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113.5

BRAIN AROMATASE ACTIVITY OF FETAL AND ADULT GUINEA PIGS. P.B. CONNOLLY*, C.E. ROSELLI, J.A. RESKO* (Spon: H. Spies). Physiology Dept., Oregon Health Sci U, Portland, OR 97201, Oregon Reg Primate Res Ctr, Beaverton OR 97006

Conversion of androgens to estrogens by aromatase activity (AA) may be important for organizing nervous tissues that mediate sexual behavior or gonadotropin release. Although testosterone (T) is a definite effector of androgen action in the guinea pig (GP), the role of *in situ* conversion to estradiol in sexual differentiation of the brain is less clear. We undertook a study to characterize and localize microsomal AA in brains of fetal, neonatal and adult male GP. Hypothalamic tissues from 50-day fetuses and adult males contained AA with an apparent Km of 19.6 and 16.6 nM, respectively. Fetal and neonatal brain AA showed significant ($p < 0.01$) between tissue differences (amygdala [AMG] > preoptic area [POA] > basal hypothalamus > septum > cortex); no sex difference was apparent. AA was highest at 40-days gestation, declined ($p < 0.01$) with gestational age (50 and 60 days) and was lowest at 5-days post-partum. Adult male brains showed a similar distribution of AA to fetus with greatest activity in AMG and POA. AA in adults was greater ($p < 0.01$) than in neonates. Castration (2 weeks) had no effect on AA in adult brains. These data demonstrate the existence of AA in fetal, neonatal and adult GP brain and suggest that AA in the brain of this species may not be androgen dependent. Supported by HD-07133 and HD-16022.

113.7

FETAL ETHANOL EFFECTS ON AROMATASE ACTIVITY IN THE HYPOTHALAMIC-PREOPTIC AREA IN THE MALE NEONATAL BRAIN. P.K. Rudeen, J.A. Creighton*, W. Kelce* and V.K. Ganjam*. Depts. of Anatomy and Vet. Biomed. Sci., Univ. of Missouri School of Medicine and College of Vet. Medicine, Columbia, MO 65212.

The fetal ethanol induced demasculinization of the sexually dimorphic nucleus of the preoptic area in male rats may be due to the inhibition of fetal testosterone synthesis by a 50% reduction of 17 α -hydroxylase activity. This study was conducted to determine the effects of fetal ethanol exposure on aromatase activity in the anterior hypothalamic-preoptic area of neonatal male rats. Estrogen formation in individual brains was assayed *in vitro* using the stereospecific production of H_2O from (1 β -3H)- androstenedione as a measurement of aromatase activity. Aromatase activity was significantly higher ($p < 0.05$) in the fetal ethanol exposed animals compared to enzyme activity in animals whose mothers were given the chow diet (92.2 ± 7.5 and 61.1 ± 6.4 pmoles/hr/mg protein, respectively). Animals exposed to the pair fed diet had intermediate enzyme activity. The increase in aromatase activity in FEE animals may be due to a compensatory increase in enzyme activity due to reduction in the availability of testosterone from fetal testes. (Supported by Grants AA05893 and AA00107).

113.9

ESTROGEN STIMULATES THE INCORPORATION OF NEW NEURONS INTO AN AVIAN SONG NUCLEUS DURING ADOLESCENCE. E.J. Nordeen and K.W. Nordeen. Psychology, U. Rochester, Rochester, NY, 14627.

The avian song nucleus hyperstriatum ventralis pars caudalis (HVC) contains more neurons in adult males (who sing) than in females. In part, this sex difference develops because HVC neurons born during song learning are added in greater numbers in young males than in females. We report here that estradiol (E2) masculinizes HVC by stimulating the addition of these newly-generated neurons.

Two days after hatching, female zebra finches received silastic implants of E2. Beginning 20 days after hatching, these females and normal males and females were injected with $[^3H]$ -thymidine daily for 20 days. On day 25, the E2-treated females were implanted with either empty or dihydrotestosterone (DHT)-filled silastic tubes. Birds were killed at 64 days of age and coronal sections (10um) were processed for autoradiography.

In females, early E2 treatment increased the addition of HVC neurons born after 20 days of age. Exposure to DHT during the juvenile period did not augment this increase. The percentage of labeled HVC neurons in males (19.9%), E2-treated females (23.4%) and E2+DHT-treated females (19.0%) was greater than in normal females (11.9%). These data suggest that sex differences in HVC neuron number arise because in males, early E2 exposure promotes the production or survival of HVC neurons born during the period of song learning.

