CASE STUDY INVESTIGATING DAILY FLUCTUATIONS IN CORE AND REGIONAL SKIN TEMPERATURES IN A PERSON WITH TETRAPLEGIA

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Abstract

Introduction: Spinal cord injury (SCI) directly affects to a person's ability to regulate core temperature, increasing their risk for hypo- and hyperthermia. Cognitive performance is also affected when exposed to low ambient temperatures. Although anecdotal reports of hypo- and hyperthermia exist, there are significant gaps in understanding how frequently core temperature fluctuations daily, and how varied ambient temperatures and exercise affect core temperature. An abbreviated literature review was conducted to partially address these gaps.
Objective: To determine the presence of circadian rhythm and the effects of environmental temperature and exercise on the regulation of core temperature in a person with cervical SCI.
Methods: An individual with cervical-level SCI had their core temperature continuously recorded over two seven-day periods during a warm (July) and a cold (November) season. Surface skin temperature and daily activity were also recorded in November. Daily minimum-maximum fluctuations were measured as well as periods of hypo- and hyperthermia.
Results: Daily core temperature fluctuated an average 2.36°C ± 1.4°C in November, and 1.89°C ± 0.8°C in July. The participant demonstrated 17 instances of sub-normal core temperature and 3 instances of hyperthermia in November. An additional 12 instances of sub-normal core temperature and 12 instances of hyperthermia were observed in July. These findings demonstrate the relatively high frequency and duration of sub-normal and hyperthermic core temperatures experienced by this person with cervical SCI, despite taking steps to maintain a comfortable core temperature.
Conclusion: These findings indicate temperature-related life quality of persons with cervical level SCI may be commonly and significantly impaired. This suggests the need to identify better means to monitor and pre-emptively regulate core temperatures in this population under different environmental conditions.

Introduction

An estimated 86,000 Canadians are currently living with the effects of a spinal cord injury (SCI), with an additional 3,675 new cases presenting each year.(1,2) This corresponds to fifty-two cases of SCI per million persons worldwide, with greater than 50% of those being classified as tetraplegia (spinal cord lesion above the first thoracic vertebra (T1)).(3) While this may represent a smaller subset of the general population in comparison to other chronic conditions, the associated impacts on the medical system are disproportionately high for each person with SCI. Economic costs can range from $1.5-3.0 million per person throughout their lifetime post-injury while incurring over eight times the direct healthcare costs when compared to able-bodied (AB) people.(1) A number of these hospital visits and associated costs may be attributed to people with SCI presenting with symptoms of either hyper- or hypothermia. It is well documented that SCI can significantly impair the body's ability to regulate core temperature (Tcore), increasing the risks for both hyper- and hypothermia post-injury.(4–7) These risks are most prevalent in individuals with SCI above T1.(8) Not only does this inability to regulate Tcore lead to emergency hospital visits, but it has also been demonstrated to impair cognitive function in these individuals, particularly when Tcore drops below normal levels.(4) However, there is very little data regarding the frequency or duration that a person with SCI spends with sub-normal Tcore.

Background

Neural Mechanisms of Temperature Regulation

In neurologically intact individuals, internal Tcore regulation is an important function that is tightly monitored and controlled by the hypothalamus through negative feedback loops

(Figure 1). This process has multiple components which include the afferent thermoreceptors, the control center, and the efferent neurons. The thermoreceptors detect temperature changes, then send a signal up through the brainstem to the hypothalamus. The hypothalamus interprets the message and provides descending response signals via the brainstem to sympathetic preganglionic neurons (SPGN) that are located in the spinal cord (T1 to L2). The SPGN relay signals to the muscles, organs, and glands that provide the necessary bodily responses that maintain an appropriate Tcore (Figure 2). These autonomic responses include sweating, shivering, vasodilation, vasoconstriction, and hormonal thermogenesis. These feedback mechanisms work collaboratively to maintain a relatively constant Tcore of 37°C ± 0.6°C.(9)

Temperature Regulation Post-SCI

The impacts of SCI on the regulation of body temperature are still not fully understood. One of the earliest studies conducted to investigate these challenges by Guttman et al in 1958 found that persons with SCI above T1 routinely experienced significant fluctuations in Tcore when exposed to various ambient temperatures.(10) Handrakis suggested that this is largely caused by limited sensory information from below the level of injury (LOI) reaching the hypothalamus for interpretation.(11) However, the descending signals to the SPGN, which are located in the thoracic spinal cord, may also be impaired depending on the level and extent of the person's injury.(1) This potential degradation in signal pathways would preclude sudomotor responses to temperature change such as sweating or shivering. Interruption of these processes causes Tcore in persons with SCI to fluctuate more drastically than AB people when subjected to various ambient temperatures.(4,9,10) For example, with complete injury at C8, no messages would descend to thoracic SPGN to activate the needed effectors and provide the bodily responses to maintain Tcore. Impaired reception of sensory information from skin regions below

LOI further delays the person from feeling hot or cold. This poses further challenges to the implementation of preventative measures to preserve a constant Tcore.(5)

Hypo- and Hyperthermia in People with SCI

There are an estimated 53,000 hypothermia-related deaths per year between Canada, the USA, and Great Britain.(12) Emergency room visits attributed to heat-related illness in the US were reported at a prevalence of 1.34 visits per 100,000 people between 2009 and 2010.(13) While there is limited information available in research literature about the numbers of hypo- and hyperthermia cases specifically in individuals with SCI, it is reasonable to assume that they would account for a potentially substantial proportion of reported cases given their increased risk factors. Refinement of first aid measures and preventative strategies to maintain a constant Tcore is vital to ensure that individuals with SCI receive better evidence-based care from medical professionals while enjoying an optimal quality of life. When examining first aid for an AB adult experiencing heat stroke, for example, current literature outlines full-body (from the neck down) immersion in cold water (1-26°C) as the most rapid method of reducing Tcore.(14) Depending on LOI, full-body immersion of SCI individuals may be challenging or even impossible. There has been limited research examining the efficacy of this or other cooling and heating methods in SCI individuals, particularly before they reach crisis stages of either hyper- or hypothermia. Improved understanding of these practices is vital for both persons with SCI as well as medical professionals to ensure that treatment methods are tailored to address instances of heat- and cold-related illnesses as effectively as possible. Therefore, this is an important consideration for the physician assistant practice given their involvement in patient treatment in both clinical and emergency settings.

Core Temperature and Sleep-Wake Cycles

Numerous regulatory processes within the body have been demonstrated to follow a circadian rhythm, which is a predictable pattern of variation based on the time of day or night. One of the most prominent cycles in humans mediated by a circadian rhythm is the sleep-wake cycle (SWC).(15) Initiation of sleep has been linked to the release of melatonin during the evening hours before sleep,(16) paced by the suprachiasmatic nuclei of the hypothalamus.(15) Melatonin has also been shown to play a role in the initiation of heat loss, suggesting that Tcore is also regulated by a circadian rhythm, one that is linked to SWC.(16) Studies have shown that humans typically initiate sleep when Tcore and skin temperatures are in sharp decline, while simultaneously melatonin levels are on the rise during evening hours before sleep.(17,18) While it is well documented that 15-40% of individuals with SCI experience some form of sleep disorder,(19) specific breakdown of cases based on neurological LOI is limited. It is believed that the neural pathway responsible for the secretion of melatonin passes through the cervical spine.(19) In other words, this pathway may involve communication with components of the sympathetic autonomic nervous system. Given this pathway will be disrupted to some degree in SCI individuals with an injury at or above T1, it is reasonable to assume that these individuals will account for a higher percentage of sleep disorder reporting amongst all persons with SCI. Physician Assistants and other medical professionals will benefit from a better understanding of how circadian rhythms are altered in persons with SCI to enable better treatment of sleep disorders that may result in this population.

Regulating Core Temperature During Exercise

Exercise is a key element in maintaining physical fitness and overall health for all individuals. As the intensity and duration of exercise increase, localized vasodilation and sweating are initiated to cool the body, avoiding a corresponding increase in Tcore.(20) These mechanisms can be severely impaired in individuals with SCI, depending on LOI. Those with a complete cervical injury cannot compensate for increased Tcore resulting from exercise, particularly in warm environments.(20,21) For those with SCI below T1, their ability to sweat will be absent below the level of lesion,(11) contributing to elevated Tcore during exercise which takes longer to return to baseline levels afterward.(11,19–21) While thermoregulatory responses to warm and cold temperatures post-SCI are reasonably well understood, there is limited research literature examining the particular effects of exercise under hot and cold conditions on the regulation of Tcore in SCI individuals. A better understanding of these responses has the potential to identify strategies for better temperature regulation in persons with SCI to maintain a relatively stable Tcore during exercise. This could be particularly beneficial for high-performance athletes with SCI who train year-round.

