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TITLE PAGE

Cold stress impacts cognitive performance in healthy volunteers: results from a randomized, controlled, cross-over study

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KEY WORDS: Cold; Stress; Cognitive performance; Attention; Risk-taking behaviour

ABSTRACT

Background: Humans exposed to cold environments for leisure or occupational activities may experience cold stress. Cold-related physical and mental stress can negatively affect cognitive performance. A recent literature review has pointed out that a single acute exposure to cold under controlled laboratory conditions (e.g., cold air or cold water) induces cognitive impairment with attention, processing speed, memory, and executive function being most affected cognitive domains. Males and females seem to respond differently to short-term cold exposure, although results are not consistent. The aim of the study was to investigate the effect of acute and brief (15 min) exposure to low ambient temperatures of -10 °C compared with 5 °C and 20 °C (up to -10°C) on selected cognitive performance (reaction time, processing speed, and risky decision-making). We hypothesized that cognitive performance decreases at low temperatures with a gender difference, before core temperature changes.

Methods: This randomized, controlled, crossover study was conducted in an environmental chamber (terraXcube) under controlled, replicable, and safe conditions in twenty-four healthy volunteers, females and males, aged between 18 and 60 years. Measurements included Psychomotor Vigilance Test (PVT), Balloon Analogue Risk Task (BART), and Digit Symbol Substitution Test (DSST). Cognitive performance, stress and cold were subjectively rated with a visual analogue scale (VAS). Physiological data (including core and skin temperature) were continuously recorded with a physiological monitoring system. Data were analysed using repeated measures analysis of variance (ANOVA), Friedman test, Generalised Estimating Equations (GEE) and correlation analysis.

Results: We identified transient impairments in cognitive performance in individuals wearing appropriate clothing. Cold exposure (-10 °C) affected attention by slowing response times and increasing the lapses, and decision-making by reducing risky behaviour. Heart rate, cold sensation, and stress, as well as thermal sensation and

comfort, but not Tc were different in the three experimental temperature exposures. No differences were found between male and female subjects in their cognitive performance.

Conclusions: Our data support the distraction theory in the decline of cognitive performance even during a short exposure to cold temperatures. Such impairment should be carefully considered in people performing different activities in cold environments, even for a short time.

INTRODUCTION

Humans exposed to cold environments for leisure (e.g. recreational winter activities, alpinism, diving) or occupational activities (e.g. search and rescue, military, farming) may experience cold stress [1]. Cold stress occurs when heat loss exceeds heat production, potentially leading to cold-related strain. Cold strain refers to the physiological responses attempting to compensate for heat loss through vascular changes, shivering and increasing metabolic heat production mediated by the hypothalamic thermoregulatory center through peripheral and central thermoreceptors [2–4]. There are also behavioural responses to cold, which involve intentional activities, such as seeking and adding clothing, movements, and adopting a closed body position with the goal of maintaining or reversing slight temperature variations [5,6].

Cold-related physical and mental stress can negatively affect cognitive performance (CP) [6]. A recent literature review has pointed out that a single acute exposure to cold under controlled laboratory conditions (e.g., cold air or cold water) induces cognitive impairment with attention, processing speed, memory, and executive function being the most affected cognitive domains. The duration and temperature of exposure, along with individual physiological response, play an important role in the degree of impairment [6]. Previous studies investigating cold exposure (e.g., cold air or cold water) and cognitive or physiological responses have used an exposure duration ranging from 30 to 180 minutes [6], often focusing on steady-state thermoregulatory response. In contrast, short-duration cold exposures (<15 min) remain comparatively underexplored, particularly in relation to concurrent cognitive performance and sex-related responses. Investigating short cold exposure better reflects real-world

scenarios, such as brief or intermittent occupational cold exposure, where individuals are not exposed long enough to reach thermal steady state. Experimental evidence indicates that early-phase cold exposure elicits rapid autonomic, metabolic, cardiovascular, and perceptual responses (e.g., cutaneous vasoconstriction, increased thermogenesis, thermal sensation) [2]. There are also strong perceptual and attentional demands due to sudden thermal discomfort. Such responses may differ from those observed during longer exposure and are particularly relevant when assessing tasks requiring attention or decision-making.

Cold stress and early stages of hypothermia can be associated with confusion, and a retrospective study on mortality on Mount Everest reported a noticeable cognitive impairment with fatigue before developing severe hypothermia in climbers who died [8,9]. Two hypotheses have been considered to explain the effect of cold exposure on different cognitive aspects. The distraction theory [8] explains the decline in CP in relation to the discomfort caused by cold exposure that reduces concentration. On the other hand, the arousal theory supports an improvement of CP with a slight decrease in core temperature (Tc) [8,9].

