TRANSMITTERS. Adamik, A., Telegdy G. Dept. Pathophysiology, Neurohumoral Research Group, University of Szeged, Szeged, Hungary. H-6701. The effects of PACAP-38 on the extinction of active avoidance learning were studied in rats. The action of transmitter mediation was followed by pretreating the animals with specific receptor antagonists. PACAP-38 administered into the lateral brain ventricle caused a transitory facilitation of the extinction of a learned active avoidance response at 3 and 6 h following extinction, which had returned to even above the control level at 24-testing. PACAP 6-38, which is an antagonist of PACAP-38, and an antibody against PACAP-38, prevented this action. The following receptor blockers diminished the action of PACAP-38 on extinction: propranolol, haloperidol, naloxone, bicuculline and nitro-L-arginine. The latter acts by blocking nitric oxide formation. Phenoxybenzamine and atropine were ineffective. The data demonstrate that the transitory action of PACAP-38 on the facilitation of extinction is mediated by beta-adrenergic, dopaminergic, GABA-ergic and opiate receptors and nitric oxide.

22. ROLE OF THE PONTOCEREBELLAR PATHWAY IN MOTOR SKILLS AND MOTOR LEARNING IN THE RAT. [1]Gasbarri A; [1]Pompili A.; [1]Pacitti C.; [2]Cicirata F. [1]Dept of Sciences and Biomed Technol, Univ. of L'Aquila; [2]Dept. of Physiology, University of Catania, ITALY. Emerging evidences support the role of the cerebellum in learning of complex motor sequences and spatial memory. Previous studies showed that the olivary projections to the cerebellum are involved in motor learning, suggesting a direct involvement of climbing fibers. On the other hand, since the pontine nuclei are the other main relay nucleus in the cerebro-cerebellar pathway, and the pontine nuclei are the main source of mossy fibers to the cerebellum, our purpose is to verify the involvement of the ponto-cerebellar pathway in motor skills and spatial learning, by comparing these functions in intact animals and in rats with selective injury of the olivary or pontine neurons. Two group of male Wistar rats were used: the first group was treated with 3-acetylpiridine (3-AP)i.p.to destroy the inferior olivary complex (IOC), the second group received electrolytic lesions of the middle cerebellar peduncle (mcp), to interrupt the ponto-cerebellar pathway. To verify their equilibrium, motor-coordination and spatial learning, different groups of lesioned and sham-operated animals

were then submitted to the following behavioral tests: unrotated-rod, rota rod at 20 r.p.m. and Morris water maze (MWM). When trained on the unrotated-rod, either 3-AP-treated rats or mcp-lesioned rats showed at the beginning some static equilibrium deficiencies but, with training, they were able to reach the maximal score as the control rats. On the other hand, the rats submitted to a complex motor task, the rota-rod at 20 r.p.m., obtained scores significantly inferior to the controls. In fact, they were unable to improve their performances by training. These findings show that either the lesion of the IOC or the lesion of the mcp prevent learning of complex motory sequences. Finally, the animals were submitted to a MWM, spatial version. The results of this behavioral test indicate that both the lesion of the IOC and the lesion of the mcp alter learning of spatial task. These findings show that both the ponto- and the olivo-cerebellar pathways are involved in learning complex motor sequences and spatial tasks. Since both projections (from olivary and pontine neurons) converge onto Purkinje cells, the evidences collected in this study suggest that motor learning is supported in the cerebellum by anatomical re-arrangement of synaptic interactions of Purkinje cells with both climbing and parallel afferent fibers.

23. CONNEXIN30 GENE-INACTIVATION IN MICE IMPAIRS MOTOR-COORDINATION, DECREASES EXPLORATORY ACTIVITY AND INDUCES AMNESIA FOR SPATIALLY DISPLACED OBJECTS. E. Dere[1], M. A. De Souza-Silva[1], C. Frisch[1], B. Teubner[2], K. Willecke[2], and J.P. Huston[1]*. [1]Heinrich-Heine-University, D-40225 Düsseldorf; [2]University of Bonn, D-53117 Bonn, Germany. Gap junction channels in the brain, formed by connexin proteins, with distinct regional/cell type distribution, allow intercellular electrical and metabolic communication. The majority of these gap junctions connect astrocytes (expressing predominantly Cx43 and Cx30, besides other connexins), which interact with neuronal networks. The functional implications of coupled astrocytic networks are not well understood and data regarding their behavioral functions have not yet been published. Therefore, the behavioral and neurochemical consequences of a mouse connexin30 (Cx30) gene-inactivation were investigated. Connexin30-/- mice showed a) decreased exploratory activity in a Y-maze and an open-field, but not in an object exploration task, b) an impaired detection of a spatially displaced familiar object and c) motor-coordination impairments in the rotarod task. Biochemical analysis suggested that Cx30 deficiency only marginally affected acetylcholine systems in the brain. The striatal dopaminergic system was altered in Cx30+/- mice, with lower dopamine-levels in the ventral striatum relative to the wild types. With respect to the serotonergic system, the Cx deficient mice differed from each other in limbic and neostriatal regions (e.g. Cx30-/- had higher 5-HT levels in the hippocampus and neostriatum than Cx30+/-), but were otherwise similar to controls. Our results indicate that the expression of Cx30 is necessary for normal behavior which, thus, appears to depend on astrocytic gap junctional intercellular communication. Possible differences in brain region specific and either genetically hard-wired or activity dependent compartimentalisation patterns of astrocytic networks of Cx30-/- and wild type mice may also account for the present findings. Supported by the Deutsche Forschungsgemeinschaft Grant HU 306/24-1.

24. DISTINCT PATTERNS OF ACH RELEASE IN THE FRONTAL CORTEX, AMYGDALA AND HIPPOCAMPUS IN RESPONSE TO NK-1 ANTAGONIST SR140333 - A MICRODIALYSIS STUDY IN THE ANAESTHETIZED RAT. Kart,E.; Huston, J.P.; de Souza Silva, M.A. Institute of Physiological Psychology, and Center for Biomedical Research, University of Düsseldorf, Universitätsstr. 1, D-40225, Düsseldorf, Germany. The neuropeptide Substance P (SP) has been implicated in processes subserving learning, reinforcement and emotionality. Recently it has been reported that NK-1 receptor antagonists can have antidepressant action. It is known that SPergic terminals make synaptic contact with cholinergic neurons in the basal forebrain and modulate cholinergic activity. In order to investigate the effect of NK-1 receptor blockade on the cholinergic system of the basal forebrain, we dialysed three major areas of cholinerigc projections: frontal cortex, amygdala and hippocampus in anaesthetised rats. Intraperitoneally injected SR140333, a potent centrally active NK-1 antagonist, in doses of 1, 3 and 9 mg/kg transiently increased ACh levels as assessed by HPLC. In the frontal cortex ACh increased from 160 to 220 minutes after injection of the antagonist, whereas in the hippocampus an immediate dose-dependent increase up to 186% of baseline occurred. In the amygdala only injection of the highest dose had an effect on ACh levels. These results indicate that this NK-1 antagonist applied peripherally has an effect on the cholinergic system. The differential effects of this NK-1 antagonist on distinct brain structures may have relevance to the understanding of the function of SP in processes governing learning, attention, antidepression and anxiety.

25. NEUROCHEMICAL AND BEHAVIORAL CONCOMITANTS OF EXTINCTION OF WATER MAZE ESCAPE BEHAVIOR IN OLD AND ADULT RATS. Topic, B.; Jocham, G.; Schulz, D.; De Souza Silva, M.A.; Huston, J.P. Institute of Physiological Psychology, University of Düsseldorf, 40225 Düsseldorf, Germany. Water maze experiments generally include multi-trial acquisition sessions followed by a non-reinforced, so-called "probe" trial. However, since an adequate analysis of water maze extinction performance requires multiple non-reinforced sessions, we employed a protocol that included 8 extinction trials given over 3 days, and related performance during these trials to acquisition scores as well as to various post-mortem neurochemical parameters in diverse brain areas in adult and aged rats. In summary, (a) adult rats displayed a conventional extinction curve, characterized by trial-dependent decrease in total time in previously reinforced platform quadrants, whereas the aged animals showed very little resistance to extinction. (b) In adult, but not aged rats, overall resistance to extinction was correlated with performance during the final acquisition trials. (c) In the aged, but not adult animals, resistance to extinction correlated positively with acetylcholine (Ach) in frontal cortex and hippocampus and negatively with dopamine in neo striatum. (d) During extinction the parameter mean distance to arena wall correlated negatively with serotonin in the cerebellum in adults, and negatively with Ach in frontal cortex and hippocampus of aged subjects. (d) Performance during 6 "cued trials", administered after extinction, correlated negatively with mean distance to arena wall during extinction. Thus, a multi-trial extinction protocol can provide important information relevant to the dynamics of non-reinforced behavior. Extinction takes a different course in adult and aged rats, it is related to performance during acquisition as well as to neurochemical parameters that may have no bearing to acquisition measures.

26. THE EFFECTS OF SELECTIVE DOPAMINE AGONISTS ON PASSIVE AVOIDANCE LEARNING IN THE DAY-OLD-CHICK. Hale, M.W.; Crowe, S.F. School of Psychological Science. La Trobe University, Bundoora, 3083. Australia. Whilst it has reported that high doses of dopamine agonists disrupt memory consolidation the specificity of this effect remains unclear. Recent examination of the mixed dopamine agonist apomorphine suggests that dopamine inhibits both passive avoidance and response suppression learning. The present study investigated the effects of selective dopamine agonists on passive avoidance learning in the day-old chick. The dopamine D1 agonist, SKF 38393, the D2 agonist, Quinpirole, and D4 agonist, PD 168077 all failed to disrupt memory consolidation when injected prior to training. Chicks injected with 6.0mg/kg of the dopamine D3 agonist 7-OH-DPAT displayed memory impairment at 180 minutes after aversive training. Time of retention data indicated that 7-OH-DPAT produced the memory disruption 90 minutes after aversive training. Pre-treatment with the dopamine D3 antagonist U 99194 eliminated the disturbance to passive avoidance learning induced by 7-OH-DPAT. These results lead to the suggestions that dopamine is involved in later stages of the memory formation processes and that the D3 receptor may be involved in this disruption.

27. BEHAVIOURAL EFFECTS OF NEONATAL EXPOSURE TO CHLORPYRIFOS IN MICE. Ricceri L.(1); Markina N.(2); Valanzano A.(1); Puopolo M.(1); Calamandrei G.(1) (1) Section of Comparative Psychology, Lab. FOS Istituto Superiore di Sanità, Rome Italy; (2) Dept. Biology, Moscow State University, Moscow, Russia. Chlorpyrifos (CPF) is a common organophosphorous pesticide. Several studies showed that developing rats are more sensitive than adults to the neurotoxic effects of CPF. We evaluated short- and medium-term behavioural effects of neonatal administration of CPF in the mouse species. Neonatal mice were given 1 or 3 mg /Kg of CPF either on postnatal day (PND) 1-4 or PND 11-14 and the effects were evaluated on several behavioural endpoints during infancy and adolescence. Number of ultrasound vocalizations (USVs) was assessed on PND 8,11 and 14, homing test was performed on PND 12, a locomotor activity test on PND 25 and a novelty seeking paradigm on PND 45. No effects of the CPF treatment was evident on the body weight gain, the number of USVs, and homing performance. A significant dose-dependent increase in locomotor activity was evident on PND 25 in mice receiving CPF on PND 11-14. On PND 45 in the novelty seeking test, the expected increase of locomotion induced by the exposure to a novel environment was evident in both control and CPF treated mice, but whereas control and PND 1-4 CPF activity levels subsequently return to baseline levels, pnd 11-14 CPF activity remained significantly higher throughout the session. These data suggest that CPF administered during the second postnatal week has detrimental effects on locomotion and habituation to a novel environment. These effects are likely not mediated by the well-known anticholinesterase action of CPF, but involve other mechanisms of long-term neurotoxicity, not limited to the cholinergic pathways.

28. NEONATAL BASAL FOREBRAIN CHOLINERGIC LESIONS DISRUPT SOCIALLY TRANSMITTED FOOD PREFERENCES IN ADULT RATS. Ricceri L.1; Moles A.2; Scattoni M.L.1; Calamandrei G.1 1Section of Comparative Psychology, Lab. FOS Istituto Superiore di Sanità, Rome Italy 2Istituto di Psicobiologia e Psicofarmacologia, CNR, Rome Italy. Previous studies using selective neonatal lesions of basal forebrain cholinergic neurons showed mild long-term effects on spatial discrimination capabilities, whereas water maze learning appeared intact. In the present study, we examined whether neonatal cholinergic basal forebrain lesions performed on postnatal day 7 using 192 IgG saporin affect a form of non-spatial associative memory, the social transmission of food preferences at adulthood. The cholinergic lesion impaired 4-h and 24-h retention of a learned social food preference relative to controls, despite performance on an immediate retention trial was indistinguishable from controls. In a second experiment neophobia towards unfamiliar scented food was assessed; levels of novel food consumption did not differ between neonatally saporin-lesioned and control rats. A marked reduction of ChAT was evident in the hippocampus and cortex of lesioned rats. These data provide the first evidence that early removal of the cholinergic input to hippocampus and neocortex has long-term effects on memory processes relative to socially transmitted-food preferences, without affecting consumption on novel foods.

29. COGNITIVE ABILITIES IN A NONSTORER BIRD SPECIES SELECTED FOR DIFFERENT COPING STYLES: COMPARING A VISUAL AND A NONVISUAL TASK. Carere, C.; Havekes, R.; Oorebeek, M; Groothuis, T. G.G. Dept. of Anim. Behav., University of Groningen P.O. Box 14, 9750 AA Haren, NL. In the great tit (*Parus major*), a nonstoring bird species, individuals can be categorised as fast or slow explorers on the basis of tests assessing the reaction to a novel object and the exploration of artificial trees. Bidirectional selection showed that these differences have a genetic basis leading to the establishment of two lines, which also differ in other behavioural domains. We aimed at characterising the cognitive abilities of the two lines. Since most studies on cognition in passerine birds have been focused on food-storers, which seem to be specialised in the use of spatial information, a second aim was to test the performance of a nonstorer in a visual and a nonvisual task. Birds of the selection lines (5th generation) kept in outdoor aviaries were challenged with a sequence of three tasks: (i) to find a hidden reward relying on a small visual cue; (ii) to find a hidden reward when the visual cue was removed; (iii) to find a hidden reward relying on a visual cue after a long retention interval (65 hrs). In all tests the reward was hidden in one of nine paper-covered bowls. No line differences in the number of errors (uncorrect visits) were found in the first and second task. In the third task the fast explorers made few errors compared to slow explorers, suggestive of better associative memory abilities. The comparison of the performance between the first (visual cue) and the second task (visual cue removed) indicated that birds made few errors and no revisits to previously visited bowls when the reward could be visually localized. The number of errors and revisits drastically increased when the cue was removed. When this latter situation was repeated the birds did not decrease the errors, but became more efficient by decreasing the number of revisits. These results suggest that nonstorers might be specialised on visual information.

30. RATS WITH NEGLECT PRODUCED BY LESIONS OF THE DORSAL CENTRAL STRIATUM DO NOT DEMONSTRATE SPONTANEOUS RECOVERY. T.M. Van Vleet, J.V. Corwin, R.L. Reep, and S. Heldt. Dept. of Psych., Northern Illinois University., and Dept. of Physiological Sciences, University of Florida. As found in humans, rats with severe neglect induced by cortical lesions recover spontaneously over the course of weeks to months. Recent studies examining the physiological correlates of spontaneous recovery from severe neglect induced by unilateral medial agranular cortex (AGm) destruction found that severe neglect was correlated with an asymmetry in IEG expression and a significant reduction in glutamatergic receptors in the dorsolateral striatum; spontaneous recovery from neglect was correlated with a return to symmetrical levels of IEG expression and a return to normal or slightly elevated levels of glutamatergic receptors in this same region. These findings are significant because the dorsal lateral striatum encompasses the site of the AGm and posterior parietal cortex (PPC) efferents to the dorsal central striatum (DCS) which may be a crucial site for the mechanisms of recovery. Recently, Van Vleet et al. (2000) demonstrated that, like unilateral destruction of the AGm, unilateral destruction of the DCS produced severe multimodal neglect. However, it remained to be determined whether animals with DCS lesion-induced neglect would also exhibit spontaneous recovery. The present study examined the effects of unilateral DCS lesions on orientation to visual, auditory, and tactile stimulation over the course of 15 weeks to evaluate the potential for spontaneous recovery from neglect. The results indicated that unlike shams or control lesioned animals, subjects in the unilateral DCS lesion group demonstrated severe neglect over the course of 15 weeks and evidenced no sign of spontaneous recovery. These findings suggest that the DCS may be a crucial site for the mechanisms of recovery and may be necessary for spontaneous recovery to occur.

31. EFFECT OF GAMMA-HYDROXYBUTYRATE IN TWO RAT MODELS OF FOCAL CEREBRAL DAMAGE. Ottani, A.; Zaffe, D.; Botticelli, A.R.; Bertolini, A., Dept. of Biomedical Sciences, Section of Pharmacology, University of Modena and Reggio Emilia; via G. Campi 287, 41100 Modena, Italy. Protective effects of GHB in animal models of cerebral ischaemia/hypoxia, as well as in human conditions of head injury-induced coma, have been described. Aim of our present work was to evaluate the effect of GHB on the behavioural and histological consequences of focal cerebral damage, either induced by ischaemia or by excitotoxicity. Adult male Wistar rats were used. Brain damage was induced by injecting 1 µl of either endothelin-1 or kainic acid (ischaemic or excitotoxic lesion, respectively) in the right striatum. Two hours later animals received GHB at the dose of 300mg/kg, i.p., followed by 100mg/kg twice daily for the following 10 days. Control-ischemized and sham-operated rats received 2ml/kg of saline, with the same schedule. Nineteen and thirty-nine days after endothelin-1 injection animals were submitted to the Morris water maze test to evaluate learning ability and to Bjorklund test to score sensory-motor activity; ten days after kainic-acid injection, animals were observed for circling behaviour induced by 2mg/kg apomorphine, s.c. Behavioural tests were followed by histological examination. The ischaemic lesion produced a significant impairment in sensory-motor activity (scores: 82 and 74, in the first and second trial, respectively) and in cognitive processes (seconds: 182.5±17.5 and 90.5±11.61); GHB significantly attenuated the phenomenon (scores:36 and 32; seconds: 110.3±22.6 and 71.3±14.5). In kainite-lesioned rats, apomorphine induced 275.67±59.86 ipsilateral turns/h; GHB significantly reduced this behaviour (28.17±8.65). Both models of damage produced areas of necrotis, demyelination and gliosis, which appeared much reduced after GHB. These results indicate that GHB provides significant protection against neurodegeneration in both experimental models.

32. BDNF IN VIVO ADMINISTRATION AFFECTS SPATIAL LEARNING IN ADULT RATS. Berry, A.; Chiarotti, F.; Alleva, E.; Cirulli, F. Section of Behavioural Pathophysiology, Laboratorio di Fisiopatologia di Organo e di Sistema, Istituto Superiore di Sanità, Viale Regina Elena 299, Rome, Italy (cirulli@iss.it). Brain-derived neurotrophic factor (BDNF) is a neurotrophin which has been shown to be involved in specific aspects of activity-dependent synaptic plasticity. The present study tested the effects of intrahippocampal administration of this neurotrophin on memory retention in a Morris Water Maze (MWM) task and on animal's behavior in a plus-maze. Sixty-day-old male Sprague Dawley rats were implanted with a stainless steel cannula (Plastic One, USA) in the right hippocampus. One week later, the experimental subjects were trained to locate a hidden platform for 6 consecutive trials in the MWM test (experimental day one). Immediately after the last training trial, all animals were divided into two groups and injected with either BDNF (24 micrograms) or PBS (inj. volume 1 microliter). On day 2, rats were tested in a probe trial, followed by 6 reversal trials in which the platform was moved to a new location. While the experimental groups did not differ in the probe trial, BDNF treated subjects showed a lower latency to reach the platform during the reversal task. In the afternoon of day 2 (trial 1) and at the same time on day 5 (trial 2) all subjects were tested in the plus maze test to assess their emotionality. The BDNF group showed a higher frequency of grooming behavior and of the stretched attend posture, but no differences in locomotion. Overall, these results indicate that a single administration of BDNF affects learning in a spatial memory task and has enduring effects (up to 72 hrs) on emotional behavior. Supported by ISS and the Italian Ministry of Health (Ricerca Finalizzata 2000, Fasc. 34F).

33. KNOCKOUT OF ERK1 MAPK FACILITATES MICE PERFORMANCES IN AVOIDANCE TASKS Vincenzo Cestari, Cristina Mazzucchelli, Chiara Vantaggiato, Alessandro Ciamei, Stefania Fasano, Gilles Pagès, Jacques Pouysségur and Riccardo Brambilla Istituto di Psicobiologia e Psicofarmacologia (CNR) Roma, Italy. San Raffaele Institute, Milano, Italy. ISDBCR-CNRS UMR 6543, Nice, France. Extracellular-signal regulated kinases (ERK1 and 2) are synaptic signaling components necessary for several forms of learning. Mice lacking ERK1 show a dramatic enhancement of long-term memory in two different operant conditioning tasks (active and passive avoidance). This behavioral observation correlates with region-specific changes in synaptic signaling. At the molecular level, we find that ablation of ERK1 results in a stimulus-dependent increase of ERK2 activity and immediate early gene transcription, particularly in the striatum but also in the cortex. We show that this effect is due to enhanced interaction of ERK2 with the upstream kinase MEK, resulting in an overall increase in ERK signaling. Attenuation of MEK activity in mutant cells by treatment with sub-optimal concentrations of the specific inhibitor

UO126 restores normal ERK2 activity even in the absence of ERK1. Our results reveal an unexpected complexity of ERK- dependent signaling in the brain and a critical regulatory role for ERK1 in the long-term adaptive changes underlying behavioral plasticity.

34. ULTRASOUNDS AS AN INDEX OF SOCIAL MEMORY IN FEMALE MICE: EFFECT OF AGE AND REPRODUCTIVE CONDITION. Rizzi, R.; Costantini, F.; Moles, A.; D'Amato, F.R. Dep. Psicol., Univ. "La Sapienza"; Ist. di Psicobiol. e Psicofarmacol., CNR, Roma, Italy. Three minutes of female-female interaction in mice is characterised by ultrasonic vocalisations (about 70 kHz) and olfactory investigation. The resident female is the individual who vocalises and shows higher levels of social exploration. Re-exposure to the same female after 60 min interval results in a decrease in the amount of calls: this decrease can be used as an index of social memory. Ultrasonic calls can be used in female subjects to evaluate the role of the reproductive condition and age on memory processes. Pregnant, in comparison with cycling females, show very low levels of ultrasonic emission and are not able to recognise a partner after an interval longer than 30 min. This change in social memory could be due either to the reduced interest shown by these females towards conspecifics, or to changes in mechanisms underling memory processes. One-year old females also show a reduction in ultrasounds in the presence of female partners and a shorter retention of social memory. The comparison of female performances in non social memory tests could help to understand if these effects of age and reproductive conditions are peculiar of social memory or also affect other non-social memory tasks.

35. TRANSPLACENTAL EXPOSURE TO TCDD AND B(A)P IMPAIRS LTP IN F1 OFFSPRINGS. Reasor, J.; Wormley, D.; Zhang, W.; Nayar, T.; Greenwood, M.; Chirwa, S.; Hood, D.B. Anatomy and Physiology & Pharmacology, Meharry Medical College, Nashville, USA. We have begun to investigate the effects of two environmental toxicants, tetrachlorodibenzodioxin (TCDD) and benzo(a)pyrene (B(a)P), on long-term potentiation (LTP; a cellular correlate of learning and memory) in F1 generation. Briefly, laparotomy on gestational day (GD) 8 was performed on two randomly assigned pregnant dams, the control (CON) and exposed (EXP) groups. On GD14, pregnant dams in the EXP group were administered TCDD (700 ng/kg bolus) by gavage. In addition, each rat was exposed to B(a)P in a carbon black aerosol (100 *g/m3) for 4 hours on GD8 through to GD17. The CON group was not exposed to TCDD and B(a)P. After birth pups were weaned on postnatal day (PD) 30, and housed separately by sex. On PD 60-62 randomly selected male rats were anesthetized (urethane,1500 mg/kg i.p.) and access holes were made in the skull through which electrodes were lowered to stimulate the entorhinal cortex, with recording in dentate gyrus. Using this animal model, it was found that robust LTP was readily produced in the CON group (4 of 4 rats). LTP exhibited decreased onset latencies and left-ward shifts of the input-output plots. In addition, paired-pulse facilitation decreased after LTP indicating synaptic potentiation. In contrast, only one out of five rats in the EXP group developed a "weak" LTP, while others did not develop LTP (4 of 5 rats). In fact, paired-pulse facilitations, onset latencies and input-output plots were unchanged in this group. Together, our results suggest that exposure to TCDD/B(a)P in utero decreases the capacity for synaptic plasticity in the progeny. (Supported in part by NIH grants RR03032 and MH 57067).

36. STEROIDS EFFECT FOS EXPRESSION INDUCED BY GLUTAMATE INFUSIONS INTO THE POSTERODORSAL MEDIAL AMYGDALA (MEAPD). M.L. Lehmann, G.M. Sable, and M.S. Erskine. Department of Biology, Boston University, Boston, MA 02215 USA. Estrogen influences the sensitivity of ER-containing neurons by increasing NMDA-R synthesis. MEApd neurons responsive to vaginocervical stimulaton (VCS) also contain estrogen receptors (ER), and stimulation of these neurons with glutamate induces pseudopregnancy. The present experiment examined c-fos activation in known VCS responsive nuclei by glutamate infusions within the MEApd and further explored the influence of estrogen (EB) and progesterone (P) on this activation. Ovariectomized female rats were implanted with unilateral cannulas directed at the MEApd. Females were treated sc with steroids, [10ug EB followed 44h later by 500 ug P] or oil. 4 hrs after injection, females were given 3 MEApd infusions of 10 uM Asp + 5 uM Glu + 1uM Gly in 0.4ul PBS, each separated by 20 min. 90 min after the first infusion, females were perfused, brains collected, and analyzed for Fos expression. Ipsilateral (IPSI) to infusion, EB-P treated females exhibited a 3-fold increase in Fos within the mPOA and VMH, and a 2-fold increase in PVN, MEApd, and BNST when compared to the contralateral (CON) side. Large increases of Fos were also noted within the IPSI cortex, thalamus, central AMYG (CE) and basolateral AMYG (BLA). Although there was no FOS response within the IPSI mPOA, BNST, VMH, or PVN in oil treated rats, a 3-fold increase was observed within the IPSI MEApd, and within IPSI areas of the cortex, thalamus, CE, and BLA compared to the CON side. These results suggest that EB-P priming increases the probability that neurons within the mPOA, VMH, BNST, and PVN will be activated in response to chemical stimulation of the MEApd. Supported by MH64187 and MH01435.

37. NORADRENERGIC LESIONS CAUSED BY ANTI-DOPAMINE-β-HYDROXYLASE SAPORIN INFUSIONS IN THE MEDIAL AMYGDALA. Carey, P.S.; Erskine, M.S.; Cameron, N. Department of Biology, Boston University, Boston, MA 02215 USA. Previous research has shown that the A2 noradrenergic cell group (NTS) is activated following mating. The immunotoxin anti-dopamine-β-hydroxylase-saporin (DBH-SAP) selectively lesions noradrenergic cells, and was used to determine whether A2 cells project to the medial amygdala (MePD). Ovariectomized female rats were given bilateral infusions stereotaxically in the MePD of either 0.2 µl (20 ng) DBH-SAP or 0.2 µl aCSF. Eight days later the animals were given estradiol benzoate (10 µg sc) followed by progesterone (P, 500 µg) to induce estrous behavior. Four hours after the P injection the rats received 15 intromissions from an experienced male and were perfused two hours later. The forebrain and brainstem were sectioned in 30 µm slices on a microtome. The forebrain was stained with cresyl violet to visualize the infusion sites and the brainstem was processed with ICC to stain for DBH. Noradrenergic cells in A1, A2 and A5 were counted bilaterally with the A2 group being subdivided into rostral, middle and caudal regions. Due to the high cell density in A6, the area was drawn using a camera lucida and the area in μm^2 was calculated. Bilateral infusion of DBH-

SAP in the MePD caused a significant reduction of noradrenergic cells in the middle A2 region. There were no significant effects on the numbers of cells in the rostral and caudal regions of A2, nor were any seen in A1, A5 and A6. Since A2 neurons are activated following mating stimulation and their projections to the MePD can be selectively lesioned by DBH-SAP infusions, the role these neurons play in mating-induced fos expression in the forebrain can be elucidated. Supported by MH64187 and MH01435 to M.S.E.

38. BEHAVIORAL AND PHYSIOLOGICAL CORRELATES OF SOCIAL BONDS IN MONGOLIAN GERBILS. Razzoli M., Polidori M. and Valsecchi P. Dipartimento di Biologia Evolutiva e Funzionale, Università di Parma, Parma Italy. A main feature of monogamy is the existence of specific social bonds. Monogamous individuals are expected to display high selectivity in partner choice and selective intraspecific aggression in mate/territory defense. Mongolian gerbils are monogamous, group-living rodents. In a first experiment aimed to examine the monogamous features of this species, female's aggression before and after pair-bond formation has been tested against same-sexed intruders. Before pairing females displayed very low aggression, while a dramatic increase of aggression occurred after pair-bond formation with a male. Females' preference towards males has also been tested. Pair-bonded females clearly preferred their partner, aggressively reacting to an unfamiliar male and displaying affiliation exclusively towards their partner. Following pair disruption, animals were tested in a free exploratory paradigm. Males' marking behavior was significantly depressed by separation, while separated females increased their exploratory activity. Pair-bond disruption did not altered any of the physiological parameters considered in females, while it negatively affected males' scent glad size. In a second experiment the effect of sibling social bond has been examined. Sibling females kept in pairs have been individually tested against female intruders. Only few females behaved aggressively. This suggests that the social bond with a sibling does not represent a crucial resource to be defended against unfamiliar conspecifics. Females were then separated from their sisters and tested in a free exploratory paradigm. Behavioral parameters and activity were unaffected by separation. The analysis of physiological parameters showed an increase in ventral gland size and ovarian weight in separated females. Sibling-bond disruption could have mimicked the abandonment of natal nest site and a subsequent hormonal activation in gerbil females.

39. Withdrawn

40. A FEMALE COOLIDGE EFFECT. Turi, A.L.; Ellingsen, E.; Larsson, K.; Agmo, A. Dept. of Psychology, Universitetet i Tromso, Tromso, Norway. The Coolidge effect can be defined as the restoration of mating behavior in males exposed to a novel female after reaching sexual satiation. When a novel female is introduced, the exhausted male will resume copulation. It has not been explored whether a similar effect exists in the female, probably due to the difficulties in establishing a criterion for female exhaustion. By employing the pacing procedure in which the female is given the opportunity to control the rate of stimulation received, it is possible to infer female satiety. This would occur when the female remains inaccessible to the male for a prolonged period of time, corresponding to the male's postejaculatory interval normally used to define exhaustion. When females are tested using the pacing procedure, it becomes evident that the time the female chooses to be inaccessible to the male is exponentially prolonged after each ejaculation. In the present experiment we wanted to determine if we could find a Coolidge effect in female rats. Eight female Wistar rats were tested to sexual satiety (return latency > 15 min)in an observation cage that was divided by a plexiglass wall with holes through which the female could enter or exit the half of the cage in which the male was confined. After reaching the satiety criterion the male was removed and a new male or the original partner was immediately introduced. The female rats in the experimental condition showed a significant increase in proceptive and approach behaviors including returns to the males compartment subsequent to the introduction of a new male compared to the control condition, i.e. the reintroduction of the original male. The female rats in this experiment displayed a Coolidge effect similar to what has been described for male rats.

41. COCAINE AND MATERNAL AGGRESSION: INTERGENERATIONAL EFFECTS. Johns, J.; Lubin, D.; Elliott, J.; Black, M.; Joyer, P.; Lomas, L.; Middleton, C. Dept. of Psychiatry. Unviersity of North Carolina, Chapel Hill, NC 27599 USA. Previous research indicates chronic gestational cocaine administration increases maternal aggressive behavior in rats while acute cocaine administration decreases aggression and is often associated with mothers leaving the offspring unprotected. In the current study we examined the effects of chronic and intermittent acute cocaine, chronic and intermittent acute saline and no treatment, on maternal aggression in rat dams (rearing their own or pups from each of the other groups) on postpartum day 8 (PPD 8). Second generation females of all dams were also bred and tested for aggression towards an intruder (with their own litter present) on PPD 8 to assess effects of prenatal drug exposure and rearing condition on aggression. Preliminary data indicate that original dams treated with either cocaine regimen were somewhat more aggressive than saline treated or untreated dams, as evidenced by increased fight attacks, aggressive posture and threatening behavior. Dams rearing pups prenatally exposed to chronic or acute cocaine took longer to initially respond to the pups, spent less time engaging in maternal behavior and displayed fewer maternal behaviors during the aggression test than those rearing saline exposed or untreated pups. Second generation dams prenatally exposed to chronic cocaine threatened more, took longer to engage in and engaged in less maternal behavior than other groups. Prenatal exposure to acute cocaine increased nipping/biting and decreased maternal behavior compared to other groups. Preliminary results suggest that dam treatment, prenatal exposure and, in offspring, rearing condition alters maternal aggression on postpartum day 8. This work was supported by NIH grant DA13362.

42. PERINATAL AZT ADMINISTRATION AND EARLY MATERNAL SEPARATION AFFECT SOCIAL AND EMOTIONAL BEHAVIOUR OF CD-1 MICE. Venerosi, A.; Cirulli F.; Capone, F.; Alleva, E. Sect. Behavioural Pathophysiology, Lab. Fisiopatologia O.S., Istituto Superiore di Sanità, Viale Regina Elena 299, I-00161 Roma Italy. Zidovudine (AZT) is an effective treatment in preventing perinatal trasmission of HIV-1,

however a continuos re-evaluation of the risk-benefit ratio of human exposure to this drug is suggested by both clinical and animal studies. Medium and long-term effects of pre-postnatal AZT treatment on mouse social and emotional behaviour were assessed. Possible interactions between AZT exposure and disruptions in the mother-infant relationship were also analysed. Pregnant CD-1 mice were administered per os with AZT (160 mg/kg) from pregnancy day 10 throughout delivery to lactation day 10. In half of the litters, the offspring was separated from the mother for 3 hours from postnatal day 2 (PND2) to PND14. On PND35 a 30 min social interaction test was performed. On PND80 AZT long-term effects on emotionality were assess by means of an elevated plus-maze. On PND35, AZT affected social behaviour of the experimental subjects, reducing aggressive interactions in males, while decreasing Investigative behaviours in females. At adulthood, AZT inhibited exploratory behaviour in the plus-maze, while increasing the frequency of risk-assessment postures in male mice. As for maternal deprivation, this early manipulation exerted a pro-aggressive effect in adolescent male mice, deprived subjects being overall characterised by higher activity levels and a deficit in habituation, an effect also observed in the plus-maze. A significant interaction between AZT and maternal deprivation was found for Affiliative behaviours. In conclusion, results indicate that both AZT exposure and maternal deprivation induced gender-dependent changes in social and emotional behaviour both during adolescence and at adulthood. Supported by AIDS grants 30C/A and 30D/1 and an AIDS fellowship by the Italian Ministry of Health to A.V.

43. RESTORATION OF COGNITIVE FUNCTION FOLLOWING ESTROGEN REPLACEMENT. Markowska, A.L. and Savonenko, A. Johns Hopkins University, Baltimore, MD 21218, USA. Recent studies suggest that some aspects of learning and memory may be altered due to the midlife loss of estrogen, indicting a potential causal relationship between the deficiency of ovarian hormones and cognitive aging. In the present study, the effects of estrogen withdrawal in middle-aged Fischer-344 rats followed by estrogen replacement were tested in memory tasks. The results revealed that estrogen withdrawal accelerated the rate of cognitive aging. Following ovariectomy the deficit occurred after four months in working memory tested in delayed-non-matching-to-position task and progressed from long-delay to short-delay trials. The efficacy of estrogen in restoration of cognitive deficit in old rats depended upon the type of treatment (chronic or acute) and whether an aging-related decline in a particular cognitive process was aggravated by the estrogen withdrawal. Chronic estrogen treatment (implants) was effective in improving working memory only when primed with repeated injections of estrogen simulating the natural fluctuation during the estrous cycle. The challenge with scopolamine revealed that ovariectomy-induced cognitive deterioration coincided with a compromised cholinergic system. However estrogen replacement did not protect cognition of old ovariectomized females against scopolamine challenges suggesting that estrogen-induced improvement in working memory was not dependent on cholinergic mechanisms. Taking into consideration the activating effect of estrogen on the cholinergic system when tested in young-adult rats, these data emphasize that the protective effect of estrogen on cognition relies on different mechanisms in the old rats with an already compromised cholinergic system than in young rats. Supported by AG15947 to ALM.

