

## Abstract

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## Administration of L-menthol results in increased metabolic heat production in humans

L-menthol activates the cold-receptor transient receptor potential melastatin 8<sup>(1)</sup> which is located on the cell membrane of brown adipocytes<sup>(2)</sup> and sensory neurons on the skin.<sup>(3)</sup> Both skin<sup>(4, 5)</sup> and diet<sup>(2)</sup> L-menthol treatments increase metabolism, non-shivering thermogenesis activity, and body weight loss in mice. This study examined the effect of skin versus diet L-menthol treatment on metabolism and thermoregulation in humans. Nine healthy male volunteers were randomly distributed into either L-menthol skin (ST; n=4) and diet (DT; n=5) treatments groups. Fasted participants seated at thermoneutral condition were treated with 10 mg/kg L-menthol (ST: gel; DT: capsule) and placebo (ST: water; DT: lactose) in a random order on two different days. Core temperature (T<sub>c</sub>), heat storage (S), metabolic rate (M), and mean skin temperature (T<sub>sk</sub>) were assessed for 15 min at baseline, immediately following each treatment, and every hour thereafter for 7 hours. 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 T<sub>sk</sub> within 2 hours and increased S, M, and T<sub>c</sub> 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 T<sub>sk</sub> (p<0.05)] that resulted in a greater increase in S, M, and T<sub>c</sub> (p<0.05). Concluding, L-menthol ST and DT treatments result in cutaneous vasoconstriction and increased metabolic heat production showing a stronger effect by ST.

## References

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**Figure 1.** Median $\pm$ 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.



