Cold water ingestion improves exercise tolerance of heat-sensitive people with MS

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Abstract

Purpose: Heat intolerance commonly affects the exercise capacity of people with multiple sclerosis (MS) during bouts of hot weather. Cold-water ingestion is a simple cooling strategy but its efficacy for prolonging exercise capacity with MS remains undetermined. We sought to identify whether cold-water ingestion blunts exercise-induced rises in body temperature and improves exercise tolerance in heat-sensitive individuals with MS.
Methods: On two separate occasions, 20 participants (10 relapsing-remitting MS (EDSS: 1-5); 10 age- and fitness-matched healthy controls (CON)) cycled at 40% VO_2max at 30°C, 30%RH until volitional exhaustion (or a maximum of 60 min). Every 15 minutes, participants ingested 3.2 $mL \cdot kg^{-1}$ of either 1.5°C (CLD) or 37°C (NEU) water. Rectal (T_{re}) temperature, mean skin (T_{sk}) temperature, and heart rate (HR) were measured throughout.
Results: All 10 CON, but only 3 of 10 MS participants completed 60 minutes of exercise in NEU trial. The remaining 7 MS participants all cycled longer (P=0.006) in CLD (46.4±14.2 min) compared to NEU (32.7±11.5 min), despite similar elevations in absolute T_{re} (NEU: 37.32±0.34˚C; CLD: 37.28±0.26˚C; P=0.44), change in T_{re} (NEU: 0.38±0.21˚C; CLD: 0.34±0.24˚C), absolute T_{sk} (NEU: 34.48±0.47˚C; CLD: 34.44±0.54˚C; P=0.82) and HR (NEU: 114±20 $b{\bullet}pm^{-1}$; CLD: 113±18 $b{\bullet}pm^{-1}$; P=0.38) for the same exercise volume.
Conclusions: Cold-water ingestion enhanced exercise tolerance of MS participants in the heat by ~30% despite no differences in core and mean skin temperatures or heart rate. These findings support the use of a simple cooling strategy for mitigating heat intolerance with MS, and lend insight into the potential role of cold-afferent thermoreceptors that reside in the abdomen and oral cavity in the modulation of exercise tolerance with MS in the heat.

Keywords: Uhthoff’s phenomenon, fatigue, physical activity, heat sensitivities.

Introduction

It is well documented that during physical activity and/or exposure to hot environments individuals with multiple sclerosis (MS) can experience heat intolerance (1), which is typically characterized by a rapid onset of fatigue (2). Despite its prevalence, the underlying mechanisms responsible for this phenomenon (Uhthoff's) remain somewhat inconclusive. Nevertheless, since the work by Davis (3) and Rasminsky (4) it has been generally considered that a rise in core temperature of ~0.5˚C induces heat-related fatigue secondary to slowed or blocked conduction of demyelinated nerves. As such, people with MS are regularly advised to remain indoors during hot weather, and limit physical activity, which can substantially impact employability and/or quality of life (5).

Some cooling strategies administered before and/or during heat exposure successfully mitigate the development of heat-related fatigue in people with MS (6). However, these methods, such as 30 minutes of lower body cold water immersion (7) or donning an ice vest (8) can prove impractical in the context of everyday life and incompatible with many jobs. Cold fluid ingestion during physical activity is a simple strategy that is presently recommended by, among others, the National MS Society (9) the MS Society (UK) (10) and MS Queensland (Australia). Indeed, drinking cold water could effectively mitigate elevations in core temperature and associated fatigue as it introduces an internal heat loss avenue (via conduction) in addition to evaporative and convective heat loss from the skin surface. Nevertheless, to the best of our knowledge, no study has yet assessed whether cold fluid ingestion during exercise in the heat can mitigate rises in core temperature and accompanying fatigue in people with MS.

The aim of this study was to examine the effect of ingesting cold (1.5˚C) compared to thermoneutral (37˚C) water on exercise time to exhaustion at a fixed low relative intensity (~40%VO_{2max}), and the elevation in core temperature of heat-sensitive relapsing-remitting MS participants in a warm (30°C) environment. It was hypothesized that with thermoneutral water ingestion, exercise time to exhaustion would be shorter for MS compared to age- and fitness-matched control participants. It was also hypothesized that compared to thermoneutral water ingestion exercise time to exhaustion in MS participants would be extended with cold water ingestion due to a blunted rise in core temperature.