44. CHRONIC EFFECTS OF EARLY PARENTAL DEPRIVATION ON STRESS AND REWARD SYSTEMS IN THE MARMOSET MONKEY. Pryce, C.R.; Dettling, A.C.; Feldon, J. Behavioural Neurobiology Laboratory, Swiss Federal Institute of Technology Zurich, CH-8603 Schwerzenbach, Switzerland. Epidemiologic studies indicate that children exposed to early-life stress (abuse, neglect) are at chronic increased risk for depression. Rodent models of neuropsychiatric symptoms based on repeated deprivation of maternal care have been developed but this approach has received scant attention in primates. Marmoset monkeys were exposed to daily 1-2 hr parental deprivation across month 1 of life (early deprivation, ED) whilst controls and their parents were briefly restrained (CON). Subjects aged 2-14 months were monitored in terms of social behaviour and conditioned behaviour, HPA physiology, and cardiovascular autonomic status (using radio-telemetry), both under basal and psychosocial challenge conditions. ED infant subjects were more distressed and less social compared with CON. From juvenility to young adulthood, ED subjects exhibited basal autonomic hyperarousal in the form of elevated urinary output of epinephrine and norepinephrine, and increased blood pressure. When challenged via repeated social separation in a novel environment, juvenile ED subjects exhibited lower basal urinary cortisol levels, reduced activity, greater sympathetic autonomic arousal, and reduced social behaviour at reunion, compared with CON. When tested on computerized tests with positive reinforcement as young adults, ED subjects were equivalent to CON in terms of simple visual discrimination learning but performed less trials per session, suggesting impaired motivation. Quantification of motivation per se using the progressive ratio schedule in the absence of food or water deprivation confirmed reduced reward sensitivity in ED subjects. The robust depression-like characteristics of this primate model provide an important opportunity for advancing understanding of the neurobiology and pharmacology of depression and related disorders.

45. EFFECTS OF EXPOSURE TO ESTROGENIC ENDOCRINE DISRUPTERS ON MATERNAL BEHAVIOR AND OFFSPRING DEVELOPMENT IN MICE. Palanza, P; Howdeshell, K.; Parmigiani, S.; vom Saal F. Dip. Biol. Evol. Funz., Parma University, Italy; Division Biol. Sci, University of Missouri-Columbia, USA. Maternal behavior in mammals is the result of a complex interaction between the lactating dam and her developing offspring. Slight perturbations of any of the components of the mother-infant interaction may result in alterations of the behavior of the mother and/or of the offspring. We studied the effects of exposure of female CD-1 mice to the estrogenic chemical bisphenol A (BPA) or to diethylstilbestrol (DES) during fetal life or/and in adulthood during the last part of pregnancy on subsequent maternal behavior. Pregnant females were fed daily doses of corn oil (controls), 10 microg/kg bw BPA or 0.1 microg/kg bw DES from gestation day 14 to 18. As adults, the prenatally-treated female offspring were time-mated and again fed either corn oil (controls) or the same doses of BPA or DES on gestation day 14 to 18. Maternal behavior was then observed on postnatal days 2 to 15 and the development of reflex responses was examined in the offspring. Dams exposed to BPA either as fetuses or in adulthood spent less time nursing their pups and more time out of the nest compared to the control group. Females exposed to BPA both as

fetuses and in adulthood did not significantly differ from controls. Females that were exposed to DES as fetuses, regardless of DES exposure as an adult, spent less time nursing and engaging in nest-related behaviors early in lactation but spent more time with their pups than controls in the latter part of lactation. No significant alterations in postnatal reflex development were observed in the offspring of the females exposed to BPA or DES.

46. ESTRADIOL TREATMENT AT BIRTH AFFECTS THE SEROTONINERGIC SYSTEM IN THE DORSAL RAPHE NUCLEUS (DRN), BUT NOT IN THE MEDIAN RAPHE NUCLEUS (MRN). Domínguez, R. 1,3; Cruz-Morales, S.E.2,3; Carvalho, M.C.3 1UIBR, FES-Zaragoza, UNAM. México. AP 9-020. CP 15000. México. D.F. 2 FES-Iztacala., UNAM. 3 Laboratório de Psicobiologia, FFCLRP-USP, Ribeirão Preto, Brasil. There are significant differences in the serotoninergic system in the DRN and MRN between male and female rats. Because the sexual differentiation of the brain is provoked by the transformation of androgens in estrogens during the beginning of postnatal life, we analyzed the effects of estradiol benzoate (EB) 5 micrograms injection on new-born female rats, on the concentration of dopamine (DA), dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA), in the MRN and DRN when the rats were adult, measured by HPLC. In the DRN significant differences in DA, DOPAC and HVA concentrations between EB-treated and control rats were not observed. A significant increase in 5-HT (1207+/-132 vs. 750+/-76, $p<0.05$), without differences in 5-HIAA concentration, were observed. In the MRN no significant differences in the serotoninergic and dopaminergic system were observed. Present results suggest that the reactivity of the MRN and the DRN to the differentiation effects of estradiol is different.

47. PERMANENT CHANGES IN SEXUAL BEHAVIOR INDUCED BY MEDIAL PREOPTIC AREA KINDLING LIKE STIMULATION. Portillo, W.; Basañez, E.; Paredes, R.G. Centro de Neurobiologia, UNAM. Juriquilla,Qro. Mexico. There are apparently normal rats that fail to initiate copulation after repeated exposure to receptive females, these animals are called "noncopulators". We have previously demonstrated that kindling in the medial preoptic area (MPOA, a brain structure important for the expression of sexual behavior in male rats), induces sexual behavior in previously noncopulating male rats. The purpose of the present study was to determine if the behavioral effects induced by MPOA kindling on sexual behavior are permanent. As well we investigated if kindling needs to be completely established to induce sexual behavior or if the development of an intermediate kindling stage is sufficient to induce sexual behavior in noncopulating male rats. Noncopulating male rats were implanted with a bipolar electrode in the right MPOA. The subjects were divided into: 1) sham (rats without electrical stimulation); 2) intermediate kindling (rats with aftherdischarge or stage 2 seizures), and 3) fully kindled (rats with 3 consecutive stage 5 seizures). After kindling rats were tested with receptive females once a week for 30 weeks. We found that previously noncopulating male rats displayed sexual behavior even 8 months after kindling like stimulation had ceased. In addition, elicitation of an afterdischarge (AD) or stimulation until stage 2 of kindling were sufficient to induce sexual behavior in previously noncopulating male rats. These results suggest that kindled like stimulation, without seizure development, can induce permanent behavioral changes.

48. OESTRADIOL α-RECEPTOR EXPRESSION IN MULTIPAROUS AND PRIMIPAROUS SHEEP BRAIN AT PARTURITION AND OESTRUS. Meurisse, M.; Gonzalez*, A.; Delsol, G.; Poindron, P*.; Lévy, F. Equipe de Comportement, PRC, INRA, 37 380, Nouzilly, France. *CNB UNAM, AP 1-1141, Querétaro 76001 QRO, Mexico. The presence of cells containing oestrogen α-receptors (ER) in brain regions relevant for maternal behavior was compared in nulliparous and multiparous ewes at parturition and at estrus, using immunohistochemistry with 1D5 antibody (n = 7 to 10 animals by group). Brains were collected at parturition or at oestrus onset. In all regions (medial preoptic area-MPOA, paraventricular nucleus-PVN, supraoptic nucleus-SON, mediobasal hyptothalamus-MBH, medial amygdala-MeA), labelled cell densities were significant lower at parturition than at estrus. These results could be due to a down regulation of ER by the high prepartum levels of oestradiol, or to the effect of a long term progesterone exposure during gestation. Furthermore, no differences were found between nulliparous and multiparous animals, indicating that the first maternal experience does not regulate the expression of ER as it was found in mice. Finally, whereas in the PVN and the SON, nuclear labelling was observed at oestrus, expression of ER was mainly cytoplasmic and axonal at parturition. These different locations suggest a distinct regulation of the receptor at parturition, and the presence of ER in the PVN is congruent with the necessity of a combined action of estradiol and intracerebral oxytocin liberation for maternal behavior activation at parturition. Supported by ECOS M98-S04.

49. MATERNAL SEPARATION IN THE MOUSE AS A MODEL FOR EARLY TRAUMATIC SOCIAL EXPERIENCE. Weiss, I.C.; Lesslauer, A.; Knobloch, M.; Mansuy, I.M. Institute of Cell Biology, Swiss Federal Institute of Technology, ETH Hönggerberg, Zürich, Switzerland. Borderline Personality Disorder (BPD) is a severe and complex pathology characterized by a combination of impulsive, affective and cognitive symptoms. Adult BPD patients display severe emotional instability, destructive social relationships, and often experience episodes of high internal tension that are frequently stopped by self-mutilations. BPD affects 1-2% of the adult population. Although its etiology is poorly understood, it is thought to result from acquired and/or developmental brain dysfunctions associated with early traumatic experience. Indeed, 40 to 70% of BPD patients report a history of abuse or familial separation as young children. We are developing a mouse model for specific symptoms of BPD pathology, based on maternal separation (MS), in an attempt to explore the possibility that the altered emotional status of BPD is governed by early environmental factors. In this study, MS was conducted from post-natal day 1 to 14 for 3h/day, at different time of the day (unpredictable stress; MSU). Further to MSU, some of the lactating mothers were subjected to chronic stress (restraint stress, forced swim; MSUS). Control litters were left undisturbed with their mother. In adulthood, MSUS mice demonstrated an anxiogenic profile, as revealed by reduced activity in the open field center and in unprotected arms of the elevated plus maze. In contrast, MSU had no detrimental effect on anxiety-related behavior of adult mice. Finally, both MSU and MSUS tended to enhance stress-induced analgesia. The present

findings suggest that MS in mice is a promising model for vulnerability to environmental stressors, which could be eventually combined with genetically modified mice.

50. ENDOCANNABINOIDS MODULATE ORIENTING AND SCANNING PHASES OF ATTENTION IN THE NAPLES HIGH-EXCITABILITY RATS. G. Grammatikopoulos, M. Pignatelli, L.A.Ruocco and A.G. Sadile Lab. Neurophysiol., Behav. & Neural Networks, Dept. Exptl. Medicine, II Univ. Naples, Naples, Italy. Experiments have been carried out in an animal model of Attention -Deficit Hyperactivity disorder (ADHD), the Naples High-Excitability (NHE) rats, by manipulating endogenous cannabinoids. This was achieved by reuptake inhibition with AM404 or CB1 receptor blockade with SR141716A. Adult male NHE or random-bred (NRB) rats received a single parenteral injection of AM404 (1 or 10 mg/kg) or SR141716A (0.025 or 0.250 mg/Kg) or vehicle 30-min before testing in a spatial novelty. The behavior was videotaped and analyzed for orienting frequency (OF) and scanning duration (SD). The OF in the NHE was decreased by both doses of AM404 in the first part and by 10mg/kg in the second part of the test. In contrast, in NRB rats OF was increased in the first part in a dose-dependent manner followed by a decrease in the second part of the testing only by 10mg/kg. Moreover, SD in the NHE was decreased during the entire test by 1mg/kg and increased in the first part by 10mg/kg. In contrast, SD was decreased by 1mg/kg during the entire test in NRB and was increased only by 10mg/kg during the second part of the test. In addition, OF was reduced in NHE by both doses of SR141716A, whereas it was increased in NRB rats. Conversely SD was increased in NHE and decreased in NRB rats. The differential strain, time and dose dependent effects of AM404 and SR141716A on orienting and scanning phases of attention reveal a different network regulation of Mesocorticolimbic dopamine neurons in NHE and control rats. This, in turn, might explain drug abuse behavior by a subset of ADHD cases.

51. NEUROPEPTIDE Y IN BRAINS OF THE FLINDERS SENSITIVE LINE RAT, A MODEL OF DEPRESSION. EFFECTS OF ELECTROCONVULSIVE STIMULI AND D-AMPHETAMINE ON PEPTIDE CONCENTRATIONS AND LOCOMOTION. Jiménez Vasquez PA [1,3], Salmi P [2], Ahlenius S [3], Mathé AA [1,3]. [1]Inst. of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden. [2]Center for Genomics Research, Stockholm, Sweden. [3]Dept. of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. Neuropeptide Y (NPY), has been implicated in the pathophysiology of depression and the mechanisms of action of electroconvulsive treatment (ECT). In this series of experiments, we explored whether there are differences between Flinders Sensitive Line (FSL) rats, an animal model of depression, and controls, Flinders Resistant Line (FRL) in (1) baseline brain NPY-LI concentrations, (2) effects of ECS on locomotion and brain neuropeptides, (3) amphetamine effects on behavior, and (4) effects of ECS pretreatment on subsequent effects of amphetamine on behavior. Both strains were divided into two groups, receiving eight ECS or ShamECS. Twenty-four hours after the last session, animals were habituated in activity boxes for 45 min before given d-amphetamine (1.5 mg/kg, subcutaneously) or vehicle. Locomotor activity was then recorded for an additional 45 min. Twenty-four hours later, rats were sacrificed by microwave irradiation, the brains dissected into frontal cortex, occipital cortex, hippocampus, hypothalamus and striatum, and the neuropeptides extracted and measured by radioimmunoassay. No differences between FSL and FRL rats in baseline locomotor activity were found. FSL compared to FRL animals showed a significantly larger locomotion increase following saline and a significantly smaller increase following amphetamine. ECS pretreatment significantly decreased the saline effects on locomotion in the FSL and the amphetamine effects in the FRL rats. 'Baseline' NPY-like immunoreactivity (LI) concentrations were lower in the hippocampus of the 'depressed' rats. ECS increased NPY-LI in frontal cortex, occipital cortex and hippocampus of both strains. The hippocampal NPY-LI increase was significantly larger in the FSL compared to FRL animals.

52. PCP INJECTIONS IN ADULT OR NEONATE RATS INDUCE SELECTIVE ATTENTION DEFICITS IN SOCIAL RECOGNITION: REVERSAL BY SSR125047A, A SIGMA LIGAND WITH POTENTIAL ANTIPSYCHOTIC PROPERTIES. Terranova, J-P.; Poncelet, M.; Perrault, Gh.; Soubrié, Ph. CNS Department. Sanofi-Synthélabo Recherche, 34184 Montpellier, France. There is evidence for the potential activity of sigma ligands (σ) in schizophrenia. Attention deficit is considered to be one of the features of cognitive dysfunction in schizophrenia, which may underlie social withdrawal in this disease. We have therefore evaluated in the rat, the effects of SSR125047A a highly selective σ ligand, in the different procedures analyzing disturbances of information processing associated with social context. SSR125047A (2.5 to 10 mg/kg ip) unlike the atypical antipsychotic clozapine (0.1 mg/kg, ip) and the classical antipsychotic haloperidol (0.1 mg/kg, ip), did not improve spontaneous selective attention disruptions. However, in an experimental condition in which rats were able to differentiate relevant (novelty) from irrelevant information, an acute injection of PCP (3 mg/kg ip) induced selective attention deficits that were reversed by SSR125047A (1.25 to 5 mg/kg ip), and clozapine (0.1 mg/kg ip) but not by haloperidol (0.05 to 0.3 mg/kg ip). Moreover, after neonatal PCP injections, SSR125047A like clozapine and haloperidol, reduced selective attention deficits when tested in the corresponding adult animals. In addition, and as with the previous results demonstrating that SSR125047A displays an atypical antipsychotic profile in rodents similar to that of clozapine, these results suggest that σ ligands such as SSR125047A may possibly alleviate social deficits associated with schizophrenia

53. GENETIC DIFFERENCES IN FEAR-POTENTIATED STARTLE: A PARADIGM FOR BEHAVIORAL ASSESSMENT S. A. Miller, M. C. Cook[1], M. R. Murphy, J. H. Merritt, and P. A. Mason, U.S.A.F. Research Laboratory, Human Effects Directorate, Directed Energy Bioeffects Division, Radio Frequency Radiation Branch, and [1]Veridian Engineering, Inc., Brooks AFB, TX. The reflexive nature and extreme sensitivity of fear-potentiated startle (FPS) make it a particularly useful tool for studying the bioeffects of stressors (e.g., radio frequency radiation, toxins, psychological stress). While the startle reflex is present in most species, it is possible that genetic differences in emotionality might significantly affect baseline startle (BLS) or FPS. Four genetically diverse strains of rats were tested: Lewis, Wistar Kyoto (WKY), Wistar, and Sprague Dawley (SD). Experimental subjects were exposed to 30

pairings of light and shock. Twenty-four hours later, all subjects received 30 trials of a 120-dB white noise startle stimulus preceded by a light (L+WN) and 30 trials of white noise alone (WN). FPS is evidenced when startle magnitude during L+WN trials exceeds that exhibited during WN trials. Clear strain differences emerged. FPS was found in Wistar, Lewis, and SD subjects. WKY subjects showed little or no FPS. Additionally, differences in BLS differed greatly between the strains. Lewis and WKY strains both showed a lower level of BLS compared to the SD and Wistar groups, eliminating the possibility that WKY rats show no FPS merely because they are hypo-reactive. The Wistar group's BLS far exceeded any of the other groups. These baseline strain differences are so profound that an experimenter, blind to the strain identity, was able to properly identify the groups based solely on their BLS. Funded, in part, by the VA/DoD Combat Casualty and Wound Repair Initiative.

54. D1 DOPAMINE RECEPTORS REGULATE PREPULSE INHIBITION OF STARTLE IN C57BL/6 MICE [1]Lehmann-Masten, V.; [3]Ralph-Williams, R.; [2]Otero-Corchon, V.; [2]Low, M.J.; [1]Geyer, M.A. [1]Dept Psychiatry, University of California San Diego, La Jolla, CA, 92093 USA. [2]Vollum Institute, Oregon Health Sciences University, Portland, OR 97201 USA. [3]Dept Psychiatry, Harvard Medical School, Belmont, MA 02478 USA. Deficits in prepulse inhibition (PPI), an operational measure of sensorimotor gating, are characteristic of schizophrenia and related neuropsychiatric disorders. Clinical and animal studies have demonstrated a contribution of dopamine (DA) and the D2-family of DA receptor subtypes to the modulation of PPI, while little is known about the role of D1-like DA receptors. Therefore, we used a combined pharmacological and genetic approach to determine whether the D1 receptor is involved in PPI of startle in mice. The experimental animals were wildtype (D1WT) and D1 receptor-deficient (D1KO) siblings of both sexes derived from mating pairs of D1+/- B6.129S4-Drd1atm1Jcd mice (N6 backcross to C57BL/6). There were no consistent differences in PPI or the acoustic startle response in D1WT and D1KO mice. The indirect DA agonist d-amphetamine produced significant disruptions of PPI in both D1WT and D1KO mice. However, both the direct D1 DA agonist SKF82958 and the mixed D1/D2 DA agonist apomorphine disrupted PPI only in the D1WT mice, and were ineffective in the D1KO mice. These results suggest that the D1 dopamine receptor is an important modulator of sensorimotor gating in mice.

55. EFFECTS OF AMPHETAMINE WITHDRAWAL ON THE MORRIS WATER MAZE TASK. Russig, H.; Durrer, A.; Murphy C.A.; Feldon, J. Laboratory of Behavioral Neurobiology, Swiss Federal Institute of Technology, ETH Zurich, Schorenstrasse 16, CH-8603 Schwerzenbach, Switzerland. Previous studies have shown that withdrawal from an escalating dosage schedule of amphetamine (AMPH; 3 injections per day, 1 – 5 mg/kg) reduced latent inhibition in rats, suggesting an animal model of attentional and/or cognitive schizophrenic symptoms. In addition it has been shown that post training AMPH injections affects water maze performance. We tested AMPH-withdrawn rats in different water maze procedures for spatial reference memory, and working memory as well as for their switching capacity in a reversal task. All testing was conducted between withdrawal days 3 and 5, with half of the animals receiving acquisition before, and half, after AMPH treatment. There were no differences between AMPH-withdrawn rats and their controls treated with drug either before or after acquisition. In contrast, AMPH-treated animals showed behavioural sensitization, as reflected by an augmentation of locomotor activity after an AMPH challenge compared to saline pre-treated animals. Taken together with previous studies these results suggest that AMPH withdrawal may model specific attentional or cognitive deficits of schizophrenic patients without inducing general memory impairment.

56. HYPERACTIVITY EXHIBITED BY SPONTANEOUSLY HYPERTENSIVE RATS (SHR) DIFFERS. WITH APPARATUS AND ACTIVITY TYPE. Ferguson, S.A.; Cada, A.M. Div. of Neurotoxicology, National Center for Toxicological Research/FDA, Jefferson, AR 72079 USA. The SHR is often used as a model of childhood Attention Deficit Hyperactivity Disorder (ADHD) due, in part, to its hyperactivity relative to the normotensive strain, the Wistar-Kyoto (WKY). Most often, however, activity levels are measured using the open field test which provides little in the way of exploratory incentives. Moreover, use of the WKY as the control strain has been questioned. Here, the activity levels in postnatal day 57 male and female SHR, WKY and Sprague-Dawley (SD) rats were measured in three substantially different apparatus: a typical open field (12 min), a residential running wheel (10 min), and the figure 8 residential maze (an ethologically-relevant alleyway-type apparatus designed to mimic burrows) (12 min). There were no sex differences in activity levels in any test, nor did sex interact significantly with strain. In each test, however, there were significant main effects of strain. In the open field, the SD rats were much more active than either the SHR or WKY which did not differ from one another. Number of wheel revolutions in the running wheel was higher in the WKY than the SHR; the SHR and SD strains did not differ from one another. In the figure 8 maze, the SHR were more active than the WKY and the WKY and SD were similar in activity. These results provide evidence that strain differences in activity levels are exquisitely test-specific. If the SHR are to be thoroughly validated as a model of childhood ADHD, assessments should be made not only of various types of activity, but such results compared to those obtained from other common laboratory strains, such as the Sprague-Dawley.

57. PERIPHERAL ADMINISTRATION OF GLYCOSILATED DOPAMINE MODULATES THE ACTIVITY AND FUNCTION OF CENTRAL DOPAMINE SYSTEMS IN MICE AND RATS. D. Viggiano[1], L.A. Ruocco[2], G. Rimoli[3], D. Melisi[4], P. De Caprariis[5], L. Annunziato[4] and A.G. Sadile[2]. Inst. Human Anatomy[1], Lab. Neurophysio[1]., Behav. & Neural Networks, Dept. Expt[1]. Medicine, II Univ. Naples[2], Depts. Pharmaceut. and Toxicol., Fac. Pharmacy, Univ. Naples "Federico II"[3] and Salerno[5], Dept. Neurosci., Med. Sch., Univ. Naples "Federico II"[4], Naples, Italy. The involvement of the mesocorticolimbic system in activity and attention has been addressed in mice and rats following peripheral administration of a glycosilated form of dopamine (GAL-DA) that is likely to cross the blood-brain barrier more easily using the membrane glucose transporter. Adult male Swiss albino or C57 mice and random bred Sprague-Dawley or Naples Hight-Excitability (NHE) rats received an i.p. injection of GAL-DA (0.0, 10 or 100 mg/Kg). In Exp. 1 rats were perfused and brains analyzed using a galactose-specific lectin. Image analysis

showed a 10% increase in GAL-DA entry into the striatum between 0.5 and 3.0 h that waned by 6 h. In Exp. 2 rats received GAL-DA (0.0, 10 or 100 mg/Kg, i.p.) 3.0 h before a 30-min. exposure in a spatial novelty. The behavior was videotaped and analyzed for traveled distance, orienting frequency and scanning duration. GAL-DA decreased traveled distance in NHE rats, increased it in C57 mice with no effects in Swiss mice and random bred rats. Conversely, GAL-DA did not affect orienting frequency but decreased scanning duration by 20% in random bred rats only at 10 mg/Kg. Thus, GAL-DA crosses the blood-brain barrier in the striatum an modulates the activity and function of dopamine systems in a dose and genotype-dependent manner. These findings promise new strategies in the treatment of some neuropsychiatric disorders with modified forms of neurotransmitters, whose entrance into the brain can be facilitated through the utilization of the plasma membrane carrier for sugars (Supported by MIUR-COFIN 2001 Grant).

58. DOMINANT BEHAVIOR MEASURED IN A COMPETITION TEST AS A MODEL OF MANIA. Ewa Malatynska, Robert Rapp and Glenda Crites. Indiana University School of Medicine, Department of Pharmacology & Toxicology, Evansville, IN 47712, USA. Our previous studies demonstrated that submissive behavior measured in a pair of rats competing for food can be used as a test for antidepressant drug activity (Malatynska et al, 1984, 1995 & 2002). The bipolar character of dominant – submissive behavior leads us to consider the dominant behavior as a model of mania for antimanic drug development. Our working hypothesis was that dominant behavior, as observed under our experimental conditions, can serve as a model of mania that is sensitive and selective to antimanic drugs. The dominance test was performed according to the method of Malatynska and Kostowski (1984). The rats were randomly paired and put into an apparatus consisting of two plexiglass boxes connected with a narrow hallway containing a small feeder with a sweetened milk in the center . Only one rat has comfortable access to the feeder at a time but two rats can drink milk during the five minutes of experimental session. The dominant rat spends significantly more time on the feeder than its submissive partner. Dominant rats were treated with drugs commonly used to alleviate mania in the clinic. These included lithium (100 mg/kg), sodium valproate (30, 200, and 300 mg/kg), carbamazepine (20 mg/kg) and clonidine (0.05, 01, 0.2 mg/kg). We have shown that (1) Dominant behavior as defined by the conditions of our experiment is reduced by lithium, carbamazepine and a low dose (30 mg/kg) of sodium valproate. (2) The activity of lithium is delayed, mimicking the effect of this drug in the clinic. (3) Dominant behavior is reduced by clonidine, a drug used to rapidly alleviate symptoms of mania, after brief treatment. We conclude that dominant behavior is sensitive to a range of drug used to treat mania in humans. However, further studies are required to determine the validity of dominant behavior as a model of mania.

59. SPATIAL LEARNING IS SELECTIVELY IMPAIRED BY REPEATED ADMINISTRATION OF AMPHETAMINE AND MK-801: A POSSIBLE MOUSE MODEL OF COGNITIVE DEFICITS. Rinaldi A; Mandillo S; Oliverio A; Mele A - Dept Gen Mol Biol, Univ La Sapienza, Rome, Italy. The dopaminergic and the glutamatergic systems have been indicated as possible substrates of cognitive deficits found in psychiatric syndromes. Both amphetamine and the NMDA receptor antagonist MK-801 have been used in pharmacological animal models of schizophrenia but none focused so far on non-reinforced learning. The objective of this study was to test if repeated administration of AMPH or MK-801 influenced the performance of mice in a non-associative spatial learning task. CD-1 male mice were given i.p. daily injections of either saline, AMPH (2.5, 5 mg/kg) or MK-801 (0.3, 0.6 mg/kg), for 5 days. On day 6 all mice were tested in an open field containing 5 different objects. After 3 sessions of habituation, the animal reactivity to the displacement or substitution of an object was assessed by scoring the time spent exploring each object. Five days of repeated AMPH or MK 801 administration dose-dependently impaired the mouse ability to discriminate a spatial change; the animals treated with AMPH or MK-801 spent a comparable amount of time re-exploring both displaced and non-displaced objects while the controls explored the displaced significantly longer than the non-displaced objects. No significant differences among treatment groups were observed in the animal locomotor activity or in the ability to detect a new object. It is proposed that alterations of both dopaminergic and glutamatergic systems and possibly of their interaction underlies spatial learning deficits. These findings could provide initial evidences to study the neural mechanism of cognitive and attention deficits induced by drugs of abuse or observed in psychiatric disorders like schizophrenia.

60. CIRCADIAN RHYTHM AND CYTOCHROME OXIDASE ACTIVITY OF THE SUPRACHIASMATIC NUCLEUS IN TWO EXPERIMENTAL MODELS OF HEPATIC INSUFFICIENCY. López, L.; Aller, M.A.; Arias, J.; González-Pardo, H.; Begega, A.; Conejo, N.; Miranda, R.; Arias, J.L. Dept. of Psychology, University of Oviedo, SPAIN. Porta-caval shunt (PCS) and portal hypertension (PH) performed by stenosis of the porta vein, are two of the animal models frequently used to test the consequences of hepatic insufficiency. In the human clinic both conditions are usually associated, since the patients that have a deviation of portal blood to the systemic circulation, develop portal hypertension simultaneously. Among the consequences of hepatic insufficiency we can find alterations in circadian rhythms of several biological systems. Our work aimed to test the rhythmic locomotor activity in three groups of rats (n= 7 each group): PCS, PH and sham-operated rats (SO). We have also determined by optical densitometry cytochrome oxidase activity (CO), a marker of neural metabolic activity, in the suprachiasmatic nucleus from the experimental groups. The results show that the animals with PCS display an altered circadian rhythm, (hypoactivity during the darkness phase and a very low rhythm percentage as compared to the SO and PH groups). At the same time, the quantification of CO has shown that the suprachiasmatic nucleus of the rats with PCS have a low CO activity level with reference to the other two groups. Additionally, there are no differences between CO activities from the groups PH and SO. These tests seem to confirm that the consequences in the nervous system are different in both models. Probably, the massive deviation of portal blood to the systemic circulation would cause the reported alterations in both the locomotor activity and CO activity from the suprachiasmatic nucleus.

61. SEX DIFFERENCES IN BRAIN OXIDATIVE METABOLISM AFTER SPATIAL LEARNING. Conejo, N.M.; González-Pardo, H.; Vallejo, G.; Arias, J.L. Dept. of Psychology. University of Oviedo, E-33003 Oviedo, SPAIN. Sexual dimorphism has been reported frequently in spatial learning processes evaluated with the Morris water maze in rodents. Differences between sexes in the rat are more pronounced during the early postnatal development, particularly about 30 days of age. However, little is known about its functional expression in the brain. In our study, we used 30 day-old Wistar rats from both sexes. The experimental groups (N=20) were trained in the Morris water maze, where animals must find a hidden escape platform beneath water level. Additionally, rats had only one visual landmark attached to one of the four curtains that surrounded the pool. Control animals (N=20) swam in the pool with no escape platform available during the same time. Our results show that males learn to locate the escape platform two days earlier than female rats. The metabolic activity measured in selected brain regions using cytochrome oxidase (CO) histochemistry was clearly dimorphic in the experimental groups. Particularly, we detected a significant increase in CO activity of mamillary bodies in females and anterior thalamus in males as compared with the respective control groups. However, both experimental groups had higher CO activity in the prelimbic cortex. Moreover several neurobehavioral correlations were found between the metabolic activity in the selected brain regions and the escape latencies measured in both experimental groups. Research supported by grants PB-SAL-96- from Ministerio de Educacion y Cultura and grant GE-EIS01-04 from FICYT.

62. INVOLVEMENT OF DIFFERENT RECEPTORS IN PACAP 38-INDUCED OPEN-FIELD ACTIVITY IN RATS. Telegdy, G.; Adamik, A. Dept. Pathophysiology, University of Szeged, Szeged, Hungary H-6701. The action of PACAP 38 was tested in an open field 3o min and 3 h after icv PACAP 38 administration. The effects on locomotion, rearing and grooming were measured. The possible roles of different receptors were tested in animals pretreated with different receptor blockers followed by PACAP 38 administration. PACAP 38 increased the locomotion, rearing activity and grooming at 3o min after administration whereas at 3 h there was no change in grooming, while the locomotion and rearing activity were decreased. PACAP antiserum, a PACAP antagonist (PACAP 6-38), a CRF antagonist (CRF 9-14), propranolol and naloxone prevented the changes observed at 30 min and 3 h. Atropine and nitro-L-arginine were ineffective. The data demonstrate that the action of PACAP 38 on the open-field activity is regulated by different receptors.

63. CLASSICAL CONDITIONING OF BREATHING PATTERN IN TWO-DAY-OLD MICE. Durand, E.; Dauger, S.; Vardon, G.; Gressens, P.; Gaultier, C.; de Schonen, S.; Gallego, J. INSERM. E9935, Hôpital Robert-Debré, 75019 Paris, France. It has been proposed that higher brain centers may participate in breathing control through learning processes. Because breathing adapts to metabolic needs at birth, the possible contribution of learning processes to breathing should be examined postnatally. We performed a conditioning experiment in two-day-old mice using an odor (lemon) as the conditioned stimulus (CS) and maternal care after one hour without the mother as the unconditioned stimulus (US). Each pup underwent two acquisition trials, in which the CS was presented immediately before (experimental paired group, n=30) or 30 min before (control unpaired group, n=30) contact with the mother. Conditioning was tested by using non-invasive whole-body plethysmography to measure the respiratory response to the CS for one minute. We found significantly stronger respiratory responses to the CS in the experimental group than in the control group. In contrast, somatomotor activity did not differ significantly between groups. To our knowledge, this is the first study showing that classical conditioning can be achieved in mouse pups as young as two days of age. Our results confirm the sensitivity of breathing to conditioning and indirectly support the hypothesis that learned feedforward processes may complement feedback pathways during postnatal maturation of respiratory control.

64. DOSE-RESPONSE EFFECTS OF CHRONIC LITHIUM TREATMENT ON SPATIAL MEMORY IN THE BLACK MOLLY FISH. Creson, T.K.; Rasch E.M.; Monaco P.J.; Woodruff, M.L. Dept. of Anatomy & Cell Biology. East Tennessee State University, Johnson City, TN 37614 USA. Reference memory has been assessed utilizing place learning spatial discrimination tasks in rodents. Results of a previous study in our lab indicate that chronic lithium regimens impair working memory in the black molly fish (*Poecilia latipinna*) as assessed by a forced-choice spontaneous alternation task. Lithium is widely used in the management of bipolar disorder, yet memory impairment is a serious side effect. To assess the behavioral effects of lithium on reference memory, we have employed a four-arm maze in a spatially constant environment identical to that used in our working memory study. Four treatment groups (N=141) were gavaged with 20 microliters of one of three different concentrations of lithium chloride (10 mM, 100 mM, 1 M) or vehicle (water) for controls every 12 hours for 25 days. On day 15, subjects began a 10 day, four trials per day, place learning task. Several measures of performance were analyzed to evaluate reference memory. Results indicate that the 1 M dose group needed significantly more trials to reach criterion and made significantly fewer correct first choices than the other dose groups. Latencies to reward were not significantly different among groups indicating performances were not compromised by lack of motivation nor locomotor disabilities. Capillary ion analysis determinations of plasma and brain lithium levels demonstrate a linear dose-response effect for plasma. Collectively, the results indicate that chronic lithium administration impairs spatial reference memory. This study and other work in our lab suggest that the fish may be an appropriate animal model subject for further pschopharmacological studies in the field of cognition.

65. EFFECTS OF L-DOPA TREATMENT WITH ANTIOXIDANTS ON ADRENAL CHOMAFFIN CELLS USING A RAT MODEL FOR PARKINSON'S DISEASE. Corona-Morales, A. A.; Castell, A.; Hernández-Peñaloza, A.; Roldán-Roldán, G; Zhang, L. Facultad de Medicina, Universidad Nacional Autónoma de México, México 04510 D. F. México. L-DOPA - the metabolic precursor of dopamine - has been extensively used clinically during the last three decades to remedy the striatal dopamine deficiency in Parkinson's Disease (PD). This drug was also used in adrenal chromaffin cell (ACC) transplanted patients during the immediate post-surgery period. We have previously demonstrated that L-DOPA caused chromaffin cell death either by necrosis or apoptosis and reported the

beneficial effects of combined application of L-DOPA with Fullerene (C_{60}) and ascorbic acid (AA) in cell culture. Here, we aimed to determine whether these beneficial effects observed *in vitro* can influence the survival cell density, neurite sprouting and neurogenesis on ACC transplant in parkinsonian rats developed by 6-hydroxidopamine (6-OHDA) model of PD. Placebo, L-DOPA (50mg/kg)/carbidopa (5mg/kg) and L-DOPA (50mg/kg)/carbidopa (5mg/kg) + AA (50mg/kg) were administrated for 10 days separated in two doses per day to food of 6-OHDA lesioned rats with satisfactory rotation test and transplanted with ACC. Animals were then perfused and forebrain sections containing transplants were obtained for pre-embedding immunocytochemistry. Increased TH+ cell density was observed in L-DOPA+AA administrated rat brain transplant regions whereas the ACC transplants from the group received only L-DOPA had higher rate of cell death. These observations may have important implications for the development of new strategies for combining cell and pharmacological therapies for PD. *Supported by DGAPA-UNAM grant IN200300 and scholarship from CONACYT-MEXICO to AACM.*

66. STATISTICAL METHODS FOR THE ANALYSIS OF THE BEHAVIOURAL SEQUENCES. Puopolo, M.; Venerosi Pesciolini, A.; Valanzano, A.; Chiarotti, F.; Calamandrei, G.; Ricceri, L. Sections of Comparative Psychology and Behavioural Pathophysiology, Lab. of Pathophysiology, Istituto Superiore di Sanità, Rome, Italy. In ethological and behavioural toxicological studies, elaborate behavioural patterns shown by the animals in well established experimental paradigms or naturalistic conditions are routinely observed and split in single behavioural items. Subsequently these items are analysed in terms of their frequencies and/or durations. Behavioural observations are usually videotaped and scored by dedicated softwares, which collect the sequences of behavioural items together with frequencies and durations. So far, the Cox proportional hazards model, a method originally developed for the analysis of time-to-event data, has been employed for the analysis of the time-structure of behaviour but its usefulness has been limited because of not allowing the inclusion of random effects in the model. However recent developments in mixed models for the analysis of time-to-event data may overcome these limitations and improve the analysis of behavioural patterns. Data on the effects of exposure to some toxicants on social interactions in mice will be presented to illustrate the use of these new statistical methods. The study of behavioural sequences may highlight the role of the investigated conditions in setting behavioural organizations. In addition the refinement of this statistical approach may contribute to a reduction in the number of animals used in this field of the life sciences.

