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The Effects of Thoracic and Cervical Spinal Cord Lesions on the Circadian Rhythm of Core Body Temperature

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Individuals with a spinal cord injury (SCI) have compromised afferent and efferent information below the lesion. Intact afferent information regarding skin temperature and the ability to regulate skin blood flow lead to an altered heat balance, which may impact the circadian variation in core body temperature (Tcore) and sleep-wake cycle. The authors assessed the circadian variation of Tcore in SCI individuals and able-bodied controls matched for the timing of the sleep-wake cycle. The authors examined subjects who had a high (cervical) or a low (thoracic) lesion. Intestinal Tcore (telemetry system) and physical activity (ambulatory activity monitor) levels were measured continuously and simultaneously in 8 tetraplegics, 7 paraplegics, and 8 able-bodied controls during one 24-h period of "normal" living. The regression slope between activity and Tcore was also calculated for each 2-h bin. Circadian rhythm parameters were estimated with partial Fourier time-series analysis, and groups were compared with general linear models, adjusted for the influence of individual wake-time. The (mean ± SD) dominant period length for controls, paraplegics, and tetraplegics were 24.4 ± 5.4 h, 22.5 ± 5.0 h, and 16.5 ± 5.1 h, respectively ($p = .02$). A significantly more pronounced 8-h harmonic was found for the variation in Tcore of SCI individuals ($p = .05$). Tetraplegics showed the highest nocturnal mean Tcore ($p = .005$), a 5-h phase-advanced circadian trough time ($p = .04$), and more variable relationships between physical activity and Tcore ($p = .03$). Taken together, tetraplegics demonstrate a pronounced disturbance of the circadian variation of Tcore, whereas the variation of Tcore in paraplegics was comparable to able-bodied controls. (Author correspondence: D.Thijssen@fysiol.umcn.nl)

Keywords: Circadian variation, Paraplegia, Sleep problems, Tetraplegia

INTRODUCTION

The circadian rhythm of core body temperature (Tcore) in diurnally active humans shows a nadir in the morning between 04:00 and 06:00 h and a peak 1–4 h before habitual bedtime (Waterhouse et al., 2005). The main temperature regulator in the hypothalamus depends on afferent feedback to adequately regulate Tcore (Berner & Heller, 1998; Satinoff, 1978). An intact sympathetic nervous system is necessary for vasoregulation and sweat gland activity in order to elicit heat loss through the skin (Johnson & Kellogg, 2010). Interestingly, such changes in skin temperature may affect the ability to initiate and maintain sleep (Raymann et al., 2007). The peripheral nervous system also enables heat production via muscle activity (Morton et al., 2006). If the afferent and efferent arms of the sympathetic nerve system are lost, regulation of Tcore is impaired (Boot et al., 2006; Price & Campbell, 1999). We were interested in determining whether this impairment alters the circadian variation in Tcore.

Dependent on the site and extent of the lesion, individuals with a spinal cord injury (SCI) have an impaired autonomic involvement and sudomotor dysfunction below the level of the lesion (Mathias & Frankel, 2002). Consequently, SCI individuals primarily depend on the region above the lesion for thermoregulation (Guttmann et al., 1958; Sawka et al., 1989), resulting in an impaired afferent input to, and efferent signals from, the central thermoregulatory center (Freund et al., 1984; Theisen et al., 2001), consequently leading to thermal dysfunction (Boot et al., 2006; Guttmann et al., 1958; Khan et al., 2007). Thermoregulatory and soporific mechanisms are thought to be linked (Atkinson & Davenne, 2007). Indeed, research has identified a high prevalence of sleep disorders in SCI (Scheer et al., 2006). The elevated 15–40% prevalence of sleep disorders in SCI individuals (Biering-Sorensen &

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Biering-Sorensen, 2001; Burns et al., 2000; Hyyppa & Kronholm, 1989; Jensen et al., 2009) is higher than the ~4% prevalence typically reported in middle-aged men (Young et al., 1993). This higher prevalence may be related to an altered sleep-wake cycle and/or altered Tcore circadian variation in SCI individuals. However, no previous study has examined, with formal chronobiological analyses, the hypothesis that an altered circadian variation of Tcore is present in SCI, when the timing of the sleep-wake cycle is taken into account.

