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ORIGINAL ARTICLE

Neck cooling and cognitive performance following exercise-induced hyperthermia

Jason K. W. Lee · Aldrich C. H. Koh · Serene X. T. Koh · Glen J. X. Liu · Amanda Q. X. Nio · Priscilla W. P. Fan

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Abstract
Purpose To assess the efficacy of neck cooling on cognitive performance following exertional hyperthermia.
Methods Twelve healthy men completed two experimental trials [control (CON) and neck cooling collar (NCC)] in a counter-balanced design. They ran on a treadmill at 70 % VO_{2peak} under warm and humid conditions (dry bulb temperature: 30.2 ± 0.3 °C, relative humidity: 71 ± 2 %) for 75 min or until volitional exhaustion. Gastrointestinal, neck and skin temperatures, heart rate and subjective ratings were assessed. Serum brain-derived neurotrophic factor (BDNF) levels were measured before and after each run. Cognitive performance comprising symbol digit matching, search and memory, digit span, choice reaction time and psychomotor vigilance test (PVT) were assessed before and after exercise.
Results Mean gastrointestinal temperature was similar after exercise between trials (CON: 39.5 ± 0.4 °C vs. NCC: 39.6 ± 0.3 °C; $p = 0.15$). Mean neck temperature was lowered in NCC compared to CON after the run (36.4 ± 1.6 °C vs. NCC: 26.0 ± 0.3 °C; $p < 0.001$). Exercise-induced hyperthermia improved mean reaction time in the symbol digit matching test (−134 ± 154 ms; $p < 0.05$) and the PVT (−18 ± 30 ms; $p < 0.05$). Maximum span was increased in the digit span test (1 ± 2; $p < 0.05$). Application of NCC reduced the number of search errors made in level 3 of the search and memory test ($p < 0.05$). Mean serum BDNF levels were increased following exercise-induced hyperthermia in both trials ($p < 0.05$).
Conclusion Exercise-induced hyperthermia improves working memory and alertness. Neck cooling may only enhance performance in tasks of higher complexity.

Keywords Hyperthermia · Perceptual heat strain · Short-term memory · Working memory alertness · Neurotrophin · S100B

Abbreviations

CON	Control
NCC	Neck cooling collar
BDNF	Brain-derived neurotrophic factor
PVT	Psychomotor vigilance test
T_{gi}	Gastrointestinal temperature
S100B	S100 calcium binding protein B
VO_{2peak}	Peak aerobic capacity
RPE	Rating of perceived exertion
RTS	Rating of thermal sensation
SPES	Swedish performance evaluation system
TrkB	Tropomyosin receptor kinase B

Introduction

Maintaining a high level of physical and cognitive performance is pertinent in both sporting and occupational

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J. K. W. Lee (✉) · P. W. P. Fan
Combat Protection and Performance Programme, Defence Medical and Environmental Research Institute, DSO National Laboratories, Singapore, Republic of Singapore
e-mail: lkaiwei@dso.org.sg

J. K. W. Lee · A. C. H. Koh · S. X. T. Koh · G. J. X. Liu
Department of Physiology, National University of Singapore, Singapore, Republic of Singapore

J. K. W. Lee
Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Republic of Singapore

A. Q. X. Nio
Cardiff School of Sport, Cardiff Metropolitan University, Cardiff, UK

settings. Although the effects of hyperthermia and the resultant impact on endurance performance have been well documented, its impact on cognitive function remains inconclusive (Hancock 1984; Ramsey 1995). Several confounding factors such as gender (Allen et al. 2003; Gur et al. 1999; Haier et al. 2005), dehydration (Cian et al. 2001; Tomporowski et al. 2007), cognitive task skill level (Hancock 1984; Ramsey 1995), duration (Hancock and Vasmatzidis 2003; Lorist et al. 2000) and difficulty (Brisswalter et al. 2002; Hogervorst et al. 1996; Moore et al. 2012) may explain the inconsistencies amongst studies. Cognitive performance improves with mild heat strain, but impairment will ensue at high levels of hyperthermia (Racinais et al. 2008).

As impairments in cognitive performance have been observed at a high level of hyperthermia (gastrointestinal temperature; T_{gi} >39.0 °C, Racinais et al. 2008; T_{gi} >38.7 °C, Gaoua et al. 2011), it is important to investigate strategies to mitigate this decay. Due to its proximity to the thermoregulatory center of the central nervous system (Hammel et al. 1963), the neck is an appropriate site for cooling to reduce heat strain (Tyler and Sunderland 2011). While neck cooling during exercise may serve as an ergogenic aid for endurance performance (Tyler et al. 2010; Tyler and Sunderland 2011), data supporting its efficacy in enhancing cognitive performance following exercise-induced hyperthermia is limited.

The blood–brain barrier is a semi permeable membrane regulating the transport of selected substances, and changes to its permeability may allow the entry and exit of substances that affect metabolism, brain function and a wide range of homeostatic mechanisms (Ballabh et al. 2004). An increase in serum S100 calcium binding protein B (S100B) concentration is indicative of functional or morphological disruption of the blood–brain barrier (Kapural et al. 2002). During exercise, elevated serum S100B levels (Bailey et al. 2011; Dietrich et al. 2003; Otto et al. 2000; Watson et al. 2005) indicate increased permeability of the blood–brain barrier, which may be the pathway for the transport of brain-derived neurotrophic factor (BDNF) from the brain to the periphery (Rasmussen et al. 2009). Indeed, a single bout of aerobic exercise has shown to elevate serum BDNF levels (Griffin et al. 2011) and most of the increase in serum BDNF levels following exercise is derived centrally (Rasmussen et al. 2009). As BDNF is believed to selectively improve performance in hippocampal-dependent learning tasks (Griffin et al. 2011), there may be a link between BDNF and cognitive function.

With this background in mind, the aim of the present study was to investigate the efficacy of neck cooling on cognitive performance following exercise-induced hyperthermia. Concurrently, we investigated the relationships between serum S100B and BDNF levels, and cognitive performance following exercise. We hypothesized that the use of a neck-cooling collar would improve cognitive function following a moderate-intensity run in the heat. We also hypothesized that the moderate-intensity run would elicit increases in serum S100B and BDNF levels, and that the latter would be associated with cognitive function.

