Modulation of Salt and Mineralocorticoid Sensitivity of Blood Pressure by the Circadian Clock Protein Per1

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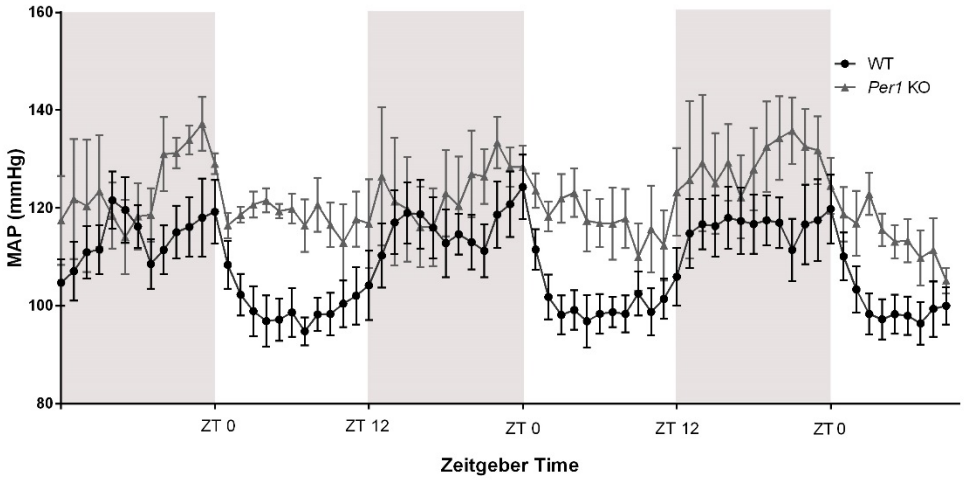
The circadian clock is important for maintaining rhythms in physiological functions including blood pressure (BP). Circadian disruption leads to increased disease risk. The clock has also been implicated in the maintenance of a normal dip in BP at night. In humans, non-dipping (night/day difference in BP<10%) is associated with an increased risk of cardiovascular and kidney disease. Dipping status can also be affected by salt intake and by hormones such as the mineralocorticoid aldosterone. The goal of this study was to determine the effects of a high salt (HS, 4% NaCl) diet plus mineralocorticoid (deoxycorticosterone pivalate (DOCP)) on BP regulation by the circadian clock protein Per1 in C57BL/6J mice. BP was monitored in conscious, unrestrained male mice by radiotelemetry and values are reported as mean arterial pressure (MAP) ± SEM. Under control conditions, MAP in male WT mice was 112.5 ± 1.08 mmHg during the night when mice are active and decreased to 102.1 ± 1.7 mmHg during the day, a "dip" in MAP of 9.2 ± 1.3%. Similarly, Per1 KO mice dip 14 ± 1.4%, with night time MAP of 119.8 ± .9 mmHg which decreased to 103 ± 1.4 mmHg during the day. On HS/DOCP, WT mice MAP decreased from 114.5 ± 1.1 mmHg to 101.5 ± 1.92 mmHg (night indicated by shaded bars in figure). This 11.4 ± 1.9% dip in WT mice was not significantly different from what was observed under control conditions. In contrast, Per1 KO mice display a significantly attenuated dip of 5.7 ± 1.4% with night time MAP of 125.3 ± 1.5 mmHg dropping to 118.1 ± 1 mmHg during the inactive day period ($p<0.05$). Thus, HS/DOCP treatment in Per1 KO mice leads to non-dipping hypertension. This is the first report of this phenotype in a single clock gene KO.



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