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Menthol in neck cooling improves subjective comfort but does not affect vascular or temperature regulation

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Abstract
Background: This study aimed to compare the effects of traditional neck cooling and menthol-enhanced neck cooling on physiological and perceptual responses in healthy males.
Methods: Thirteen participants (mean age: 28.2±5.3 years) underwent two experimental conditions (control and menthol) in a randomized crossover design. Each session involved a 60-minute cooling protocol with measurements of tympanic temperature, cutaneous blood flux, cutaneous vascular conductance (CVC), mean arterial pressure (MAP), and perception of frostiness taken at baseline and at 10-minute intervals.
Results: Tympanic temperature decreased significantly over time in both conditions ($p<0.0001$), with no significant differences between them. Cutaneous blood flux and CVC remained stable across both conditions, indicating no significant impact of menthol on microvascular function. A transient decrease in MAP was observed at 30 minutes in the menthol condition ($p<0.05$). Perception of frostiness was significantly higher in the menthol condition at the onset and up to 30 minutes of cooling ($p<0.0001$).
Conclusion: Both traditional and menthol-enhanced neck cooling effectively reduce core body temperature. Menthol-enhanced cooling provides a stronger subjective cooling sensation without significantly altering peripheral blood flow or vascular conductance, making it a valuable addition to thermoregulatory interventions where comfort and adherence are critical. Further research is needed to explore long-term effects and cardiovascular implications of menthol application.

Keywords: Neck cooling, menthol, cutaneous blood flux, vascular conductance, perceived cooling

1. Introduction

Neck cooling is a therapeutic intervention widely utilized for mitigating hyperthermia and its associated adverse effects. Traditional methods, such as the application of cold packs or cooling devices, are designed to reduce core body temperature and alleviate symptoms related to heat stress and stroke. Poli and colleagues emphasized the efficacy of neck cooling in lowering brain temperature following a stroke, highlighting its potential to minimize neurological damage [1]. Recent advancements suggest that combining traditional cooling techniques with pharmacological agents, such as menthol, can enhance their effectiveness. Menthol, known for its cooling sensation and vasodilatory properties, has shown promise in improving cooling efficiency [2, 3]. Recent investigation indicated that the application of a topical analgesic containing menthol accelerates heat loss during skin cooling, optimizing the cooling process and potentially offering a rapid and sustained reduction in core body temperature [4]. Combining menthol with traditional cooling methods can mitigate cutaneous vasoconstriction, which often reduces the effectiveness of cooling treatments [4]. This approach has been explored in various settings, from exercise-induced hyperthermia to clinical applications in stroke management [5, 6]. Menthol has been shown to activate cold-sensing receptors in the skin, enhancing vasodilation and cooling effects [2, 3].

Menthol-enhanced cooling has also been linked to improved cognitive function during heat stress. Lee *et al.* found that neck cooling with menthol improves cognitive performance following exercise-induced hyperthermia [7]. Similarly, Ando reported positive effects on cognitive function during strenuous exercise in hot environments when using temporal neck cooling with menthol [8].

This suggests that menthol not only aids in physiological cooling but also supports overall performance and recovery during heat stress conditions. Additionally, it is demonstrated that self-paced exercise performance in the heat improved with menthol-enhanced neck cooling [9]. These findings underline the dual benefits of menthol in physiological and cognitive aspects during heat stress.

This study aims to compare traditional neck cooling methods with a novel approach incorporating menthol cream. By evaluating physiological variables such as skin blood flow, and cardiovascular responses, we seek to determine the superiority of the menthol-enhanced cooling technique in managing heat stress and its implications for clinical practice in stroke management. The comparative analysis of these methods could provide valuable insights into developing more effective and practical cooling interventions. This could ultimately improve patient outcomes in hyperthermic conditions [9-12]. Effective cooling interventions are crucial not only for athletes and individuals performing intense physical activities but also for clinical scenarios where managing body temperature is critical, such as during heatwaves and for patients suffering from heat strokes [13, 14].

2. Materials and Methods

The study was conducted in accordance with the Declaration of Helsinki (2013) and all study procedures used in the current experiment were approved by the Institutional Review Board (IRB) at Jeonbuk National University (IRB #: JBNU 2022-01-004-002). Thirteen healthy male participants (mean age: 28.2±5.3 years; mean height: 179.0±6.7 cm; mean weight: 74.8±8.7 kg; mean BMI: 23.3±1.8 kg/m²) were recruited for this study. The participants were screened for cardiovascular, respiratory, and metabolic disorders through a detailed health questionnaire and medical history review. Written informed consent was obtained from each participant prior to the commencement of the study, and the study was conducted in accordance with the Declaration of Helsinki.