67. SPONTANEOUSLY HYPERTENSIVE RATS DO NOT PRESENT AGING-INDUCED OROFACIAL DYSKINESIA: A POSSIBLE PROTECTIVE EFFECT OF CATALASE. Abílio, V. C.; Carvalho, R.C.; Ribeiro, R. de A.; Frussa-Filho, R. Departamento de Farmacologia, UNIFESP, São Paulo, Brazil. Reserpine-induced orofacial dyskinesia has been proposed as an animal model of tardive dyskinesia (Neisewander et al., Psychopharmacol.,116:79-84, 1994), a syndrome that seems to be related to nigroestriatal dopamine supersensitivity (Baldessarini & Tarsy, Int. Ver. Neurobiol., 21:1-45, 1979) as well as to oxidative stress (Lohr, Arch. Gen. Psychiat., 48:1097-1106, 1991). Six month old Spontaneously Hypertensive Rats (SHR) do not develop reserpine-induced orofacial dyskinesia (Queiroz et al., Eur. J. Pharmacol., 356:105-108, 1998). Considering that aging is the main risk factor for tardive dyskinesia (Wolfarth and Ossowska, Prog. Neuro-Psychopharmacol. Biol. Psychiat., 13:799-840, 1989) and that saline-treated old Wistar rats present orofacial movements similar to those induced by reserpine (Bergamo et al., Neurobiol. Aging 18:623-629, 1997), the aim of this work was to compare the development of aging-induced oral dyskinesia in normotensive Wistar rats (WR) and in SHR. In addition, striatal catalase (an antioxidant enzyme) activity was also quantified. WR and SHR at 45 days, 6 months and 18 months of age were used. All animals were observed for quantification of spontaneous orofacial movements. Animal of these same ages were used for striatal catalase quantification. Senescent WR but not senescent SHR presented increased orofacial movements. Striatal catalase activity was increased in SHR when compared to WR at all ages. In addition, aging induced an enhancement of striatal catalase activity only in SHR. As previously reported for reserpine-induced orofacial movements, our results show that SHR do not develop aging-induced orofacial dyskinesia. An enhancement of striatal catalase activity could be a neuroprotective factor responsible for the absence of aging-induced orofacial dyskinesia in SHR. Financial Support: FAPESP.

68. EFFECTS OF CLASSICAL CONDITIONING ON CYTOCHROME OXIDASE ACTIVITY IN THE CEREBELLUM OF GOLDFISH. Álvarez E; Gómez A; Rodríguez F; González JA; González-Pardo* H; Arias* JL; Salas C. Laboratorio de Psicobiología. Universidad de Sevilla. Sevilla (Spain). *Laboratorio de Psicobiología. Universidad de Oviedo. Oviedo (Spain). Determination of cytochrome oxidase activity has been suggested as a method to examine sustained baseline change in cellular metabolic activity. Several lines of evidence indicate that the cytochrome oxidase histochemistry can be used to reveal learning-related changes on neural activity. In the present study, quantitative cytochrome oxidase histochemistry was applied to study changes in metabolic activity of neurons in the teleost cerebellum following training in an “eye-blink” like classical conditioning paradigm. Goldfish (Carassius auratus) were randomly distributed in three groups: i) delay conditioning, ii) uncorrelated conditioning, iii) untrained. Goldfish in the delay group received 300 conditioning trials. Each trial consisted of the paired presentation of a light as conditioned stimulus (350 ms in duration) followed by a single shock (0.2-0.5 mA pulse of 0.15 ms) at the base of the dorsal fin as unconditioned stimulus. The intertrial interval was 30"6 sec. Untrained and uncorrelated groups were used as control. The uncorrelated group received unpaired presentation of the same conditioned and unconditioned stimulus whereas the untrained group did not receive any experimental manipulation. After training sessions, between groups differences were found in the level of cytochrome oxidase activity. Animals trained in the delay procedure showed an increase in cytochrome oxidase activity level in the molecular and granular layers of the cerebellum in relation to the control groups. These results are consistent with those showing learning-related changes in the cerebellum in response to associative conditioning in mammals.

Friday, June 21

8:00-9:00 Oral Session 2: Behavioral endocrinology

PERINATAL EXPOSURE TO PHYTOESTROGENS ALTERS ENDOCRINE-IMMUNE INTERACTIONS IN MALE RATS. Klein, S.L.; Wisneiwski, A.B.; Marson, A.L., Glass, G.E.; Gearhart, J.P. Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA. Although several studies illustrate that endogenous estrogens alter immune function, few studies have examined the hormonal effects of phytoestrogens (i.e., plant-derived estrogens) on the immune system. Because phytoestrogen consumption is associated with health-related outcomes, we hypothesized that ingestion of genistein, an estrogenic isoflavonoid from soybeans, may affect immune function. To examine the effects of perinatal phytoestrogen exposure on immune function, pregnant female rats were exposed to no, low, or high genistein diets throughout gestation and weaning, and endocrine and immune function were assessed in adult male offspring. Although relative spleen masses were not affected by genistein exposure, thymus masses were heavier among males exposed to high genistein than among males exposed to low or no genistein. Percentages of splenic and thymic helper T cells were not altered by genistein. The percentage of cytotoxic T cells in the spleen was higher among males exposed to the high genistein diet than among males exposed to low or no genistein. The percentage of B cells in the spleen was higher among males exposed to no genistein than among males exposed to either low or high genistein diets. Although estradiol concentrations were not affected by genistein exposure, testosterone concentrations were lower among males exposed to low and high genistein diets than among males that received no genistein. Males with lower testosterone concentrations had heavier spleen and thymus masses and higher helper and cytotoxic T cell numbers than males with higher testosterone concentrations. Whether genistein exposure affects cytokine production will be discussed. In summary, these data illustrate that perinatal exposure to phytoestrogens alters the endocrine and immune systems and may affect responses to disease.

NEUROSTEROID EXPOSURE DURING NEONATAL DEVELOPMENT PRODUCES SEX-SPECIFIC EFFECTS ON ANXIETY-RELATED BEHAVIORS IN THE ADULT RAT. Fortis, A. [1]; Bonet, Y. [2]; Cruz, N. [3]; Barreto, J. [1]; Rivera, J.C. [2]; Corretjer, G.[4]; Jorge, J.C.[4]. Departments of Chemistry[1], Biology[2], and Psychology[3], Rio Piedras Campus. Department of Anatomy[4], Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico 00936. Pregnenolone sulfate (PREG-S) is a neurosteroid that acts as an allosteric modulator of receptor-channel complexes in the brain. Sixty four Sprague Dawley pups were injected with PREG-S (1mg/kg) from postnatal (PN) day PN1 to PN14. Starting on PN 30, we monitored the day of vaginal opening, and we assessed the pattern of estrous cycle with vaginal smears to determine pubertal onset. At PN 75, behavioral tests were performed to measure locomotor and anxiety-related behaviors with the automated Activity Monitoring System and the Elevated Plus-Maze from AccuScan Instruments (Ohio-IL). After behavioral assessment, rats were sacrificed by decapitation, and blood was collected to measure hormone levels. Gonads (ovaries, uterine tubes, and testicles) were collected and weighted. While PREG-S exposure had no effect on locomotor behaviors (rearing activity, stereotypic count, total locomotor activity) in either sex, the same treatment produced sex-specific differences on anxiety-related behaviors. Specifically, PREG-S had anxiolytic effects in females and anxiogenic effects in males. These modulatory effects on behavior cannot be attributed to permanent changes on the hypothalamo-pituitary axis since gonadal weight, day of vaginal opening, pattern of estrous cycle, and plasma levels of progesterone, estradiol, and testosterone in adult animals were not altered by PREG-S neonatal exposure. Therefore, modulation of neuronal activity by PREG-S during neonatal development might contribute to the sexual differentiation of anxiety-related behaviors in the rat. Funding provided by the MBRS-RISE- MSC (GM61838) to Fortis, Bonet, and Ramos, the COR- RPC to Cruz. Study funded by RCMI-MSC (G12RR03051) and the NIH (RR15565) to JC Jorge.

NEONATAL TEMPERATURE/SEPARATION STRESS ALTERS EXPLORATORY BEHAVIOR IN MALE BALB/CBYJ MICE. Hohmann, C.F.; Karikari, P.D.; Lipscomb, D. Dept. of Biology, Morgan State University, Baltimore, MD USA. Despite intensive research, the neurobiology of many mental health disorders is still poorly understood. Clearly, genes are not the only way that mental disorders are transferred; environmental factors are increasingly recognized as major factors in morbidity. The goal of the current study is to assess, in a mouse model, behavioral and cortical changes that result from exposure to early postnatal stress. One half of 64 Balb/CByJ mice were subjected to alternating cold (5˚C) and hot (37˚C) stress from postnatal day [PND] 2-7, for 30 minutes per day, followed by additional maternal separation of 30 minutes at room temperature. The other half of each litter remained with the dam. Beginning with PND 60, 16 males and 16 females from each the control and stressed group were handled and subsequently subjected to an Open Field Object Recognition (OFOR) task. Videotapes of OFOR performances were analyzed using the Observer Video Pro II (Noldus). Following the OFOR task, all mice were subjected to a neurological test battery. Statistical data analysis was conducted using factorial Anovas (StatView). Results show significantly less object exploration throughout the OFOR task in stressed male but not female mice compared to non-stressed controls. No significant differences appeared between stressed and control mice in general activity, object novelty and object displacement, largely due to substantial inter-animal variability in performance. No neurological impairments were seen but differences in anxiety levels between stressed and non-stressed mice were apparent. We are currently preparing the cortices of all subjects for morphometric analysis. Supported by NIGMS RR 11606-05 and GMS51971.

ADRENAL RESPONSE INDUCED BY SOCIAL STRESS IN A TERRITORIAL BIRD SELECTED FOR DIFFERENT COPING STYLES. Carere, C.; Groothuis, T.T.G.; Möstl, E.; Koolhaas J.M. Dept. of Anim. Behav. and Dept. Anim. Physiol., University of Groningen, P.O. Box 14, 9750 AA Haren, NL. In this study we tested whether in a passerine bird (great tit, *Parus major*) individuals different for coping strategies differ in the magnitude of the adrenal response to social stress. Furthermore, we aimed at characterizing daily rhythms in corticosteroid

release before and after social stress. We used sixteen males from either of two selection lines (fast and slow explorers). Social stress was induced by confrontation with an aggressive resident male. Corticosteroid metabolites were analyzed in faeces collected at 90-min intervals from 9 to 1630 on a baseline day, on the day of the social conflict and on the following day. In both days and in both lines levels varied with time of day in a robust rhythm with a peak in the first sample of the morning, and a trough at the end of the light phase. This rhythm correlates strongly with activity (perch-hopping). An increase in levels relative to baseline day was observed between 30 and 140 min after the challenge. Birds of the less aggressive and more cautious line (slow explorers) showed a higher response compared to birds of the more aggressive and bolder line (fast explorers), which showed almost no response. The birds of the slow line also had reduced corticosteroids 24 hrs after the challenge, likely reflecting an increased negative feedback. The results provide evidence for a physiological basis of different coping strategies, emerging in response to social stress. Since both strategies coexist in natural populations, possible ecological consequences are discussed.

9:00-10:00 Presidential Lecture: John P. Bruno

THE BASAL FOREBRAIN CORTICAL CHOLINERGIC SYSTEM: ITS ROLE IN ATTENTIONAL PROCESSING AND CONTRIBUTION TO NEUROPSYCHIATRIC DISORDERS. Bruno, J.P.; Depts. of Psychology and Neuroscience. The Ohio State University, Columbus, OH 43210 USA. Attentional processing, involving the detection, selection and resource allocation among multiple stimuli, is a necessary component of cognitive processing and is impaired in a number of neuropsychiatric disorders such as Alzheimer's dementia, schizophrenia, and drug addiction. The continued erosion of attentional processing may contribute to subsequent cognitive deficits seen in these disorders. Evidence from humans and animals strongly suggests that the integrity of the basal forebrain cortical cholinergic system is necessary for normal attentional processes. Recent animal studies from our laboratory and others demonstrate that cortical cholinergic transmission is enhanced during performance of operant tasks that explicitly tax attentional processes. Collectively, our research identifies a distributed neural system involving cortical (prefrontal, posterior parietal) and subcortical (nucleus accumbens and basal forebrain) regions in the mediation of attention. Using intact rats as well as animal models of aspects of Alzheimer's disease, schizophrenia, and drug abuse, we will present neurochemical (release of multiple neurotransmitters) and neuropharmacological (effects of drugs on this release) data within this distributed system, explicitly comparing baseline conditions (animals at rest) with the effects seen during performance of the attentional task.

10:15-12:15 Symposium II: Cannabinoid receptor genetics, signaling and behavior

EFFECTS OF CANNABINOIDS ON MEMORY, OR "WHERE DID I PARK MY CAR?" Hampson, R; Deadwyler, S. Physiology & Pharmacology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157-1083, USA. Potent cannabinoids such as delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient in marijuana, and the aminoalkylindole WIN 55,212-2, have been shown to disrupt short term memory in animals performing a variety of behavioral tasks. Studies have shown that the mammalian hippocampus is essential for certain types of short-term memory, and that there is a concentration of cannabinoid CB1 receptors in this structure. Recent reports have shown that endogenous cannabinoids mediate GABAergic inhibition of hippocampal pyramidal cells via a diffusible reverse-messenger, and suggest that cannabinoids may modulate memory by reducing inhibition and causing less specificity of neural activity. However, there are differences between this proposed mechanism and cannabinoid effects on neural activity in the hippocampus of behaving animals. The effects of delta-9-THC and WIN 55,212-2 have been characterized on behavior and hippocampal neural activity during performance of a short-term memory task. Electrophysiological recordings reveal that neural firing of the presumed pyramidal cells in hippocampus encode task-relevant information during specific phases of a short-term memory task, and that behavioral performance in the task can be correlated to the strength of that encoding. CB1 receptor agonists inhibit cell firing of specific neurons that fire only during the during phases of the task in which information is encoded. These effects are dose-dependent, blocked by the CB1 receptor antagonist SR141716A and develop tolerance to both the electrophysiological and behavioral effects with chronic exposure to cannabinoids. Thus, the impairment is primarily during the encoding of task-specific information, with little to no effect on firing at other times. These effects will be discussed in terms of the still-developing role of the endogenous cannabinoid system in memory processing.

NEUROBIOLOGICAL BASIS FOR THE ADDICTIVE POTENTIAL OF CANNABINOIDS. Gardner, E.L. Intramural Research Program, National Institute on Drug Abuse, NIH, Baltimore, MD 21224 USA. With few exceptions, addictive drugs enhance electrical brain-stimulation reward and act as direct or indirect dopamine agonists in the reward-relevant dopaminergic projections of the medial forebrain bundle (MFB). Further, basal aberration in dopaminergic function within these MFB-associated circuits may constitute a major vulnerability factor for drug addiction. Cannabinoids were long considered to be "anomalous" addictive drugs, lacking pharmacological interaction with these brain reward substrates. However, 15 years of consistent research shows that cannabinoids act on these brain reward substrates in strikingly similar fashion to other addictive drugs. Cannabinoids enhance MFB electrical brain-stimulation reward, and enhance both basal and stimulated dopamine release in reward-relevant MFB projection loci. Cannabinoid action on these mechanisms is tetrodotoxin-sensitive, calcium-dependent, and naloxone-blockable. Furthermore, cannabinoids modulate brain mu and delta opioid receptors, and interact with dopamine receptor-activated transduction mechanisms. Cannabinoid withdrawal produces neurophysiological and neurochemical sequelae strikingly similar to those seen in withdrawal from other addictive drugs. Behaviorally, cannabinoids produce conditioned place preferences and support intravenous self-administration. Thus, cannabinoid interaction with brain reward systems is fundamentally similar to that of other

addictive drugs. However, major gaps in understanding persist - especially regarding the neuroanatomical site(s) of cannabinoid action on brain reward substrates.

BLOCKADE OF EFFECTS OF SMOKED MARIJUANA IN HUMANS BY THE CB1-SELECTIVE CANNABINOID RECEPTOR ANTAGONIST SR141716. Gorelick, D.A.; Heishman, S.J.; Preston, K.L.; Nelson, R.A.; Moolchan, E.T.; Frank,R.A.*; & Huestis, M.A. Clinical Pharmacology & Therapeutics Branch, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD 21224 USA, and *Sanofi-Synthelabo, Inc., Malvern, PA 19355 USA. The CB1-cannabinoid receptor antagonist SR141716 blocks acute effects of CB1 agonists in animals, suggesting that CB1 receptors mediate many of the effects of marijuana. We present evidence that this is also the case in humans. Sixty-three healthy males (mean [SD] age 27.7 [5.4] years, 70% African-American, 10.3 [5.9] years of lifetime marijuana use, 15.3 [10.2] days of marijuana use in the prior month) were randomly assigned to receive a single oral dose of SR141716 or placebo double-blind in an escalating dose (1, 3, 10, 30, 90 mg) design. Each subject smoked an active (2.64% THC) or placebo marijuana cigarette two hours later. Subjective response, heart rate, and blood pressure were measured before and after SR141716 and marijuana administration. Marijuana produced the expected responses of subjective intoxication and tachycardia. SR141716 produced significant dose-dependent blockade of these effects. The 90-mg dose reduced the feelings of "drug high" and "stoned" by 38-43%, tachycardia by 59%, and symptomatic episodes of hypotension to 0% (vs. placebo SR141716). SR141716 by itself had no significant effects and did not affect THC plasma concentrations. These findings confirm the role of CB1 receptors in mediating smoked marijuana effects in humans. SR141716 was well tolerated, and may be a useful tool for studying the endogenous cannabinoid system in humans. Acknowledgment: Supported by NIDA intramural funds and Sanofi-Synthelabo, Inc.

THE ENDOCANNABINOID SYSTEM AS A NOVEL TARGET IN DRUG DISCOVERY. Makriyannis, A., Pharmaceutical Sciences and Molecular and Cell Biology, Center for Drug Discovery, University of Connecticut, Storrs, CT, 06269, USA. The molecular basis of cannabinoid activity is better understood with the discovery of the CB1 receptor in mammalian brain and the CB2 receptor in the periphery of the spleen. Subsequently, an endogenous CB1 receptor ligand, arachidonylethanolamide (anandamide), was isolated from porcine brain and shown to be metabolized by the enzyme anandamide amidase. Recently, we have characterized a reuptake system for the transport of anandamide across the cell membrane and shown that selective inhibition of this transporter is associated with analgesia and peripheral vasodilation. The four cannabimimetic membrane-bound proteins, including the CB1 and CB2 receptors, anandamide amidase and the anandamide transporter, are excellent targets for the development of novel medications for pain, immunosuppression, peripheral vascular disease, appetite enhancement or suppression, and mental illness. The medicinal chemistry of the above four drug targets will be discussed in the context of target-based drug design. (Supported by grants DA9158, DA03801 and DA07215 from the National Institute on Drug Abuse.)

ENDOCANNABINOID GENETICS AND BEHAVIOR. Onaivi, E.; Ishiguro, H.; Zang, P.; Akinshola, B.; Hall, F.; Leonard, C.; Lin, Z.; Darmani, Z.; Hanus, L.; Hope, B.; Uhl, G. William Paterson University, Wayne, NJ 07508, Molecular Neurobiology Branch, NIDA-NIH, Baltimore, MD 21224, Howard University School of Medicine, Washington DC 20059, Kirksville College of Osteopathic Medicine, Kirksville, MO 63501, Hebrew University, Jerusalem, Israel 91120. Significant progress has been achieved in marijuana (cannabinoid) research. However, little information is available at the molecular level about the polymorphic nature of the cannabinoid receptor gene (Cnr) structure, regulation and function. We have continued studies on Cnr genetics and signaling in order to understand the role of endocannabinoids in human behavior and physiology. Using in-vivo and in-vitro techniques we present data on human CB1 Cnr gene transcript size, splice variants, SNPs, trinucleotide repeat and linkage disequilibrium(LD) between these polymorphisms in selected ethnic populations. While the frequencies of the SNPs differed by race, there was different pattern of (LD) between the polymorpisms. Differences were observed when the effects of the endocannabinoids, anandamide, 2-AG, and noladin ether were compared on kainate activated AMPA receptor subunits in Xenopus oocytes using two-electrode voltage clamp. The presence of Cnr CB1 protein and gene expression in the shrew brain and gut, mouse and rat brains and in human blood is presented as evidence for the existence of an endocannabinoid physiological control system (EPCS). In addition the effects of Cnr agonists and the CB1 anatagonist, SR 141716 in the rodent model of withdrawal aversions from cocaine, alcohol and diazepam support a role for this EPCS in natural reward regulatory mechanism. Therefore, understanding the EPCS in the human body and brain will contribute to elucidating this natural regulatory mechanism in health and disease.

ENDOCANNABINOID MODULATION OF MOTOR FUNCTIONS. Giuffrida, A.; Piomelli, D. Dept. Pharmacol., UCI, Irvine, CA 92697. Cannabinoid receptors (CBr), the pharmacological target of the psychoactive constituents of marijuana, are physiologically engaged by a class of lipid signaling molecules termed endocannabinoids. Endocannabinoids exerts profound effects on motor behaviors and cognitive functions. These effects are consistent with the anatomical distribution of CB1 receptors (a CBr subtype), which are particularly abundant in the basal ganglia, cerebellum and sensorimotor cortex. Experimental evidence indicates that the endocannabinoid anandamide represents an important neuromodulator regulating motor functions. Indeed, microdialysis studies have shown that activation of striatal dopamine D2-like receptors induces the release of anandamide, which counteracts D2-mediated hypermotility by acting as an inhibitory feedback mechanism. The cross-talk between dopamine and endocannabinoids suggests that these lipids may participate in pathologies implicating a dopaminergic dysregulation, such as Parkinson’s disease (PD). In support of this hypothesis, altered endocannabinoids levels have been reported in the basal ganglia of 6-OHDA-lesioned rats, an animal model of PD. These observations provide a rationale for new pharmacological interventions for the treatment of motor disorders. This work is supported by PDF (to AG); NIDA (to DP); NARSAD (to DP).

2:00-4:00 Symposium III: Valid models of alcohol dependence x functional

THE ALCOHOL DEPRIVATION EFFECT AS A MODEL OF ALCOHOL RELAPSE. Spanagel, R. Dept. of Psychopharmacology. Central Institute of Mental Health (CIMH), University of Heidelberg, Mannheim, Germany. Voluntary alcohol intake and vulnerability to alcohol abuse depends on numerous genetic and environmental factors. One factor which can also affect alcohol intake is alcohol deprivation. In individuals who had voluntary access to alcohol and became deprived for several days, a pronounced transient rise in alcohol intake and preference over baseline drinking is observed following the re-presentation of alcohol. This robust phenomenon is called the alcohol deprivation effect (ADE) and is observed across several species including rats, mice, monkeys and human social drinkers. Since the ADE mimics different aspects of relapse-like drinking it became a standard model to examine the efficacy of pharmacological agents to prevent relapse drinking. Genetic factors of voluntary alcohol intake can be studied in alcohol-preferring rat lines. The introduction of genetic selection for voluntary alcohol intake in the rat yielded animals with a high preference for alcohol and high daily intake of alcohol. The most common used lines are the Finnish Alko Alcohol (AA), the Indiana University alcohol-preferring (P) and the high-alcohol-drinking (HAD) lines. In the present study the effects of alcohol deprivation in these alcohol-preferring lines is described.

GENETIC SELECTION AND OPIOID SENSITIZATION IN MODELS OF ALCOHOL PREFERENCE. Hyytia, P.; Koistinen, M.; Ojanen, S.; Tuomainen, P.; Kiianmaa, K. Dept of Mental Health and Alcohol Research, National Public Health Institute, POB 33, 00251 Helsinki, Finland. Behavioral sensitization, defined as a progressive and persistent increase in drug effects produced by repeated drug injections, has become increasingly implicated in addiction processes. Genetic differences in consumption of drugs could be reflected in susceptibility to behavioral sensitization. In the present work, we compared the susceptibility of the alcohol-prefer-ring AA (Alko Alcohol) and alcohol-avoiding ANA (Alko Non-Alcohol) rats to morphine-induced neurochemical and behavioral sensitization. Rats were given morphine injections (10 mg/kg, SC) or saline every second day, 15 injections in total. Locomotor activity and dopamine release in the nucleus accumbens were monitored in the animals after challenging them with two additional morphine doses (10 mg/kg, SC), given one and five weeks after termination of the injections. The first challenge dose increased locomotion and dopamine release more in the morphine-treated rats than in the saline-treated controls. Furthermore, the AAs were more sensitive than the ANAs to these effects of morphine. After the second challenge injection, AA rats still showed a greater response in locomotion than the ANA rats. Morphine, however, stimulated now dopamine release in the nucleus accumbens in a similar manner in both saline- and morphine-treated rats. There were no line differences in the brain and plasma morphine concentrations, suggesting that pharmacokinetic factors cannot explain the observed differences in the effects of morphine. These data show that the AAs are more susceptible to morphine-induced behavioral and neurochemical sensitization than the ANAs. More work is needed to elucidate the neuronal mechanisms of the differential sensitivity to the effects to repeated morphine and its contribution to the line difference in alcohol drinking.

PROGRESSION TO LOSS OF CONTROL IN LONG TERM VOLUNTARY ETHANOL DRINKING IN RATS. Wolffgramm,J.;Heyne,A. Section of Addiction Research,University of Tuebingen, D-72076 Tuebingen, Germany, and Medimod Research Institute, D-72770 Reutlingen, Germany. In human alcohol addicts, loss of control is reflected by an acceptance of adverse circumstances or consequences accompanying alcohol intake and by an inability to choose attractive alternatives instead of alcohol drinking. Once loss of control has been established, it does not disappear spontaneously even after long periods of abstinence (high risk of relapse). Outbred Wistar rats without any innate preference for alcohol can become addicted after one year of voluntary ethanol intake. In a retest after some months of abstinence, these rats reveal a persistently increased voluntary intake of alcohol. They even accept an unpleasant bitter taste of the solutions and take alcohol when a sucrose solution is offered as an alternative. Only voluntary access, but not forced administration leads to addiction. In contrast, the alcohol-preferring CAA line of rats turned out not to be addicted after long-term alcohol experience. Like other non-addicted rats, they ceased alcohol intake in the presence of a sucrose solution. In the development of opiate addiction, the transition to loss of control takes place during a clearcut sensitive period lasting 6-8 weeks after 25-40 weeks of controlled consumption. In the development of alcohol addiction, no such phase can directly be observed. Nevertheless, experiments with varying periods of voluntary and forced alcohol drinking have shown that a (hidden) sensitive period also exists in the development of alcohol addiction. Furthermore, these and other experiments suggest that phases of withdrawal occuring during this period may be crucial for the development of loss of control.

STRESS AND CUE-INDUCED REINSTATEMENT OF ALCOHOL SEEKING BEHAVIOR AS A MODEL FOR RELAPSE. R. Ciccocioppo, M.Massi, X.Liu*, F. Weiss*. Dept. of Pharmacol. Sci. and Exp. Med. University of Camerino, Italy. *Dept. of Neuropharmacology, TSRI, La Jolla , CA. Alcoholism is a chronic relapsing disorder characterized by compulsive drug-seeking and use. Stress and environmental conditioning play a crucial role in the maintenance of drug abuse, and represent the major determinants of relapse in abstinent individuals. Recently, new animal models of cues and stress-induced reinstatement of alcohol-seeking have been developed. Evidence obtained from these animal models showed that cues-induced alcohol-seeking is under the control of the mesocorticolimbic DA and opioid systems and that administration of D1 and D2 receptor antagonists or the opioid antagonist naltrexone prevent the reinstatement. Other evidence, instead, shows that stress-induced alcohol-seeking is under the control of the extrahypotalamic corticotropin-releasing factor (CRF) system and is blocked by administration of CRF antagonists. Moreover, it has been demonstrated the existance of interactions between the response-reinstating effects of stress and cues, and that these effects are enhanced in rats with a history of ethanol dependence. Finally, recent data showed that the activation of the opioid receptor four (OP4), by its endogenous ligand nocicepin/orphanin FQ (NC), which possesses "anti-opioid" and "anti-CRF" properties blocks both cues and stress-induced reinstatement of ethanol-seeking. Altogether these studies demonstrated that stress, environmental conditioning or the combination of both factors are critical for the maintenance of alcohol abuse. The development

of these animal models of drug-seeking could give an important contribution for the study of mechanisms of relapse, and for the development of new medication strategies for the treatment of alcoholism.

PROLONGED ETHANOL PREFERENCE FOLLOWING REPEATED CYCLES OF ETHANOL VAPOUR EXPOSURE. Rimondini, R.; Sommer, W.; Arlinde, C.; Heilig, M. Dept. of Neurotec. Karolinska Institute, S-14186 Stockholm, Sweden. Animal models of alcohol self-administration with a predictive validity are essential for identifying new medication targets. However, difficulties remain in modelling the progression from low to high alcohol consumption in the laboratory rat, since non-selected rats do not readily self-administer alcohol. Exposure to ethanol vapor has been reported to increase ethanol consumption, but this increase is transient, and might partly be to counter acute withdrawal. Persistent neuroadaption may be more likely to result if brain alcohol levels fluctuate. Starting from these observations, we have developed an animal paradigm based on repeated cycles of alcohol vapor exposure, accompanied by periods of mild withdrawal. After 2-weeks of habituation at low ethanol concentrations, rats are intermittently exposed to ethanol vapor for 7 weeks. During 17h "on" phases, blood ethanol levels are kept between 150 and 250 mg/dl, and drop to 0 during 7h "off"-phases. When 3-6 weeks of post-exposure recovery are allowed in order to eliminate effects of acute withdrawal, exposed rats still consume markedly increased amounts of alcohol in a two-bottle free choice paradigm, and in an operant task. Elevated alcohol consumption is observed up to a total of 9 weeks following completion of the vapor exposure procedure. We have studied the time course of the progression from low to high consumption. Our data indicate the existence of a threshold at a time point between 4 and 7 weeks for induction of persistent voluntary alcohol consumption. Initial pharmacological evaluation of the model has been obtained using acamprosate, a molecule used clinically to treat relapse in alcoholics. Acamprosate fully counteracts exposure induced increase in ethanol consumption, without affecting alcohol intake in non-exposed subjects. These findings suggest that our intermittent exposure paradigm is adequate to induce long-term, or even persistent changes in the motivation to consume alcohol, and may serve as a useful tool for identification of novel pharmacological treatment targets.

FUNCTIONAL GENOMICS FOR TARGET GENE IDENTIFICATION IN ANIMAL MODELS WITH GENETICALLY AND ENVIRONMENTALLY INDUCED ETHANOL PREFERENCE. Heilig, M.; Arlinde, C.; Rimondini, R.; Sommer, W. Dept. of Neurotec. Karolinska Institute, S-14186 Stockholm, Sweden. As in humans, both genetic and environmental factors are involved in the development of ethanol preference in model organism. We hypothesize that these two aspects of the disease may converge into common mechanisms leading to the expression of the behavior, and that these mechanisms leave permanent traces in the pool of expressed mRNAs in a cell. These traces, i.e. changes in the expression of a relatively few number of genes, can be extracted out of the total pool of expressed genes by modern microarray technology. Using the Affymetrix Rat Neurobiology U34 GeneChip, expression profiles were examined from key brain areas, in two animal models. Genetically selected AA (alcohol accepting) rats display ethanol preference and behavioral disinhibition, a behavioral constellation similar to that seen in human type II alcoholism, for which considerable genetic loading has been shown. These rats were compared with two alcohol non-preferring rat strains, ANA (alcohol non-accepting) and Wistar. A limited number of genes was differentially expressed in the cingulate cortex of the AA line. To examine molecular substrates of the transition from a non-dependent to a dependent state which results from environmental factors, we developed a novel model, wherein repeated cycles of intoxication and mild withdrawal induce a persistent ethanol consumption comparable to the genetically selected rat lines. This model was pharmacologically validated using acamprosate, a compound clinically effective in human alcoholics. Expression analysis of cingulate cortex and amygdala reveals a set of long-term upregulated transcripts in this model. Despite the limited number of genes analyzed (ca. 1200) we found interesting overlaps in gene expression between the two animal models. This may point to important function of such genes in the regulation of the phenotype, i.e. ethanol preference, and may delineate novel targets for pharmacological treatment of alcoholism.

4:15-6:25 Student Travel Award Winners' Symposium

THE DOPAMINE D2 RECEPTOR ANTAGONIST RACLOPRIDE BLOCKS SOCIAL LEARNING OF FOOD PREFERENCES IN MALE AND FEMALE RATS. Choleris, E.; Forder, J.P.; Kavaliers, M. & Ossenkopp, K.-P. University of Western Ontario, London, Ontario, Canada, N6A 5C2. Through social learning an animal "exploits the expertise of others" thus circumventing the disadvantages of individual learning. The neurobiological bases of social learning of food preferences where an "observer" animal acquires a flavor preference after a brief interaction with a recently fed "demonstrator" are still largely unknown. The dopaminergic system mediates several behavioral reward effects during mating, sociality, feeding and learning, with the dopamine D2 receptor modulating social behavior and learning. We examined the effects of a D2 receptor antagonist, raclopride, in the social learning of food preferences in male and female rats. Raclopride (0.1 mg/kg, ip) was administered to the observer rats (RACLO group) 20 min before a 30 min interaction with a same sex demonstrator that had just eaten either a cocoa or a cinnamon flavored diet. Additional groups of rats either received saline (SAL group) or were left undisturbed (untreated group). When given a choice between the cocoa and cinnamon flavored novel diets the untreated and the SAL, but not the RACLO observers, showed a significant preference for their demonstrator's food. Computerized analysis of the observers' feeding behavior over 24 hours showed that the socially acquired preference was expressed immediately after the social interaction and continued throughout the first major feeding bout at the beginning of the dark phase. Feeding behavior per se as well as the demonstrator-observer's interactions were either unaffected or minimally affected by the drug treatment. These results show an involvement of the dopaminergic system, through the D2 receptor, in the mediation of social learning of food preferences in rats. Supported by NSERC.

EFFECT OF POSTNATAL HANDLING ON EMOTIONAL BEHAVIOR IN ADULT AMYGDALA-KINDLED RATS. Lee, A.W.; Kalynchuk, L. Department of Psychology. Dalhousie University, Halifax, NS B3H 4J1 Canada. Long-term amygdala kindling in adult rats produces high levels of anxiety, and is often used as an animal model for studying the emotionality associated with human temporal lobe epilepsy. Brief handling in early-life decreases anxiety and the behavioral responses to stressors encountered in adulthood. The present study examined whether postnatal handling would reduce the development of emotionality in adult amygdala-kindled rats. Male rats were handled (separated for 15 min daily) for the first 14 days of life or left undisturbed. At adulthood, rats were either left undisturbed in their home cage or received sham stimulations, or 10, 25, or 60 amygdala kindling stimulations and were tested for changes in anxiety (open field and elevated-plus maze) and depression (forced swim). Kindled rats displayed increases in resistance to capture and decreases in activity in the open field and increases in open-arm activity on the elevated-plus maze. The magnitude of these effects increased as the animal received more kindling stimulations. There was no effect of postnatal handling on any of the tests. The results of this experiment show that kindling produces increases in emotional behavior, consistent with previously published findings. However, postnatal handling had no effect on kindling-induced emotionality, suggesting that variations in early environmental experience do not play a role in the development of epilepsy-induced emotionality.

EVIDENCE OF INATTENTIVE AND IMPULSIVE SUBPOPULATIONS IN THE ADOLESCENT SHR STRAIN, AN ANIMAL MODEL OF ADHD. Adriani, W.; Caprioli, A. (*); Laviola, G. Sect. of Behavioural Pathophysiology, Lab FOS, Istituto Superiore di Sanità, Roma, Italy, and (*) Behavioural Pharmacology Lab, Sigma-Tau, Pomezia, Italy. Email: adriani @ iss.it or laviola @ iss.it . Attention-deficit/Hyperactivity Disorder (ADHD) is a neuropsychiatric disorder consisting of peculiarities in the attentional process but also an impulsive behavioral trait. This study investigated the SHR strain (a validated animal model for ADHD). METHODS - Food-deprived SHRs were compared to Wistar-Kyoto controls (WKY). Rats were tested during peri-adolescence (i.e. the ontogenetic period around puberty, post-natal days 30 to 45), in operant chambers provided with two nose-poking holes. Nose-poking in one hole (H1) resulted in the immediate delivery of a small amount of food, whereas nose-poking in the other hole (H5) resulted in the delivery of a larger amount of food after a delay. The delay increased progressively each day (0 to 100 sec). As expected, all animals showed a shift in preference from the large to the immediate reinforcer as far as delay increased. Impulsivity was assessed by the steepness of this preference-delay curve. RESULTS - As a whole, no differences in impulsivity were found between the two strains. However, when looking at individual differences, two separate subgroups were evidenced within the SHR one. A first subgroup showed a steeper preference-delay curve (i.e. a quicker shift towards the immediate reinforcer). Such an elevated intolerance to reward delay is an index of enhanced impulsivity. A second subgroup showed a flat curve (i.e. little or no shift towards the immediate reinforcer), suggesting that animals payed reduced attention to the experimental contingencies. Such a profile was completely absent within the WKY strain. As for frequency of "inadequate" responding, SHRs showed as a whole higher nose-poking during the delays, thus indicating an enhanced restlessness. CONCLUSION - When compared to the WKY strain, two separate subpopulations were evidenced within the SHR one. Adolescent rats of the SHR strain represent a suitable animal model for the study of some of the prominent features of the human-infant ADHD syndrome.