Males and females seem to respond differently to short-term cold exposure, although results are not consistent. Some studies indicated that females exposed to cold air exhibited more pronounced metabolic and hormonal changes [10], and a cognitive impairment [11,12]. Conversely, Solianik et al. [4] and Kong et al. [12] showed a cognitive impairment only in males after cold water-immersion. However, only few studies have been performed to compare CP response to cold in males and females, where participants were exposed to cold ambient air at around 5 to 10 °C in a climate chamber [11,12], and to cold water at around 10 to 15 °C [4,12,13].

The aim of the study was to investigate the effect of acute and short (15 min) exposure to low ambient temperatures (up to -10°C) on selected cognitive performance (reaction time, processing speed, and risky decision-making) in females and males, as well as to evaluate the distraction and the arousal theories. To this aim,

subjects completed three sessions of cognitive tests during exposure to three different ambient temperatures (Ta: 20 °C, 5 °C, and -10°C), performed in random order, under physiological monitoring. We hypothesized that CP decreases at low temperatures with a gender difference, before core temperature (Tc) changes.

MATERIALS AND METHODS

This randomized, controlled, crossover study was approved by the Institutional Review Board of Bolzano (Protocol Number 42-2021 BZ). The study was conducted according to the Declaration of Helsinki (World Medical Association, 1997) and the CONSORT guidelines [14].

Participants

Twenty-four healthy volunteers were recruited in the study. Inclusion criteria were age between 18 and 60 years, class I according to the American Society of Anaesthesiologists (ASA) [15], no fever (temperature above 37.5 °C) no acute disease or COVID-19, no neurological or psychiatric disorders, no history of cold injuries no of cold disorders (i.e., Raynaud's disease).

All participants underwent a medical examination prior to the study initiation. Participants were asked to avoid sleep deprivation before the session day, and to avoid smoking, caffeine, tea, or alcohol intake at least two hours before the study.

Sample size calculation and randomization

The sample size was determined based on the criteria for a pilot study, which recommend a minimum of 12 subjects to obtain reliable estimates of the mean and variance [16]. To account for the experimental conditions, the randomization, and the potential risk of participant drop-out, the sample size was increased to 24 subjects, gender balanced, comprising 12 male and 12 female participants.

Randomization was conducted using computer-generated sequences. The randomization variable was the order of the three test sessions, each corresponding to a different Ta exposure (see Study Protocol).

This combination yielded six unique session sequences (Figure 1). Each sequence was assigned to four subjects, balanced in terms of gender.

Study protocol

The study was performed in the terraXcube climate chamber (terraXcube, Eurac Research, Bolzano, Italy, https://terraxcube.eurac.edu). Upon arrival, a medical check was performed to assess the eligibility of the participants and familiarize with the study protocol. Before starting the experimental sessions, the participants rested for about 15 min at 20 °C and performed the baseline session measurements. Each participant was exposed on the same day to three experimental sessions (15 min) at three different Ta, interspersed by a 15 °C step (neutral 20 °C, cold 5 °C, and very cold -10 °C), each followed by a wash-out resting period of 15 min at 20 °C to allow physiological recovery [17,18]. During each session (baseline and test sessions) the participants performed cognitive tests along with the completion of several questionnaires and physiological parameters were continuously acquired (Figure 1). All participants wore appropriate and similar garments (underwear, long-sleeves shirt and thick sweaters, trousers and down jacket). Participants were allowed to take off the down jacket during the session at 20°C to avoid thermal discomfort.

Physiological monitoring and self-assessment of the participant's status

Demographical data (age, gender, education) were collected. The participants were equipped with an oesophagus temperature probe (ER400-12 Level 1® Esophageal Temperature Probe, Smiths Medical ASD, Inc., Minneapolis, MN, USA; probe accuracy: ≤ 0.2°C in the range 5°C to +45°C), which was inserted in the lower third of the oesophagus according to the current guidelines [19], to measure Tc and display it on

an emergency medicine monitor (Corpuls 3, Corpuls GS Elektromedizinische Geräte G. Stemple GmbH, Kaufering, Germany). Together with Tc, additional physiological parameters, such as skin temperature (Tsk), heart rate (HR), and peripheral oxygen saturation (SpO_2) were measured during all the sessions. Tsk was measured on the chest and recorded using the Equivital system (EQ02, Hidalgo, UK; probe accuracy: ≤ 0.3°C in the range -10°C to +50°C). HR and SpO_2 were measured by a pulse oxymeter (Masimo Corporation, Irvine, CA, USA; HR accuracy: ≤3 bpm in the range 30 - 240 bpm; SpO_2 accuracy: ≤ 2% in the range 70 - 100 %) on the participant's index finger of the non-dominant hand and displayed on the emergency medicine monitor.

