A13

ORAL CONTRACEPTIVE AND CHRONIC ETHANOL INDUCED CHANGES IN REPRODUCTIVE FUNCTION IN THE FEMALE RAT. Charles D. Lox* and F. S. Messiha
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The relationship between ethanol (ETOH) and reproductive function in the female rat has been studied by evaluating the effect of consumption of various ethanol (ETOH) concentrations on male serum hormonal levels and on hepatic enzymes involved in the metabolism of ETOH and acetaldehyde. Female rats were placed on water (H_2O), 5% ETOH, or 20% ETOH drinking solution for 8 weeks. The last two weeks, the rats received orally either ethynyl estradiol (EE), 4 ug/kg/day, norethindrone acetate (NED) 8 ug/kg/day, or a combination of both in identical concentrations once daily for 14 days.

Luteinizing hormone (LH) decreased due to ETOH drinking and was undetectible subsequent to steroidal treatment. The intake of 5% ETOH solution concomitant with EE or EE plus NED had a significant (p 0.05) 2 fold increase in prolactin from controls where as to the 20% ET drinking rats this was limited to those receiving NE. This may reflect a possible synergistic effect between EE level and exposure to 5% ET indicating a possible different site of action of the steroids which might be modified by the level of exposure to ETOH.

Hepatic alcohol dehydrogenase (ADH) enzyme was inhibited due to EE when compared to water controls in the 5% drinking animal, whereas aldehyde dehydrogenase (ALDH) was induced in combination with NED in both the 5% and 20% drinking rats. The modulation of these enzymes by the contraceptive agents studied in ETOH drinking rats from corresponding water controls suggestive of a toxic metabolic ETOH contraceptive interactions.

A14

MOUSE ETHANOL PREFERENCE AS A FUNCTION OF GENOTYPIC LEVELS OF WHOLE BRAIN METHIONINE ENKEPHALIN. Blum, K., Elston, S.F.A., Briggs, A.H. and DeLallo, L., Division of Substance and Alcohol Misuse, University of Texas Health Science Center, San Antonio, Texas 78284.

Our laboratory has proposed common mechanisms of action for alcohol and opiates. The common mechanism resides in the formation of isoquinolines which function as a "link" between these two highly addictive substances by direct or indirect interaction with opiate receptors. Most recently, we proposed the psychogenetic theory of drug seeking behavior. The basic element of the theory involves the concept that alcohol desire as an example, may be dependent in part on a genetic deficiency of the internal opiates (enkephalins or endorphins) along with certain environmental factors. Thus, it was decided to evaluate the levels of whole brain enkephalin in various strains of mice with different degrees of prefernece for ethanol. Results obtained illustrate that a negative correlation exists between methionine-enkephalin and ethanol 14-day mean preference ratios. DBA non-alcohol preferring mice were found to possess higher levels (339 ± 12 pu/g) than C3H (316 ± 28 pu/g), an intermediate strain in terms of ethanol desire. In addition, C57 (307 ± 0.4 pu/g) and C58 (268 ± 18 pu/g) mice, which are high preferring mice, had significantly lower levels than both DBA and C3H strains of mice. The correlation coefficient calculated for DBA, C3H and C57 was 0.93. These results suggest that the baseline brain levels of methionine-enkephalin may be a predictor for degrees of ethanol desire in mice.

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A15

IMMUNOCYTOCHEMICAL LOCALIZATION OF ALCOHOL DEHYDROGENASE. Goldstein, B. and Maxwell, D.S., University of California, Los Angeles, California.

Alcohol dehydrogenase (ADH) activity has been demonstrated biochemically in several organs. Biochemical, immunochemical, and immunocytochemical studies were completed to determine the cellular localization of rat brain and liver alcohol dehydrogenase. The ADH-containing cells were examined with light and electron microscopy following the utilization of the peroxidase-antiperoxidase method. Observations in the cerebral cortex included stained cortical neurons and apical dendrites continuing towards the surface of the brain. Cells in the deeper layers of the cortex were the only cells that contained reaction product after staining. Electron microscopy revealed reaction product in cell bodies, processes, and specific synapses. Glial elements did not stain specifically. In the liver, the cytoplasm of all hepatocytes stained intensely. Nuclei were unstained, as well as other cytoplasmic organelles. Kupffer cells and endothelial cells did not contain the reaction product. Parallel control sections were all negative. This study has established a means for correlative biochemical and morphological studies of the localization of alcohol dehydrogenase. This method offers an approach to study the distribution of this enzyme in different brain regions, in several organs, and following various experimental conditions. In addition, alcohol dehydrogenase might prove to be a useful neuronal-specific enzyme.