Methods

Participants

Twelve healthy men were recruited for this study, which was approved by the Ethics Committee of the Defence Medical and Environmental Research Institute, DSO National Laboratories, Singapore, and conformed to the standards set by the Declaration of Helsinki. They undertook endurance running and/or cycling regularly (approximately 5 times per week; each session lasting at least an hour). Following a detailed briefing explaining the nature, benefits and risks of the study, participants gave their informed consent verbally and in writing. Participants were certified fit for participation in this study by a physician. Before the commencement of each trial, participants completed a health status questionnaire to ensure that they were well.

Preliminary measurements

Height was measured to the nearest 0.1 cm using a stadiometer (Seca, Brooklyn, NY, USA), and baseline body mass was obtained to the nearest 0.05 kg using a digital scale (ID1 Plus/KCC150, Mettler-Toledo, Germany). Skinfold measurements were taken at four sites (biceps, triceps, subscapular and suprailiac) using skin-fold callipers (Model HSK-BI-3; Baty International, West Sussex, UK), and the mean values were used to calculate total skinfolds. Body density (Durnin and Womersley 1974) and body fat (Siri 1956) were calculated.

Experimental design

Prior to the full familiarisation trial, two cognitive test practice sessions were conducted to familiarise participants with the cognitive test battery (Ely et al. 2013). In these two cognitive test practice sessions, anthropometric measurements were taken on the first session and peak aerobic capacity (VO_{2peak}) was determined on the second. Following the full familiarisation trial, two experimental trials were conducted in a counter-balanced design [control: CON (no neck collar) and neck cooling collar: NCC]. Trials were separated by at least 7 days to allow recovery. Including the two cognitive test practice sessions, all trials

were conducted in the environmental chamber (Heraeus Votsch, Germany) programmed to maintain a dry bulb temperature of 30 °C and 70 % relative humidity.

Participants were required to standardize their dietary intake, as well as refrain from alcohol and strenuous activity in the 24-h period prior to each trial. A dietary record sheet was provided to the participants to aid them in standardizing their dietary intake. Each participant ingested a Jonah™ core temperature capsule (Mini Mitter Co., Inc., Bend, OR, USA) at least 8 h prior to the commencement of trial as a measurement of T_{gi}. Participants were also instructed to consume 500 ml of water 90 min before the commencement of each experimental trial and refrain from drinking thereafter.

Experimental procedure

Upon arrival at the laboratory for the experimental trials, a urine sample was collected and nude body mass was measured. Urine osmolality was measured using freezing point depression (Osmomat 030-D, Gonotec, Germany). A telemetric check was performed before the initiation of each trial to ensure the sensor resided within the participant. The VitalSense® temperature logger was sealed in a waterproof bag fitted into a padded pouch and worn on a customized lightweight harness around the waist positioned in the lumbar region of the participant. Skin temperatures were measured using telemetric iButtons (Maxim Integrated Products, Inc., Sunnyvale, CA, USA) attached with waterproof tape (Transpore; 3M, Minnesota, USA) on various sites on the participant (four on the neck and one each on the right chest, tricep, anterior thigh and calf). Each participant also wore a chest band and wristwatch heart rate monitor (Model S610i; Polar Electro Oy, Kempelem, Finland).

Participants entered an environmental chamber, and a baseline blood sample was obtained after 10 min of rest. Participants then commenced with the battery of cognitive tests in the following order: symbol digit matching, search and memory, digit span, choice reaction time and psychomotor vigilance test (PVT). The cognitive tests were performed before and after exercise in the environmental chamber.

Participants were asked to run on a motorized treadmill set to an individual speed calculated to produce an oxygen requirement of 70 % of their VO_{2peak}. Participants consumed 1 ml kg^{-1} body mass of water (at approximately 30 °C induced by the ambient temperature) immediately before the commencement of the run, every 15 min during exercise and after the first, second, third and fourth cognitive sub-test post-run. Rating of perceived exertion (RPE) and rating of thermal sensation (RTS) were assessed before the start of the run and every 15 min thereafter until the cessation of the run. Trials were terminated prematurely when a participant's T_{gi} reached 40 °C, in adherence with pre-determined ethical guidelines. Following completion of the run, blood sampling, body mass measurement and urine sampling were performed before participants completed the post-exercise cognitive test battery. Mass of iButtons were then measured and subtracted from body mass readings taken post-exercise.

Measurement of VO_{2peak}

Peak aerobic capacity was measured during the second session. Each participant ran at four different speeds on a treadmill (h/p/cosmos Mercury, Germany), starting at a speed 1 km h^{-1} slower than his expected pace for a 10-km race, with increments of 1 km h^{-1} every 3 min, for a total of 12 min. During the last 10 s of each 3-min stage, heart rate and RPE were recorded. Oxygen uptake (VO_2) was assessed over the final minute of each stage through a mouthpiece connected to a metabolic cart (Cortex Metalyser 3B, Germany). Following 5–10 min rest, the participant started on a continuous treadmill run with an initial gradient of 1 %, which increased by 1 % every 1 min until he reached volitional exhaustion. VO_{2peak} was recorded as the mean oxygen uptake over the last minute before volitional exhaustion. The relationship between VO_2 and speed was determined, and the speed corresponding to 70 % VO_{2peak} for each participant was used in subsequent experimental trials.

Neck-cooling collar

The neck-cooling collar was modified from a commercially available neck-cooling device (Black Ice LLC, Lakeland, USA). The cooling component was drained and replaced with 120 g of gel refrigerant (BDH Laboratory Supplies, Poole, Dorset, England, UK; Tyler and Sunderland 2011). The neck collar was held in direct contact with the skin by a 600-mm neoprene wrap secured with Velcro fastenings at the anterior aspect of the neck. Details of the collar are described by Tyler et al. (2010). Prior to the NCC trial, the collar was frozen for at least 24 h in a freezer at −80 °C and left in ambient conditions for 5 min before application. In the NCC trial, participants only donned the cooling collar 5 min into the run and through the post-exercise cognitive tests.

