

## Time-Dependent Modulation on Depressive Responses and Circadian Rhythms of Corticosterone in Models of Melatonin Deficit

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**Abstract :** Melatonin deficit can cause a disturbance in emotional status and circadian rhythms of the endocrine system in the body. Both pharmacological and alternative approaches are applied for correction of dysfunctions driven by changes in circadian dynamics of many physiological indicators. In the present study, we tested and compare the beneficial effect of agomelatine (40 mg/kg, i.p. for 3 weeks) and endurance training on depressive behavior in two models of melatonin deficit in rat. The role of disturbed circadian rhythms of plasma melatonin and corticosterone secretion in the mechanism of these treatments was also explored. The continuous exercise program attenuated depressive responses associated with disrupted diurnal rhythm of home-cage motor activity, anhedonia in the sucrose preference test, and despair-like behavior in the forced swimming test were attenuated by agomelatine exposed to chronic constant light (CCL) and long-term exercise in pinealectomized rats. Parallel to the observed positive effect on the emotional status, agomelatine restored CCL-induced impairment of circadian patterns of plasma melatonin but not that of corticosterone. In opposite, exercise training diminished total plasma corticosterone levels and corrected its flattened pattern while it was unable to correct melatonin deficit in pinealectomy. These results suggest that the antidepressant-like effect of pharmacological and alternative approach might be mediated via two different mechanism, correction of the disturbed circadian rhythm of melatonin and corticosterone, respectively. Therefore, these treatment approaches might have a potential therapeutic application in different subpopulations of people characterized by a melatonin deficiency. This work was supported by the National Science Fund of Bulgaria (research grant # № DN 03/10; DN# 12/6).

**Keywords :** agomelatine, exercise training, melatonin deficit, corticosterone

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