2.1. Experimental Design

This study employed a randomized crossover design, ensuring that each participant served as their own control. The participants underwent two experimental conditions: control and menthol, with each session separated by a minimum washout period of one week to eliminate any carryover effects. The order of the sessions was randomized. Each session was conducted in a temperature-controlled room maintained at 24±1 °C. Upon arrival, participants rested for 15 minutes to acclimatize to the room temperature. The cooling protocol involved the application of either a standard cold pack (control condition) or a cold pack combined with menthol cream (menthol condition) to the neck region for 60 minutes. The menthol cream used in the study contained 6% L-menthol. Baseline measurements were taken after the acclimatization period, followed by measurements at 10-minute intervals during the 60-minute cooling period. The cold packs were stored in a freezer at -18 °C and were applied immediately after removal.

2.2. Measurements

Tympanic Temperature

Tympanic temperature was measured using an ear thermometer (Braun ThermoScan, Germany) to ensure accurate core temperature readings. Measurements were taken at baseline and at 10-minute intervals throughout the cooling protocol.

Cutaneous Blood Flux

Cutaneous blood flux was assessed using laser Doppler flowmetry (Periflux System 5000, Perimed, Sweden). This technique involves the use of a laser Doppler probe placed on the forearm to measure microvascular blood flow, expressed in arbitrary units (A.U.). Measurements were recorded at baseline and at 10-minute intervals.

Cutaneous Vascular Conductance (CVC)

CVC was calculated as the ratio of cutaneous blood flux to mean arterial pressure (MAP), providing an index of microvascular function. CVC values were obtained by dividing the blood flux values by the corresponding MAP values at each time point.

Rating of Perceived Exertion (RPE)

The Rating of Perceived Exertion was assessed using the Borg scale, a numerical scale ranging from 6 to 20, with higher values indicating greater perceived exertion. Participants were asked to rate their perceived level of effort and discomfort at baseline and at each measurement interval during the cooling period.

Mean Arterial Pressure (MAP)

MAP was measured using an automated sphygmomanometer (Omron HEM-907XL, Omron Healthcare, USA). Measurements were taken at baseline and at 10-minute intervals. MAP was determined as one-third pulse pressure plus diastolic blood pressure.

2.3. Statistical Analysis

All data were analyzed using repeated measures ANOVA to examine the effects of the cooling condition (control vs. menthol) and time on the measured variables. Interaction effects were explored using post-hoc analyses with Bonferroni correction for multiple comparisons. Statistical significance was set at $p<0.05$. Data are presented as mean±standard deviation (SD).

3. Results

3.1. Tympanic Temperature

Tympanic temperature decreased significantly over time in both the control and menthol conditions ($p<0.0001$) (Figure 1A). At baseline, the mean tympanic temperature was 36.9±0.1 °C in the control condition and 36.9±0.1 °C in the menthol condition. After 60 minutes of cooling, the temperatures decreased to 36.7±0.1 °C in the control condition and 36.7±0.1 °C in the menthol condition. There was no significant difference between the two conditions at any time point (Figure 1A), indicating that both cooling methods were equally effective in reducing tympanic temperature.

3.2. Cutaneous Blood Flux

Cutaneous blood flux did not show significant changes over time or between the control and menthol conditions (Figure 1B). At baseline, the mean cutaneous blood flux was 117.8±13.2 A.U. in the control condition and 116.4±12.7 A.U. in the menthol condition. At the end of the cooling period, these values were 112.7±12.8 A.U. for control and

110.9±13.0 A.U. for menthol (Figure 1B). The absence of significant differences suggests that the addition of menthol did not significantly alter microvascular blood flow compared to the control condition.

3.3. Cutaneous Vascular Conductance (CVC)

CVC values did not show significant differences between the control and menthol conditions across the cooling period. At baseline, the mean CVC was 1.42±0.15 Flux/mmHg in the control condition and 1.41±0.14 Flux/mmHg in the menthol condition (Figure 1C). By the end of the cooling period, CVC values were 1.37±0.14 Flux/mmHg in the control condition and 1.36±0.13 Flux/mmHg in the menthol condition (Figure 1C). The stable CVC values indicate that the menthol cream did not significantly impact cutaneous vascular conductance.

