TITLE

Modulation of cold-induced shivering activity by intermittent and continuous voluntary suppression.

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RUNNING TITLE

Voluntary control of shivering.

ABSTRACT

Introduction: This investigation assessed the physiological effects of voluntary suppression of shivering thermogenesis in response to whole-body cooling. ***Method:*** Eleven healthy volunteers underwent passive air cooling (10°C), across three visits: *NO_SUP*, where participants allowed their body to freely regulate against the cold; *FULL_SUP*, where participants constantly suppressed shivering; *INT_SUP*, where participants intermittently suppressed shivering (5 min phases), interspersed with 5 min free regulation. Shivering was assessed via electromyography (EMG), mechanomyography (MMG) and whole-body oxygen uptake ($\dot{V}O_2$), while body temperature and heat exchange were assessed via skin temperature, rectal temperature, and heat flux sensors. ***Results:*** A 29 % increase was observed in shivering onset time in the FULL_SUP trial compared to NO_SUP ($p = 0.032$). Assessing shivering intensity, EMG activity decreased by 29 % ($p = 0.034$), MMG activity decreased by 35 % ($p = 0.031$), while no difference was observed in $\dot{V}O_2$ ($p = 0.091$) in the FULL_SUP trial compared to NO_SUP. Partitioning the no-suppression and suppression phases of the INT_SUP trial, acute voluntary suppression significantly decreased $\dot{V}O_2$ ($p = 0.001$), EMG ($p < 0.001$) and MMG ($p = 0.012$) activity, compared to the no suppression phases. Shivering activity was restored in the no-suppression phases, equivalent to that in the NO_SUP trial ($p > 0.3$). No difference was observed in thermal metrics between conditions up to 60 min ($p > 0.4$). ***Conclusions:*** Humans can both constantly and periodically suppress shivering activity, leading to a delay in shivering onset and a reduction in shivering intensity. Following suppression, regular shivering is resumed.

KEY WORDS

Cold, Shivering, Suppression, Voluntary, Autonomic

INTRODUCTION

The physiological response to the cold is categorized by a distinct set of thermoeffectors, including behavioral adjustments, vasoconstriction, and both shivering and non-shivering thermogenesis. While behavioral thermoregulation is primarily governed by conscious control, vasoconstriction and shivering thermogenesis are often considered as autonomic processes, free from conscious inputs (24). For example, whereas the afferent spinothalamocortical neurological pathway provides perceptual feedback in relation to a cold stimulus, removal of this pathway in rats returns little effect on the overall sympathetic thermogenic response to a given drop in body temperature (21, 23). However, while the investigation of the thermoregulatory mechanisms in small mammals provides a good indicator of those which can be expected in humans, the direct translation of such data should be undertaken with caution. To date, limited evidence has quantified the extent to which humans can directly suppress and alter shivering activity through voluntary control during progressive whole-body cooling, and importantly the resultant impact on body temperature. Interestingly, case-study evidence documents the unique ability of some individuals to develop control over key components of the autonomic nervous system, including activation of the primary control centers for descending pain/cold stimuli modulation in the periaqueductal gray (PAG), possibly initiating a stress-induced analgesic response, enabling both improved psychological and physiological tolerance to adverse environmental stress (19).

Several investigations document modulated shivering activity by a range of thermal and non-thermal mechanisms, highlighting a potentially wider network of feedback inputs to autonomic thermogenic activity than previously assumed. In humans for example, both altered shivering onset and shivering activity are reported under hypoxic or hypercapnic conditions and following nitrate supplementation (1, 3, 14). In animals, attenuated shivering activity is

observed with concomitant peripheral nerve stimulation (5, 16), while noxious stimuli appear to exacerbate shivering activity (26). Focusing of feedforward mechanisms, early case studies note that shivering activity may be consciously ceased with voluntary restraint, while this may be difficult, if not impossible, during intense shivering, and that momentary exacerbations in shivering activity often follow voluntary restraint in the muscles concerned (6). Later investigations demonstrate that shivering thermogenesis can coexist alongside voluntary muscular activation (i.e. exercise), and that both shivering onset and shivering intensity can be altered with voluntary muscular activation and/or changes in posture (9, 12, 20). It has been suggested that the modulation of shivering activity by voluntary muscular activation is of 'central' origin, and not due to competition at a muscular level, given that voluntary activation of a specific muscle may independently alter the shivering activity of a muscle elsewhere in the body (12).