Objectives and Relevance to Current Research

Recent efforts to examine the potential circadian rhythm of temperature regulation, as well as the effects of exercise on thermoregulation post-SCI continue to identify gaps in understanding. Given the potential adverse effects of SCI on everyday life, it is promising to see that the limitations and challenges imposed by SCI continue to be studied to improve our understanding of them. This can contribute to the development of optimal treatment and

prevention strategies. Therefore, this study sought to examine Tcore variation in a SCI individual over seven-day periods in summer and fall time frames with the following aims:

- determine the potential presence of a circadian rhythm,
- examine changes in Tcore relative to ambient environmental temperature,
- examine the effects of exercise under hot and cold conditions on Tcore.

We hypothesize that:

- Tcore and skin temperatures will demonstrate circadian fluctuations, but the extent of those fluctuations will either be blunted in cool environmental conditions and/or exaggerated in a warm environment when compared to an AB individual,
- persons with tetraplegia will be unable to regulate either Tcore or skin temperature to the same extent as AB individuals in response to varying environmental conditions,
- that exercise in a hot environment will speed up Tcore increases in a person with tetraplegia; conversely, exercise under cold conditions will delay or prevent increases in Tcore.

Literature Review

Circadian Rhythm

To date, the body of literature examining the circadian rhythm of temperature regulation as it relates to sleep in individuals with SCI is extremely limited. At this point, only three published articles were available on the subject. The nocturnal release of melatonin, which contributes to normal sleep patterns, is controlled at the cervical level.(22) Thijssen et al hypothesized that this release could be altered or stopped in people with cervical SCI.(19) To test this hypothesis, Tcore values were measured over 24 hours across 23 participants: 8 tetraplegics,

7 paraplegics, and 8 AB controls. All SCI participants had complete lesions between C5 and T12 that had existed for at least 5 years.(19) Tcore data across all 3 groups was largely consistent throughout the day, but markedly different at night. AB controls saw a decrease in Tcore when going to sleep, followed by a plateau and then a trough. SCI participants showed no plateau, with Tcore continuing to rise slightly after the trough(19). This was more pronounced in tetraplegics compared to paraplegics.(19)

This study was limited as it did not examine changes in surface skin temperature and the potential correlation to Tcore circadian rhythm. Jones et al addressed this limitation in their 2014 study, while simultaneously examining salivary melatonin levels in people with SCI, comparing them to an AB control group.(16) Skin temperature in the lower half of the body was seen to decrease between 1900h and 2300h in both the control and paraplegic groups, but no such decrease was observed in tetraplegics. Conversely, tetraplegic participants saw an increase in lower body skin temperature over the same period.(16) The melatonin levels increased significantly in the control and paraplegic groups, while the tetraplegic group decreased slightly.(16)

It is important to note that both these studies examined Tcore changes in their participants in their own community-based settings.(16,19) While this provided a realistic set of parameters under which to study Tcore fluctuations, it did introduce external (largely behavioural) variables that could not be controlled. Baschieri sought to address this issue by using a controlled laboratory setting to measure the circadian rhythm and modulation of Tcore in SCI participants over 48 hours.(17) Both rectal Tcore and SWC were observed in 5 cervical SCI (cSCI) participants, 7 thoracic SCI (tSCI) participants, and 7 AB controls.(17) All participants remained in a temperature- and humidity-controlled room (24^{o}C, 40-50% humidity), in pyjamas and with

bed sheets, their activities video recorded to assess SWC. Participants were to remain lying in bed except during meals and toilet breaks.(17) Rectal Tcore was measured every 2 minutes, with Tcore and sleep times tabulated and averaged for each sleep stage.(17) Similar to Thijssen et al, tSCI participants showed a comparable pattern of Tcore values to AB controls, gradually increasing through the late afternoon before decreasing overnight.(17,19) The cSCI group started with lower Tcore values that increased more sharply through the afternoon while continuing to increase later in evening (until ~10 pm).(17) Further, overnight decrease in Tcore in cSCI participants was also markedly slower than in the other groups, and remained a full 1^{o}C higher overnight.(17)

When examining the body of research literature about the circadian rhythm of temperature regulation post-SCI, it is apparent that the most limiting factor to its application is its scope and depth. Regarding participants with SCI in particular, further studies are required to refine the link between circadian rhythms regulating Tcore and sleep. Given the prevalence of sleep disorders in SCI,(23) studies could be crafted to determine the efficacy of interventions intended to improve sleep, while examining the potential impacts of these interventions on Tcore during overnight hours. It was specifically noted by Baschieri that they did not require participants with SCI to discontinue any medications they had been taking; however, their methods did not specify what these medications or dosages were.(17) This information would be useful in the analysis of results as a means of explaining any anomalous data points. This practice should be considered for incorporation into any future study of circadian rhythms for either thermoregulation or SWC in persons with SCI. Also, participants remained lying in their beds with covers and pyjamas in a 24^{o}C room. It is possible that Tcore of those with cSCI

remained high due to an inability to activate heat loss mechanisms while sleeping in warm environmental conditions.

Thermoregulation Under Different Environmental Conditions

The body's ability to regulate Tcore is significantly impaired post-SCI, with the effects being most profound in tetraplegia (injury above T1).(8) Numerous studies have examined Tcore fluctuations in people with SCI in varying environmental conditions. Handrakis examined the effects of exposing SCI participants to cold and heat stress independently in separate studies between 2015 and 2017 respectively.(4,5) In addition to changes in Tcore, each study also examined cognitive function pre- and post-temperature stress, while comparing participant values to AB controls. (4,5)

In Handrakis' first study, seven SCI participants and seven AB controls were exposed to a Cool Challenge of 18°C for 120 minutes or less if Tcore dropped to or below 35°C.(4) Tcore decreased in all SCI participants by an average of 1.2°C after only 109 minutes of Cool Challenge. Controls showed no change after the full 120 minutes. Cognition levels were initially the same in both groups, but the SCI participants saw a decreased performance in Stroop Interference score post-Cool Challenge.(4) While it is reasonable to conclude that cognitive performance is directly linked to Tcore, Handrakis acknowledged that their study did not assess cognition once Tcore had returned to baseline (BL) levels.(4) This degree of study could further strengthen the linkage of Tcore and cognitive performance.

The effects of heat challenge (HC) on Tcore in people with SCI were examined by exposing 10 persons with tetraplegia and 9 AB control participants to HC (35°C) for 120 minutes to determine the resulting impacts on Tcore and cognitive performance.(5) The HC was

terminated if Tcore reached 38°C or if participants reported discomfort. The control group saw no significant change past-HC, while the SCI participants saw an increase in Tcore of 0.78±0.18°C over an average of 118 minutes.(5) Not all SCI participants completed the full 120 minutes of HC due to these increases in Tcore.(5) Interestingly, people with tetraplegia demonstrated improved cognition post-HC, but no significant change was observed in the control group.(5) The limited duration HC saw tetraplegic Tcore rise from sub-normal to levels close to hyperthermia, which reinforces the premise that this group has higher risk of hyperthermia compared to AB individuals. While cognitive functions improved at higher Tcore, it is possible that cognition is sub-optimal in those with tetraplegia at BL Tcore levels compared to AB controls.(5) Active measures to bring tetraplegic Tcore into the high-normothermia range may optimize cognitive performance.

Mneimneh built on previous research to develop a Bioheat model that would predict the responses of tetraplegics to various temperature stimuli and metabolic output.(8) The model was designed to take into consideration all changes in tetraplegic physiology and thermoregulatory functions. This new model was validated by predicting Tcore and mean skin temperature for participants previously included in various studies, comparing predicted results to those measured during each study. The greatest variance observed for Tcore, and mean skin temperature was 0.86°C and 0.9°C respectively.(8) While this model has proven effective as a starting point for predicting Tcore and skin temperature changes in tetraplegics, it could be further modified for application to paraplegics as well.(8)

Within research literature, Tcore is most commonly reported as an average across all participants with SCI, comparing them to an AB control group. Limited studies are focusing on changes to Tcore based on the specific degree and level of SCI. The American Spinal Injury

Association Impairment Scale (AIS) defines a Grade A SCI as a “complete impairment”, with no sensory or motor function remaining below the point of injury.(24) Grade B is classified as "incomplete impairment", with the sensory function being preserved below LOI and motor function being absent.(24) Future studies should be crafted to deliberately examine the effects of the degree of SCI on Tcore, skin temperature, and cognition. Finally, numerous studies examining thermoregulation in SCI were conducted across relatively small sample sizes (≤10). While there are many challenges in coordinating larger numbers of participants, every effort should be taken to include additional SCI participants in future studies. This will allow for greater flexibility and viability in statistical analyses while strengthening the validity of any trends identified in the results obtained.