A Visual Analogue Scale (VAS) was used to evaluate self-assessment of stress (low to high), cold sensation (not cold to very cold), and cognitive test performance (very good to very bad) by placing a mark on a 100-mm horizontally positioned VAS [20]. Thermal sensation was assessed using a 9-degree subjective judgment scale (ranging from -4, "extremely cold" to 4, "extremely hot"), and thermal comfort using a 5-degree scale (ranging from 0, "comfortable", to 5, "extremely uncomfortable") [21].

Cognitive tests

Cognitive performance was assessed using three different computerized cognitive tests installed on a portable personal computer as previously described [22,23]. Six different versions of the Digit Symbol Substitution Test (DSST) were administered across the three experimental sessions and the baseline session to avoid learning effect. All the tests were developed using PsychoPy (version 3.1.0, www.psychopy.org) and were modularly designed.

Psychomotor Vigilance Test (PVT)

A brief 3-minute version of the Psychomotor Vigilance Test (PVT), similar to that described by Basner and Dinges [24], was used to assess sustained attention and reaction time (RT). One key advantage of the PVT is that repeated administration does not affect the results, because PVT has no aptitude or learning effects. RT (in

milliseconds [ms]) - excluding lapses and false starts- was recorded, along with the number of omission errors or "lapses" (defined as RTs ≥ 355 ms), false starts or errors of commission (defined as a response with no stimulus or RT <100 ms), and performance score [defined as 1 - (the number of lapses and false starts)/(the number of all trials), and expressed as percentage from 0 to 100%] [44].

Balloon Analogue Risk Task (BART)

The Balloon Analogue Risk Task (BART) [25] was used to evaluate the risky decision making. The mean earning that equals mean pumps (because each pump = 1) of the unexploded balloon was measured. For this outcome, the higher the number of pumps, the greater the risk-taking behaviour.

Digit Symbol Substitution Test (DSST)

The Digit Symbol Substitution Test (DSST) was used to assess different cognitive performance, including processing speed and low-level visual search. The total mean number of correct and incorrect responses, as well as the mean RT for the correct responses, were analysed. Parallel forms were randomly assigned to each participant to avoid practice effects [26].

Statistical analysis

The analysis was performed with SPSS version 29 statistical software (IBM Corp., Armonk, NY). Normal distribution was assessed by means of Shapiro-Wilk test and normal Q-Q plots. Comparison of normally distributed parameters at the three ambient temperatures (-10 °C, 5 °C and 20 °C) was performed by means of repeated measures analysis of variance (ANOVA) with post hoc tests, while comparison of not normally distributed parameters was performed by means of Friedman test, using Wilcoxon signed-rank test for pairwise comparisons. Generalised estimating equations (GEE) [27] were used to analyse the effects on cognitive test parameters of Ta (-10 °C, 5 °C

or 20 °C), gender and interaction of Ta with gender. To control for an effect on cognitive test parameters, also age (two groups considering the median age of the participants, 31 years, as the cut-off) and years of education (≤13 or >13 years, where the cut-off of 13 years corresponded to the completion of high-school education) were inserted in the GEE as factors, while test number and value of cognitive parameter at baseline were inserted as covariates. GEE with normal distribution were used for BART mean earnings, PVT mean RT, PVT performance score (after arcsin transformation) and DSST mean RT of correct responses. GEE with Poisson distribution were used for PVT number of lapses, PVT number of false starts, DSST number of correct responses and DSST number of incorrect responses. GEE models were also estimated inserting age and years of education as covariates instead of factors to further check for an effect of these two variables. To determine whether variations in CP were associated with subjective or physiological responses during the different cold exposure conditions, Pearson correlation was calculated between cognitive and subjective/physiological parameters. Multiple comparisons were adjusted by means of Holm-Bonferroni correction. $P<0.05$ (two-sided) was considered as statistically significant. Values are reported as mean ± standard deviation for normally distributed variables, and as median (range) otherwise. Estimates of the GEE are reported as mean (95% confidence interval, CI).

RESULTS

Twenty-four healthy volunteers were enrolled in the study, and 23 completed the study because one participant could not tolerate the oesophageal probe. Demographic data are shown in Table 1. The median age of the participants was 31 (24 - 53) years, 11 (48%) were female and the median of the years of education was 18 (10-22).

Physiological parameters

Physiological values (Tc, Tsk, SpO$_2$, HR) obtained during the three sessions are reported in Table 2. SpO$_2$, Tc, and Tsk were not different in the three conditions. HR at - 10 °C was significantly higher (p<0.001) than at 5 °C and at 20 °C.