Cognitive tests

Cognitive performance was assessed using the Swedish Performance Evaluation System (SPES) and PVT. Four SPES sub-tests were selected to test specific cognitive functions—symbol digit matching, search and memory, digit span and choice reaction time. Each sub-test took 8–10 min

to complete. Cognitive testing commenced immediately after the run, regardless of whether participants completed the full 75 min of running, and the battery of tests was completed in approximately 45 min.

The symbol digit matching test was used as an assessment of working memory, particularly perceptual capacity and speed. During the test, a table of nine numbers, with each number corresponding to a specific and unique symbol, was provided. While referring to the table, participants were tasked to enter numbers in the sequence according to the rearranged symbols that appeared in the row below. The test ended after ten sets of symbol–digits were presented.

The search and memory test was used to evaluate the executive control function of the brain. Each participant was presented with a letter on the computer screen for 1 s and required to reproduce the letter on the keyboard following its disappearance. Levels 2 and 3 of the test would have 2 and 3 letters appearing for 2 and 3 s, respectively. If the letter(s) was successfully reproduced, a row of 30 letters was presented. In the shortest time possible, participants were required to search the row and to press a key when they recognized any of the letters that appeared in the previous task.

The digit span test is an assessment of working memory. During the test, a string of digits was presented on the computer screen. Each digit appeared a second after the other. Beginning with three digits, a maximum of up to 15 could be displayed. Immediately after all the digits appeared, participants were required to reproduce the string of digits using a number pad. A successful attempt extended the string by one digit; an unsuccessful attempt shortened the string by one number. The test was stopped when six attempts on the same digit span were made.

The choice reaction time test is a sustained attention task measuring the speed of response, which involves decisional making. A cross with one arm shorter than the others was presented on the computer screen. The four directional keys on the number pad corresponded to each arm of the cross. Participants were required to identify the short arm and to press the representative key on the number pad. The test ended after 128 presentations.

After the SPES sub-tests were completed, PVT (Model PVT-202, CWE, Inc., USA) was used to measure alertness and response latency, the time between onset of a stimulus and response. During this 5-min test, participants monitored the screen for the random appearance of a stimulus. The stimulus was a number that increased according to the amount of time (in milliseconds) that elapsed from its time of first appearance. Participants were instructed to press a designated button immediately when the visual stimulus was detected to stop the number from increasing. The mean reaction time to several exposures of the stimulus was used as a measure of vigilance.

Blood analyses

Venous blood samples (5 ml each) were collected after the participants were rested for 10 min. The blood was dispensed into an anticoagulant-free tube and was temporarily stored in ice until the end of each trial. Blood samples were centrifuged (Jouan Br44i Centrifuge, DJB Labcare, UK) at 3,500 rpm, 4 °C for 10 min to obtain serum. From the samples, S100B concentrations were determined using enzyme-linked immunoabsorbant assay (ELISA) (Human S100B ELISA, BioVendor Inc., Czech Republic). BDNF concentrations were determined using ELISA (Quantikine Human BDNF ELISA, R&D Systems Inc., USA).

Statistical analyses

All statistical computations were performed using the Statistical Package for Social Sciences version 15.0. Normality of experimental trial data was assessed using Shapiro–Wilk test. Paired *t* tests were performed on data that were normally distributed. Data which did not follow the normal distribution were analyzed using Wilcoxon matched-pair signed rank test. As intra-individual inter-day variability in cognitive performance is inevitable (Ely et al. 2013), changes from pre- to post-exercise were compared between trials. Two-factor repeated measures ANOVA was used to evaluate the changes in variables over time. Coefficient of determination (r^2) was used to detect any association between the cognitive test results and the change in BDNF levels before and after exercise. A statistical significance of $p < 0.05$ was used. Unless otherwise stated, all data are presented as mean ± SD.

Results

Participant characteristics

Participants' age and physical characteristics are detailed in Table 1.

Table 1 Physical characteristics of participants ($n = 12$)

Characteristic	Mean ± SD	Range
Age (years)	24 ± 2	21–27
Mass (kg)	61.6 ± 8.1	51.9–75.7
Height (m)	1.72 ± 0.05	1.65–1.78
Body fat (%)	11.7 ± 3.4	8.3–19.3
VO_{2peak} (ml kg^{-1} min^{-1})	59.4 ± 5.3	53.6–70.4

Exercise duration

No difference was detected in the duration of the run for participants between the two trials (CON: 67 ± 8 min; NCC: 71 ± 5 min; $p = 0.09$). Three participants exercised for a shorter duration in the CON trial due to exhaustion (Participant 4, CON: 64 min vs. NCC: 75 min; Participant 8, CON: 50 min vs. NCC: 75 min; Participant 11, CON: 68 min vs. NCC: 75 min). Removal of these participants from the analysis of cognitive, physiological, perceptual and blood data had no effect on the interpretation of results, and hence their data were included. No participant terminated the exercise session due to T_{gi} reaching 40 °C. Participants were considered euhydrated prior to each trial, demonstrated by pre-trial urine osmolality (CON: 247 ± 194 mOsmol kg^{-1} vs. NCC: 241 ± 168 mOsmol kg^{-1}; $p = 0.92$).

Environmental conditions and ingested fluid temperature

There were no differences in ambient temperature, relative humidity or ingested fluid temperature between trials.

Body mass changes

There were no differences in body mass between trials before the pre-exercise cognitive tests. Body mass was similar between conditions prior to the run, after the run, and 2 h after exercise was terminated. A decrease in body mass following the run for both CON (pre-CON: 61.6 ± 8.5 kg vs. post-CON: 60.2 ± 8.3 kg; $p < 0.001$) and NCC trials (pre-NCC: 61.5 ± 8.5 kg vs. post-NCC: 60.1 ± 8.3 kg; $p < 0.001$) was observed.

