Neuroprotective effect of long-term low dose hormone replacement therapy on postmenopausal women brain hippocampus

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Objective:

To investigate the differences between the long-term low dose hormone replacement therapy (HRT) in postmenopause group and control group in hormone level, peripheral benzodiazepine receptor (PBRs) level and volume of hippocampus with the same susceptibility of genotype to Alzheimer's disease (AD).

Methods:

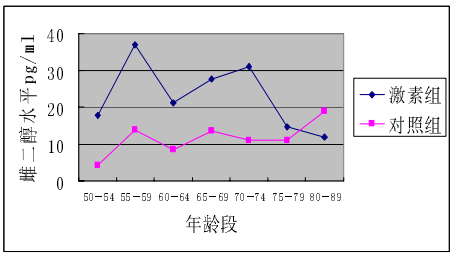
182 employees at the age of 50~87 who were in their postmenopause of Peking Union Medical College Hospital were chosen and allocated to HRT and control groups. The volunteers from the former group had taken a 1/2 ~ 1/4 dose for 4~33 years. The concentrations of estradiol (E_2,) progesterone (Pro) and testosterone (T) were measured through Ezyme linked immunosorbent assay (ELISA), the activity of PBRs on the peripheral platelet membranes was determined by ^{3}H-PK11195; after DNA was extracted from the white blood cells of the volunteers, the gene types of ApoE and ERa were measured through PCR method; then the persons with susceptible genes of AD (ApoE ε 3/ ε 4) were screened, whose hippocampus volumes between two groups were compared through MRI. The scanning protocol include axial T2 weighted image, matched FLAIR image, T1 weighed image(oblique coronal, vertical to the hippocampus, slice thickness 3mm, without gap, and including the whole body of hippocampus), and 3D image including the whole brain. High signal abnormalities were rated by three experienced neuroradiologists on T2WI or FLAIR images. The sites and grades of hyperintensities were described in Table 1. Volume of bilateral hippocampus was manually measured and then calculate the ratio of hippocampus and the whole volume of the brain. Then the statistical method were taken to analyse the results.

Results:

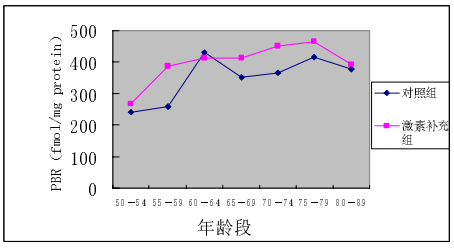
Compared with control group (99 cases), the concentrations of E_2 at each age stages in the HRT group (83 cases) were obviously higher (P<0.05, picture 1); there were no statistical differences in the concentrations of Pro and T between the two groups. The activity of PBRs on the peripheral platelet membranes in the HRT group was higher than the control group at each age stages(picture 2), and there was obvious correlation between the concentration of HRT and E2 in the blood. There was no obvious difference in ApoE and ERa subtypes distribution between the two groups. The results of hippocampus MRI for the persons with susceptible genes ApoE ε 4 (HRT group 14 cases, control group 11 cases) showed that the left and right hippocampus volumes in the HRT group were larger than the control group, and there were obvious differences (P<0.05, picture 3).

Conclusion:

To those postmenopausal women，long-term low dose HRT maintain the E_2 physiological concentration in blood plasma, and which can keep PBR activity staying at high level. Because PBR modulate synthesis of hormone，up-regulation of PBR significantly decrease the degree of anxiety in postmenopausal women. Furthermore, the hippocampus MRI result from the persons with ApoE ε 4 gene showed that the volume of left and right hippocampus in the HRT group were larger than the control group's, which indicate that long-term low dose HRT can avoid hippocampus atrophy, which is beneficial to maintaining function of brain and prevention of AD.



Picture 1: the concentrations of E2 in each group



picture2: The activity of PBRs on the peripheral platelet membranes