

mounting rates compared to controls which were accounted for by their significantly higher rates of mounts without pelvic thrusts (EFM =  $1.29 \pm 0.32$ , control =  $0.25 \pm 0.09$ ,  $F = 7.29$ ,  $p = 0.005$ ). EFM's also had increased thrusting-mounts without intromissions (EFM =  $2.37 \pm 0.46$ , control =  $0.81 \pm 0.28$ ,  $F = 4.87$ ,  $p = 0.02$ ). When degree of genital masculinization was used as a covariate, these differences disappeared. Females presented to EFM's more than to controls (EFM =  $1.87 \pm 0.42$ , control =  $0.73 \pm 0.24$ ,  $F = 4.28$ ,  $p = 0.03$ ), which correlated with male T level ( $r = 0.517$ ;  $p = 0.020$ ). LFM's did not differ behaviorally from controls. Contrary to our predictions, prenatal androgen blockade early in gestation affected adult sexual behavior probably resulting from EFM's reduced genital masculinization. (Support: NSF agreement #IBN-9876754, RR-00165, MH50268).

**47. ENZYMES NECESSARY FOR DE NOVO STEROID SYNTHESIS ARE EXPRESSED ALONG LATERAL VENTRICLES IN DEVELOPING ZEBRA FINCH BRAINS.** London, S.E.,<sup>1,2</sup> Alday, N.A.,<sup>2</sup> Tam, H.,<sup>2</sup> and Schlinger, B.A.<sup>1,2</sup> *Interdepartmental Neuroscience Program,<sup>1</sup> Physiological Science Department,<sup>2</sup> UCLA.*

During posthatch development, male zebra finches organize a complex neural circuit that supports song learning and production but females have a minimal circuit that does not allow singing. Steroids functionally masculinize the song system, but gonadal manipulations do not alter the "sex" of the circuit, suggesting that an alternative steroid source may contribute to masculinization. We hypothesize that steroids are synthesized de novo in the brain during the first week posthatch when steroids are most masculinizing and prior to identification of song nuclei. Neural aromatase is abundant, but expression of the three enzymes upstream of aromatase in the steroidogenic pathway was undefined in normal developing brain. Therefore, we cloned three zebra finch steroidogenic enzymes: CYP11A1, 3 $\beta$ -HSD, and CYP17. Relative quantitative RT-PCR demonstrates that these genes are expressed in male and female P5 whole brains, a finding confirmed by Northern blots for 3 $\beta$ -HSD and CYP17, though no sex differences were detected. In situ hybridization identified label for these genes in the cells surrounding the lateral ventricle during the first week posthatch. Biochemical assays confirm 3 $\beta$ -HSD activity in P5 brain regions and in slices containing the lateral ventricle region. Steroidogenic enzyme expression surrounding the lateral ventricle may be particularly important because it is a site of cell proliferation and contributes cells to song nuclei. Further, steroids modify postmitotic aspects of cell proliferation in this region and can increase the number of cells migrating into song nuclei. Therefore, early expression of CYP11A1, 3 $\beta$ -HSD and CYP17 suggests that neurosteroidogenesis along the lateral ventricle may contribute to song system organization as well as more general brain development. Supported by NIH MH65114(SEL) and MH61994(BAS).

**48. PROLACTIN RECEPTOR mRNA EXPRESSION IN HYPOTHALAMIC NUCLEI OF A PATERNAL HAMSTER, PHODOPUS CAMPBELLI.** Elva Ma and Katherine E. Wynne-Edwards. *Queen's University, Kingston, Canada K7L 3N6.*

No previous research has described prolactin receptor (PRLR) mRNA expression in a paternal mammal. This study investigated the expression in selected hypothalamic nuclei of a naturally biparental hamster, *Phodopus campbelli*. Paired males and females were analyzed on gestation day 17 (G17), lactation day 1 (L1), and lactation day 5 (L5), and compared to unpaired animals of the same sex. Brains were dissected into the following sections and snap frozen in liquid nitrogen: preoptic area (POA), median eminence (ME), choroid plexus (ChP), and cerebral cortex (CC). Expression of PRLR mRNA was evaluated by reverse transcription-PCR. Results revealed marked changes in males between pre-pairing and gestation/lactation. Levels in ChP were significantly lower at G17 and L1 compared to unpaired males, while expression at L5 was elevated to prepairing levels. This trend was repeated in the POA and ME of males, although not to the point of significance. As controls, females displayed a PRLR mRNA expression profile similar to female laboratory rats. Expression in the ChP was significantly higher in pregnant and lactating female hamsters

