

The dysregulation of circadian clock genes in insomnia combined with anxiety and depressive disorders

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Objective: This project aims to investigate the expression of circadian clock genes in patients with insomnia combined with anxiety and depressive disorders and examine whether they could serve as biomarker to evaluate the outcome of melatonin receptor agonist treatment.

Methods: In this 12- week follow-up study conducted from January 2016 to January 2017, 9 healthy controls and 9 eligible patients with sleep disturbance comorbid with anxiety and depressive disorders were recruited after comprehensive psychiatric assessment. The patients received pharmacological treatments based on the mutual decision between clinicians and patients. The participants who received melatonin receptor agonist; ramelteon (RMT) (8-16 mg/day, n=30) were considered for laboratory analyses. The peripheral blood was collected at weeks 0, 4 and 8 and circadian clock gene expression in mononuclear blood cells (PMBCs) was quantitated by real time PCR.

Results: The real time PCR analysis revealed that period homolog 1 (PER1) and period homolog 2 (PER2) were significantly downregulated in PMBCs of patients with insomnia combined with anxiety and depressive disorders compared with healthy controls. RMT recovers PER1 and partially PER2 mRNA levels during the 8-week treatment. The protein expression of PER1 and PER2 in PMBCs is consistent with mRNA change. The recovery of PER1 and PER2 is significantly correlated with the response to RMT treatment in patients.

Conclusion: PER1 and PER2 genes have strong correlation with the insomnia combined with anxiety and depressive disorders, and both genes could serve as potential biomarkers to evaluate the outcome of patients receiving RMT treatment.

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