INPLASY

Metabolic effects of brown adipose tissue activity due to cold exposure in humans: A systematic review and meta-analysis of RCTs and non-RCTs

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ADMINISTRATIVE INFORMATION

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 December 2023 and was last updated on 11 December 2023.

INTRODUCTION

*R*eview question / Objective How cold exposure affects the glucose and lipid metabolism parameters at the fasting level?

Condition being studied This systematic review and meta-analysis assessed the metabolic effects of cold exposure-induced brown adipose tissue activation in healthy humans, examining changes in glucose and lipid metabolism compared to thermoneutrality.

METHODS

Participant or population Healthy individuals.

Intervention Studies were included if the temperature range of cold exposure was between 12-19°C.

Comparator Studies were included if the temperature range of thermoneutrality between 20-25°C.

Study designs to be included Randomized controlled trails (RCTs) and non-RCTs.

Eligibility criteria Additionally to intervention and comparator, studies with personalized cooling protocols, in which cold exposure temperature was set above the shivering threshold of each subject individually, were also included. Lastly, concerning metabolic outcome parameters, research was restricted to studies reporting basal glucose, insulin, triglyceride, and free fatty acid concentrations. Studies with either lower (26°C) temperatures were considered "not mild cold exposure" or "warm but not thermoneutrality" and were, therefore, excluded. Studies reporting a

shivering observation during the cold exposure protocol used and studies with shorter (i.e., nighttime fasting lower than 8h) or longer fasting periods (i.e., 24h or more) were also excluded.

Information sources A computerized search was performed in PubMed (MEDLINE) and Web of Science, respectively.

Main outcome(s) When comparing thermoneutrality (TN) and cold exposure (CE) under fasting conditions, there were no significant changes in glucose, insulin, or triglyceride (TG) concentrations (all $p > 0.36$). In contrast, CE significantly increased free fatty acid (FFA) concentration ($p = 0.002$; $n = 38$). Bias was absent for all parameters, but heterogeneity was observed for insulin ($I2 = 74.8\%$). CE primarily affects FFA concentration, likely reflecting cold-induced BAT activity.

Quality assessment / Risk of bias analysis Publication bias was assessed by funnel plots, where the standard error was plotted on the vertical axis with a reversed scale, placing larger studies towards the top, and effect estimates were given on the horizontal axis.

Strategy of data synthesis The meta-analysis procedure was performed using the RStudio library package "metafor" (version 2.0-0). Means and standard deviations (SD) of fasting glucose, insulin, triglyceride (TG), and free fatty acid (FFA) concentrations during both CE and TN were extracted. If needed, a 95 % confidence interval (CI) was converted to standard deviation. A random-effects model was used to measure the impact of thermoneutrality vs. cold exposure on glucose, insulin, TG, and FFA concentrations.

Subgroup analysis NA.

Sensitivity analysis NA.

Language restriction English.

Country(ies) involved Deutschland and Chile.

Keywords Brown adipose tissue (BAT); cold exposure (CE); glucose metabolism; lipid metabolism; humans.

Contributions of each author
Author 1 - Shirin Tabei - writing—original draft preparation, methodology (ST).
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