Methods

Participants

Twenty participants, 10 individuals with relapsing-remitting MS, an expanded disability status scale (EDSS) range of 2-4.5 (1 = No disability, slight dysfunction in one area, 4.5 = significant disability with some limitation of daily activities (11)) and 10 age, height and weight-matched healthy controls (Table 1) were recruited for this study based on a power calculation (Heinrich-Heine-Universität Düsseldorf, Germany) employing an α of 0.05, a 1-β of 0.95 and an effect size of 1.55 for the main outcome variable of exercise performance with cold fluid ingestion in the heat (12). All MS participants had a self-reported intolerance to the heat. All participants were informed of any risks associated with the study before providing written informed consent. The study was approved by the University of Sydney Human Research Ethics Committee (HREC No: 2016/214).

Measurements

Rectal (T_{re}) temperature was measured using a general-purpose pediatric thermistor (TM400, Covidien, Mansfield, MA, USA) self-inserted to a depth of 12 cm past the anal sphincter. Skin temperature was measured at four sites on the right side using thermistors (Concept Engineering, Old Saybrook, CT, USA) attached with hypoallergenic tape (Blenderm, 3M, Sydney, NSW, Australia). Mean skin temperature (T_{sk}) was estimated using a weighted average in accordance to Ramanathan (13). All thermometric measurements were sampled at 5 seconds intervals (NI cDAQ-91722 module, National Instruments, Austin, TX, USA) and displayed in real-time using LabView (v7.0).

Heart rate (HR) was measured using a wireless 6-lead ECG (Quark T12x Asia Pacific PTY, Sydney, NSW, Australia) monitoring system. Electromagnetic gel was applied to 4 foam electrodes, which were then placed under the right and left clavicle, the right and left 6th intercostal and then covered with tape. Prior to the placement of the electrodes, the skin surface was shaved and cleaned with alcohol to ensure minimal signal interference.

Protocol

Each participant completed one preliminary trial and two experimental trials. During the preliminary trial, participants performed an incremental submaximal exercise protocol (beginning at 45 W increasing 20 W every three minutes for a total of four stages) on a semi-recumbent cycle ergometer (Corival Recumbent, Lode BV, Groningen, Netherlands) in a 20˚C room. Heart rate and oxygen consumption (Quark CPET, Cosmed, Asia Pacific PTY, Sydney, NSW, Australia) were measured during each 3-min stage. A least square regression equation was employed using sub-maximal heart rate and oxygen consumption at the end of each stage and extrapolated to the maximum age-predicated heart rate (220-age) (14) to determine VO_{2max} using the YMCA protocol (15). Individualized workloads (40% of predicted VO_{2max}) were calculated for the subsequent experimental trials.

Participants completed two experimental trials separated by a minimum of 48 h in a climate-controlled chamber at 30˚C and 30% relative humidity until i) volitional exhaustion, or ii) a maximum of 60 minutes. Participants were required to complete both trials at the same time of day to avoid any disparity in resting core temperature due to circadian rhythm. If any participant presented with a resting T_{re} more than 0.2˚C away from the other trials, then the trial would not commence. Participants cycled on a semi-recumbent cycle ergometer at a fixed relative intensity (~40%VO_{2max}) and consumed a 3.2

ml·kg^{-1} aliquot of water (in <1 minute) after the 15th, 30th and 45th minute of exercise. Participants consumed either thermoneutral (37˚C) water (NEU) or cold (1.5˚C) water (CLD) during each experimental trial. The presentation of trials was balanced between participants. The temperature of the water ingested in the NEU trial was maintained using a hydrostatic controlled water bath (DA05A, Polyscience, Niles, IL, USA). The temperature of the water ingested in the CLD trial was maintained in a thermos filled with ice. Immediately prior to fluid ingestion, the temperature of the fluid was verified using a factory-calibrated glass precision thermometer (Durac Plus, Blue Spirit, Cole-Parmer, Vernon Hills, IL, USA) with a certified range between –1°C and +100°C and with an accuracy of ±0.1°C, and the required mass of water was measured using a balance with a precision of 0.1 g (MS12001L, Mettler Toledo, Columbus, OH, USA). Breath by breath oxygen consumption was continuously monitored to ensure participants were performing at the same relative intensity throughout both trials.