In a comparison of different methods for the voluntary suppression of shivering, Israel et al (13) assessed four techniques; relaxation, warm water ingestion, mental arithmetic and breath holding. They observed conscious relaxation to be significantly more effective in reducing electromyographic activity, a metric for shivering activity, compared to the other techniques. Given that mental arithmetic was also effective in suppressing shivering, the potential for a central cognitive input to shivering control seems plausible. Note, all four experimental variables were consecutively tested in the same session, for 30 s to 1 min each, thus the extent to which shivering can be suppressed over time remains unclear, and the potential for carry-over between conditions is unknown. As such, a number of questions remain with regards to voluntary inputs to shivering control; for instance, whether shivering can be consciously suppressed over longer periods; the impact of shivering suppression on the estimation of shivering onset; whether shivering suppression is initiated through a corresponding increase

muscular tone (also thermogenic) or via muscular relaxation; and importantly, the resultant impact of shivering suppression on body temperature. Elucidation of such questions helps to inform methodological considerations in designing and interpreting future thermoregulatory investigations, for example the extent to which the manipulation of conscious control may contribute to residual variability in both shivering onset and intensity, beyond that of measure error (2). Secondly, the efficacy of the conscious suppression as an operational countermeasure to overcome the deleterious effects of shivering, on for example, fine motor control, weighted against the thermal impact of shivering suppression. Thus, this investigation firstly aimed to quantify the capacity to consciously suppress shivering thermogenesis, both intermittently and continuously, in response to progressive whole-body cold stress. Secondly, to quantify the impact of shivering suppression on body temperature and heat exchange. It was hypothesized that: *1)* participants would be able to constantly suppress shivering activity, leading to a temporal delay in shivering onset as well as reduced shivering intensity, 2) with intermittent suppression, shivering activity is exacerbated when conscious suppression is released, and 3) core cooling rate is increased with continuous shivering suppression, but not intermittent shivering suppression.

METHODS

Ethical approval was granted by the Ethics Committee at Loughborough University (approval number, R19-P237). Research was conducted in accordance with the Declaration of Helsinki, 2013, expect for registration into a database. All participants provided written informed consent prior to participation.

Participants

Eleven healthy volunteers, nine male and three females (age, 21 ± 2 yrs; stature, 1.79 ± 0.06 m; body mass, 76.9 ± 10.0 kg; BMI, 24 ± 2 kg·m^2; body fat, 18 ± 6 %) were recruited from the Loughborough area, UK between January and March 2020. All participants were non-smoking, physically active individuals, over 18 years of age. Exclusion criteria included any individuals currently exhibiting, or with a history of muscular, neurological, or cardiovascular debilities. Females were not taking oral contraceptives and underwent experimental sessions between days 1-6 of their respective menstrual cycle, wherein levels of sex hormones remain low. This control was deemed necessary, as previous research has shown female hormones to alter the mechanisms underlying cutaneous vasoconstriction, thus the net physiological response to cold exposure (25).

Study Design

The study utilized a repeated measures randomized design, in which participants were exposed to a standardized whole-body cooling stimulus, set across four independent sessions; a familiarization session, followed by three experimental sessions: ***NO_SUP***, in which participants were instructed to allow their body to freely and autonomically regulate against the cold, with no conscious suppression or voluntary input; ***FULL_SUP***, in which participants were instructed to constantly suppress perceptible shivering activity for the duration of the trial. Specifically, individuals were informed, that when they perceived any increase in muscular tone ('tense muscles') or shivering activity, they should consciously relax these muscles to the best of their ability (13). Participant were encouraged to ask questions to aid understanding; ***INT_SUP***, in which participants were instructed to intermittently suppress shivering for 5 min phases, as per the full suppression trial, interspersed with 5 min phases of no suppression, as per the no suppression trial. The leading phase of the intermittent suppression trial was counterbalanced across participants. For each condition, participants were reminded every 5

147 min of the respective session aim and protocol. Visits were scheduled a minimum of 24 hrs
148 apart to minimize any carryover effects between experimental sessions or adaptation in
149 response to the cold (2). Sessions were undertaken at the same time each day for each
150 individual, to exclude the extraneous impact of the circadian rhythms upon thermoregulation,
151 as previously reported (15).
152
153 ***Procedure***
154 During the first laboratory visit, participants were briefed with regards to the session aims,
155 followed by a familiarization session involving the same cooling stimulus as experimental
156 trials. Additionally, in this session participants were also asked to perform several brief
157 maximal isometric contractions prior to cooling, to facilitate normalization of EMG data for
158 future comparison between studies. Maximum voluntary contractions (MVC) of the pectoralis
159 major, deltoid, trapezius and rectus femoris and vastus lateralis (EMG sensor placement
160 detailed in 'Measurements') were determined as the best of three separate contractions on a
161 static resistance cable rig. Following isometric exercises, participants were exposed to the
162 cooling stimulus, where they rested supine in an air-conditioned room wearing shorts and socks
163 (also sports bra for women), and passively cooled with cold air circulation (air temperature,
164 10.8 ± 0.3 °C; relative humidity, 58 ± 3 %; air velocity, 0.14 ± 0.03 $m \cdot s^{-1}$). Cooling of the
165 underside of the body by the bed was provided by a water perfused mattress, circulating water
166 clamped at 25 °C (PlastiPad®, Gentherm, OH, USA). The mattress temperature was selected
167 to provide comparable cooling rates of the skin by the ambient air and bed, established during
168 pilot work with a thermal imaging camera. Participants were progressively cooled for a
169 minimum of 60 mins, after which they remained cooling until 10 mins after they were deemed
170 to be continuously whole-body shivering via visual assessment. At this point the test ended,
171 participants were removed from the cold and actively re-warmed on a cycling ergometer in

thermoneutral conditions. A hot shower was also offered. At the point of leaving the laboratory, participants were reminded to refrain from alcohol and any non-routine vigorous activity 24 hrs preceding each subsequent trial. Furthermore, they were instructed to hydrate ad-libitum, avoid caffeine 6 hrs prior to each trial and eat only a light meal no later than 60 min prior to each trial, where possible replicating this meal as best as possible across subsequent visits.

