Abstract

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Acute effect of dietary and skin TRPM8 ion channel stimulation on human thermoregulation and metabolism

Transient receptor potential melastatin 8 (TRPM8) is the receptor for cold sensation and is located on the cell membrane of brown adipocytes(1) and sensory neurons on the skin,(2) and can be activated by both cold and L-menthol.(3) Indeed, both skin(4, 5) and dietary(1) L-menthol treatments increase brown adipose tissue activity and metabolism in mice, leading to reduced body weight. However, the effects of these treatments in humans remain incompletely understood. The aim of this study was to examine the effect of dietary and skin TRPM8 stimulation on metabolism and thermoregulation in humans. After obtaining University of Thessaly ethical approval, nine healthy male volunteers were randomly distributed into either L-menthol skin (ST; n=4) and dietary (DT; n=5) treatment groups. Participants in both groups were treated with 10 mg/kg L-menthol (ST: gel; DT: capsule) and placebo (ST: water; DT: lactose capsule) in a random order on two different days. Fasted participants remained seated in a 24-25°C and 40-50% relative humidity environment. Core temperature (Tc), heat storage (S), metabolic rate (M), and mean skin temperature (Tsk) were measured at baseline, immediately following each treatment, and every hour thereafter for 7 hours. Each assessment lasted 15 min. The placebo condition data were subtracted from the L-menthol condition data to eliminate the effect of diurnal variation. Kruskal–Wallis one-way ANOVA was used to assess the effect of each treatment on all variables showing a change across time for both ST and DT (Figure 1; $p<0.05$). Post hoc Mann-Whitney U tests showed that ST reduced Tsk within 2 hours and increased S, M, and Tc within 4 hours ($p<0.05$). A similar, albeit weaker, effect was observed following DT ($p<0.05$). Between-treatments comparisons showed that ST produced a strong vasoconstriction [evident by a greater reduction in Tsk ($p<0.05$)] that resulted in a greater increase in S, M, and Tc ($p<0.05$). It is concluded that TRPM8 stimulation via L-menthol ST and DT result in cutaneous vasoconstriction and increased metabolic heat production. Moreover, the effects produced by ST appear to be stronger, as compared to those of DT.

References

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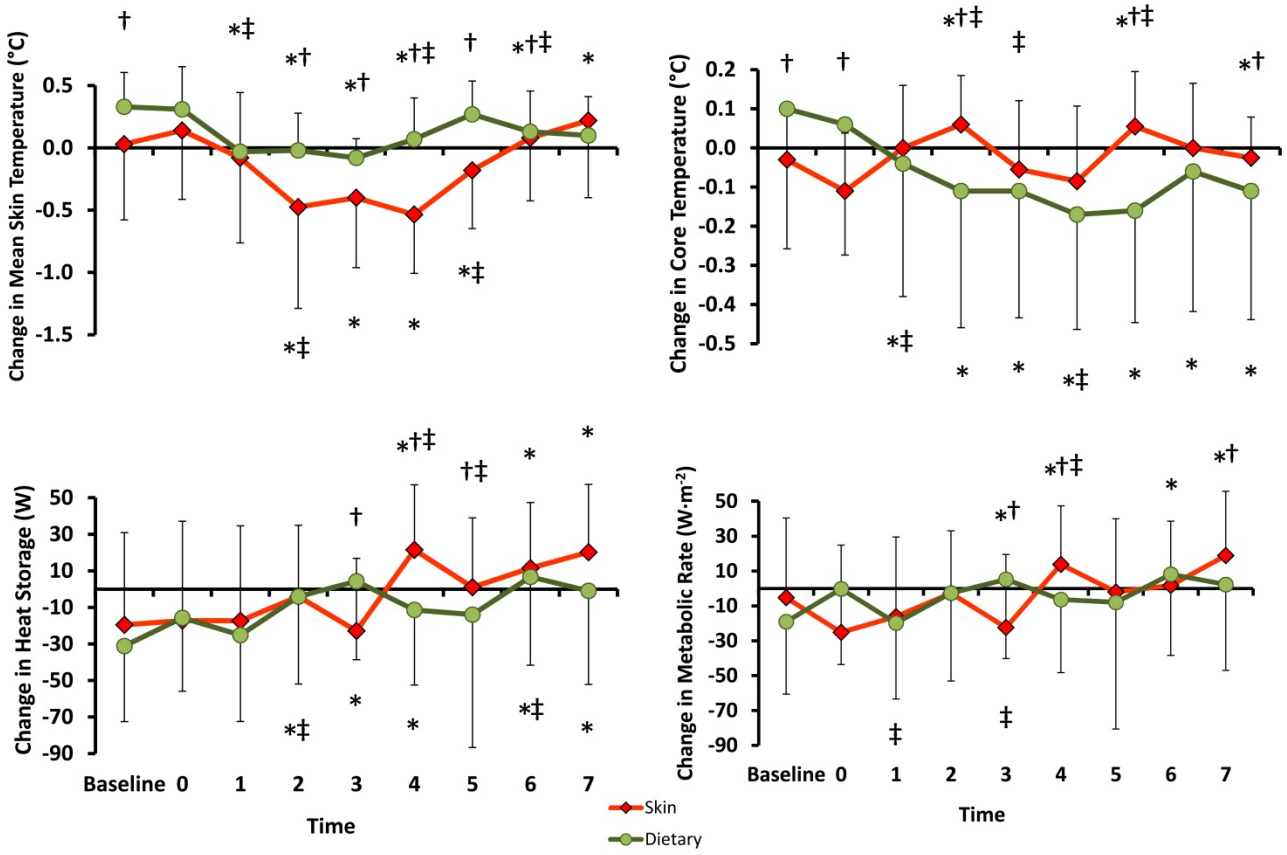
Figure 1. Median±SD change (L-menthol condition minus placebo condition) in mean skin temperature, core temperature, heat storage, and metabolic rate in the skin and dietary treatment groups. Symbols are placed at the respective end of the SD bars: * = difference from baseline for the same treatment; ‡ = difference from the previous time-point for the same treatment; † = difference between treatments for the same time-point.



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