Effects of a cooling vest with sham condition on walking capacity in heat-sensitive people with Multiple Sclerosis

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Abstract

Purpose Heat sensitivity is a common contraindication in people with Multiple Sclerosis (pwMS), and physical fatigue is one of the most frequently reported symptoms that can affect quality of life. Increases in body temperature may exacerbate fatigue and heat-related symptoms. Decreasing body temperature via cooling devices may mitigate disease symptoms and improve physical abilities and quality of life. This study evaluates the effects of a cooling vest with sham condition on walking capacity using a commercially-available cooling vest specifically designed for pwMS.

Methods A counter-balanced, cross-over design was used to assess the effects of a cooling vest (CryoVest Comfort, Cryo-Innov, France) (COLD) from a menthol-induced sham condition (CON) on ground walking time to exhaustion (T_{ex}, s) and distance at exhaustion (D_{ex}, m) in ambulatory pwMS. Secondary outcomes were heart rate (HR, bpm), thermal sensation (Tsens), skin chest (Tchest) and back (Tback) temperature.

Results Ten females with Multiple Sclerosis (59 ± 9 years, EDSS 3.0–5.5) participated to the study. During COLD, pwMS walked significantly longer (1896 ± 602 vs. 1399 ± 404 s, $p < 0.001$) and farther (1879 ± 539 vs. 1302 ± 318 m, $p < 0.001$) than CON. Importantly, Tsens and HR at exhaustion were not significantly different between conditions, although Tchest (-2.7 ± 1.8 °C, $p < 0.01$) and Tback (-3.9 ± 1.8 °C, $p < 0.001$) were lower at volitional fatigue during COLD.

Conclusion The lightweight cooling vest improved total walking time and distance in heat-sensitive pwMS. These physiological improvements were likely due to feeling perceptually cooler in the COLD trial, compared to the corresponding point of fatigue in the CON condition.

Keywords Fatigue · Cooling · Multiple Sclerosis · Walking · Uhthoff phenomenon

Abbreviations

6MWT	6 Min walking test
ANOVA	Analysis of variance
COLD	Cold vest condition
CON	Control condition
CWS	Comfortable walking speed
D_{ex}	Distance to exhaustion
EDSS	Expanded disability status scale
HR	Heart rate
MS	Multiple Sclerosis
PP	Primary progressive
pwMS	People with Multiple Sclerosis
RH	Relative humidity
RR	Relapsing remitting
T	Time (different time points during the exercise)
T25-FW	Timed 25-Foot Walk
Tback	Mid-scapular skin temperature
Tchest	Mid-pectoral skin temperature
Tcom	Thermal comfort
T_{ex}	Time to exhaustion
Tsens	Thermal sensation
TUG	Timed up and go
VAS	Visual analog scale

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Introduction

Patients with Multiple Sclerosis (pwMS) often report being more susceptible to high environmental temperature-associated strain (Davis et al. 2010, 2018), which can influence their quality of life. Patients are often recommended to carefully consider embarking on outdoor activities during hot weather, a suggestion which can limit their independence (Julian et al. 2008). Indeed, 80% of pwMS report the presence of some degree of physical fatigue, and 55% considers that this symptom significantly impairs daily life (Rottoli et al. 2017). Uhthoff's phenomenon is a physiological mechanism commonly reported by 60–80% of pwMS which is associated with increased fatigue; it results in a temporary worsening of clinical signs and neurological symptoms specifically manifesting during heat exposure (Davis et al. 2010). In pwMS for example, a small rise of 0.8 °C core temperature can negatively affect central motor conduction time and cortical excitability (White et al. 2013), likely as a consequence of the slowed or blocked nervous conduction in demyelinated lesions within the CNS, causing altered central activation (Sheean et al. 1997; Humm et al. 2004). Uhthoff's phenomenon may thus represent a both a cause, and consequence, of the increased energy cost of locomotion observed in pwMS (Buoite Stella et al. 2020). This is due to the altered gait biomechanics and muscle contractions required to overcome impaired neuron conductivity, ultimately resulting in higher amounts of energy needed to produce simple locomotion. Simultaneously, the increased energy requirements of walking will produce higher metabolic heat that will, in itself, further influence the conduction of nervous stimuli (Krupp 2006; Chung et al. 2008; Davis et al. 2010). Worryingly, the prevalence of MS is increasing (Logroscino et al. 2018), and it may be speculated that more pwMS, and others with chronic illnesses, will have their independence further affected by climate change.

There have been many cooling methods proposed to improve exercise performance in pwMS by reducing one's core and/or skin temperature before taking on physical work (Kaltsatou and Flouris 2019). For an historical perspective of the beneficial effects of lowering body temperature in pwMS, we recommend the paper by Watson (Watson 1959). For example, wearing a cooling suit for 45 min was found to improve motor function in both ambulatory and wheelchair pwMS (Kinnman et al. 1997), and these improvements were confirmed in selected activities of daily living (Flensner and Lindencrona 1999; Kinnman et al. 2000). Moreover, a 60-min cooling protocol induced via cooling garment was associated with modest improvements in motor and visual function, and subjective perception of fatigue (Schwid et al. 2003). More recently, head and neck precooling, (including a sham condition), found improvements in ambulatory capacity (Reynolds et al. 2011). Other cooling methods besides cooling suits include cold water immersion, or whole-body cryotherapy, which have each shown similar physical improvements in pwMS (White et al. 2000; Miller et al. 2016). Although effective methods, most of the tools used to induce the cooling outlined above were attached to cooling units or limited the person's mobility and are therefore rather impractical for use in daily life.

