

Alexandra L. Holmes, Helen J. Burgess and Drew Dawson

J Appl Physiol 92:2578-2584, 2002. First published Feb 22, 2002; doi:10.1152/jappphysiol.01106.2001

You might find this additional information useful...

This article cites 34 articles, 9 of which you can access free at:

<http://jap.physiology.org/cgi/content/full/92/6/2578#BIBL>

This article has been cited by 1 other HighWire hosted article:

Increased sympathetic and decreased parasympathetic cardiovascular modulation in normal humans with acute sleep deprivation

X. Zhong, H. J. Hilton, G. J. Gates, S. Jelic, Y. Stern, M. N. Bartels, R. E. DeMeersman and R. C. Basner

J Appl Physiol, June 1, 2005; 98 (6): 2024-2032.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Updated information and services including high-resolution figures, can be found at:

<http://jap.physiology.org/cgi/content/full/92/6/2578>

Additional material and information about *Journal of Applied Physiology* can be found at:

<http://www.the-aps.org/publications/jappl>

This information is current as of September 1, 2010 .

Effects of sleep pressure on endogenous cardiac autonomic activity and body temperature

ALEXANDRA L. HOLMES, HELEN J. BURGESS, AND DREW DAWSON
*Centre for Sleep Research, University of South Australia,
Woodville, South Australia 5011, Australia*

Received 5 November 2001; accepted in final form 19 February 2002

Holmes, Alexandra L., Helen J. Burgess, and Drew Dawson. Effects of sleep pressure on endogenous cardiac autonomic activity and body temperature. *J Appl Physiol* 92: 2578–2584, 2002. First published February 22, 2002; 10.1152/jappphysiol.01106.2001.—This study investigated the effects of variations in sleep pressure on cardiac autonomic activity and body temperature. In a counterbalanced design, 12 healthy, young subjects (6 men and 6 women) remained recumbent during 30 h of wakefulness (high sleep pressure) and 6 h of wakefulness (low sleep pressure). Both periods of wakefulness were immediately followed by a sleep opportunity, and the first 2 h of sleep were analyzed. During extended hours of wakefulness, a reduction in heart rate was mediated by a decline in cardiac sympathetic activity (measured via preejection period) and the maintenance of cardiac parasympathetic activity (measured via respiratory sinus arrhythmia). In subsequent high-pressure sleep, parasympathetic activity was amplified and sympathetic activity was negatively associated with electroencephalographic slow-wave activity. Sleep deprivation had no impact on foot temperature, but it did alter the pattern of change in core body temperature. A downregulation of cardiac autonomic activity during both extended hours of wakefulness and subsequent sleep may respectively provide “protection” and “recovery” from the temporal extension of cardiac demand.

slow-wave activity; sympathetic; heart rate variability; parasympathetic; constant routine

IT IS GENERALLY ACCEPTED THAT sleep deprivation affects a significant proportion of the population (3, 6). Shift workers are particularly likely to experience a sleep debt (23), and there is also an association between shift work and an increased incidence of cardiovascular disease (5, 19). Factors suggested to partially mediate the risk of cardiac disease in shift workers include a higher body mass index (33), lower socioeconomic status (34), and an increased incidence of smoking (4). In addition, it is possible that the extended hours of wakefulness often experienced by shift workers may have direct negative effects on cardiac activity.

In laboratory studies controlling for environmental and behavioral influences such as light, sleep, and activity, acute sleep deprivation (24–30 h) reportedly

reduced heart rate (HR) in healthy young subjects (8, 10, 17). This decline is typically superimposed on a 24-h rhythm. In controlled environments, acute sleep deprivation has also reduced other measures of physiological activity, such as muscle sympathetic nerve activity (16) and plasma cortisol (36) and plasma catecholamine levels (10).

The effects of extended hours of wakefulness on the two branches of cardiac autonomic activity have only been examined in one study. During a 24-h period of supine enforced wakefulness, cardiac sympathetic activity (SNS) was assessed with preejection period (PEP) via impedance cardiography, and cardiac parasympathetic activity (PNS) was assessed with respiratory sinus arrhythmia (RSA) from the spectral analysis of the electrocardiograph signal (8). Both branches decreased linearly; however, PNS activity was deemed to be influenced more strongly by the circadian system than the absence of sleep.