Gastrointestinal temperature

There were no differences in T_{gi} between CON and NCC trials before exercise (CON: 36.7 ± 0.2 °C vs. NCC: 36.8 ± 0.3 °C; $p = 0.21$; Fig 1), throughout the run (CON: 38.2 ± 0.3 °C vs. NCC: 38.2 ± 0.4 °C; $p = 0.31$), after exercise (CON: 39.5 ± 0.4 °C vs. NCC: 39.6 ± 0.3 °C; $p = 0.15$) and at the end of the post-exercise cognitive tests (CON: 37.3 ± 0.3 °C vs. NCC: 37.4 ± 0.3 °C; $p = 0.19$).

Neck temperature

No differences were observed in the neck temperature between trials prior to the run (CON: 34.2 ± 0.3 °C vs. NCC: 34.4 ± 0.3 °C; $p = 0.26$; Fig 2). Application of the neck collar 5 min into the run resulted in lower mean neck temperature in the NCC trial (CON: 34.9 ± 0.1 °C vs. NCC: 24.6 ± 2.1 °C; $p < 0.001$). Mean neck temperature was lowered in the NCC trial compared to the CON trial throughout the run (CON: 35.9 ± 0.4 °C vs. NCC: 26.3 ± 1.5 °C; $p < 0.001$), after the run (CON: 36.4 ± 1.6 °C vs. NCC: 26.0 ± 0.3 °C; $p < 0.001$) and following the post-exercise cognitive tests (CON: 34.4 ± 1.9 °C vs. NCC: 25.1 ± 0.2 °C; $p < 0.001$).

Weighted mean skin temperature

Mean skin temperature was similar for both trials before the run (CON: 32.6 ± 0.3 °C vs. NCC: 32.8 ± 0.4 °C; $p = 0.12$), throughout the run (CON: 30.1 ± 4.8 °C vs. NCC: 30.2 ± 5.3 °C; $p = 0.69$), following the termination of the run (CON: 34.7 ± 2.3 °C vs. NCC: 34.8 ± 2.3 °C;

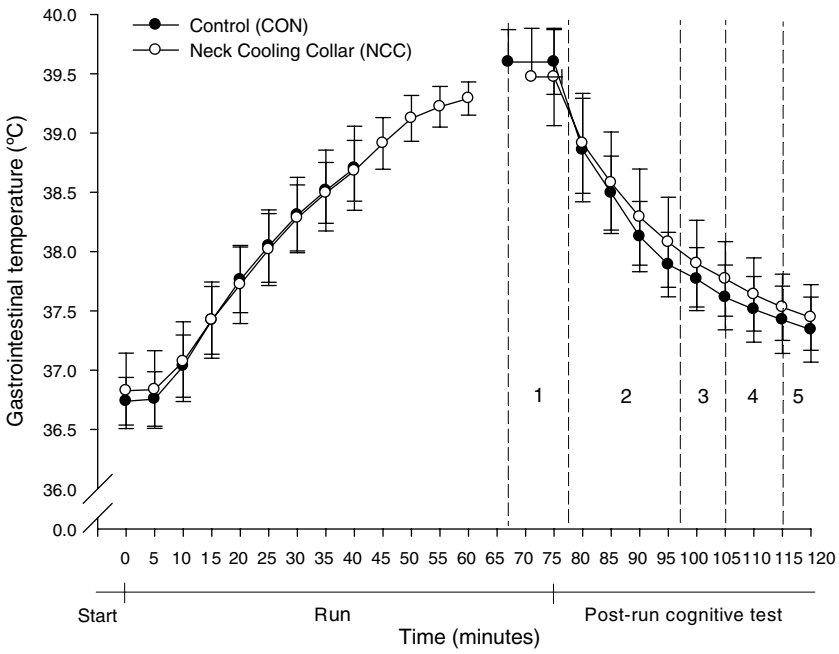

Fig. 1 Gastrointestinal temperature (°C) of participants in experimental trials. Mean gastrointestinal temperature was similar at pre-exercise ($p = 0.21$), throughout exercise ($p = 0.31$), exercise termination ($p = 0.15$) and at the end of post-exercise cognitive tests ($p = 0.19$) in both CON and NCC trials. The sequences of the cognitive tests being administered were as follows: *1* symbol digit matching, *2* search and memory, *3* digit span, *4* choice reaction time, and *5* psychomotor vigilance test

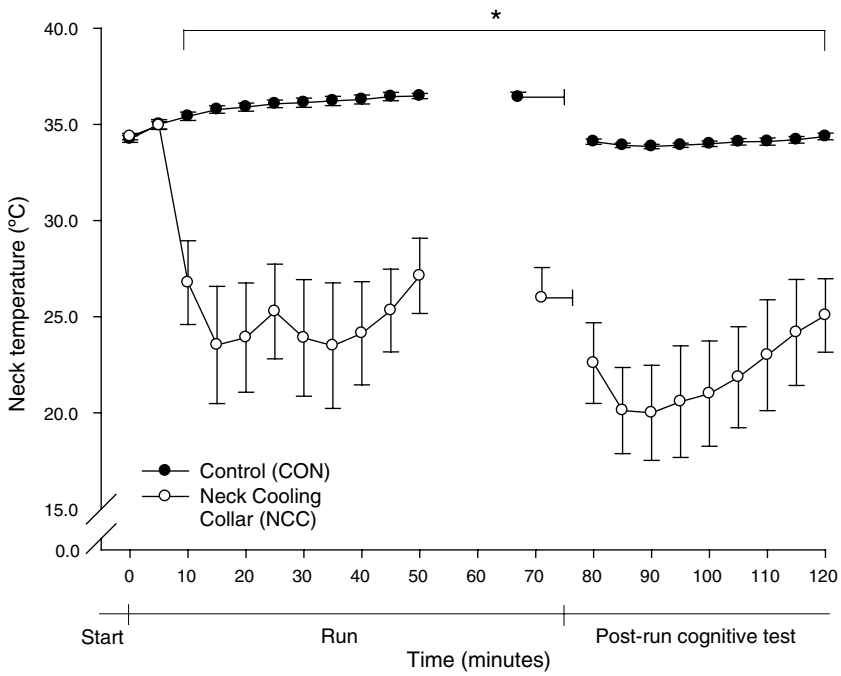

Fig. 2 Neck temperature (°C) of participants in experimental trials. Mean neck temperature was lower in NCC trial than CON trial during the run ($p < 0.001$)

$p = 0.97$) and after the post-run cognitive tests (CON: 32.5 ± 1.8 °C vs. NCC: 32.2 ± 2.2 °C; $p = 0.80$).