VAS and thermal scales

Cold sensation rated with the VAS was significantly different (p<0.001) at different Ta. Stress rated with the VAS was significantly higher (p<0.001) at the coldest Ta (-10 °C). Subjective performance on cognitive tests rated with the VAS was not rated differently at the three Ta.

Thermal sensation and thermal comfort were significantly different at different Ta (Table 2), but they were not different according to gender (Supplemental Table S1).

Cognitive tests (DSST, BART, PVT)

GEE analysis results (Table 3) showed an effect of Ta on BART mean earnings, PVT mean RT, and number of lapses, and DSST mean RT of the correct responses. No effect of gender, age, nor years of education was observed on the cognitive test parameters. Individual curves of cognitive test parameters are shown in Supplemental Figure S1. When age and years of education were inserted in the GEE as covariates instead of factors, the results were the same in terms of statistical significance (Supplemental Table S2).

BART mean earnings were lower at -10 °C in comparison with 5 °C (*p*=0.046) and with 20 °C (*p*=0.006).

The estimated BART mean earnings at -10 °C were 8.8 (95% CI 8.6-9.1), while they were 9.1 (95% CI 8.8-9.4) at 5 °C and 9.1 (95% CI 8.9-9.4) at 20 °C. No effects on the other BART parameters were observed.

The average PVT RT was slower at -10 °C than at 5 °C (p=0.013) and at 20 °C (p=0.004). The estimated mean PVT RT at -10 °C was 277 (95% CI 272-282) ms compared to 271 (95% CI 266-276) ms at 5 °C and to 267 (95% CI 262-272) ms at 20 °C. The PVT number of lapses was higher at -10 °C in comparison with 5 °C (p=0.013) and with 20 °C (p=0.048). The estimated PVT number of lapses at -10 °C was 3.6 (95% CI 2.8-4.8), while it was 2.6 (95% CI 1.9-3.5) at 5 °C and 2.5 (95% CI 1.9-3.2) at 20 °C. There was no effect of Ta on the number of false starts (p=1.000) nor on the performance score (p=0.057) of the PVT.

The mean RT of correct responses to the DSST was slower at -10 °C in comparison with 5 °C (p=0.006). The estimated DSST mean RT for correct responses was 1.652 (95% CI 1.606-1.697) s at -10 °C, compared to 1.598 (95% CI 1.559-1.637) s at 5 °C and 1.602 (95% CI 1.567-1.638) s at 20 °C. GEE analysis showed no effect of Ta on the number of correct and incorrect responses on DSST (p=0.268 and p=0.145, respectively; Table 3).

Correlations
A positive correlation was found between mean RT at PVT and participants' rating of their performance on a VAS at both -10 °C (r=0.632; p=0.005; Table 4) and at 20 °C (r=0.496; p=0.032). HR was positively correlated with mean RT of PVT at 20 °C (r=0.623; p=0.004). No correlation was found between the other cognitive tests variables and self-assessment (VAS) of stress, cold, cognitive test performance, thermal sensation and comfort, Tc, Tsk and SpO_2. VAS performance was not significantly correlated with PVT performance score.

DISCUSSION

In this randomized, controlled, cross-over study, we identified transient impairments in cognitive performance during a short (15 min) exposure to cold Ta of -10 °C compared

with cold Ta of 5 °C and to ambient Ta 20 °C in participants wearing appropriate clothing. Cold exposure at -10 °C primarily affected attention, as reflected by slower response times and a higher number of lapses, and decision-making, as evidenced by a reduction in risk-taking behaviour. Significant differences were also observed across conditions in heart rate, thermal and cold sensations, and self-reported stress and comfort, while core temperature (Tc) did not change. No significant differences were observed between male and female participants in cognitive performance. Our data support the distraction theory, suggesting that cold-induced sensory discomfort can transiently divert attentional resources, even during short cold exposure.

Our results showed an impairment of attention even with a short exposure to cold. Such changes are in agreement to and extend the findings of a previous study [28], where participants were similarly exposed to -10 °C cold air, albeit with a longer exposure duration (30 min vs. 15 min) and a different attentional test employed. In that study, decreased perceptual motor speed, motor steadiness, and executive function were also reported [28]. Other studies with different designs and neuropsychological tests have yielded mixed results. For example, Watkins et al. [29] reported reduced attention after exposure to -5 °C cold air for 45 min, Muller et al. [9], and Spitznagel et al. [26] after exposure to 10 °C cold air for 2 hours and Enander et al. [11] after exposure to 5 °C cold air for 60 min. Kong et al. [12] reported slower RT only in women at the beginning of exposure to cold air (10 °C) up to 140 min. Other studies have reported no effects on attention after a single exposure to cold air at 2 °C for 3 hours [30], at 10 °C for 2 hours [31], and at 5 °C for 90 min [11]. Differently from our study, processing speed was affected by cold air exposure [11,28]. These discrepancies probably arise from methodological differences, such as exposure duration, clothing insulation, Tc monitoring, and whether cognitive testing occurred during or after cold exposure.