The extent of thermal dysfunction in SCI individuals may depend on the level of the lesion. Indeed, SCI individuals with a cervical lesion have an increased risk of developing hypo- or hyperthermia compared with subjects with a thoracic spinal cord lesion (Boot et al., 2006; Guttmann et al., 1958; Khan et al., 2007). Nocturnal release of melatonin, a hormone that contributes to the normal sleep pattern (Pandi-Perumal et al., 2008), contributes to the 24-h variation of Tcore. Interestingly, melatonin is released via the central nervous system at the cervical level (Pandi-Perumal et al., 2008) and, therefore, may be altered or even absent in SCI individuals with a cervical lesion, i.e., tetraplegia (Li et al., 1989; Scheer et al., 2006). We hypothesized that a higher lesion level would have a larger impact upon the changes in Tcore circadian variation than a lower lesion. Therefore, the aims of the study were to compare the Tcore during a 24-h recording of SCI individuals and able-bodied controls matched for sleep-wake timing, and to examine the impact of lesion level by comparing subjects with a high (cervical) and low (thoracic) lesion.

METHODS

Subjects

Eight healthy recreationally active men and 15 healthy recreationally male subjects with SCI were recruited from the local community (Table 1). Eight of the SCI subjects presented with a complete cervical spinal cord lesion (tetraplegics), whereas seven subjects had a complete thoracic spinal lesion (paraplegics). All SCI subjects had a complete spinal cord lesion (ASI A), varying between C5 and T12 that had existed for at least 5 yrs. No subject reported having been diagnosed with cardiovascular disease or associated elevated risk factors, such as hypercholesterolemia or hypertension. Subjects who were on sleep medication or drugs influencing the cardiovascular system were excluded. Due to the use of the telemetry system for Tcore measurements, participants with known bowel disease were excluded from study. The study procedures were approved by the Ethics Committee of the Radboud University Nijmegen Medical Centre and conformed to international ethical standards (Portaluppi et al., 2010).

Experimental Design

Core body temperature was assessed using a portable telemetry system for a 24-h period, starting at 09:00 h and finishing at 09:00 h the following day. In addition, the physical activity level (heart rate recorder + activity monitor) was measured simultaneously and continuously throughout the 24-h span. Participants performed their normal daily activities, but refrained from exercise and/or physically demanding activities to minimize the impact of physical activity–induced changes on Tcore.

Procedures

The day before testing, all subjects received written information, a diary, and the ingestible telemetry pill for Tcore recording. On the day of testing, all subjects ingested the telemetry pill at 06:00 h. Able-bodied controls and paraplegics reported to the laboratory at 08:30 h for measurement of general characteristics, e.g., body mass and height. Subsequently, detailed instruction of the procedures and equipment was provided. Data recording started at 09:00 h. Subjects reported back to the laboratory on the subsequent day at 09:30 h. For practical reasons, instruction of the procedures and provision of equipment of the tetraplegics was performed at their home. Also, collection of the equipment and diary was performed at least 24 h after the start of the experiment at their home. All subjects were instructed to remain indoors to ensure constant and stable environmental conditions within and between subjects.

Core Body Temperature Assessment

A portable telemetry system was used to measure Tcore (CorTemp System; H Q, Palmetto, FL, USA) that has been demonstrated to be a safe and reliable method to examine core body temperature at rest and during physical exercise (Byrne & Lim, 2007; Gant et al., 2006). Each sensor was calibrated before use in order to ensure optimal validity and reliability of Tcore measurements (Byrne & Lim, 2007). Subjects ingested the individually calibrated telemetric temperature sensor at 06:00 h to ensure that the pill had passed the stomach and reached the intestine for stable temperature signals and was not susceptible to the potential influence of consumed (hot/cold) food or fluids (Wilkinson et al., 2008). Every 40 s, a signal was transmitted through a radiowave signal to an external receiver worn in a pouch around the waist. Finally, data were averaged over 15-min time windows to examine changes across the 24-h recording. A single 24-h period was selected, since a longer data collection period would have necessitated the ingestion of an additional independent sensor, which may have added random measurement errors and bias to our estimates of the parameters of circadian variation, as well as possible cross-talk if two thermistors were simultaneously present in the intestines. Despite individual variation, the pill typically remains in the digestive track for at least ~24 h. Indeed, in our study none of the subjects lost the pill during the 24-h recording of Tcore.

