

Study on the Regulatory Mechanism of Ginkgo Biloba Extract on the Central BDNF-TrkB-PI3K/Akt-CREB Signaling Pathway in Rats with Depression

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Abstract

Objective: To investigate the mechanism of antidepressant effects of Ginkgo biloba extract through the BDNF-TrkB-PI3K/Akt-CREB signaling pathway, Ginkgo biloba ketoester tablets and Yinxing Mihuan oral liquid were studied in the hippocampus of rats with liver depression and spleen deficiency syndrome. **Methods:** A 21 day chronic unpredictable mild stress (CUMS) method was used to prepare a rat model of liver depression and spleen deficiency syndrome. The appearance, body weight, food intake and open field experiment of the rats were observed to determine the success of the model. The rats were divided into five groups: normal group, model group, Western medicine control group and two treatment groups including Ginkgo biloba ketoester tablets group and Yinxing Mihuan oral liquid group. Using RT qPCR, immunohistochemistry, Western blot and Elisa, etc, the key molecular indicators on the BDNF-TrkB-PI3K/Akt-CREB pathway were detected at the levels of mRNA and protein. **Results:** On the 21st day of the experiment, in terms of appearance, the rats in the model group exhibited clear signs of spleen deficiency, such as dry and yellow hair, watery stools and no escape behavior in the model group. Body weight, food intake, and all indicators in the open field experiment decreased significantly ($P < 0.05$), while the treatment groups showed significant improvement ($P < 0.05$). Compared with the model group, the treatment groups showed an increase in the number of neurons in the hippocampal tissue of the rats with more regular cell morphology, smaller intercellular gaps, relatively neat cell arrangement, and clearer nucleolus. There was no significant difference in the morphology of hippocampal tissue between the normal group and the control group. Compared with the normal group, the levels of mRNA and protein expression of BDNF, Akt and CREB in the hippocampus of the model group were significantly decreased ($p < 0.01$). While, compared to the model group, the levels of mRNA and protein expression of BDNF, TrkB, Akt, mTOR, and CREB in the hippocampal tissue of the Ginkgo biloba extract treatment group were significantly upregulated ($p < 0.05$). **Conclusion:** The levels of mRNA and protein expression of BDNF, TrkB, Akt, and CREB in the hippocampus of CUMS rats with liver depression and spleen deficiency syndrome were significantly reduced compared to the normal group. Ginkgo biloba extract has a significant improvement effect on depressive behavior in model rats, and can reverse the damage of depressive stimuli to hippocampal tissue cells. Its mechanism may play an antidepressant role by regulating the BDNF TrkB-PI3K/Akt CREB signaling pathway.

Keywords

Ginkgo Biloba Extract, Signaling Pathway, Liver Depression and Spleen Deficiency Syndrome