While previous cooling studies in pwMS have focused on investigating the effects of precooling i.e., reducing body temperature prior to exercise or heat stress (White et al. 2000; Schwid et al. 2003; Reynolds et al. 2011), more recent work uses percooling, the cooling of an individual while they are still performing the exercise (Nilsagard et al. 2006; Meyer-Heim et al. 2007; Grahn et al. 2008; Gonzales et al. 2017; Chaseling et al. 2018). To this end, cooling vests represent a promising tool to help reduce the inevitable increase in core temperature that occurs during physical activity, and its accessibility may facilitate its use among pwMS in several working and exercising scenarios (Nilsagard et al. 2006; Meyer-Heim et al. 2007; Gonzales et al. 2017). Cooling vests have shown potential benefits in terms of functional capacity (Kaltsatou and Flouris 2019), with some authors focusing on walking (White et al. 2000; Schwid et al. 2003; Nilsagard et al. 2006; Grahn et al. 2008). The general limitation with both pre- and per-cooling research to date is an inability to fully blind participants to the condition in which they are being tested, and precooling literature conducted under laboratory conditions can over-value the precooling effect, especially when realistic airflow or other real-world conditions are not considered in the study design (Morrison et al. 2014). Thus, there remain significant gaps in our understanding of the mechanisms behind the purported cooling benefits observed in pwMS, and most crucially, to what extent do the exercise/performance alterations derive their benefits from physiological, or perceptual cooling.

To the best of the authors' knowledge, the effects of commercially available cooling vests on walking capacity have been under- investigated in ecologically-valid conditions, including at warm ambient temperatures, and especially in clinical populations. When studies do use ecologically-valid walking protocols, the ones commonly used have been shown to be relevant in terms of predictors of life quality (Cohen et al. 2014). Ground walking, which can be subject to increased thermal load via radiant energy reflecting from that surface, especially in a warm environments, does represent a common physical activity for many pwMS. Thus, considering all the points raised above, the aim of this study was to quantify the efficacy of a commercially-available cooling vest on walking capacity in a warm environment, as evaluated by volitional time to exhaustion at constant speed and in a moderately warm environment, and additionally, to compare the results with a sham cooling condition which would induce the perception of cooling but without ample physical cooling per se. It was hypothesized that time to exhaustion would be improved in the actual cooling trial and there would be no significant differences in the thermal perception at exhaustion between trials.

Materials and methods

Participants

This repeated-measures, cross-over study was approved by the Institutional Review Board and regional Ethics Board (CEUR) and was conducted following the guidelines of the declaration of Helsinki. Ten female participants with a confirmed diagnosis of MS, eight with relapsing remitting (RR) MS and two with primary progressive (PP), were recruited for this study. Inclusion criteria for participants were as follows: aged between 18–64 years, report being 3–5.5 on the Expanded Disability Status Scale (EDSS), and report being at least 12 months from their last relapse, they must also have self-reported the presence of fatigue and heat-sensitivity as part of their symptom makeup. Participants with PP MS did not take any disease modifying therapy at the time of the study, whereas RR MS did not modify their standard therapy which did not include interferon beta or other drugs that have been shown interfering with thermal sensation (Christogianni et al. 2018). Patients were excluded in the case of reporting other concomitant vascular, neurologic or orthopedic conditions that may have had an effect on temperature regulation or their walking capacity, or if they needed assistance to walk for more than 10 min. Analgesics or taking anti-inflammatory drugs in the previous 72 h before testing was a further exclusion criterion. Sample size was estimated using the G*Power software (Faul et al. 2007) and based on previous results obtained during pilot testing, using the same protocol and main outcomes of $\alpha = 0.05$ and power of 0.80 (Buoite Stella et al. 2016).

Measurements

Main outcomes of the study were the time to exhaustion (T_{ex}, s) and the distance to exhaustion (D_{ex}, m) measured during the constant speed walking test. Skin temperature was measured at four skin sites (two on the right side and two on the left side) using thermistors and a data logger (SmartReader Plus, ACR Systems Inc., Canada) attached with hypoallergenic tape (Blendem, 3 M, Sydney, Australia). The skin sites were selected based on the cooling vest shape (mid-pectoral, Tchest, and mid-scapular, Tback, °C), and average was provided for left and right sites together. All thermometric measurements were sampled at 10-s intervals) and downloaded. Heart rate (HR) was measured using a wireless heart rate sensor (H10, Polar, Finland) and processed every 10-s intervals. Skin temperature measurements and HR were analyzed to obtain 1 min averages and compared between conditions at 5 min intervals. Thermal comfort (Tcom) was evaluated on arrival to the lab using a 1–5 Likert scale (1—comfortable, 5—extremely uncomfortable) (Gagge et al. 1967). To rate the participants' subjective temperature perception, two 10-cm visual analog scales (VAS) were administered by asking the participant "by how much do you think you perceive more heat than a person without Multiple Sclerosis?" (VAS—heat perception), and "indicate by how much do you think heat might worsen your quality of life?" (VAS—heat symptoms). Thermal sensation (Tsens) was established using a 12-point Likert scale which ranges from 1- 'unbearable cold', to 7- 'neutral', and up to 12- 'unbearable hot', with descriptors, and numbers for the values between the extremes). The scale used in this particular study was an adapted version of a previously used scale (Buratti and Ricciardi 2009), where participants score integer values. All participants had the opportunity to familiarize themselves with these questionnaires before the experimental sessions and ask researchers for clarification if anything remained unclear. Like Tcom, Tsens was evaluated on arrival to the lab, before starting the exercise, 20 min after wearing the vest (for baseline acclimatization purposes), and then every 5 min during the exercise bout until exhaustion.