Effects of Exercise on Thermoregulation

As identified by Sawka et al through their literature review in 1989, there was limited research examining the effects of exercise on Tcore in SCI participants specifically.(25) Previous studies conducted with individuals with SCI had examined Tcore, sweat responses, and subcutaneous blood flow after passive exposure to varying ambient temperatures. It was generally observed that while some sweating can occur over the insensate skin, it was not in sync with the sweat response observed over the sensate skin, providing early evidence of individuals with SCI being at a thermoregulatory disadvantage compared to AB controls.(25) One additional study by Gass et al examined Tcore changes among a group of SCI participants after a period of prolonged wheelchair exercise, with Tcore readings measured via rectal and esophageal probes simultaneously.(25,26) This study noted a higher increase in esophageal compared to rectal readings. Sawka’s interpretation of Gass’ data led to the conclusion that the disparity in observed

Tcore values was likely caused by lower metabolic output in the lower body region. This in turn would result in limited localized heating above basal levels during exercise.(25)

A recent study conducted by Price and Campbell targeted the effects of prolonged exercise and recovery on Tcore and skin temperature between AB, paraplegic, and tetraplegic individuals.(21) Tcore and skin temperatures were continually monitored during arm crank exercise at 60% VO_2 max over 60 minutes in cool ambient conditions (21.5°C, 47% humidity).(21) TCore in AB and paraplegic participants saw a relatively minor increase (0.6 ± 0.3°C), whereas the tetraplegic participant saw a steady increase in Tcore totalling 0.9°C.(21) During 30 minutes of passive recovery, AB participants saw a quicker decline in Tcore compared to paraplegic participants(21). Tcore in the tetraplegic group continued to rise during recovery, hitting its plateau with 5 minutes remaining.(21) This study's conclusions reaffirm previous findings that Tcore in tetraplegics is prone to substantially greater fluctuation during exercise as well as protracted recovery times to return to BL levels compared to AB controls and those with paraplegia.

Although those with tetraplegia show reduced temperature regulation during exercise, not every form of exercise causes rapid increases in Tcore in every environmental condition. For example, Grossman et al., sought to compare performance parameters and activity profiles during wheelchair basketball (WCB) games played under hot (HOT) and temperate (TMP) conditions.(27) A total of 8 people with varying degrees of SCI participated in the study, with two participants playing in both games (one under TMP (21.6°C, 30% humidity) conditions, one under HOT (30.3°C, 52% humidity) conditions.(27) LOI for each participant was noted to facilitate statistical analysis.(27) While there were no statistically significant differences between data for HOT and TMP games, it was suggested by Grossman that a low level of overall intensity

during the game was likely a contributing factor behind the lack of observed disparity.(27) It was postulated that there was insufficient metabolic heat production during either game to result in a meaningful difference in the data collected for each game.(27)

While the literature examining the effects of exercise on Tcore post-SCI continues to evolve, one area that warrants further research is the correlation between exercising in varying ambient temperatures on Tcore and skin temperature in people with SCI. Testing the effects of exercise on Tcore regulation under varying ambient temperatures in a clinically controlled setting will be crucial in improving understanding of these mechanisms post-SCI. Further studies could also examine the variance in responses observed based on LOI. Finally, it must once again be acknowledged that most studies examining the effects of exercise on thermoregulation post-SCI suffer from a limited sample size. Larger sample sizes will afford a much higher degree of fidelity to a study's findings while enabling statistical and trend analyses that may otherwise be impossible. This will be particularly impactful in studies targeting variation in thermoregulation based on LOI.

Methods

This study involved continuous recording of Tcore in an individual with cervical-level spinal cord injury (cSCI) (level of injury=C8, AIS grade=B) over two different seven-day periods (November and July). Regional skin temperature was also monitored during the seven days in November. The participant remained in their community-based setting for the duration of the study. Tcore was measured using an Ecelcius® system, which includes wireless sensor transmitter pills, receiver and data-logger, and proprietary software. Skin temperatures were also monitored by Etact® skin sensors attached to the skin over five different body regions (calf,

thigh, abdomen, chest, forearm). TCore and skin temperature were recorded every 30 seconds in conjunction with a timestamp for each sensor, while skin sensors also monitored the quantity of movement and acceleration through their incorporated accelerometers. Logged data was exported into Excel and time-aligned (based on each sensor's timestamp). Data from each sensor was then converted for analysis within the Spinal Cord Research Centre's in-house developed research software. Each time series was plotted for visualization and separated into 24-hour periods (e.g., Figure 3). The time-series temperature and accelerometer data were annotated based on the participant's log of activities during each seven-day period. Data were visually inspected to observe any obvious relationships between Tcore and skin temperature as well as to assess the effect(s) of different daily activities and environmental conditions. The participant maintained a daily journal logging entries related to physical activities, clothing level, exercise, sedentary status, ambient environmental temperature as well as outside temperature in the vicinity of their home when exercising or performing activities outdoors. Any specific actions or measures taken to affect their perception of temperature were also recorded, such as applying heat packs, taking a bath, or removing layers of clothing. The participant maintained a constant ambient temperature within the home (22.5°C in November, 23.5°C in July), recording any changes made to the temperature setting in the home. The participant also wore a Garmin vivoactive®3 fitness watch throughout the study. Exercise data, including ambient temperature, were downloaded for each seven-day period, and correlated with the appropriate timeframe for comparison to Tcore and skin temperature recordings. Data collected from Tcore and skin temperature was imported into Excel, time-aligned based on each sensor's time stamp, edited for conversion to text, and then converted to a format compatible for use in *Analysis*. These converted temperature files were synchronized concerning time and plotted in 24-hour epochs to

facilitate observation of daily variations in temperature. Timestamps and markers were reviewed and the temperature data was annotated with the time-stamped events recorded in the participant's journal. External ambient temperatures and clothing conditions were added to the dataset to assist in the identification of anomalous data points.

Maximum, minimum, and total temperature fluctuation (max-min) were calculated for each day and recorded for Tcore and each skin temperature sensor. Movement data from each skin temperature sensor was also plotted and synchronized by time with temperature readings. A qualitative analysis of the resulting temperature graphs was conducted to determine potential trends in temperature over the two seven-day periods, and to assess the effect(s) of the logged activities on Tcore and skin temperature based on the time of day.

Results

Overall, this participant demonstrated wide fluctuations in temperature during both seven-day observation periods. The light blue/grey boxes (Figures 3, 4 and 5) indicated periods during which this participant experienced sub-normal temperatures (< 36.5 °C),(11) accounting for 17 episodes (> 25 hours) of sub-normal temperatures during November and 12 episodes (> 29 hours) in July. This represents 15-17% of this time period. While awake, sub-normal temperatures were experienced for approximately 12 hours in July and 15 hours in November, with each episode ranging from 30 minutes to 6 hours in duration. These periods could be interrupted or influenced by altering the ambient conditions or initiating exercise or movement (Figures 3, 4, and 5).

Daily periods of hyperthermia were experienced, typically in response to exercise or external ambient conditions. Nine periods of hyperthermia occurred in July with only three

observed in November (Figure 3 and 4). Tcore was also noted to drop 0.5 to 1°C at the onset of sleep for each day in November and July (Figure 3 and 4). Tcore observed in July saw slightly elevated average values recorded before the onset of sleep, with the nightly decline commencing at an average of 36.7°C ±0.34°C (Figure 4), compared to 36.4°C ± 0.34°C in November (Figure 3).

Examining a typical day spent indoors at an ambient temperature of 22°C shows several temperature-related observations (Figure 6). First, when comparing Tcore and skin temperature at the onset of sleep, it becomes apparent that skin temperatures hit their overnight trough before Tcore begins its nightly decline. This was consistent for each of the six days in November in which Tcore and skin temperature were simultaneously monitored, indicating that there is an obvious trend for a circadian-based reduction in Tcore at the onset of sleep. It should be noted that reductions in Tcore were curtailed by the body's response to warmer ambient temperatures (caused by covering the body during sleep (Figure 6)), masking the circadian reductions.

Tcore in this individual has demonstrated significant instability in response to a variety of external and internal (i.e., exercise) conditions (Figure 5).

External conditions seemed to have relatively little effect on mitigating Tcore increases during exercise in cold ambient conditions, given the observed 1.56°C increase in Tcore despite significant reductions in regional skin temperature. However, the participant's logged entries indicate that exercise in this condition was considered 'exhilarating' and that they could have continued indefinitely. Conversely, the participant used repeated application of ice-cold water on cooling neck and wristbands to feel 'able' to continue exercising in the heat. Tcore in each of these situations was relatively similar, demonstrating that perception of heat is highly influenced

by ambient temperatures yet poorly indicative of the actual heat stress situation of the individual (Figure 7).