Physical Activity

An accelerometer was used (SenseWear Pro3; BodyMedia, Pittsburg, PA, USA) to continuously monitor physical

TABLE 1. General characteristics of the subjects

Variable	Controls (n = 8)	Paraplegics (n = 7)	Tetraplegics (n = 8)	*p* value
Age, yrs	34 ± 10	43 ± 8	44 ± 8	.06
Body mass, kg	78 ± 9	71 ± 13	84 ± 16	.99
Height, cm	181 ± 4	181 ± 7	181 ± 10	.20
BMI, kg/m^2	23.5 ± 1.8	21.7 ± 3.2	25.4 ± 4.5	.13
Sleep reported during data collection				
Time-to-sleep (h:min)	23:36 ± 0:46	23:53 ± 1:01	23:40 ± 1:16	.88
Time-wake up (h:min)	07:25 ± 0:54	07:30 ± 0:28	07:51 ± 1:03	.60
Total sleep (h)	8.00 ± 0:55	7:46 ± 0:52	8:14 ± 1:12	.69
Sleep reported during typical day*				
Time-to-sleep (h:min)	23:33 ± 0:51	23:11 ± 1:09	22:42 ± 1:46	.11
Time-wake up (h:min)	07:07 ± 0:42	07:17 ± 1.11	07:25 ± 0:44	.53
Activity monitor				
Time-to-sleep (h:min)	23:57 ± 0:31	24:10 ± 0:45	23:58 ± 0:54	.79
Time-wake up (h:min)	07:13 ± 0:48	06:53 ± 1:04	07:57 ± 1:00	.25
Total sleep (h:min)	7:29 ± 0:47	6:46 ± 2:34	7:55 ± 1:26	.46
Time lying (h:min)	8:50 ± 2:16	7:38 ± 3:09	8:13 ± 1:16	.64
Time sleeping (h:min)	7:17 ± 1:57	5:50 ± 2:27	6:29 ± 1:30	.43

Data are presented as mean ± SD. *P* value represents a one-way ANOVA between the three groups.
*Data collection from 7 controls, 6 paraplegics, and 6 tetraplegics due to failure of reporting this information.

activity level, and to exclude physical activity level as the primary factor causing alteration of Tcore in this field study. The accelerometer was worn around the right upper arm throughout the 24-h period. Physical activity was expressed in metabolic equivalent units (METs) (Pitta et al., 2008). Data were calculated in 15-min time windows to match with the data analysis of the Tcore. Previous studies have demonstrated that this activity monitor is a valid and accurate means of measuring energy expenditure in free-living situations (Fruin & Rankin, 2004; King et al., 2004; Malavolti et al., 2007). Recently, a close relation between energy expenditure during various types and levels of physical activities and energy expenditure of the Sensewear was reported in manual wheelchair users (Hiremath & Ding, 2009). In addition, since the accelerometer is able to record lack of movement, it is also able to determine the periods when subjects were supine. By taking skin heat flux into account, the accelerometer also estimated sleep duration. A recent study found that accelerometry is a valid tool for this purpose (Weiss et al., 2010).

Heart Rate

A chest band was used to continuously measure heart rate (Polar RS800; Polar Electro Oy, Kempele, Finland). To achieve constant signalling throughout the day, a gel (Aquasonic 100, ultrasound transmission gel; Fairfield, NJ, USA) was applied to the back of the polar band. Data were recorded continuously and were used to filter artefacts and identify changes in Tcore due to increased physical activity only.

Diary

Participants also kept a diary and reported their physical activities throughout the 24-h recording. This assisted the filtering of artefacts and identifying changes in Tcore due to increase in metabolic demand during periods of elevated physical activity (Sarabia et al., 2008). Participants also reported the time when they went to bed, when the light was switched off, and when they awoke.