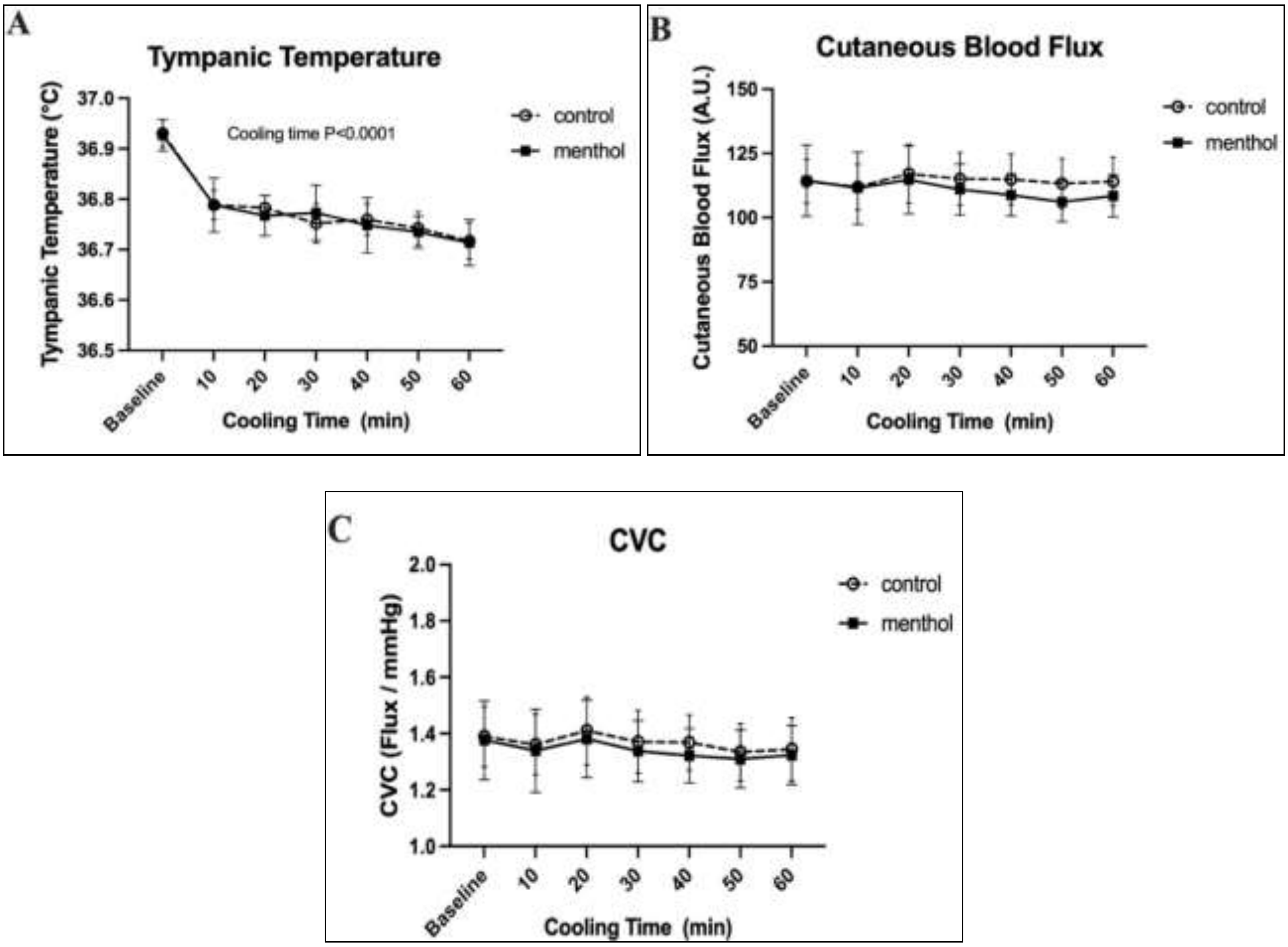

Fig 1: (A) Tympanic temperature over time during control and menthol conditions. (B) Cutaneous blood flux over time during control and menthol conditions. (C) Cutaneous vascular conductance (CVC) over time during control and menthol conditions.