In examining the relative and absolute daily maximum and minimum Tcore values, it is apparent that the participant demonstrated significant daily fluctuations in Tcore. Daily maximum and minimum Tcore had a difference of 2°C or more on seven days between July and November, with a difference of 1.5°C over an additional 5 days. These fluctuations in Tcore are significantly higher than those typically observed in AB persons, with circadian fluctuations in Tcore averaging <0.5°C.(17) (Figure 8)

Discussion

This study measured Tcore and skin surface temperature in an individual with cervical SCI throughout two seven-day periods in fall and summer timeframes as they progressed through their daily routine at home, work, and activities in the community. Overall, Tcore readings demonstrated the presence of a circadian rhythm, while being susceptible to significant fluctuations in response to external environmental conditions. This person also experienced significant periods of sub-normal and above-normal temperatures.

In terms of a sleep-related circadian rhythm, the participant demonstrated a consistent daily reduction in Tcore upon initiating sleep, similar to what has been described under controlled conditions in an experimental setting in persons with SCI.(17) However, as noted during both observation periods, circadian reductions in Tcore occurred despite rising skin temperatures, brought on by increasing the local insulation around the skin with blankets and coverings. Thus, circadian reductions in Tcore were disrupted by the participant's inability to maintain temperature when sleeping with blankets. Accelerometer data and logged entries

marking when covers were removed or replaced show a strong correlation between removing blanket covers and corresponding reductions in Tcore and regional skin temperature, as well as immediate increases upon replacing covers. These findings are consistent with the single other community-based study comparing participants with tetraplegia to those with either paraplegia or neurologically intact controls. All groups demonstrated a circadian rhythm in Tcore, although SCI subjects saw a greater degree of fluctuation in Tcore during waking hours.(19) Mean nighttime Tcore in tetraplegics was also significantly higher compared to paraplegics and controls.(19)

The second key finding of relatively large periods during which this person experienced sub-normal temperatures is consistent with case series anecdotal reports by persons with tetraplegia of feeling cold during the fall and winter seasons.(11) Our observation that 15-17% of the participant's time was spent with sub-normal temperatures, and that these periods also occur during the summer (in air-conditioned conditions), suggest this represents a potential risk for impaired cognitive and functional performance. These episodes occurred despite the participant taking measures to try to maintain a comfortable condition, suggesting the need to better monitor and maintain Tcore in this population. Handrakis et al showed that those with tetraplegia had an average Tcore at BL (after 15 minutes of exposure to 27°C ambient conditions, although it is also indicated that participants rested in these conditions for 30 minutes first) of 36.9°C, then increased to 37.7°C during a 120-minute HC at 35°C.(5) At BL, Tcore was significantly different (36.9°C ± 0.3°C for tetraplegia and 37.3°C ± 0.3°C in AB controls), while cognitive performance measured through Stroop testing also differed significantly.(5) These results are similar to our participant in this study during the periods in July with exposure to outdoor hot temperatures as well as in response to bathing in November.

During HC, Tcore in those with SCI increased dramatically (0.78°C ± 0.18°C), whereas Tcore in AB controls remained unchanged (-0.02° ± 0.22°C).(5) Interestingly, each cognitive test showed significant increases in performance after HC for those with SCI but remained stable in the AB control group.(5) As such, the mean Tcore post-HC for those with tetraplegia increased from 36.9°C ± 0.3°C to 37.7°C ± 0.4°C, suggesting that even non-hypothermic, yet slightly sub-normal temperatures may contribute to impaired cognition in this population.(5) Given that BL measurements were taken at an ambient temperature of 27°C,(5) which is 3-5°C above typical room temperature, it is quite likely that the Tcore of these individuals under normal environmental conditions would be lower than the mean reported in this study. The implications relating to cognition raise the importance of noting that in our study, the participant spent at least 15% of each day with Tcore <36.5°C, despite making efforts to maintain a 'comfortable' environment. These efforts included going outside in the heat during summer, spending large portions of their time in a room with the temperature set >27°C, and sleeping with a heated blanket in both summer and winter. None of these temperature reductions warranted an emergency visit, but together, these observations suggest better means of maintaining Tcore are required so that this population can engage in more community-based activities without discomfort or possible reductions in function or cognitive performance. Given the extended time periods our participant experienced sub-normal temperature, it also suggests the need for more rigorous testing for temperature-related impairments in this population. This will help determine whether earlier reports of reduced cognitive performance after only a limited amount of time spent in cooler temperatures,(4) are widespread and common phenomena. It also indicates further testing for temperatures at which optimal cognition is thought to occur in this population, suggested to be when Tcore is slightly elevated above normal levels.(5)

Compared to responses in the general population, our results demonstrated extreme temperature responses in our participant with cervical SCI in response to external heat and cold stressors as well as the internal stressor of exercise. The data support the suggestion of several trends regarding temperature fluctuation as they pertain to the circadian rhythm in people with cervical SCI. During both November and July periods, average daily temperature fluctuations of 2.36°C in November and 1.89°C in July occurred. These fluctuations were brought on by either external ambient conditions or in response to the internal heat stressor, exercise.

When examining Tcore fluctuation during the July period specifically, it was observed that Tcore continued to rise after ceasing exercise and returning to a cool environment (Figure 4 and 6). Given that the participant's Tcore was already elevated due to a higher ambient temperature, the continued rise in Tcore poses an additional risk for hyperthermia and related heat stress injuries. This makes it imperative for people with cervical SCI to closely monitor Tcore during exercise to avoid excessive increases that could lead to hyperthermia. When coupled with environmental temperature readings, an optimal temperature range can be proposed for people with cervical SCI to exercise outside, including an upper threshold limit above which exercise outside should be avoided. However, it should be noted that the rise in Tcore was much less when exercising at similar (or higher) temperatures after sunset in this participant (Figure 4 HC on July 23 at 23 ^{o}C in the day compared to HC on July 25 at 28.9 ^{o}C after sunset with a relatively limited rise in Tcore). Together, these findings suggest further research is required to determine the conditions under which exercise should optimally be performed in this population to minimize risk of heat stress injuries.

Limitations and Further Research

It is acknowledged that this study is limited in scope, particularly regarding its number of participants. While the single-participant nature of the study facilitated a rapid design and conduct, the lack of additional participants limited the potential for further statistical analysis (e.g.: differences in Tcore fluctuation based on LOI). Repetition of this study with a larger number of participants along with the incorporation of a control group would be warranted to validate these case study findings. Cervical SCI participants could be compared against a control group comprised of either AB or thoracic-level SCI individuals. Additional studies should record skin temperature readings under both hot and cold environmental conditions, as this study measured skin temperature during a cold environment only. Future studies should also use an additional sensor, located on the chair wheel axis, to record nearby ambient temperature and wheeling movements to document ambient and activity conditions. This will alleviate the need for the participant to log this information.

With an increase in the number of participants, it will also be necessary to implement a degree of control over participants' methods of cooling and warming themselves. A standardized set of methods and tools for self-temperature regulation should be established, and where required, tools provided to participants. They should also be strongly discouraged from using any warming or cooling methods beyond those provided while continuing to log the use of those that are provided. Additional studies could also focus on the time required for Tcore to stabilize to an established BL after the removal of an external stimulus, building on previous research to better appreciate the ability of SCI individuals to thermoregulate under varying environmental conditions.

While this study showed that there remains a correlation between Tcore and skin temperature post-SCI, additional research is necessary to target the effects of heating or cooling various skin regions on Tcore. While it is common to apply ice packs to the neck, back, armpits, and groin of a hyperthermic AB individual to facilitate Tcore reduction(14), similar parameters could be studied to determine the impacts on Tcore for individuals with SCI. It should be noted that during 2 exercise episodes in this study (July 22 and 23, 2021), the participant employed the use of cooling cloths on themselves and despite these measures, Tcore continued to increase during exercise. Thus, further studies are needed to identify better strategies and timing of when such cooling or heating methods should be applied before or during exercise to allow for a greater duration of peak performance.

Conclusion

In relation to our three hypotheses, we demonstrated that:

- Tcore and skin temperature demonstrated circadian fluctuations, and the extent of these fluctuations were blunted in a warm environment,
- our participant with tetraplegia was unable to regulate either Tcore or skin temperature in response to varying environmental conditions,
- exercise in a hot environment sped up Tcore increase; conversely, exercise in cooler conditions delayed or reduced increases in Tcore.

These extreme fluctuations in daily temperature and the relative inability to maintain a stable Tcore under different environmental conditions suggest the need for better strategies to maintain Tcore in an optimal range for persons with SCI as well as practical guidelines to assist such persons to achieve this goal. Further research is required to develop tools for people with

SCI to help monitor and control body temperature under varying conditions such as exercise or prolonged exposure to heat or cold.

