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Temporal Pattern of Salt Intake and Circadian Blood Pressure Rhythm

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Summary

To explore how the circadian expression of genes regulating salt absorption is controlled by the mineralocorticoid receptor (MR) and circadian clock, the large intestine and serum of the male gut-specific Bmal1 knockout mice, gut-specific MR knockout mice, and control mice aged from eight to twelve weeks-old was collected every four hours over the circadian cycle (zeitgeber time [ZT] 0, 4, 8, 12, 16, 20, wherein the light phase starts from ZT0 and the dark phase begins from ZT12). The circadian clock was expressed in the large intestine and in phase with the clock in other tissues such as the liver. The Bmal1 target gene expression displayed circadian oscillation, which was disrupted in the gut-specific Bmal1 knockout mice. Additionally, the circadian variation of the MR-target gene expression was attenuated in the gut-specific Bmal1 knockout mice, suggesting that the considerable portion of the MR target genes are controlled by BMAL1. On the other hand, the clock gene expression was unaffected in the gut-specific MR knockout mice, while the oscillation of the MR-target gene expression was perturbed by the MR deletion. The serum aldosterone and corticosterone abundance exhibited daily fluctuations, whereas the MR protein levels did not. Thus, the circadian rhythms of the MR-target genes were likely driven by the daily aldosterone variations and the gut-intrinsic circadian clock. The transcriptomic analysis is performed in the intestinal epithelial cells of the gut-specific Bmal1 knockout, gut-specific MR knockout, and control mice to decipher the gut genomic rhythms driven by the BMAL1 and MR using the RNA-seq and JTC-Cycle analysis, a statistical analysis through which the oscillatory expression is determined. Nighttime- and daytime-restricted feeding of the high and low salt diet will be conducted in the control mice aged from eight to twelve weeks-old to establish the impact of the concerted transcriptional dynamics of BMAL1 and MR on time-of-day salt intake.