On experimental days, participants were first provided with a rectal thermistor (400-AC Temperature Probe, Viamed Ltd., UK), and instructed to self-administered 100 mm beyond the anal sphincter (8). A urine sample was also obtained to confirm hydration status; urine specific gravity (USG) less than 1.020 (22). Body mass and stature were assessed, after which the participant rested seated in a thermoneutral prep-room for a standardized 20 min period, allowing skin temperature to normalize and relevant measurement probes and equipment to be appended (see below). Once ready, the participant was transported through to the temperature controlled experimental room and instruction was provided to adopt a supine position on the bed, remaining as still and relaxed as possible. The participant was immediately covered with blankets, shielding the body from the cold for the first 20 mins, allowing baseline data to be collected. At 20 mins, blankets were removed, the mattress under the participant was perfused with water, and the cooling phase began. Every 5 mins participants were reminded of the of the suppression protocol for the respective condition.

Measurements

All metrics were continuously assessed from baseline, through until completion of the whole-body cooling phase, while monitoring of rectal temperature also continued throughout the recovery phase for safety reasons. Shivering thermogenesis was assessed as per Arnold et al. (1) using three metrics: Breath-by-breath pulmonary oxygen uptake ($\dot{V}O_2$) via metabolic cart

(Quark CPET, Cosmed, ITL), with a two-point calibration (ambient air and a 16.00% O_2 / 5.02% CO_2 gas mix) prior to each trial. Electromyography (EMG) via wireless surface electrodes (DataLITE Wireless, Biometrics Ltd, UK, probe mass, 17 g), sampled at 1000 Hz with a gain of 1000, the signal rectified, and filtered to remove spectral components at 50 Hz and related harmonics. Finally, mechanomyography (MMG) via custom-built tri-axial accelerometer (NXP Semiconductors, NL; range, ± 7G; sensitivity, 200mV/G; size, 30 mm x 20 mm x 10 mm; mass, 13 g), with movement across X, Y and Z axes, sampled at 1000 Hz, and collated using a root sum of squares in DasyLab™. Both EMG and MMG sensors were placed on the right-hand side of the body, over the center of the muscle belly, with an MMG sensor located at the right pectoralis major, and EMG sensors located at the pectoralis major, deltoid, trapezius, vastus lateralis and rectus femoris. Mean EMG was established, taking an equal weighting from all sites. Diligence was paid in relation to the reproducibility of sensor placement and the preparation of the skin in accordance with SENIAM recommendations (11). The associated merits, limitations, and reliability of each shivering metric is detailed in Arnold et al. (2).

Mean skin temperature was assessed via surface thermistors (Grant Instruments, UK), equally weighted at 14 sites as per ISO 9886 (8), while deep-body temperature was assessed via rectal thermistor. Heat transfer from the skin to the ambient air was assessed via heat flux sensors (Model-FR-025-T-6, Concept Engineering, USA), positioned on the righthand aspect of the mid abdomen and the pectoralis major. Both skin thermistors and heat flux sensors were appended to the skin surface with Hypafix® tape to minimize thermal insulation (BSN medical, UK). The rectal thermistor, skin thermistors and heat flux sensors all fed into a data logger (SQ2020, Grant, UK), sampling every 1 s. Finally, mean arterial pressure and heart rate were

sampled every 5 min from the left arm via automated sphygmomanometer (Tango M2, SunTech Medical, USA).

Data Analysis

Data across all variables was subsampled into 1 min time block averages. Baseline values were determined as a mean of the final 2 mins of each respective 20 min baseline phase. Inflections points were first established in $\dot{V}O_2$, EMG and MMG data, denoting onset of continuous shivering thermogenesis. For each condition, shivering onset was categorized as the mean of six observations; the time elapsed at the inflection point in $\dot{V}O2$, EMG and MMG data, each quantified by both segmental linear regression and visual inspection of graphs, as detailed in Arnold et al. (1). Comparisons of shivering onset time between the NO_SUP trial and the FULL_SUP trial was assessed via paired samples T-test (Hypothesis 1). Shivering onset in the INT_SUP trial was not considered due to the sinusoidal nature of the intermittent suppression trial obscuring the quantification of the inflection point both mathematically and visually.