Understanding that Tcore tends to fluctuate more frequently and substantially in those with SCI compared to AB persons, additional research examining the extent of this volatility will help to develop appropriate guidelines for healthcare providers. This will ensure they are equipped to provide optimal treatment and advice for the SCI population.

As demonstrated by Handrakis et al in 2015, individuals with tetraplegia exhibit impaired cognitive performance after exposure to cold temperatures for even a moderate amount of time.(4) When coupled with their increased sensitivity to changes in Tcore and associated risk for hypo- and hyperthermia, individuals with SCI may seek to avoid situations that could entail prolonged exposure to the outside environment. By continuing to improve our understanding of thermoregulation post-SCI, individuals living with these injuries will be better enabled to prepare for and cope with prolonged exposure to diverse environmental conditions. This can help to reduce the number of incidents of accidental hypo- or hyperthermia, reducing the potential drain on the medical system while improving overall quality of life in this population.

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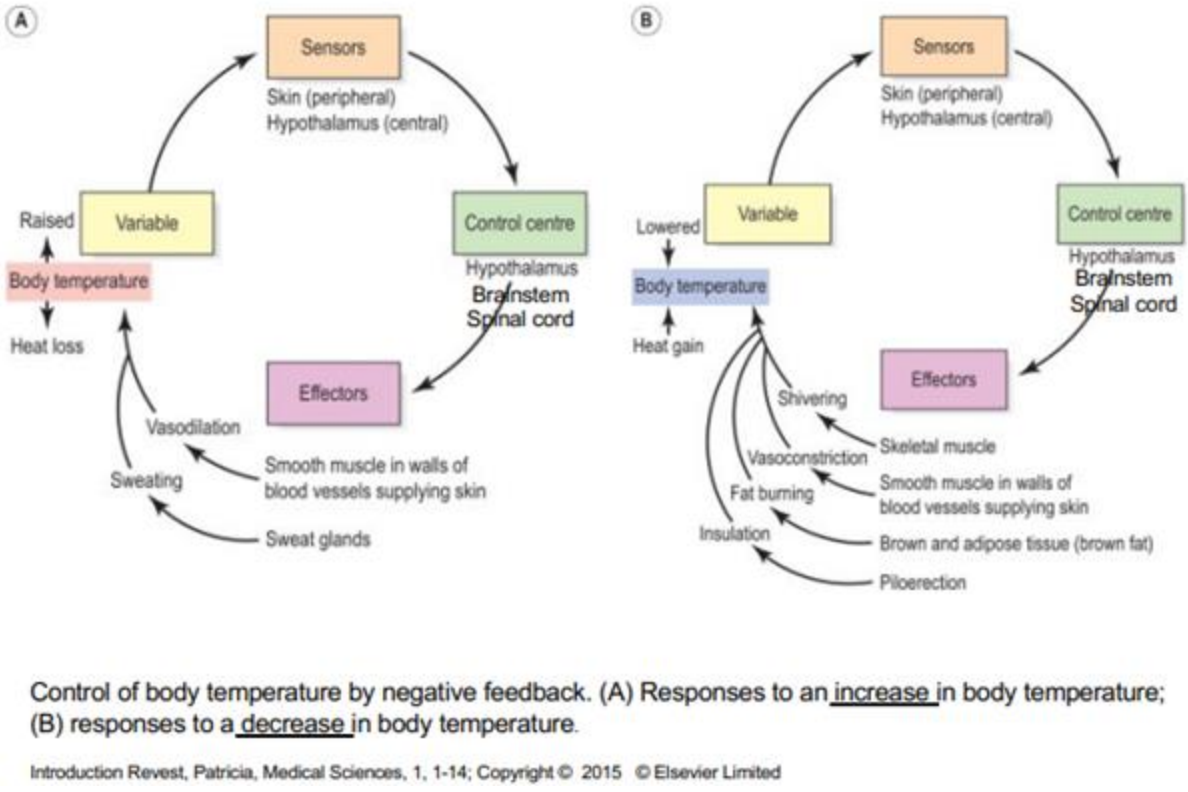
Appendix

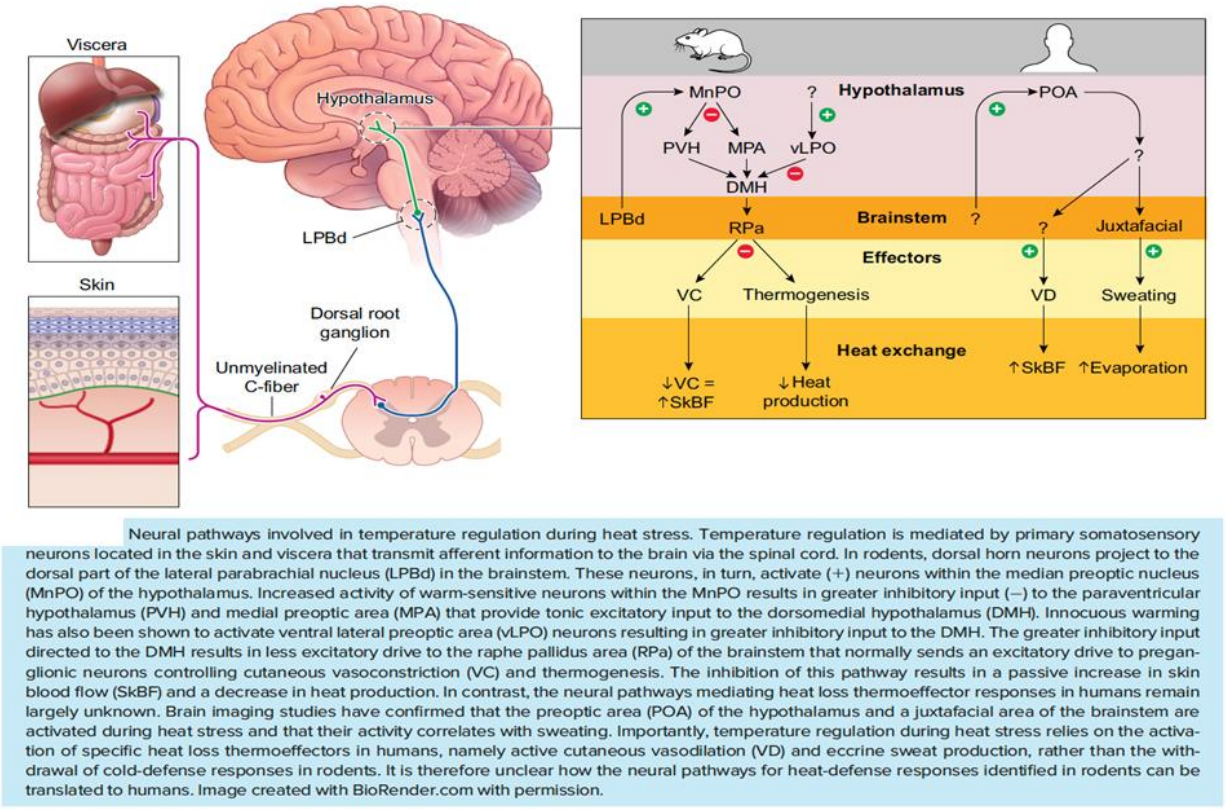
Figure 1. Negative Feedback Control of Temperature Regulation



Control of body temperature by negative feedback. (A) Responses to an increase in body temperature; (B) responses to a decrease in body temperature.

Figure 1. Negative feedback control of temperature regulation in mammals. Figure and legend are from Nash et al (2022) (28), used here in accordance with s.29.1 of the Copyright Act for education purposes only.

Figure 2. Model of Neural Pathways



Neural pathways involved in temperature regulation during heat stress. Temperature regulation is mediated by primary somatosensory neurons located in the skin and viscera that transmit afferent information to the brain via the spinal cord. In rodents, dorsal horn neurons project to the dorsal part of the lateral parabrachial nucleus (LPBd) in the brainstem. These neurons, in turn, activate (+) neurons within the median preoptic nucleus (MnPO) of the hypothalamus. Increased activity of warm-sensitive neurons within the MnPO results in greater inhibitory input (—) to the paraventricular hypothalamus (PVH) and medial preoptic area (MPA) that provide tonic excitatory input to the dorsomedial hypothalamus (DMH). Innocuous warming has also been shown to activate ventral lateral preoptic area (vLPO) neurons resulting in greater inhibitory input to the DMH. The greater inhibitory input directed to the DMH results in less excitatory drive to the raphe pallidus area (RPa) of the brainstem that normally sends an excitatory drive to preganglionic neurons controlling cutaneous vasoconstriction (VC) and thermogenesis. The inhibition of this pathway results in a passive increase in skin blood flow (SkBF) and a decrease in heat production. In contrast, the neural pathways mediating heat loss thermoeffector responses in humans remain largely unknown. Brain imaging studies have confirmed that the preoptic area (POA) of the hypothalamus and a juxtafacial area of the brainstem are activated during heat stress and that their activity correlates with sweating. Importantly, temperature regulation during heat stress relies on the activation of specific heat loss thermoeffectors in humans, namely active cutaneous vasodilation (VD) and eccrine sweat production, rather than the withdrawal of cold-defense responses in rodents. It is therefore unclear how the neural pathways for heat-defense responses identified in rodents can be translated to humans. Image created with BioRender.com with permission.