Statistical Analysis

Tcore data were analyzed using the Statistical Package for the Social Sciences (version 17) and with Chronos-Fit Version 1.04 (Zuther & Lemmer, 2004). Daytime was predetermined as 06:00–22:59 h and the nighttime as 23:00–05:59 h. Full details of the Chronos-Fit parameters and the Fourier analysis that Chronos-Fit allows are provided in Zuther and Lemmer (2004). First, the following simple summary statistics were calculated: 24-h mean, daytime mean, nighttime mean, and day-night mean difference. A Fourier series essentially alters time series data into a sum of oscillating harmonics based on sine and/or cosine functions. Periodicity in each of our data sets was analyzed by partial Fourier series with up to six (i.e., 24, 12, 8, 6, 4.8, and 4 h) harmonics. The following summary statistics were calculated for the fitted curve of each subject: mesor (24-h time series mean), acrophase (time of maximum value of each harmonic), peak and trough values of the combined Fourier analysis, and time-to-peak and time-to-trough of the fitted Fourier analysis. These summary statistics are typically useful in describing a longitudinal time-series in chronobiological studies (Paul & Lemmer, 2007). The dominant period length, the %-rhythm (an index of the amount of variance accounted for by the fitted model), and the statistical significance of the model were calculated. Mean differences between the three groups in all the above summary statistics were examined with one-factor (group) general linear models. Although groups were matched for mean sleep-wake characteristics, individual wake-time was added as a covariate in order to control for random

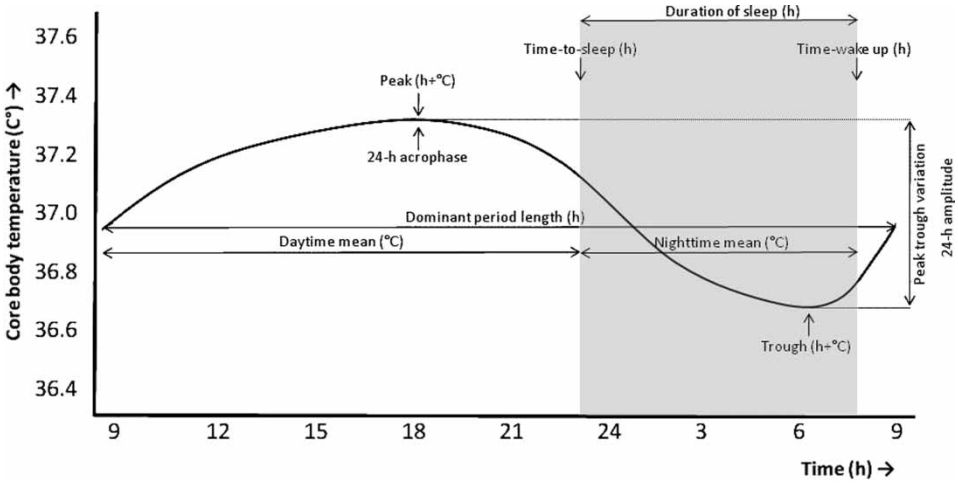

FIGURE 1. Graphical presentation of the 24-h rhythm of Tcore (▬), with the grey region representing the time of sleep. All parameters for the analysis of the 24-h variation in Tcore (dominant period length, %-rhythm, daytime mean, nighttime mean, peak-trough variation, peak value, peak time, trough, trough time), and sleep (time-to-sleep, time-wake up, and total duration of sleep) are identified in the figure. Please note that only with a dominant period length of exactly 24 h do the 24-h amplitude and acrophase correspond with the peak-trough variation and peak value, respectively. The mesor, which represents the rhythm-adjusted mean, is not presented in this figure.

interindividual variability in this factor, thereby improving statistical power (Miller & Chapman, 2001). Significant *F*-values were followed up with multiple comparisons using the Fisher's least significant difference procedure. Data are presented as mean ± SD unless otherwise stated. Figure 1 illustrates the phases and time points used in our chronobiology analysis. Note that the analysis of some parameters is based on a Fourier analysis and detects patterns in individual participants. Therefore, peak or minimal values in Tcore may not coincide exactly to the data presented at individual time points, as in Figure 2.

In chronobiological field studies, it is relevant to attempt to "purify" the circadian variation in a physiological function for the masking influence of physical activity, typically with a statistical approach (Waterhouse et al., 2005). Therefore, we also examined circadian variation in the reactivity of Tcore to physical activity. Using methods similar to those described by Atkinson et al. (2009), we calculated the least squares regression slope between activity and Tcore in 2-h bins for each subject, with time expressed relative to the individual wake-time. A two-factor (group × time-of-day) general linear model was employed to analyze these data.

RESULTS

The three study groups did not differ significantly in terms of the timing of the sleep-wake cycle and sleep length, both during the data collection period and via self-reports of their typical living (Table 1). There were also no significant differences between study group means in body mass, height, or BMI (Table 1), although there appeared to be more inter-individual variability as shown by the SD in the SCI groups compared with the healthy controls (Table 1). Although the controls were somewhat younger than the SCI group, this difference did not reach statistical significance (Table 1).

