Roles of Cardiovascular Autonomic Regulation and Sleep Pattern in Mild Cold Exposure-Induced High Blood Pressure in Rats

***Hypertension Research*, 2021, 44.6: 662-673.**

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Introduction

- Increased blood pressure (BP) due to exposure to cold temperatures can partially explain the increased incidence of cardiovascular events in winter. However, the physiological mechanisms involved in cold-induced high BP are not well established. Many studies have focused on physiological responses to severe cold exposure.
- In this study, we aimed to perform a comprehensive analysis of cardiovascular autonomic function and sleep patterns during exposure to mild cold in rats, a condition relevant to humans in subtropical areas, to clarify the physiological mechanisms underlying mild cold-induced hypertension.

Materials and Methods

- 10-week-old male Wistar-Kyoto rats (WKY, n=11)
- 24-h telemetry recording of electroencephalogram, electromyogram, electrocardiogram, core temperature and BP signals from freely-moving WKYs
- Each rat was recorded individually in a recording chamber at a specific ambient temperature, either 23 °C, 18 °C or 15 °C.
- The sequence of ambient temperature changes for the three recording days were randomized for each rat.
- Assessment of autonomic function based on heart rate variability (HRV) analysis; sleep analysis based on electroencephalogram and electromyogram; baroreflex sensitivity based on BP and heart rate.

Results

① **Mild cold exposure induced higher BP and heart rate during both wakefulness and sleep.**

② **Mild cold exposure-induced changes in BP and heart rate were more prominent during sleep than during wakefulness.**

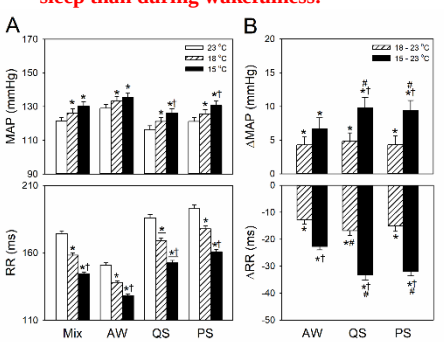

Figure 1. (A) Effects of different ambient temperatures (23 °C, 18 °C and 15 °C) on mean arterial pressure (MAP) and R-R intervals (RR) of 24-h recording without sleep scoring (Mix) and with distinguishing active waking (AW), quiet sleep (QS), and paradoxical sleep (PS) in rats. *p<0.05 vs 23 °C, †p<0.05 vs 18 °C by Fisher's least-significant difference test following a significant one-way repeated measures analysis of variance (ANOVA); ±p<0.05 vs 23 °C, ‡p<0.05 vs 18 °C by Dunn *post hoc* method following a significant Friedman test. (B) The changes in MAP and RR from 23 °C to 18 °C (18-23 °C) and from 23 °C to 15 °C (15-23 °C) during AW, QS and PS stages. All variables were normally distributed. *p<0.05 vs 0 by one-sample t test; †p<0.05 vs 18-23 °C by paired t test; #p<0.05 vs AW by Fisher's least-significant difference test. Values are presented as means ± SEM; n=11.

Mild cold exposure induced higher vascular sympathetic activity but lower overall autonomic activity and parasympathetic activity during both wakefulness and sleep.

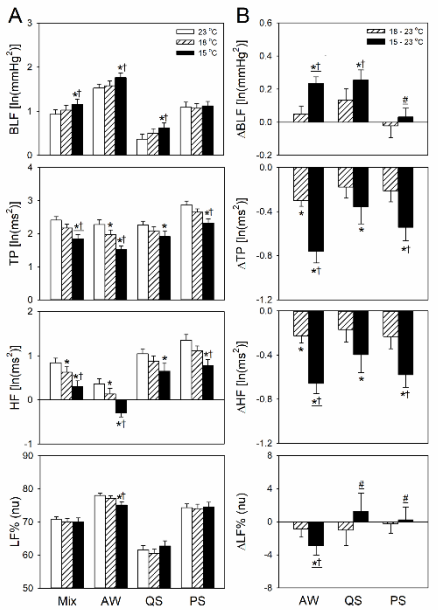

Figure 2. (A) Effects of different ambient temperatures (23 °C, 18 °C and 15 °C) on cardiovascular autonomic variables of 24-h recording without sleep scoring and with distinguishing AW, QS, and PS in rats. *p<0.05 vs 23 °C, †p<0.05 vs 18 °C by Fisher's least-significant difference test following a significant one-way repeated measures ANOVA; ±p<0.05 vs 23 °C, ‡p<0.05 vs 18 °C by Dunn *post hoc* method following a significant Friedman test. (B) The changes in cardiovascular autonomic variables from 23 °C to 18 °C (18-23 °C) and from 23 °C to 15 °C (15-23 °C) during AW, QS and PS stages. *·±p<0.05 vs 0 by one-sample t test for normality and one-sample Wilcoxon signed rank test for non-normality, respectively; †·‡p<0.05 vs 18-23 °C by paired t test for normality and Wilcoxon signed rank test for non-normality, respectively; #p<0.05 vs AW by Dunn *post hoc* method for non-normality; there was no significant difference between AW and either QS or PS by Fisher's least-significant difference test for normally distributed variables. Values are presented as means ± SEM; n=11. BLF, low frequency power of BP variability; TP, total power of HRV; HF, high frequency power of HRV; LF%, normalized low frequency power of HRV; ln, natural logarithm; nu, normalized units.