COMPUTATIONAL APPROACH TO IDENTIFICATION OF LABORATORY FACTORS THAT INFLUENCE GENETIC STUDIES OF PAIN BEHAVIOR. [1]Chesler, E.J.; [1]Wilson, S.G.; [1]Lariviere, W.R.; [2]Rodriguez-Zas, S.L.; [3]Mogil, J.S. [1]Department of Psychology, Neuroscience Program, [2]Dept. of Animal Sciences, University of Illinois at Urbana-Champaign, Champaign, IL 61820, USA. [3]Department of Psychology, McGill University, Montreal, QC H3A 1B1, Canada. The interaction between mouse genotype and laboratory environment has a demonstrated influence on the genetic study of behavioral traits. These effects have the capacity to limit the reliability and generalizability of behavioral genetic experiments. Standardization and systematic variation of laboratory conditions have been proposed as solutions to this problem, but until the relevant environmental factors are identified these measures can not be used. A computational approach employing classification and regression trees (CART) followed by linear modeling was applied to a data archive of 8034 observations of basal thermal nociceptive sensitivity to identify and rank the relative influence of laboratory related factors. This analysis revealed that the experimenter performing the test was a more important factor than even mouse genotype in determining baseline pain sensitivity, and that nociception can be affected by many other additional factors including season/humidity, cage density, time of day, sex and order of testing. The results of this approach were validated experimentally, and allowed partitioning of the variance of this complex trait among genetic (27%), environmental (42%), and genetic x environmental (18%) sources. The use of modern 'data-mining' techniques may be profitably applied to large-scale phenotyping efforts to elucidate environmental factors that influence the study of complex traits.

ROLE OF THE DORSAL HIPPOCAMPUS IN THE ACQUISITION AND EXPRESSION OF DISCRIMINATION REVERSAL IN AUDITORY FEAR CONDITIONING. Quinn, J.J.*; Ma, Q.D.; Tinsley, M.R.; Fanselow, M.S. Dept. of Psychology, UCLA, Los Angeles, CA 90095 USA. The hippocampus is necessary for a variety of spatial and non-spatial tasks. Many investigations of hippocampus function have utilized pre-training manipulations such as lesions and genetically altered mice. Such investigations do not allow for distinctions between proposed hippocampus involvement in the acquisition and the expression or consolidation of a memory. Previous investigations using eyeblink conditioning have shown that pre-training lesions of the hippocampus spare initial discrimination of two auditory cues, but impair the subsequent reversal of that discrimination. The present series of experiments addresses the role of the dorsal hippocampus in the acquisition and expression of discrimination and discrimination reversal using Pavlovian fear conditioning. We show that hippocampus lesions given prior to or following acquisition of an initial auditory discrimination do not alter performance. However, these lesions do appear to alter the rate at which the animals learn the reversal of that discrimination. In addition, lesions given following reversal training produce a large deficit in the expression of the reversed discrimination. These data

indicate that the hippocampus may be more critically involved in the expression and/or consolidation, rather than acquisition, of discrimination reversal in fear conditioning.

IMMUNOHISTOCHEMICAL LOCALIZATION OF THE VASOPRESSIN V1a RECEPTOR IN THE MONOGAMOUS PRAIRIE VOLE BRAIN. Lim, M; Sharer, C; Insel, T; Zohar, N; Hoffman, G*; Young, L. Center for Behavioral Neuroscience, Emory University, Atlanta, GA. *Dept of Anatomy and Neurobiology, University of Maryland, Baltimore, MD. The neuropeptide vasopressin (AVP) plays a critical role in pairbond formation in the monogamous prairie vole (Microtus ochrogaster). Past evidence using receptor autoradiography and transgenic approaches suggest that the pattern of vasopressin V1a receptors (V1aR) in the vole brain is important for monogamous-typical behavior in vole species. However, the poor cellular resolution of receptor autoradiography limits subcellular discrimination of V1aR fibers and cell bodies. In the present study, we used immunohistochemistry to investigate the distribution of V1aR at the cellular level in prairie vole brain sections. Rabbit antiserum was generated to the extracellular N-terminus 20 amino acid sequence of the V1aR peptide. Brains were perfused with a 4% paraformaldehyde and 2.5% acrolein fixative. Punctate labeling (suggesting points of synaptic contact) were observed in the lateral septum, bed nucleus of the stria terminalis, and ventral pallidum, which are all regions containing AVP fibers. Cell membrane labeling was seen in the cingulate cortex, hippocampus and central amygdala. Large scattered pyramidal neurons were labeled in the deep layers of the cortex, as well as in CA1 of the hippocampus. This staining is consistent with the general pattern of binding seen with V1aR autoradiography. To our knowledge, this is the first report of immunohistochemical localization of the V1aR in the mammalian brain. This antibody can now be used to further characterize the neural circuitry that regulates pairbond formation in the prairie vole.

PHARMACOLOGY OF FEAR POTENTIATED STARTLE IN MICE. Risbrough, V.B.; Geyer, M.A. Dept. of Neuroscience, University of California, San Diego, La Jolla, CA 92093 USA. Fear potentiated startle (FPS) has been used as a model of anxiety to explore the neurochemistry and neural circuitry involved in fear-related behaviors in rats. The FPS paradigm assesses fear conditioning by pairing a noxious unconditioned stimulus (US) with a neutral conditioned stimulus (CS). The degree of conditioned fear subsequently induced by the CS is reflected by the modulation of the acoustic startle reflex (ASR). With the advent of transgenic technology in the mouse, the roles of specific genes in the expression, acquisition, and pharmacology of fear-related behaviors may be further elucidated. The use of the FPS model in mice, however, has remained relatively rare, and the pharmacology of FPS in mice has yet to be explored. Therefore, after establishing robust and reliable FPS in DBA/J mice, we tested the effects of clinically effective anxiety-modulating compounds on the expression of fear conditioning. Mice trained with a light-CS and footshock-US pairing exhibited significantly greater ASR modulation by the CS than mice trained without explicit CS-US pairing. Additionally, the anxiolytic GABA-A receptor agonists diazepam and chlordiazepoxide were found to significantly reduce the ASR in the presence of the CS at doses that did not disrupt baseline ASR. The clinically effective anxiolytic and serotonin-1A receptor partial agonist buspirone also significantly reduced the modulation of the ASR by the CS. These data support the predictive validity of the FPS model of anxiety in mice.

ESTROGEN ENHANCES DEVELOPMENT OF BEHAVIORAL SENSITIZATION AND DOPAMINE RELEASE. Jackson, L.R.; Becker, J.B. Dept Psychology, Reproductive Sciences Program, Neuroscience Program. University of Michigan, Ann Arbor, MI 48109 USA. There are effects of estrous cycle on the behavioral responses to cocaine in that females in estrus show greater psychostimulant-induced behaviors relative to other days of the cycle. In rodents, psychomotor stimulants produce a progressive and long-lasting increase in the behavioral responsiveness with repeated drug administration, a process referred to as behavioral sensitization. Experiment one examined the ability of 5mg estradiol benzoate (EB) to mediate induction of behavioral sensitization to 5 mg/kg cocaine HCl. Experiment two examined the ability of EB to increase stimulated dopamine release in vitro. Four groups of animals were tested: ovariectomized (OVX) females treated with cocaine (OVXcoc), OVX females treated with saline (OVXsal), OVX females treated with EB and cocaine (OVX+Ecoc), OVX females treated with EB and saline (OVX+Esal). On each test day, groups received 5 mg/kg cocaine or saline i.p. after hormone treatment or control. After twelve intermittent test days, animals underwent drug withdrawal for 10 days, then received a challenge dose of 5 mg/kg cocaine. Stereotyped head and forelimb movements, as well as vertical and horizontal locomotion were quantified and analyzed. After behavioral analysis, animals were sacrificed, the striatum dissected and superfusion was performed. Brain effluent samples were analyzed via HPLC-EC. On the challenge day, OVX+E females had greater stereotyped and locomotor behaviors than every other group. In addition, on the challenge day, stereotyped head and forelimb movements were enhanced in cocaine treated animals relative to saline-treated controls, which received cocaine on this day for the first time. Further, DA release was enhanced in OVX+Ecoc animals compared to OVX+Esal or OVXcoc animals. Estrogen treatment of ovariectomized females results in a significant enhancement of the effect of 5 mg/kg cocaine on stereotyped behaviors relative to oil treated females. Estrogen treatment of animals sensitized to 5 mg/kg cocaine results in greater stimulated DA release compared to oil treated sensitized animals or estrogen-treated non-sensitized animals.

EFFECTS OF A CHRONIC TREATMENT WITH IMIPRAMINE IN PRENATALLY STRESSED RATS. Morley-Fletcher S., Darnaudery M., *Mocaer E., Maccari S. Lab. Neurosciences du Comportement, Villeneuve d'Ascq, * IRIS, France. Early ontogeny is a markedly plastic and crucial stage, and alterations of prenatal milieu may have a great influence in modulating developmental trajectories that in turn will influence subsequent behavioral responses. In this view, the experience of stressful experience in early life can exert profound and long-lasting perturbations of an organism's physiological homeostasis which can lead to the development of psychological disturbances, in particular depression. Interestingly, many of the abnormalities found in prenatally restrain stressed (PNRS) rats, such as increased anxiety, emotionality and disturbances in a variety of circadian rhythms (locomotor activity,

corticosterone secretion, and changes in sleep wake parameters) parallel those found in human depression. Taken together, these data suggest that PNRS rat may be a useful animal model of depression, making it an attractive model for the design and testing of new therapeutic strategies in mood disorders. In this view, a study was conducted in order to investigate the effects of a chronic treatment with a classic tricyclic antidepressant as imipramine (IMI, 10 mg/kg i.p. for 21 days) in PNRS and Non-stressed (NS) rats. When assessed in the social interaction test, PNRS rats spent longer time in aggressive investigation of the partner than NS animals, whereas such profile was reduced following IMI-treatment. In the elevated plus maze test, PNRS rats spent less time in the open arm than NS rats, and IMI-treated PNRS animals presented a slight reduction of such profile of anxiety. In the forced swim test, a behavioural test classically used to test antidepressant efficacy, chronic IMI-treatment reversed in PNRS rats the increment in immobility normally observed in the VEH-PS group with respect to NS animals. Overall, these results indicate PNRS animals as more sensitive to the effects of antidepressant treatment, and reinforce the idea of the usefulness of PNRS rats as an appropriate animal model to study human depression.

EARLY DEPRIVATION LEADS TO REDUCED MOTIVATION AND INCREASED BEHAVIOURAL DESPAIR IN THE ADULT RAT. Rüedi-Bettschen, D., Feldon, J., Pryce, C.R. Behavioural Neurobiology Laboratory. Swiss Federal Institute of Technology Zürich, CH-8603 Schwerzenbach, Switzerland. Objective: In humans it is known that early stressful life events enhance the probability to develop a depressive episode in adulthood. Some core symptoms of depression are reduced motivation for pleasurable events (anhedonia) and behavioural despair. In this study we investigated the effects of daily 4-hr deprivation of maternal care and littermates in rat pups on motivation for sucrose and behavioural despair in adulthood. Methods: Rat pups were isolated daily for 4 hours on postnatal days 1-14 (early deprivation, ED). Control animals were left undisturbed during that time (non-handling, NH). ED was performed during the light (inactive) phase or dark (active) phase. At age 5 months subjects were tested in a progressive ratio schedule of reinforcement for 7% sucrose solution following minimal (2 hr) water deprivation. At age 6 months subjects were tested in the Porsolt forced swim test. Results: When tested on a progressive ratio schedule ED demonstrated reduced lever pressing for sucrose reward compared to NH. In the Porsolt forced swim test ED showed decreased distance swam (which corresponds to more floating time) compared to their NH counterparts. Both effects were obtained in the ED-dark subjects only. Conclusion: This study suggests that experience of ED during the active circadian phase leads to a trait of reduced motivation for sucrose reward and increased behavioural despair in adult rats. These behaviours in the rat simulate core symptoms of depression disorder, suggesting that early deprivation provides an animal model for anhedonia and behavioural despair.

THE ABILITY OF LAMOTRIGINE TO REVERSE KETAMINE BUT NOT AMPHETAMINE-INDUCED PPI DEFICITS IN MICE. [1]Henry, S.A.; [1]Geyer, M.A.; [2]Large, C.H. [1]Dept. of Psychiatry and Neurosciences. University of California - San Diego, La Jolla, CA 92093-0804 USA. [2]Neuropharmacology, GlaxoSmithKline, 37135 Verona, Italy. Lamotrigine, a sodium channel blocker which has been used as an effective anticonvulsant, appears effective in the treatment of patients with bipolar disorder, perhaps by virtue of its ability to reduce glutamate release. Furthermore, it has recently been found that lamotrigine decreases the perceptual abnormalities produced by the NMDA antagonist ketamine in humans, similar to the effects of the atypical antipsychotic clozapine. Acutely manic bipolar patients, like patients with schizophrenia, Tourette's, and obsessive compulsive disorder, show decreases in sensorimotor gating, as measured by prepulse inhibition of the startle response (PPI). Here, we assessed the ability of lamotrigine to reduce the PPI-disruptive effects of ketamine and the dopaminergic agent amphetamine in two inbred mouse strains, C57Bl/6J and 129SvPasIco. In the 129SvPasIco mice, lamotrigine reversed the ketamine-induced PPI deficit, without altering PPI in control mice. In C57Bl/6J mice, however, 27mg/kg lamotrigine generally increased PPI in both control and ketamine-treated mice. Lamotrigine did not ameliorate the amphetamine-induced PPI deficit in either strain. Hence, PPI may prove to be a useful measure of the apparent interaction between lamotrigine and glutamatergic compounds, with implications for possible treatments in bipolar disorder and schizophrenia.

WITHDRAWAL FROM REPEATED AMPHETAMINE ADMINISTRATION, A MODEL OF SCHIZOPHRENIA? Russig, H.; Murphy C.A.; Feldon, J. Laboratory of Behavioral Neurobiology, Swiss Federal Institute of Technology, ETH Zurich, Schorenstrasse 16, CH-8603 Schwerzenbach, Switzerland. Latent inhibition (LI) is a behavioral phenomenon whereby repeated exposure to a non-reinforced stimulus retards subsequent conditioning to that stimulus. Deficits in LI reflect an inability to ignore irrelevant stimuli and are studied as a model of the cognitive/attentional abnormalities found in schizophrenia. We recently determined that pretreatment with escalating doses of the indirect dopamine agonist, amphetamine (AMPH; 1-5 mg/kg, i.p., over 6 days) disrupts LI in rats tested in a two-way active avoidance paradigm during at least the first 2 weeks of withdrawal. We have also now evaluated the effects of the atypical neuroleptic clozapine and the typical neuroleptic haloperidol on the expression of LI on day 4 of AMPH withdrawal. Neuroleptic injections were given either 45 min prior to each of two tone preexposure sessions and prior to a subsequent tone-shock avoidance test session or only prior to the test session. As expected, saline-injected control groups showed LI during the test session, as reflected by significantly reduced avoidance in tone preexposed vs. non-preexposed rats. In contrast, animals pretreated with escalating doses of AMPH did not show LI, due to the improved avoidance of the preexposed animals. Clozapine (5 mg/kg) and to a lesser degree haloperidol (0.03 mg/kg) largely reversed the disruptive influence of AMPH on LI regardless of whether these drugs were administered prior to both preexposure and test sessions or only prior to the test session. These results provide pharmacological validation for AMPH withdrawal as a model of schizophrenic symptoms. Future studies will investigate whether AMPH withdrawal produces behavioral deficits associated with other schizophrenic symptoms as well.

FOS EXPRESSION IN THE FOREBRAIN AFTER MATING IS ALTERED BY ADRENALECTOMY. Cameron, N.; Erskine, M.S. Department of Biology, Boston University, Boston, MA 02215. In a previous experiment we showed that mating-induced prolactin release is affected by adrenalectomy. We hypothesized that mating activates forebrain areas containing corticotropin-releasing hormone and/or ß-endorphin, peptides that are altered by adrenalectomy. In this experiment, we looked at mating-induced FOS responses in adrenalectomized (adx) or sham-operated female rats. Adx (n=21) or sham (n=21) rats were treated sc with estrogen (10 ug) and progesterone (500 ug) 2 weeks later. They received 15 intromissions (15I), 5 intromissions (5I) or 15 mounts-without-intromission (MO) from males or no treatment (home cage, HC). Two hours after mating rats were perfused with paraformaldehyde and their brains were collected and processed for immunocytochemical labeling for FOS. FOS-positive cells in the ventromedial hypothalamus (VMH), medial preoptic area (mPOA), bed nucleus of the stria terminalis (BNST) and medial amygdala (mAMYG) were counted bilaterally. There was a significant effect of mating on cellular activation in all areas, with both 5I and 15I groups showing a similar increase in FOS over the MO or HC levels. Adx affected the FOS expression only in the VMH and mPOA; although 15I animals showed an increased response over MO or HC, the response was significantly suppressed compared to the 5I animals. These results suggest that in Adx rats a large number of intromissions may suppress FOS activation in the VMH and mPOA, perhaps due to an increase in ß-endorphin release in the VMH, mPOA or other areas. Supported by MH64187 and MH01435 to M.S.E.

6:30-8:30 Poster Session II: Behavioral Toxicology, Neuroimmunology, Addiction, Learning And Memory, Stress And Anxiety, Kindling, Behavioral Genetics

69. CYTOLOGICAL AND ULTRASTRUCTURAL CHANGES OF OLFACTORY MUCOSA AND BULB INDUCED BY OZONE EXPOSURE. Colín-Barenque L., Avila-Costa M.R., Fortoul T., Rugerio-Vargas C., Borgonio-Pérez G., Pasos F. and Rivas-Arancibia S. Depto. de Neurociencias FES Iztacala, Depto. de Biología Celular y Depto. de Fisiología, Facultad de Medicina, UNAM. México, D.F: México. Ozone toxicity is related to the production of free radicals. Olfactory dysfunction has been reported in patients with neurodegenerative diseases in which oxidative stress has been detected. The objective of this study was to analyze the changes in olfactory epithelium and bulb caused by oxidative stress produced by ozone exposure. Male Wistar rats were exposed to ozone (1 ppm) for 4 hours. Control animals were exposed to flowing air. The experimental groups were sacrificed at 2h, 24h, 5, 10 and 15 days after the ozone exposure had finished. All animals were perfused and processed for Golgi technique and ultrastructural analysis. The olfactory mucosa showed cytotoxic changes such as: Bowman's glands vacuolation, partial cilia loss, pycnotic changes in the basal stratum of the olfactory epithelium and a decrease in the thickness at 24 h and an increase at 5 days. The number of spines of the granule cells in the olfactory bulbs decreased at 2 h, 24 h, 5 days and 10 days, but at 15 days after the exposure had finished the number of spines increased to values similar to those found in controls. The ultrastructural findings, were that granule cells exhibited cytoplasmic vacuolation, lipofucsin granules, swollen mitochondria and endothelial changes. In animals sacrificed after 2 h and 5 days, vacuolation and mitochondrial changes were prominent; while endothelial damage and lipofucsin granules were found mostly at 5 days. Supported by DGAPA IN213501 to S R-A.

70. TAURINE EFFECTS ON PROGRESSIVE ASTROCYTE DAMAGE IN HIPPOCAMPUS CAUSED BY OXIDATIVE STRESS. Pereyra-Muñoz, N., Acosta-Vázquez F., Rodríguez-Martínez E, Rugerio-Vargas C., Borgonio-Pérez G. and Rivas-Arancibia S. Depto. de Fisiología, Facultad de Medicina, UNAM. México, D.F. Astrocytes participate in synapse formation and transmission efficacy, through metabolic and morphological changes. Oxidative stress produces progressive damage to the hippocampus and memory deterioration. The objective of this study was to analyze the effect of taurine on astrocyte changes in hippocampus caused by oxidative stress produced by long term ozone exposure. Forty two male Wistar rats were exposed to O3 (0.25 ppm) for 4 h daily, except the control group. Seven experimental groups (n=6) received one of the following treatments each: 1) control group, 2) 8 days O3 exposure, 3) 8 days O3 exposure + 43 mg/kg ip taurine, 4) 15 days O3 exposure, 5) 15 days O3 exposure +43 mg/kg ip taurine, 6) 30 days O3 exposure, 7) 30 days O3 exposure +43 mg/kg ip taurine. After ozone exposure had finished, animals were processed for glial fibrillary acidic protein (GFAP) immunohistochemistry. Results indicate: 8 days of O3 exposure show a 50% decrease in size and an increase in processes thick; at 15 days these changes ameliorate, however at 30 days astrocyte number and processes width increase, and processes length decreases. Taurine administration partially recovers astrocytic alterations in the 8 days group, and in the 15 days group astrocytes are alike to the controls. In the 30 days group, taurine diminishes astrocyte damage, and astrocyte number and processes are similar to those in the control group. In conclusion, ozone exposure produces progressive astrocytic alteration and these changes can be reverted by taurine. Supported by DGAPA IN213501 to S R-A.

71. ANTIOXIDANT EFFECT OF TAURINE ON OXIDATIVE DAMAGE IN HIPPOCAMPUS CAUSED BY 3-NP ADMINISTRATION IN RATS. Rodríguez-Martínez E., Acosta-Vázquez F., Juárez-Meavepeña M., Borgonio-Pérez G., Pereyra-Muñoz N., and Rivas-Arancibia S. Depto. de Fisiología, Facultad de Medicina, UNAM. México, D.F. Reactive oxygen species (ROS) are increased by 3-nitropropionic acid (3-NP) administration. It produces a decrease in ATP synthesis and activation of NMDA receptors, which lead to cell death by excitotoxicity. Taurine is an antioxidant that protects against neuronal damage caused by ROS. In this study we evaluated the antioxidant effect of taurine on lipid peroxidation levels caused by 3-NP administration in hippocampus. Immunohistochemistry for glial fibrillary acidic protein (GFAP), enolase and S-100 was also carried out. Eighteen male Wistar rats (400g), were separated into 3 groups and received one of the following ip treatments: (1) Control, (2) 20 mg/kg 3-NP, (3) 20 mg/kg 3-NP + 43 mg/kg taurine. After four hours the animals were sacrificed, and lipid peroxidation levels were quantified. Our results showed that 3-NP increased lipid peroxidation levels, while taurine clearly decreased them in hippocampus. GFAP immunohistochemistry showed a 30% decrease in astrocyte size in the group treated with 3-NP

when compared to the control group and a significant recovery when treated with taurine. Enolase immunoreactivity decreased and S-100 immunoreactivity increased with 3-NP. However, when animals were treated with taurine 10 min after 3-NP administration these alterations were reverted. In conclusion, taurine ameliorates neuronal damage and protects astrocytes from oxidative stress caused by ozone. Supported by DGAPA IN213501 to S R-A.

72. OXIDATIVE CHANGES IN HIPPOCAMPUS CAUSED BY OZONE EXPOSURE MODIFY SHORT-TERM MEMORY IN RATS. González-Rivas S.; Sánchez-Vega R., Acosta-Vázquez F. Rugerio-Vargas C., Quintana-Rojas Y., Borgonio-Perez G. and Rivas-Arancibia S. Dept. of Physiology, Faculty of Medicine, UNAM, México D.F. Some research indicates that oxidative signals might be involved in the modulations of plasticity phenomena. In previous reports we found that, an increase in oxidative stress caused by ozone (O3) exposure, (0.7t o 1.0 ppm), produces behavior, biochemical and morphologic alterations,. The objective of this work, was to study the effects of changes in oxidative signals produced by different O3 doses on brain plasticity, To carry out this study, 50 male Wistar rats were individually housed, with free access to water and food. Animals were randomly assigned to each of the following groups (n= 10): (1) control, air exposed. (2) 0.2 ppm O3, (3) 0.4 ppm O3, (4) 0.8 ppm O3, (5) 1.6 ppm O3. Animals were exposed for 4 h to ozone. One hour after the O3 exposure session had finished, all groups were trained in a one-trial passive avoidance conditioning and short-term memory was registered. Afterwards 5 rats of each group were deeply anesthetized and processed for GFAP, synaptophysin, enolase and S-100 immunohistochemistry. Results indicate:short-term memory improvement at 0.2 ppm and impairment with the increasing ozone doses. Results also show changes in GFAP inmunoreactivity. 0.2 ppm of ozone show some alteration with a more than 50% increase in astrocytic size which decreases with progressive ozone doses. Synaptophysin an enolase inmunoreactivity show changes depending on O3 dose. In conclusion, low O3 doses could be facilitating brain plasticity for a short time period, while higher O3 doses cause deterioration of these processes. Supported by DGAPA IN213501 to S R-A.

73. BEHAVIORAL AND GLIAL CHANGES IN STRIATUM, INDUCED BY 3-NITROPROPIONIC ACID TREATMENT IN RAT Juárez-Meavepeña M.; Acosta-Vázquez F.; Pineda-Solis K.; and Rivas-Arancibia S. Depto. de Fisiología, Facultad de Medicina, UNAM. México D.F., México. 3-nitropropionic acid (3-NP) is an irreversible inhibitor of succinate dehydrogenase that inhibits complex II activity of the electron transport chain and is used as a model of Huntington's disease. 3-NP is associated with increased production of reactive oxygen species (ROS), which lead to oxidative stress and cell damage. The objective of this study was to correlate the damage induced by different doses of 3-NP, with glial and behavioral changes, as well as learning and memory alterations. Seventy five male Wistar rats were randomly assigned to 5 groups (n=15) and received one of the following treatments (1) saline, (2) 5 mg/kg 3-NP, (3) 10 mg/kg 3-NP, (4) 15 mg/kg 3-NP, and (5) 20 mg/kg 3-NP. After four hours of 3-NP (pH 7.4) administration, motor activity and behavior were registered in 12 rats of each group, later the rats were trained with passive avoidance conditioning and short and long term memory were measured. In 3 other animals of each group, brains were processed for glial fibrillary acidic protein (GFAP) immunohistochemistry. Results indicate that 3-NP administration produces astrocytic alterations which are dose dependent. Astrocytes present loss of normal morphology such as changes in the size, processes and number. On the other hand, alterations in short and long term-memory were found with 5 mg/kg of 3-NP and motor behavior alterations began at 10 mg/kg of this toxin. The results obtained indicate that: 1) astrocytic alterations are dose dependent and 2) learning and memory processes are more vulnerable to degenerative damage than motor behavior. Supported by DGAPA IN213501 to S R-A.

74. EFFECTS OF TAURINE ON OXIDATIVE STRESS CAUSED BY FRONTAL CORTEX LESION. Berlanga Taylor A.; Acosta-Vázquez F.; Rugerio-Vargas C.; Fernández-Barocio F.; Durán-Vázquez A.; Borgonio-Pérez G. and Rivas-Arancibia S. Depto. de Fisiología, Facultad de Medicina, UNAM. México D.F., México. Oxidative stress plays an important role in cell deterioration. It can be caused by frontal cortex lesions. When provoked by head trauma it generates free radicals such as reactive oxygen and nitrogen species (ROS and RNS) in damaged cells. Taurine acts as an antioxidant with neuroprotective properties. The objective of our work was to determine if taurine, administered for 5 days, could ameliorate damage caused by frontal cortex lesions. Nineteen male Wistar rats between 230 g. and 290 g. were randomly assigned to 3 groups and received one of the following treatments: (1) control, (2) lesion and (3) lesion + taurine treatment (a daily 43 mg/kg dose was administered i.p. for 5 days). On day 4 after the lesion was provoked all groups were trained with passive avoidance conditioning. Short and long term memory was measured. Motor activity and behavior were registered and lipid peroxidation levels were determined. Brains were then processed immunohistochemically for glial fibrillary acidic protein (GFAP). Results indicated the neuroprotective effects of taurine. Statistical analysis demonstrated significant differences between groups in behavior (freezing and shaking), short and long term memory and motor activity tests. Rats treated with taurine showed improved short and long term memory and diminished motor activity. Immunohistochemical analysis showed morphological changes in astrocytes with ameliorated damage to taurine treated rats. In conclusion, taurine administration after the lesion favors recovery and decreases damage. Supported by DGAPA IN213501 to S R-A.

75. GROOMING BEHAVIOR ALTERATIONS IN RATS CAUSED BY PROLONGED OZONE EXPOSURE. Dorado-Martínez C., Borgonio-Pérez G. and Rivas-Arancibia S. Depto. de Fisiología, Facultad de Medicina, UNAM. México D.F., México. Ozone exposure causes an increase in reactive oxygen species (ROS) that alter brain cell plasticity. ROS oxidate dopamine and increase its release. Grooming behavior sequence depends on mesostriatal dopaminergic pathways maturation and integrity. The purpose of this work was to study grooming behavior alterations produced by oxidative stress, caused by prolonged exposure to low levels of ozone. With this aim we used 20 male Wistar rats; one group used as control (n=10), and the other (n=10) exposed to 0.25 ppm ozone for 28 days for 4 hours and animals were evaluated at 2, 4, 7, 14 21 and 28 days. Each rat was observed for 10 minutes and the time it spent grooming as well as the grooming sequence were registered. The grooming sequence was taken as

follows: for head grooming "A", for chest and abdomen grooming "B", for back grooming "C", and for loins and croup grooming. "D" We analyzed if grooming sequence was A, B, C, D, and if the sequence was completed. Results show that, there was no difference in the frequency of the behavior but there were important sequence alterations. After 4 days of O3 exposure the sequence was more often begun but not completed and from the 14th day of exposure the rats began sometimes from D or C instead of A as the controls always did. These results indicate that ROS induced by ozone exposure, cause grooming behavior changes that could be related with dopaminergic pathway and neurotransmitter release alterations. Supported by DGAPA IN213501 to S R-A.

76. A PROGRESSIVE DAMAGE IN HIPPOCAMPUS CAUSED BY CHRONIC OZONE EXPOSURE IN RATS. Valencia-Reyes R., Rugerio-Vargas C., Rodríguez-Mata V., Dorado-Martínez C., Borgonio-Pérez G. and Rivas-Arancibia, S.; Depto. de Fisiología, Facultad de Medicina, UNAM. México, D.F., México. Oxidative stress has proved to be involved in many neurodegenerative diseases. Chronic ozone exposure at low doses is a non invasive model of oxidative stress. When ozone is inhaled it can form Reactive Oxygen Species (ROS) in the lung. This molecules reach the brain via the systemic circulation. ROS cause damage in the nervous system depending on the dose, time of exposure and the sensitivity of the brain structure. The objective of this study was to determine the effect of ROS in hippocampus of rats exposed to ozone . Materials and methods: 66 male Wistar rats were individually housed with free access to food and water. Rats were randomly assigned to 3 groups (n=22): 1) Control; 2) 15 days ozone exposure and 3) 30 days ozone exposure. Ozone was administered at 0.25 ppm for 4 hours daily . After ozone exposure had finished, each group was separated as following: 6 rats were used to quantify lipid peroxidation levels (lipoprotein-lipase and ascorbic acid oxidase technique); 3 rats for the Klüver Barrera histological technique ; 3 rats for a modified histological technique with Prussian blue and eosin; and 10 rats were used to measure short and long term memory. Results show: a) a significant increase in lipid peroxidation levels, b) morphological changes in the hippocampus (particularly in cells located in the CA1 region and dentate gyrus) and c) significant deterioration of short and long term memory. We conclude that ROS are able to cause direct and progressive damage to the hippocampus depending on the dose used and the duration of the exposure. Supported by DGAPA IN213501 to S R-A.

77. THE ROLE OF PRO-INFLAMMATORY CYTOKINES IN THE ETIOLOGY OF AUTOIMMUNITY-INDUCED NEURODEGENERATION AND BEHAVIORAL DYSFUNCTION. David A. Ballok and Boris Sakic, Dept. of Psychiatry and Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada L8N 3Z5. Anxiety, depression and psychosis of unknown etiology are common manifestations of the systemic autoimmune/inflammatory disease lupus erythematosus. Increased levels of pro-inflammatory cytokines were reported in the cerebrospinal fluid (CSF) of patients suffering from psychiatric manifestations. Similarly, increased expression of mRNA for IL-6 and IFN-gamma were detected in brains of behaviorally impaired lupus-prone MRL-lpr mice. We have recently observed that the CSF from aged (but not young) MRL-lpr mice is neurotoxic to brain stem cells and neuronal cultures. Taken together, the above evidence has led to the hypothesis that systemic and/or intrathecal production of pro-inflammatory cytokines play a role in neurodegeneration and behavioral dysfunction during systemic inflammatory disease. The present study examines whether circulating levels of pro-inflammatory cytokines are associated with behavioral deficits in MRL-lpr mice and whether pre-absorption of CSF with monoclonal antibodies to IL-1beta, TNF-alpha, IL-6 and IFN-gamma prevents toxicity of brain stem cells *in vitro*. Animals are presently examined in an established battery of behavioral tests and serum/CSF samples will be collected at 15 weeks of age, i.e. when CSF reliably shows the neurotoxic property. Results are pending and will be reported at the meeting.

78. EFFECTS OF INTERLEUKIN-2 ON MALE SEXUAL BEHAVIOR IN MICE. Genedani, S.; Saltini, S.; Filaferro, M.;Ottani, A.; Benelli, A. Dept. of Biomedical Sciences, Section of Pharmacology, University of Modena and Reggio Emilia, Italy. It has been previously reported that the cytokines interleukin-1 (IL-1) and tumor necrosis factor a (TNFalfa) induce behavioral effects different from those induced by interleukin-2 (IL-2), at least in part. As far as sexual behavior is concerned, it as been shown that IL-1 and TNFalfa inhibit female sexual behavior, while having no effect on male copulatory activity. The purpose of our present research was to study the influence of IL-2 on male sexual behavior, in order to possibly obtain other data of differentiation between the behavioural picture induced by IL-2 and that induced by IL-1 and TNFalfa. We used both sexually responsive and sexually sluggish mice, in order to detect either an inhibitory or a stimulatory effect on male sexual behavior. We found that IL-2, while having no influence on both sexual motivation and performance in sexually sluggish mice, significantly increased ejaculation latency (588.33±61.00 vs. 211.66±48; $p<0.004$) and the number of mounts with intromission (11.66±1.17 vs. 4.00±0.60; $p<0.005$) (=increased sexual potency) in sexually responsive mice, at the intraperitoneal dose of 200 ng/animal. Our present data confirm the notion that cytokines can act as neuroregulatory agents and influence behavior, and support previous observations indicating that in male sick animals there is no impairment of sexual activity; yet, according to our present data, the mating success is enhanced.

79. HYPOACTIVITY AND BEHAVIORAL TOLERANCE TO LIPOPOLYSACCHARIDE ARE DIFFERENTIALLY EXPRESSED ACROSS THE LIGHT AND DARK PERIODS IN MALE AND FEMALE RATS. Franklin, A.E.; Engeland, C.G.; Kavaliers, M.; Ossenkopp, K.-P. Neuroscience Program, University of Western Ontario, London, Ontario, Canada N6A 5C2. Behavioral responses to bacterial infection typically include anorexia, hypodipsia and hypoactivity; a set of symptoms collectively termed sickness behaviors. Sickness behaviors and the development of tolerance have not yet been examined across the light-dark cycle. We examined the hypoactivity response of male and female rats following systemic injection with lipopolysaccharide (LPS) during either the light or dark phase of the light-dark cycle. Both male and female Long-Evans rats housed on the same light-dark cycle (12:12hr) were injected with either LPS (200μg/kg) or saline on Day 1 and Day 4 during either the light or dark period. Two hours following injection the locomotor activity of each animal was assessed

using a non-novel automated open-field (Digiscan Animal Activity Monitor). LPS treatment on Day 1 during the light period induced robust activity decrements in both male and female rats. A significant sex difference was also apparent during the light period such that males showed greater activity reductions compared to females at this time. During the dark period, LPS treatment on Day 1 caused some activity decrements however, such reductions were not as large as in animals injected during the light period. No sex difference in activity reductions was apparent during the dark period. After a second treatment with LPS on Day 4, all animals showed behavioral tolerance as evidenced by attenuated hypoactivity compared to Day 1. However, animals injected during the dark period exhibited a greater degree of behavioral tolerance to LPS than animals tested during the light period. These results indicate that hypoactivity and behavioral tolerance to LPS are modulated by the light-dark cycle.

80. SIMILARITIES IN THE BEHAVIORAL RESPONSES OF PREWEANING GUINEA PIGS TO CRF, LPS, AND ISOLATION: DO STRESS-INDUCED SICKNESS BEHAVIORS CONTRIBUTE TO THE RESPONSE TO MATERNAL SEPARATION? Hennessy,M.B.;Deak*,T.;Schiml-Webb,P.A.;Schwartz,K.; Stewart,H.;Wilson,S.E. Dept. of Psychology, Wright State University, Dayton, OH 45435 USA and *Dept. of Psychology, SUNY-Binghamton, Binghamton, NY, 13902 USA. "Sickness behaviors" refer to a class of passive behaviors characteristic of illness, which presumably act to conserve heat and energy. Recently, it was demonstrated that both physical and psychogenic stressors can sometimes elicit this same class of behaviors. We suggest that stress-induced sickness behaviors may be elicited by maternal separation. Early studies demonstrated that during prolonged separation from the maternal attachment object, humans and some other primates showed an initial active behavioral stage known as "protest", followed by a passive behavioral stage referred to as "despair". "Despair" is marked by lethargy and such behaviors as crouching and self-clasping, and has long been considered an animal model for human depression. We have found that the preweaning guinea pig, which also exhibits evidence of attachment to its mother, responds to separation with an initial active stage characterized by vocalizing and locomotor activity, followed by a passive stage marked by crouching, eye-closing, and piloerection. Similar passive responses are induced by both the stress-related neuropeptide, CRF, and by the endotoxin, LPS, and are reversed with a CRF receptor antagonist. These findings suggest that some portion of the "despair" stage may represent sickness behaviors induced by the stress of the maternal separation procedure. This hypothesis can accomodate findings in widely divergent species, does not require assumptions regarding the ability to express complex emotional states, and aligns the separation model with recent notions regarding the nature and ontogeny of depressive illness.

