5087872720: MAJOR PHYSIOLOGY
KEYWORDS: ANXIETY / BENZODIAZEPINE / ESTROGEN / $GABA_A$ RECEPTOR / OVARIECTOMIZED RAT

SUWAPORN DAENDEE: EFFECTS OF ESTROGEN ON $GABA_A$ RECEPTOR PLASTICITY AND ANXIETY-LIKE BEHAVIOR IN OVARIECTOMIZED RATS.ADVISOR: ASST.PROF.SARINEE KALANDAKANOND THONGSONG, D.V.M., Ph.D., CO-ADVISOR: ASSOC.PROF. BOONRIT THONGSONG, D.V.M., Ph.D., 114 pp.

In the present study, the effects of estrogen on anxiety-like behavior and the alterations of GABAergic and serotonergic systems were focused. It was hypothesized that the length of estrogen deprivation had a negative effect on the level of anxiety-like behavior measured with the elevated T-maze (ETM); and this effect may be related to the alteration of $GABA_A$ receptor subunits and/or serotonergic activity in the brain areas associated with anxiety. In order to test these hypotheses, this study was divided into 3 parts. In part 1, to determine the length of estrogen deprivation on anxiety behavior and the $GABA_A$ receptor subunit mRNA expressions along with the changes in serotonin levels, the female Wistar rats were divided into 2 groups, ovariectomized-rat (Ovx) and ovariectomized-rat with estrogen replacement (E_2). Then the rats from each group were randomly selected for behavioral test at 7, 14, 21 or 28 days after ovariectomy,. The behavioral data from the ETM demonstrated that the rats that were deprived of estrogen for 21 and 28 days had higher level of anxiety compared to those at day 7 and 14. Moreover, a significant negative correlation between the time of estrogen deprivation and the level of anxiety was found. For the E_2 groups, the number of day following ovariectomy had no significant effect on anxiety behavior. After behavioral tests, the measurement serotonin (5-HT) and its metabolite (5-HIAA), and $GABA_A$ receptor subunit gene expression were examined. In conjunction to the behavioral data, the serotonergic activity was more fluctuated in the Ovx rats compared to the E_2 rats. For $GABA_A$ receptor subunit gene expression, the α2-, α3- and α4 $GABA_A$ receptor subunit gene expressions in the midbrain were higher in the Ovx than the E_2 groups especially for α2- and α3-$GABA_A$ receptor subunits. Interestingly, the α3- and α4- receptor subunits were markedly up-regulated at day 21 in the Ovx groups. Contrarily, the expression levels in the E_2 groups were rather stable. These results suggested the alteration in GABAergic and serotonergic systems in relation to behavior. In part 2, the $GABA_A$ receptor function was determined in the 3 weeks-Ovx rats with or without E_2 supplementation by injecting benzodiazepine agonist (diazepam, 0, 0.25, 0.5 and 1 mg/kg) 30 min before behavioral test. The results in this part indicated that the $GABA_A$ receptor sensitivity was increased in the 3 week ovariectomized rats. In part 3, to determine the effect of estrogen in treating anxiety along with the alteration of $GABA_A$ receptor function; the rats were first ovariectomized for 3 weeks to warrant the estrogen depletion, before supplemented with or without E_2 for 4 weeks. On the behavioral test day, the rats from each group were subdivided into 2 groups receiving vehicle or diazepam (0.25 mg/kg; the effective dose from part 2) in order to test the function of $GABA_A$ receptor. In this part, the data indicated that estrogen could alleviate anxiety in anxious rats. For the serotonergic activity following diazepam administration as in parts 2 and 3, there was no difference in the levels of 5-HT and 5-HIAA or the ratio of 5-HIAA/5-HT in the Ovx groups in all examined brain areas; whereas, in the E_2 groups, the 5-HT levels was significant increased in some areas. Therefore, this information contributes to the roles of estrogen in generating anxiety in relation to the GABAergic system.

Field of Study: .....Physiology..... Student's Signature.....

Academic Year:.....2011..... Advisor's Signature.....

Co-advisor's Signature.....