Statistical Analysis

A two-way mixed ANOVA employing the repeated factor of water temperature (CLD, NEU) and the non-repeated factor of group (MS, Control) was used to examine exercise time to exhaustion. The T_{re}, T_{sk} and HR at the time of exhaustion in the shortest trial for each individual were also compared to the same time point in the other trial within the MS and CON groups using paired sample t-tests. A within-group analysis was employed for measures of T_{re} and T_{sk} due to the different exercise time between the con and MS groups. Furthermore, within the CLD trial T_{re} and T_{sk} at the time of exhaustion in the NEU was compared to the end-exercise values of the CLD within the MS group using a paired sample t-test. Finally, an unpaired t-test was used to examine HR between control and MS participants at 30 minutes of exercise for both the NEU and CLD trials..All statistical analyses were performed using GraphPad Prism (v6.0, LA Jolla, CA, USA).

Results

Exercise time to exhaustion was shorter in the MS group compared to the CON group ($P=0.002$), however an interaction was observed between water temperature and group ($P<0.001$). Specifically, all 10 control participants completed 60 minutes of exercise in both the NEU and CLD trials (Figure 1). On the other hand, while only 3 of 10 participants in the MS group completed 60 minutes of exercise in the NEU and CLD trial, all 7 MS participants who could not complete the NEU trial cycled longer (Figure 1) in the CLD trial (NEU: 32.7±11.5 min; CLD: 46.4±14.2 min; $P=0.006$). After 30 minutes of exercise, HR responses in the NEU trial (MS: 104±15 b•pm^{-1}; CON: 96±10 b•pm^{-1}; $P=0.22$) and the CLD trial (MS: 103±17 b•pm^{-1}; CON: 92±12 b•pm^{-1}; $P=0.17$) were not different, despite being moderately higher for the MS group throughout exercise.

In the MS group, at the time of exhaustion in the NEU trial, T_{re} ($P=0.44$; Figure 2A), T_{sk} ($P=0.82$; Figure 2C) , change in T_{re} ($P=0.66$; Figure 2E) and HR (NEU: 114±19 b•pm^{-1}; CLD: 113±17 b•pm^{-1}; $P=0.45$) were not different after the same amount of exercise time elapsed in the CLD trial. All 7 MS participants who cycled for longer in the CLD trial did so despite T_{re} ($P=0.001$) and T_{sk} ($P=0.03$) rising to higher values above baseline when they did stop exercise (ΔT_{re}: 0.26±0.12°C vs. 0.40±0.23°C; ΔT_{sk}: 1.27±0.72°C vs. 1.47±0.79°C).

In the CON group, end-exercise (i.e. after 60 min in all CON participants) T_{re} ($P=0.25$; Figure 2B), T_{sk} ($P=0.33$; Figure 2D) , change in T_{re} ($P=0.7$; Figure 2F) and HR (NEU: 99±11 bpm; CLD: 99±13; $P=0.33$) were not different between the NEU and CLD trial. Due to equipment problems, HR values are only displayed for 8 control participants.

Discussion

This study is the first to report the efficacy of cold-water ingestion for improving exercise tolerance in the heat in people with MS. Importantly, all MS participants that could not complete 60-min of exercise with the ingestion of thermoneutral water (NEU trial) due to volitional exhaustion, cycled for longer with ingestion of cold water (CLD trial). However this longer exercise time to exhaustion in the CLD trial in the MS group was observed despite no influence of a lower ingested water temperature on core and skin temperatures as well as heart rate.

