

The Role of DNA Methylation Regulating BDNF Expression in Depressive Behavior of Mice Under Acute Restraint Stress

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Abstract

Depression is a common and serious neurological disorder, but the molecular mechanisms underlying its development and the corresponding treatments are still limited. Therefore, in the present study, mice were subjected to 24 h restraint stress stimulation to construct a model with acute depressive-like behaviour, and to investigate the molecular mechanism of DNA methylation regulating brain-derived neurotrophic factor (BDNF) expression in the depressive behaviour of mice. ICR male mice were used as experimental subjects and randomly divided into Control group and Restraint group, detection of depression-like behaviour in mice after acute restraint stress stimulation using the open field test and sucrose preference test. Subsequently, the expression of BDNF and its receptors TrkB, DNA methyltransferase1 (DNMT1), 3A (DNMT3A) and 3B (DNMT3B) were measured in the hippocampal region of mice. Finally pyrophosphate sequencing examined the methylation level of BDNF promoter region. The results revealed that compared with the Control group, mice in the Restraint group had a shorter total distance travelled in the open field test; a decrease in sucrose consumption in the sucrose preference test; a decline in body weight. The acute restraint stress downregulated BDNF expression at both the mRNA and protein levels in hippocampus of the Restraint group mice, while it had no effect on protein and mRNA expression of TrkB. In DNA methylation studies, mRNA expression of DNMT3A and DNMT3B was elevated in hippocampus of the Restraint group mice compared with the Control group, and the difference in mRNA expression of DNMT1 was not statistically significant. In addition DNA methylation in the BDNF promoter region was significantly higher in the Restraint group compared to the Control group. The above results suggest that mice might be induced to develop significant depressive-like behaviours after 24 h of restraint stress, accompanied by upregulation of DNA methylation levels to downregulate BDNF expression.

Keywords

Depression, 24-Hour Restraint Stress, Brain-Derived Neurotrophic Factor, DNA Methylation