Control subjects demonstrated typical circadian variation in Tcore (Figure 2A), with a dominant period that did not differ significantly from 24 h ($p > .10$), acrophase ~9.0 h after waking, and amplitude of 0.4°C (Table 2). In SCI individuals, the phase and amplitude of the circadian variation of Tcore was different and depended on lesion level (Figure 2A). The absolute values and timing of both the peak and trough in Tcore did not differ significantly between controls and paraplegics (Table 2). Nevertheless, the trough time of the Fourier curve and 24-h acrophase were significantly earlier in the tetraplegics compared with paraplegics (Table 2). The implication of the difference in the 24-h amplitude between the groups should be interpreted with caution, since the dominant period length differed substantially from 24 h in tetraplegic subjects. In tetraplegics, the mean dominant period length was 6–8 h shorter, whereas the mean Tcore during the nighttime was significantly higher (Table 2). A significantly higher amplitude of the 8-h harmonic was found for SCI individuals compared with controls (Table 2). No group differences were found for the other Fourier subharmonics. The study groups did not differ in terms of the number of harmonic periods fitted to each subject's time-series data ($p = .46$).

Physical activity significantly varied over time in the controls ($p < .0005$) and paraplegics ($p < .0005$), whereas physical activity in tetraplegics was relatively stable across the 24 h, with less physical activity being recorded during the daytime than in the paraplegics and healthy controls (Figure 2B). Nonetheless, the differences in the 24-h variation in physical activity between groups did not reach significance ($p = .08$). We also examined the change in Tcore relative to the change in physical activity, i.e., the "reactivity" of the Tcore. A significant