81. THE EFFECTS OF CHRONIC LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION ON LOCOMOTOR ACTIVITY AND WATER MAZE PERFORMANCE IN RATS. Saber, A.J.; Engeland, C.G.; Ossenkopp, K.-P.; Kavaliers, M.; Cain, D.P.; Neuroscience Program. University of Western Ontario. London, Ontario, Canada, N6A 5C2. Brains of patients with Alzheimer dementia (AD) show inflammation co-occurring with characteristic plaques and tangles. In the laboratory, neuroinflammation can be induced by intracerebroventricular infusions of lipopolysaccharide (LPS), a component of gram negative cell walls. Previous histological studies have shown that chronic LPS infusions into the 4th or lateral ventricle of rats causes an increase in the number of activated microglia and astrocytes throughout the brain with associated cell death. Previous research also has shown that rats are impaired on the Morris water maze task (MWM), an assessment of spatial learning and memory. In the current study, rats were implanted with osmotic minipumps, delivering LPS (1.0 µg/µl) or cerebrospinal fluid into the lateral ventricle for 37 days (0.25 µl/h). After this time, locomotor activity and behavior were assessed in an automated open-field, and motor co-ordination evaluated on a beam walking task. Half of the rats were then tested in the MWM where search time, time spent in the periphery, and direct swims were quantified. The remaining rats were given strategies pretraining prior to spatial testing to separate the two components of the task. If LPS-treated animals acquire the strategies but are spatially impaired this will imply that LPS-induced neuroinflammation contributes specifically to a spatial learning impairment. If impairments are not detected in pretrained rats, then the behavioral deficits reported in previous studies are likely due to an inability to learn the strategies necessary for successful completion of the MWM. The results from this study will provide a more detailed behavioral analysis of MWM performance in rats given chronic LPS infusions than has been reported to date. The utility of using neuroinflammation as a model of AD will also be addressed.

82. FUNCTIONAL INTERACTIONS BETWEEN GROUP III METABOTROPIC GLUTAMATE RECEPTORS AND DOPAMINE RECEPTORS IN THE RAT NUCLEUS ACCUMBENS. David, H.N.; Abraini, J.H. UMR CNRS 6551, Centre CYCERON, BP 5229, Université de Caen, Bd H. Becquerel, 14074 Caen Cedex, France. Functional interactions between metabotropic glutamate (mGlu) receptors and dopamine (DA) neurotransmission is now clearly established. In the present study, we investigated interactions between group III mGlu receptors and D1-like and D2-like receptors in the nucleus accumbens (NAcc). Administration in the NAcc of the selective group III mGlu receptor agonist AP4 resulted in an increase in locomotor activity, which was blocked by pretreatment with the group III mGlu receptor antagonist MPPG. In addition, pretreatment with AP4 further blocked the increase in locomotor activity induced by the D1-like receptor agonist SKF 38393, but potentiated the locomotor responses induced by either D2-like receptor agonist quinpirole or co-infusion of SKF 38393 + quinpirole. MPPG reversed the effects of AP4 on the motor responses induced by D1-like and/or D2-like receptor activation. These results confirm that glutamate transmission may control DA-dependent locomotor function through mGlu receptors and further indicate that group III mGlu receptors oppose the behavioural response produced by D1-like receptor activation and favor those produced by D2-like receptor activation.

83. BLOCKADE OF THE NMDA RECEPTORS BY THE LAUGHING GAS NITROUS OXIDE AND XENON PREVENT AMPHETAMINE SENSITIZATION. David, H.N.; Abraini, J.H. UMR CNRS 6551, CYCERON, Université de Caen, BP 5229, Bd Henri Becquerel, 14074 Caen cedex France. N-methyl-D-aspartate (NMDA) antagonists are well known to prevent the development of the sensitization of the psychoactive drug amphetamine

when co-injected with it. However, Blockade of NMDA receptors leads to serious side effects. Nitrous oxide and xenon have been reported in vitro to inhibit NMDA receptors, without neurotoxic effect when used at normobaric pressure. Therefore, the aim of the present study was to investigate the potential neuroprotective effect of nitrous oxide and xenon on the development of sensitization by amphetamine in rats. From day 1 to day 3, rats were pretreated with either saline (1 ml/kg, ip) or amphetamine (1 mg/ml/kg, ip) and then immediately exposed to either air, nitrous oxide (50 % and 75 %) or xenon (50 % and 75 %). Thereafter, locomotor activity was assessed after an injection of saline (1 ml/kg) on day 6 and amphetamine (1 mg/ml/kg) on day 7. Nitrous oxide at 50 % (with 50 % oxygen) and 75 % (with 25 % oxygen) respectively decreased and totally prevented the development of sensitization by amphetamine. 50 % xenon (with 50 % oxygen) totally prevented the development of sensitization by amphetamine; surprisingly 75 % xenon (with 25 % oxygen) only diminished sensitization by amphetamine.

84. BEHAVIOURAL AND PHARMACOKINETIC PROFILE FOLLOWING MDMA ("ECSTASY") ADMINISTRATION IN ADOLESCENT RATS: INFLUENCE OF PRENATAL STRESS. [1]S. Morley-Fletcher, [1]M. Puopolo, [2]S. Macri, S. [2]Gentili, [2]T. Macchia, [2]G. Laviola. [1]Labor. F.O.S., [2] Labor. Clinical Biochemistry, Istituto Superiore di Sanità, Viale Regina Elena 299 - 00161 Rome, Italy. Ecstasy (3,4-methylenedioxymethamphetamine, MDMA) is a recreational drug of increasing use among youth because of its stimulant and empathogenic properties, such as euphoria and friendliness. Likewise, affective and psychotic disturbances are being increasingly recognised in association with MDMA abuse, together with the potential to affect psychomotor skills. In the present study, the issue of a possible influence of prenatal stress (PS group) on vulnerability to MDMA effects was addressed in female adolescent rats (pnd 30). 1st EXP: Following oral administration of MDMA, a time-course analysis (3 hours) of animals performance in a simple motor coordination task, pain sensitivity and analgesia levels in a hot-plate test, as well as measurement of MDMA levels in the blood was carried out. A time-dependent increment of locomotor activity as well as analgesia profile was observed following drug exposure. Such profile was also positively correlated with drug levels in the blood. Significantly higher values of circulating MDMA, as well as episodes of drug-induced altered motor coordination were evidenced in the PS group than in NS (no-stress) animals. 2nd EXP: NS and PS rats had two hours/day free access to MDMA oral consumption in the home cage. Alterations in basal motor activities were measured during the dark phase of the L/D cycle. Interestingly, PS group appeared to be the most sensitive to such effects. As a whole, this study provides a detailed characterisation of the effects of MDMA exposure during adolescence and indicates a differential vulnerability to the effects of such a drug as a function of early stress conditions during prenatal life.

85. THE NAPLES HIGH-AND LOW EXCITABILITY RATS: SELECTIVE BREEDING, BEHAVIORAL PROFILE, BRAIN MORPHOMETRY AND MOLECULAR BIOLOGY. Davide Viggiano[1], Daniela Vallone, Adolfo G. Sadile. Lab. Neurophysio[1]., Behav. & Neural Networks, Dept. Exptl. Medicine and Inst. Human Anatomy1, II Univ. Naples, Italy. The present report reviews published and unpublished data gathered so far on the Naples-High (NHE) and Low-Excitability (NLE) rat lines. Historically, NHE and NLE rats were selected ever since 1976 on the basis of behavioral arousal to novelty (Làt-maze) from a population of Sprague-Dawley rats. Selective breeding has been obtained under continuous genetic pressure with no brother-sister crossing. This divergent selection has lead to a line with a high score (NHE) and one with a low score (NLE), along with a random bred parental line (NRB). This review covers research carried out in the last ten years scanning behavioral, morphometric and molecular biology studies. The behavioral analysis pertains to (i) activity in environments of different complexity such as holeboard and Làt maze, (ii) maze learning such as hexagonal tunnel maze, Olton-maze and Morris water maze, (iii) learning and memory tasks such as two-way active avoidance and conditioned taste aversion. Morphometric analysis pertains to brain dopamine systems in their origin and target sites, and by density of dopamine transporter immunoreactivity. Molecular biology analysis pertains to reset experiments on the prefrontal cortex (PFc) by cloning and identifications of differentially expressed genes using subtractive libraries and by RNAase protection. The data suggest that the PFc of NHE rats overexpress at least 51 over 200 isolated genes, which include mitochondrial components, and underexpress dopamine D1 receptors. Altogether, the evidence gathered so far supports on hyperfunctioning mesocorticolimbic system that makes NHE rats a useful tool in the study of hyperactivity and attention deficit, learning and memory disabilities and drug abuse. (Supported by MIUR-COFIN 2001 Grant).

86. ESTROGEN, WHEEL-RUNNING AND INBRED SACCHARIN PREFERENCE: PREDICTORS OF ACCELERATED DRUG SELF-ADMIINISTRATION IN RATS. Carroll, M.E; Morgan, A.D.; Roth, M.E.; Cosgrove, K.P.; Lynch, W.D. Department of Psychiatry, University of Minnesota, Minneapolis, MN 55455, USA. Female rats were ovariectomized (OVX) or sham-operated (SH) and treated with estradiol benzoate (EB) or vehicle while they acquired i.v. cocaine or heroin self-administration. Other groups of in tact female rats were selected for high and low wheel-running and tested for acquisition of cocaine self-administration. Male and female rats selectively bred for high (HiS) and low (LoS) intake of a saccharin solution were compared on their rate and success of acquisition of i.v. cocaine and heroin self-administration. It was hypothesized that factors such as estrogen, elevated wheel-running and saccharin preference would sensitize the rats and yield faster acquisition of drug self-administration and successful acquisition for more rats in the group than controls. With both cocaine and heroin, the OVX rats receiving EB or SH with vehicle treatment acquired faster and at higher group percentages than the OVX vehicle groups. There was a similar finding with cocaine acquisition in females selected for high rates of wheel-running. In the rats bred for saccharin preference, the HiS females acquired cocaine self-administration more rapidly than the LoS females, and females of both phenotypes met the acquisition criteria more rapidly than males. In both HiS and LoS cocaine groups a greater percentage of females (vs. males) met the acquisition criteria within 30 days. The female (vs. male) heroin groups showed a more rapid rate of acquisition, but there was no difference due to saccharin phenotype. All of the heroin groups met the criteria within 30 days. These results indicate that there are several endogenous factors that predict and accelerate cocaine and heroin self-administration, being female, having

estrogen, higher wheel-running and saccharin preference. This work was supported by NIDA grants R37 DA03240 (MEC), T32 DA07097 (ADM), F31 AA05575 (KPC), F31 DA14161.

87. CENTRALLY ADMINISTERED ETHANOL PRODUCES PLACE PREFERENCES AND POTENTIATES OPIATE REWARD. Walker, B. M.; Ettenberg, A. Behavioral Pharmacology Laboratory, Psychology Department, University of California, Santa Barbara, CA 93106 USA. Valid and reliable measures of ethanol (EtOH) reward have proven difficult to establish in animals. Oral EtOH self-administration studies are complicated by the bitter taste of ethanol and/or the need to employ deprivation conditions to obtain reliable operant responding by the subjects. To avoid these issues, the present study evaluated the rewarding properties of centrally administered EtOH using a conditioned place preference paradigm. Male rats were implanted with intracerebroventricular (ICV) cannula and subsequently administered EtOH and saline on alternate days. EtOH was paired with one of two distinct environments and saline was paired with another different environment over an 8 day protocol. Following conditioning, a single 15min behavioral test revealed that ICV EtOH produced reliable preferences for the drug-paired environment compared to the saline-paired environment. In a second experiment, ICV EtOH was also found to potentiate the size of conditioned place preferences produced by IV heroin administration. Thus, the rewarding properties of ethanol (by itself and in conjunction with heroin) can be reliably observed following central application in laboratory rats. (Supported by DA 05041 awarded to AE and a NRSA (DA 06019) awarded to BW.)

88. DIFFERENTIAL SENSITIVITIES OF ENDOCANNABINOIDS AND VANILLOIDS. Akinshola, B.; Fryar, E.; Taylor, R. Howard University College of Medicine, Washington, D. C., William Paterson University Wayne, NJ and NIDA-NIH, Baltimore, MD 21224. There is growing evidence for the existence of an endocannabinoid physiological control system (EPCS)which has been implicated in the treatment of pain, whereas the vanilloid receptor system (VRS) is involved in the sensory perception of pain. In this study, the effects endocannabinoid and vanilloid agonists were compared on kainate activated AMPA receptor subunits in Xenopus oocytes using the two-electrode voltage clamp, in-vitro. The order of potency of inhibition of receptor current were arvanil> 2-AG>olvanil>methanandamide and 2-AG>arvanil>methanandamide>olvanil at the GluR1 and GluR3 respectively. The in-vitro data suggest similar roles for the EPCS and VRS in long term potentiation. In-vivo, the effects of cannabinoid receptor (Cnr) agonists and CB1 antagonist, SR 141716 in the mouse model of withdrawal aversions from cocaine, alcohol and diazepam support a role for this EPCS in natural reward regulatory mechanism.

89. THE ROLE OF DOPAMINE AND GLUTAMATE IN THE EXTINCTION OF COCAINE INDUCED CONDITIONED INCREASES IN LOCOMOTOR ACTIVITY. Pert,A.;Sundstrom,J.;Hall,S.Biological Psychiatry Branch, NIMH, Bethesda, MD 20892 USA. Contextual stimuli associated contiguously with cocaine develop the ability over time to elicit increases in locomotor activity when presented in the absence of the drug. Although considerable effort had been made toward understanding the mechanisms underlying the acquisition and expression of such conditioning, nothing is known regarding its extinction.The purpose of these studies was to determine whether dopamine stimulation or blockade or glutamatergic blockade would alter the extinction process.Groups of rats were conditioned for five days to associate environmental stimuli with the pharmacological effects of cocaine. Following conditioning, various conditioned and control groups were pretreated over five consecutive days with either SCH 23390 (50 and 150 ug/kg), eticlopride (125 ug/kg), apomorphine (1 mg/kg), MK-801 (0.25 mg/kg) or saline and then placed in the conditioning chambers for a 30 min extinction session.D1 DA receptor blockade and enhanced DA activity did not appear to alter extinction, although the D1 receptor blocker SCH 23390 did seem to attenuate the expression of the conditioned behavior.D2 DA receptor blockade, on the other hand, completely blocked the expression of the conditioned behavior and inhibited the extinction process.In order for extinction to proceed it appears that intact D2 DA function is necessary. We have previously reported that cocaine associated cues elicit increases in locomotor activity by enhancing mesoaccumbens DA release. Extinction may require the activation of D2 DA mesoaccumbens DA receptors in the absence of reinforcement (e.g.,cocaine). Intact glutamate function was also necessary for extinction to proceed.

90. EFFECTS OF TACRINE ON MEMORY AND ANXIETY OF MICE TESTED IN THE PLUS-MAZE DISCRIMINATIVE AVOIDANCE TASK Silva, R.H.; Abilio, V.C.; Frussa-Filho, R. Department of Pharmacology, UNIFESP, São Paulo, Brazil. The cholinesterase inhibitor tacrine has been shown to improve memory in several animal models. The aim of the present study was to verify the effects of tacrine on a new animal model of learning/memory: the plus-maze discriminative avoidance task. This paradigm allows the evaluation of learning/memory and, at the same time, provides information about motor behavior and anxiety levels of the animals. Mice received saline solution (SAL) or 5 mg/kg of tacrine. Sixty minutes after the injection, each animal was placed for 10 minutes in a modified elevated plus-maze, with 2 open arms opposite to two enclosed arms (one of which with a 100 w lamp – aversive arm). A 3-min test was performed 24 h later. In the training session, percent time spent in open arms by tacrine-treated group was lower than saline-treated group, indicating a higher anxiety level. In the test session, percent time in aversive arm by tacrine group was lower than saline group, indicating better retention of the task. In conclusion, tacrine increased the retention of the discriminative avoidance task. However, this improvement could be explained by the anxiogenic-like action of this drug. Financial Support: FAPESP.

91. EFFECTS OF ETHANOL ON MEMORY AND ANXIETY OF MICE TESTED IN THE PLUS-MAZE DISCRIMINATIVE AVOIDANCE TASK. Silva, R.H.; Kameda, S.R.; Araújo, N.P.; Frussa-Filho, R. Department of Pharmacology, UNIFESP, São Paulo, Brazil. Ethanol abuse is often followed by cognitive deficits, and several clinical and experimental studies have demonstrated the amnestic effects of ethanol. The aim of the present study was to verify the effects of ethanol on a new animal model of learning/memory: the plus-maze discriminative avoidance task. This paradigm allows the evaluation of learning/memory and, at the same time, provides information about motor behavior and anxiety levels of the animals. Mice received saline solution (SAL) or 1.2, 1.8

or 2.4 g/kg ethanol (ETOH). Five minutes after the injection, each animal was placed for 10 minutes in a modified elevated plus-maze, with 2 open arms opposite to two enclosed arms (one of which with a 100 w lamp – aversive arm). A 3-min test was performed 24 h later. In the training session, percent time spent in open arms by ETOH 1.8 and 2.4 groups was higher than SAL group. Percent time spent in the aversive arm presented by ETOH 1.8 and 2.4 groups was higher than SAL and ETOH 1.2 groups. Total number of entries did not differ among the groups. In the test session, percent time in aversive arm by ethanol 1.8 group was higher than SAL group. In conclusion, ethanol caused a reduction in the retention of the discriminative avoidance task. However, this deficit could be explained by ethanol anxiolytic action. In fact, it has been already demonstrated that alterations in anxiety can modify the retention of this task. Financial Support: FAPESP.

92. INHIBITION OF ETHANOL SELF-ADMINISTRATION AND RELAPSE BY NOCICEPTIN/OP4 RECEPTOR SYSTEM STIMULATION. R.Ciccocioppo, A. Fedeli, D. Economidou, M.Massi. Dept of Pharmacol. Sci. and Exp. Med. University of Camerino, Camerino, Italy. Nociceptin (NC) is the endogenous neuropeptide that binds the opioid OP4 receptors. ICV injection of NC inhibits ethanol intake and ethanol-induced conditioned place preference in genetically selected Marchigian Sardinian (msP) alcohol-preferring rats(1). The present study investigated the effect of NC on ethanol self-administration under FR1 and progressive ratio(PR) contingency, as well as, on cues-induced reinstatement of ethanol-seeking. For ethanol self-administration, rats were trained to lever press for 10% alcohol (30 min/day). When a stable baseline of responding was established NC was tested. Chronic ICV injection (6 days) of NC (500 or 1000 ng/rat), significantly reduced ethanol responding ($p<0.01$). Lever presses returned to a baseline level within 4 days from the last NC injection. Under PR contingency, the breaking point for ethanol self-administration was also reduced ($p<0.05$). In another experiment, msP rats were trained to self-administer 10% ethanol or water on an FR1 schedule in the presence of cues associated with the availability of ethanol (S+) vs. water (S-). The rats were, then, given daily extinction sessions during which lever presses progressively decreased. At this point re-exposure to S+ but not S- significantly reinstated responding in the control group ($p<0.01$). ICV pretreatment with 2000-4000 ng/rat of NC significantly ($p<0.05$) inhibited the effect of S+. Overall, the results demonstrate that NC reduces the reinforcing effects of alcohol and decreases the vulnerability to relapse elicited by environmental conditioning factors. Ciccocioppo R. et al., 1999 Psychopharmacology 141:220-224.

93. IMPROVING TRANSPLANT SURVIVAL FOR PARKINSON'S DISEASE: AN EXPLORATION OF A DIFFERENTIATED HUMAN DOPAMINERGIC CELL LINE. [1]Glasper, E., [2]Paul, G., and [2]Brundin, P. [1]Department of Psychology, Randolph-Macon College, Ashland, VA 23005, USA. [2]Wallenberg Neuroscience Center, Section for Neuronal Survival. Lund University, Lund, Sweden, SE-221-00. Parkinson's disease (PD), the second most common neurodegenerative disorder, is characterized by the death of dopaminergic neurons and accompanying motor disturbances. Treatment is limited due to severe complications as the disease progresses. Transplants of immature neurons have been shown to successfully reverse the effects of PD; however, survival of the transplanted tissue is poor and tissue availability is limited. Therefore, our aim was to characterize a human immortalized cell line with respect to its use for neural transplantation. Human embryonic ventral mecencephalic cells were immortalized using a tetracycline-regulatable v-myc oncogene. We examined different methodological approaches to improve survival of differentiated cells. Three coating protocols were utilized to indicate maximum adhesion and survival of cells to chamber slides. Cells were exposed to differentiation factors for 6 hours, 24 hours, or continuously. Subsequently, cells were exposed to standard immunocytochemistry to determine the presence of β3 Tubulin (early neuronal marker), TH (dopaminergic marker), and Hoechst (nuclear stain). Based on morphological and immunocytochemical observations, it was determined that these cells need to be differentiated at least 24 hours before TH-immunoreactivity, a necessary criterion for PD transplantation, is observed.

94. EFFECT OF CANNABIS ON PARKINSON'S DISEASE SYMPTOMS: QUESTIONNAIRE-BASED STUDY. Venderova, K.[1]; Ruzicka, E.[2]; Visnovsky, P.[1] ([1] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Charles University, Hradec Kralove, Czech Republic [2] Movement Disorder Centre, Department of Neurology, 1st Medical Faculty, Charles University, Prague, Czech Republic). Following the information presented in the media we realised that some of our patients decided to use cannabis to alleviate their Parkinson's disease (PD) symptoms. To evaluate their possible experience, all patients with PD registered at the Movement Disorder Centre (MDC) were asked to anonymously complete a questionnaire. Out of 630 questionnaires sent, 339 (53,8%) were returned. The responders' mean age was 65,7 years (range 36-92 years) and the average PD duration was 8,6 years (ranging from 1 to 46 years). 85 patients (25,1%) reported to have an experience with cannabis, most of them using fresh or dried cannabis leaves orally. In this group, 39 patients (45,9%) described mild or substantial alleviation of their PD symptoms in general, 26 (30,6%) improvement of rest tremor, 38 (44,7%) alleviation of bradykinesia, 32 (37,6%) alleviation of muscle rigidity and 12 (14,1%) improvement of levodopa induced dyskinesias. According to the information obtained from the patients, this alleviation in average occurred 1,7 months (ranging from 1 hour to 6 months) after their first cannabis use. There was a correlation between the duration of cannabis use and subjective feeling of improvement in general PD symptoms ($p<0,001$, ÷2 test), tremor ($p<0,01$), bradykinesia ($p<0,01$) and muscle rigidity ($p<0,01$). In case of dyskinesias, the beneficial effect did not correlate with the length of cannabis use, but the patients using cannabis with higher frequency reported alleviation of dyskinesias more often ($p<0,05$). It seems some of the cannabinoids or compounds targeting the cannabinergic system might be useful in the treatment of PD symptoms or drug-induced dyskinesias. Supported by grants 2223/02 and CEZ:J13/9811600004.

95. EFFECTS OF PRENATAL COCAINE AND/OR NICOTINE ON INDICES ON MENTAL ILLNESS IN ELDERLY RATS. Sobrian, S.K.; Ressman, K.; Marr, L. Dept. of Pharmacology Howard Univ. Col. of Med., Washington, DC 20059 USA. The use of cocaine and withdrawal from the drug have been linked to mental illness. Changes in emotional behavior were assessed using behavioral paradigms developed as animal analogs of

psychiatric disorders in 12-15 month old Sprague-Dawley rats exposed on GD 8-20 to cocaine and nicotine, either alone or in combination. Results from the elevated plus maze, used to assess anxiety-related behaviors, indicated that offspring prenatally exposed to high dose nicotine (5.0 mg/kg/day) or high dose cocaine (40 mg/kg/day) were less timid. Animals from these two groups spent the most time in the open arms, and had the highest percent of entries into open arms. Combined exposure to cocaine and nicotine reversed these effects; offspring in these groups had the largest numbers of closed-arm entries. Cocaine challenge (20 mg/kg) did not interact with prenatal treatment but reduced anxiety in all groups. Sucrose preference was used as a measure of anhedonia, a cardinal symptom of depression. Sex differences in sucrose intake, but not preference (F > M), were still evident at 15 months of age. Reduced sucrose preference was seen only in the HC/LN group, and reflected an increase in water intake. A mild stress (23-hr water deprivation) eliminated these differences. Pre-pulse inhibition of the acoustic startle response, which tests sensory gating of external stimuli, has been used to model some aspects of schizophrenia. Prenatal treatment did not impact startle amplitude on the pre-pulse trails. However, control offspring exhibited a deficit in response to the acoustic stimulus (110 dB tone) alone. These data indicate that prenatal exposure to cocaine and/or nicotine has a long-term effect on emotional behavior. Combined exposure contributes to the development of both depression and anxiety, but not schizophrenia. In contrast, exposure to high doses of either drug alone reduced cautionary behavior. (Supported by NIH Grant S06 GM 08016-28).

96. INCREASED ALCOHOL INTAKE AFTER PRENATAL ALCOHOL EXPOSURE IN THE RAT: A CONDITIONED RESPONSE? Chotro, M.G.; Arias, C. Universidad del Pais Vasco, San Sebastian, Spain. Previous studies have shown that the administration of a moderate alcohol dose during gestational days (GD) 17-20 in the rat results in enhanced alcohol consumption by the offspring. During this last gestational period the rat fetus can perceive chemosensory characteristics of substances present in the amniotic fluid and these experiences may modify their preference for those flavors through associative or non-associative processes. It is also known that at this stage the opioid system is functional, that the opioid antagonist Naloxone can modify fetal responses known to be regulated through this system, and that opiate antagonists may reduce reinforcing properties of alcohol. Considering this information, it was hypothesized that the increased alcohol consumption after prenatal ethanol exposure could obey to a conditioned preference resulting from the association between sensory and reinforcing properties of alcohol mediated by the opioid system. The associative nature of the effect was tested in a series of three experiments. In Experiment 1, with the aim of interfering with the establishment of the association, pregnant dams received an injection of Naloxone together with the alcohol administration during GD 17-20. In Experiment 2 subjects were exposed prenatally to alcohol and during postnatal days 10-12 were re-exposed only to the sensory properties of alcohol, in order to extinguish the association. In the last experiment, subjects were exposed prenatally to alcohol and postnatally were aversively conditioned to alcohol taste. Results suggest that the opioid system plays an important role in the augmented alcohol intake effect observed after prenatal alcohol exposure. Also seem to support the hypothesis of a conditioned preference response established in utero after maternal alcohol administration.

97. EFFECT OF CHRONIC NICOTINE ADMINISTRATION ON ACCUMBAL DOPAMINERGIC TRANSMISSION IN MICE Tammimäki, A.; Gäddnäs, H., Ahtee, L. Div. of Pharmacology and Toxicology, Dept. of Pharmacy, POB 56, FIN-00014 Univ. of Helsinki, Finland. Sensitisation of mesolimbic dopaminergic system is believed to be central in the development of drug addiction. The sensitisation phenomenon may be due to changes in dopamine receptors (Vanderschuren et al., Psychopharmacology 143:244-253, 1999). In the present study we explored the changes in the sensitivity of dopamine autoreceptors and the role of nicotinic receptor activation in dopamine (DA) release in mice during chronic oral nicotine treatment. Male NMRI mice had for 7 weeks either nicotine solution or tap water as the sole source of fluid. Locomotor activities of the mice were measured immediately after D_2/D_3-receptor agonist, quinpirole (0.01 or 0.03 mg/kg s.c.) or saline for 60 min. In microdialysis experiments the probe was placed in the nucleus accumbens. After collection of four baseline samples mecamylamine (2 mg/kg s.c.) or quinpirole (0.03 mg/kg s.c.) was given. Samples were collected at 20 min intervals and their DA, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) contents were measured using HPLC–EC. On the 50th day of nicotine administration the basal DA concentration in dialysate was higher in the nicotine-treated than in control animals as reported before (Gäddnäs et al., Pharmacol Biochem Behav 70:497-503, 2001). Mecamylamine reduced DA outflow in nicotine-treated but not in control mice. Quinpirole reduced the locomotor activity and DA release similarly both in nicotine-treated and control mice. Thus, this data suggests that the sensitivity of presynaptic D_2-receptors does not change during chronic oral nicotine treatment in spite of elevated extracellular DA levels.

98. INTERACTION BETWEEN MK-801 AND MORPHINE IN DIFFERENT BEHAVIOURS. Costanzi M.; Pavone F.; D'Amato F.R.; Castellano C.; Cestari V. Istituto di Psicobiologia e Psicofarmacologia CNR Rome Italy. A number of studies indicate that NMDA and opioid receptors are involved both in pain modulation and in learning and memory processes.In the present research we investigated the interaction between the NMDA receptor antagonist MK-801 and morphine in behavioural responses to acute pain and in memory consolidation in CD1 mice. In a first series of experiments the involvement of the glutamatergic system in the opioid-induced analgesia was investigated. For this purpose CD1 mice were i.p. injected with MK-801 (0, 0.1, 0.125, 0.15 mg/kg) and morphine (0, 5, 10 mg/kg) alone or in combination and tested in the tail flick test. The results showed that a otherwise ineffective dose of MK-801 potentiated the antinociceptive response induced by morphine in a time-dependent manner. In a second series of experiments we investigated the involvement of NMDA and opioid receptors in memory consolidation in a non associative spatial learning task and in the active avoidance test. In these experiments CD1 mice, i.p. injected immediately post training with different doses of MK-801 (0, 0.15, 0.3 mg/kg), morphine (0, 5, 10, 20 mg/kg) or a cocktail of the drugs, showed performances impairment in both tests. In a third set of experiments we investigated the involvement of NMDA and opioid receptors in the modulation of

emotionality in a social and in a non-social context. MK-801 (0, 0.15 mg/kg), morphine (0, 10 mg/kg) and combined i.p. administration of the drugs induced an alteration of the emotional perception of the stimuli rather than modifying anxiety The results of the three series of experiments suggest a functional link between NMDA and opioid receptors in different neural mechanisms.

99. REGIONAL DIFFERENCES IN NALOXONE MODULATION OF THC-INDUCED C-FOS EXPRESSION IN RATS. Allen, K.V; Mallet, P.E.; Singh, M.; McGregor, I. S. Department of Psychology, University of Sydney, NSW 2006, Australia and School of Psychology, University of New England, Armidale NSW 2351, Australia. Recent behavioral and pharmacological research shows extensive interplay between the cannabinoid and opioid neurochemical systems of the brain. For example, the opioid receptor antagonist, naloxone inhibits cannabinoid-induced activation of reinforcement circuitry, cannabinoid-induced hyperphagia and cannabinoid antinociception. Here we sought to more rigorously examine the neural basis of such phenomena. We compared c-fos expression in groups of Wistar rats treated with either vehicle, THC (10 mg/kg), naloxone (10 mg/kg) or THC/naloxone in combination. Locomotor activity was depressed in both THC treatment groups and moderately inhibited in rats given naloxone alone. Naloxone inhibited THC-induced c-fos immunoreactivity in several key brain regions including the ventral tegmental area, striatum and ventrolateral periaqueductal grey. Conversely, naloxone potentiated THC- induced c-fos expression in the central nucleus of the amygdala and the paraventricular nucleus of the thalamus. Naloxone had no effect on THC-induced c-fos expression in the paraventricular nucleus of the hypothalamus, Edinger-Westphal nucleus and nucleus accumbens core. These findings compliment earlier pharmacological results suggesting a potent modulation of cannabinoid-induced analgesia and reinforcement by the opioid system. The effects of naloxone on THC-induced c-fos expression in the ventral tegmental area and periaqueductal grey point to these structures as key sites involved in cannabinoid-opioid interactions.

100.ACOUSTIC STARTLE AS A MEASURE OF SPONTANEOUS AND PRECIPITATED MORPHINE WITHDRAWAL IN RATS. Harris, A.C.; Brier-Bauder, G.; Vasserman, E.Y.; Gewirtz, J. C. Department of Psychology. University of Minnesota, Minneapolis, MN 55455 USA. Fear and anxiety induces an elevation of the startle reflex in humans and rodents, an effect that is blocked by anxiolytic drugs. Anxiety is frequently reported as a symptom of withdrawal from alcohol, opiates and other drugs of abuse. The current study evaluated the effects of spontaneous and precipitated opiate withdrawal on acoustic startle in rats, using an acute dose of morphine. In Experiment 1, spontaneous withdrawal from a single injection of morphine sulfate administered over 4 consecutive days produced a significant increase in baseline startle 2 hours (3.2 mg/kg), or 4 hours (10 mg/kg) after injection. In Experiment 2, morphine withdrawal (10 mg/kg morphine sulfate) precipitated by the opioid antagonist naloxone (2.5 mg/kg) also produced a significant increase in baseline startle. These results suggest that both spontaneous and precipitated withdrawal from an acutely administered opiate produce anxiogenic-like effects on acoustic startle. Preliminary data indicate that the benzodiazepine chlordiazepoxide (10 mg/kg) blocks the opiate withdrawal-induced elevation of startle. We are currently investigating the effects of other anxiolytic drugs on this phenomenon. Research supported by NIDA T32 DA07097 to A.C.H. and a University of Minnesota Grant in Aid of Research to J.C.G.

101.BUPRENORPHINE FALLS SHORT AS A POSTOPERATIVE ANALGESIC IN RODENTS. Thompson, A.C.[1]; Sallaj, A.S.[2]; Acheson, A.[2]; Martin, L.B.E.[3]; Martin, T.[3]; Kristal, M.B.[2]. [1]Research Institute on Addictions, [2]Dept. of Psychology, and [3]Dept. of Comparative Medicine. University at Buffalo, Buffalo NY 14260. Buprenorphine is a widely prescribed postoperative analgesic in rodents at doses of 0.05 mg/kg SC, or 0.5mg/kg PO in flavored gelatin. We previously compared the analgesic efficacy of the recommended oral dose of buprenorphine and its SC counterpart, and found significant differences. In fact, the PO dose of buprenorphine must be increased to 5mg/kg to yield an analgesic response comparable to that produced by 0.05mg/kg SC. Several new experiments extend this analysis and show that the findings of our original study are not unique to the strain of rat used or method of buprenorphine preparation. Furthermore, these studies show that the 5mg/kg PO dose of buprenorphine must be mixed in a highly palatable substance, such as peanut butter paste, for the rats to eat it reliably, although it is still detectable to the rats. Additionally, these clinically relevant doses of buprenorphine also induced a conditioned taste aversion, indicating that they induced gastrointestinal distress. Finally, in Sprague-Dawley rats, but not in Long-Evans rats, these doses (either SC or PO) induce significant pica. Overall, the present studies support our previous finding that a 5mg/kg PO dose is necessary to achieve an analgesic response similar to the standard therapeutic SC treatment, and indicate that this dose can be given PO in a highly palatable substance. But our data also suggests that the SC and PO dosing regimes induce nausea as well as analgesia. Nausea, in turn, may slow the recovery process and induce unproductive and potentially harmful behaviors such as pica.

102.CHRONIC EXERCISE ATTENUATES THE PAIN RELIEVING PROPERTIES OF NICOTINE IN FEMALE RATS. Kanarek, R.B.; Mathes, W.F. Dept. of Psychology Tufts University, Medford, MA 02155, USA. Chronic exercise alters the behavioral consequences of psychoactive drugs. For example, rats housed in activity wheels are less sensitive to the pain relieving actions of opioid agonists than rats housed in standard laboratory cages. These findings raise the question of whether exercise only modifies the actions of opioid drugs or also affects the analgesic properties of other psychoactive agents. To answer this question, female Long-Evans rats were housed either in running wheels or standard cages for 3 wk. Rats then were tested for nicotine-induced analagesia using the radiant heat tail flick (TF) test. After determining baseline TF latencies, rats were injected every 5 min with increasing doses of nicotine leading to cumulative doses of 0.1, 0.3, 1.0 and 3.0 mg/kg. Latency to TF was measured immediately before each drug injection. Decay of nicotine's analgesic effect was evaluated by measuring TF latencies every 5 min for 40 min after the last injection. The analgesic actions of nicotine increased as a function of drug dose. However, active rats were significantly ($p<0.01$) less sensitive to the pain relieving actions of nicotine than inactive rats. Additionally, analgesic responses decreased as a function of time after the last nicotine injection.

However, analgesic responses of active rats were significantly lower ($p<0.01$) and returned to baseline sooner than those of inactive rats.

103.CONTRIBUTION OF CENTRAL ALPHA1-ADRENOCEPTORS TO FORMALIN-PAIN MODULATION IN MICE. Borghi V*.; Nalepa I.°; Kowalska M.°; Przewlocka B.°; Vetulani J.°; Pavone F.* *CNR-Ist. Psychobiology and Psychopharmacology, Viale Marx 43, 00137 Rome-Italy, f.pavone@ipsifar.rm.cnr.it °Department of Molecular Neuropharmacology, Institute of Pharmacology, Polish Academy of Sciences, Krakòw-Poland. The noradrenergic system has been extensively studied for its role in pain and analgesia: the descending noradrenergic pathway, together with the serotoninergic one, is considered a crucial link in the supraspinal modulation of nociceptive transmission. Most studies on pain noradrenaline-mediated effects have been focused on alpha-2 receptors since noradrenaline itself exerts its inhibitory effect on pain transmission mainly through alpha-2 adrenoceptors. However sporadic, and not always consistent, reports showed that also alpha-1 adrenergic receptors are involved in pain control. Our interest was to investigate the role of this subtype adrenergic receptors in the inflammatory pain induced by formalin by both behavioral and biochemical analyses. The effects of the prototypic alfa-1 antagonist Prazosin (from 0.01 to 1 mg/Kg i.p.) were investigated in CD1 male mice. The characteristic biphasic behavioral responses induced by formalin were differently modulated by Prazosin, with only the first phase inhibited by this compound. Different groups of mice were used to analyze, by autoradiography, the effects of formalin on alpha-1 adrenoceptor density in several structures of CNS (spinal cord, thalamus, amygdala, cortex). A decrease in the alfa-1 adrenoceptors density was observed in the spinal cord and the cortex, while an opposite effect was evident in the amygdala. The results obtained support a role of central alpha-1 adrenoceptors in the inflammatory pain modulation.

