THE IMPACT OF BODY SURFACE AREA EXPOSURE TO MENTHOL ON HUMAN TEMPERATURE REGULATION AND PERCEPTION

Honors Thesis

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V. CONCLUSION

Inclusion of an overlap abstract and important characteristics pulled from all analysis of the data. A statement of support of hypothesis and reference to findings.

VI. REFERENCES

Listed annotated bibliography which will in detail will describe prior studies and their findings.

This research was supported by both the athletic training and sports and movement science department. I want to thank Dr. Jason Gillis, Dr. Joseph Gallo Prof. Kevin Silva, Dr. Bret Ely, and my former research partner Jacob Moriarty from Salem State

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Menthol is an active ingredient derived from mint commonly used in sports medicine practices to treat injuries. Although known for its capacity to cause cool sensations without actually cooling the skin temperature, menthol's effect on skin blood flow has not been clearly classified. Some research has shown menthol to increase skin blood flow (vasodilation), while others show decreases (vasoconstriction). It is hypothesized that body surface area (BSA) exposed to menthol influences blood flow. The purpose of this study was to test if large BSA exposures induce vasoconstriction while smaller exposures induce vasodilation. Twelve participants were placed into a controlled environment with a specific amount of their BSA (left middle finger, left arm, left upper/lower body) exposed to a menthol or placebo gel for 30 minutes. Thermal sensation, skin temperature, and skin blood flow were measured throughout testing. Vasodilation was not observed for small BSA. Participants exposed to large BSA experienced enhanced vasoconstriction and felt significantly cooler without change in skin temperature; partly supporting the hypothesis. Research supports menthol activation of cold receptors in the skin and causing cold sensations. Data also provides support that BSA exposure to menthol influences skin blood flow.

Menthol is considered a terpene alcohol that is either produced synthetically or derived from mint (Eccles, 1994). Menthol is an active ingredient found in many topical pain relievers (analgesics) in addition to producing a cooling sensation (Peier et Al, 2002). Menthol's chemical makeup has allowed it to be used to relieve muscle soreness and is a key ingredient in many commercial products. Menthol can be found in many active forms. The L isomer that plays a major role in the effect of menthol is what allows for the cooling sensations felt when applied to the skin all while being nontoxic to humans (Eccles et al., 1988). Menthol influences skin blood flow by eliciting a cold sensation by acting on transient receptor potential melastin 8 cold sensing channels (TRPM8) (Peier et al., 2002). Both menthol and temperatures below 28 °C activate TRPM8 stimulated by transition of ion channels, which are embedded in terminals of primary afferent nerve endings (McKemy Neuhausser & Julius, 2002; Piere et Al., 2002). These thermo-sensitive neurons are thought to project to the somatosensory cortex, where temperature is perceived (Craig, 2002) and towards the hypothalamus, where body temperature is regulated (Morrison & Nakamura, 2011). In this way, menthol has been shown to influence both human temperature perception and body temperature regulation (Gillis, House & Tipton, 2010; Gillis et al., 2015). Prior research has indicated menthol to induce cutaneous vasodilation (Craighead et al., 2016). Research has also indicated for menthol to driven by a stimulus of skin receptors/ sensory nerves that may vasoconstriction (Gillis et al., 2015). This is driven by activation of peripheral nerves- skin receptors leading to heat storage response due to repeated exposure. Effects are suggested to be based upon body surface area exposure. Prior research has shown menthol to have an effect on both

perceptual and physiological functions, but the influence of the body surface area exposed to menthol on body temperature regulation and perception has not been investigated. The purpose of this study is to navigate this relationship with particular emphasis on menthol's influence on skin blood flow.

II. METHODOLOGY

Procedure:

In a single-blinded study, participants were exposed to menthol application on the left side of three different body surface areas (left middle finger, left arm, and left upper and lower body) and one exposure to a placebo condition. Twelve subjects were to rest in an environmentally controlled tent for 30 minutes pre and post intervention for a total of 60 minutes. Perceptual measures taken included thermal sensation. Thermoregulatory measures of skin temperature and skin blood flow were monitored and recorded throughout testing. Skin blood flow was measured via laser Doppler flowmetry on the middle finger. On both the right and left side of the participants skin temperature was recorded (chest, forearm, thigh, and calf).