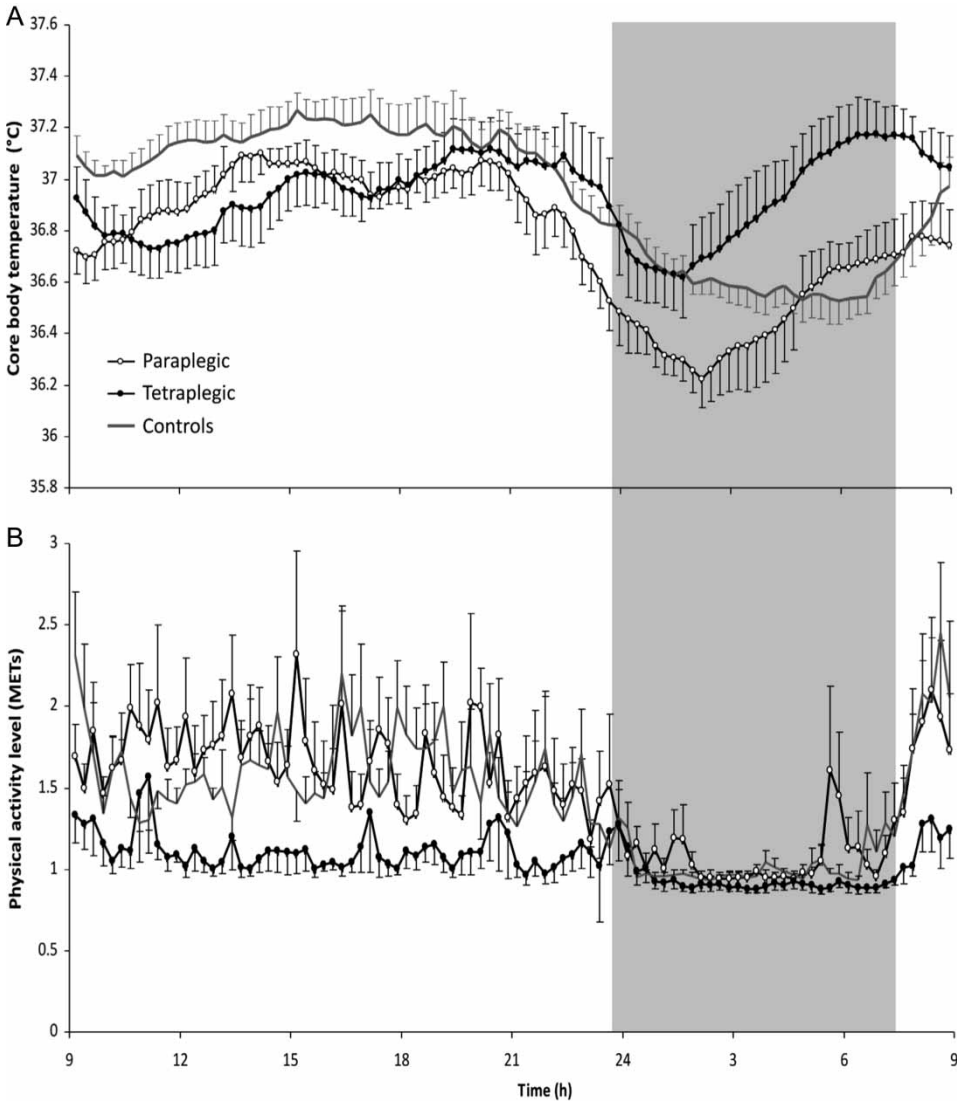

FIGURE 2. 24-h rhythm of Tcore (A) and physical activity (B) levels in able-bodied subjects (▬), paraplegic (○), and tetraplegic (•) subjects. The grey region represents the average time of sleep for all subjects. Tcore and physical activity recording started at 09:00 h and was performed continuously for a 24-h period. Data are presented as the mean over a 15-min period, whereas error bars represent SE. Physical activity level was measured using an activity monitor, which calculated the metabolic equivalent (MET), representing the fold change in baseline metabolic rate. Note that the mean MET level during the awake hours is ~1.5, whereas during sleep MET levels are ~1. Moreover, no significant differences between groups for physical activity level were found.

impact of time-of-day was found for Tcore reactivity ($p = .01$; Figure 3). Although no interaction between time-of-day and group was found ($p = .56$), the variability in the Tcore–physical activity relationship was significantly higher for tetraplegics (one-factor general linear model [GLM] on within-subjects SD over time-of-day: $p = .03$). In tetraplegics, the relation of Tcore to physical activity changed markedly 4–10 h after sleep. This is consistent with the early afternoon increase in Tcore in tetraplegics, despite little change in physical activity (Figure 2B).

DISCUSSION

The main purpose of this study was to examine the circadian variation of the Tcore in able-bodied controls and SCI individuals with a "high" (cervical) or "low" (thoracic) lesion. Tcore across the 24-h period in able-bodied controls demonstrated typical 24-h variation, i.e., an early evening peak in Tcore followed by a rapid decline and subsequent plateau phase in Tcore during sleep (Lack et al., 2008). However, dependent on lesion level, SCI subjects demonstrated a marked difference in the circadian variation of Tcore. Tetraplegics showed a shorter time period during which the biphasic variation in Tcore was completed and an earlier nocturnal phasing of the Tcore trough value. These differences cannot be fully explained by physical activity levels, since physical activity was consistent over the 24-h period in these individuals, thus making relationships between Tcore and physical activity rather weak. Even though paraplegic subjects have a significantly reduced

TABLE 2. Differences between groups in the various individual rhythm summary statistics for the parameters of core body temperature obtained after analysis with chronos-fit

Variable	Controls (C) (n = 8)	Paraplegics (P) (n = 7)	Tetraplegics (T) (n = 8)	*p* value	Multiple comparisons
Dominant period length (h)	24.4 ± 5.4	22.5 ± 5.0	16.5 ± 5.1	.02	C = P > T
%-rhythm	94.9 ± 3.7	94.6 ± 3.4	94.5 ± 3.4	.97	N/A
Mesor (°C)	36.9 ± 0.3	36.8 ± 0.3	36.9 ± 0.3	.11	N/A
Daytime mean (°C)	37.1 ± 0.3	36.9 ± 0.3	37.0 ± 0.3	.25	N/A
Nighttime mean (°C)	36.6 ± 0.3	36.5 ± 0.3	36.9 ± 0.3	.005	C = P < T
Peak-trough variation (°C)	1.0 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	.45	N/A
Peak value (°C)	37.4 ± 0.3	37.3 ± 0.3	37.5 ± 0.3	.07	N/A
Peak time (h after waking)	9.0 ± 6.2	8.5 ± 5.8	4.3 ± 5.7	.11	N/A
Trough value (°C)	36.4 ± 0.3	36.0 ± 0.3	36.3 ± 0.3	.04	C = T > P
Trough time (h before waking)	2.9 ± 5.1	6.0 ± 4.8	9.9 ± 4.8	.05	C = P < T
24-h amplitude (°C)	0.4 ± 0.3	0.4 ± 0.3	0.3 ± 0.3	.44	N/A
24-h acrophase (h after waking)	8.6 ± 5.1	8.1 ± 4.8	2.6 ± 4.8	.05	C = P > T
8-h amplitude (°C)	0.07 ± 0.09	0.17 ± 0.09	0.18 ± 0.09	.05	C < P = T
8-h acrophase (h after waking)	4.1 ± 2.0	6.1 ± 2.1	5.8 ± 2.0	.10	N/A