A16

ETHANOL EFFECTS ON SERUM GONADOTROPIN LEVELS IN MALE RATS. Ring, D., Evans, P., Joanning, S., and Menendez, C.E. Endocrinology Section, Department of Internal Medicine, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, Texas 79430.

It has long been recognized that chronic ethanol abuse causes hypogonadism in males. Not much is known, however, about the short term effects of ethanol on the gonadotropin levels in the rat. The present study examines the effect of large doses of ethanol on serum luteinizing hormone (LH) - follicle stimulating hormone (FSH) levels in adult, male castrated rats. Rats were injected intraperitoneally (IP) with 3.0 g/kg body weight (BW) of ethanol or an equivalent volume of saline for 1, 3, or 5 days. After 5 days serum LH levels were significantly lower in the ethanol group than the saline group, indicating an inhibition of the normal post-castrational rise in serum LH. Other LH and all FSH levels were not significantly different from the saline controls. This study demonstrates that short-term ethanol administration can lower LH levels, which may be a mechanism contributing to the hypogonadism associated with more chronic use of ethanol.

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A17

ISOLATION AND PARTIAL CHARACTERIZATION OF γ-GTP FROM MICE DIFFERING IN ETOH SENSITIVITY.
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The present study was undertaken to determine the biochemical and physical properties of the membrane bound enzyme γ-glutamyl transpeptidase (γGTP) in two strains of mice selectively bred for their sensitivity to ethanol. Male mice (90-120 days of age) were decapitated and the brains and livers excised and placed in cold Tris buffered saline. The tissues were homogenized and let stand for 24 hours in 1% deoxycholic acid. The long sleep mice were found to have a higher level of γGTP in liver than did the short sleep mice but the brain level was lower. The individual brain samples were then pooled and purified as previously described in our laboratory utilizing deferential centrifugation and ammonium sulfate precipitation. The enzyme preparation from the long sleep mice was fractionated into 3 peaks of enzyme activity on a DEAE column while the short sleep mice preparation only produced 2 peaks of enzyme activity. Km's and Vmax's were determined for each peak. It was also noted that γGTP isolated from liver also differed. The difference in γGTP between these strains of mice may account, at least in part, for the difference in ethanol sensitivity between the strains.

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A18

The Effects of "Week-end" Drinking on Activity of Sinclair (S-1) Miniature Swine. J.D. Dexter, M.E. Tumbleson and C.C. Middleton, School of Medicine and Sinclair Research Farm, Univ. of MO, Columbia, MO 65212

24 six month old Sinclair S-1 miniature were divided into three groups. Groups I and II were fed one and three grams of ethanol/Kg/day and Group III were allowed free choice alcohol ad lib for 2.5 days out of each week for 40 weeks. The animals were observed for withdrawal signs after the completion of the 2.5 days of exposure to ETOH. Every second cycle one animal from each group was placed in an activity chamber which measured total activity for 9 days (2 days prior to alcohol, 2.5 days of ETOH treatment and 4½ days post alcohol). Then Voluntary consuming group (III) consumed 3.3±1.5gm/Kg/day (range 1.4 to 4.5).

The clinical observation revealed only a small amount of behavioral lethergy which could not be quantified. However the results of the activity chambers revealed the following variations from the mean of the 7 days (1 day prior to ethanol 2.5 days of ethanol exposure and 4 days following ethanol).

Day	1	2	3	4	5	6	7
Group I	107± 7	96±14	103±10	117±14	113±17	86±11	75±16
Group II	152±16	139±12	103±15	118±13	91±18	78±19	48±17
Group III	105±15	130±15	152±17	108±15	68±20	69±13	69±15

The significant change was the marked decrease in activity during the 4 days following alcohol consumption which is most obvious in Groups II and III.

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