Our participants showed a lower risk-taking related decision making during cold exposure. To the best of our knowledge, this is the first time that risk-taking behaviour during cold exposure has been studied in humans. Our results align with data from animal experiments showing that exposure to cold environments (8 °C) induces avoidance behaviour with activation of implicated neuronal pathways from the paraventricular thalamic nucleus to the nucleus accumbens, bed nucleus of stria terminalis, and central nucleus of the amygdala [32].

Both Tsk and Tc did not differ significantly among the three conditions, probably due to short duration of exposure and clothing, suggesting that Tc and Tsk were not the main driver of cognitive impairment that we observed. However, Tsk was measured at the chest, which might have been better insulated and thus less affected by the short exposure. Conversely, cold stress may have led to a reduction in peripheral Tsk, particularly at the extremities, triggering sensory input from peripheral hand thermoreceptors. This input may have diverted attentional resources away from the primary cognitive task, causing distraction within the cognitive system and resulting in decreased vigilance, as reflected by slower RTs and an increased number of lapses [8]. Participants reported changes in thermal sensation and thermal comfort, which may be associated with a reduction in peripheral Tsk (i.e., local at the hand). Not all the studies investigating the effects of cold air exposure on CP included detailed temperature measurements. However, in those that assessed both Tsk and Tc, minimal variation was observed. More recently, Wallace et al. [33] intentionally examined the impact on cognitive function of cold air exposure (0 °C for up to 180 min) until the reduction of Tsk (Δ-0.3 °C) and Tc (Δ-0.8 °C). Despite these physiological changes, no significant effects were found on measures of attention, working memory, and processing speed.

Our study found no significant differences in cognitive performance between male and female participants.

Although previous studies have reported sex-specific physiological responses to cold, such as

more pronounced metabolic and hormonal changes [10] and a faster cooling rate in females [34,35], relatively few studies have assessed the effects of cold exposure on cognitive performance in both genders. Studies that included both sexes revealed inconsistent findings. Enander [11] exposed 12 males and 12 females to cold air at around 5 °C and found an impairment of attention, processing speed, and executive function only in females, despite the fact that females had received shorter exposure (60 min vs. 90 min). Kong et al. [12] recently reported a gender difference in CP in 41 subjects: females showed reduced CP during exposure to cold air at 10 °C up to 140 min, such as slower RTs in spatial manipulation and procedural tasks, while cold-water immersion at 15 °C up to 80 min affected the immediate memory performance of males. Solianik et al. [4] exposed 32 volunteers to an intermittent cold-water (14 °C) immersion up to the level of the manubrium for a maximum immersion time of 120 min. They found an impairment in cognitive flexibility in both genders, while visual recognition and short-term memory were impaired only in males. Mahoney et al. [13] exposed 19 participants to immersion up to the chest in a pool of water at 10 °C to assess tyrosine as a countermeasure to cold-induced CP impairment, regardless of gender. Conflicting data on gender difference in the effect of cold exposure on CP could depend on the different study design, duration, degree and mode of cold exposure (water or air), thermal protection, and individual response. Water immersion is another experimental modality to investigate the effects of cold exposure. Most studies in the literature report that cold exposure through immersion can affect CP, including attention, executive function, processing speed, memory, and visuospatial abilities [6]. Cold-water immersion, where thermal conductivity is approximately 25 times greater than air (Castellani & Young, 2016), has been shown to induce more

pronounced impairments in attention, memory, cognitive flexibility, accompanied by stronger sympathetic nervous system and hypothalamic-pituitary-adrenal axis activation [36,37]. These distinctions limit the generalizability of findings to other cold modalities, as results obtained under cold-air exposure cannot be assumed to apply to cold-water immersion, and vice versa.

Overall, our results suggest that the observed impairment of CP is likely due to the distracting effects of cold-induced discomfort. From both occupational and recreational perspectives, it is essential to minimize reductions in peripheral Tsk to maintain optimal cognitive function. Occupational injuries and fatalities have been reported among professionals exposed to cold environments, such as Alaskan fishermen and military personnel. The most commonly employed strategy to mitigate the adverse effects of cold is the use of protective clothing and equipment [38]. Other potential interventions, though supported by limited evidence, include tyrosine supplementation [13] and cold acclimatisation. Tyrosine may mitigate the cold-induced decline in CP, as cold exposure has been shown to alter catecholamine levels [39]. Repeated cold exposure, or cold acclimation, can trigger physiological adaptations that reduce the stress associated with cold environments, improving CP and enhancing thermal comfort and cold sensation. Cold acclimation has the advantage in unplanned situation or exposure to cold, whereas tyrosine supplementation for instance has to be taken at least two hours before exposure. However, very little data are available on this topic [40,41].

