修士論文要旨

Estradiol is a key factor modulating daily changes of body temperature and heart rates

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Introduction Women are physically and psychologically affected by the female sex hormones (i.e., estradiol and progesterone). There are some indirect evidences showing that estradiol may affect daily rhythms of body temperature (T_b) and heart rates (HR). In addition, problems in peri- and postmenopausal women may be related to disturbance of the rhythms. The aim of the present study was to investigate how change in plasma estradiol affects rhythms of T_b and HR. I used ovariectomized rats with estradiol replacement or withdrawal, and 3-wks continuous measurements of T_b and HR were conducted.

Methods

Experiment 1 Female Wistar rats (n=14, age of 9 w) were bilaterally ovariectomized, and implanted a radio transmitter for T_b and activity (ACT) measurements (PDT-4000 HR E-Mitter) in the abdominal cavity. Two electrode lead-wires for ECG measurement were subcutaneously placed in the chest wall. Two silicon tubes containing 17β-estradiol (50–60 mg) were subcutaneously placed in one group (n=7, E_2 (+)), and empty tubes for the other group (n=7, E_2 (–)). The tubes were removed 10 days after the placement (defined as Day 0).

Experiment 2 Female Wistar rats (n=9, age of 7–9 w) were bilaterally ovariectomized, and implanted a radio transmitter for HR and arterial pressure (AP) measurements (TL11M2-C50-PXT) in the abdominal cavity. AP was assessed through a thin catheter place in the descending aorta.

Experiment 3 One day before the removal of the tubes (defined as PRE), on Days 7 and 21, female Wistar rats (n=30) were killed. The heart was excised, and the cell membrane of the ventricle of the heart was prepared for the protein determination of β_1 and β_2-adrenoreceptors (AR) was determined by Western blotting.

Results On PRE, T_b in the E_2 (–) group was lower ($P < 0.05$) than that in the E_2 (+) group at 23:30–1:30 (37.4±0.1℃ and 38.0±0.3℃, respectively). On Day 14, T_b in the E_2 (+) group was higher ($P < 0.05$) than PRE at 14:30–18:30 (36.8±0.1 and 36.7℃, respectively). On PRE, HR was greater ($P < 0.05$) in the E_2 (–) group than that in the E_2 (+) group (388±15 and 337±13 beats/min (bpm) in the light phase; and 450±12 and 390±12 bpm in the dark phase, respectively). On Day 14, HR in the E_2 (+) group was greater ($P < 0.05$) than PRE (377±15 bpm in the light phase; and 431±14 bpm in the dark phase). On Day 21, HR in the E_2 (–) group became lower ($P < 0.05$) than the PRE (330±17 bpm in the light phase; and 388±20 bpm in the dark phase). Mean AP was not different between the two groups on each day, and remained unchanged in each group. On PRE, both β_1-AR and plasma noradrenaline were greater ($P < 0.05$) in the E_2 (–) than E_2 (+) group. On Day 7, both β_1-AR and plasma noradrenaline decreased from the values of PRE; however, on Day 21, plasma noradrenaline became higher again. On PRE, β_2-AR was greater ($P < 0.05$) in the E_2 (+) than E_2 (–) group. On Day 21, β_2-AR in the E_2 (+) group decreased ($P < 0.05$).

Discussion T_b in the E_2 (–) group showed a short-term (2 h) reduction in the middle of the dark phase, whereas the reduction was not observed by estradiol replacement. Therefore, estradiol may have an effect on a daily change of T_b in female rats. At the same time of the T_b reduction, ACT seemed to decrease to the level in the light phase. Thus, the T_b reduction may be related to smaller activity. Another possible reason for the reduction of T_b may be augmented tail vasodilation. Although Gonadotropin-releasing hormone (GnRH), which facilitates tail vasodilation, level was not assessed in the present study, higher GnRH due to low estradiol level may have increased the vasodilation, resulting in hypothermia. After the removal of estradiol, T_b increased in the last half of the light phase. When increase of T_b was observed in the light phase, ACT remained unchanged. Thus, the T_b elevation may not be related to ACT.

HR decreased on Day 21, although HR significantly increased in PRE. The increase of HR after ovariectomy was transient. The expression of β_1-AR decreased on Days 7 and 21 in the E_2 (–) group, although greater expression of that was observed on PRE. Thus, the increase of the expression of β_1-AR after ovariectomy was also transient. An increase of plasma noradrenaline level seems to be linked with a reduction of plasma estradiol level. Greater expression of β_1-AR and plasma noradrenaline level may have worked together to increase of HR on PRE.

Conclusion The present study indicated that a reduction of plasma estradiol in female rats modulates daily rhythm of T_b and transiently increased HR with augmented β_1-AR expression and plasma noradrenaline level. These results may enable us to understand mechanisms for disturbance of the rhythms of T_b and HR, which are observed as peri- and postmenopausal syndrome (i.e., hot flushes and palpitation).