Figure 2. This figure summarizes current research in animals to develop a hypothetical model of the neural mechanisms and pathways involved in the response to heat stress in humans. Figure and legend are from Cramer et al (2022) (29), used here in accordance with s.29.1 of the Copyright Act for education purposes only.

Figure 3: Daily Core Temperature Fluctuations in November

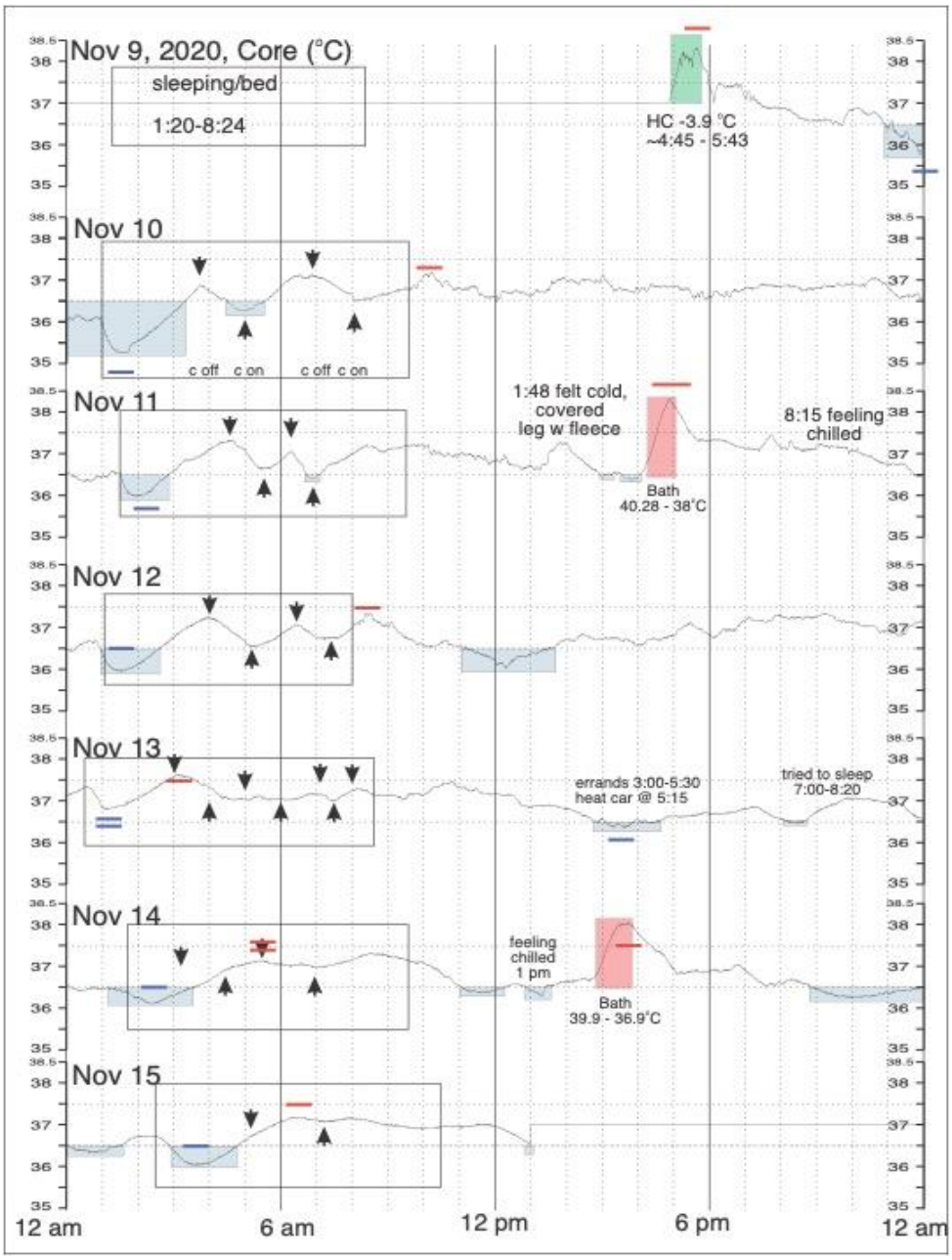


Figure 3. Core temperature data continuously recorded and annotated for the period of 9 to 15 November 2020 in a person with C8 level tetraplegia. Indoor temperature maintained at 22 ºC, unless otherwise noted. In this and Figure 4, blue bars indicate daily minimum and red bars daily maximum values (respectively). Overnight sleeping periods are denoted by a box, down arrowheads indicate times when covers were removed and up arrowheads when covers replaced. Blue/grey-shaded regions indicate periods where core temperature dropped $\leq$ 36.5 ºC. Note that during sleep, there was a daily reduction in Tcore (trough) prior to a subsequent increase in temperature. Red-shaded regions indicate heat exposures (i.e., warm bath), with significant increases in core temperature. The average difference between minimum and maximum core temperature values for this period were 2.4°C ±1.2°C.

Figure 4: Daily Core Temperature Fluctuations in July

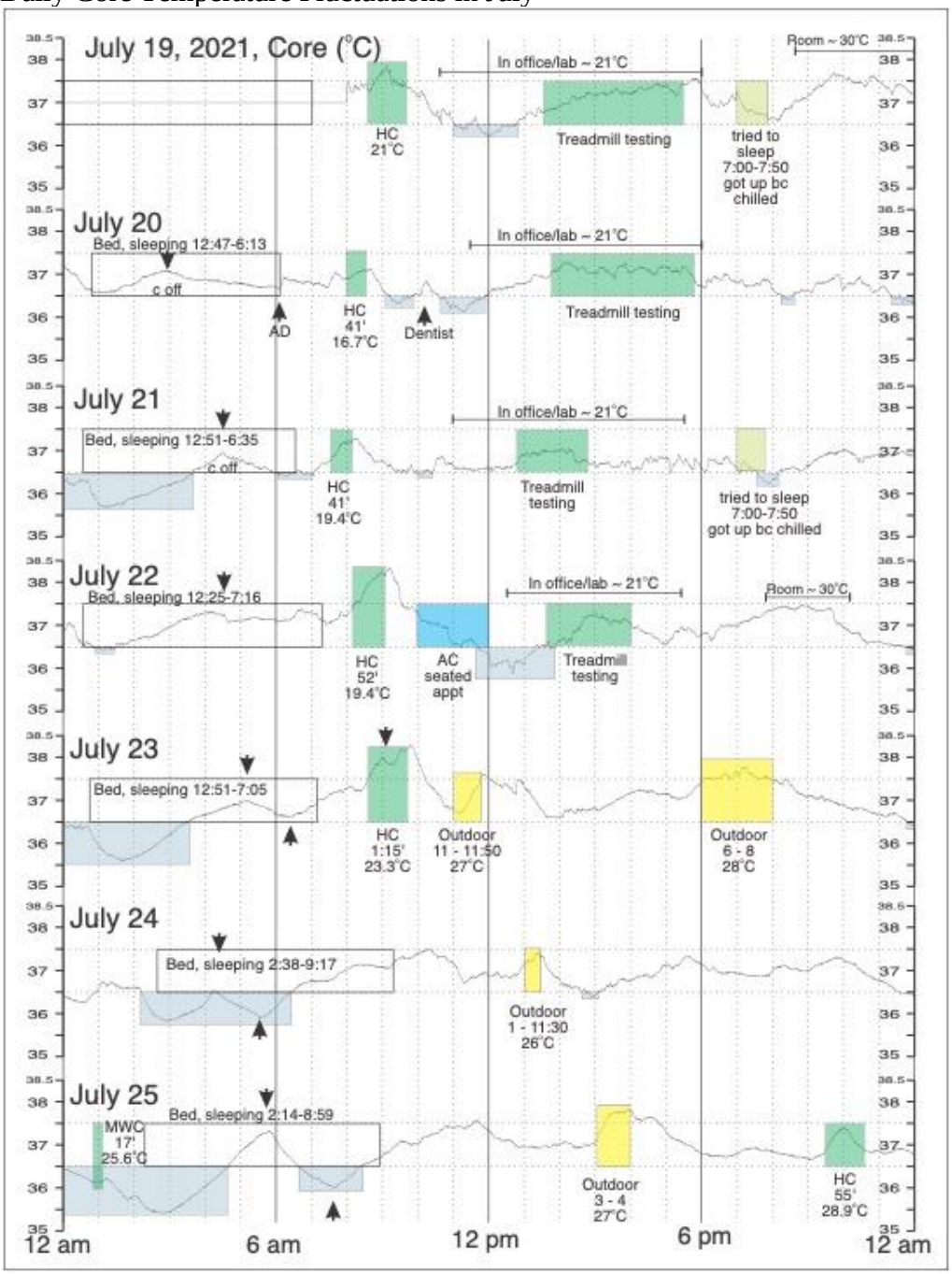


Figure 4. Tcore data were continuously recorded and annotated for the period of 19 to 25 July 2021 in a person with C8-level tetraplegia. Indoor temperature at home was maintained at 23°C, work temperature ~20-21°C unless otherwise noted. Blue/grey-shaded regions indicate periods where Tcore dropped $\leq$ 36.5 °C. Note that during sleep, there was a daily reduction in Tcore (trough) prior to a subsequent increase upon initiating sleep. Green-shaded regions indicate periods of exercise, while yellow-shaded regions indicate periods spent outdoors, with the external environmental temperature annotated for each of these periods. The average difference between minimum and maximum Tcore values for this period is 1.8°C ±1.2°C.