To our knowledge, only one study has measured the effect of sleep pressure on cardiac autonomic activity during sleep (14). This study investigated the effects of overnight sleep deprivation on cardiac activity during subsequent day sleep. During the first 90 min of recovery sleep, vagal tone measured via a beat-by-beat index of cardiac parasympathetic activity was significantly lower compared with normal nighttime sleep. However, because daytime sleep was compared with nighttime sleep, the effect was likely to be confounded by circadian phase. Furthermore, no measures of SNS activity were made.

The effects of variations in sleep pressure on endogenous cardiac autonomic activity during both wakefulness and sleep are not known. Therefore, the aim of this study was to systematically investigate the effects of acute sleep deprivation (high sleep pressure evoked by 30 h of wakefulness) on cardiac autonomic activity and to compare these effects with those of a short period of wakefulness (low sleep pressure evoked by 6 h of wakefulness). A sleep opportunity immediately followed both periods of wakefulness, and this occurred at the same time of day in both conditions to control for any circadian influences.

Address for reprint requests and other correspondence: A. L. Holmes, Centre for Sleep Research, Level 5 CDRC Bldg., The Queen Elizabeth Hospital, Woodville Rd., Woodville SA 5011, Australia (E-mail: alex.holmes@unisa.edu.au).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

It was hypothesized that extending wakefulness would decrease HR and that this would primarily be due to a reduction in SNS activity, rather than an increase in PNS activity. We also hypothesized that the decline in cardiac activity during sleep would be determined by the degree of prior wakefulness. Finally, because previous work indicates that SNS activity is primarily influenced by sleep (8), we anticipated that SNS activity during sleep would be related to electroencephalographic (EEG) slow-wave activity (SWA), a measure of sleep homeostasis.

METHODS

Subjects

Twelve healthy subjects (6 men and 6 women) aged between 18 and 30 yr (23.2 ± 2.0 yr) with an average body mass index (23.4 ± 2.9 kg/m²) participated in the study. Subjects and their parents had no cardiovascular or respiratory disease, and subjects were nonsmokers. All subjects were free from sleep disorders and did not regularly take daytime naps. Subjects did not regularly consume large amounts of caffeine (<350 mg/day) nor alcohol (≤ 5 standard drinks/wk) and participated in a moderate amount of exercise (≤ 10 h per wk). They were not taking any medication (presently or in the past week), except that all female subjects were taking an oral contraceptive. Subjects had not undertaken any shift work or transmeridian travel in the past 3 mo and were not experiencing major stress.

The laboratory procedures were approved by The Queen Elizabeth Hospital Human Research Ethics Committee and the University of South Australia Human Research Ethics Committee. All subjects gave written, informed consent before their participation, and the experiment conformed to the Declaration of Helsinki. Subjects received financial reimbursement for their time.

Design

The experiment was conducted at The Centre for Sleep Research at The Queen Elizabeth Hospital. Subjects were required to participate in two experimental conditions separated by at least 4 days (Fig. 1). Subjects were informed of the order of the two conditions before the study and maintained a self-selected constant sleep-wake cycle for 7 days before their first condition and between conditions. Wrist actigraphy recordings and sleep-wake diaries were collected to verify subjects' compliance. Participants abstained from alcohol, caffeine, and other stimulants for 24 h before and during the experiment.

Subjects slept at the laboratory for the two nights (adaptation and baseline) before both conditions. On these nights, the monitoring equipment detailed below was attached, and at each subject's normal sleep onset time the lights were turned out and they were permitted to sleep. All subjects were left undisturbed until their normal wake time, at which time they either left for a normal day or commenced one of the experimental conditions.