Description of the testing sessions:

For four days with a 24hour non-testing period between them. Shorts were necessary to perform the tasks of this study as well as removal of the shirt in order to easily access the body for randomized application of the menthol. Subjects were weighed, measured for height and questioned for caffeine intake and exercise prior to testing sessions (which is an exclusion of the study). Participants were also asked background questions which

included age and history of exercise lifestyle. Upon entering the temperature controlled tent, participants hey would then be instrumented with a laser Doppler probe on the left side and skin temperature thermistors. Participants rested in a supine position for 30 minutes pre and post intervention. Thermal sensation was assessed every 5 minutes and recorded. Rectal temperature were also recorded every minute. Blow flow perfusion, skin temperature, and time were monitored from the computer screens. Once the full 60 minutes was up, the test was finished.

Data Analysis:

Data were collected over 60 minutes of testing, but only the data over the last 30 minutes of testing were analyzed. Specifically, the area under the curve (AUC) from minutes 30 to 60 was calculated by summing all of the data points together (i.e. min 35 + min 40 + min 45 + min 50 + min 55 + min 60 = AUC). This produced four different numbers for each condition. These four different numbers where then compared using data obtained from 12 participants, using a 1-way Repeated Measures Analysis of Variance, with an alpha level of 0.05.

III. RESULTS

Thermal sensation, skin temperature, and skin blood flow were measured throughout testing. Vasodilation was not observed for small BSA. Participants exposed to large BSA experienced enhanced vasoconstriction and felt significantly cooler without change in skin temperature; partly supporting the hypothesis.