Figure 5. Effects of Ambient Temperature and Exercise on TCore

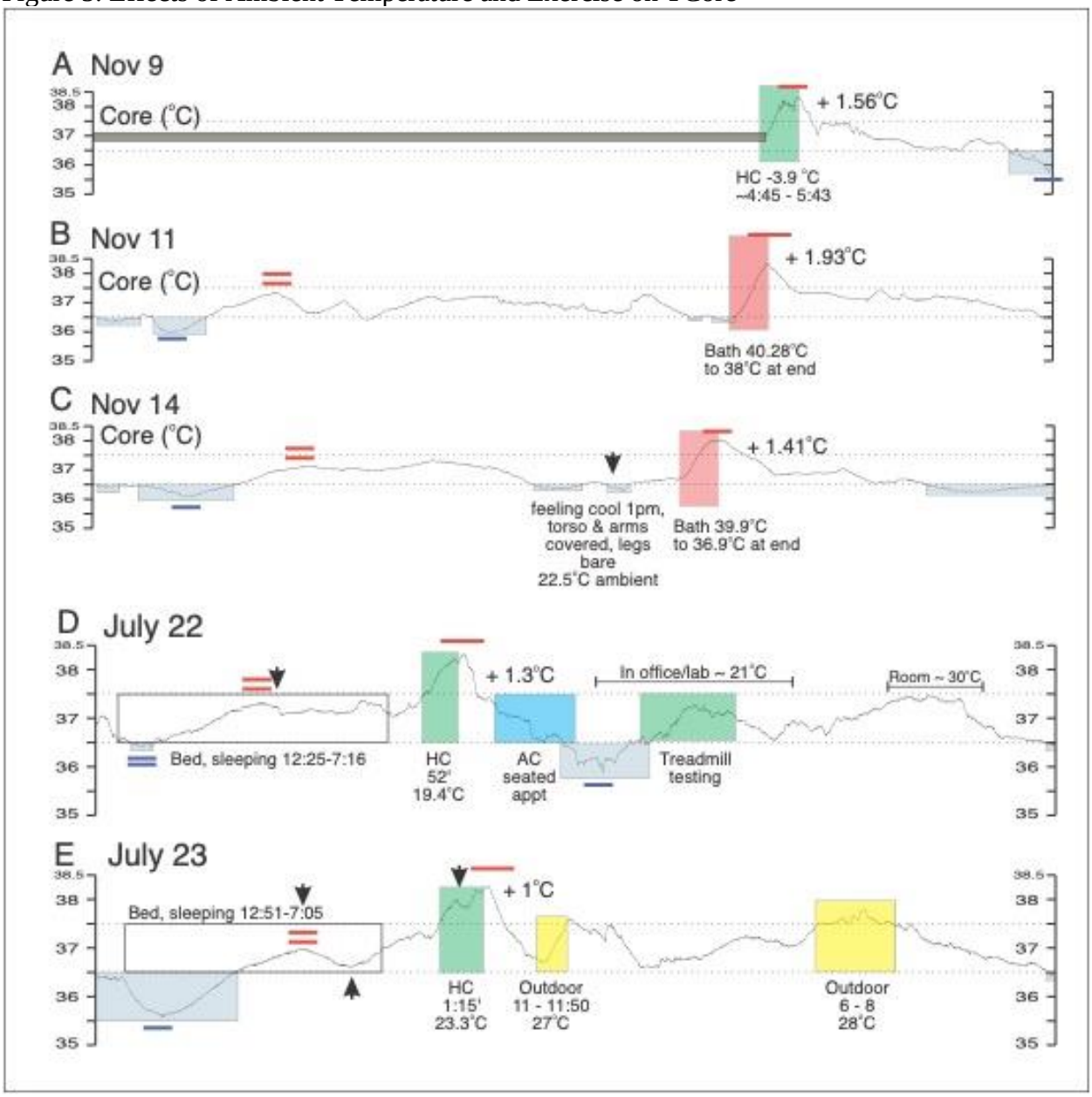


Figure 5. As in previous figures, exercise is shown in green, bathing in red, outdoor exposure in yellow and seated in a normally air-conditioned room in blue. Note the widely varying temperatures in this individual, as well as extended periods of time with sub-normal Tcore (blue-grey).

Figure 6. Data Points Recorded for TCore and Skin Temperature for a Single Day in November