Assessing the impact of constant voluntary suppression on shivering intensity (Hypothesis 1), mean $\dot{V}O_2$, EMG and MMG activity was compared between NO_SUP and FULL_SUP, determined from data between the participant-specific shivering onset time observed in the NO_SUP trial, and the end of the standardized 60 min cooling phase. For two participants, the analysis window was extended to 70 min, given the protracted onset of shivering in these individuals. Comparisons between NO_SUP trial and FULL_SUP were assessed via paired samples T-test for each metric. Mean assessment of post-shivering data, along with the corresponding T-test, was selected as a preferential mode of analysis due to the highly individualized nature of this time-course data; however, a two-way repeated-measures ANOVA (condition*time) was also undertaken on 5 min time-bins for each shivering metric, thus

checking for, and acknowledging that any difference in NO_SUP and FULL_SUP could conceivably be time sensitive.

Assessing for any compensatory shivering activity or increased voluntary suppression during the acute suppression/no-suppression periods of the INT-SUP trial (Hypothesis 2), mean $\dot{V}O_2$, EMG and MMG across the no-suppression phases and suppression phases (5 mins each) of the INT_SUP trial were compared with the corresponding temporal phases of the NO_SUP and the FULL_SUP trial. Specifically, compensatory shivering activity during the no-suppression phases of the INT_SUP trial was compared with the NO_SUP trial via paired samples T-test, while increased voluntary suppression during the suppression phases of the INT_SUP trial was compared with the FULL_SUP trial. Again, data following shivering onset through until 60 mins (70 mins for two individuals) was assessed in this analysis. As with hypothesis 1, an additional two-way repeated-measures ANOVA (condition*time) was undertaken on this data to assess for time-sensitive effects.

Addressing hypothesis 3, skin temperature, rectal temperature and heat flux were considered as delta (Δ) changes, determined from the final minute of the cooling phase, against the final 2 min of the baseline period. Thermal metrics were compared across conditions via one-way repeated measures ANOVA (3 levels, 'NO_SUP', 'FULL_SUP' and 'INT_SUP'). Data are presented as mean ± SD. Statistical significance was established at $p = 0.05$.

RESULTS

Pre-Experimental and Baseline Measurements

No differences were observed in environmental conditions or hydration status between experimental visits (air temperature, $p = 0.8$; relative humidity, $p = 0.9$; air velocity, $p = 0.9$;

USG, p = 0.5). Furthermore, no differences were observed in baseline values between visits for each of the shivering metrics or thermal metrics ($\dot{V}O_2$, p = 0.7; EMG, p = 0.9; MMG, p = 0.3; mean skin temperature, p = 0.7; rectal temperature, p = 0.5; heat flux, p = 0.9).

Shivering Activity

Hypothesis 1 - A significant 29 % increase was observed in shivering onset time in the FULL_SUP trial compared to the NO_SUP trial (NO_SUP, 2301 ± 894 s vs. FULL_SUP, 2961 ± 703 s; p = 0.032; *Fig. 1*). Assessing shivering intensity between trials, EMG activity was decreased by 29 % (NO_SUP, 9.88 ± 4.21 µV [2.6 ± 1.2 % MVC] vs. FULL_SUP, 6.99 ± 2.20 µV [1.6 ± 0.5 MVC]; p = 0.034; *Fig 2*), and MMG activity was decreased by 35 % in the FULL_SUP trial compared to the NO_SUP trial (NO_SUP, 1.00 ± 0.52 $m \cdot s^2$; FULL_SUP, 0.65 ± 0.23 $m \cdot s^2$; p = 0.031). In contrast to EMG and MMG, no difference was observed in $\dot{V}O_2$ activity between the NO_SUP and FULL_SUP trial (NO_SUP, 6.1 ± 1.4 $ml \cdot kg^{-1} \cdot min^{-1}$; FULL_SUP, 5.3 ± 0.7 $ml \cdot kg^{-1} \cdot min^{-1}$; p = 0.091). No interaction was observed between experimental condition (NO_SUP and FULL_SUP) and time for either $\dot{V}O_2$ (p = 0.3), EMG (p = 0.4) and MMG (p = 0.4), assessed via two-way repeated-measures ANOVA.

Hypothesis 2 - Partitioning the discrete phases of the INT_SUP trial, acute voluntary suppression significantly decreased $\dot{V}O_2$ (p = 0.001), EMG (p < 0.001) and MMG (p = 0.012) activity, compared to the no suppression phases. Further assessing for any compensatory shivering activity during the no-suppression phases of the INT_SUP trial, and comparing them with the temporal equivalent phases of NO_SUP trial (*Fig 3*), no difference was observed in $\dot{V}O_2$ (NO_SUP, 5.9 ± 1.5 $ml \cdot kg^{-1} \cdot min^{-1}$ vs. INT_SUP, 6.4 ± 1.2 $ml \cdot kg^{-1} \cdot min^{-1}$; p = 0.2), EMG (NO_SUP, 8.01 ± 3.66 µV [2.0 ± 0.9 % MVC] vs. INT_SUP, 10.07 ± 2.73 µV [2.9 ± 0.6 % MVC]; p = 0.2) or MMG activity (NO_SUP, 0.89 ± 0.56 $m \cdot s^2$ vs. INT_SUP, 1.03 ± 0.39 $m \cdot s^2$;