Data are presented as mean ± SD. *p* value represents a one-way general linear model between the three groups adjusted for individual differences in wake-time.

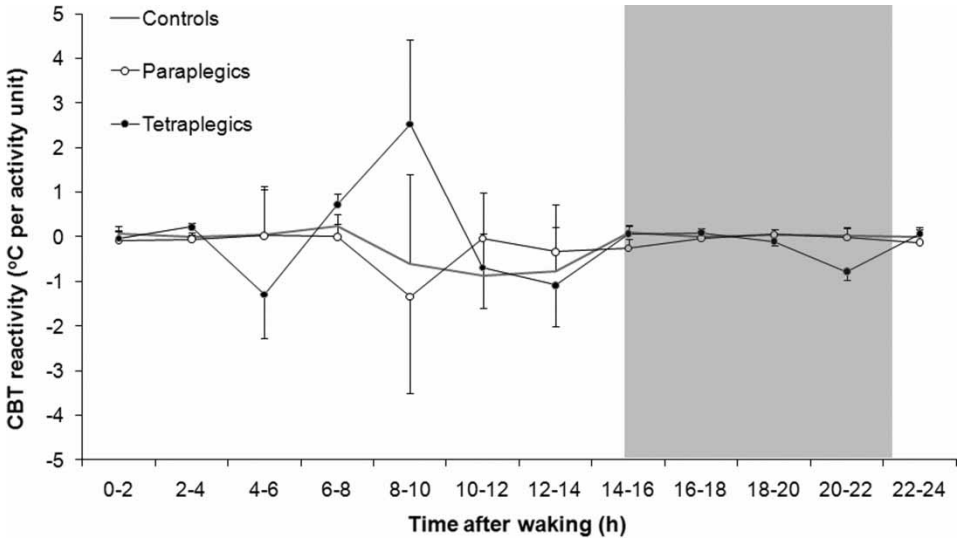

FIGURE 3. The 24-h variation in Tcore reactivity for able-bodied subjects (▬), paraplegic (○), and tetraplegic (•) subjects. The regression slope of body temperature versus physical activity was calculated for each 2-h bin. The grey region represents the average time of sleep for all subjects. Error bars represent SE.

surface area available for thermoregulation, no important differences in the 24-h variation in Tcore were found compared with controls. This suggests that mechanisms other than skin thermoregulation explain the altered 24-h regulation of Tcore. Taken together, these data indicate that the circadian variation of Tcore is altered in tetraplegics, but largely preserved in paraplegics, compared to able-bodied controls.

Using a detailed analysis of the Tcore pattern across the 24-h recording, we found no difference between groups in the Tcore changes during the daytime. This indicates that SCI individuals, even in those with a cervical lesion, are able to maintain a normal Tcore during the daytime. The pronounced change in the dominant period in tetraplegics, however, is primarily explained through characteristic changes in Tcore during the sleep period. Able-bodied controls demonstrated a typical decrease in Tcore when going to sleep, followed by a plateau, and thereafter a trough ~3 h before waking. SCI individuals with a cervical lesion, however, demonstrated no plateau in Tcore during sleep, but showed an increase in Tcore after reaching the trough (Figure 2). The absence of a plateau in Tcore during sleep was also reflected in the significantly higher mean Tcore during sleep in tetraplegics. Taken together, the differences in Tcore variation between able-bodied controls and tetraplegics are primarily explained by specific changes in Tcore during the sleep.