On waking, in both conditions subjects were allowed out of bed for 20 min during which time they ate breakfast and used the toilet; no showers were allowed. Subjects then returned to bed and remained awake for either 30 h in the high-sleep-pressure condition or 6 h in the low-sleep-pressure condition. Subjects were required to lie on their back, with their head and neck propped up by two pillows, and were requested to keep movement to a minimum. Continuous wakefulness was ensured by the constant observation of subjects in their bedrooms or via EEG signals. Ambient temperature was maintained at $22 \pm 1^\circ\text{C}$, and light intensity was <300 lux at the angle of gaze. During the experimental procedure, subjects wore shorts and a T-shirt. While in bed, they were covered by a sheet and were allowed to self-select the position of the bed covering with the restriction that this remained constant throughout the experiment. Subjects' feet remained covered by bedding at all times. They were allowed to read or watch television and had ad libitum access to water. At 2-h intervals, subjects were offered equicaloric (250 cal) snacks. After the designated period of wakefulness, bedroom lights were switched off and subjects were permitted to sleep in a quiet environment. In the 6-h condition, subjects left the laboratory after 3 h in bed. In the 30-h condition, they were allowed to leave the laboratory after 3 h in bed and were woken if they were still asleep after 5 h.

Assessment of sleep-wake state. Each subject's sleep-wake state was assessed according to standardized criteria by a central (C₃-A₂) and occipital (O₁-A₂) EEG, an electrooculogram (left and right outer canthi displaced vertically), and an electromyogram (26). Electrodes were connected to a Medilog MPA-2 sleep analysis system (Oxford Medical Limited, Oxtown, UK).

Assessment of HR. An electrocardiogram (ECG) was obtained from disposable pregelled Ag-AgCl ECG spot electrodes (Meditrace) that were placed at the jugular notch of the sternum, 4 cm under the left nipple and the right lateral side (ground). The electrodes were connected to a Vrije Universiteit ambulatory monitoring system (VU-AMS, version 4.6, TD-FPP, Vrije Universiteit, Amsterdam, The Netherlands). The ECG was recorded by the VU-AMS device by using an amplifier with a time constant of 0.3 s, 1 M Ω impedance, and a low-pass software filter of 17 Hz. Each

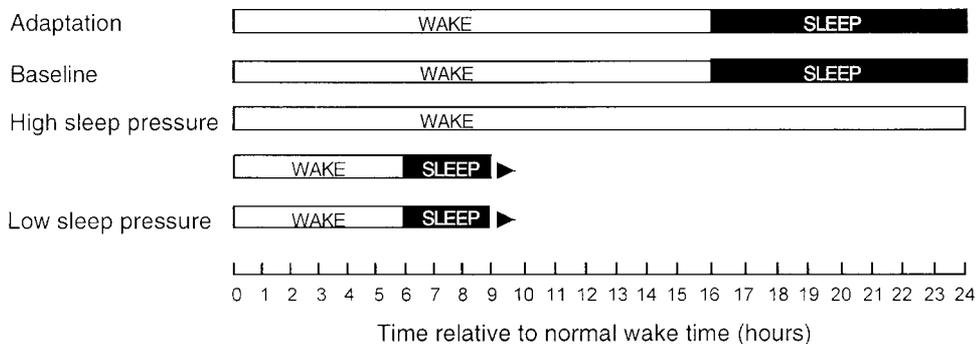


Fig. 1. Schematic diagram of the experimental protocol. Adaptation and baseline nights (subjects were not in the laboratory during the wake periods) and high-sleep-pressure (30 h of wakefulness in the laboratory) and low-sleep-pressure (6 h of wakefulness in the laboratory) conditions are illustrated. In both experimental conditions, the first 2 h of sleep were analyzed.

R peak was detected with a level detector with automatic level adjustment (32). From the R-peak time series, an average value for HR was obtained for each 30-s period.