It is well documented that even small increases in body temperature are associated with a transient worsening of symptoms for individuals with MS (3, 4), otherwise known as Uhthoff's phenomenon (16). The development of fatigue, manifested by sensations of tiredness, is a common characteristic associated with Uhthoff's phenomenon and explains the shorter exercise time for 7 of the 10 MS who could not complete 60 minutes of exercise compared to CON group in the NEU trial as both participant groups were matched for age and aerobic fitness. In addition, the relative exercise intensity was moderately low (~40%VO_{2max}) and should have been easily sustainable for 60 minutes, as evidenced by all 10 CON participants completing the exercise bout in both trials.

Within the MS group, the longer exercise to time to exhaustion in the CLD trial occurred despite a similar T_{re}, T_{sk}, and HR at a comparable time point (i.e. same volume of exercise) than the time to exhaustion in the NEU trial for each individual. In other words, exercise tolerance in the heat was improved in the MS group with cold-water ingestion despite no independent influence of ingested water temperature on the development of thermal and cardiovascular strain with exercise time. Indeed, from the time point at which exercise exhaustion was reached in the NEU trial, T_{re} and T_{sk} in the CLD trial continued to rise to higher values by the time exercise stopped. It has been previously suggested that the underlying mechanism responsible for heat-related reduction in exercise performance in healthy athletes is potentially similar to heat sensitivity with MS, but with fatigue onset occurring alongside much smaller rises in body temperature with MS (17). It follows that heat-related decrements in the aerobic performance of healthy athletes can potentially be attenuated via the stimulation of cold-afferent receptors located in the oral cavity (12) and on the skin surface (18), without necessarily lowering core temperature. The present findings potentially support the notion that research examining the mitigation of heat-related decrements in exercise performance in healthy athletes may, at least to an extent, be translatable to the management of Uhthoff's phenomenon in the MS population.

Irrespective of participant group, for the same volume of exercise, any alteration in core and skin temperature due to theingested fluid temperature were minimal (Fig. 2A, C and E), despite the greater internal heat loss via conduction with cold fluid ingestion. A recent series of studies (19-21) described fluid temperature-dependent alterations in sweating during exercise that are modulated, independently of core and skin temperatures, by visceral thermoreceptors located in the abdomen. Ultimately, the reduction in evaporative heat loss from the skin surface with cold fluid ingestion was found to counterbalance the greater internal heat loss, thereby yielding similar changes in whole body heat storage and thus similar changes in core temperature, irrespective of ingested fluid temperature (19). Although sweating rates are not reported in the present study, a similar fluid temperature-dependent modulation of skin surface evaporation could explain the similar levels of thermal strain between the NEU and CLD trials within both the MS and CON group. Another consideration is that the absolute amount of heat transfer generated by each 3.2 ml·kg^{-1} aliquot of 1.5°C water, even without any parallel alterations of skin surface evaporation, would only be ~35 kJ, which for a 82.5 kg individual with a mean body specific heat of 3.49 kJ·kg^{-1}·°C^{-1} would yield a reduction in mean body temperature of only ~0.1°C.

Despite the profound impact of regular exercise on the physical and psychological health of individuals with MS (22), it has been reported that people with MS are less physically active (23), partly to avoid a temporary worsening of symptoms associated with an elevation in body temperature. Moreover, heat intolerance has been shown to greatly impact the capacity for many people with MS to remain among the workforce (5). Cold water ingestion is a simple strategy for improving exercise tolerance in the heat, which could be used as an alternative to other less practical but currently recommended cooling strategies such as partial immersion in cold water prior to heat exposure (7), or donning an ice vest (24). It should be noted that for individuals with MS susceptible to urinary incontinence, additional fluid ingestion might not prove an optimal solution. Therefore, future research must establish whether independently stimulating cold-afferent thermoreceptors in the oral cavity, via a cold mouth rinse, would be sufficient to mitigate heat-related decrements in exercise tolerance with MS, as reported with complete cold-water ingestion in the present study.