Experimental protocol including cooling techniques

All the participants who met inclusion criteria were invited to one preliminary visit and two experimental sessions, each separated by at least 96 h. During the preliminary visit, inclusion and exclusion criteria were verified, and any adverse reaction(s) to the menthol spray were tested. The participant was then asked to walk along the clinic hall at a speed they deemed "comfortable" for a length of 30 m. Individual speed was calculated by measuring the time it took them to walk the 30 m distance. This was then defined as the patient's comfortable walking speed (CWS). Included patients were then randomly assigned to two groups and the two experimental sessions were performed using a cross-over design.

The two experimental sessions were identical with the exception that the cooling properties of the vest were different. During the cold vest condition (COLD), participants wore a commercially available cooling vest, specifically designed for MS patients (CryoVest Comfort, CryoInnov, France). The vest was appropriately prepared with cooling packs (~ – 0.4 °C, per manufacturer data). The vest with cooling packs weighted 1.8 kg, covered the upper part of the torso from the collarbone to the upper abdomen and through to the mid-neck, posteriorly. During the control condition (CON) participants wore the same vest, but the cooling packs were in place at ambient temperature. To encourage blinding of both sessions, the participants' torso was first sprayed with a 0.05% menthol solution to induce an immediate cold sensation, as previously described elsewhere (Gillis et al. 2010). The vests were then installed after menthol application.

After full instrumentation, participants rested in a quiet room, for 20 min to allow for vest familiarization and standardize the waiting time between trials. Temperature and humidity were indicated by the room (25 °C and 30% RH) and hall (29–30 °C and 30% RH) digital thermometers. Participants started walking in a near hallway following a 30 m trace at a constant speed, calculated based on their CWS, which was then increased by 20%. We decided to use a faster speed than their CWS to find a speed that induced fatigue in most pwMS patients, while also allowing for at least 10 min of walking; the 20% increase in exercise load was based on previous pilot testing (Buoite Stella et al. 2016). Walking speed was maintained constant by using an acoustic signal corresponding to the time needed to reach the end of the trace. During the first minute of walking, participants were free to familiarize themselves with the walking speed and the acoustic signals. A researcher blinded to the COLD or CON condition walked near the participant to prevent falls and to help maintaining the pace. This researcher also collected data about thermal sensation during the exercise. Participants continued walking until exhaustion, defined by their voluntary termination of the exercise, or if they were not able to reach the extremity of the trace, concomitantly with the acoustic sound, for more than two consecutive times. Both experimental sessions were performed at the same time of day to avoid the effects of circadian rhythm.

Statistical analyses

Continuous variables were tested for normality with the Shapiro–Wilk test. We summarized data by means ± standard deviation (SD) or median and range, as appropriate, for continuous variables, and absolute frequencies and percentages for categorical variables. The paired *t* test was used to compare main outcomes of the study, including exercise time (T_{ex}, s) and distance (D_{ex}, m). Comparisons of HR, Tchest and Tback were between CON and COLD at the time of exhaustion (CON) or iso-time i.e., point during COLD trial which corresponded to the CON exhaustion time, respectively. Tsens was not normally distributed and was thus analyzed with the non-parametric Wilcoxon test for paired data. The unpaired *t* test or Mann–Whitney *t* test were used to compare Delta HR, Delta Tback, Delta Tchest and Delta Tsens between CON and COLD.

The effect of the intervention on physiological outcomes (HR, Tchest and Tback) was analyzed using a two-way mixed repeated measures ANOVA with condition (CON v COLD) as the between-subject factor and time (T) (i.e., baseline, T0, T5…T20) as the within-subject factor. Effect sizes were calculated as partial eta squared (η2) for ANOVA results. Post hoc planned pairwise comparisons were conducted through t-tests, with Bonferroni correction for multiple comparisons performed when main effects for a given factor was observed. For Tsens, the statistical analysis was performed using a nonlinear mixed-effect models (fixed effects: Time and Group; random effect: individual subject using "nlme" package of R). The longitudinal models (ANOVA and NLME) were performed up to time-point T20, at which point there remained equal, and adequate, number of participants before the patients began to volitionally fatigue. The significance level was set at 0.05. A post-hoc analysis confirmed power > 0.80 for the main outcomes of this study. Statistical analyses were performed with R version 3.5.3 (2019), The R Foundation for Statistical Computing.