① **Mild cold exposure induced lower baroreflex sensitivity during wakefulness and sleep.**

② **Mild cold exposure-induced changes in baroreflex sensitivity were more prominent during sleep than during wakefulness.**

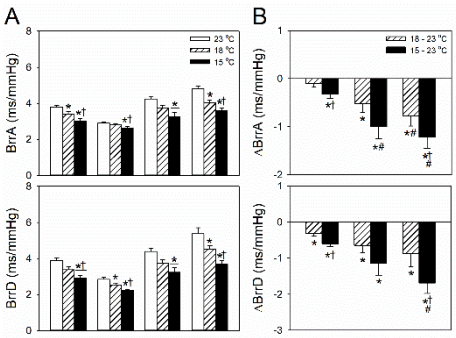

Figure 3. (A) Effects of different ambient temperatures (23 °C, 18 °C and 15 °C) on baroreflex sensitivity indices of 24-h recording without sleep scoring and with distinguishing AW, QS, and PS in rats. *p<0.05 vs 23 °C, †p<0.05 vs 18 °C by Fisher's least-significant difference test following a significant one-way repeated measures ANOVA; ±p<0.05 vs 23 °C, ‡p<0.05 vs 18 °C by Dunn *post hoc* method following a significant Friedman test. (B) The changes in baroreflex sensitivity indices from 23 °C to 18 °C (18-23 °C) and from 23 °C to 15 °C (15-23 °C) during AW, QS and PS stages. All variables were normally distributed. *p<0.05 vs 0 by one-sample t test; †p<0.05 vs 18-23 °C by paired t test; #p<0.05 vs AW by Fisher's least-significant difference test. Values are presented as means ± SEM; n=11. BrrA, baroreflex sensitivity of ascending MAP-RR pairs; BrrD, baroreflex sensitivity of descending MAP-RR pairs.

Mild cold exposure led to sleep disturbance, which included decreased cumulative QS and PS time as well as increased interruptions and decreased delta power percentage of QS.

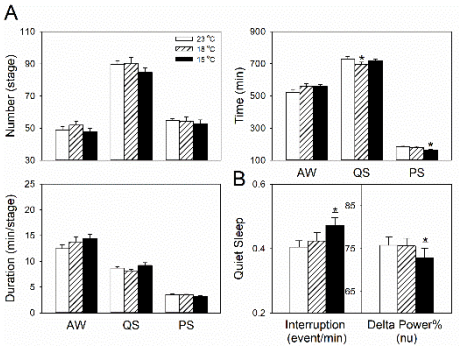

Figure 4. (A) Effects of different ambient temperatures (23 °C, 18 °C and 15 °C) on number, average duration and cumulative time of 24-h recording with distinguishing AW, QS, and PS and (B) interruption and delta power percentage of QS in rats. Values are presented as means ± SEM; n=11. *p<0.05 vs 23 °C by Fisher's least-significant difference test following a significant one-way repeated measures ANOVA; ±p<0.05 vs 23 °C by Dunn *post hoc* method following a significant Friedman test; there was no significant difference between 18 °C and 15 °C by Fisher's least-significant difference test or Dunn *post hoc* method.

Mild cold-induced autonomic dysregulation and sleep problems were associated with elevation of BP.

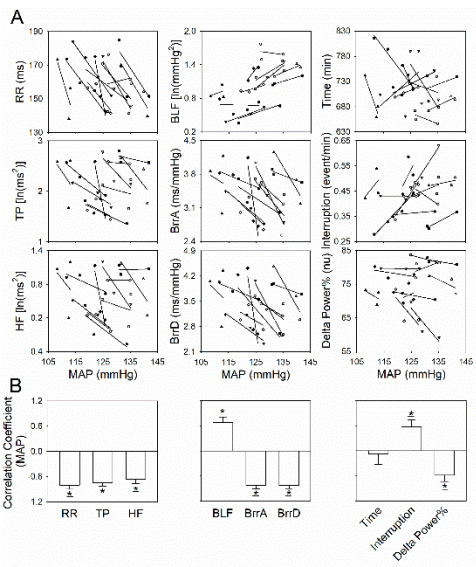

Figure 5. (A) Two-dimensional scattergram and (B) the correlation coefficients displaying the relationship between the variations of MAP and the corresponding cardiovascular response measures without sleep scoring and sleep pattern variables during QS across three different ambient temperatures in rats. Values are presented as means ± SEM; n=11. *·±p<0.05 vs 0 by one-sample t test for normality and one-sample Wilcoxon signed rank test for non-normality, respectively. RR, R-R intervals; TP, total power of HRV; HF, high frequency power of HRV; BLF, low frequency power of BP variability; BrrA, baroreflex sensitivity of ascending MAP-RR pairs; BrrD, baroreflex sensitivity of descending MAP-RR pairs; ln, natural logarithm; nu, normalized units.

Conclusions

Mild cold exposure elicits autonomic dysregulation and poor sleep quality to elevate BP, which may have critical implications for cold-related cardiovascular events.