Assessment of PEP. The VU-AMS also determined PEP via impedance cardiography. PEP is the most strongly validated and reliable noninvasive measure of cardiac β -adrenergic sympathetic activity (e.g., Refs. 1, 9). PEP approximates the isovolumetric contraction time of the left ventricle: as SNS activity increases, PEP shortens. To measure PEP, a 350- μ A current at 50 kHz was passed through the body via "current" electrodes on the base of the neck over vertebrae C₃–C₄ and on the back over vertebrae T₈–T₉. Two "recording" electrodes, on the jugular notch and xiphoid process of the sternum, measured the resulting impedance, from which the change in impedance with time (dZ/dt) was derived. The dZ/dt signal was sampled at 250 Hz and time locked to the R wave to enable 30-s ensemble averaging of the dZ/dt signal. Thus, for each 30-s period, PEP was later determined off-line as the time period between the R wave on the ECG signal and the upstroke on the ensemble-averaged dZ/dt signal. Reliability and validity of the VU-AMS device are described elsewhere (13, 37).

Assessment of RSA. The most valid and reliable noninvasive measure of PNS activity is RSA, a specific index of HR variability (e.g., Refs. 1, 9). Five-minute periods of cardiac beat-to-beat intervals (determined previously by the VU-AMS; see above) were selected for spectral analysis. Frequency domain analysis of the interbeat intervals was calculated by the CARSPAN program (ProGAMMA) that is based on sparse discrete Fourier transformation and produces a power spectrum from 0.01 to 0.50 Hz. The spectrum is based on a series of equidistant samples representing HR, obtained from low-pass filtering of the R-wave series as unit pulses. RSA was calculated as the power in the range of 0.15–0.40 Hz divided by the total power (0.04–0.50 Hz; e.g., Ref. 25).

Assessment of respiratory rate. Variations in respiratory rate (RR) can alter the magnitude of RSA independently of alterations in cardiac vagal tone (e.g., Ref. 2). To control for this, respiration was assessed using a thermistor (Thermocouple, Pro-tech, Washington, DC) taped under each subject's nose. The thermistor was attached to the Oxford system (used for sleep-wake assessment), and the number of breaths per second was calculated off-line.

Assessment of body temperature. Core temperature (T_c) was recorded by use of indwelling rectal thermistors (Steri-Probe 491B, Cincinnati Sub-Zero Products, Cincinnati, OH), self-inserted by the participants to 10 cm. Foot temperature (T_f) was measured by use of thermistors (Steri-Probe 499B, Cincinnati Sub-Zero Products) attached to the arches of the soles of both feet. Thermistors were connected by cable to a 486 computer, and the data were analyzed using a purpose-built temperature system (Strawberry Tree, Sunnyvale, CA). All temperatures were recorded at 30-s intervals with a sensitivity of 0.05°C.

Data Analysis

Sleep-wake activity. Polysomnographic data were collected during the 2 h after sleep onset in the high- and low-sleep-pressure conditions. The sleep recordings were visually scored in 30-s epochs according to standard criteria (26). Sleep-onset latency was calculated as the time from lights out to sleep onset (first of three consecutive 30-s epochs of scored sleep). SWA (0.33–3 Hz) was assessed for each 30-s epoch, with a period amplitude analysis of the central EEG signal as calculated by the sleep-analysis software (Medilog SAC Operator's Manual, Oxford Instruments).

Cardiac autonomic activity and body temperature. HR, PEP, T_c , and T_f (the temperatures of both feet were averaged to give a single measure) were automatically calculated for every 30-s period by using the AMS system and the temperature-analysis software. These values were averaged into 1-h bins for the wakefulness periods and 15-min bins for the sleep periods.

To obtain an hourly measure of RSA while subjects were awake, 5-min periods of data were selected from the half hour surrounding each new hour of wakefulness. During sleep, 5-min periods were selected continuously and then averaged into 15-min bins. A period was selected on the basis that it contained no abrupt changes in HR and minimal body movement. RR was calculated from the respiratory signal presented by the SAC. As a test of the integrity of the RSA data, the within-subject relationship between RR and RSA was examined (e.g., Ref. 2).

For all measures, the first hour of wakefulness data was not included to avoid major effects of changes in body fluid distribution associated with the initial commencement of the recumbent position. Data contaminated by movement were also discarded.

Statistical Analyses

Because baseline cardiac activity and body temperature can vary widely between individuals, measurements were recalculated for each subject relative to their individual mean during both conditions. These normalized data were used in the statistical analyses.