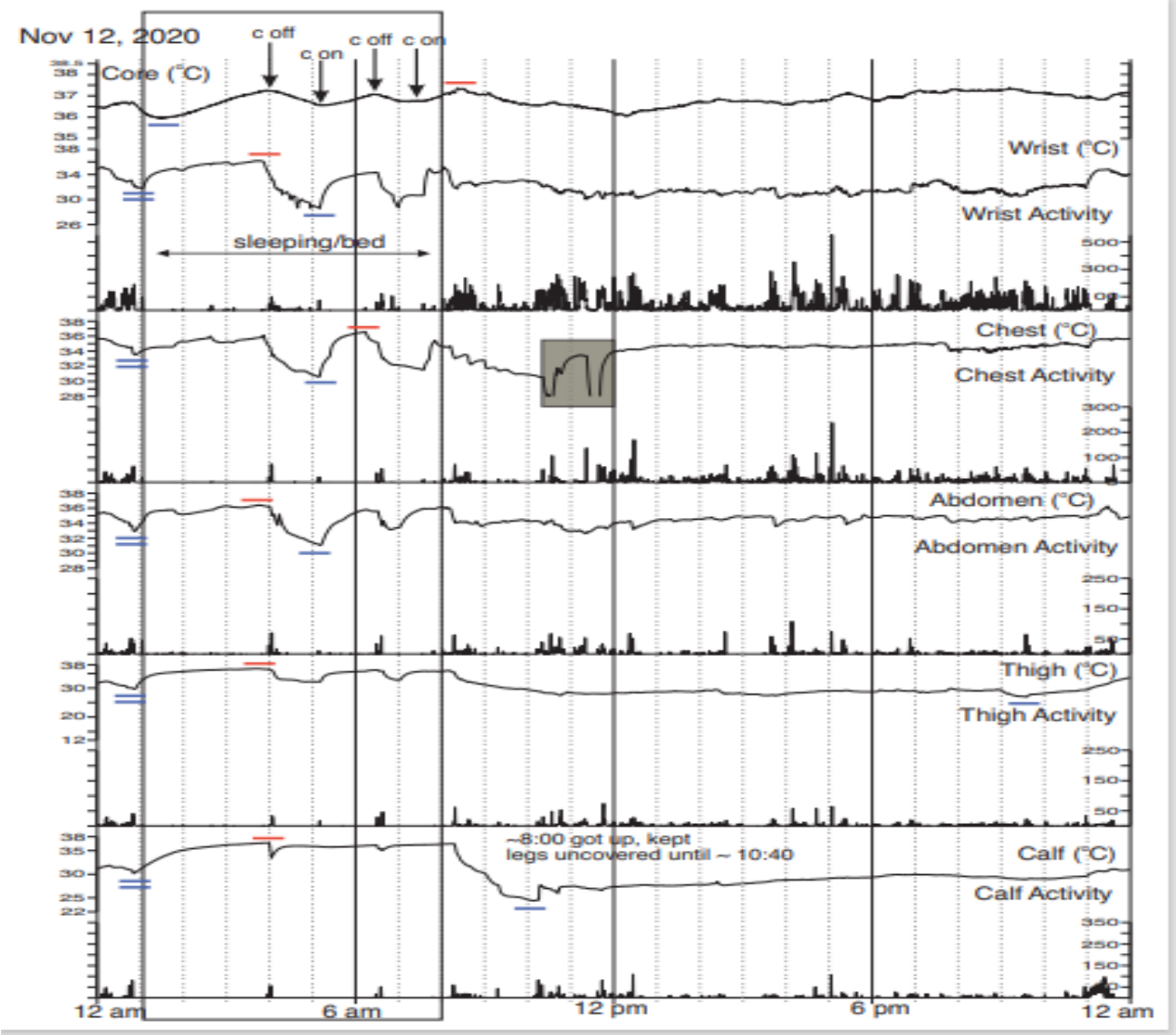


Figure 6. Tcore, skin temperature, and regional accelerometer data from a representative 24-hour period were continuously recorded in November 2020 in a person with C8-level tetraplegia. Temperature scales are shown on the left and accelerometer values on the right. Blue bars indicate daily minimum and red bars daily maximum values (respectively). Overnight sleeping periods are denoted by a box. If the minimum observed during the first three hours of sleep did not correspond to the minimum temperature for that day, the sleep minimum is indicated with a double blue bar. Greyed regions indicate periods when either Tcore or skin temperature data were excluded when sensors were being charged or were not in contact with the body. Covers were in place initially overnight while sleeping, and an initial decrease in Tcore and skin temperature was observed. Note that the initial reduction in Tcore (1 -2 am) occurred while skin temperatures were increasing (likely due to being covered). After 2 am, Tcore began to increase in concert with elevated skin temperatures until covers were removed (down arrow) at 4 am, at which time all temperatures decreased. Arrows indicate when covers were removed (c off) or replaced (c on), which correspond with subsequent decreases and increases in Tcore and skin temperature respectively. On this day, the fluctuation in Tcore was 1.4°C and the participant remained indoors for the entire period with a house temperature set at 22.5°C, but portions of the house were kept at warmer temperatures when feeling chilled.

Figure 7. Tcore Fluctuations During Exercise in a Cold Environment

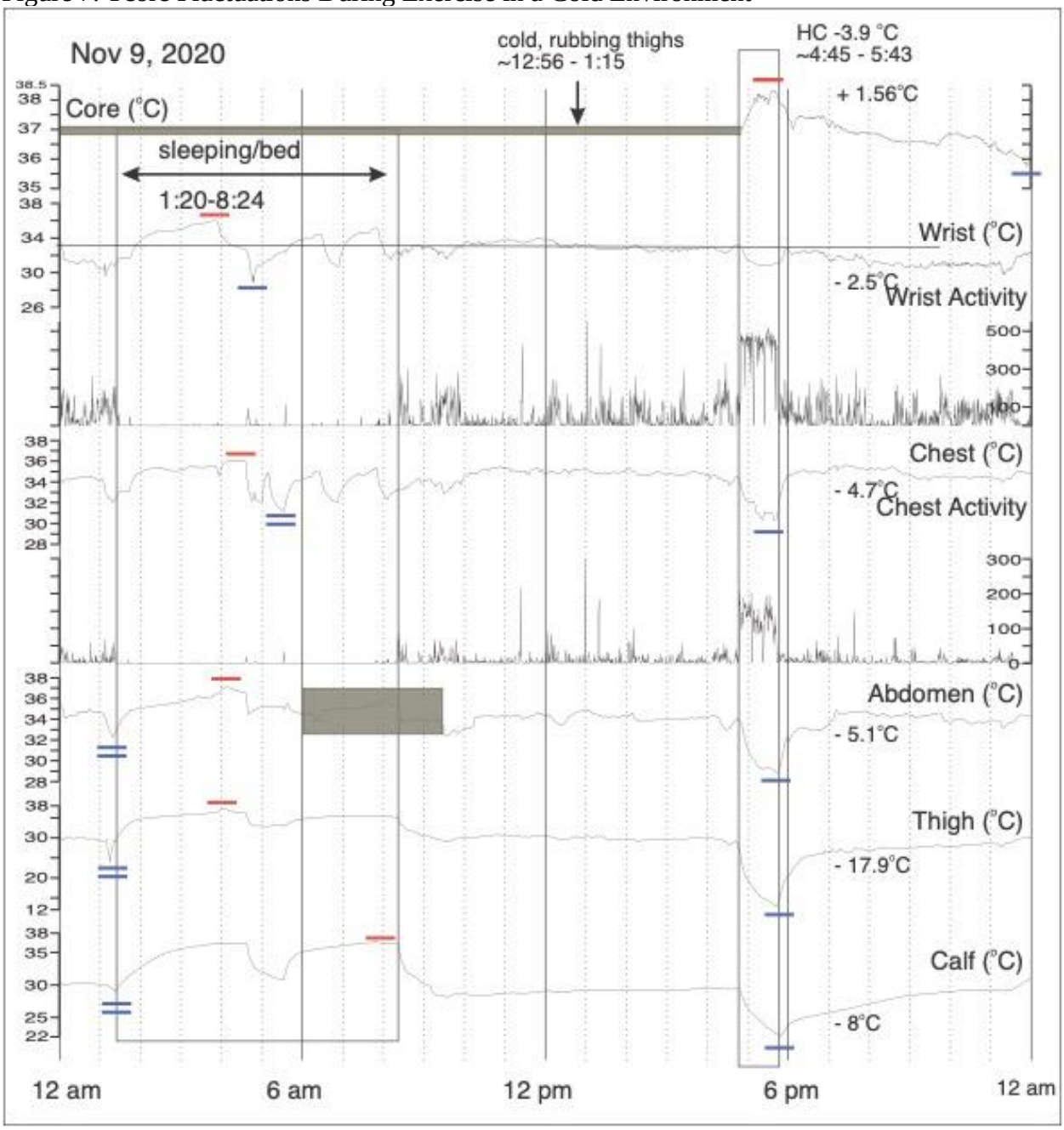


Figure 7. Core temperature increases during exercise at an ambient temperature of -3.9 ºC despite large reductions in regional skin temperature. The period of exercise is boxed, while wrist and chest accelerometer data indicate the increase in activity. Note Tcore increased by 1.56°C despite skin temperatures decreasing by as little as 2.5°C at the wrist, or as much as 17.9°C at the thigh.

Figure 8. Absolute and Relative Daily Tcore Fluctuations

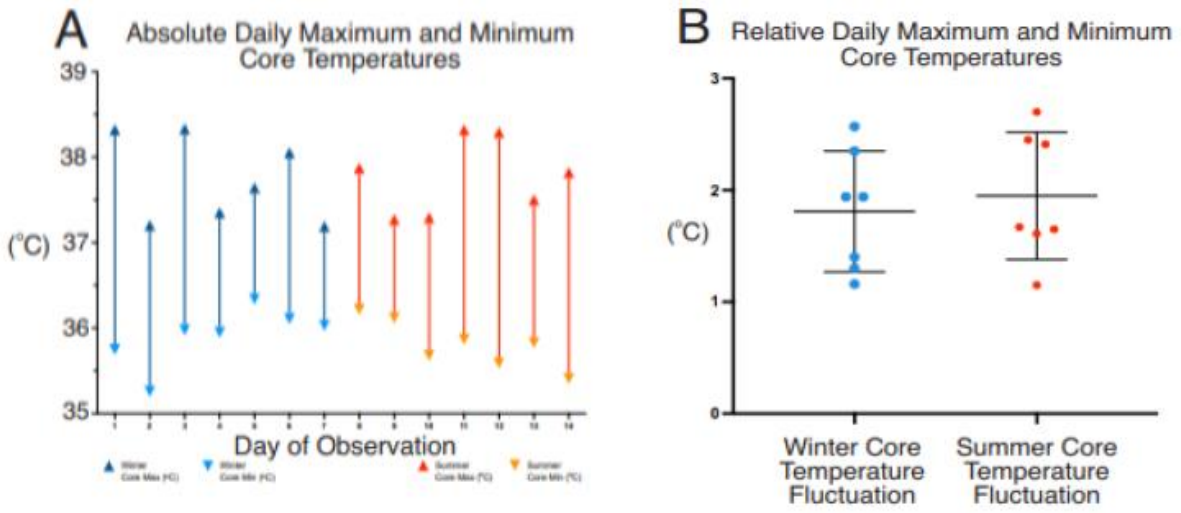


Figure 8. This figure compares the absolute (Graph A) and relative (Graph B) daily maximum and minimum Tcore observed during the November and July timeframes. Absolute values are depicted for each of the seven days during each observation period using an arrow, with the endpoints representing the recorded maximum and minimum Tcore. The arrows are colour-coded based on the timeframe they were observed, with blue arrows representing data collected during November, while the orange-yellow arrows representing temperature values from July. Graph B represents the daily change observed between maximum and minimum Tcore for each day, using the same colour coding as Graph A.