compared to diestrus females, consistent with known actions of PRL on the brain during lactation, including the onset of maternal behaviour. Finally, PRLR mRNA was present at minimal levels in the CC, and did not increase expression after pairing in either males or females. Until now, no research has investigated the PRLR in the context of parental behaviour in naturally paternal mammals. Contrary to prior hypotheses regarding the evolution of mammalian parental care, these results are the first to suggest that the neuroendocrine mechanisms evoking such behaviours may differ between naturally biparental males and females.

**49. EFFECTS OF 3-NITROPROPIONIC ACID ON HISTAMINERGIC NEURONAL SYSTEM AND BEHAVIORAL ACTIVITIES OF THE GOLDEN HAMSTER.** Madeo, M., Giusi, G., Alò, R., Granata, T., Facciolo, R.M., Carelli, A., and Canonaco, M. *Comparative Neuroanatomy Laboratory, Ecology Department, University of Calabria, Arcavacata di Rende (CS), Italy.*

Hibernating mammals are useful models to study neurophysiological functions of the biogenic amine, histamine. This neuromediating system consists of four receptors (H<sub>1-4</sub>R) and is involved in the control of physiological and behavioral functions such as sleep-wakefulness and pain. Of these subtypes, the different H<sub>3</sub>R isoforms seem to control waking and attention as well as modulating its mRNA expression level in some basal ganglia nuclei of Parkinson's disease (PD) patients. It is our intention with *in vivo* intraperitoneal administration of 3-nitropropionic acid (3-NPA), an irreversible inhibitor of mitochondrial succinate dehydrogenase which mimics PD motor disorders, to identify the neuroprotective role of H<sub>3</sub>R in encephalic nuclei that are linked to the regulation of physiological and hibernating functions of the golden hamster and compared to that of the rat. Interestingly, whereas two acute doses (50 mg/Kg) were sufficient to induce behavioral motor abnormalities (hindlimb dystonia and clamping) in the latter rodent, two 100 mg/Kg doses were instead required to produce similar behavioral alterations in hamster. Moreover an accumulation of chronic doses (90 mg/Kg in three days) was tolerated by the rat while an accumulation of 920 mg/Kg (eight days) was instead tolerated by the hamster. At the hamster brain level, both type of treatment modalities accounted not only for a greater expression level of H<sub>3</sub>R<sub>(445bp)</sub> isoform, aside the striatum, in the cortex and amygdala, but also of fewer shrunken and dark neurons with swollen processes and chromatin condensation. Thus the elevated quantities of H<sub>3</sub>R in these brain regions might represent a major element capable of exerting a neuroprotective role in PD-like syndromes.

**50. DIMORPHISM AND EFFECTS OF ESTROUS CYCLE ON THE NITRINERGIC SYSTEM IN MOUSE HYPOTHALAMUS.** Martini, M., Sica, M., Eva, C., Viglietti-Panzica, C., and Panzica, G.C. *Dept. Anatomy and Pharmacology, University Torino, Italy.*

Nitric oxide (NO) plays an important role in the regulation of rodent reproductive activities including sexual behavior. NO-producing neurons have been localized, by means of immunohistochemistry for neuronal NO synthase (nNOS) in several hypothalamic and limbic nuclei, as the medial preoptic area (MPOA), the arcuate (ARC), ventromedial (VMH), and Stria terminalis (BST) nuclei. Hypothalamic nNOS expression is affected by testosterone in male and by estrogens in female rat. We have here investigated male and female mice to detect the presence of sexually dimorphic nNOS distribution, as well as the effect of cyclic hormonal changes linked to estrous cycle.

Two month-old C57BL/6-DBA2 male (n = 5) and female mice (n = 20, 5 for each stage of estrous cycle, detected by means of vaginal smears) were perfused with 4% paraformaldehyde and brains were dissected, frozen, serially sectioned, and processed for nNOS immunocytochemistry. In proestrous females, MPOA and VMH have a smaller number, whereas BST has a higher number of nNOS-ir neurons in comparison to male. No statistically significant differences were observed in the ARC and PVN. The number of nNOS-ir elements is not varying along the estrous cycle in VMH and BST, but they vary in MPOA and ARC, showing the highest number at the estrous or proestrous respectively.