Wake. To assess the reliability of the data, a repeated-measures ANOVA compared the first 5 h of data collected during the high-sleep-pressure condition with that collected during the low-sleep-pressure condition. These were expected to be similar.

To determine the effects of sleep pressure, a repeated-measures ANOVA compared data collected during the first and last 5 h of the high-sleep-pressure condition. Furthermore, a linear regression was performed on all of the wakefulness data from the high-sleep-pressure condition to identify how much variance could be accounted for by the effects of increasing hours of wakefulness. This variance was removed before a 24-h fundamental curve with 12-h harmonic curves was fitted (KaleidaGraph version 3.08c, Synergy Software) to identify any circadian rhythmicity in the data.

Sleep. ANOVAs were conducted to assess the effect of sleep under different conditions of sleep pressure on each dependent variable. Data collected 2 h before and 2 h after sleep onset were used in analyses. A 2×2 ANOVA with repeated measures on each variable was used to compare state (wake vs. sleep) with condition (high vs. low sleep pressure). To investigate more closely the influence of prior wakefulness on cardiac activity, body temperature, and SWA during sleep, repeated-measures ANOVAs compared these variables during sleep in the two conditions.

Pearson product-moment correlations were performed between SWA and the other variables to investigate the possible influence of SWA on cardiac activity and/or body temperature. Each individual Pearson product-moment correlation was transformed to a Fisher Z score, the scores were averaged, and then the average Z score was reconverted back to a correlation. To confirm that RSA was not unduly influenced by RR, correlations were also calculated between RSA and RR within each subject. A group average was then calculated.

To account for the large number of repeated-measures analyses, all P values were based on the Huynh-Feldt corrected degrees of freedom. Statistical significance was determined at $P < 0.05$.

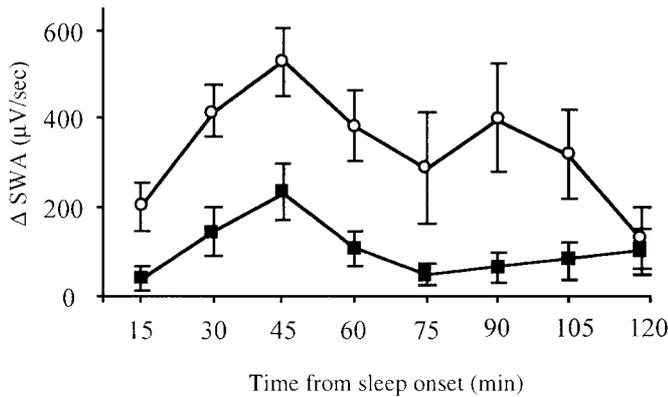


Fig. 2. Slow-wave activity (SWA) for 2 h after sleep onset in a high-sleep-pressure (\circ) and low-sleep-pressure (\blacksquare) condition. Data are averaged across 10 subjects. Values are means \pm SE (see RESULTS for explanation).

RESULTS

Preliminary Analyses

All variables were normally distributed. Because of technical difficulties, SWA and temperature data were lost from two subjects (1 man and 1 woman) during the high-sleep-pressure condition. All subjects slept for at least 2 h during the sleep opportunities in both conditions. After 30 h of continuous wakefulness, sleep-onset latency was significantly [$t(7) = 2.39, P < 0.05$] shorter (mean \pm SD: 4.08 ± 1.37 min) compared with after only 6 h of wakefulness (mean \pm SD: 12.33 ± 3.25 min). SWA was significantly higher [$F(1,9) = 25.43, P < 0.05$] in the high-sleep-pressure condition compared with the low-sleep-pressure condition, indicating that two conditions of differing sleep pressure were created (Fig. 2). SWA changed significantly over time [$F(7,63) = 3.6, P < 0.05$] in a manner that was not significantly different between conditions.

Cardiac autonomic activity (HR, PEP, and RSA) was not significantly different during the first 5 h of data collected in the two conditions. RR showed no significant effects of condition, time, or interaction between time and condition. No significant correlations between RR and RSA were identified, and the average correlation was 0.17 for the 30-h condition and -0.07 for the 6-h condition. Therefore, RR changes were not considered to have significantly affected the RSA data.