3.4. Mean Arterial Pressure (MAP)

MAP remained stable during the cooling period in both conditions. However, a significant interaction was observed between cooling condition and time ($p<0.05$) (Figure 2A). At baseline, the mean MAP was 82.3±3.4 mmHg in the control condition and 82.0±3.2 mmHg in the menthol condition. At 30 minutes, MAP in the menthol condition decreased significantly to 79.2±3.1 mmHg compared to 82.6±3.3 mmHg in the control condition ($p<0.05$). This decrease was transient, as MAP values returned to baseline levels by the end of the cooling period (Figure 2A).

3.5. Perception of Frostiness

Participants reported a higher perception of frostiness in the menthol condition compared to the control condition ($p<0.0001$) (Figure 2B). At the onset of cooling, the perception of frostiness was rated at 5.3±0.7 on the visual analogue scale (VAS) in the menthol condition compared to 4.2±0.6 in the control condition ($p<0.05$). At 10, 20, and 30 minutes, the menthol condition maintained higher ratings of 5.1±0.6, 4.9±0.5, and 4.8±0.5, respectively, compared to 3.8±0.5, 3.7±0.4, and 3.5±0.4 in the control condition ($p<0.05$ for all comparisons) (Figure 2B). This enhanced perception of cooling suggests that the menthol cream provided a stronger subjective cooling sensation, which may be beneficial for improving comfort during cooling interventions.

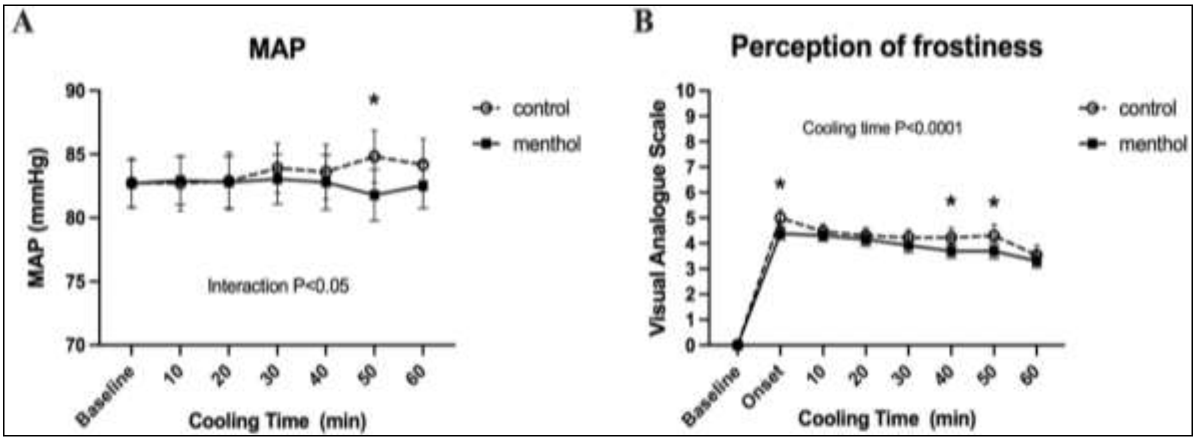

Fig 2: (A) Mean arterial pressure (MAP) over time during control and menthol conditions. (B) Perception of frostiness over time during control and menthol conditions.

4. Discussion

The present study investigated the effects of traditional neck cooling and menthol-enhanced neck cooling on physiological and perceptual responses during a 60-minute cooling period in a group of healthy male participants. The key findings indicated that while both cooling methods were effective in reducing tympanic temperature, the addition of menthol significantly enhanced the perception of cooling without significantly affecting cutaneous blood flux or cutaneous vascular conductance. These results provide new insights into the potential benefits and limitations of menthol-enhanced cooling in thermoregulatory interventions.

Our findings demonstrated that tympanic temperature decreased significantly over time in both the control and menthol conditions, with no significant differences between the two conditions. This suggests that both cooling methods were equally effective in lowering core body temperature. These results are consistent with previous studies that have highlighted the effectiveness of neck cooling in reducing core temperature during heat stress [13, 14]. For instance, Lee *et al.* found that neck cooling significantly reduced core temperature in athletes performing high-intensity exercise in hot conditions [7]. Similarly, it was reported that temporal neck cooling was effective in lowering core temperature during strenuous exercise [8]. The lack of significant differences between the control and menthol conditions in our study suggests that the primary mechanism of core temperature reduction is the direct cooling effect of the cold pack, regardless of the presence of menthol.