Limitations of the present study
Some limitations should be acknowledged. Tsk was measured only on the chest, without inclusion of peripheral sites, which may have limited the detection of localized/peripheral/uncovered thermal response. Although clothing was largely standardised, allowing removal of the down jacket at 20 °C to maintain thermal

neutrality may have introduced minor residual clothing-related effects, which cannot be entirely excluded. Additionally, menstrual cycle phase was not recorded, despite evidence that hormonal fluctuations can influence both thermoregulation and cognitive performance [42,43]. The sample-size was relatively small, and the age range of participants was narrow, which may limit the generalizability of the findings. Future studies would benefit from broader participant demographics and more comprehensive physiological monitoring. Additionally, individual physical traits - such as body mass, body surface area, fat distribution, and, in females, menstrual cycle phase - are known to influence thermoregulatory responses and hormonal balance during cold exposure [44]. These factors differ between sexes and may have introduced variability or confounding effects in the observed cognitive and physiological responses. Although such characteristics were not systematically controlled or recorded in the present study, they should be considered in future research to improve the accuracy and generalizability of findings related to sex-specific thermo-physiological and cognitive outcomes.

CONCLUSIONS

This randomized, controlled, crossover pilot study found that a single, short, cold exposure of 15 minutes   transiently impaired neurocognitive performance even in the absence of changes in Tc. Cold impacted decision-making, reducing risky behaviour, and impaired attention, slowing RTs and increasing the number of lapses. HR, cold sensation and stress, as well as thermal sensation and comfort but not Tc were different in the three experimental temperature exposures. No differences were found between male and female participants in their cognitive performance. Our data support the distraction theory in the decline of CP even during a short exposure to cold temperatures. Such impairment should be carefully considered in people performing different activities in cold environments, even for a short time, to implement evidence-based prevention and mitigations strategies.

TABLES

Table 1. Demographical data (*n*= 23 participants). Continuous variables are reported as median (range) and frequencies as absolute frequency (percentage).

Feature/Variable	Median (range) or n (%)
Age, years	31 (24 - 53)
Females, n (%)	11 (48%)
Education, years	18 (10 - 22)

Table 2. Comparison of mean values of physiological parameters during the cognitive test, visual analogue scale (VAS) for stress, cold, and performance, thermal sensation and comfort at the three different ambient temperatures during the cognitive tests. Values are reported as mean ± standard deviation if parameters were normally distributed, and as median (range) otherwise. *P*-values were adjusted by means of Holm-Bonferroni method. HR, heart rate; SpO$_2$, peripheral oxygen saturation; Tc, core temperature; Tsk, skin temperature.

Parameter	Ambient temperature			P-value			
	-10 °C	5 °C	20 °C	-10 °C *vs.* 5 °C *vs.* 20 °C	-10 °C *vs.* 5 °C	-10 °C *vs.* 20 °C	5 °C *vs.* 20 °C
Tc	36.7 ± 0.4	36.7 ± 0.4	36.7 ± 0.4	0.974	-	-	-
Tsk	34.0 ± 1.3	33.8 ± 1.1	33.9 ± 1.0	1.000	-	-	-
SpO$_2$	100 (98; 100)	100 (98; 100)	100 (99; 100)	0.459	-	-	-
HR	66.2 ± 9.6	61.5 ± 9.5	59.9 ± 9.1	**<0.001**	**<0.001**	**<0.001**	**0.026**
VAS cold	75.5 (45; 97)	49 (12; 86)	21 (1; 65)	**<0.001**	**<0.001**	**<0.001**	**<0.001**
VAS stress	56.5 (5; 86)	35 (5; 74)	24 (3; 65)	**<0.001**	**0.001**	**<0.001**	**0.018**
VAS performance	47.2 ± 17.3	42.9 ± 17.8	38.1 ± 15.5	0.101	-	-	-
Thermal sensation	-3 (-4; 1)	-2 (-4; -1)	0 (-3; 2)	**<0.001**	**0.007**	**0.002**	**0.001**
Thermal comfort	2 (0; 4)	1 (0; 4)	0 (0; 2)	**<0.001**	**0.001**	**<0.001**	**<0.001**

Table 3. *P*-values, after adjustment with Holm-Bonferroni method, of the effect of climatic and demographic factors on cognitive test parameters, estimated by generalized estimating equations (GEE). BART, Balloon Analogue Risk Task; DSST, Digit Symbol Substitution Test; PVT, Psychomotor Vigilance Test; *, interaction.