296 p = 0.3). In addition, no increase was observed in conscious suppression during the suppression
297 phases of the INT_SUP trial, when compared with the temporal equivalent phases of the
298 FULL_SUP trial, observed as no difference in $\dot{V}O_2$ (INT_SUP, 5.6 ± 0.7 $ml \cdot kg^{-1} \cdot min^{-1}$ vs.
299 FULL_SUP, 5.3 ± 0.7 $ml \cdot kg^{-1} \cdot min^{-1}$; p = 0.2), EMG (INT_SUP, 5.91 ± 1.57 μV [1.4 ± 0.3 %
300 MVC] vs. FULL_SUP, 6.69 ± 2.09 μV [2.5 ± 0.5 % MVC]; p = 0.084) or MMG activity
301 (INT_SUP, 0.67 ± 0.11 $m \cdot s^2$ vs. FULL_SUP, 0.65 ± 0.31 $m \cdot s^2$; p = 0.8). Again, two-way
302 repeated-measures ANOVA yielded no interaction between condition and time for each of these
303 assessments (p > 0.05).
304
305 ***Thermal and Cardiovascular Metrics***
306 *Hypothesis 3* - Following 60 mins of whole-body cooling, no significant difference was
307 observed between conditions in the delta change in rectal temperature (NO_SUP, 0.20 ± 0.27
308 ºC; FULL_SUP, 0.29 ± 0.24 ºC; INT_SUP, 0.22 ± 0.13 ºC; p = 0.5), mean skin temperature
309 (NO_SUP, 6.23 ± 0.77 ºC; FULL_SUP, 6.21 ± 1.43 ºC; INT_SUP, 6.34 ± 0.76 ºC; p = 0.9) or
310 heat flux (NO_SUP, 0.028 ± 0.003 $W \cdot m^2 \cdot mV^{-1}$; FULL_SUP, 0.021 ± 0.001 $W \cdot m^2 \cdot mV^{-1}$;
311 INT_SUP, 0.015 ± 0.009 $W \cdot m^2 \cdot mV^{-1}$; p = 0.4). Furthermore, no differences were observed
312 between conditions in mean arterial pressure (NO_SUP, 92 ± 7 mmHg; FULL_SUP, 93 ± 8
313 mmHg; INT_SUP, 92 ± 7 mmHg; p = 0.9) or heart rate (NO_SUP, 60 ± 6 bpm; FULL_SUP,
314 59 ± 7 bpm; INT_SUP, 61 ± 6 bpm; p = 0.5) across the 60 min cooling phase.
315
316 **DISCUSSION**
317 This investigation examined the extent to which shivering thermogenesis is modulated by
318 voluntary suppression, and the corresponding impact of shivering suppression on body
319 temperature. The principal findings of the study follow: *1)* onset of continuous whole-body
320 shivering can be temporally delayed with voluntary suppression, *2)* following onset, the

intensity of shivering activity is decreased with continuous voluntary suppression, *3)* shivering can be intermittently suppressed, after which shivering activity immediately resumes to an equivalent intensity observed when the body is left to freely regulate, and *4*) the body temperature response to whole-body cooling remains unchanged with voluntary suppression of shivering for a duration up to 60 min.

In agreement with Hypothesis 1 and previous work, the current investigation provides evidence that autonomic shivering activity can be voluntarily suppressed during whole-body cooling (6, 13). It is also evident that suppression of shivering is possible, not only acutely, but during sustained whole-body cooling, resulting in a 29% delay in shivering onset time. The feedforward suppression of shivering by conscious relaxation is expected to result from direct cortical inhibitory projections on shivering centers in hypothalamus and brainstem reticular formation, or on spinal cord circuits (17). The findings herein offer an important methodological consideration for future investigations seeking to quantify the impact of experimental variables on thermoeffector responses to the cold, specifically shivering thermogenesis. For example, investigations should first acknowledge, in part, the potential for conscious relaxation to introduce residual variability and influence observable data, thus the importance of briefing participants prior to testing. This may also be of interest to individuals both working and performing in cold environments and require a simple, yet effective countermeasure, where detrimental effects of shivering activity are observed on fine motor control in specific muscle groups (18). It is possible that the ability to resist and suppress shivering activity via conscious relaxation is trainable, however this has yet to experimentally determined, along with the impact of shivering suppression on thermal comfort and should be the focus of future research.

Observations suggest that participants were particularly able to continuously suppress shivering activity registered via EMG and MMG, while no difference was observed in $\dot{V}O_2$ when comparing the NO_SUP and FULL_SUP trial. This discrepancy could be explained by several possibilities. Firstly, it is conceivable that $\dot{V}O_2$ lacks the sensitivity to track subtle changes in shivering intensity, that were otherwise observable with EMG and MMG, or that the lack of effect observed in $\dot{V}O_2$ might result from insufficient statistical power. However, while no a-prior power calculation was undertaken due to the limited data available in this area, previous work conducted in ten individuals of a similar demographic, highlights $\dot{V}O_2$ to be both a reliable and valid metric for shivering activity during acute cold exposure (2). Alternatively, it is possible that humans can consciously suppress shivering activity in the proximal muscles (detectable by EMG, MMG and $\dot{V}O_2$), but to a lesser extent in deeper muscles groups (only detectable by $\dot{V}O_2$). Indeed, from an evolutionary standpoint, it could be speculated that the ability to voluntarily suppress mechanical tremors in peripheral muscles would increase survival odds, given that intense shivering compromises locomotion (10). In this situation, thermogenic activity from deeper muscle groups, which are known to contribute to thermogenesis (4, 7), might be sustained and possibly even upregulated to defend body temperature, reflecting no significant change in $\dot{V}O_2$ or thermal metrics.