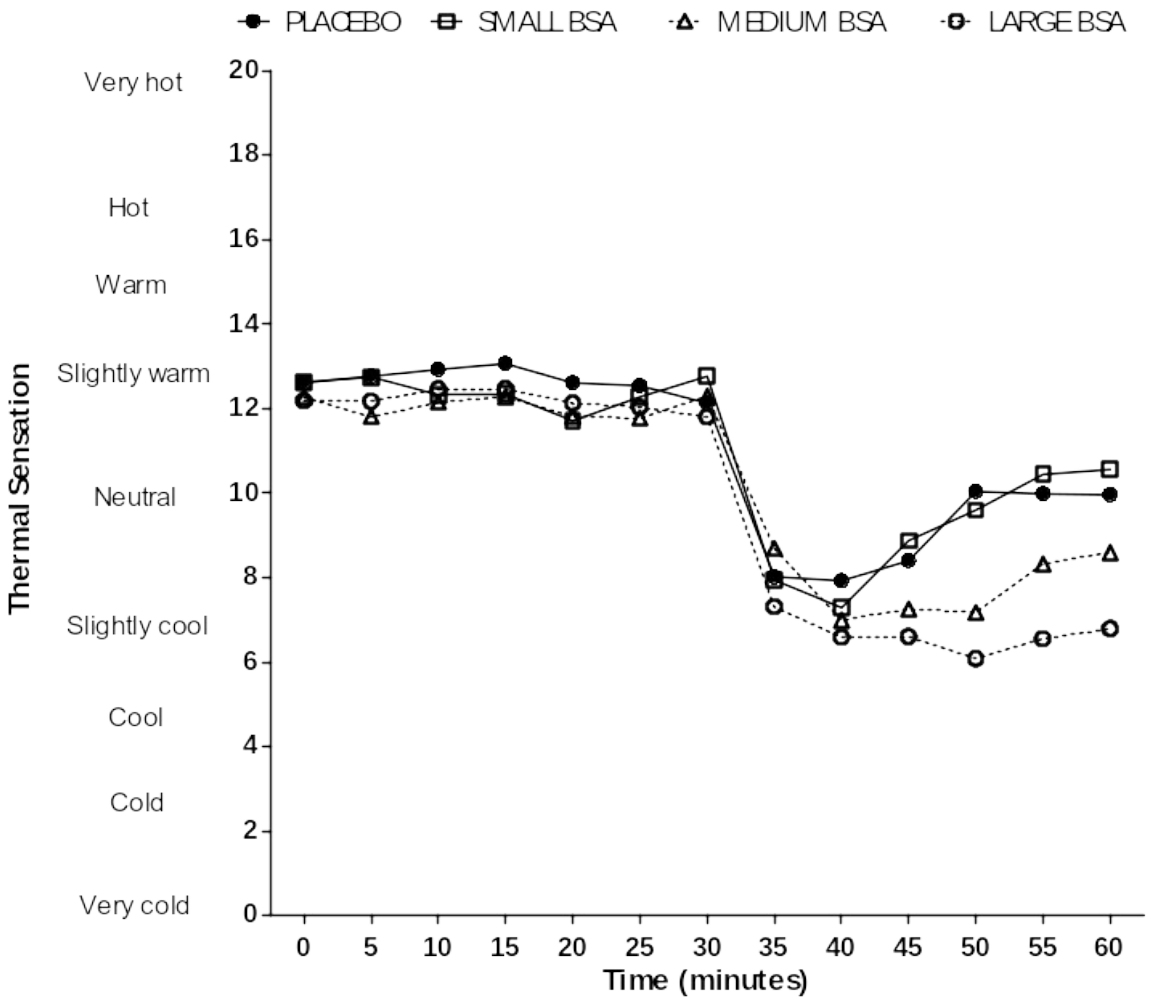

Fig 1: Thermal Sensation following the application of three different menthol exposures (Small, Medium, and Large Body Surface Area exposures), compared to a Placebo Condition at minute 30 in twelve participants. An analysis of the area under the curve from minute 30 to 60 found a significant difference (1-way ANOVA, $p < 0.05$) between conditions. These data indicate that participants exposed to the largest body surface area of menthol felt the coolest.

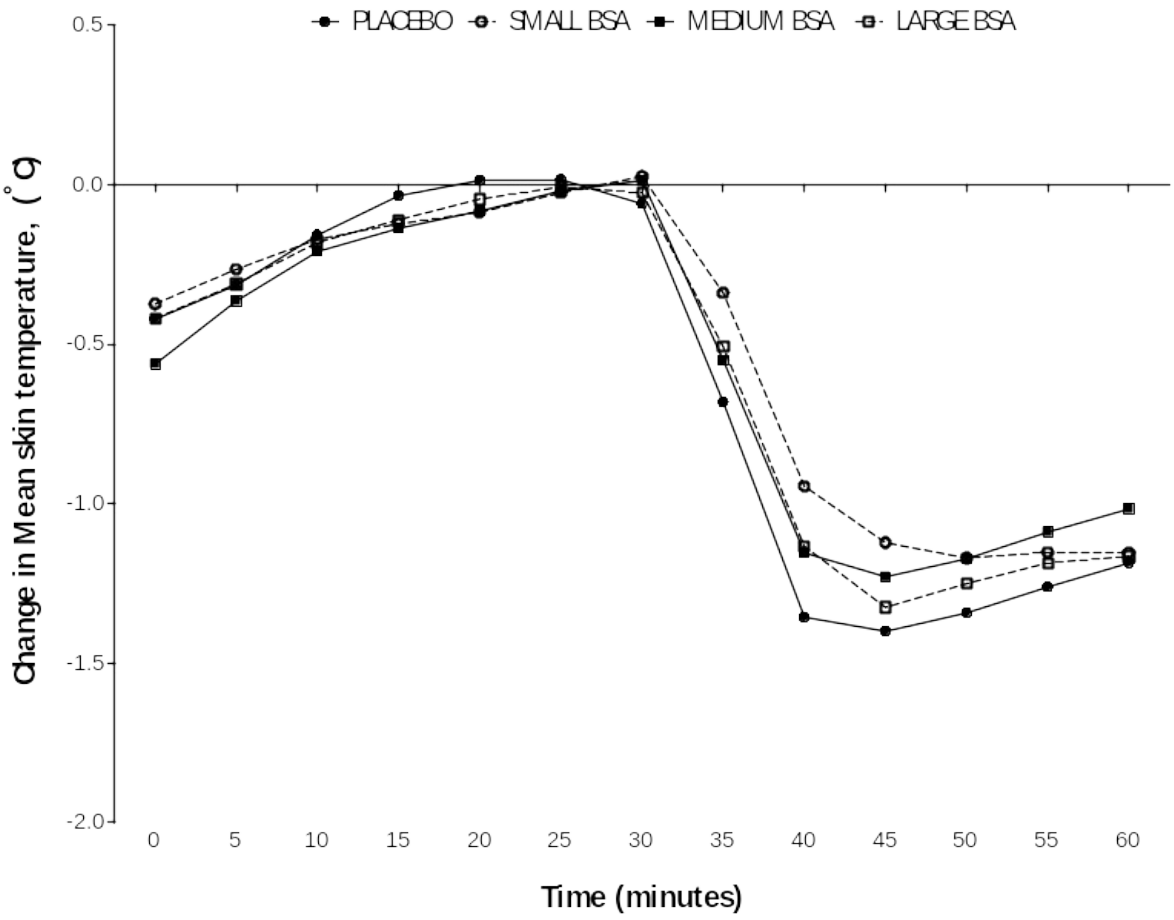

Fig 2: Mean Skin temperature following the application of three different menthol exposures (Small, Medium, and Large Body Surface Area exposures), compared to a Placebo Condition at minute 30 in twelve participants. An analysis of the area under the curve from minute 30 to 60 found no significant difference (1-way ANOVA, $p > 0.05$) between conditions. These data indicate that the increased cool sensations felt by participant in the Large BSA condition in Figure 1 was not due to a lower skin temperature.