Results

Clinical and demographic data are reported in Table 1. Absolute time to exhaustion (T_{ex}) was ~ 36% longer after COLD (s) compared to CON condition (1896 ± 602 vs. 1399 ± 404 s, $p < 0.001$). This resulted in participants walking 46% farther (D_{ex}) before volitional exhaustion in the COLD compared to CON (1879 ± 539 m vs. 1302 ± 318 m, $p < 0.001$, Fig. 1). Ambient temperature (T_a) was not different between conditions, and did not change during the exercise ($p = 0.729$).

At baseline, there were no significant differences in Tsens ($p = 0.06$), Tcom ($p = 0.34$), Tchest ($p = 0.18$), and Tback ($p = 0.54$), whereas HR was slightly higher in COLD by ~ 3 bpm ($p = 0.02$). Before starting the exercise, there were no significant differences in Tsens ($p = 0.34$), HR ($p = 0.06$), and Tchest ($p = 0.15$), whereas Tback was significantly lower during COLD compared to CON (− 0.6 ± 0.3 °C, $p = 0.01$). Compared to CON, Tsens at the relative time to exhaustion (iso-time) was significantly lower (− 1.3, 95% CI − 0.6, − 2.1; $p < 0.01$), as were Tchest (− 2.8 °C, 95% CI − 4.3, 1.4; $p < 0.01$) and Tback (− 3.5 °C, 95% CI − 4.7, − 2.2; $p < 0.001$) (Fig. 2). Cardiovascular strain was also marginally lower at this relative timepoint by ~ − 2 bpm (95% CI − 4, 0; $p < 0.05$). The mean differences between values at exhaustion for CON and iso-time (COLD) are summarized in Table 2.

During exercise, Tsens showed a significant time effect ($p < 0.001$), a group effect ($p = 0.04$) and an interaction effect (time × group, $p = 0.004$). HR showed a significant

Table 1 Participants' individual demographics and clinical characteristics

Personal characteristics	1	2	3	4	5	6	7	8	9	10	Total
Age [years]	70	54	62	68	66	50	58	64	50	45	59 ± 9
Body mass [kg]	70	67	74	80	71	66	82	78	71	85	74.4 ± 6.5
BMI [kg/m^2]	27.3	24.0	26.5	31.6	27.7	24.8	28.7	28.7	24.0	33.2	27.67 ± 3.07
Disease duration [years]	21	17	31	36	11	14	12	10	11	7	17 ± 10
EDSS	3.5	5.0	3.5	4.5	4.0	4.0	4.5	4.0	4.5	3.5	4.1 ± 0.5
PDDS	3	4	3	3	3	4	4	3	4	3	3.4 ± 0.5
VAS—heat perception [cm]	6.5	9.3	5.8	10.0	7.8	8.0	7.1	6.9	7.8	7.9	7.7 ± 1.2
VAS—heat symptoms [cm]	7.6	8.8	8.0	10.0	9.0	9.5	9.2	9.0	9.7	9.2	9.0 ± 0.7
CWS [m/s]	0.91	0.71	0.83	0.74	0.80	0.90	0.95	0.89	0.90	1.0	0.86 ± 0.09

Notes: Participants' reported age (years), body mass (kg), body mass index (BMI, kg/m), disease duration (years), expanded disability status scale (EDSS), patient determined disease steps (PDDS), heat perception self-reported on a visual analog scale (VAS—heat perception, cm), severity of heat related symptoms self-reported on a visual analog scale (VAS—heat symptoms, cm), comfortable walking speed (CWS, m/s)

