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The Short-Day Cycle Induces Intestinal Epithelial Purine Metabolism Imbalance and Hepatic Disfunctions in Antibiotic-Mediated Gut Microbiota Perturbation Mice

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Abstract: Intestinal microbiota dysbiosis is related to many metabolic diseases in human health. Meanwhile, as an irregular environmental light–dark (LD) cycle, short day (SD) may induce host circadian rhythm disturbances and worsen the risks of gut dysbiosis. Herein, we investigated how LD cycles regulate intestinal metabolism upon the destruction of gut microbes with antibiotic treatments. The growth indices, serum parameters, concentrations of short-chain fatty acids (SCFAs), and relative abundance of intestinal microbes were measured after euthanasia; intestinal contents, epithelial metabolomics, and hepatic transcriptome sequencing were also assessed. Compared with a normal LD cycle (NLD), SD increased the body weight, spleen weight, and serum concentration of aspartate aminotransferase, while it decreased high-density lipoprotein. Meanwhile, SD increased the relative abundance of the Bacteroidetes phylum while it decreased the Firmicutes phylum in the gut of ABX mice, thus leading to a disorder of SCFA metabolism. Metabolomics data revealed that SD exposure altered gut microbial metabolism in ABX mice, which also displayed more serious alterations in the gut epithelium. In addition, most differentially expressed metabolites were decreased, especially the purine metabolism pathway in epithelial tissue. This response was mainly due to the down-regulation of adenine, inosine, deoxyguanosine, adenylsuccinic acid, hypoxanthine, GDP, IMP, GMP, and AMP. Finally, the transcriptome data also indicated that SD has some negative effects on hepatic metabolism and endocrine, digestive, and disease processes. Overall, SD induced an epithelial and hepatic purine metabolism pathway imbalance in ABX mice, as well as the gut microbes and their metabolites, all of which could contribute to host metabolism and digestion, endocrine system disorders, and may even cause diseases in the host.

Keywords: light–dark cycles; antibiotics; gut microbes; metabolomics; purine metabolism; transcriptome sequencing

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1. Introduction

Mammalian biological rhythms regulate physiological activities, habits, nutrient digestion, and metabolism in a 24 h cycle. This system relies on the generation and regulation of the central clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus and the peripheral clock in peripheral organs [1,2]. A stable circadian rhythm is achieved by oscillation in the transcription of genes and their proteins in a process called