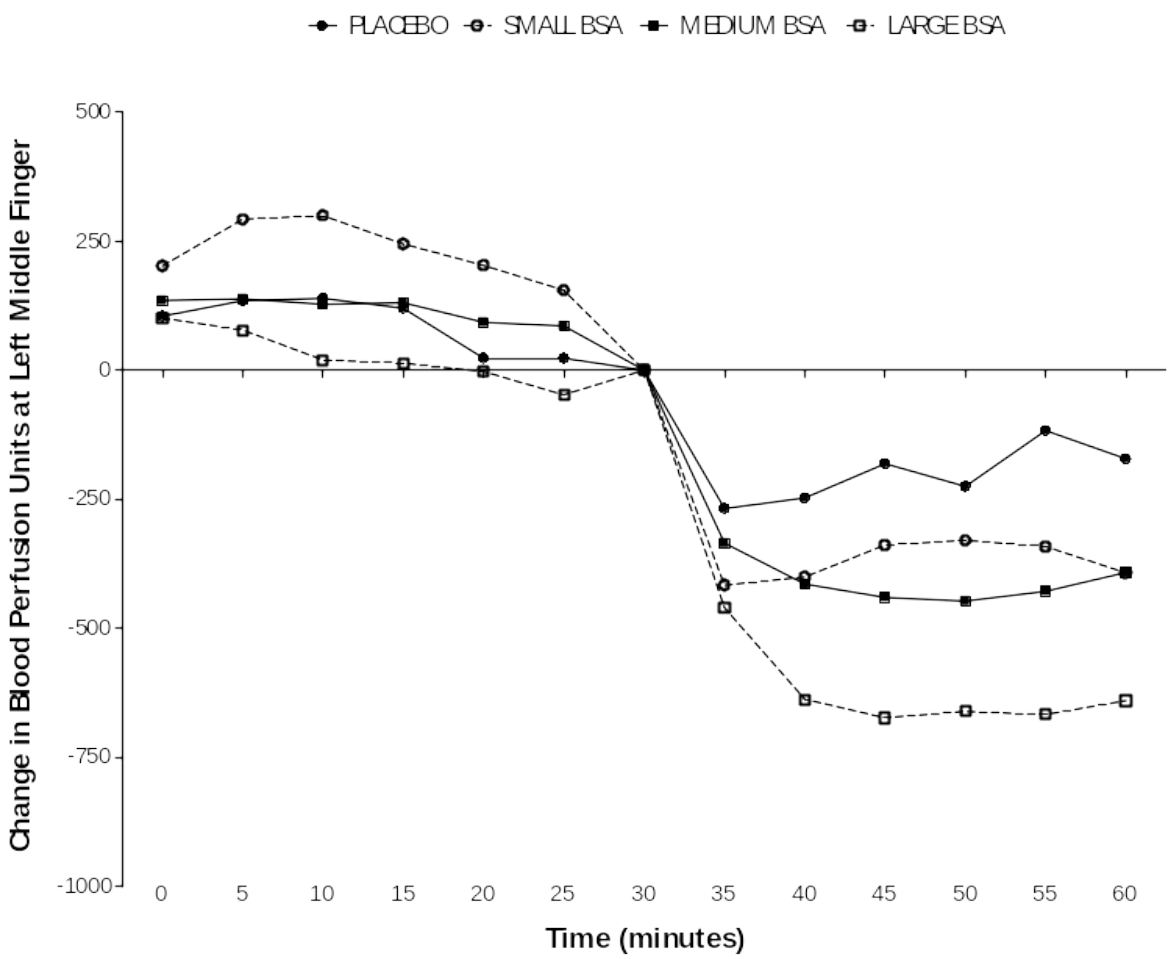

FIG 3. Blood Flow following the application of three different menthol exposures (Small, Medium, and Large Body Surface Area exposures), compared to a Placebo Condition at minute 30 in twelve participants. An analysis of the area under the curve from minute 30 to 60 found a significant difference (1-way ANOVA, $p < 0.001$) between conditions. These data indicate that participants exposed to the largest body surface area of menthol had a significant reduction in skin blood flow.