104.INFLUENCE OF SEX AND BREEDING STATUS ON THE BEHAVIOR OF MEADOW VOLES IN THE AUTOMATED DIGISCAN LIGHT-DARK ANXIETY TEST. K.-P. Ossenkopp, S. Anderson, C. G. Engeland, & M. Kavaliers. Neuroscience Program and Dept. of Psychology, University of Western Ontario, London, Ontario, Canada, N6A 5C2. The light-dark test was developed to assess anxiety and/or fear related behaviors in small mammals. This test is based on an innate aversion of rodents to novel, brightly illuminated spaces which could pose a threat from encounters with potential predators. This test has been most commonly used with laboratory mice (a nocturnally active species) and involves exposing the animals to a 2 compartment chamber in which one half is white and brightly illuminated and the other half is black and dark (low illumination). The subjects are allowed access to either compartment during the test session. The present study examined the behavior of breeding or non-breeding, male and female meadow voles (a diurnally active species) in an automated light-dark test apparatus. This apparatus used a Digiscan activity monitor to quantify a variety of behaviors by means of infratred light beams, in a light area (approx. 900 lux) or a dark box (both 40 X 20 cm). The meadow voles were exposed to this apparatus for 30 min on 3 consecutive days. All animals spent significantly less time in the light area relative to the dark box. Breeding voles, especially females, spent less time in the light area than did non-breeding voles. On the first test day breeding voles also made fewer transitions across areas relative to non-breeding voles. In general all voles were more active in the light area relative to the dark for horizontal movements as well as rearing responses. Breeding status affected activity levels in the dark box on Day 1 with breeding voles less active than non-breeding animals. These results show that breeding voles are more anxious in this situation than non-breeding voles, especially when the apparatus is novel, and that breeding females avoid the light area the most. Thus, both breeding status and sex can influence situation based anxiety levels in this species. (Supported by NSERC).

105.EFFECTS OF A BRIEF EXPOSURE TO FOX ODOR ON ANXIETY AND LOCOMOTOR ACTIVITY LEVELS IN THE LIGHT-DARK TEST IN MALE AND FEMALE MEADOW VOLES. S. Anderson, C. G. Engeland, M. Kavaliers, & K.-P. Ossenkopp. Neuroscience Program and Dept. of Psychology, University of Western Ontario, London, Ontario, Canada, N6A 5C2. Previous research has shown that brief exposure to a predator odor can influence the behavior of small rodents. These animals depend on olfactory detection of a predator prior to actual contact and in the wild will avoid objects tainted with predator odor. In the laboratory we have found that meadow voles, especially males, will exhibit reductions in open-field locomotion in response to brief exposures to a fox odor. In the present study we tested male and female meadow voles, housed in opposite sex pairs under a 16h L: 8h D photoperiod, in an automated light-dark test apparatus. This apparatus used an automated Digiscan activity monitor to quantify a variety of behaviors by means of infrared light beams in a light area (approx. 900 lux) or a dark box (both 40 X 20 cm). Following 3 days of baseline testing (30 min/day) all animals were exposed (in odor exposure boxes), on 3 consecutive days, to either 3 min of fox odor or a control odor and then tested for 30 min in the light-dark test apparatus. All animals spent significantly less time in the light area compared to the dark box. Voles exposed to the fox odor spent more time in the light area than did controls and males spent more time in the light area than did females. Horizontal locomotor activity in the light area was greater than in the dark box and fox odor exposure increased activity levels in the dark box but not the light area. Rearing responses were greater in the odor exposed voles relative to controls in both areas, but only on the second day of odor exposure. Thus, brief exposure to fox odor in the present study increased locomotor activity levels and time spent in the light area in both males and females. This finding contrasts with previous studies in our laboratory which obtained reductions in activity in a brightly illuminated familiar open-field apparatus following fox odor exposure. The present findings are perhaps indicative of increased vigilance in the voles exposed to the predator odor. (Supported by NSERC).

106.AN EXPLORATION OF COPING STRATEGY CONSISTENCIES IN MALE AND FEMALE RATS EXPOSED TO MULTIPLE STRESSORS. [1]Campbell, T.; [1]Lin, S.; [2]DeVries, C.; [1]Lambert, K. [1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005 USA; [2]Dept. of Psycholgy, The Ohio State University, Columbus, OH 43210 USA. Because of the pathogenic effects of chronic stress exposure, it is important to identify factors that may mitigate stress-induced pathology. Although the physiological response to stress (i.e., activation of the HPA axis) has been well documented, less is known about the robustness of behavioral response strategies to

various stressors. Of interest in the present study was the consistency of responses across various stressors as well as the influence of behavioral strategies on the intensity of the stress response [e.g., corticosterone levels (CORT), *fos* activation in the central amygdala (CEA)]. Sixteen male and 16 female Long-Evans rats were assigned to either a stress or control group. The stressed animals were subsequently exposed to a battery of ecologically-relevant stressors (e.g, predator odor, novel stimuli, immunological challenge) in order to determine trends in coping strategies. Following behavioral tests, CORT levels were determined (following a one-hour recovery period from predator odor in stressed animals). Standard immunohistochemistry was performed on all brains to determine *fos*-immunoreactivity in the CEA and paraventricular hypothalamus. Results indicated that certain response strategies (e.g., passive vs. active) persist across several behavioral tests. Focusing on neurobiological data, stressed animals exhibited more *fos*-immunoreactive cells in the CEA and higher CORT levels were observed in the females.

107.POSTNATAL HANDLING HAS POSITIVE EFFECTS ON ANXIETY DURING PREGNANCY IN RATS. Lointier, L.; Roy, V.; Chapillon, P. Equipe Neurobiologie de l'Apprentissage. UPRES PSY.CO – EA 1780, Université de Rouen, 76821 Mont-Saint-Aignan, FRANCE. E-mail: louiselointier@hotmail.com. Pregnancy in rats has been reported to increase anxiety in the elevated plus maze. In addition, postnatal handling has been shown to reduce emotional reactivity in a lot of behavioral tests. In the present study, we investigated the potential effects of handling (consisting in a short daily maternal separation during the first 21 days of life) during a stressful situation in pregnant rats. For that purpose, different groups of DA\HAN female rats were tested independently in three tests of emotional reactivity: the elevated plus maze test, the probe burying test and a cat exposition test. At the age of 10-14 weeks, control and handled females were housed with males during the dark phase of their cycle. At the end of this phase, pregnant females, as determined by the presence of spermatozoids in the vaginal smear, were isolated (Day 0 of gestation). In parallel, non-pregnant females were also isolated (Day 0 of isolation). On day 12, pregnant and non-pregnant females were subjected to one of the three emotional reactivity tests. Pregnant rats (control and handled) showed lower coping abilities with stressing situations than non pregnant rats, as measured by the time spent in open arms of the elevated plus maze and locomotion in the two other apparatus. However, postnatal handling effects were obvious in the three experiments: handled animals (non pregnant and pregnant) displayed more behaviors related to a lower emotional reactivity than control animals, as measured by exploration or locomotion behaviors. So, handled pregnant rats seem less anxious than control pregnant rats. The present experiment demonstrates that the positive effects of postnatal handling on anxiety persist at a given day of pregnancy. Moreover prenatal psychological stress influences behavior of the offspring. So, in a current study we investigate whether the better coping abilities of handled females confronted to a stressful situation could have positive effects on their offspring development and behavior.

108.EFFECTS OF CHRONIC STRESS AND SOCIAL CONTACT ON HIPPOCAMPAL APOPTOSIS AND STRESS RESPONSIVITY IN *PEROMYSCUS CALIFORNICUS* .[1]Lin, S.; [1]Campbell,T.; [2]DeVries, C.; [1]Lambert,K.G.[1]Dept. of Psychology, Randolph-Macon College, Ashland, VA 23005 USA;[2]Dept. of Psychology, The Ohio State University, Columbus, OH 43210 USA. A plethora of research suggests that chronic stress threatens the hippocampus, evidenced by decreased hippocampal volume and atrophied hippocampal neurons. In this study, we investigated potential mechanisms of hippocampal atrophy by examining the effect of chronic unpredictable stress on programmed cell death, or apoptosis, within the hippocampus. Also of interest was the variable of social contact; past research suggests that social contact may mitigate some of the harmful effects of chronic stress. In the present study, 36 adult male mice *Peromyscus californicus* were assigned to either a chronic stress or control group. In each group, animals were further assigned to a social contact or isolate condition. All animals were exposed to an open field test prior to and following the experimental procedure. Following sacrifice, subfields CA1, CA2, CA3, and dentate gyrus of the hippocampus were examined for presence of apoptotic cells (via caspace-3 immunoreactivity). Results indicated that stressed animals exhibited significantly more apoptotic cell bodies in the CA3 and dentate gyrus than control animals. Blood samples taken at sacrifice indicated increased corticosterone levels in the stressed animals as well. Behaviorally, socially-stressed animals were more active in the open field than their isolate-stressed counterparts. In sum, these findings suggest that psychological stress may play a significant role in cellular death in the hippocampus and, further, that social contact mitigates some of the negative consequences of chronic stress.

109.BRAIN-STIMULATION REWARD AS A BEHAVIOURAL MEASURE OF CHRONIC MILD STRESS IN FEMALE RATS. Kentner, A.C.; Baker, S.; Konkle, A.T.M.; Fouriezos, G.; and Bielajew, C. University of Ottawa, Ottawa, ON, CANADA. The chronic mild stress paradigm was developed in rodents to generate anhedonia, a major symptom of depression. Typically, hedonic status is assessed by a decrease in either intake of or preference for a mild sucrose solution. However, there is some concern that change in consumption is associated with fluctuations in body weight. In order to avoid this problem of interpretation, some investigators instead index hedonic status by tracking thresholds for brain stimulation reward following chronic exposure to a series of mild stressors. Using this measure, an increase in reward thresholds has been reported with stressor experience, returning to basal levels with antidepressant treatment (Moreau et al., 1992, 1994, 1996). Although the exact role played by gonadal hormones in the etiology and development of major depression is unclear, it is important that animal models of human disorders be investigated in both male and female subjects; up to now, there has been a gender bias towards males, even though in humans, depressive disorders appear to predominantly target females. The goal of the present study was to investigate the effects of chronic mild stressors on threshold changes for brain stimulation reward in female rats. The behavioural data collected thus far suggest little effect of the stressors on reward thresholds, at least in the female Sprague-Dawley rat. Because strain differences in stressor reactivity have been reported in males, we are currently assessing whether such differences exist in females by evaluating thresholds in female rats of the Long-Evans strain.

110.INVESTIGATING THE EFFECTS OF CHRONIC MILD STRESS ON SUCROSE PREFERENCE IN TWO FEMALE RAT STRAINS. Baker, S.L.; Kentner, A.C.; Konkle, A.T.M.; and Bielajew, C. University of Ottawa, ON K1N 6N5 Canada. Stress has long been implicated in the etiology of depression. The chronic mild stress (CMS) paradigm is one that models, in rodents, the everyday life stressors that humans encounter (Willner, 1987). It is employed both for the purpose of assessing the effects of antidepressants and to further examine the neurobiological basis of this disorder. Typically, preference for a weak sucrose solution, used as an index of reward, is decreased over time in male rats exposed to CMS versus their control counterparts. However, little work has been done to assess the effects of such paradigms in female rats, which is surprising, given that the incidence of depression is much higher in women than in men. The purpose of this study was to examine the effects of CMS in two strains of female rats, using physiological indices of stress and a behavioural index of reward - sucrose intake after 1 and 24 hours. We included three groups, CMS, single, and group-housed Long Evans and Sprague-Dawley rats. Analysis of the body weight data revealed a slower rate of weight gain in the CMS animals with all Long-Evans animals gaining weight more quickly than Sprague-Dawley ones. This group, CMS, typically had heavier adrenal glands and spleen. The behavioural data show a slight increase in 1-h sucrose intake over time for the singly-housed groups; no change from baseline was observed for the CMS and group-housed animals. Finally, although statistical analyses reveal significant effects of treatment and/or time for 1 hour sucrose preference, the 24 hour intake and preference for sucrose, no real patterns emerge from the data. These results demonstrate the importance of including data from females in the evaluation of animal models and further advance the notion of an interaction between genetic and environmental factors in the etiology of depression.

111.5-HT1A RECEPTOR ACTIVITY AT A STRESSFUL EVENT MODIFIES LATER BEHAVIOR ALTERED BY THE STRESSFUL EXPERIENCE. Seoul Lee, Jeong Won Jahng, and Dong Goo Kim Dept. of Pharmacology and Yonsei Brain Research Institute, Brain Korea 21 Project for Medical Sciences, Yonsei University College of Medicine, Seoul 120-752, Korea. We have previously reported that an experience of early life stress modified later behavior of the organism. In this study, we aimed to determine the role of 5khydroxytryptamine (5-HT) 1A receptor activity at a stressful event on the experience-dependent behavioral alteration. Sprague-Dawley rats were subjected to footshocks (0.6 mA, 50 times, 5 s duration, at random intervals) on PND 14, and a 5-HT1A agonist, 8-OH-DPAT or a 5-HT1A antagonist, NAN-190 was administered 30 min after the footshock session. The number of footshocks necessary to elicit helplessness behavior was chosen as an index of behavioral stress response. On PND 21, the same footshock stress was delivered and the behavioral response was measured. The control rats showed helplessness behavior earlier during the stress session on PND 21 than on PND 14. Interestingly, this altered pattern of behavioral expression under stressful event was abolished by the treatment with 8-OH-DPAT, but not with NAN-190. On PND 42, these rats were subjected to a novel environment and measured the exploratory activities for 5 min. Experience of 8-OH-DPAT or NAN 190 increased or decreased ambulatory activities when facing with novel environment, respectively. When we measured the level of plasma corticosterone in the morning of the very next day of the last day of the water maze test, an increased corticosterone level was found in rats experienced 8-OH-DPAT early in life. The results suggest that the consolidation of stressful memory was influenced by the status of 5-HT1A receptor activities in the process of stress response, and then this memory may alter the HPA axis which influences later behavior to cope with stressful event. This research was supported by James W. Yoo Research Fund.

112.BEHAVIORAL AND NEURAL EVIDENCE OF SOCIAL STRESS AND SOCIAL SUPPORT IN CONTROL CAGE MATES OF DSP-4 TREATED RATS. McFarlane, H.; Henry, S.;Dewey, T.; Cornwell, C. Dept. of Psychology. Syracuse University, Syracuse, NY 13244 USA. Previous evidence suggests that control cage mates of rats treated with the norepinephrine (NE) neurotoxin DSP-4, experience social stress. The present study investigated whether housing individual controls exclusively with DSP-4 treated cage mates, would produce greater indices of stress than those seen in controls housed in equally mixed treatment groups. Juvenile rats were housed in 3 different conditions: groups of 8 controls, groups of 4 controls and 4 DSP-4 treated rats, and groups of 1 control and 7 DSP-4 treated rats. After 10 days, 4 measures were taken: preferences for a familiar vs. 2 unfamiliar bedding odors, body weight and hippocampal NE concentrations. Relative to control-only group means, DSP-4 group means were below normal on all 4 measures. Means of the single-control group were below normal for NE concentrations and on one of the odor preference tasks. Single-control means on the latter task were also below those of controls from the equal mix group. The results not only suggest that exposure to DSP-4 rats is stressful for controls, but additionally imply that the presence of other controls buffers the impact of this exposure. Therefore, this paradigm may provide an animal model of both social stress and social support.

113.HIPPOCAMPAL ASPIRATION DECREASES OPEN ARM AVOIDANCE IN TWO RAT STRAINS AND BOTH PLUS- AND T-MAZE TESTS OF ANXIETY. Coover, G.D.; Trivedi, M.; Heldt, S.A. Dept. of Psychology, Northern Illinois University, DeKalb, IL 60115 USA. Aspiration lesions of the hippocampus and (HIPP)/ or (CORT) overlying cortex were performed in Long-Evans hooded rats and Charles Rivers derived Sprague Dawley albino rats. The albino SHAM group emerged more rapidly than the hooded SHAM group from the enclosed arm of the T Maze, but the SHAM groups exhibited comparable passive avoidance of the open arms on the next two trials. CORT lesions reversed the latency pattern of the two strains, such that the CORT hooded rats emerged more quickly than the CORT albino group on the baseline and avoidance trials, with both lesion control groups exhibiting passive avoidance of the open arms comparable to that shown by the SHAM groups. The HIPP groups of each strain continued to emerge rapidly on the avoidance trials, thus exhibiting significantly less passive avoidance of the open arms. On the 4th trial, which assessed escape from the open arm, the HIPP groups were slower to escape than SHAM or CORT groups. In fact, rats with HIPP lesions walked past the entrance to the enclosed arm multiple times, suggesting disinterest in escape. Subsequently, the rats were given 5-min exposures to an elevated Plus Maze using either the same red room light used for the T-Maze test (Session 1), or a brighter, white room light (Session 2). The subjects showed less open-arm time during Session 2 than Session 1, regardless of lesion condition. The HIPP

groups spent more time on the open arms (59% collapsed over Strain and Session) than either the SHAM groups (12%) or the CORT groups (15%). Complete removal of the hippocampus clearly reduces the anxiety generated by novel, open, elevated arms.

114.SOCIAL LEARNING OF NATURAL FEAR RESPONSES IN DEER MICE: ROLES OF KINSHIP AND FAMILIARITY. Kavaliers, M.; Choleris, E.; and Colwell D., Dept. Psychology, Univ. Western Ontario, London, Canada; Rockefeller Univ.; and Agriculture and Agri-Food Canada, Lethbridge, Alberta. Social learning, whereby an "individual's behavior is influenced by observation of, or interaction with, another animal or its products" has been reported for a variety of behavioral responses. Recently we examined the roles of social learning in fear conditioning to biting flies, a natural aversive stimulus commonly encountered by animals. Brief exposure of mice to biting flies (stable flies, Stomoxys calcitrans) induces analgesia and active self-burying avoidance responses. Mice that received a single exposure to intact stable flies further displayed analgesic and avoidance responses when exposed 24 h later to biting flies that were altered to be incapable of biting. This "one trial" conditioned analgesia and avoidance self-burying could also be acquired through social learning without direct individual aversive experience with biting flies. Mice (observers) that witnessed other mice (demonstrators) being attacked by biting flies but themselves were not bitten, displayed analgesic responses. Upon subsequent (24 h) exposure to altered biting flies the observers displayed socially acquired conditioned analgesic and self-burying avoidance responses. Normally social learning occurs withing the complex framework of an animal's social interactions that are markedly affected by factors such as family bonds and kinship, familiarity and dominance hierarchies. Using deer mice, Peromyscus maniculatus, we describe here the significant facilitatory effects of relatedness (kinship) and familiarity on the social learning and retention of fear responses to biting flies. As well, we show that dominance-subordinate relationships between the demonstrator and observer can modulate the social learning of fear responses with subordinates displaying enhanced learning. Supported by NSERC and Agriculture and Agri-Food Canada.

115.FIFTY-kHz CALLS INDUCED BY A DIRECT ACTIVATION OF THE DOPAMINERGIC SYSTEM IN THE RAT BRAIN. Brudzynski, S.M. Dept. of Psychology and Neuroscience Program, Brock University, St. Catharines, ON L2S 3A1 Canada. It has been known that adult rats emit short, high frequency calls (termed 50 kHz calls) in a number of behavioual situations associated with social affiliation. Recent data have implicated the dopaminergic system in the initiation of these calls. The goal of the present study was to a) demonstrate that 50 kHz calls could be induced by a local activation of the dopaminergic system in the nucleus accumbens - the main target structure for the ascending dopaminergic projection, and b) that the pharmacologically-induced 50 kHz calls have species-typical acoustic characteristics known from other behavioural studies. Twenty adult, male Wistar rats were stereotaxically implanted with chronic cannulae in the nucleus accumbens. After recovery, rats were intracerebrally injected with amphetamine (5-25 ug), which potentiates dopaminergic transmission, or with quinpirole (5-10 ug), a slective D2-like dopamine receptor agonist. Amphetamine significantly increased the number of 50 kHz calls as compared to the baseline after vehicle injection while quinpirole had less pronounced action. The acoustic characteristics of the calls (average sound frequency, call duration, and bandwidth) did not differ significantly among the groups. It is concluded that dopamine is implicated in production of species-typical 50 kHz calls and that D2-like receptors are likely to be involved in this process. Supported by the Natural Science and Engineering Research Council of Canada.

116.DUAL 5-HT MECHANISMS IN BASOLATERAL AND CENTRAL NUCLEI OF AMYGDALA IN THE REGULATION OF THE DEFENSIVE BEHAVIOR INDUCED BY ELECTRICAL STIMULATION OF THE INFERIOR COLLICULUS. Macedo, C.E.; Castilho, V.M.; Brandão, M.L. Laboratório de Psicobiologia, Faculdade Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo (USP), 14040-901, Ribeirão Preto, SP Brazil. Regulatory mechanisms in the basolateral nucleus of the amygdala (BLA) serves as a filter for unconditioned and conditioned aversive information that ascend to higher structures from the brainstem whereas the central nucleus (CNA) is the main output for the resultant defense reaction. We have shown that neural substrates in the inferior colliculus are activated by threatening stimuli of acoustic nature and have important functional links with the amygdala. In this work we examined the influence of lesions with 5,7- dihydroxytryptamine (DHT) of these nuclei of amygdala on the aversive responses induced by electrical stimulation of the inferior colliculus. Thus, rats were implanted with an electrode in the central nucleus of the inferior colliculus for the determination of the thresholds of alertness, freezing and escape responses. Each rat also bore a cannula implanted in the BLA or CNA for injection of DHT (5.0 μg/0.6 μl). The obtained data show that CNA lesions increase the thresholds of aversive responses whereas BLA lesions decrease the thresholds of these responses. From these evidence it is suggested that defensive behavior induced by activation of the neural substrates of aversion in the inferior colliculus seems to depend on the integrity of the amygdala. BLA regulates the input and CNA functions as the output for these aversive states generated at brainstem level. It is likely that aversive information ascending from the inferior colliculus may receive either inhibitory or excitatory influences of 5-HT mechanisms in the BLA or CNA, respectively.

117.BEHAVIORAL CHARACTERIZATION OF MECP2 MUTANT MICE - A RETT SYNDROME MODEL. Stearns, N.A.; Floerke-Nashner, L.; Berger-Sweeney, J. Dept. Biological Sciences, Wellesley College, Wellesley, MA USA. Rett syndrome (RS), which affects primarily females, is characterized by reduced postnatal head growth; regression of hand use and speech; stereotyped repetitive hand movements; gait apraxia, and severe cognitive deficits. The apparent cause of RS is the mutation of an X-linked gene encoding Mecp2, a gene expression regulatory protein. We characterized behavior in an RS mouse model in which the MECP2 gene is knocked out. Heterozygous MECP2 females were mated to wildtype males, producing offspring in 4 categories: wildtype females, wildtype males, heterozygous females and hemizygous males. Genotypes of the offspring were confirmed by PCR analysis. The offspring were characterized by weighing and observation, a neurological battery, locomotor activity, a 1-day swim maze task, and contextual fear conditioning. By six weeks of age, there was a trend toward

increased body weights in mutants vs. wildtypes. Also, stereotypic movements of the forepaws were noted in some mutant males. Reaching and righting reflexes were normal, but grip strength was reduced in hemizygous males. Mutant mice of both sexes exhibited reduced dark-cycle locomotor activity. The mutants also exhibited impaired swim maze performance vs. controls, however, the data were confounded by motility difficulties in the mutant males. There was a suggestion of heightened fear conditioning in the mutants, though the data were not statistically significant. These data suggest that knocking out the MECP2 gene results in behavioral abnormalities that resemble some of those noted in individuals with RS. Further testing will be necessary to characterize the nature of any cognitive deficits.

118.FEAR POTENTIATED STARTLE IS MAINTAINED IN CHRONICALLY STRESSED RATS. Heldt, S.A.; Gouilland, A.M.; & Matuszewich, L. Department of Psychology, Northern Illinois University, DeKalb, IL 60115 USA. Exposure to chronic unpredictable stress may be a potentially useful animal model of post-traumatic stress disorder (PTSD) (Foe et al., 1992). Rats pre-exposed to stress may be more vulnerable to the effects of an acute traumatic event, such as the foot shock used in fear conditioning. Previous research has used the fear potentiated startle paradigm for fear conditioning in rodents and as a model of the arousal symptoms associated with PTSD (Morgan et al., 1995). The current study investigated the persistence of fear potentiated startle following exposure to chronic, variate stress. Male Sprague-Dawley rats were exposed to 10 days of the following unpredictable stressors: cold room (4°C) for 50 min, shaker table for 60 min, swimming for 3 min, alterations in light cycle, restraint stress for 60 min, isolation housing, and food and water deprivation for 13 hours. The stressors were presented at variable times, 2-3 times during the 10 days. On the 11th day, stressed and non-stressed rats were given training that consisted of 5 trials of noise and shock pairings. Fear potentiated startle was assessed one hour, 3 days and 7 days after training. In the absence of the noise conditioned stimulus, startle responses did not differ between the two groups. However, the magnitude of fear potentiated startle declined over time in non-stressed control rats, indicative of extinction ($p<.01$). In contrast, stressed rats maintained their potentiated startle response 7 days after training. These findings suggest that the stressed rats fail to extinguish their startle response to the conditioned stimulus and may be an appropriate model for PTSD. Current studies are investigating the neurochemical alterations in the stressed rats that may contribute to the maintenance of fear potentiated startle.

119.EFFECTS OF RESTRAINT STRESS DURING PREGNANCY ON COPING STRATEGIES IN LACTATING DAMS. Darnaudéry M. ; Del-Favero F. ; Maccari S. University of Lille 1, Villeneuve d'Ascq, FRANCE. Prenatal and postnatal environments exert complex and long-term influences on the development of individuals. In rat, prenatal stress has been demonstrated to induce several permanent behavioural disorders under stressful conditions, including enhanced anxiety and depressive-like behaviour. While the impact of chronic stress applied to pregnant rodents has been well documented on offspring's behaviour, few studies have explored their effects on the behaviour of stressed dams. Aim of this study was therefore to characterise in rats, the influence of chronic restraint stress applied during gestation on mother behavioural response. Two groups of parameters were investigated: the first one was relative to maternal environment quality (mother's body weight gain, nest building quality, pup care and food hoarding behaviour), and the other assessed mother's ability to cope with stressful situations (reactivity to novelty and to a male intruder). During pregnancy we observed that chronic prepartum stress impaired female's body weight gain, nest quality and increased their anxiety in the black-white box test. Stressed dams showed behavioural disturbances also after parturition. In fact, food-hoarding behaviour was decreased; when exposed with their pups to stressful situations, they showed a decrease of maternal aggression towards an intruder and an increase of self-directed behaviours. In conclusion, our results show that chronic restraint stress during pregnancy affects female's behaviour both in prepartum and postpartum periods. It is important to further investigate how such disturbances of mother behaviour can affect the later vulnerability of the stressed offspring.

120.REGIONAL-SPECIFIC CHANGES IN CATECHOLAMINE INNERVATION FOLLOWING MATERNAL SEPARATION Teicher, M.H.; LeBlanc, C.; Andersen, S.L.. Dept. of Psychiatry. Harvard Medical School and McLean Hospital, Belmont, MA 02478 USA. Maternal separation is a species-relevant stressor and has been used as an animal model to enhance our understanding about the effects of early life stress on brain development. Studies have shown that early stress dramatically reduces the size and function of the hippocampus and the nucleus accumbens. In this study, rats were assigned to three conditions: 1) isolated from the dam for 4 hours a day between postnatal (P) days 2-20 (ISO); 2) handled briefly each day and returned to the dam (MOM); or 3) left undisturbed until sacrifice (COLONY). Subjects were then perfused at P25, 40, 60, 80, and 100 days of age and the striatum, nucleus accumbens, prefrontal cortex, and cerebellum were immunolabeled with an antibody to tyrosine hydroxylase (TH) to assess catecholamine innervation patterns. All regions demonstrated an overproduction and elimination of TH immunopositive neurons across the periadolescent period in the COLONY group. However, maternal separation influenced this process in a regionally-selective manner. No effect of Condition was observed in the striatum or the prefrontal cortex. In contrast, TH immunoreactivity was reduced in the nucleus accumbens shell and core in the ISO condition ($F2,202= 2.86$ and 2.98, $p<0.05$). Reduced TH levels were also observed with subregional specificity within the posterior lobes of the cerebellum. While lobes IX and X both overproduced and eliminated TH neurons during periadolescence, lobe X was significantly reduced in the males of the ISO group (Group X Sex:$F2,155=3.01$, $p<0.05$). These data are consistent with a reduction in the cerebellar vermis due to early childhood abuse (Anderson et al 2002). The cerebellum plays an important role in the manifestation of a number of psychiatric illnesses, including abuse, schizophrenia, depression, and ADHD. These data provide additional evidence that this brain region is vulnerable to postnatal stress that in turn, alters its development.

121.MATERNAL SEPARATION DOES NOT ALTER STRIATAL RESPONSIVENESS Andersen, S.L.; Thompson, A.; Teicher, M.H. Dept. of Psychiatry. Harvard Medical School and McLean Hospital, Belmont, MA 02478 USA.. Tourettes Syndrome (TS) begins in childhood and is characterized by excessive motor disturbances and vocal tics. The motor symptoms of TS vary across development, becoming worse with puberty and receding in 90% of affected patients in adulthood. This waxing and waning of symptoms follows the timecourse of D2 receptor density in the striatum, where an overexpression of D2 receptors is observed during adolescence that declines by 40% by adulthood. Furthermore, Wolf et al (1997) observed a 0.99 correlation between D2 receptors in twins discordant for TS severity. Given these observations, we wanted to determine if stress, a factor known to exacerbate TS symptoms, would alter D2 receptor density in the striatum during puberty and endure into adulthood. We used maternal separation as a species-relevant stressor. Rats were either isolated from the dam for 4 hours a day between postnatal (P) days 2-20 (ISO condition) or left undisturbed until sacrifice (COLONY condition). Subjects were tested for responsiveness to the mixed D1/D2 dopamine receptor agonist apomorphine (1 mg/kg,ip) to determine if early stress increased dopamine sensitivity. Surprisingly, no differences were observed in locomotor responsiveness to apomorphine, suggesting that pre-exposure to chronic stress does not increase the risk for the worsening of symptoms. A separate group of subjects were sacrificed at 40 or 80 days of age for autoradiography. Analysis of receptor density also did not reveal any significant differences in striatal D2 receptor density between the ISO and COLONY conditions. However, a significant Condition X Sex interaction ($F_{1,50}=6.24$, $p<0.05$) was observed for striatal D1 receptors. D1 receptor density was significantly reduced in males, but increased in females in the ISO condition. These data suggest that early life stress does not influence striatal D2 receptor density and therefore does not impose an increased risk for the exacerbation or perseverance of TS symptoms.

122.TMT AND CAT FECES FAIL TO SUPPORT CONDITIONING OF DEFENSIVE BEHAVIORS Blanchard, D.C. & Blanchard, R.J. Division of Neurosciences, University of Hawaii at Manoa, Honolulu, HI 96822. High levels of trimethylthiazoline (TMT), a derivative of fox feces, fail to support aversive conditioning as a UCS. As high levels of this repugnant odor might have produced illness or guarding that interfered with conditioning, we evaluated very low TMT levels (.01 - .1 µl) in a paradigm previously shown to produce conditioning with cat fur/skin odor. While each level produced defensiveness to the odor itself, none resulted in a significant change in behavior the following day to the same context and cue stimuli when the odor was not present. To determine if this inability to support conditioning is related to the type of predator odor, Exp. 2 evaluated cat urine, cat feces, and cat fur/skin odor against a no odor control in the same situation. Cat feces and cat fur/skin odors elicited virtually identical patterns of change in defensive behaviors during exposure, but only the cat fur/skin group showed significant differences on a conditioning day for each of the defensive behaviors elicited during exposure. The cat feces group showed no conditioning test day differences on any measure. These results suggest that failure of TMT to support conditioning may relate to the type of predator odor (feces) rather than 1) the amount used; 2) the species of predator (fox vs. cat); or 3) the possibility that TMT omits important odor components that are present in natural feces. Predator feces may be less effective as a UCS because they are poorly predictive of the actual presence of the predator, a possibility that suggests the need for a re-evaluation of the functions of the UCS in aversive conditioning.

123.PSYCHOLOGICAL AND PHYSIOLOGICAL REACTIONS TO ANXIETY INDUCED BY THE STROOP COLOR-WORD TEST IN HEALTHY VOLUNTEERS – EFFECTS OF DIAZEPAM. Teixeira Silva, F.; Bordini, G.; Leite, J.R. Department of Psychobiology, Universidade Federal de São Paulo, São Paulo, Brazil. From among the few human experimental models that can be used to predict the clinical activity of new anxiolytic drugs, the Video Recorded Stroop Color-Word Test (VRSCWT), which uses subjective scales to evaluate anxious states, is noteworthy. However, considering that the choice of treatment for anxiety disorders is heavily dependent on the level of somatic symptomatology, a quantitative evaluation of the physiological alterations elicited by the anxiogenic situation of the VRSCWT would also be of great interest. In the present study, 36 healthy male and female volunteers were submitted to either the VRSCWT or to a non-anxiogenic test. The results showed that, as well as a sensation of anxiety, the VRSCWT elicited increases in heart rate and gastrocnemius tension. Subsequently, a further 48 healthy men and women were randomly assigned to three treatments: placebo, 5mg and 10mg of diazepam, and were submitted to the VRSCWT. The results showed that in men diazepam blocked the feeling of anxiety elicited by the test, although it did not prevent the physiological alterations. In women there was no response to the anxiolytic action of the drug. Taken as whole, these results suggest that the VRSCWT is an efficient method of inducing anxiety experimentally. It is able to elicit observable psychological and physiological alterations and can detect the blocking, by an anxiolytic, of the feelings of anxiety in healthy men. Furthermore, the results suggest that the neural pathways for the control of the psychological and physiological manifestations of anxiety might be separate. This study also draws attention to the fact that gender is an important variable in the evaluation of anxiolytic drugs.

124.INFLUENCE OF SAMe ON THE BRAIN POLYAMINE LEVELS AND NMDA RECEPTOR EXPRESSION IN AN ANIMAL MODEL OF DEPRESSION. Saltini, S.; Genedani, S.; Benelli, A.; Filaferro, M.; Ottani, A.; Bertolini, A. Dept. of Biomedical Sciences, Section of Pharmacology, University of Modena and Reggio Emilia, Italy. Two new hypotheses on the pathophysiology of depression have been recently put forward: the neurotrophic hypothesis, linked to the expression of neurotrophic proteins, and the neuronal plasticity hypothesis, linked to the activity of NMDA receptors. The involvement of these systems in the therapeutic activity of antidepressant drugs have been experimentally demonstrated. It is well known that the ODC/polyamine system is involved both in synaptic plasticity and in neurogenesis. This evidence prompted us to suppose a possible involvement of this system in both the development of depression and the mechanism of action of antidepressant drugs. Using the “chronic unpredictable mild stress” as an animal model of depression, we studied the possible modifications of brain polyamine levels in such condition. Three weeks of stress produced a significant decrease ($p<0.01$) of all the three polyamines (putrescine from 51.00±5.10 to 34.88±4.53, spermidine from 300.26±30.02 to 158.47±20.54 and

spermine from 156.15±15.61 to 81.73±10.62) in the hippocampus and of putrescine (from 66.00±8.58 to 35.00±6.3) in the nucleus accumbens. S-adenosyl-L-methionine (SAMe), -a molecule essential for the synthesis of polyamines, and endowed with antidepressant activity- at the antidepressant dose of 300mg/kg i.m., daily for 7 days, significantly ($p<0.01$) increased the content of both spermidine (from 158.47±20.54 to 219.24±17.53) and spermine (from 81.73±10.62 to 102.27±8.18) in the hippocampus, and completely restored to normal the content of putrescine (from 35.00±6.3 to 68.00±5.44; $p<0.01$) in the nucleus accumbens. On the other hand, no modification of the content of any polyamine in the frontal cortex was observed. The expression of NMDA receptors, explored by in situ hybridization, in the same brain areas has also been studied.