113.6

SEX AND AGE-RELATED DIFFERENCES IN NUCLEAR ESTROGEN BINDING CAPACITY AND PROGESTIN RECEPTOR INDUCTION IN THE RAT BRAIN T.J. Brown, N.J. MacLusky, E.E. Jones and F. Naftolin. Dept. of Ob/Gyn, Yale Univ. Medical School, New Haven, CT 06510

Previous studies have suggested parallels between the mechanisms underlying sexual differentiation and age-related loss of reproductive cyclicity in the female rat. Both appear to involve the actions of estrogen on the brain; and are associated with a reduction in hypothalamic estrogen sensitivity. The present studies were performed to directly compare the effects of sex and aging on cell nuclear estrogen receptor (ERN) capacity and cytosol progesterin receptor (PRc) induction in the rat brain and pituitary gland. Young (2.5 mo) and middle-aged (8-10 mo) male and female, and old (19 mo) female rats were gonadectomized and adrenalectomized two weeks before use. ERn capacity and estrogen induction of PRc were measured in the pituitary (PIT), periventricular preoptic area (PVPOA), medial preoptic area (mPOA), bed nucleus of the stria terminalis, arcuate-medial eminence region, ventromedial nucleus (VMN) and corticomedial amygdala. RESULTS: ERn levels and PRc induction were lower in the PVPOA, mPOA and VMN of the male as compared to the female. In the female, although the level of PRc induction in the PIT and the six different brain regions was unaffected by age, ERn capacity in the mPOA, VMN and PIT was significantly lower at 19mo than at either 2.5 or 8-10mo. ERn capacity in the PVPOA was identical in young and old animals. CONCLUSIONS: These results demonstrate that the effects of sexual differentiation and aging on the hypothalamus involve similar, but not identical, region-specific reductions in ERn binding capacity. The consequences of these reduced ERn levels in terms of the PRc response to an estrogen challenge are, however, different in male as compared to old female rats. (Supported by NIH grants HD13587, AG05004 and NS07807)

113.8

DEVELOPMENTAL CHANGES AND SEX DIFFERENCES IN THE ACTIVITY OF TESTOSTERONE-METABOLIZING ENZYMES IN THE BRAIN OF THE ZEBRA FINCH. A. Vockel*, E. Pröve* and J. Balthazar. Dept. Ethology, Univ. Bielefeld, FRG and Lab. Gen. and Comp. Biochemistry, Univ. Liège, Belgium.

Many effects of testosterone (T) in the zebra finch (*Taeniopygia guttata*) can be mimicked by T metabolites, mainly oestradiol and 5 α -dihydrotestosterone. We have therefore characterized T-metabolizing enzymes and studied their neuroanatomical distribution by means of the Palkovits punch technique combined with radioenzyme assay in the brain of adult and young male and female zebra finches. The kinetic parameters (Km, Vmax) of the aromatase, the 5 α - and 5 β -reductase were first determined in the hypothalamus of birds of both sexes at different ages between 5 and 100 days post-hatch. We observed a large decrease of the Vmax and Km of the 5 β -reductase and a substantial decrease of the Km of the aromatase with increasing age. No significant sex difference in these parameters was detected. The activity of these enzymes was then studied by a one point assay in 4 nuclei of the song system (X, RA, ICo, HVC), 2 nuclei of the visual system (*ectostriatum*, *n. rotundus*) and in limbic and hypothalamic areas. Very noticeable was the presence of a very high not sexually dimorphic aromatase activity in the hippocampal region and in the *nucleus taenialis* and the absence of this enzyme in ICo. We found a higher aromatase activity in male than female preoptic area-anterior hypothalamus and a higher 5 α - but lower 5 β -reductase activity in RA of males compared to females. Many age-related metabolic differences were also detected but these do not have a clear interpretation since the Km of these enzymes also changes with age. Extremely low levels of 5 β -reductase activity were found in the nuclei of the visual system in adult birds while this enzymatic activity was very high in young birds. The function of this change with age remains obscure. Correlations are thus observed between the neuroanatomical distribution of T-metabolizing enzymes and of androgen and estrogen receptors with the important exception of ICo which has no aromatase but contains high concentrations of estrogen receptors. T-metabolizing enzymes are however also present in areas which are not known as steroid targets.

113.10

EFFECT OF HVC LESIONS ON ESTRADIOL-INDUCED MASCLINIZATION OF ZEBRA FINCH SONG SYSTEM. K. Hermann* and A.P. Arnold (SPON. S.C. Lee) Dept. of Psychology, UCLA, Los Angeles, CA 90024.

The song system of male zebra finches is much larger than in females. Early treatment with estradiol (E2) can masculinize female song areas by increasing both the number and size of neurons. The mechanism by which this masculinization occurs is unknown. One hypothesis is that E2 acts transsynaptically by first masculinizing one nucleus which then masculinizes the development of other song regions. We tested this idea by lesioning HVC (caudal nucleus of the ventral hyperstriatum) unilaterally in 20 day old female zebra finches which were implanted with a 200 ug E2 pellet. At day 60 the birds were sacrificed and the volume of RA (robust nucleus of the archistriatum), area X and MAN (magnocellular nucleus of the anterior neostriatum) were analyzed for interhemispheric differences.

Most pronounced left/right differences after unilateral HVC lesions were seen in area X which was virtually absent or very small on the side of the lesion. RA volume was reduced by about 30% ipsilateral to the lesioned HVC, whereas MAN seemed to be masculine in morphology and symmetric and therefore not affected by the lesion. These data suggest that the E2-induced masculinization of area X, and to a lesser degree of RA, is dependent on the presence of HVC, whereas the masculinization of MAN does not seem to require an intact HVC.

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