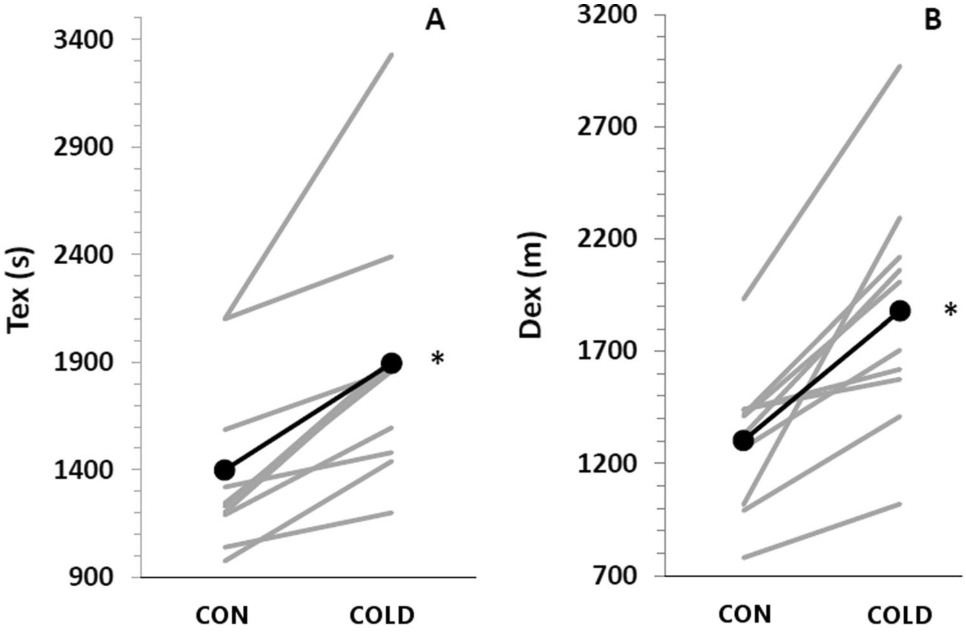


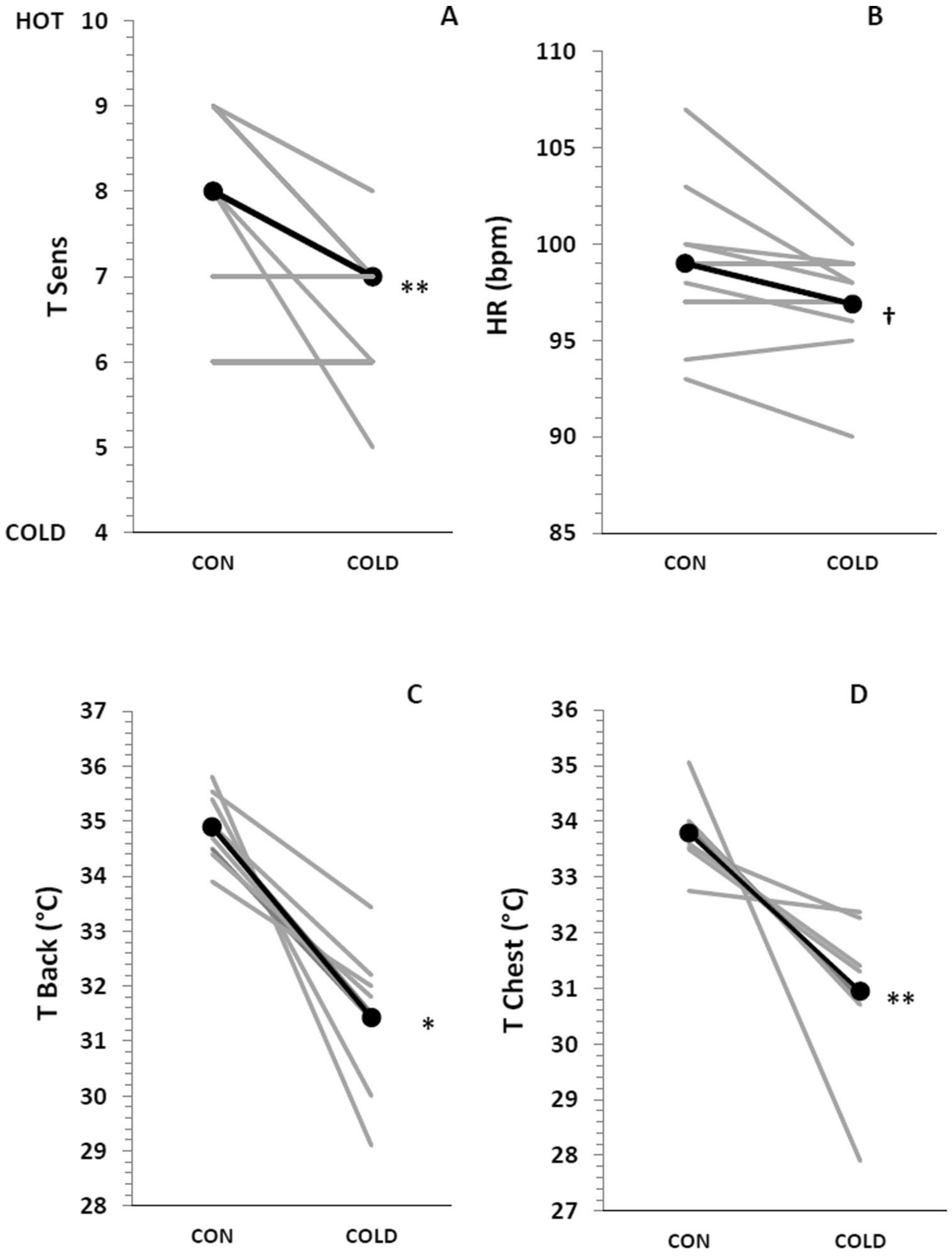
Fig. 1 Individual data (gray lines) and group means (black line with marker) showing the total walking time to exhaustion (T_{ex}, s) and the total walking distance to exhaustion (D_{ex}, m) during the control (CON, $n = 10$) and cooling (COLD, $n = 10$) conditions. Both outcomes show significant differences between conditions (*$p < 0.001$)

time effect ($p < 0.001$), with no effect of group ($p = 0.0.07$) or interaction (time × group, $p = 0.09$). Conversely, Tchest was characterized by a significant time effect ($p = 0.65$), a significant group effect ($p < 0.001$), and a significant interaction (time × group, $p < 0.001$). Similarly, Tback was characterized by a not significant time effect (p = 0.05), a significant group effect ($p < 0.001$), and a significant interaction (time × group $p < 0.001$). Results at the different time points and intergroup comparisons are summarized in Table 3.