Heart rate

There was no difference in heart rate between trials prior to the run (CON: 58 ± 7 beats min^{-1} vs. NCC: 58 ± 7 beats min^{-1}; $p = 1.00$), throughout the run (CON: 149 ± 8 beats min^{-1} vs. NCC: 150 ± 6 beats min^{-1}; $p = 0.72$), at the end of the run (CON: 171 ± 10 beats min^{-1} vs. NCC: 173 ± 9 beats min^{-1}; $p = 0.29$) and after the post-exercise cognitive tests (CON: 82 ± 10 beats min^{-1} vs. NCC: 80 ± 8 beats min^{-1}; $p = 0.28$).

Cognitive test results

Results of the cognitive tests are shown in Table 2. Exercise-induced hyperthermia improved reaction time in the symbol digit matching test and the PVT for both trials ($p < 0.05$). Maximum span was increased in the digit span test for the CON ($p < 0.05$), but not in the NCC ($p = 0.61$) trial after exercise. In relation to the CON trial, wearing the neck collar in the NCC trial caused a slight improvement in the level 3 search and memory test, as the change in number of errors was reduced from 0 to −1 ($p < 0.05$). Exercise-induced hyperthermia had no effect on the remaining cognitive tests.

Subjective ratings

Rating of perceived exertion was similar prior to the run for both trials (CON: 7 ± 1 vs. NCC: 7 ± 1; $p = 0.37$). Throughout the run, RPE was lower in the NCC trial compared to the CON trial (CON: 13 ± 1 vs. NCC: 12 ± 1; $p < 0.05$). RPE was similar at the end of the run (CON: 17 ± 2 vs. NCC: 16 ± 1; $p = 0.12$). RTS was similar prior to the run for both trials (CON: 3.8 ± 0.6 vs. NCC: 3.7 ± 0.7; $p = 0.34$) and throughout the run (CON: 5.5 ± 0.7 vs. NCC: 5.0 ± 0.4; $p = 0.14$). At the end of the run, RTS was lower in the NCC trial compared to the CON trial (CON: 6.7 ± 0.8 vs. NCC: 5.9 ± 0.8; $p < 0.05$), but was similar after the post-run cognitive tests (CON: 4.3 ± 0.4 vs. NCC: 4.1 ± 0.4; $p = 0.08$).

Serum S100B and BDNF levels

Baseline serum S100B levels were similar for both trials prior to exercise ($p = 0.88$). An increase in serum S100B levels was observed after exercise in both control (pre-CON = 7.7 ± 4.4 pg ml^{-1} vs. post-CON = 16.1 ± 4.8 pg ml^{-1}; $p < 0.05$) and collar trials (pre-NCC = 6.8 ± 3.2 pg ml^{-1} vs. post-NCC = 12.2 ± 5.2 pg ml^{-1}; $p < 0.05$). There was no difference in the change in S100B levels at the end of exercise for both trials (CON: 8.4 ± 5.4 pg ml^{-1} vs. NCC: 5.4 ± 7.1 pg ml^{-1}; $p = 0.19$). Baseline serum BDNF levels were similar in both trials prior to exercise ($p = 0.61$). Following exercise, an increase in mean serum BDNF levels was observed in both CON (pre-CON: 23.2 ± 5.6 ng ml^{-1} vs. post-CON: 29.1 ± 5.0 ng ml^{-1}; $p < 0.05$) and NCC trials (pre-NCC: 21.7 ± 5.1 ng ml^{-1} vs. post-NCC: 32.1 ± 12.4 ng ml^{-1}; $p < 0.05$). There was no difference in the change in BDNF levels at the end of exercise for both trials

Table 2 Summary of cognitive test results comparing (mean ± SD) pre-CON/NCC and post-CON/NCC trials ($n = 12$)

Cognitive test	Measures	Pre-CON	Post-CON	Change	Pre-NCC	Post-NCC	Change
Symbol digit matching	Mean reaction time (ms)	1,624 ± 279	1,490 ± 232	−134 ± 154*	1,645 ± 226	1,516 ± 244	−129 ± 75*
	No. of errors	2 ± 3	2 ± 2	0 ± 4	1 ± 2	2 ± 2	1 ± 3
Search and memory level 1	Mean reaction time (ms)	4,437 ± 1,661	4,311 ± 1,309	−126 ± 807	4,455 ± 1,431	4,279 ± 1,478	−176 ± 673
	No. of errors	1 ± 1	0 ± 0	0 ± 1	1 ± 1	1 ± 1	0 ± 1
Search and memory level 2	Mean reaction time (ms)	6,984 ± 2,406	6,693 ± 3,331	−291 ± 1,955	7,147 ± 2,769	6,682 ± 2,126	−464 ± 1,140
	No. of errors	1 ± 1	2 ± 2	1 ± 2	1 ± 1	2 ± 2	1 ± 2
Search and memory level 3	Mean reaction time (ms)	9,711 ± 3,799	9,384 ± 4,314	−328 ± 2,077	9,481 ± 3,140	9,022 ± 3,365	−460 ± 1,609
	No. of Errors[#]	2 ± 2	2 ± 1	0 ± 1	3 ± 2	2 ± 1	−1 ± 2
Digit span	Maximum span	10 ± 2	11 ± 2	1 ± 2*	11 ± 2	11 ± 2	0 ± 1
	No. of directional changes	8 ± 2	9 ± 2	1 ± 3	9 ± 2	9 ± 2	0 ± 3
Choice reaction time	No. of correct responses	121 ± 6	120 ± 15	−1 ± 13	125 ± 4	126 ± 3	1 ± 4
	Mean reaction time (ms)	574 ± 88	522 ± 71	−51 ± 84	564 ± 145	531 ± 97	−32 ± 61
Psychomotor vigilance	Median reaction time (ms)	262 ± 55	244 ± 46	−18 ± 30*	238 ± 30	218 ± 29	−20 ± 25*
	No. of errors	3 ± 3	1 ± 2	−2 ± 3	1 ± 2	0 ± 1	−1 ± 2