Test	Parameter	Intercept	Ambient temperature	Gender	Age	Education in years	Test number	Parameter's value at baseline	Ambient temperature * gender
BART	Mean earnings	0.793	**0.034**	1.000	1.000	1.000	1.000	**<0.001**	1.000
PVT	Number of lapses	**0.009**	**0.044**	1.000	1.000	1.000	1.000	**<0.001**	1.000
	Number of false starts	0.216	1.000	1.000	0.891	1.000	0.254	**0.001**	1.000
	Mean reaction time	0.202	**0.020**	0.865	1.000	1.000	1.000	**<0.001**	1.000
	Performance score [1]	1.000	0.057	1.000	1.000	1.000	1.000	**<0.001**	1.000
DSST	Number of correct responses	**<0.001**	0.268	1.000	1.000	1.000	1.000	**<0.001**	0.296
	Number of incorrect responses [2]	**0.009**	0.145	0.110	1.000	1.000	1.000	**0.006**	1.000
	Mean reaction time of correct responses	0.289	**0.043**	1.000	1.000	1.000	1.000	**<0.001**	0.053

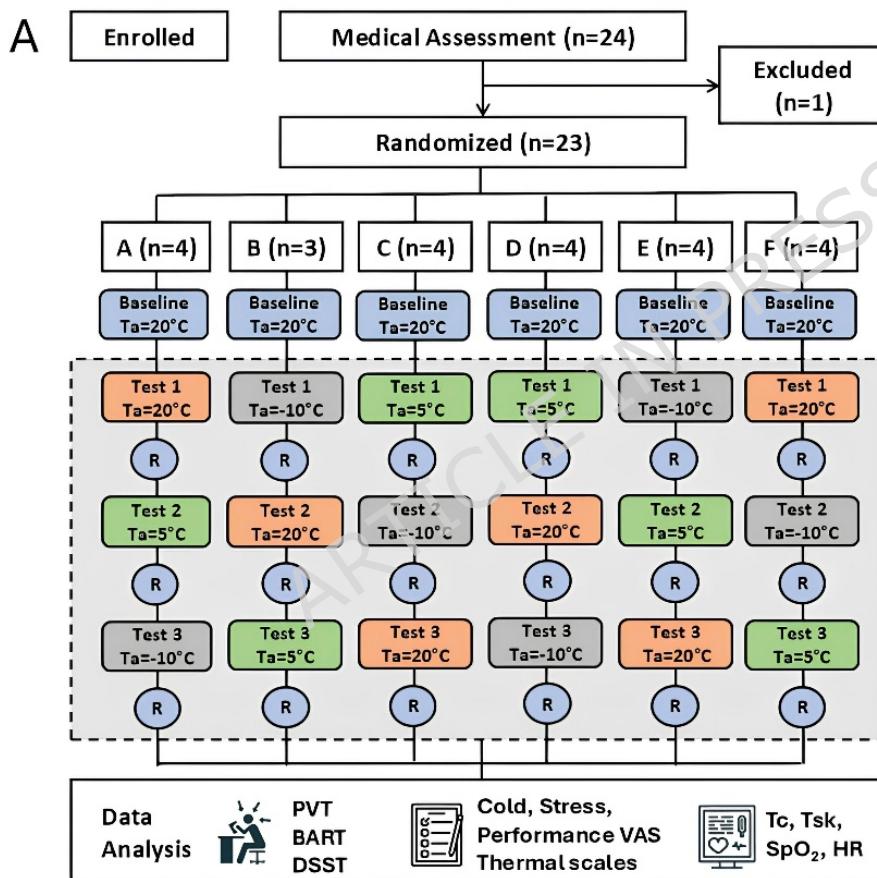[1] arcsin transformation was used to obtain normal distribution
[2] one test excluded from analysis because outlier

Table 4. Pearson correlation (r) between main cognitive test parameters and self-assessment, by means of visual analogue scale (VAS), of stress, cold, and performance, thermal sensation and comfort and mean value of physiological parameters during the test. P-values were adjusted by means of Holm-Bonferroni method. BART, Balloon Analogue Risk Task; DSST, Digit Symbol Substitution Test; HR, heart rate; PVT, Psychomotor Vigilance Test; SpO_2, peripheral oxygen saturation; Tc, core body temperature; Tsk, skin temperature.