125.EFFECTS OF MIDAZOLAM IN THE ELEVATED T-MAZE. Cruz-Morales, S.; Saldívar, N.; Gómez-Romero, J.; González-López, M. Lab. of Psychopharmacology, FES-IZTACALA, UNAM, MEXICO. P.O. Box 314, Tlalnepantla, Edo. Mex. 54030. The benzodiazepines are used for the treatment of anxiety, and amnesic effects have been reported after their administration. Because an overlapping between memory and anxiety could be present, we evaluated the effects of the administration of midazolam on avoidance and escape responses in rats exposed to the T-maze. Male Wistar rats (250-300g) assigned to independent groups were treated with saline or midazolam (1, 2 mg/kg, ip) 15 min before been exposed to the T-maze. The T-maze consisted of an enclosed arm and two open arms elevated 50 cm above the ground. The first day the subjects were placed in the enclosed arm and the time remaining in this arm was registered (Baseline), two subsequent trials were given. After avoidance trials, the subjects were placed in the open arm and the latency to escape was recorded. After 24 hrs the latencies of avoidance and escape were recorded without administering the drug. Significant effects for trials were observed in avoidance latencies suggesting acquisition and consolidation of this response, midazolam (2 mg/kg) significantly reduced the avoidance latency evaluated 24 hrs later. For escape latencies significant effects were detected for drug, trials and the interaction. The subjects treated with midazolam showed higher latencies in the first escape, suggesting an anxiolytic effect, and no differences were observed in escape 2. These results suggests that midazolam affects both memory and anxiety processes.

126.Withdrawn.

127.Withdrawn.

128.IN VITRO TISSUE SLICE INDICATORS OF NEUROBEHAVIORAL COMPETENCE. Rossi III, J.; McInturf, S.; McDougle, F; Ritchie, G.D.; Bekkeda, M.Y.V. Neurobehavioral Effects Laboratory (NHRC/TD), Wright-Patterson AFB, OH, 45433-7903 USA. We are currently developing an in vitro system that will predict behavioral change resulting as a consequence of exposure to toxicants and compounds of pharmaceutical interest. This system incorporates state-of-the-art microelectrode array technology to probe brain slices for electrophysiological patterns induced by various pharmacological agents and toxicants. We have chosen a strategy which implements a system using 7 anatomically distinct brain slice preparations incorporating known neural circuits that underlie various subunits of neurobehavioral/cognitive competence. The final product will be a modeling system that will be capable of assessing compounds and classify-ing them for likely neuropharmacological activity through comparison to signature profiles we are currently compiling. Once this library of signature profiles has been established we can compare the 3-D response patterns obtained from agents to be screened to the profile library to predict therapeutic or toxicological efficacy, selectivity and potency. In addition, the completed system should be capable of prediction of perturbations in neurobehavioral per-formance based on the correlative relationships with behavioral signatures determined using the same compounds with the whole animal Neurobehavioral Toxicology Assessment Battery (NTAB). We have completed several pharmacological dose response studies using hippocampus and cerebellum slices, and have recently begun the development of a model for epilepsy based on the kindled amygdala slice. Data are presented for preliminary work with the convulsants trimethylolpropane phosphate (TMPP) and pentylenetetrazole, and ethanol.

129.PARACHLOROAMPHETAMINE TREATMENT INDUCES ALTERATIONS ON THE NITRIC OXIDE SYSTEM. Tagliaferro P, Ramos AJ, López-Costa JJ, Brusco A. Instituto de Biología Celular, Fac. Medicina. Universidad de Buenos Aires. Paraguay 2155 (1121) Argentina. Serotonin (5HT) is a neurotransmitter expressed early during development. Parachloroamphetamine (PCA) damages ascending 5HT projections, we had previously found that neonatal PCA treatment results in striatal and cortical 5HT denervation in rat pups. NO also plays a role in neuronal development. Morphologic and functional relationship between NO and 5HT has been demonstrated and alterations of the nitrergic system were observed after a 5HT depletion. It has been hypothesized that NO may be related with the neuronal damage produced by some 5HT neurotoxins. In order to study the effects of a 5HT depletion on NO system during postnatal development, Wistar rat pups were injected subcutaneously twice on P3 and P4 (P0=day of birth) with PCA (15 mg/kg each dose). Control rats received the same volume of sterile saline solution. Neuronal nitric oxide synthase (nNOS) immunoreactivity and NADPH diaphorase reactivity were performed on brain sections from P5, P7, P12, P19, P29 and P62 animals. There was no difference between the expression pattern of NADPH-d activity and nNOS immunoreactivity in both, control and treated animals. After the treatment, we found a higher NADPH-d staining from PND5 to PND19, which would be indicating an increase in the NOS activity. The intensity of nNOS immunostaining was also increased after the treatment at the same ages. Interestingly, NADPH-d staining and nNOS immunostaining were higher when 5HT denervation was more evident. From PND19 the expression of both NO-neuronal markers in the treated animals was similar to the control ones. Supported by grants: UBACYT and Ministerio de Salud.

130.SELECTIVE BLOCKADE OF NEURAL NITRIC OXIDE SYNTHASE (nNOS)INTO THE NEOSTRIATUM IMPAIRS CONSOLIDATION AND RETRIEVAL OF INHIBITORY AVOIDANCE LEARNING. González-Sánchez H.; Roldán G. Dept. of Physiology, Fac. of Medicine, National University of Mexico, Mexico City. The blockade of nitric oxide (NO) production by systemic or intracerebral administration of non-selective NO synthase inhibitors produces amnesic effects in several types of learning tasks. In the present study we evaluated the contribution of the nNOS isoform in inhibitory avoidance memory consolidation and retrieval. Male Wistar rats were implanted with bilateral guide cannulae aimed at the dorsal neostritum. one week later, rats were trained in a single-trial, step-though inhibitory avoidance task, and were given infusions of 7-nitroindazole (2, 4, or 8 □g/side) or vehicle, immediately after training (consolidation), or 2 min before retention testing (retrieval). A dose-related impairment of the task performance was found in the drug-treated rats. The results suggests that nNOS into the neostriatum plays a critical role in both, memory consolidation and retrieval of inhibitory avoidance. Supported by DGAPA grant IN-216999.

131.THE BEHAVIOR GENE *YELLOW* IS DOWNSTREAM OF *FRUITLESS* IN THE *DROSOPHILA* DEVELOPING BRAIN. Radovic, A.[1]; Wittkopp, P.J.[2]; Long, A.D.[3]; Drapeau, M.D.[3]; [1]Department of Developmental and Cell Biology, University of California – Irvine, [2]Howard Hughes Medical Institute, Laboratory of Molecular Biology, University of Wisconsin – Madison, [3]Department of Ecology and Evolutionary Biology, University of California – Irvine. The central nervous system-limited *Drosophila melanogaster* gene *fruitless* (*fru*), which encodes a putative Zn-finger transcription factor, regulates an undefined genetic hierarchy specifying proper development of adult male sexual behaviors. Here we demonstrate that the male sexual behavior gene *yellow* (*y*) is downstream of the male-specific FRU isoform BM ($FRU^{M\{BM\}}$) in late-larval neuroblasts. Both *fru* and *y* mutants are known to reduce levels of wing extension during male courtship, and these $FRU^{M\{BM\}}$-Y-expressing neuroblasts are in the general region of the brain that controls the development of wing extension. Misexpression experiments show that $FRU^{M\{BM\}}$ presence is sufficient for Y, linking the *D. melanogaster* sex determination/differentiation hierarchy to a downstream gene necessary for a specific subset of male courtship behavior.

132.DISSOCIATION OF SPATIAL AND NON-SPATIAL BEHAVIORAL COMPONENTS IN TRANSGENIC MICE OVEREXPRESSING A MUTANT FORM OF THE FE65 PROTEIN. D. Viggiano1, L.A. Ruocco2, A. Gallo2, N. Zambrano3, T. Russo3 and A.G. Sadile2. Inst. Human Anatomy1, Lab. Neurophysiol., Behav. & Neural Networks, Dept. Exptl. Medicine, II Univ. Naples2, 3Dept. Biochemistry and Medical Biotechnologies, Univ. Naples "Federico II", Naples, Italy. The FE65 protein is a cytosolic ligand of the Alzheimer's ß-amyloid precursor protein APP. 6- and 18- mos old mice overexpressing either the wild-type FE65 protein or a mutant form of FE65 unable to interact with APP and 6mos old control mice (BDF1) were subjected to various behavioral tests: the spatial novelty Làt-maze and the elevated plus-maze. Moreover, 18-mos-old mice were also tested in a 8-arm radial-maze (Olton-maze). The behavior was videotaped and analyzed in a Làt-maze for travelled distance, orienting frequency and scanning duration, or in the Olton-maze for working and reference memory and reward consumption. In the Làt-maze only the 6-mos-old mice overexpressing the mutant form of FE65 showed a 100% increase in travelled distance, but not in orienting frequency, nor in scanning duration. In contrast, the 18-mos-old mice with the mutant FE65 were as active as the other two groups. However, the old mice with the mutant form showed higher running speed, a good working and reference memory in the Olton-maze, but a low reward magnitude. In the elevated plus-maze 6-mos-old mutant mice were more anxious, as they spent most of the time in the protected arms, whereas both wild-type and mutant 18-mos-old transgenic mice were more anxious, compared to controls. These findings reveal that mice overexpressing the mutant, but not the wild-type form of the FE65 protein display age-dependent hyperactivity, anxiety and dissociation between cognitive and non-cognitive behavioral components. (Supported by ISS, special fund Grant).

133.ANALYSIS OF BEHAVIOURAL ITEMS TEMPORALLY RELATED WITH ULTRASONIC VOCALISATIONS IN THE INFANT MOUSE (MUS MUSCULUS). Branchi, I., Santucci, D., †Puopolo, M., Alleva, E. Section of Behavioural Pathophyisiology, †Section of Comparative Psychology, Laboratory of Pathophysiology, Istituto Superiore di Sanità, 00161, Roma, Italy. One of the most used approaches to investigate emotional responses in mice during early ontogeny is the analysis of the ultrasonic vocalisations (USVs). The characterisation of pup behaviour during calling could provide useful information to perform a more accurate analysis of this phenomenon. Moreover, this approach could improve the power of ultrasonic vocalisation analysis in revealing subtle and limited changes during emotional development. To this purpose, we performed an analysis of the temporal sequence of behaviours shown by mouse pups (postnatal day 7, the peak-emission day for CD-1 mouse strain) while isolated from both dam and litter to investigate the sequences with which behavioural items and ultrasound emissions occur. The four behavioural items that occurred more often were analysed: locomotion, head rising, wall climbing, and lying still. The variables considered were: probability of emitting, latency to emit, probability of interrupting, and duration of USV. The results showed a marked emission of USVs in conjunction with behavioural items involving movement, and evidenced that the different variables analysed are differently modulated within each behavioural items. These findings provide an useful key to better understand the ultrasonic vocalisation per se and as a measure of emotional development in the mouse. Furthermore, USV production will be discussed in terms of the ecology of mother-offspring relationship in rodents, since the data support the hypothesis of the communicative role of these vocalisations.

134.CHARACTERISATION OF MOTION SICKNESS IN THE MOUSE. Santucci, D.; Francia, N.; Aloe*, L.; Alleva, E. of Behavioural Pathophysiology Section, Laboratorio di Fisiopatologia di Organo e di Sistema, Istituto Superiore di Sanità, Viale Regina Elena 299, I-00161 Roma (Italy) and *Istituto di Neurobiologia, Consiglio Nazionale delle Ricerche, Viale Carlo Marx 15, I-00137 Roma (Italy). Motion sickness (MS) is an illness triggered by a "sensory conflict" involving the vestibular system, occurring when sensory inputs regarding body position in

space are contradictory or different from those predicted from experience. In a large variety of animal species MS is associated with the occurrence of an emetic response. In rat, a species incapable of emetic response, pica behaviour (the consumption of non-nutritive substances, such as kaolin, sawdust and wood) has been considered an appropriate index of MS. Our studies were aimed to characterise MS in CD-1 mice and to evaluate possible age-related differences in the susceptibility to this syndrome during late postnatal development in this rodent specie. The occurrence of MS was evaluated in both male and female mice on postnatal day (PND) 28, 42, 60 and at adulthood. The animals were exposed to a rotation-induced change in the vestibular inputs using a custom-made centrifuge device. Pica behaviour (measured through kaolin consumption) and ethological-type scoring of different items were used to evaluate the behavioural response before, during, and after rotation. Moreover, in order to correlate behavioural changes with alterations in central levels of neurotrophins, brain levels of Nerve Growth Factor (NGF) and Brain Derived Nerurotrophic Factor (BDNF) were assessed following 1h of rotation.

135.MODULATION OF APPROACH-AVOIDANCE BEHAVIOR IN A NOVEL OBJECT EXPLORATION PARADIGM IN MICE. Powell, S.B., Paulus, M.P., Geyer, M.A. Dept. of Psychiatry, UCSD, La Jolla, CA 92093. Approach and avoidance are critical components of novelty seeking, which plays an important role in susceptibility to drug abuse and aspects of cognition. This experiment was designed to examine the effects of handling and duration of exposure to a novel environment on various measures of novel object exploration in mice. Mice were either handled by the experimenter or received minimal exposure to human contact. Additionally, some groups of mice were exposed to the open field for either 2 or 3 days and thus had the opportunity to explore the novel object in the center of the enclosure once or twice, respectively. A total of 40 male C57/Bl6 mice were used in this study. This study yielded three main results. First, handled mice explored the novel object more than non-handled mice as measured by the time spent in the vicinity of the novel object. Second, on their second exposure to the novel object, handled mice showed less exploration of the object relative to the first exposure. Third, non-handled mice with prior exposure to the novel object showed more object exploration compared to non-handled mice without previous object exposure. These results are consistent with the hypothesis that a certain degree of familiarity with the object or with the experimenter decreases avoidance and increases exploration of novel stimuli. In contrast, repeated exposure to the novel object decreases exploration and is consistent with the hypothesis that novelty is a critical factor for approach behavior. In combination, these results show that the approach and avoidance dimension of novelty seeking can be experimentally manipulated and may be used to examine the effects of drugs of abuse.

136.INCREASED IMPULSIVITY AND LOW AMPHETAMINE-INDUCED REWARD AS RISK FACTORS FOR DRUG ABUSE DURING ADOLESCENCE. Adriani, W. & Laviola, G. Sect. of Behavioural Pathophysiology, Lab FOS, Istituto Superiore di Sanità, I-00161 Roma, Italy. Email: adriani @ iss.it or laviola @ iss.it. Human adolescents use a number of psychoactive agents. Such age-related willingness may be explained by an impulsive behavioral trait and/or age-related peculiarities in the rewarding effects of psychoactive agents. To study these variables, periadolescent (PND 30 to 45) and adult (PND > 60) mice were compared for levels of impulsivity and d-amphetamine-induced place conditioning. Exp. 1: Food-deprived mice were tested in operant chambers provided with two nose-poking holes. Nose-poking in one hole (H1) resulted in the immediate delivery of a small amount of food, whereas nose-poking in the other hole (H5) resulted in the delivery of a larger amount of food after a delay. The delay increased progressively each day (0 to100 sec). As expected, all animals showed a shift in preference from the large (H5) to the immediate (H1) reinforcer as far as delay increased. Adolescent mice showed as a whole enhanced preference for the immediate reinforcer, suggesting an elevated intolerance to reward delay (i.e. increased impulsivity). Adolescent mice also exhibited elevated demanding for the immediate reinforcer during delays, when nose-poking response was inadequate, thus suggesting increased restlessness. Exp. 2: AMPH administration (0, 1, 2, 3.3 or 5 mg/kg once/day for three days) was paired with one compartment of the apparatus, saline with the other compartment. Subjects were then given free access to the whole apparatus in drug-free condition. When compared to adults, the magnitude of place conditioning was significantly less marked in adolescent mice, thus suggesting lower rewarding effects of amphetamine. CONCLUSION - Adolescent mice appear to be more impulsive and restless, being also less sensitive to the immediate rewarding effects of psychostimulants. These behavioral traits have been proposed as risk factors for drug abuse. Interestingly, epidemiological as well as experimental studies on animal models suggest that drug exposure during adolescence may sensitize neurobehavioral systems responsible for vulnerability to addiction.

137.DO CB1 AGONISTS AFFECT LONG-TERM POTENTIATION? Diana, G.; Pieri, M.; Valentini G. Pharmacology, Istituto Superiore di Sanità, Roma, Italy. Marijuana is thought to affect memory by an action at the CB1 receptor site. It has been shown that CB1 agonists impair hippocampal Long-Term Potentiation (LTP), which is widely regarded as a cellular model of learning. However, molecules in this class are also able to reduce hippocampal neurotransmission. To separate the two activities, we studied the effects of Win 55,212-2, a potent and selective CB1 agonist, on responses evoked by two independent pathways, one of which was potentiated with a tetanic stimulation. This is possible thanks to an intrinsic property of LTP, i.e. input specificity. The experiments were performed on 400 ìm thick transverse hippocampal slices prepared from 3-month old male Sprague Dawley rats (Charles River Italia, Calco, Lecco). Rats were anesthetized with urethane 1.5 g/kg and killed by decapitation. The brain was rapidly removed and hippocampal slices were prepared with a McIllwain tissue chopper. The slices were perfused at 24° with artificial cerebral spinal fluid and DMSO (0.1% in volume) in a submerged type recording chamber. Potentials were recorded using a glass microelectrode (filled with 0.5M Na-acetate, 1.5-2 MΩ) placed into the pyramidal cell body layer of CA1 area. Two monopolar stimulating electrodes were placed in the stratum radiatum. Field potentials were evoked by alternate stimulation of two afferent pathways (0.0166 Hz, squared waves, 60 ìs, constant current, 18-100 ìA). The results of the study show the following: a) Win 55,212-2 induces a decrease of EPSP slope ($F=2.38$, $df=8$, $p=0.026$ by repeated measurement ANCOVA). The depression is of similar magnitude in both control and potentiated P1 pathway ($F=0.122$, $df=1$, $p=0.736$ by repeated measurement

ANCOVA), thus suggesting a lack of effect on LTP maintenance; b) the drug increases Post-Tetanic Potentiation ($t=2.92$, $p=0.043$ at 30 s post tetanus by paired t test); c) on condition that the responses are compared to those obtained by activation of the unpotentiated pathway, Win 55,212-2 does not change LTP ($F=0.029$, $df=1$, $p<0.869$ at 25 min post tetanus by repeated measurement ANCOVA). The study suggests that marijuana does not cause amnesia by affecting activity dependent changes in synaptic efficacy.

Saturday, June 22

8:30-10:30 Symposium IV: Stress effects on limbic function and behavior

NEUROPLASTICITY IN LIMBIC CIRCUITS IN RESPONSE TO SEVERE STRESS Adamec, R.; Blundell, J., Dept. of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada, A1B3X9 Predator stress increases anxiety like behavior (ALB) up to 3 weeks after the exposure. Initiation, but not maintenance of increases in ALB and acoustic startle depend on NMDA receptors, consistent with an LTP-like mechanism. Predator stress appears to selectively potentiate and depotentiate evoked responses in several afferent and efferent amygdala pathways. Path analyses suggest that stress induced changes in afferent transmission to the basolateral amygdala (BLA) and efferent transmission from BLA to periacqueductal gray (PAG) act cooperatively to alter ALB in the plus maze. In contrast neither pathway contributes to changes in the light/dark box or startle tests of ALB. Finally degree of LTP in right hemisphere pathways and degree of reduction of transmission in left hemisphere together predict anxiogenic-like effects on behavior. These data suggest that changes in particular emotional behaviors in rats depend upon changes in neural transmission in particular limbic pathways in particular hemispheres, as has been found in cats. Study of stress effects on pCREB expression suggest initiation of neuroplastic changes involve the pCREB cascade.

SOCIAL STRESS OF AGONISTIC INTERACTION: THE VISIBLE BURROW SYSTEM. R.J. Blanchard and D.C. Blanchard, University of Hawaii, Honolulu, HI 96922. Different stressors may produce difference physiological and behavioral consequences. This emphasizes the need for models that utilize the stressors that have been crucial during evolution, in order to understand the stress-mediating and stress-impacting systems that have evolved in response to these crises. The Visible Burrow System (VBS) was designed to provide a seminatural and desirable habitat for fossorial rodents. In VBS, males of mixed-sex rat or mouse groups show high levels of agonistic behavior without any further experimental manipulation. Fighting among male rats results in dominance hierarchies that produce chronic social stress for subordinates; this fighting is so fierce in mice as to make the VBS unsuitable for use with mixed-sex groups. This presentation will outline a number of physiological and behavioral responses of subordinate males in VBS. Both the brain and behavioral changes in these animals are similar to many of the markers and symptoms of depression. Dominant males and females in the VBS also show high levels of agonistic behavior but the behavior and brain changes of these are less similar to those of depression. Female aggression occurs largely in the context of fending off sexual advances, and involves little tissue damage or subsequent avoidance on the part of the female. While dominants fight more than other colony males, and may be wounded, the fighting of these animals appears to be positively reinforcing, leading to further attack rather than avoidance of other colony males.

HEMISPHERIC, SEX-RELATED LATERALITY IN AMYGDALA INVOLVEMENT IN THE STORAGE OF MEMORY FOR EMOTIONALLY AROUSING EVENTS. Larry Cahill, Department of Neurobiology and Behavior, Center for the Neurobiology of Learning and Memory, University of California, Irvine, 92697-3800, USA. Converging evidence from animal and human subject studies suggests that the amygdala is critical for enhanced long-term memory associated with emotionally arousing (sympathetic nervous system activating) events. Its role in memory clearly extends beyond any isolated domain of emotion, such as fear. Rather, the degree of arousal associated with a learning situation seems the key determinant of amygdala participation in memory for that situation. Recent human brain imaging studies, while lending new support to this conclusion, also suggest that subject sex significantly impacts amygdala participation in memory for emotionally arousing material. Specifically, evidence suggests a preferential involvement of the right hemisphere amygdala in men, and of the left hemisphere amygdala in women, in memory of emotionally arousing material. Other evidence related to these imaging findings suggests that beta-adrenergic receptor blockade differentially impairs memory for emotionally arousing events in men and women. We suggest that understanding the seemingly interrelated influences of subject sex and cerebral hemisphere represents an important new avenue for investigations of brain mechanisms of emotionally influenced memory.

ENDOCRINE BACKGROUND AND ENDOCRINE RESPONSIVENESS IN BEHAVIORAL AND BRAIN RESPONSES TO STRESS, József Haller, Institute of Experimental Medicine, Budapest. Recent results from our laboratory show that stress not only contributes to the development of anxiety, but also affects pharmacological reactivity. This suggests that both acute and chronic stressors induce changes in brain function that are relevant for the efficacy of anxiolytic drug treatment. Acute stressors applied concomitantly with pharmacological treatments affect both the effects of benzodiazepines and serotonergic anxiolytics. The anxiolytic effects of chlordiazepoxide were not changed by acute stressors, however, the sedative effects of this compound were markedly increased. The anxiolytic effects of buspirone were potently suppressed by glucocorticoids and acute stressors, while the locomotor suppressive effects of this compound were increased. Chronic stressors did not affect the behavioral effects of chlordiazepoxide. In contrast, social isolation as well as repeated social stress markedly increased the anxiolytic efficacy of buspirone, provided that buspirone was administered in a period lacking an acute stressor. Recent results from our group suggests that such phenomena occur also during the pharmacological treatment of anxiety patients in a clinical setting. Thus, the efficacy of pharmacological treatments depends to a large extent on concurrent and/or

previous stressors, and the result of the interaction appears compound specific. These data tentatively suggest that the selection of anxiolytic medication may be improved by taking into account the frequency and temporal distribution of stressful events to which patients are exposed.

STRESS, ANXIETY AND LIMBIC CRH. [1]Merali, Z.; [2]Khan, S.; [2]Michaud, D.; [3]Anisman, H. [1]Institute of Mental Health Research; Psychology and Cellular & Molecular Medicine, University of Ottawa; [2]Psychology, University of Ottawa; [3]Psychology and Neuroscience, Carleton University. The corticotropin-releasing hormone (CRH) system(s) within the brain is (are) activated by stressful stimuli and may contribute to behavioral and emotional responses. The present investigation assessed anxiety-like responses and neurochemical alterations at the central nucleus of the amygdala (CeA) evoked by exposure to an unfamiliar environment. Placement into an unfamiliar environment (new cage) markedly suppressed ingestion of a palatable snack, and this effect was antagonized by diazepam in a dose-dependent fashion. As such, this behavioral change was utilized as an index of anxiety in the rodent. This stressor also stimulated the release of CRH and glutamate at the CeA. However, various CRH antagonists (e.g. ah-CRF, CP-154,526, antisauvagine-30, preproTRH178-199) did not attenuate the behavioral effects elicited by the stressor. As well, central infusions of CRH (2 mg i.c.v.) failed to suppress the amount of snack consumed in the home cage. Despite the potent anxiolytic effect of diazepam in this paradigm, it failed to prevent the stressor-associated release of CRH and glutamate at the CeA. Thus, although exposure to an unfamiliar environment may be interpreted as being "stressful" by neural circuits involving CRH and/or glutamatergic receptors at the CeA, the data do not support the view that activation of CRH and/or glutamate receptors is necessary for the expression of anxiety-like behavioral responses. Rather than provoking anxiety, it is suggested that these systems might serve to draw attention to events or cues of biological significance, including those posing a threat to survival.

STRESS, STRESS HORMONES AND MEMORIES FOR EMOTIONAL EVENTS, LIMBIC SYSTEM INVOLVEMENT. Roozendaal, B.; McGaugh, J.L. Center for the Neurobiology of Learning and Memory, Department of Neurobiology and Behavior, University of California, Irvine, CA 92697-3800, USA. It is well established that glucocorticoid hormones, secreted by the adrenal cortex after a stressful event, influence cognitive performance. Some studies have found glucocorticoid-induced memory enhancement. However, many studies have reported impairing effects of glucocorticoids on memory function. I will review recent findings from our laboratory on the acute effects of glucocorticoids in rats on specific memory phases, i.e., memory consolidation and memory retrieval. The evidence suggests that the consequences of glucocorticoid activation on cognition depend largely on the different memory phases investigated. Post-training activation of glucocorticoid-sensitive pathways involving glucocorticoid receptors enhances memory consolidation in a pattern highly similar to that previously described for adrenal catecholamines. Also, similarly to catecholamine effects on memory consolidation, glucocorticoid influences on memory consolidation depend on noradrenergic activation of the basolateral nucleus of the amygdala and interactions with other brain regions. By contrast, memory retrieval processes are usually impaired with high circulating levels of glucocorticoids or following infusions of glucocorticoid receptor agonists into the hippocampus. The hypothesis is proposed that these apparently dual effects of glucocorticoids on memory consolidation and memory retrieval might be related and that the basolateral nucleus of the amygdala is a key structure in a memory-modulatory system that regulates, in concert with other brain regions, stress and glucocorticoid effects on both memory consolidation and memory retrieval. Research supported by USPHS Research Grant MH12526 from NIMH (JLM).

10:45-12:00 Oral Session 3: Models of disorders and neuroplasticity

CANNABINOID CB1 ANTAGONISTS AMELIORATE FUNCTIONAL DEFICITS IN PARKINSONIAN RATS AFTER EXTENSE BUT NOT MODERATE NIGRAL DEGENERATION. Espejo, E. Fdez.; Caraballo, I.; El Banoua, F.; Flores, J.A. Dept. of Medical Physiology, University of Seville, 41009 Sevilla, Spain. Modulation of endocannabinoid system has been proposed that might be useful in treating Parkinson's disease. Here we show that, in hemiparkinsonian rats, systemic administration of cannabinoid CB1 receptor antagonists (SR141716A and AM251) exerts wide beneficial antiparkinsonian effects (within a limited dose range) after extense but not moderate nigral neuronal loss, as measured through stereology. In search for the basal ganglia locus of action, regional infusions of SR141716A revealed that motor effects were much stronger in the denervated circuit vs the nondenervated one. Local injections into the denervated striatum and corresponding globus pallidus increased basal ganglia output in a dose-dependent manner ($p<0.05$), this effect being linked to stimulation of striatal D1 dopamine receptors and blocking of D2 dopamine receptors. However, intranigral injections reduced basal ganglia output ($p<0.01$), except after intense nigral loss (>94%) where the nigral-mediated inhibitory effect disappeared. Biphasic effects were obtained after subthalamic nucleus injections. These results suggest that: i) systemic administration of cannabinoid CB1 antagonists in parkinsonian rats with moderate nigral degeneration is ineffective because the stimulatory motor effects mostly mediated by striatopallidal neurons are antagonised by nigral activity, and ii) CB1 antagonists exert antiparkinsonian effects after extense nigral degeneration because nigral-mediated inhibition disappeared and basal ganglia output is then enhanced. Cannabinoid CB1 receptor antagonists, unlike CB1 receptor agonists, lack psychoactive effects, and they could be of therapeutic value in the control of symptoms of advanced Parkinson's disease in humans, where extense nigral degeneration is a hallmark. (Study supported by Plan Andaluz de Investigacion, Spanish Ministerio de Educacion and Laboratorios Dr. Esteve)

AGING OF THE BASAL FOREBRAIN CORTICOPETAL CHOLINERGIC SYSTEM: INTERACTIONS BETWEEN THE EFFECTS OF AGE AND PRIOR LOSS OF CORTICAL CHOLINEGIC INPUTS ON CORTICAL ACH EFFLUX AND ATTENTIONAL PERFORMANCE. Sarter, M.; Bruno, J.P.; Burk, J.A.; Herzog, C.D.; Nowak, K.A. Dept. of Psychology and Neuroscience Program. The Ohio State University, Columbus, OH 43210 USA. Although some studies have suggested that subgroups of aged and behaviorally impaired subjects exhibit significant changes in the cortical cholinergic input system, chronological age per se does not reliably predict such changes, particularly not with respect to in vivo measures of extracellular cortical acetylcholine (ACh) levels. Our research is guided by the general assumption that the demonstration of robust age-related changes in the cortical cholinergic input system, and in the attentional abilities mediated via this system, depend on interactions between prior pathological events affecting this system and the aging process. Accordingly, data from our lab demonstrated that activation of a diminished cortical cholinergic input system, indicated by increases in cortical ACh efflux, is attenuated in aged rats. As cortical cholinergic inputs have been extensively demonstrated to mediate attentional performance, a longitudinal study assessed the attentional performance of rats with partial loss of cortical cholinergic inputs. The degree of the 192 IgG-saporin-induced loss of cortical cholinergic inputs was limited to ensure that the lesioned animals' immediate post-lesion performance was identical to sham-lesioned controls. All animals were trained/tested continuously until the age of 36 months. Lesioned animals' performance did not dissociate from the control until the age of 31 months. Thereafter, lesioned animals exhibited a specific impairment in attentional performance. While these data support the general hypothesis that aging of the basal forebrain cholinergic system interacts with pre-existing loss of cholinergic neurons, the aging process that reveals the consequences of such pathology remains unsettled. Our recent data have suggested that the local cortical GABAergic regulation of ACh efflux may be exacerbated by the aging process. We speculate that in aged animals with partial loss of cortical cholinergic inputs, such enhanced inhibitory regulation of cortical ACh efflux further limits the degree to which cortical cholinergic inputs can be activated, thereby mediating the cognitive decline occurring in such animals as they age. Collectively, these data may contribute to the determination of the neuronal mechanisms that mediate the enormous differences between individual subjects' age-related cognitive capacities. Supported by PHS Grant AG10173.

DIFFERENTIAL AUTISM-LIKE NEURODEVELOPMENTAL DAMAGE IN "VULNERABLE" FISHER344 RATS AND "RESISTANT" LEWIS RATS. Pletnikov, M.; Dietz, D.; Vogel, M.; Moran, T.H.; Carbone, K. Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21205, MPRC, University of Maryland, Baltimore, MD 21208. Neonatal Borna disease infection (BDV), as an experimental teratogen, produces selective neuroanatomical, neurochemcal, neuroimmunological and behavioral abnormalities similar to the symptoms of autism. We evaluated BDV-induced neurodevelopmental damage in two inbred rat strains, Fisher344 and Lewis, characterized by opposite responsivity to environmental insults. Despite similar viral replication and weight gain inhibition, neonatal BDV infection produced greater thinning of the neocortex in Fisher344 rats compared to Lewis rats at day 30 and 120 post infection (p.i.), while degeneration of the dentate gyrus of the hippocampus and hypoplasia of the cerebellum were similar in the two rat strains at day 30 and 120 p.i. Greater virus-associated up-regulation of serotonin (5-HT) tissue contents and densities of postsynaptic 5-HT1a and 5-HT2a receptors were observed in Fisher344 rats compared to Lewis rats at day 14 p.i., followed by BDV-associated decrease in receptor density in both rat strains. BDV-associated alterations in dopamine neurotransmission were predominantly found in Fisher344. Virus-associated monoamine disturbances might explain strain-related impairments of prepulse inhibition of the acoustic startle and hyper-reactivity to novelty as well as differential sensitivity to 5-HT compounds. The present findings emphasize the utility of the BDV model for studying the pathogenic events leading to varying disease outcomes and responses to treatment in animals with different vulnerability to environmental teratogens. Supported by MH-48948.

BRAIN IMAGING OF PAVLOVIAN DIFFERENTIAL INHIBITION OF BEHAVIOR. Gonzalez-Lima, F.; Jones, D. Dept. of Psychology and Institute for Neuroscience. The University of Texas at Austin, Austin, Texas 78712, USA. The associative inhibitory control of behavior is a major component of Pavlovian learning theory, but little is known about its functional neuroanatomy. The associative effects of differential inhibition of conditioned behavior were investigated by mapping learning-related changes in brain activity of the rat with fluorodeoxyglucose autoradiography. Of interest was how a tone is processed in auditory and extra-auditory systems of the rat brain under similar behavioral, but different associative conditions. Conditioned emotional suppression to drink was used to assess training, and summation tests were used to verify that the tone became an inhibitor of conditioned behavior. In the Inhibitor group, presentations of a tone stimulus alone were intermixed with presentations of a light stimulus followed by footshock. In the Pseudorandom group, the same numbers of tone, light and footshock presentations were used, but they were presented in a pseudorandom fashion. After training, fluorodeoxyglucose uptake was measured during tone presentations. Behavioral responding to the tone was similar during fluorodeoxyglucose uptake in the two groups, yet associative effects were found in brain activity. In the auditory system, the tone produced reduced fluorodeoxyglucose uptake in major relay nuclei (cochlear nucleus and inferior colliculus) in the Inhibitor group relative to the Pseudorandom group. The tone inhibitor produced similar decreases in the septohippocampal system and the retrosplenial cortex. In contrast, the tone inhibitor produced activity increases in somatosensory and reticulocerebellar systems. The findings provide the first detailed map of neural regions involved in the learned associations controlling differential inhibition of behavior. Supported by NIH R01 NS37755.

SYNAPTIC PROTEIN SYNTHESIS: MODULATION BY TRAINING. Eyman M.; Mandile P.; Crispino M.; Giuditta A. Dept. of General and Environmental Physiology, University of Naples "Federico II", Naples, Italy. In addition to its main somatic localization, neuronal protein synthesis also occurs in dendritic, axonal and presynaptic regions. This conclusion is supported by experiments on mammalian brain as well as on model systems. In the squid, cytoskeletal proteins, cytosolic enzymes and nuclear-encoded mitochondrial proteins are synthesized by the giant axon and nerve terminals. We have used synaptosomal fractions from rat brain containing nerve endings, dendritic fragments and glial processes to compare the electrophoretic patterns of newly-synthesized proteins, and show that protein bands of 66 and 87 kDa are more intensely synthesized in trained rats that in control animals, and that several additional proteins differ between adult and old rats. Furthermore, using RT-PCR methods we have shown that synaptosomal fractions contain mRNAs coding for presynaptic (GAT-1), dendritic (MAP2) and glial proteins (GFAP). The data indicate that a translation system is present in synaptic regions, and that its activity is modulated by age and training.

2:00-4:05 Symposium V: Analyzing neonatal behavior to understand brain development: human and animal data

NEUROBEHAVIORAL DEVELOPMENT OF HUMAN PERINATE. Monk, C.; Fifer W.P.; Tseng A.; Anderson, K. Depts. of Psychiatry and Pediatrics. Columbia University, NY, NY, 10032 USA. The current surge of interest in fetal origins of adult disease and recent findings on the relationship between fetal brain insult and subsequent risk for neurobehavioral disorders including SIDS have refocused attention on the study of brain behavior continuities during the perinatal period. Though direct assessment of brain activity remains largely an unfulfilled promise, indirect reflections of CNS activity and capacities are shedding light on early brain development and assessment of risk. In the absence of a gold standard of global neurologic integrity, integration of new and established technologies for measuring autonomic nervous system activity, and reactivity, offers one approach for assessing brain function and maturity. Mechanisms underlying ANS development are vulnerable to effects of untimely exposure to a wide range of agents during pregnancy and early infancy. Advances in quantification of periodicities in autonomic activity and assessment of reactivity to a range of environmental challenges offer non-invasive indices of central nervous system function during this vulnerable period. Data describing early developmental continuities in autonomic function and indices of CNS capacity to respond to sensory stimulation and physiological challenges will be presented.

ONTOGENY OF EARLY MOTOR BEHAVIOR PATTERNS AND BRAIN DAMAGE. Cioni G. Div. Child Neurology & Psychiatry, University of Pisa and IRCCS Stella Maris, 56018 Calambrone, Pisa, Italy. Fetuses and newborns show a large number of endogenously generated motor patterns, produced by central pattern generators located in different parts of the brain. Of the whole repertoire of endogenously generated motor patterns, general movements (GMs), gross movements involving the whole body, have received most of the attention of both researchers and clinicians. At 6-9 weeks postterm age, the form and character of GMs of normal infants changes from the writhing to a fidgety type of movement pattern. Fidgety movements (FMs) are circular movements of small amplitude and moderate speed and variable acceleration of neck, trunk and limbs in all directions. They are continual in the awake infant, except during focused attention. FMs may be seen until 15-20 weeks, for term as well as for preterm infants after correcting the age. GMs are the most appropriate target for clinical assessment, because of their complexity, long duration and frequent occurrence. Studies carried out on high-risk fetuses, brain-damaged preterm and term infants, as well as infants during the first months of life, have shown that it is not the incidence of GMs but the quality of their execution which is a good indicator of infant neurological status. The GMs of abnormal infants lack complexity; they are slow and monotonous or brisk and chaotic, with a marked reduction in subtle fluctuations of amplitude, force and speed. Several studies (Ferrari et al., 1990; Cioni et al., 1997; Prechtl, 1997; Prechtl et al, 1997; Bos et al., 1998; Cioni et al., 2000). indicate that GM findings correlate highly, and better than traditional neurological examination, with the presence of brain lesions, as shown by neuroimaging, and with the neurological outcome.