One potential explanation for the variation in Tcore is physical activity level, as exercise increases muscle metabolic rate and heat production, which will induce a change in Tcore. The physical activity level in all participants was estimated to fluctuate between 1 and 2 METs, which indicates that subjects refrained from moderate to intense physical activity (Fruin & Rankin, 2004). Moreover, tetraplegics demonstrated an even lower physical activity level than paraplegics or controls, which is in line with previous findings (Ginis et al., 2010). As tetraplegics also demonstrated a more variable relationship between physical activity and Tcore (Figure 3), it is unlikely that differences in the circadian variation of Tcore in tetraplegics can be explained by physical activity. Also, the main difference in core body temperature occurred at night, when physical activity level was at the resting level and comparable between groups. Therefore, other factors besides physical activity explain the differences in the 24-h variation in Tcore.

Skin thermoregulation relates to the circadian variation of Tcore, since changes in skin temperature may causally affect the ability to initiate and maintain sleep (Raymann et al., 2007). Previous studies of Price and Campbell (1997, 1999, 2003) and the review of Price (2006) establish lower skin temperatures below the lesion, whereas the physiological responses of skin temperature below the lesion to exercise are altered, especially in those with a tetraplegia. Despite these observations and the significantly reduced body surface for thermoregulation in paraplegics, we found no important differences in the 24-h regulation of Tcore between paraplegics and controls. This finding contrasts with our hypothesis and indicates that differences in skin thermoregulation, such as between paraplegics and controls, do not simply lead to changes in the 24-h variation in Tcore. Future studies should examine skin distal and proximal thermoregulation in SCI to gain better insight into this matter.

Our results may relate to group-specific endocrinologic changes, such as the nocturnal release of melatonin, a hormone that contributes to a normal sleep pattern, and which is produced via neural pathways (Pandi-Perumal et al., 2008). Melatonin is released via the central nervous system at the cervical level (Pandi-Perumal et al., 2008). Interestingly, two previous observational studies suggested that tetraplegics who demonstrate an interruption of efferent and afferent information at the cervical level show no nocturnal release of melatonin (Li et al., 1989; Scheer et al., 2006). This change in endocrine function in tetraplegics may contribute to the marked difference in Tcore observed in our study, especially since tetraplegics demonstrate the most pronounced change in the 24-h variation in Tcore. However, no previous study examined melatonin release in cervical spinal cord injured individuals and linked these changes to Tcore.

This study took advantage of the inclusion of a large group of SCI individuals, including paraplegics as well as tetraplegics, and continuous measurement of Tcore and physical activity levels. A potential limitation of our study is the tendency for a younger age of the control group compared to the SCI groups. Although age is a potential factor that may contribute to sleep disorders, changes in sleep patterns are hypothesized to occur at a much later age, i.e., 50–65 yrs (Ohayon, 2002). Also, differences in the 24-h recording of Tcore were reported between paraplegics and tetraplegics, despite their similar age. Therefore, a potential age difference between the groups is an unlikely explanation of the primary findings of this study. Another potential limitation is that we did not examine sleep quality, which would have allowed direct comparison between our observations and sleep problems in SCI subjects. Indeed, we believe that a study that focuses on sleep, including a comprehensive assessment of sleep quality using polysomnography under controlled laboratory conditions, would add considerable insight to these findings. A study design such as that employed in previous research (Zaregarizi et al., 2007) whereby the sleep-onset period is tightly controlled from lights-off onwards would be useful in differentiating between sleep-related and light-response-related effects on the thermoregulatory changes prior to and during sleep.

The different Tcore circadian variation in SCI individuals compared to their able-bodied peers may present a potential pathophysiologic mechanism that contributes to the high incidence of sleep disorders in SCI individuals. Interestingly, we observed that the change in circadian variation in Tcore was larger in tetraplegics compared with paraplegics, a finding that parallels previous findings that reported a trend towards a greater prevalence of sleep disorders in tetraplegia compared with paraplegia (Burns et al., 2000). Before examining the effects of intervention on sleep quality in SCI, better insight into the underlying mechanisms for the differences in the 24-h regulation in Tcore is necessary.

In conclusion, SCI individuals demonstrate a significant disturbance in the circadian variation of Tcore, which is unlikely explained by differences in physical activity levels. Interestingly, the circadian variation of Tcore is altered in tetraplegics, but largely preserved in paraplegics, compared to able-bodied controls. As a minimum, this suggests that the level of the lesion is significantly related to the ability to regulate the circadian variation of Tcore in humans, with the most pronounced differences present in those with a cervical lesion. Finally, the disturbance in circadian variation of Tcore may contribute to the pathophysiologic mechanism that explains the frequently reported poor sleep quality in subjects with a cervical spinal cord injury.

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