Discussion

The results from this study show the effects of a commercially available cooling vest specifically designed for pwMS, on walking capacity. We found that while using the "active" cooling vest (COLD), participants were able to walk for a significantly longer time (+ 36.1 ± 19.7%) and distance (+ 45.6 ± 32.3%) compared to the control (CON) condition. The use of a menthol spray in both conditions provided a "sham effect" to help de-couple the performance and cardiovascular effects of exercise from actual body (i.e., skin) cooling and the perception of cold sensation. Subjective thermal sensation showed no difference between conditions (CON vs. COLD) at baseline after the menthol solution was applied, and while wearing the cooling vest. People did feel colder during the COLD trial at the same point they were exhausted in the CON trial. This difference disappeared when absolute volitional fatigue levels were compared.

Fig. 2 Individual data (gray lines) and group means (dotted line) at time to exhaustion during control (CON) and corresponding iso-time during cooling (COLD), for **a** thermal sensation (Tsens,$^{**}p < 0.01$), **b** heart rate (HR, bpm) $^{\dagger}p < 0.05$), **c** skin back temperature (Tback, °C, $^{*}p < 0.001$) and **d** skin chest temperature (Tchest, °C $^{**}p < 0.01$)



Effect of cooling protocol on walk performance

The present study chose a cooling vest because it (a) is commercially-available (b) easy to use and (c) represents enough cooling power to potentially affect physical activity performance outcomes without having to use impractical pumps, tubes, or other medical devices. The open-ended walking protocol used here was chosen to mimic normal conditions for most pwMS. By walking on a plane ground, at a speed slightly higher than what patents considered comfortable, and in moderately warm conditions, it was hoped that the participants would approach volitional fatigue within a reasonable timeframe to examine the testing hypothesis. Thus, the study aimed to present data that may be easily translated to daily life for these individuals. Indeed, although exercise is strongly recommended in pwMS, many of them anecdotally prefer to not engage in physical activity due to the increase in body temperature and subsequent worsening of symptoms this often provokes. Therefore, having time to exhaustion increase by over one third and distance covered increase by over 45% in this population represents a significant functional improvement. Most of the previous clinical literature also report physical performance improvements with common tests, such as the Timed Up and Go (TUG), Timed 25-Foot Walk (T25-FW), or the 6-min walking test (6MWT). However, despite being commonly used in clinical

Table 2 Participants' outcomes at volitional fatigue for the thermoneutral control (CON) trial and relative to time-matched point to CON in the COLD condition (COLD)

Outcomes	CON $n = 10$	COLD $n = 10$	Sig.
Baseline			
T_a (°C)	28.8 ± 0.2	28.8 ± 0.4	0.729
Tcom	1.1 ± 0.3	1.0 ± 0.0	0.343
Exhaustion			
T_{ex} (s)	1398.8 ± 403.8	1895.6 ± 601.7	**< 0.001**
D_{ex} (m)	1302.5 ± 318.3	1878.5 ± 539.4	**< 0.001**
Isotime			
$\Delta \text{Tsens}_{\text{ex-iso}}$	Δ 2 (− 1–3)	Δ 0 (− 1–1)	**0.018**
$\Delta \text{HR}_{\text{ex-iso}}$ (bpm)	Δ 30.8 (25.8, 35.8)	Δ 25.9 (22.7, 29.1)	0.080
$\Delta \text{Tchest}_{\text{ex-iso}}$ (°C)	Δ 1.1 (0.8, 1.3)	Δ − 1.9 (− 1.6, − 2.3)	**< 0.001**
$\Delta \text{Tback}_{\text{ex-iso}}$ (°C)	Δ 2.9 (1.6, 4.2)	Δ − 1.4 (− 2.9, 0.1)	**< 0.001**

Data are presented as means ± SD, and medians (range) and means (CI 95%) for differences at iso-time

Notes: measurements at baseline: ambient temperature (Ta, °C), participants' thermal comfort before wearing the vest (Tcom, 1-comfortable, 5-extremely uncomfortable); measurements at exhaustion: time to exhaustion (T_{ex}, s), distance to exhaustion (D_{ex}, m); measurements at isotime (exhaustion in CON vs isotime in COLD): Δ delta-change differences between baseline and at the time at exhaustion for CON and at the isotime for COLD for thermal sensation ($\Delta \text{Tsens}_{\text{ex-iso}}$), heart rate ($\Delta \text{HR}_{\text{ex-iso}}$, bpm), chest temperature ($\Delta \text{Tchest}_{\text{ex-iso}}$, °C), back temperature ($\Delta \text{Tback}_{\text{ex-iso}}$, °C). Significance value (Sig.) for intergroup comparison. Bold values for $p < 0.05$

and rehabilitation practice, those tests are not strongly reflective of everyday life mobility (Ehling et al. 2019), and may be poor estimators of total walking distance in pwMS (Phan-Ba et al. 2011). Indeed, although those tests may better at evaluating certain aspects of locomotion (e.g., balance, speed, etc.), they are not an optimal tool to evaluate fatigue and exercise-induced increases in body temperature, which is why we opted for an exercise task performed at constant speed until exhaustion as a way to determine endurance capacity (Alghannam et al. 2016). Similar to the performance results reported here, (Grahn et al. 2008) used a cooling device on one hand during a time-to-exhaustion walking test on treadmill. Their results showed a 33% increase of total walking time compared to the no-cooling condition. Despite the application of a different cooling device and walk method (treadmill vs. ground walking), the reported improvements are comparable in magnitude to the ones obtained here.