VISUAL COGNITION: CORTICAL FUNCTIONAL SPECIALIZATION AND POSTLESIONAL PLATICITY IN INFANCY. de Schonen S*; Sangrigoli S.*;Turati C.° *CNRS & INSERM, Hospital Robert Debré, Paris, France; °University of Padova, Italy. Understanding the relationships between cognitive development and cortical maturation requires combining studies on human and non human infants. Some issues can be approached by behavioural and anatomo-functional brain imaging studies on human infants. Other issues, concerned with the cellular level for instance, require animal models. Behavioural and functional brain imaging approaches were used to study the development of visual cognition in human infants. Cortical networks that are crucially involved in face processing at age 2 months involves the right Fusiform gyrus as in adult despite the fact that face processing is still crude in the second month of life. It was also found that long term effects of early unilateral and bilateral posterior brain lesions on visuo-spatial processing development (including face processing) differ according to the date of lesion before and after birth. Despite the early cortical localisation of face-related activation in the ventro-temporal right cortex, both left and right posterior unilateral perinatal brain damage can result in a long lasting face and object visual processing deficit. Deficit specific to face processing and preserving other visual objects processing is observed with damage occurring only after 14 months of age. With perinatal damage, some face processing abilities develop: they are however based on a different visual information processing than normal. Brain damages in infants as seen by MRI were compared to brain damages (Ibotenate injection) made unilaterally in the parietal cortex in mice at P1, P5, P10 (Gressens, Cohen-Salmon & de Schonen). The mice were tested when adult in a spatial task and a decision task. The results of this comparison will be commented.

ANIMAL MODELS OF EARLY BRAIN DAMAGE: A BATTERY OF TESTS FOR NEONATAL ANALYSIS OF BEHAVIOR AND RELATED STATISTICAL ISSUES. Gemma Calamandrei, Laura Ricceri, Maria Puopolo, Comparative Psychology Sect., Laboratory of Pathophysiology, Istituto Superiore di Sanità, Rome, Italy. Laboratory rodents are the most widely used animal species for modelling mental retardation and behavioral/cognitive disturbances in human infants. From a neurological view-point, a newborn rat is comparable in stage of brain development to the human fetus at the end of the second trimester of gestation, and a 7-day-old rat is comparable to an infant at term. Rats and mice are altricial species, that is they were born blind, deaf, and unable to regulate their body temperature. During the early neonatal period, the behavioral repertoire of the neonate is mainly limited to suckling and huddling in the nest with the other siblings. However, these apparently "primitive" behavior patterns, that characterize the first two weeks of postnatal life, are amenable to quantitative and qualitative analyses. Studies of selective (cholinergic) and more generalized neonatal brain damage (perinatal asphyxia) have revealed alterations in reflex development, suckling behavior, ultrasound emission and motor activity pattern in newborn rodents that are often predictive of significant behavioral impairments later on in development. Furthermore, learning tasks fitting with the ecological requirements of the neonate (i.e. olfactory conditioning) can be used to assess early learning and memory capabilities. As neonatal behavior is deeply biased by maternal care, experiments modelling early brain damage should be planned by assigning postnatal «treatments» within litter and data analyzed by adequate mixed models. Frequency, duration, intensity and latency of the different behavioral items should be analyzed by controlling for variables (i.e. body weight) that could indirectly affect the behavioral phenotype. In addition, the temporal structure of sequences of different behavioral items may be analyzed by methods originally developed for time to event data.

ULTRASOUNDS IN RODENTS: EARLY MARKERS OF ALTERATION IN CNS DEVELOPMENT. Zimmerberg, B.; Rosenthal, A.J.; Davidson, A.L. Dept. of Psychology and Neuroscience Program. Williams College, Williamstown, MA 01267 USA. The search for neural mechanisms underlying early brain damage is limited by the restricted behavioral repertoire of the neonatal rat. One behavior that has received increased attention as a model system in the last decade is the production of ultrasonic vocalizations (USVs). USVs are emitted by neonates in the range of 20-50 kHz after brief maternal separation and serve the critical function of eliciting maternal retrieval and care (Noirot, 1972). The rate of vocalization is modulated by environmental and social factors during testing, rendering it a rich system for detecting alterations on neural development. Alterations in USV rate in neonates after brief maternal separation have been used to detect effects of prenatal stress, prenatal alcohol and drug exposure, and postnatal stress. Selective breeding experiments have separated out two lines of N:NIH rats based on their USV responses to maternal separation at 10 days of age (Brunelli et al, 1996), providing new opportunities for research into neural mechanisms. USVs are also emitted by juvenile rats at 55 kHz during rough-and-tumble play (Knutson, Burgdorf, & Panksepp, 1998). Recent studies in this laboratory developing play-evoked USV production as a test for early brain damage will be presented. Social isolation stress during the second week of life was found to reduce the rate of USVs compared to controls when tested in either the maternal separation or play paradigms. Control of vocalizations appears to be multimodal, and the different neurochemical systems involved will be reviewed. Research supported in part by a grant from the NSF (No. 0074627).

5:00-6:00 Keynote Speaker: John C. Crabbe

BEHAVIORAL GENOMICS: ABUSED DRUGS AS A MODEL SYSTEM. Crabbe, J.C. Portland Alcohol Research Center, VA Medical Center, Dept. of Behavioral Neuroscience, Oregon Health & Science Univ., Portland, OR 97201 USA. Individual differences in behavior represent the integrated output of genetic influences as modulated by the environmental conditions in which genes act. With the recent dramatic advances in availability of information regarding human and non-human animal genomes, it is becoming possible to advance beyond making purely statistical inferences about genetic contributions. As specific genes are identified or targeted for experimental manipulation, it is increasingly clear that precision in behavioral analysis is crucial to the interpretation of how genes express their effects to influence behavior. Environmental interactions with specific genes' effects is pervasive, and a more sophisticated understanding of these interactions is essential to avoid inaccurate inferences of genetic determinism. Animal models of the relevant complex traits have been exploited extensively in the study of risk and protective factors for substance abuse. Because both genes and environment can be manipulated in animal models, this domain offers an excellent proving ground for enhancing our understanding of the power, and the limits, or genomic information. Supported by the VA, NIAAA and NIDA.

Sunday, June 23

8:00-10:00 Symposium VI: Hormones, behavior and the neural circuits that guide them

NEURAL CIRCUITS UNDERLYING MALE REPRODUCTIVE BEHAVIOR. Murphy, A. Dept. of Anatomy & Neurobiology and Program in Neuroscience. Univ Maryland Sch Medicine, Baltimore, MD 21201 USA. Our recent studies have established that the MPO sends a very dense and localized projection to the midbrain periaqueductal gray (PAG). The PAG, in turn, innervates the nucleus paragigantocellularis (nPGi), a pudendal premotor site essential for normal male reproductive behavior. Dual immunostaining for retrograde tracer and steroid receptor indicate that up to half of MPO-PAG or PAG-nPGi neurons contain estrogen or androgen receptor. Our recent behavioral studies show that over 70% of MPO-PAG neurons express Fos following ejaculation suggesting that this circuit is selectively engaged during copulation. These results are the first to establish an MPO-PAG-nPGi circuit, and further indicate that gonadal steroids can influence neuronal synaptic activity within these sites. We are currently using the multisynaptic tracer pseudorabies virus (PRV) to further establish the organization of the MPO-PAG-nPGi circuit. PRV (Bartha's K strain) was injected into the penile bulbocavernosus muscle of male Sprague-

Dawley rats; animals survived 120 hrs post-injection. To identify supraspinal sources of efferent drive onto PRV labeled cells, the anterograde tracer biotinylated dextran amine (BDA) was injected into the MPO, PAG or bed nucleus of the stria terminalis (BNST) in the same animal 3 weeks prior to the virus. Anterograde labeling from the MPO and BNST terminated heavily among retrogradely labeled PRV cells in the PAG. Anterograde labeling from the PAG terminated among PRV+ cells in the nPGi. In summary, we propose that the MPO-PAG-nPGi circuit forms the final common pathway whereby MPO neural output results in the initiation and maintenance of male copulatory reflexes.Supported by NIH MH59187.

HOW DO CHANGES ASSOCIATED WITH REPRODUCTIVE STATUS CONTRIBUTE TO OUR UNDERSTANDING OF SEX DIFFERENCES IN PAIN? Berkley, K.J. Program in Neuroscience, Florida State Univ., Tallahassee, FL 32306-1270 USA. Pain is a learned perceptual/emotional experience that changes across an individual's lifetime as a function of that individual's experience. Several recent reviews have concluded that there are numerous and substantive sex differences in pain. Unfortunately, specification of these differences is daunting, because the literature is wide-ranging and often contradictory. Furthermore, individual differences such as sex differences likely involve interactive combinations of genetic, genomic, molecular, physiological, hormonal, psychological, social, and cultural factors that evolve across an individual's lifetime. This situation has made it difficult to develop and test hypotheses concerning mechanisms that might underly sex differences in pain. What has made it even harder is that our understanding of the neural mechanisms of pain in general is itself still evolving. Current research has now matured enough, however, so that promising hypotheses are now beginning to emerge. What has helped considerably are studies that address the neuroplasticity that is associated with changes in reproductive status. An example of one such set of studies will be discussed. These studies examined how neurons in the rat's dorsal column system responded to gentle and noxious stimulation of healthy or inflamed pelvic visceral organs. The studies were done, however, by two groups of investigators, one using male rats, the other using female rats in different reproductive conditions. The two sets of results led to opposing hypotheses of the neural mechanisms that underly visceral pain. One group (male rats) proposed the existence of a 'new' pathway for visceral pain. The other group (female rats) proposed that visceral pain must involve a 'widely distributed and dynamic system,' some of whose components would vary with sex (as well as other factors). Supported by NIH grant NS 11892.

NEUROENDOCRINE REGULATION OF SOCIAL ATTACHMENT IN THE MALE PRIARIE VOLE Young, L.J.; Center for Behavioral Neuroscience, Emory University, Atlanta, GA 30322, USA. Voles are excellent animal models for understanding the neurobiological and biochemical mechanisms underlying affiliative behavior and social attachment. Prairie voles are highly affiliative and monogamous, forming enduring social attachments with their mates. In contrast, montane voles are more solitary and fail to form social attachments between mates. In the male prairie vole, the neuropeptide arginine vasopressin plays an important role in facilitating both affiliative behavior and pair bond formation. Monogamous and non-monogamous vole species differ in the neuroanatomical distribution of V1a vasopressin receptors (V1aR), as well as in the structure of the V1aR gene promoter. Monogamous vole species have high densities of V1aR in the ventral pallidum while non-monogamous species do not. Interestingly, other monogamous rodents and primates also have elevated V1aR density in the ventral pallidum compared to related non-monogamous species, suggesting as association between V1aR density in this region and social structure. Using viral vector gene transfer techniques, we have shown that increasing V1a receptor density in the ventral pallidum facilitates pair bond formation in male prairie vole. The ventral pallidum is part of the mesolimbic dopamine reward pathway and is a site of action of drugs of abuse. Thus, these studies suggest that perhaps social attachment and addiction share common underlying neural circuits.

NEURAL CIRCUITS THAT LINK ENERGY BALANCE TO REPRODUCTIVE SUCCESS. Schneider, J. E., Dept. of Biological Sci., Lehigh University, Bethlehem, PA 18015, USA. Reproductive processes and ingestive behaviors are controlled by overlapping systems that include metabolic sensory signals and hormonal/neuropeptide modulators. An evolutionary perspective suggests that the mechanisms that control energy balance and ingestive behavior came about primarily because they increase survival and optimize reproductive success. Thus, it might be beneficial to study these physiological systems under conditions that allow animals to engage in a variety of species-specific behaviors. We are studying the effects of metabolic sensory signals, leptin, insulin, and cortisol and their effects on ingestive behavior, hoarding, estrous cyclicity and sex behavior in Syrian hamsters. It appears that the hormones and metabolic signals that increase food intake in laboratory rats fail to do so in Syrian hamsters. Rather, these same metabolic signals and hormones influence hoarding behavior, the estrous cycle, sex behavior and energy expenditure in this species. Changes in plasma hormones , but not changes in metabolic fuel availability, can be dissociated from changes in estrous cyclicity. In rodents, the neural circutitry for control of reproduction and ingestive behavior includes projections from the caudal brain stem, in addition to hypothalamic structures traditionally associated with these physiological processes. Supported by NSF IBN 0098961.

NEUROANATOMICAL EVIDENCE FOR THE ORGANIZATIONAL AND ACTIVATIONAL EFFECTS OF GONADAL STEROIDS. Swann, J.M.; Wang, J.; Govek, E.K. Dept. of Biological Sciences. Lehigh University, Bethlehem, PA 18015 USA. A number of neural parameters including neuron number, density and morphology have been correlated with sex differences in behavior. However, the significance of sex differences in neural parameters in the regulation of behavior has not been determined primarily because the role of these sexually dimorphic structures in the regulation of sex specific behaviors is poorly defined. We have begun to examine sex differences in the chemosensory pathway that regulates male sex behavior in the hamster. Hamsters are keenly dependent on pheromonal cues from conspecifics for the initiation of social behaviors. The pathway that mediates pheromonal input to more central areas is highly conserved and well described. Pheromonal cues are relayed from the olfactory bulbs to three interconnected areas: the medial nucleus of the amygdala (Me), the bed nucleus of the

stria terminalis (BNST) and the magnocellular medal preoptic nucleus (MPN mag). The Me and BNST form bi-directional, parallel circuits that integrate pheromonal information with that from gonadal steroids. Signals from the BNST and Me are relayed to the MPN mag. The integrity of these three areas and the pathways that connect them is critical for normal mating behavior. Destruction of the BNST, Me or MPN mag immediately and permanently eliminates copulation. Our results indicate that steroids regulate pheromonal stimulation of these areas by differentially affecting cell number and synaptic efficacy. This regulation is sex specific occurring during development and in adulthood. As detection of pheromones is critical for the normal expression of male sex behavior in hamsters our results suggest that steroids regulate male sex behavior by effecting morphological changes that disrupt pheromonal processing in the BNST, Me and MPN mag.

10:15-12:15 Oral Session 4: Feeding and body weight regulation

A PARADOXICAL EFFECT OF OREXIN A: THE HYPOPHAGIA Monda, M.; Viggiano, A.; Salemme, M.; De Luca, B. Department of Experimental Medicine, Section of Human Physiology Second University of Naples, via Costantinopoli 16, 80138 Naples, Italy. Hypocretin-1 is a novel hypothalamic neuropeptide which is also named "orexin A" for the peptide's influence on food intake. Since the particularity of this peptide is its capacity to induce both the activation of thermogenesis and the hyperphagia, the aim of this experiment was to test the possibility that a previous thermogenic activation induced by orexin A can modify eating behaviour. Food intake, firing rate (FR) of the sympathetic nerves to interscapular brown adipose tissue (IBAT), IBAT and colonic temperatures (TIBAT and TC), and heart rate (HR) were monitored in 24h-fasting male Sprague-Dawley rats for 15 h after food presentation. Orexin A (1.5 nmol) was injected into the lateral cerebral ventricle 6 h before food presentation while FR, TIBAT and TC, and HR were also monitored. The same variables were controlled in rats receiving orexin A contemporaneously to food presentation. Two other groups of control animals were tested with the same procedure, however orexin A was substituted by saline. The results showed that food intake was significantly lower in the group receiving orexin A 6 h before food presentation in comparison to all the other groups. FR, TIBAT and TC, and HR were significantly higher in the rats receiving orexin A with respect to rats receiving saline. These findings demonstrate that orexin A, so-called for its orexigen action, can also induce hypophagia. On the other hand, orexin A always induces an activation of the thermogenesis. These results suggest a revision of the role played by orexin A in the control of food intake, assigning to this peptide a primary role in the thermoregulation. The possibility that orexin A can induce hypophagia is well demonstrated by this experiment, so that the scientific community should use a different name for this peptide.

THE MECHANISM OF INTERLEUKIN-1-INDUCED HYPOPHAGIA CHANGES OVER TIME. Dunn, A.J.; Swiergiel, A.H. Dept. of Pharmacology. Louisiana State University Health Sciences Center, Shreveport, LA 71130 USA. Administration of interleukin-1 (IL-1) has long been known to induce behaviours such as decreased feeding and locomotor activity characteristic of illness, and often called sickness behaviour. The mechanisms of the behavioural induction have been studied extensively, and the most effective antagonists are inhibitors of cyclooxygenase (COX). We used the ingestion by mice of sweetened milk and food pellets and locomotor activity as simple measures of sickness behaviour. The responses are largely but not completely prevented by COX inhibitors such as aspirin, and indomethacin. They are also sensitive to selective inhibitors of COX2 (NS-398 and celecoxib), the form of COX induced in association with inflammation. However, changes in milk drinking and locomotor activity are observed starting around 15 min after ip injection of IL-1beta, whereas COX2 is not induced for one hour or more, the noradrenergic response starts around 30 minutes and the serotonergic responses are delayed 2-4 hours. Thus we studied the sensitivity to COX inhibitors in mice at different times after IL-1 administration. At early times, IL-1-induced behaviour was sensitive to non-selective inhibitors and was almost absent in COX1 knockout mice, but normal in COX2 knockout mice. However, at later times the IL-1-induced behaviours were sensitive to the COX2-selective inhibitor, celecoxib, and were normal in COX1 knockout mice but diminished in COX2 knockout mice. These results suggest that the mechanisms underlying the behavioural responses change as a function of time, COX1 is involved at early times, COX2 at later times; although presumably the behavioural changes at both times are induced by prostaglandins synthesized via COX.

REPEATED DAILY ADMINISTRATION OF SALMON CALCITONIN REDUCES THE LEVEL OF DEFENDED BODY WEIGHT IN RATS. Rushing, P. A.; Seeley, R. J.; Lutz, T. A.; Woods, S. C. Department of Psychiatry, University of Cincinnati; Cincinnati, OH 45269-0559 USA; Institute of Veterinary Physiology, University of Zürich, Zürich, Switzerland. We recently observed significant reductions of food intake, body weight and body fat after repeated daily injections (ip) of low doses of salmon calcitonin (sCT) in rats. Whether these sCT-induced reductions of body weight reflect some regulatory effect on energy balance or are simply the result of some nonspecific reduction in ingestion is an important concern. In a paradigm designed to address this issue, separate groups (n = 16/group) of rats, maintained on standard rat chow, received daily ip injections of saline vehicle or 800 pmol/kg sCT for 9 consecutive days. Half of the saline and half of the sCT rats received no food for the first 2 days; the other half of the saline and sCT rats received ad lib food throughout. Consistent with our previous findings, rats that received sCT and ad lib food for the entire 9 days ate less and lost a significant amount of body weight compared to saline-treated ad lib controls. The two groups of rats that received no food for the first 2 days lost a substantial amount of weight. Interestingly, the fasted sCT rats lost significantly more weight (-39 g) than the fasted saline controls (-32 g). When food was returned to the fasted rats on day 3, both saline control and sCT animals began to regain weight. The fasted controls significantly overate compared to ad lib controls and regained body weight such that they caught up with their ad lib counterparts by day 9. The fasted sCT rats did not overeat to the same degree as the fasted controls, however, they did overeat enough to regain body weight to exactly match the reduced level of their ad lib sCT counterparts by day 7 and remained so through day 9. In summary, the data are consistent with the conclusion that sCT affected energy homeostasis such that the level of defended body weight was reduced. Additionally, the greater weight loss exhibited by the sCT-treated rats compared to saline-treated rats in the absence of food suggests that sCT may also increase energy expenditure.

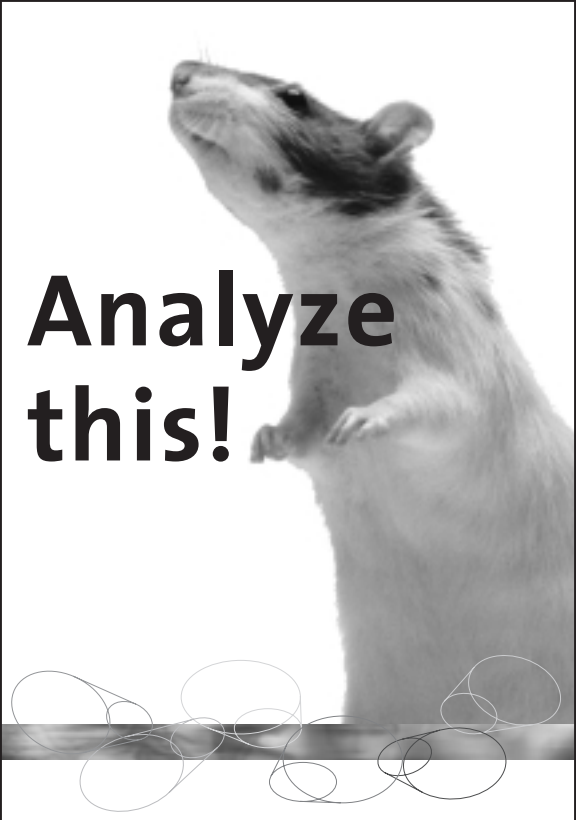
ANALYSIS OF ADULT-ONSET OBESITY AND FEEDING BEHAVIOR IN 5-HT TRANSPORTER-DEFICIENT MICE. Holmes, A.[1]; Yang, R.J.[1]; Tolliver, T.J.[2]; Huang, S.[2]; Li, Q.[2]; Ren-Patteson, R.F.[2]; Saavedra, M.C.[1]; Murphy, D.L.[2]; Crawley, J.N.[1] [1]Section on Behavioral Genomics; [2]Laboratory of Clinical Science; NIMH. A wealth of literature has implicated the brain 5-HT system in the mediation of feeding behavior. By controlling the reuptake of extracellular 5-HT, the 5-HT transporter (5-HTT) is a key regulator of 5-HT activity in both the brain and periphery. 5-HTT-deficient mice were generated to study the role of 5-HTT in body weight regulation. 5-HTT -/- develop higher body weights than +/+ controls, beginning at 4-6 months of age. Genotype differences in body weight become progressively greater with age; 5-HTT -/- mice were 28% heavier than +/+ controls by 18 months. Autopsy confirmed that 5-HTT -/- mice had significantly more white adipose tissue than +/+ controls, while other organ weights (with the exception of an enlarged liver) were similar across genotypes. 5-HTT -/- exhibited elevations of plasma leptin, and male 5-HTT -/- mice showed increased circulating levels of insulin. While analysis of daily food intake found no differences between genotypes, home cage activity was markedly reduced in 5-HTT -/- mice. Detailed microstructural analysis of feeding behavior is the subject of ongoing experiments. In a functional assay for 5-HT2C receptor function, 5-HTT -/- showed normal hypophagic responses to the 5-HT agonist, mCPP. These data suggest that obesity in 5-HTT -/- mice is unrelated to altered 5-HT2C receptor function or chronic hyperphagia. Future experiments will test 5-HTT -/- mice for metabolic abnormalities. An obesity phenotype in 5-HTT-deficient mice identifies a novel mechanism by which the 5-HT system can regulate body weight. (Supported by NIMH-IRP).

ELEVATION OF BLOOD GLUCOSE LEVEL BY GASTRIN RELEASING PEPTIDE (GRP) MICROINJECTION INTO THE RAT AMYGDALA AND ITS ELIMINATION BY SELECTIVE GRP RECEPTOR ANTAGONIST. Lénárd, L.[1]; Fekete, É.[1]; Bagi, É.[1]; Coy, D.H.[2] [1]Inst. of Physiol. and Neurophysiol. Res. Group of the HAS, Pécs Univ. Med. School, Pécs, H-7643, Hungary and [2]Peptide Res. Lab., Tulane Univ. Med. Center, New Orleans, LA 70112, USA. Our previous results showed that gastrin releasing peptide (GRP) or neuromedin B (NMB) microinjected into the central part of the amygdala (ACE) inhibit feeding. In the present experiments blood glucose level (Bgl) was studied after application of GRP or NMB into the ACE. Bilateral guide tubes were implanted and vehicle (0.4 ul of 0.15 M NaCl), GRP (150 ng/site) or NMB (30 ng/site) were injected bilaterally. Selective GRP receptor antagonist [D-Phe6]-BN(6-13)-Methyl ester (BME, 250 ng/site) was used alone or 10 min before GRP treatment. For Bgl determination samples were taken from the tail vein (enzymatic detection with Glucometer Elite, Bayer). Bgl was measured 10 min before and 10, 20, 30 and 60 min after GRP or NMB microinjections. In glucose loading experiments 0.2 g glucose/ml saline/100 g bw was applied i.p. and Bgl was measured in every 10 min for 120 min. Ten and 20 min after GRP treatment Bgl significantly increased. NMB application did not modify Bgl. BME used alone was ineffective on Bgl. Prior application of BME, however, completely eliminated Bgl increase induced by GRP. In glucose loading experiment Bgl was not modified by GRP. Results show that GRP plays a distinct role in ACE satiety mechanisms and that Bgl increase is mediated via GRP-preferring receptors. (This work was supported by OTKA T 034489, ETT 354/2000, by the HAS and the Pécs University Med. School).

AN ESSENTIAL ROLE FOR LEPTIN IN HIPPOCAMPAL SYNAPTIC PLASTICITY. Oomura, Y; Li, X.L.; Aou, S.[1]; Hori, N.[2]; Armstrong, D.L.; Wayner, M.J.[3]. Dept. of Physiology, Faculty of Medicine, Kyushu Univ. Japan[1]; Public Health, New York Univ. Albany[2]; Dept. of Biology, Univ. of Texas at San Antonio, USA[3]. Leptin released from adipocytes during feeding facilitates long term potentiation (LTP) in Schaeffer collateral afferent-CA1 pyramidal cell synapses in rats; and the enhancement of LTP is associated with improved performance in the water maze. Zucker rats and db/db mice with abnormal leptin receptors do not display the facilitaion of LTP and enhanced water maze performance. Ob/ob mic that have normal leptin receptors but do not produce normal amounts of leptin also do not display normal LTP and spatial learning nad memory. Daily intraveneous administration of leptin for three weeks, 50μg/kg, in these animals resulted in normal maze performance. The essential role of leptin in synaptic plasticity will be discussed.

A DECREASE IN THE EXPRESSION OF OREXIGENIC NEUROPEPTIDES IN THE LATERAL HYPOTHALAMUS MAY CONTRIBUTE TO THE ANORECTIC ACTION OF AMYLIN. Lutz, T.; Riediger, T.; Zünd, D.; Barth, S.; Scharrer, E. Inst. Vet. Physiol., Univ. Zurich, Switzerland. The pancreatic hormone amylin which is released in response to a meal, reduces feeding by a primary activation of neurons in the area postrema (AP). This was shown by feeding experiments since an AP-lesion blocks peripheral amylin's anorectic effect while a direct AP-infusion of amylin potently reduces feeding. Immunohistochemical (c-Fos detection) and electrophysiological studies confirmed a direct excitatory effect of amylin on AP neurons. AC 187, a specific amylin antagonist, blocked the amylin-induced excitation of AP neurons. AC 187 also reduced the c-Fos expression in the AP triggered by exogenous amylin or by endogenously released amylin as induced by refeeding of food-deprived rats. In the present study, we examined the central pathways mediating amylin's anorectic effect subsequent to the primary, amylin-induced AP signal. Similar to peripheral amylin, refeeding of food-deprived rats induced c-Fos expression in ascending relay stations, e.g. the nucleus of the solitary tract (NTS), lateral parabrachial nucleus (lPBN) and central amygdala (CeA). An AP-lesion blocked the amylin-induced c-Fos expression in these areas. Further, food deprivation induced a strong c-Fos signal in the lateral hypothalamus (LH) which was completely reversed 2 hr after refeeding, but also reversed by peripheral amylin injection in non-refed rats. Interestingly, we showed in preliminary studies that peripheral amylin and its agonist salmon calcitonin (sCT) reduce the expression of the orexigenic neuropeptides orexin A and melanin-concentrating hormone (MCH). We conclude that the primary amylin-induced activation of AP neurons is projected via various relay stations (NTS, lPBN, CeA) to the forebrain. In the forebrain, this signal may then be translated into an inhibition of neurons in the LH expressing orexigenic neuropeptides. It is possible that this inhibition contributes to the anorectic action of peripheral amylin.

All authors.



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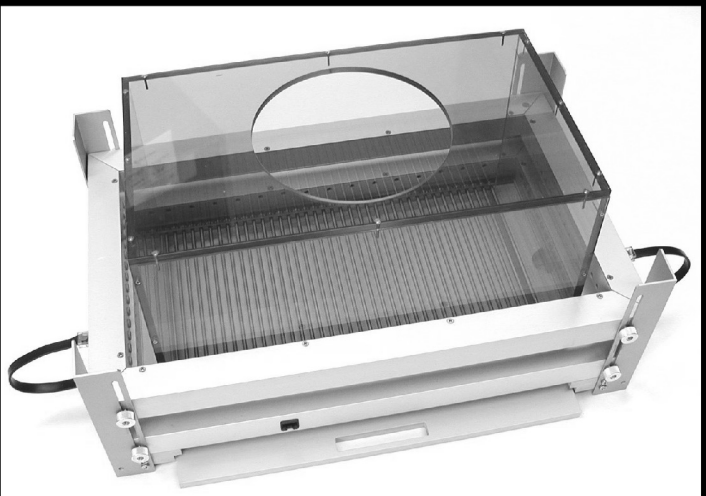

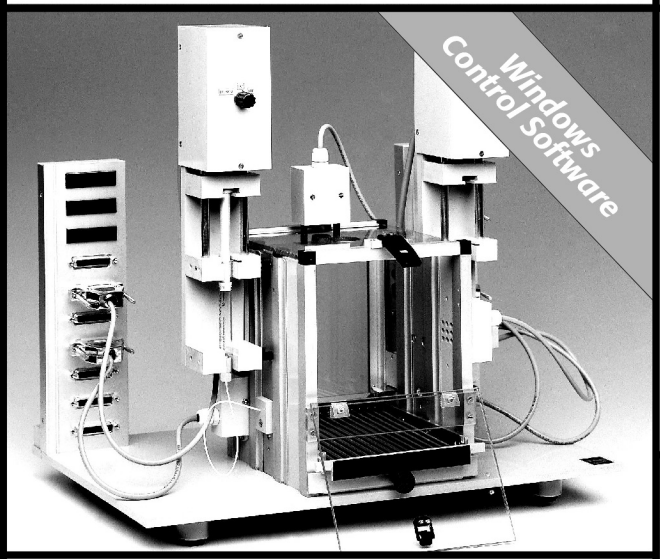

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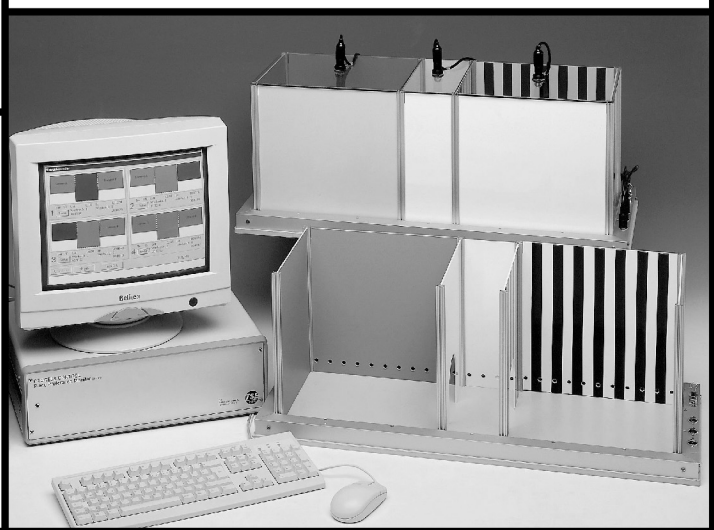

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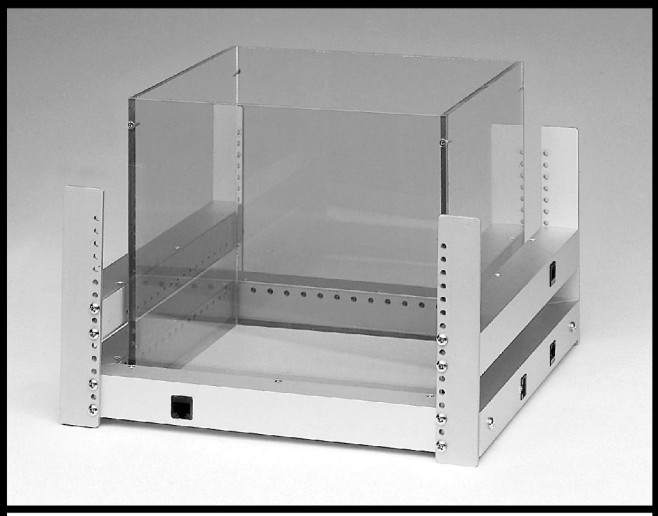

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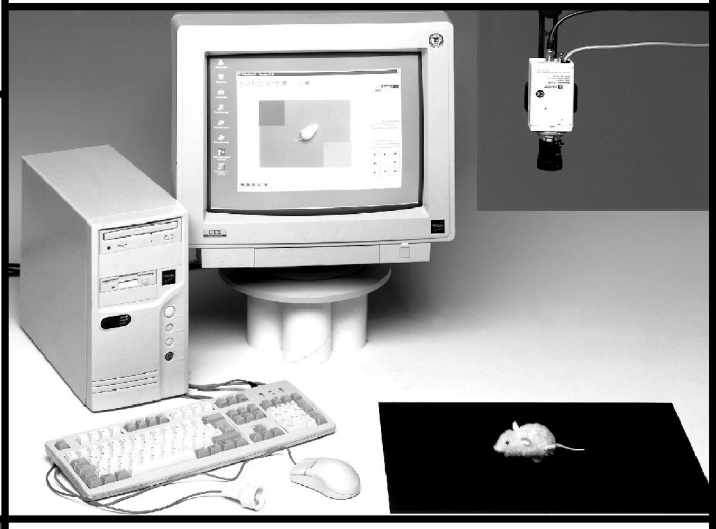

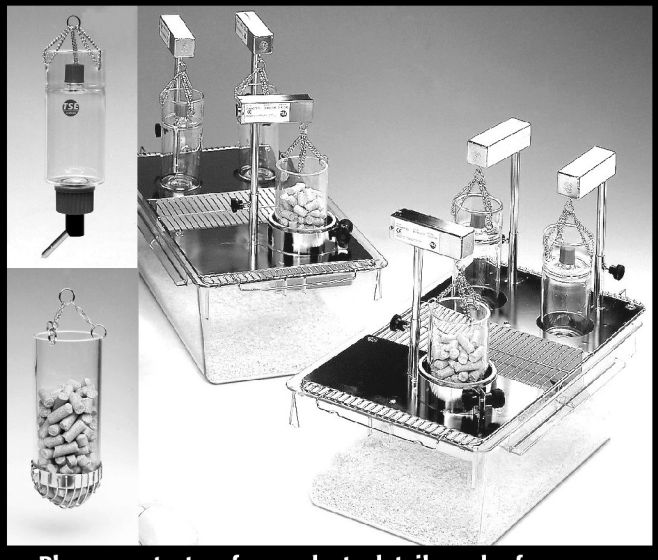

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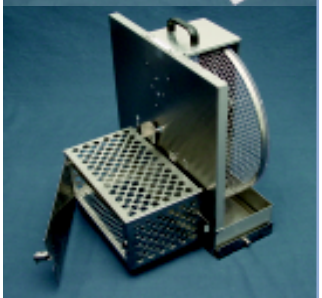

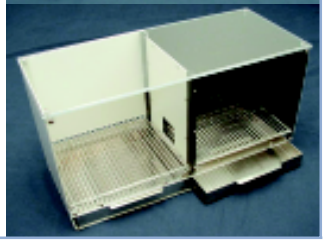

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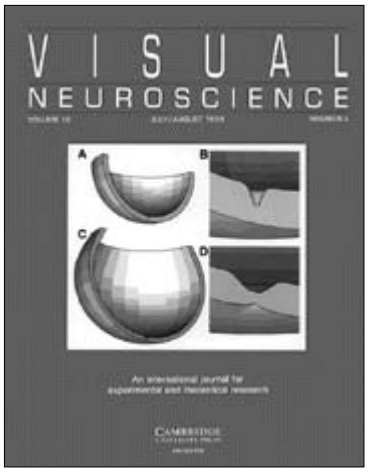

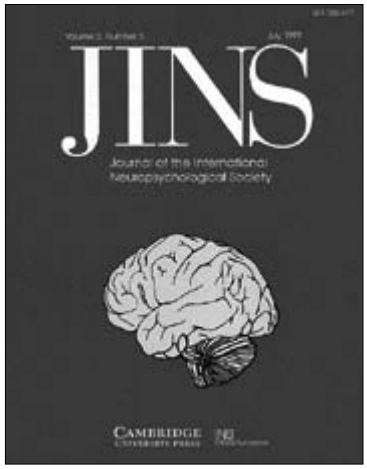

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