Participants were able to periodically suppress shivering activity during the INT_SUP trial, highlighting the ability of humans to acutely modulate autonomic activity when needed. Following periods of intermittent shivering suppression (INT_SUP trial), shivering activity immediately restored to an equivalent intensity observed when the body is left to freely/autonomically regulate (NO_SUP trial). While Deny-Brown and colleagues (6) make reference to compensatory outbursts of shivering activity following voluntary muscular movement, or periods of deep breathing, this compensatory effect was not observed the current

investigation, thus opposing Hypothesis 2. Note, such compensatory outbursts observed by Deny-Brown and colleagues (6) are report in the context of seconds, thus may not pose physiological relevance in the timeframes assessed in the current study, which were five-minutes in duration.

While shivering activity appears to be modulated by varying durations of voluntary suppression, no impact was observed on either deep-body temperature, mean skin temperature or skin-air heat flux, thus disagreeing with Hypothesis 3. As such, with 60 min whole body cooling, a combination of vasoconstriction, non-shivering thermogenesis, and possibly thermogenic shivering activity from the deep muscle groups appear to compensate for the any alteration of observed shivering activity on body temperature. The impact of shivering suppression on deep body temperature for periods greater than 60 mins, and/or the capacity and impact of shivering suppression during severe cold stress remains unclear, with limited evidence suggesting that shivering suppression may result in hypothermia if sustained for long enough (17).

Conclusion

While shivering thermogenesis is considered as an autonomic thermoeffector, humans possess a clear capacity to voluntarily modulate shivering activity via several mediums. Asking participants to suppress shivering via conscious relaxation, the current investigation showed a significant delay in shivering onset time, and a reduction in mean shivering activity in response to whole-body cooling, detectable by electromyography and mechanomyography but not whole-body oxygen uptake. Participants showed a clear ability to suppress shivering intermittently, after which shivering activity was quickly restored to normal levels when suppression was withdrawn. Shivering suppression does not compromise body temperature in

the context of 60 min whole-body cooling, thus it is conceivable that thermogenic activity is sustained in the deeper body tissues, while shivering activity is suppressed in the peripheral muscles.

AUTHOR CONTRIBUTION

JA, JL and AL were involved in the conception and design of the research. JA and JL conducted the experiment. JA, JL and AL analyzed the data. JA wrote the manuscript with amendments and suggestions made by JL and AL.

CONFLICTS OF INTEREST AND SOURCES OF FUNDING

The authors declare they have no conflicts of interests and the study did not receive funding from external sources to Loughborough University.

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FIGURE/TABLE CAPTIONS

Fig. 1: Onset of continuous shivering thermogenesis with voluntary suppression of shivering in response to passive whole-body cooling (n = 11). ***NO_SUP***, no voluntary shivering suppression, where participants were instructed to allow their body to freely regulate against the cold. ***FULL_SUP***, full voluntary shivering suppression, where participants were instructed to constantly suppress perceptible shivering activity via conscious relaxation. Data are mean ± SD, with individual data points. Each data point was categorized as the mean of six observations; the time elapsed at the inflection point in whole-body oxygen uptake, electromyography and mechanomyography data, each quantified by both segmental linear regression and visual inspection of graphs.

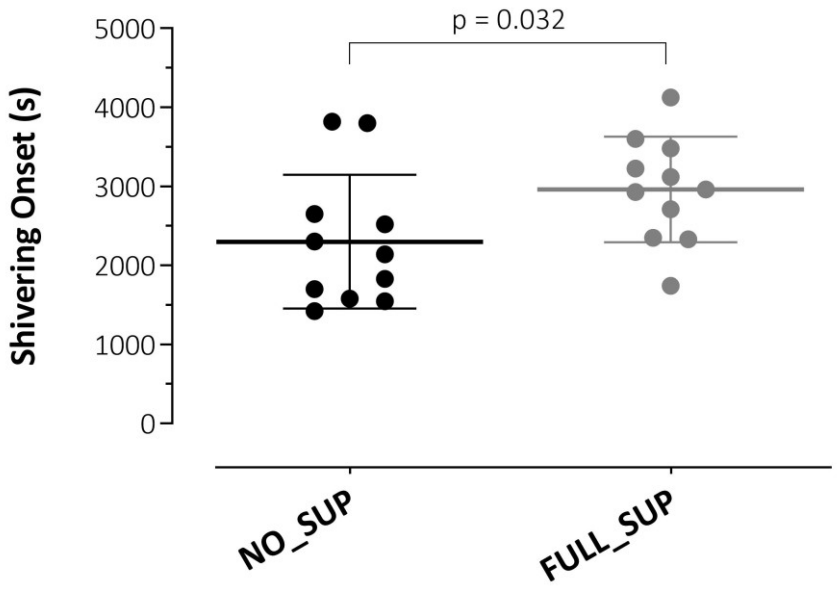
Fig. 2: Metrics of shivering thermogenesis in response to passive whole-body cooling with/without voluntary suppression (n = 11). $\dot{V}O_2$, whole-body oxygen uptake. ***EMG***, electromyography. ***MMG***, mechanomyography. ***NO_SUP***, no voluntary shivering suppression, where participants were instructed to allow their body to freely regulate against the cold. ***FULL_SUP***, full voluntary shivering suppression, where participants were instructed to constantly suppress perceptible shivering activity via conscious relaxation. Mean activity was determined from data between the participant-specific shivering onset time observed in the NO_SUPP trial, and the end of the standardized 60 min cooling phase. Data are mean ± SD, with individual data points.