Perceptual effects of vest cooling

Precooling literature in particular has been/continues to be, at risk for reporting a positive-bias in its results, not only when the activity is performed indoors in the absence of adequate airflow (Morrison et al. 2014), but also because it can be difficult to blind participants to the experimental condition. Therefore, it was critical in the current study that we attempt to blind participants to the experimental conditions. The use of a menthol solution, administered before putting the vest on, and using a standardized 20 min habituation period before commencing with exercise, appears to have been effective for the first 10 min of the experimental protocol, based on the Tsens data obtained. There were significantly higher Tsens (indicating higher heat perception) during the middle of the CON condition compared to COLD. This result implies: (1) Blinding to the trial condition was effective baseline and continued to be well-matched between trials at the start of exercise, and (2) as exercise continued,

Table 3 Univariate statistics for variables in analysis, means ± SD for HR, Tchest, Tback and median (min–max) for Tsens

Outcomes	Baseline ($n = 10$)	T0 ($n = 9$)	T5 ($n = 9$)	T10 ($n = 9$)	T15 ($n = 9$)	T20 ($n = 9$)	T25 ($n = 2$)	T30 ($n = 2$)	T35 ($n = 2$)
Tsens COLD	7 (6–7)	6 (4–7)	5.5 (4–7)	6 (4–8)[a]	7 (5–8)[a]	7 (5–9)[a]	7.5 (6–9)	8 (7–8)	8 (8–8)
Tsens CON	7 (6–9)	6.5 (5–9)	6 (5–9)	8 (5–9)[a]	8 (6–9)[a]	8.5(6–9)[a]	9 (6–9)	9 (9–9)	9 (9–9)
HR COLD	71.0 ± 1.7[a]	70.9 ± 3.1	94.1 ± 4. 8[a]	95.3 ± 3.2	95.8 ± 2.9	97.2 ± 3.6	99.9 ± 1.0	100.0 ± 1.4	98.5 ± 0.7
HR CON	68.2 ± 3. 2[a]	69.0 ± 3.0	89.8 ± 3.5[a]	94.1 ± 4.7	96.0 ± 3.8	99.7 ± 3.5	98.0 ± 1.4	102.5 ± 3.5	101.5 ± 2.1
Tchest COLD	32.9 ± 0.9	32.4 ± 1.4	31.4 ± 1. 7[a]	31.1 ± 1. 6[a]	31.0 ± 1. 5[a]	30.8 ± 1. 2[a]	30.3 ± 1.1	31.2 ± 0.5	31.8 ± 0.8
Tchest CON	32.7 ± 0.6	33.1 ± 0.2	33.6 ± 0. 4[a]	33.7 ± 0. 6[a]	33.7 ± 0.6[a]	33.9 ± 0.7[a]	33.4 ± 0.4	33.4 ± 0.3	33.1 ± 0.5
Tback COLD	32.8 ± 1.4	33.1 ± 0.5[a]	32.4 ± 0.8[a]	32.2 ± 0.7[a]	31.9 ± 0.9[a]	31.5 ± 1.1[a]	30.8 ± 0.8	30.1 ± 0.5	29.6 ± 0.6
Tback CON	32.0 ± 1.5	33.7 ± 0.6[a]	33.6 ± 1.0[a]	33.7 ± 0.7[a]	34.5 ± 0.6[a]	34.6 ± 0.3[a]	35.1 ± 0.3	35.5 ± 0.4	35.6 ± 0.3

Notes: Repeated measures for Cold (COLD) and Control (CON) conditions at different times at baseline and during exercise at corresponding walking minutes, n indicated the number of pair measurements performed (COLD vs. CON). "*T*" stands for time (Baseline: on arrival to the lab; T0: before starting the exercise but 20 min after wearing the cooling vest for baseline acclimatization purposes, and then every 5 min during the exercise bout until exhaustion-T5-T10-…). Data were analyzed up to T20, after which only $n = 2$ participants remained (T25-T35 data are included here for interest). Participants' reported thermal sensation (Tsens, 1- unbearable cold, 7- neutral, 12-unbearable hot), heart rate (HR, bpm), chest temperature (Tchest, °C), back temperature (Tback, °C)

[a] Inter-group comparison $p < 0.05$ for valid pairs at each time

there were perceptual differences that were apparent to the participants. However, it should be considered that increase in body temperature in pwMS may affect cold thermal sensation, and future studies linking exercise and thermal stimuli should carefully consider this interaction (Filingeri et al. 2017).