Limitations

The present study does not include subjective measures such as whole body thermal sensation (WBTS) or rate of perceived exertion (RPE). If a lower WBTS and RPE were observed for the same exercise load for the MS participants, this may have explained the improved exercise tolerance. Furthermore, there was no measure taken to assess the onset of symptoms, if any, for the MS participants. Therefore, we are unsure whether cold fluid ingestion mitigated the onset of heat related symptoms, or temporarily dampened sensations of heat intolerance. Future research should investigate whether prolonged exercise time effects heat related symptoms, or whether ingesting cold water is sufficient to mitigate the onset of symptoms during exercise in a hot environment. As some participants reported a mild discomfort with the cold fluid ingestion future research should assess similar outcome variables to this current research, however with slightly warmer fluid temperatures.

The exercise time to exhaustion protocol was selected to assess the capacity of an easily fatigued, non-athletic population. However, due to the large variability that is typically demonstrated in time to exhaustion studies, future research should look at investigating aerobic performance for MS individuals using a more reliable protocol such as a time trial (25) Using heart rate to predict VO_{2max} for MS individuals has not yet been validated for this population. Given that heart rate responses to exercise were quite variable for the MS group, there is a possibility that VO_{2max} results were either under or overestimated. Despite this, the relative workload was consistent within each participant, and therefore the main outcome of this study is not affected.

Conclusion

In conclusion, the present study examined the influence of ingesting cold compared to thermoneutral water on exercise time to exhaustion at a fixed low relative intensity (~40%VO_{2max}), and the concurrent elevation in core and skin temperature of heat-sensitive relapsing-remitting MS participants in a warm (30°C) environment. With thermoneutral water ingestion, exercise time to exhaustion was shorter in the MS group compared to age-matched controls, presumably due to the development of fatigue associated with Uhthoff's phenomenon. Cold-water ingestion resulted in a ~30% longer exercise time to exhaustion in the MS participants that could not complete 60 minutes of exercise in the thermoneutral water ingestion trial. However while cold-water ingestion appeared to improve the exercise tolerance of the MS group in the heat, it did not blunt the rise in core and mean skin temperature with time. These findings provide a practical and simple cooling strategy for individuals with MS performing physical activity in hot environments, and lend insight into the potential role of cold-afferent thermoreceptors that reside in the abdomen and oral cavity in the modulation of exercise tolerance with MS in the heat.

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Conflicts of Interest

There are no conflicts of interest to declare.

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Figure Legends

Figure 1. Individual data and group means (with SD) at the end of exercise in NEU (yellow) trial compared to the same time point in the CLD (black) trial for multiple sclerosis (MS: squares) and healthy controls (CON: circles). Values given for: Exercise time to exhaustion with a maximum of 60 min. Asterisk (*) indicates $P \leq 0.05$.

Figure 2. Individual data and group means (with SD) at the end of exercise in NEU (yellow) trial compared to the same time point in the CLD (black) trial for multiple sclerosis (MS: squares) and healthy controls (CON: circles). Values given for: Rectal temperature (Panels A-B), mean skin temperature (Panel C-D) and heart rate (Panel E-F) Asterisk (*) indicates $P \leq 0.05$.