* Significant difference between pre-CON/NCC and post-CON/NCC ($p < 0.05$)

[#] Significant difference between changes in CON and NCC ($p < 0.05$). Change = post-CON/NCC − pre-CON/NCC

(CON: 6.6 ± 5.1 ng ml^{-1} vs. NCC: 10.5 ± 13.6 ng ml^{-1}; $p = 0.45$). A strong association was found between the change in serum BDNF levels and change in maximum span for the digit span test in the CON trial ($r^2 = 0.81$; $p < 0.001$; Fig 3), but not in the NCC trial ($r^2 = 0.14$; $p = 0.26$). No association was found between serum BDNF levels and the remaining cognitive tests ($p > 0.05$).

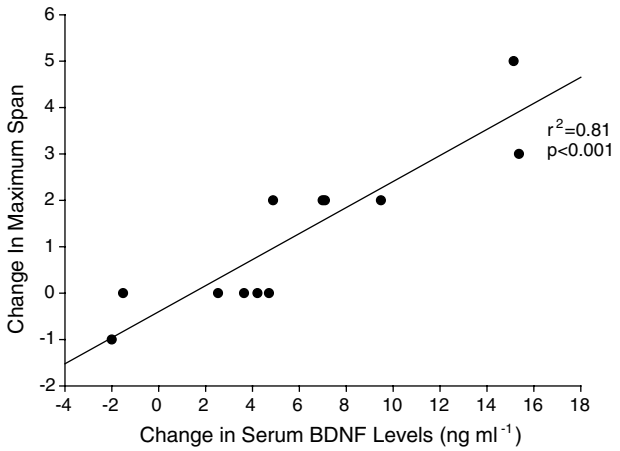

Fig. 3 Association between change in maximum span in digit span test and change in serum BDNF levels post-exercise in CON trial

Discussion

This study aimed to assess the efficacy of a neck-cooling collar on improving cognitive performance following exercise-induced hyperthermia. Memory and alertness were found to improve after exercise. The neck-cooling collar was found to enhance performance in the highest level (level 3) of the search and memory test, indicating that neck cooling was beneficial only in cognitive tasks of higher complexity. The rise in serum S100B concentrations after exercise for both trials provides some evidence that running in the heat could have caused a disruption of the blood brain barrier. An improvement in the digit span test paralleled the increase in serum BDNF levels after the run in the absence of neck cooling.

Reaction time as measured by the PVT was improved following exercise-induced hyperthermia. This is consistent with a previous study by Gaoua et al. (2011), in which participants completed tests associated with attention and memory over three separate trials (control: 20 °C, 40 % rH; hot: 50 °C, 50 % rH; hot with head kept cool). Reaction time improved with heat exposure until T_{gi} exceeded 38.7 °C. It is noteworthy that participants' T_{gi} in the present study following the run had dropped to 37.6 °C by the time they attempted the final cognitive test PVT. Therefore,

participant's T_{gi} was below the stipulated threshold of 38.7 °C as defined by Gaoua et al. (2011). Future studies should explore maintenance of hyperthermia following exercise on cognitive functions. Although a previous study by Racinais et al. (2008) demonstrated that heat exposure increases reaction time, it was based on a passive approach of heating (ambient temperature of 50 °C). Comparatively, the present study employed exertional heat stress on the participants. Similarly, the improvements on the digit span and symbol digit matching tests following the run indicate that exercise-induced hyperthermia enhances memory function. However, the results obtained were different from observations by Racinais et al. (2008), whereby hyperthermia resulted in an impairment of working memory in Spatial Span Test and Pattern Recognition Memory Test. McMorris (2009) proposed that moderate-intensity exercise was able to elicit optimal levels of arousal that improve cognitive function. This was suggested to be more evident with relatively simple cognitive tasks compared with more complex memory tasks (McMorris 2009). Therefore, a lack of arousal from a passive approach to hyperthermia in the study by Racinais et al. (2008) may account for the difference in outcomes for reaction time and memory function in the present study. Johnson and Kobrick (2001) have suggested that cognitive performance improves as arousal increases above a comfortable level caused by exposure to mild heat, but would degrade at high temperatures for a sustained duration of time.

With less complex cognitive tests, it appears that the impact of neck cooling on performance is minimal and is not dependent on whether hyperthermia is achieved actively with exercise, as in the present study, or passively (Simmons et al. 2008). Simmons et al. (2008) demonstrated that cognitive function was heavily dependent on core and skin temperature, and that cooling the head and neck did not affect cognitive performance. In addition, some degree of cognitive resilience compensates for the negative distraction of alterations in skin temperatures during heat stress (20–40 °C; Ely et al. 2013), but not cold stress (2 °C; Adam et al. 2008). Interestingly, neck cooling with exercise-induced hyperthermia may have a greater influence on more complex cognitive tasks in the heat. Previous studies have suggested that cognitive disturbances due to hyperthermia are dependent on task complexity (Pilcher et al. 2002; Ramsey 1995) and perceived heat strain may be a plausible limiting factor for more complex cognitive performance in the heat. In the present study, lowered RPE and RTS with neck cooling resulted in a reduced error rate in level 3 of the search and memory test. It is also possible that the cognitive domain tested could be different, and that NCC is only effective in improving cognitive functions of the pre-frontal cortex, temporal lobe and the parietal cortex—brain regions, which are involved in execution of the tasks required in the search and memory tests. However, we observed no improvement in the symbol digit matching test results for the NCC condition even though the specific cognitive function tested was the most similar. Furthermore, performance in levels 1 and 2 of the search and memory test was also not significantly different between trials, although all other factors were kept constant except for task complexity. Taken together, these results point towards the influence of task complexity on the efficacy of neck cooling on cognitive performance. Tyler and Sunderland (2011) have shown that dampening perceived heat strain with neck cooling prolongs exercise time to exhaustion. Thus, neck cooling may mask the 'cognitive load' perceived with exercise-induced hyperthermia and allow a partial restoration of cognitive resources, which enhances performance of complex cognitive tasks in the heat.

