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The effect of short photoperiod on the behavior, brain serotonin system and BDNF in mice that differ in predisposition to catalepsy

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Introduction: Seasonal affective disorder (SAD) is a complex of behavioral disorders that occur due to a decrease of the light phase of the day. According to the World Health Organization, such violations are observed in about 20–25 % of people in the autumn-winter period of the year. It is now believed that the formation of SAD is associated with an imbalance in the functioning of the brain serotonin (5-HT) system, neurotrophic factors and circadian rhythms. However, the pathophysiological and genetic mechanisms of the development of SAD remain poorly understood nowadays.
Catalepsy is a prolonged motor inhibition, presenting a syndrome of several psychopathologies as schizophrenia and affective disorders. A large amount of data has been accumulated on the involvement of the brain 5-HT system and BDNF (Brain-derived neurotrophic factor) in the regulation of hereditary catalepsy in mice of CBA/Lac strain that are characterized by high genetic predisposition to a pathological cataleptic reaction. It has been suggested that CBA/Lac mice may be sensitive to the exposure of decreased daylight length. The aim was to study and compare the effects of short photoperiod on the behavior and state of brain serotonin system in mice of non-cataleptic C57BL/6J and cataleptic CBA/Lac strains.
Methods: Adult males (2 months) of the experimental groups were kept under conditions of short photoperiod (light/dark: 4/20) for 6 weeks, whereas the animals of the control groups were kept under standard conditions (light/dark: 14/10). Behavior was assessed in the "open field", "forced swimming", "tail suspension" and "pinch-induced catalepsy" tests. The levels of 5-HT and its metabolite 5-HIAA in brain structures (prefrontal cortex, hippocampus, midbrain, hypothalamus) were studied by HPLC. The mRNA levels of genes encoding a) BDNF and its TrkB, p75 receptors and b) key elements of brain 5-HT system were determined using Real-Time PCR. The data were analyzed by two-way ANOVA followed by LSD post-hoc test.
Results: Exposure to a short photoperiod resulted in persistent rise of depression-like behavior in mice of both strains ($p < 0.05$), as well as an increase in duration of cataleptic freezing in CBA/Lac animals ($p < 0.05$) compared to control mice.
A decrease in the level of serotonin in the hypothalamus ($p < 0.05$) and hippocampus ($p < 0.05$) and the level of its metabolite 5-HIAA in the hypothalamus ($p < 0.05$) was observed only in mice of the cataleptic CBA strain under conditions of keeping with shortened daylight hours.
Exposure to a short photoperiod led to a decrease in the expression of 5-HT1A receptor genes in the cortex ($p < 0.05$) and 5-HT4 receptor genes in the hippocampus ($p < 0.05$) in C57Bl/6 mice, as well as a decrease in gene expression of 5 -HT1A and 5-HT7

receptors in the hippocampus ($p < 0.05$), 5-HT4 receptors in the hypothalamus ($p < 0.05$) and tryptophan hydroxylase 2 gene in the midbrain ($p < 0.05$) in CBA mice. A significant decrease in the expression of the 5-HT2A receptor gene in the hippocampus was found in C57BL/6 animals relative to CBA animals, however, a significant effect of a short photoperiod on both lines was not observed. *Bdnf* gene expression in the cortex significantly decreased in the CBA/ Lac line in comparison with the control group ($p < 0.05$). Though there were no significant changes in expression of genes encoding TrkB and p75 receptors.

Conclusion: An increase in indicators of depression-like behavior under shortened daylight hours was observed in mice of both strains and was accompanied by a decrease in the functional activity of the serotonin system, these changes were more significant in CBA animals. Thus, the CBA mouse strain can be proposed as an adequate model for studying the molecular and physiological mechanisms of SAD.

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