In conclusion, gonadal hormones control part of the nitrinergic system of female mice that show changes during the estrous cycle. The involved regions (MPOA and ARC) are characterized by a high number of estrogen receptors. Our data point also to the importance of establishing the precise stage of female cycle when performing studies on the sex dimorphism of neurochemical markers.

**51. TESTOSTERONE AND COGNITIVE FUNCTIONING IN ELDERLY MEN.** Rose H. Matousek, Ph.D Candidate, Barbara B. Sherwin, Ph.D, and Stephanie Blum. *McGill University Montreal, Canada.*

Results of studies on the relationship between hormones and cognitive function in men are contradictory, with some showing a negative (Gouchie and Kimura, 1991), and others showing a positive relationship between testosterone and spatial ability in healthy, eugonadal men (Christiansen and Knussmann, 1987; Yaffe, Lui, Zmuda, and Cauley, 2002) whereas others show no hormone-behavior relationship (McKeever, Rich, Deyo, and Connor, 1987; Kampen and Sherwin, 1996; Barrett-Connor, Goodman-Gruen, and Patay, 1999). Direct comparison of these studies is made difficult by the fact that different subject populations were tested, different hormone levels were measured, and different neuropsychological tests were used to measure cognitive function. Therefore, we examined the relationship between changing sex hormone levels and cognitive functioning in healthy, older men using a more extensive neuropsychological battery and a more thorough evaluation of the various hormones that may affect cognitive function in an effort to clarify this issue. We hypothesized that higher levels of bioavailable testosterone would be associated with better performance on certain cognitive measures (i.e., spatial and verbal abilities), and would be unrelated to others (e.g., attention and general intelligence). Fifteen healthy men between the ages of 60–75 underwent an extensive neuropsychological battery that examined verbal, visual, and spatial learning and memory, as well as attention and general intelligence. Blood samples were collected and plasma levels of total testosterone and SHBG were analyzed by radioimmunoassay at the completion of the study. Bioavailable testosterone was determined by calculating the ratio of total testosterone to SHBG. Findings from this study will be presented and their contribution to the clarification of the role of testosterone in age-related changes in cognitive function in older men will be discussed.

**52. ESTRADIOL ENHANCED ADULT HIPPOCAMPAL NEUROGENESIS IS MEDIATED BY BOTH ER ALPHA AND ER BETA IN THE FEMALE RAT.** Mazzucco, C.A., Walker, H.A., and Galea, L.A.M. *Neuroscience Program, University of British Columbia.*

The estrogen receptor (ER) exists in two known forms, ER $\alpha$  and ER $\beta$ . To determine the contribution of each receptor towards estradiol-induced enhancement in adult hippocampal neurogenesis we used specific ER agonists, an alpha agonist propyl pyrazole triol (PPT) and a beta agonist diethylpropionitrile (DPN). Study 1 determined which dose of PPT elicited female sexual receptivity. Twenty-four female ovariectomized (OVX) Sprague Dawley rats received s.c. injections of either sesame oil (OIL; 0.1 ml), estradiol benzoate (EB; 10  $\mu$ g/0.1 ml OIL), dimethylsulfoxide (DMSO; 0.1 ml) or one of 4 doses of PPT (2.5 mg, 1.25 mg, 0.625 mg or 0.3125 mg/0.1 ml DMSO) for two days followed by progesterone. Our results indicate that the ER $\alpha$  agonist PPT elicited sexual receptivity in 2 doses (2.5 mg and 1.25 mg PPT). Study 2 was conducted to determine the relative contribution of each ER agonist to enhance cell proliferation in the dentate gyrus. Twenty-four female OVX Sprague-Dawley rats were given a s.c. injection either of OIL, EB (10  $\mu$ g), DMSO, PPT (2.5 mg) or DPN (2.5 mg). The rats were then administered the cell synthesis marker, 5-bromo-2'-deoxyuridine (BrdU, i.p.; 200 mg/kg) four hours later. The animals were perfused 24 hours after BrdU administration and cell proliferation was assessed via immunocytochemistry. Estradiol increased the number of BrdU-labeled cells by approximately 50% relative to both vehicles. PPT and DPN both demonstrated a 25% increase in the number of BrdU-labeled cells relative to vehicles. Thus, estradiol enhances cell proliferation in the dentate gyrus of adult female rats by activating both the

alpha and beta estrogen receptor and female sexual receptivity can be altered via the ER $\alpha$ .