The results of the present study support previously reported increases in S100B after exercise (Watson et al. 2005) and the similar levels observed with and without neck cooling (Tyler et al. 2010). Serum BDNF was also found to increase concomitantly with serum S100B levels. Pedersen et al. (2009) found that while BDNF production increased in muscle during physical activity, it was not released into the circulation, suggesting that BDNF is derived centrally (Rasmussen et al. 2009). Furthermore, BDNF is known to be able to cross the blood–brain barrier in a saturable transport system (Pan et al. 1998). As such, with an increased permeability of the blood–brain barrier after exercise (indicated by S100B levels), we propose that BDNF is transported from the brain to the periphery, accounting for the increase in serum BDNF levels.

A strong association was observed between the change in maximum digit span scores and serum BDNF changes following exercise in the CON trial ($r^2 = 0.81$; $p < 0.001$), suggesting a link between working memory and serum BDNF levels after exercise. Although previous studies have demonstrated an improvement in memory and a concomitant increase in serum BDNF levels after exercise (Ferris et al. 2007; Griffin et al. 2011), no associations were reported. Based on this association, we hypothesize that working memory may be mediated by a BDNF-related mechanism. Griffin et al. (2011) found that acute exercise induced an increase in BDNF that paralleled improved performance in a face–name matching task. The researchers went on to conclude that acute bouts of intense aerobic exercise were selective in improving performance for hippocampal-dependent learning task mediated by BDNF expression. Furthermore, it has been found that exercise training increased the size of the hippocampus and was related to an improvement in the spatial memory test (Erickson et al. 2011). Neurological studies with rats have also uncovered a relationship between BDNF signaling after exercise and improvement in memory. Recently, Lee

et al. (2012) found that a bout of resistance wheel running was able to improve hippocampal-dependent learning and memory tasks in rats. Gomez-Pinalla et al. (2008) also found that rats displayed an improvement in spatial memory tasks that was dependent on BDNF expression in the hippocampus after physical activity. Taken together, both human and animal studies seem to indicate that an improvement in memory is related to BDNF levels following exercise, giving support to the association we found.

However, this association was only established in the CON trial. Given that the neck collar reduced participant's perceived heat stress in the NCC trial, it raises the question as to whether perceptual heat strain impacts BDNF-mediated mechanisms in improving working memory. Heat stress is a 'cognitive load' placing attentional demands on a limited global workspace, which leaves fewer resources available for the participant to use in concurrent cognitive tasks (Gaoua et al. 2011). Since the neck collar was able to reduce the perceived heat stress of participants, this would leave them with additional cognitive resources to undertake the digit span test. Therefore, although BDNF levels also increased after the run in the NCC trial, it may not have been a crucial mediator of working memory under lower perceived thermal strain. It is possible that BDNF may be selectively utilized as a mediator for synaptic plasticity only under conditions whereby perceived heat stress is more pronounced. Further investigation should be targeted at elucidating the underlying mechanisms of BDNF and synaptic plasticity during and following hyperthermia. Although we have shown that working memory improvement is correlated with a rise in BDNF post-exercise, we did not establish a causal relationship between them. Future studies can quantify TrkB binding by BDNF to establish a causal relationship when an up-regulated binding is observed after exercise in the heat.

In conclusion, exercise-induced hyperthermia improved memory and alertness. Neck cooling was only effective in enhancing cognitive performance in tasks of higher complexity after exercise-induced hyperthermia, possibly by blunting the perceptual heat stress experienced. While the neck-cooling collar was ineffective at improving less complex cognitive tasks after exercise-induced hyperthermia, it did not impair the performance of these tasks and may be applied as a strategy for personnel competing or working under heat stress to enhance the performance of more complex cognitive tasks. The strong association observed between BDNF concentrations after exercise and working memory, but only without neck cooling, suggests that working memory may be selectively regulated by a BDNF mechanism.

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Conflict of interest All authors declare they have no conflict of interest.

References

Adam GE, Carter R 3rd, Cheuvront SN, Merullo DJ, Castellani JW, Lieberman HR, Sawka MN (2008) Hydration effects on cognitive performance during military tasks in temperate and cold environments. Physiol Behav 93:748–756

Allen JS, Damasio H, Grabowski TJ, Bruss J, Zhang W (2003) Sexual dimorphism and asymmetries in the gray-white composition of the human cerebrum. Neuroimage 18:880–894

Bailey DM, Evans KA, McEneny J, Young IS, Hullin DA, James PE, Ogoh S, Ainslie PN, Lucchesi C, Rockenbauer A, Culcasi M, Pietri S (2011) Exercise-induced oxidative-nitrosative stress is associated with impaired dynamic cerebral autoregulation and blood-brain barrier leakage. Exp Physiol 96:1196–1207

Ballabh P, Braun A, Nedergaard M (2004) The blood-brain barrier: an overview: structure, regulation, and clinical implications. Neurobiol Dis 16:1–13

Brisswalter J, Collardeau M, Rene A (2002) Effects of acute physical exercise characteristics on cognitive performance. Sports Med 32:555–566

Cian C, Barraud PA, Melin B, Raphel C (2001) Effects of fluid ingestion on cognitive function after heat stress or exercise-induced dehydration. Int J Psychophysiol 42:243–251

Dietrich MO, Tort AB, Schaf DV, Farina M, Goncalves CA, Souza DO, Portela LV (2003) Increase in S100B protein level after a swimming race. Can J Appl Physiol 28:710–716

Durnin JV, Womersley J (1974) Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 32:77–97