Fig. 3: Shivering activity during intermittent voluntary suppression of shivering compared to a control (n = 11). $\dot{V}O_2$, whole-body oxygen uptake. ***EMG***, electromyography. ***MMG***, mechanomyography. ***NO_SUP***, no voluntary shivering suppression, where participants were instructed to allow their body to freely regulate against the cold. ***INT_SUP***, intermittent

voluntary shivering suppression, where participants were instructed to suppress shivering for 5 min phases, interspersed with 5 min phases of no suppression/free-body regulation. ***FULL_SUP***, full voluntary shivering suppression, where participants were instructed to constantly suppress perceptible shivering activity via conscious relaxation. Data are mean ± SD, with individual data points. Mean $\dot{V}O_2$, EMG and MMG across the no-suppression phases [***LEFT***] and suppression phases [***RIGHT***] (5 mins each) of the INT_SUP trial were compared with the corresponding temporal equivalent phases of the NO_SUP and FULL_SUP trial. Data following the participant-specific shivering onset time observed in the NO_SUP trial, through until 60 mins (70 mins for two individuals) was assessed in this analysis.

518 **FIGURES/TABLES**

519 Fig 1.



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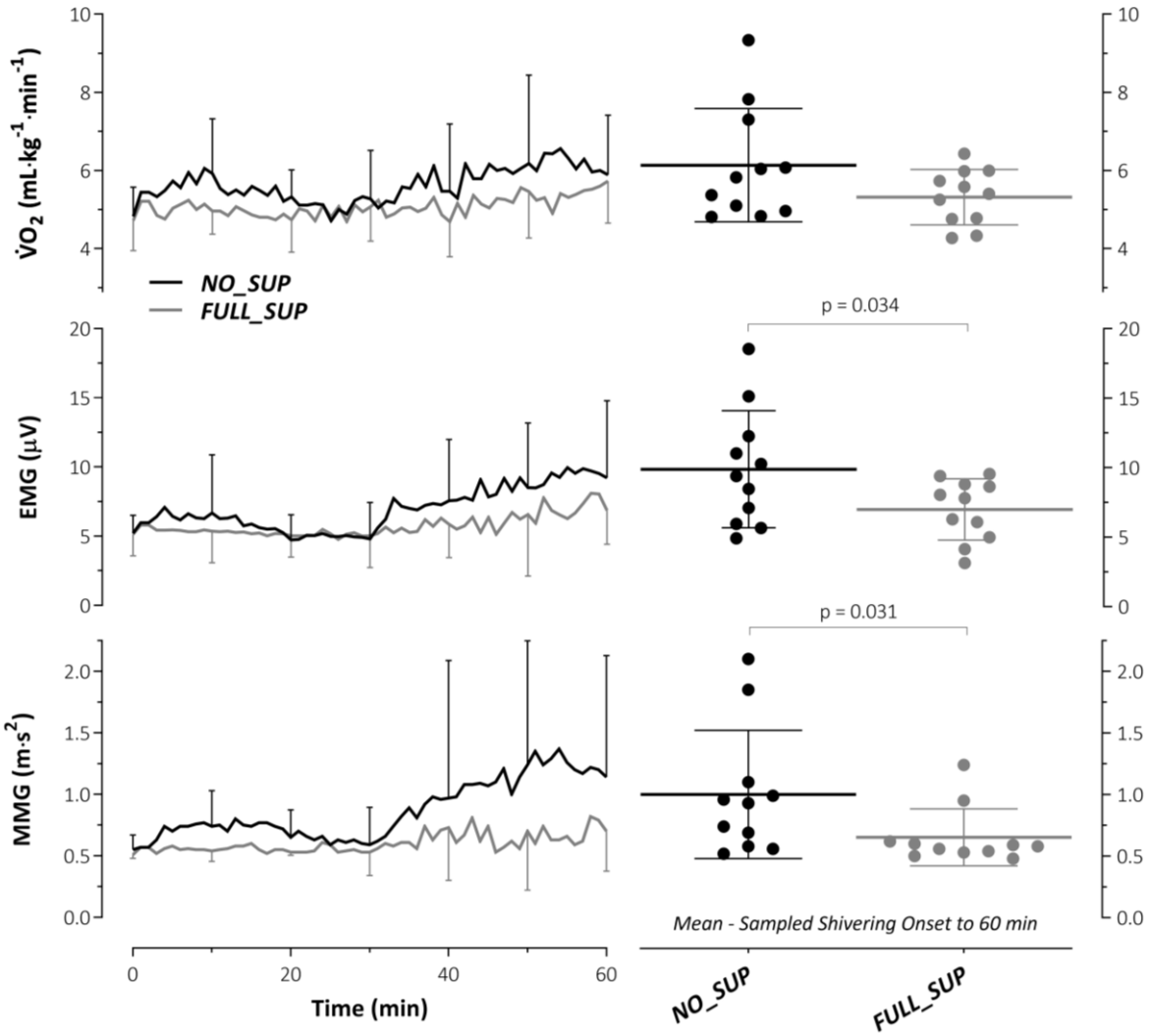
521 Fig 2.