Physiological effects of vest cooling

HR was monitored continuously from baseline to exhaustion in the present study. Despite (slightly) significantly higher values at baseline and until the 5th min of walking in the COLD condition, HR remained stable across trials from the progression of constant walking to volitional exhaustion, suggesting that cardiovascular strain was not a limiting factor to the cessation of exercise. This finding is in line with a previous well-conducted study that evaluated the effects of cold water ingestion on exercise capacity (Chaseling et al. 2018), which also reported no effects and/or independent influence of cooling on the development of cardiovascular strain.

The Chaseling et al. study (2018) did provide some evidence that exercise capacity in the heat can be extended by perceptual cooling alone (i.e., via cold water ingestion which caused no lowering of actual Tcore); but that study was not designed to address the perceptual vs. physical cooling question on performance outcomes. The methods of cooling were also different compared to the current study, since it used an internal (as opposed to external) cooling method. In contrast with the above-mentioned study, skin temperatures measured in present study did differ between conditions. Both chest and back skin temperature showed a rapid decrease during COLD. Tchest was significantly lower during COLD from the 5th min of exercise and remained different at exhaustion, while Tback was significantly lower already from the start of the exercise. Therefore, a modulation effect on exercise capacity and thermal sensation may be due to stimulation of the cold-afferent receptors on the torso skin surface, as similarly observed in healthy subjects (Tyler et al. 2015). Physiological effects on neurophysiological parameters have been studied in pwMS after cooling. Capello et al. (1995)) found that after wearing a cooling garment for two 45-min sessions, central somatosensory conduction was significantly improved in their sample, suggesting there was indeed a modulation effect of heat-related symptoms in pwMS (i.e., the Uhthoff's phenomenon).

The question is then whether the ~ 4 °C decrease in torso skin cooling observed in the present study conferred enough cooling power to significantly affect walking performance in our sample of pwMS participants, or whether their performance gains were as a result of a lower perception of thermal strain per se. Ice-vests can be powerful cooling devices; studies in elite athlete populations have shown they are capable of removing ~ 273 $\mathrm{kJ \cdot m^{-2}}$ (Cotter et al. 2001). It is conceivable that the − 4 °C cooling observed herein was significant enough to extol measurable differences in walking endurance for this clinical group. It is also well-established that skin temperature is a powerful driver of thermal perception (Cotter et al. 1996) which can affect a participant's thermal comfort, perceived exertion and ultimately, their performance as well. Since participants reported feeling cooler in the middle of this open-ended exercise, and since these decreases were largely dissipated by the time of volitional exhaustion, it remains that the pwMS participants were able to complete more work over a longer period of time, and with no greater thermal or cardiovascular strain reported at volitional fatigue; this represents a clinically-significant result for a clinical group whose life quality satisfaction stands to be greatly enhanced by even small changes in behavior.

Limitations and considerations

The focus of the present study was to determine functional outcomes to an ecologically-valid exercise test in pwMS people. Therefore, the work does lack many of the more extensive tools used to determine thermoregulatory responses at a mechanistic level, including: core temperature measurement, and a broader assessment of skin temperature, sweat loss, and vasomotor tone. Although this limits the mechanistic assessment and subsequent thermoregulatory impact of the interventions used, our paper does provide the methodological framework and proof-of-concept for future studies to follow when assessing the interactions between perceptual and physical cooling in greater detail. Patients reported feeling cooler in the COLD trial after exercising for 10 min, so although our blinding procedure was adequate in the beginning, as exercise continued, there were perceptual differences apparent between groups.

Conclusion

Heat-sensitive pwMS may be characterized by reduced physical capacity due to the negative effects of increased body temperature, therefore affecting their working capacity, independence, and quality of life. Different cooling methods can produce beneficial effects on physical and cognitive performance by reducing body temperature, but testing conditions are rarely blinded to the patients. This study adds a novel control condition which provided perceptual, but not physical cooling via the use of a menthol spray. As such, the study found that the perceptual effects of cooling were no different at the point of volitional fatigue between wearing a cooling vest and a sham cooling condition, even though participants were able to complete more work (i.e., walk a greater distance and duration) in that time. Thus, the moderate physical effects of skin cooling provided by an ice vest can mitigate the onset of heat-induced decrements in walking capacity in pwMS individuals.

Author contributions ABS: conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; resources; visualization; roles/writing—original draft; writing review and editing. FP: conceptualization; investigation; methodology; validation; roles/writing—original draft; writing—review and editing. SAM: conceptualization; data curation; methodology; resources; software; supervision; validation; writing—review and editing. MEM: conceptualization; methodology; validation; writing—review and editing. AD: investigation; methodology; writing—review and editing. AB: investigation; methodology; resources; supervision; writing—review and editing. AB: methodology; resources; supervision; writing—review and editing. AS: conceptualization; data curation; funding acquisition; investigation; methodology; resources; supervision; validation; roles/writing—original draft; writing—review and editing. FG: data curation; formal analysis; software; validation; visualization; roles/writing—original draft; writing—review and editing. PM: conceptualization; data curation; funding acquisition; methodology; project administration; resources; supervision; validation; writing—review and editing.

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Data availability The datasets generated during and/or analyzed during the current study are not publicly available due to IRB/EC requirements, but are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the Institutional Review Board of the "Azienda Sanitaria Universitaria Giuliana Isontina" and the Ethics Board of Friuli-Venezia Giulia. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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