Ely BR, Sollanek KJ, Cheuvront SN, Lieberman HR, Kenefick RW (2013) Hypohydration and acute thermal stress affect mood state but not cognition or dynamic postural balance. Eur J Appl Physiol 113:1027–1034

Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, Kim JS, Heo S, Alves H, White SM, Wojcicki TR, Mailey E, Vieira VJ, Martin SA, Pence BD, Woods JA, McAuley E, Kramer AF (2011) Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci USA 108:3017–3022

Ferris LT, Williams JS, Shen CL (2007) The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. Med Sci Sports Exerc 39:728–734

Gaoua N, Racinais S, Grantham J, El Massioui F (2011) Alterations in cognitive performance during passive hyperthermia are task dependent. Int J Hyperthermia 27:1–9

Gomez-Pinilla F, Vaynman S, Ying Z (2008) Brain-derived neurotrophic factor functions as a metabotrophin to mediate the effects of exercise on cognition. Eur J Neurosci 28:2278–2287

Griffin ÉW, Mullally S, Foley C, Warmington SA, O'Mara SM, Kelly AM (2011) Aerobic exercise improves hippocampal function and increases BDNF in the serum of young adult males. Physiol Behav 104:934–941

Gur RC, Turetsky BI, Matsui M, Yan M, Bilker W, Hughett P, Gur RE (1999) Sex differences in brain gray and white matter in healthy young adults: correlations with cognitive performance. J Neurosci 19:4065–4072

Haier RJ, Jung RE, Yeo RA, Head K, Alkire MT (2005) The neuroanatomy of general intelligence: sex matters. Neuroimage 25:320–327

Hammel HT, Jackson DC, Stolwijk JA, Hardy JD, Stromme SB (1963) Temperature regulation by hypothalamic proportional control with an adjustable set point. J Appl Physiol 18:1146–1154

Hancock PA (1984) Effect of environmental temperature on display monitoring peformance: an overview with practical implications. Am Ind Hyg Assoc J 45:122–126

Hancock PA, Vasmatzidis I (2003) Effects of heat stress on cognitive performance: the current state of knowledge. Int J Hyperthermia 19:355–372

Hogervorst E, Riedel W, Jeukendrup A, Jolles J (1996) Cognitive performance after strenuous physical exercise. Percept Mot Skills 83:479–488

Johnson RF, Kobrick JL (2001) Psychological aspects of military performance in hot environments. In: Pandoff KB, Burr RE (eds) Textbooks of Military Medicine: Medical Aspects of Hasrh Environments (Volume 1). US Army Medical Research and Material Command, Borden Institute, Washington, pp 135–159

Kapural M, Krizanac-Bengez Lj, Barnett G, Perl J, Masaryk T, Apollo D, Rasmussen P, Mayberg MR, Janigro D (2002) Serum S-100beta as a possible marker of blood-brain barrier disruption. Brain Res 940:102–104

Lee MC, Okamoto M, Liu YF, Inoue K, Matsui T, Nogami H, Soya H (2012) Voluntary resistance running with short distance enhances spatial memory related to hippocampal BDNF signalling. J Appl Physiol 113:1260–1266

Lorist MM, Klein M, Nieuwenhuis S, de Jong R, Mulder G, Meijman TF (2000) Mental fatigue and task control: planning and preparation. Psychophysiology 37:614–625

McMorris T (2009) Exercise and cognitive function: a neuroendocrinological explanation. In: McMorris T, Tomporowski P, Audiffren M (eds) Exercise and cognitive function. John Wiley, Chichester, pp 41–68

Moore RD, Romine MW, O'connor PJ, Tomporowski PD (2012) The influence of exercise-induced fatigue on cognitive function. J Sports Sci 30:841–850

Otto M, Holthusen S, Bahn E, Söhnchen N, Wiltfang J, Geese R, Fishcer A, Reimers CD (2000) Boxing and running lead to a rise in serum levels of S-100β protein. Int J Sports Med 21:551–555

Pan W, Banks WA, Fasold MB, Bluth J, Kastin AJ (1998) Transport of brain-dervied neurotrophic factor across the blood brain barrier. Neuropharmacology 37:1553–1561

Pedersen BK, Pedersen M, Krabbe KS, Bruunsgaard H, Matthews VB, Febbraio MA (2009) Role of exercise-induced brain-derived neurotrophic factor production in the regulation of energy homeostasis in mammals. Exp Physiol 94:1153–1160

Pilcher JJ, Nadler E, Busch C (2002) Effects of hot and cold temperature exposure on performance: a meta-analytic review. Ergonomics 45:682–698

Racinais S, Gaoua N, Grantham J (2008) Hyperthermia impairs short-term memory and peripheral motor drive transmission. J Physiol 586:4751–4762

Ramsey JD (1995) Task performance in heat: a review. Ergonomics 38:154–165

Rasmussen P, Brassard P, Adser H, Pedersen MV, Leick L, Hart E, Secher NH, Pedersen BK, Pilegaard H (2009) Evidence for a release of brain-derived neurotrophic factor from the brain during exercise. Exp Physiol 94:1062–1069

Simmons SE, Saxby BK, McGlone FP, Jones DA (2008) The effect of passive heating and head cooling on perception, cardiovascular function and cognitive performance in the heat. Eur J Appl Physiol 104:271–280

Siri WE (1956) The gross composition of the body. Adv Biol Med Phys 4:239–280

Tomporowski PD, Beasman K, Ganio MS, Cureton K (2007) Effects of dehydration and fluid ingestion on cognition. Int J Sports Med 28:891–896

Tyler CJ, Sunderland C (2011) Cooling the neck region during exercise in the heat. J Athl Train. 46:61–68

Tyler CJ, Wild P, Sunderland C (2010) Practical neck cooling and time-trial running performance in a hot environment. Eur J Appl Physiol 110:1063–1074

Watson P, Shirreffs SM, Maughan RJ (2005) Blood-brain barrier integrity may be threatened by exercise in a warm environment. Am J Physiol Regul Integr Comp Physiol 288:R1689–R1694