**53. SELF-PACED OR NON-PACED COPULATION AND Fos EXPRESSION IN THE REWARD PATHWAYS OF MALE AND FEMALE RATS.** Casey L. McGovern,<sup>1</sup> Antonio A. Nunez,<sup>2,3</sup> and Lynwood G. Clemens<sup>1,2</sup>. <sup>1</sup>Department of Zoology, <sup>2</sup>Neuroscience Program, <sup>3</sup>Department of Psychology, Michigan State University, East Lansing, MI 48824.

Preliminary research in this laboratory has shown a difference in Fos expression in the sexually dimorphic nucleus (Clemens, unpublished data) of female rats tested in paced versus non-paced conditions. Under these same conditions others have shown differences in c-fos expression in regions such as the medial amygdala, ventromedial hypothalamus, and bed nucleus of the stria terminalis (Erskine and Hanrahan, *J. Neuroendo.* 1997). Additional studies have shown that self-paced copulation is more rewarding than non-paced copulation for both females and males (Paredes and Vazquez, *Beh. Brain Res.* 1999; Martinez and Paredes, *Horm. Beh.* 2001). In related studies, it has been shown that dopamine release is increased in the nucleus accumbens and striatum during self-paced copulation in the female (Mermelstein and Becker, *Behav. Neurosci.* 1995) and the male (Damsma et al., *Behav. Neurosci.* 1992). Therefore, we suggest that self-paced copulation in male and the female rats will result in activation of the brain's reward pathway in both sexes. To evaluate this hypothesis, we tested male and female rats in self-paced and non-paced mating situations and examined Fos expression in the nucleus accumbens, ventral tegmental area, and amygdala.

**54. NEURONAL MORPHOLOGY OF THE MAGNOCELLULAR SUBDIVISION OF THE MEDIAL PREOPTIC NUCLEUS USING GOLGI TECHNIQUE IN INTACT AND CASTRATED MALE HAMSTERS.** A.K. Motroni and J.M. Swann. *Lehigh University, Dept. of Biological Sciences, Bethlehem, PA 18015.*

The magnocellular subdivision of the medial preoptic nucleus (MPN mag) plays a critical role in the regulation of male sexual behavior in the Syrian hamsters. Lesions that include this area eliminate copulation. The MPN mag appears to regulate behavior by integrating pheromonal and steroidal signals. Pheromonal signals that initiate mating stimulate the MPN mag in gonadally intact males but fail to do so in castrates. To further delineate neural morphology with regard to hormonal milieu, we examined the profiles of neurons in the MPN mag of intact and castrated male Syrian hamsters labeled with a modified Golgi impregnation technique. One neuron from the MPN mag of each of 3 castrates and 3 intact males were examined. These neurons were traced in their entirety and examined for dendrite number and length, dendritic spine number, and overall orientation. All spines were included whether their shape was stick-like, pedunculated, or appearing broad-based. No attempt was made to include spines projecting above or below the visual field. Striking differences were observed. The ratio of spine to dendritic length averaged 0.45 for castrated vs. 0.26 for intact males. The average dendritic length measured 98  $\mu$ m for castrated vs. 184  $\mu$ m for intact males. The predominate orientation of the dendrites was toward in vertical extension in both groups. In the castrate group, 2 neurons were bipolar and 1 was tripolar. In the intact group, 1 bipolar and 2 multipolar neurons were seen. These observations indicate significant changes in morphology in the MPN mag of castrate animals and suggest that gonadal hormones regulate male sex behavior by regulating neural processes in the preoptic area.

**55. INCREASED FOS EXPRESSION IN HYPOCRETIN/OREXIN NEURONS FOLLOWING MALE RAT SEXUAL BEHAVIOR.** Muschamp, J.W. and Hull, E.M. *Department of Psychology, University at Buffalo-SUNY, Buffalo, NY 14260.*

The hypocretin/orexin (Hcr/Orx) system of the lateral hypothalamic area is thought to facilitate arousal and behavioral activation, including