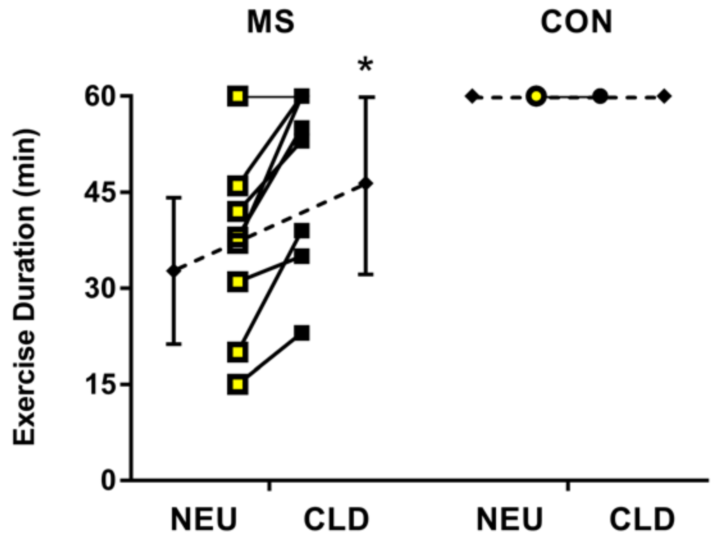
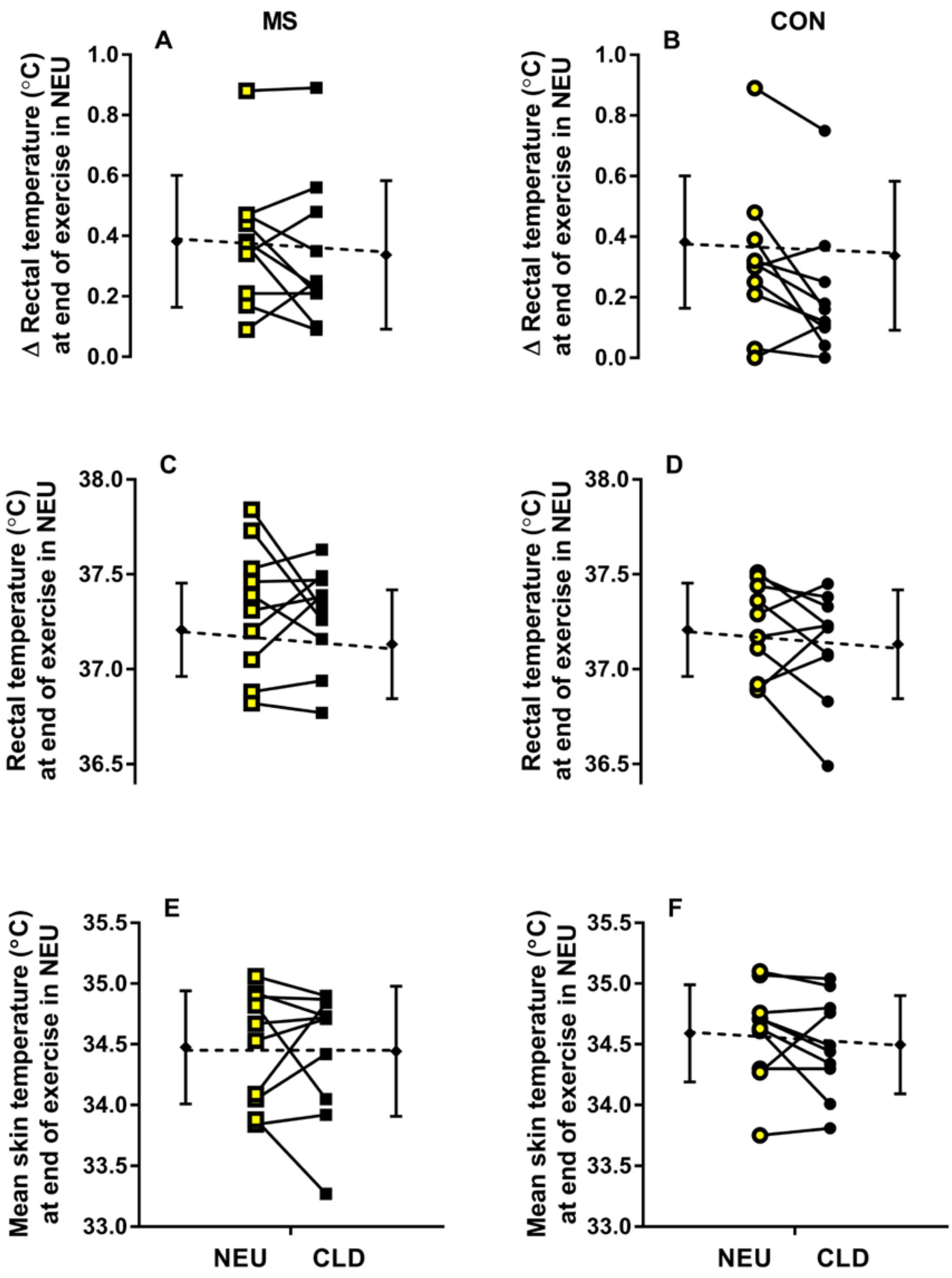


Figure 1.



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