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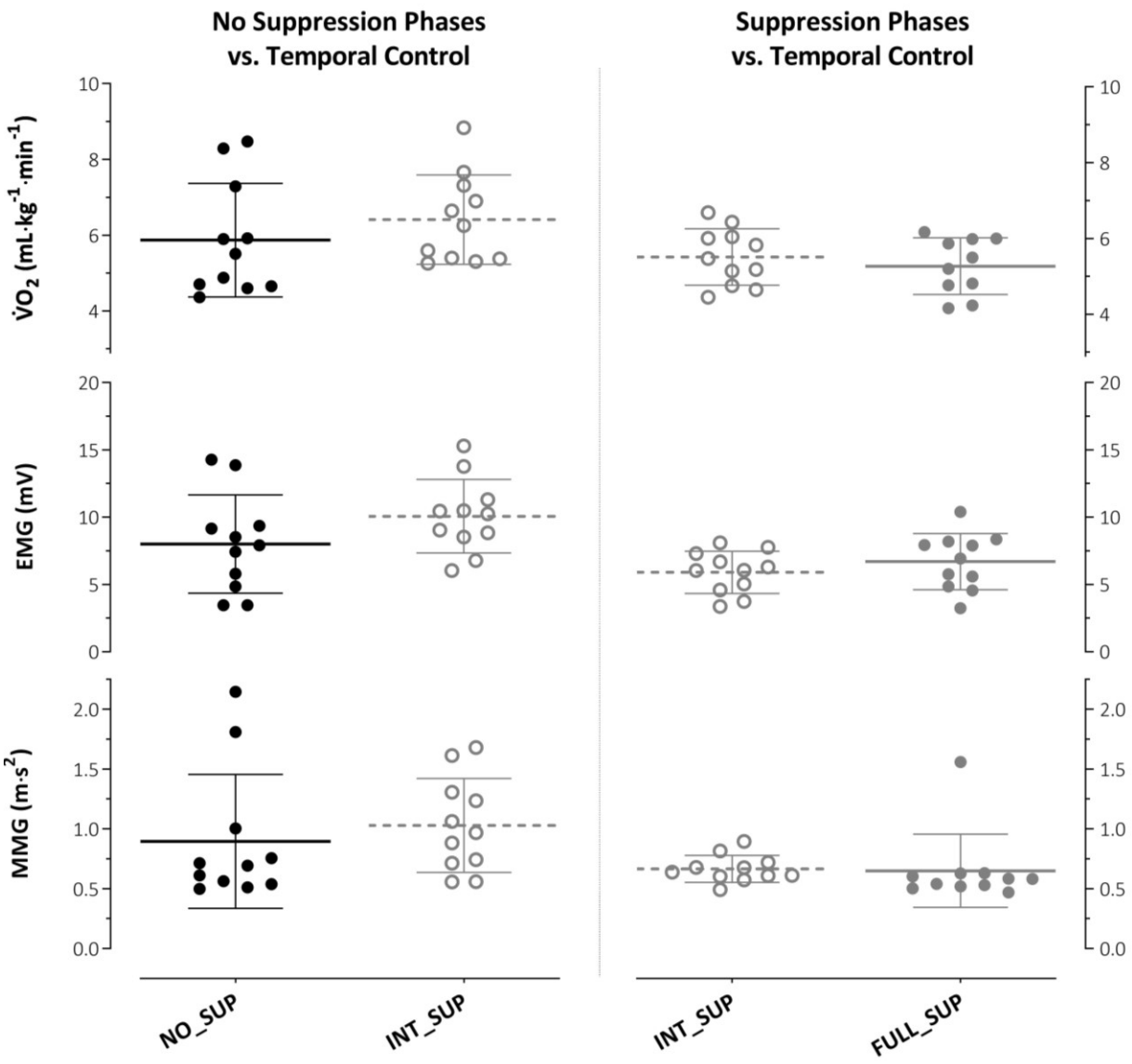
524 Fig 3.



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