Cutaneous blood flux and cutaneous vascular conductance (CVC) did not show significant differences between the control and menthol conditions throughout the cooling period. This finding aligns with previous research indicating that external cooling primarily affects core temperature without significantly altering peripheral blood flow (Wang *et al.*, 2022). The stability of cutaneous blood flux and CVC in our study suggests that the addition of menthol does not enhance or diminish the microvascular response to cooling. This is in contrast to recent findings [2], who suggested that menthol might enhance vasodilation through the activation of cold-sensing TRPM8 receptors. However, our results imply that any potential vasodilatory effects of menthol are not sufficient to produce measurable changes in cutaneous blood flux or CVC during the cooling period.

The significant interaction between cooling condition and time for mean arterial pressure (MAP) indicates a transient effect of menthol on blood pressure regulation. Specifically, MAP decreased significantly at the 30-minute mark in the menthol condition compared to the control condition, but this effect was not sustained throughout the cooling period. Previous studies have shown mixed results regarding the impact of menthol on cardiovascular responses. For example, Sun *et al*. reported that menthol application could mitigate vasoconstriction and reduce hypertension through the attenuation of the RhoA/Rho kinase pathway [3]. Conversely, other studies have found no significant cardiovascular effects of menthol [11, 12]. Our findings suggest that while menthol may have a temporary effect on blood pressure, its overall impact on cardiovascular responses during prolonged cooling is minimal.

One of the most notable findings of our study was the significantly higher perception of frostiness reported in the menthol condition compared to the control condition. This enhanced perception was particularly evident at the onset of cooling and persisted for up to 30 minutes. These results are in line with previous studies that have documented the cooling sensation associated with menthol application [7, 8]. Menthol is known to activate TRPM8 receptors, which are responsible for the sensation of cold [2]. The subjective enhancement of cooling sensation with menthol can be beneficial in improving comfort and adherence to cooling interventions, particularly in settings where psychological perception plays a crucial role, such as in sports or rehabilitation [9].

Practical Implications

The practical implications of our findings are multifaceted. First, the lack of significant differences in tympanic temperature reduction between the control and menthol conditions suggests that traditional neck cooling methods remain effective for core temperature management. However, the enhanced perception of cooling with menthol could be advantageous in situations where subjective comfort and adherence to cooling protocols are critical. For example, athletes may prefer menthol-enhanced cooling during breaks in training or competition to maintain a comfortable and refreshing sensation, potentially improving performance and recovery [5].

Second, the transient decrease in MAP observed with menthol suggests that caution should be exercised when using menthol-enhanced cooling in individuals with cardiovascular concerns. Although the effect was temporary, further research is needed to understand the mechanisms and potential long-term implications of menthol on cardiovascular function during cooling interventions.

Finally, the stability of cutaneous blood flux and CVC with menthol-enhanced cooling indicates that this method can be safely used without adverse effects on peripheral circulation. This is particularly relevant for clinical settings where maintaining stable peripheral blood flow is crucial, such as in patients with peripheral vascular disease or diabetes [11, 14].

Limitations and Future Directions

There are several limitations to our study that warrant consideration. First, the sample size was relatively small, and the study population consisted exclusively of healthy young males. Future research should include a larger and more diverse sample to improve the generalizability of the findings. Second, the study was conducted in a controlled laboratory environment, which may not fully replicate real-world conditions. Field studies are needed to evaluate the effectiveness of menthol-enhanced cooling in various practical settings, such as during athletic events or in occupational environments with high heat exposure.

Additionally, while our study focused on the acute effects of menthol-enhanced cooling, future research should investigate the long-term impact of repeated use of menthol on physiological and perceptual responses. Understanding the potential cumulative effects of menthol application is essential for developing comprehensive cooling strategies for both athletic and clinical populations.

5. Conclusion

In conclusion, our study demonstrates that both traditional neck cooling and menthol-enhanced neck cooling effectively reduce core body temperature, with menthol providing an enhanced perception of cooling without significantly altering peripheral blood flow or vascular conductance. These findings suggest that menthol-enhanced cooling could be a valuable addition to thermoregulatory interventions, particularly in settings where subjective comfort and adherence to cooling protocols are critical. However, further research is needed to explore the long-term effects and potential cardiovascular implications of menthol application. The stability of cutaneous blood flux and CVC with menthol-enhanced cooling indicates its safe use in various populations, providing a basis for future studies to optimize cooling strategies and improve outcomes in both athletic and clinical settings.

6. Conflict of Interest

None declared.

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