Parameter	Ambient temperature	VAS cold		VAS stress		VAS performance		Thermal sensation		Thermal comfort		Tc		SpO_2		HR		Tsk	
		r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
BART mean earnings	-10 °C	0.136	1.000	-0.082	1.000	-0.142	1.000	0.106	1.000	-0.188	1.000	-0.411	0.154	0.172	1.000	0.020	1.000	-0.127	1.000
	5 °C	-0.286	0.559	-0.371	0.245	0.173	1.000	-0.018	1.000	-0.180	1.000	0.192	1.000	-0.209	1.000	0.117	1.000	-0.338	0.343
	20 °C	-0.024	1.000	0.035	1.000	0.145	1.000	-0.121	1.000	-0.017	1.000	0.193	1.000	-0.279	0.591	0.059	1.000	-0.059	1.000
PVT number of lapses	-10 °C	-0.166	1.000	0.293	0.557	0.407	0.181	-0.060	1.000	0.081	1.000	-0.010	1.000	0.256	0.714	0.272	0.629	0.191	1.000
	5 °C	0.151	1.000	0.290	0.539	0.214	0.978	0.165	1.000	-0.121	1.000	-0.103	1.000	0.090	1.000	0.242	0.800	0.146	1.000
	20 °C	-0.187	1.000	0.127	1.000	0.262	0.680	0.164	1.000	-0.026	1.000	0.021	1.000	-0.344	0.324	0.330	0.373	0.235	0.841
PVT mean reaction time	-10 °C	-0.046	1.000	0.495	0.057	0.632	**0.005**	0.061	1.000	0.203	1.000	0.121	1.000	0.451	0.092	0.372	0.161	0.209	1.000
	5 °C	0.179	1.000	0.054	1.000	0.376	0.077	0.031	1.000	0.120	1.000	0.233	0.853	0.350	0.305	0.393	0.127	0.226	0.899
	20 °C	-0.046	1.000	-0.052	1.000	0.496	**0.032**	0.031	1.000	0.013	1.000	0.307	0.461	-0.138	1.000	0.623	**0.004**	0.327	0.382

PVT performance score	-10 °C	0.303	0.513	-0.249	0.791	-0.403	0.188	0.054	1.000	-0.026	1.000	0.149	1.000	0.259	0.696	-0.170	1.000	-0.155	1.000
	5 °C	0.184	1.000	0.268	0.647	0.224	0.914	0.236	0.837	0.173	1.000	0.185	1.000	-0.054	1.000	0.129	1.000	-0.086	1.000
	20 °C	0.293	0.526	-0.132	1.000	-0.246	0.773	-0.204	1.000	-0.033	1.000	0.048	1.000	0.386	0.207	0.278	0.596	-0.142	1.000
DSST mean reaction time of correct responses	-10 °C	-0.151	1.000	-0.034	1.000	-0.025	1.000	-0.019	1.000	-0.066	1.000	-0.145	1.000	0.451	0.093	0.134	1.000	-0.131	1.000
	5 °C	-0.371	0.245	-0.045	1.000	-0.196	1.000	-0.207	1.000	-0.073	1.000	-0.167	1.000	0.457	0.085	0.163	1.000	-0.274	0.617
	20 °C	-0.157	1.000	-0.152	1.000	-0.212	0.995	-0.018	1.000	-0.016	1.000	0.381	0.218	0.280	0.588	0.203	1.000	0.318	0.417

Figure 1. Study design. CONSORT scheme of the study, reporting experimental phases and randomization procedure. After medical assessment and randomization, the participants underwent a baseline session at 20 °C, followed by a sequence of three test sessions at three different ambient temperatures (Ta, baseline Ta, 20 °C; low Ta, 5 °C; very low Ta, − 10 °C), interspersed by a recovery (R) phase at 20 °C. During each session, the participants performed a Psychomotor Vigilance Test (PVT), a Balloon Analogue Risk Task (BART), and a Digit Symbol Substitution Test (DSST), they completed stress, performance, and thermal scales, and their core temperature (Tc), skin temperature (Tsk), heart rate (HR), and oxygen saturation (SpO_2) were monitored.

Author contribution

MF and GS conceived the study idea. MF, GS, MM, and AM designed the study. MF, GS, MM, AM, GR, and MJvV collected the data. MF, TDC, MM, and GS analysed the data. MF and GS wrote the first draft of the article. All the authors reviewed and approved the final manuscript.

Data availability

Data is available upon reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate

This randomized, controlled, crossover study was approved by the Ethics Committee review board of Bolzano (protocol number 42-2021 BZ). We conducted the study

according to the Declaration of Helsinki. All participants were informed about the possible risks and gave written informed consent prior to enrolment. Additionally, they gave an informed consent for the publication of images in an online open-access publication.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests with regards to items described in this article.

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