IV. DISCUSSION

Menthol has been shown to influence both human temperature perception and body temperature regulation (Gillis, House & Tipton, 2010; Gillis et al., 2015). Prior research has shown menthol to have an effect on both perceptual and physiological functions. This appears to not only be associated with dosage but also, according to the data collected in this experiment, with body surface area exposure. The fundamental purpose of this study was to test if large BSA exposures induce vasoconstriction while smaller exposures induce vasodilation. Results indicate participants that were exposed to large BSA had enhanced vasoconstriction while feeling significantly cooler without change in skin temperature. However in smaller BSA there was no clear indication of vasodilation that was observed, as had been observed by Craighead et al. (2017), partly supporting the experimental hypothesis. Preliminary data did in fact support menthol activation of cold receptors in the skin and causing cold sensations because participants in all menthol conditions felt significantly cooler than the placebo condition, with the exception of the small BSA condition. This is probably because the small BSA exposed to menthol i.e. the fingertip, was not sufficient to bring about significantly afferent inputs to register cool sensations. Data also supported that BSA exposure to menthol influences skin blood flow, with particular emphasis on large BSA exposures leading to vasoconstriction. These data did not support the work of Craighead et al., (2017) who observed increased skin blood flow with menthol. This is perhaps because their experimental set-up was different. They used a heated skin blood flow probe to control skin temperature, and infused menthol at skin temperature. In the present study, we applied menthol in gel form to the skin, which caused a reduction in skin temperature, leading to a reduction in skin

blood flow across all conditions. This reduction in skin temperature was apparently enough to eliminate menthol's vasodilator effects. Limitations of this study were mostly influenced by variability of applications per participant i.e. every participant has a unique thermoregulatory system and may respond differently to menthol, so there is a lot of variability in the data. In addition there was no direct assessment of vasodilation to completely override the conclusion found in the small BSA results.

The practical implications of the present experiment suggest that when menthol is applied in gel form, as it often is in a clinical setting, it will cool the skin and cause enhanced vasoconstriction, rather than vasodilation, and this vasoconstriction seems to be stronger and more prolonged as the BSA exposed to menthol increases.

v. CONCLUSION

Research supports menthol activation of cold receptors in the skin and causing cold sensations. Data also provides support that BSA exposure to menthol influences skin blood flow. The hypothesis is consistent with the literature and research findings in terms of menthols influence on BSA. Gel application caused large BSA applications to feel cold without any real skin reduction in temperature. Menthol has a strong perceptual stance in which skin blood flow is influenced creating the cold sensation in which the participant feels. It seems to be in the smaller body surface area vasodilation was not consistent with the data. In the larger exposures to menthol, the opposite happens.

VI. REFERENCES

Craighead DH, McCartney NB, Tumlinson JH, Alexander LM. (2017). Mechanisms and time course of menthol-induced cutaneous vasodilation. Microvascular Research. 110:43-47.

Filingeri D. (2016). Neurophysiology of skin thermal sensations. Comprehensive Physiology. 6(3):1429.

Gillis DJ, House JR, Tipton MJ. (2010). The influence of menthol on thermoregulation and perception during exercise in the heat. *Eur J Appl Physiol*. 110(3): 609-18.

Gillis DJ, Weston N, House JR, Tipton JM. (2015). Influence of repeated daily menthol exposure on human temperature regulation and perception. *Phys Behavior*. 139:511-8.

Gillis, D.J., Capone, S., Nestor, K., Snell, M. (year). The influence of menthol dose on human temperature perception, regulation and energy expenditure. Target: *Physiology & Behavior.*

Schlader Z.J., Vargas, N.T. (2018). Regulation of body temperature by autonomic and behavioral thermoeffectors (in press)

Eccles R. Menthol and related cooling compounds. (1994). *J Pharm Pharmacol.* 46: 618-30.

Eccles R, Griffiths DH, Newton CG, Tolley NS. (1988). The effect of D and L isomers of menthol upon nasal sensation of airflow. *J Laryngol Otol.* 10: 506-508.

McKemy DD, Neuhausser WM, Julius D. (2002). Identification of a cold receptor reveals a general role for TRP channels in thermosensation. *Nature.* 416: 52-58.

Morrison SF, Nakamura K. Central neural pathways for thermoregulation. (2011). *Front Biosci* 16: 74-04.