Wake

Extended hours of wakefulness significantly decreased HR [$F(1,11) = 30.33, P < 0.05$] and significantly increased PEP [reflecting a decrease in SNS activity; $F(1,11) = 16.00, P < 0.05$; Fig. 3]. Eighty-two

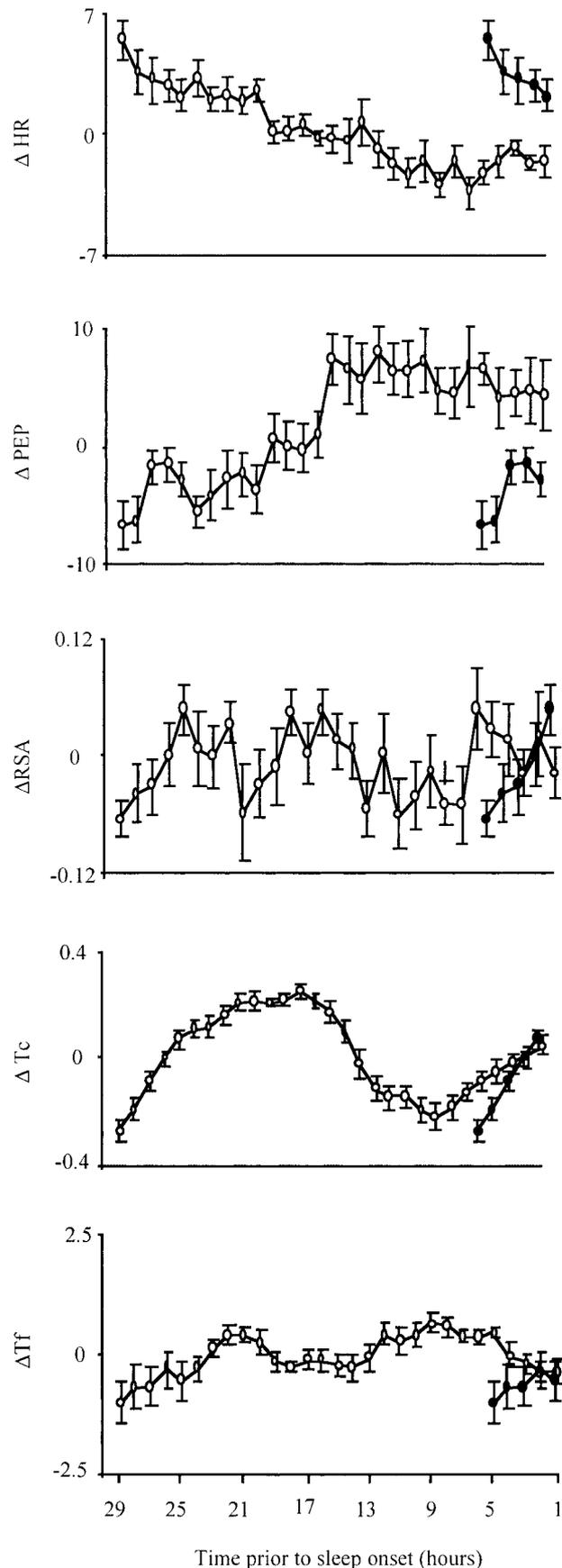


Fig. 3. Change (Δ) in cardiac and thermoregulatory variables during 30 h of wakefulness (\circ) and 6 h of wakefulness (\bullet). Data are ordered according to hours before subsequent sleep onset. Heart rate (HR, in beats/min), pre-ejection period (PEP, in ms), and respiratory sinus arrhythmia (RSA, in proportion of power spectrum) are averaged over 12 subjects; core body temperature (T_c , in $^{\circ}\text{C}$) and foot temperature (T_f , in $^{\circ}\text{C}$) are averaged over 10 subjects. Values are means \pm SE (see RESULTS for explanation).

percent [$F(1,27) = 125.87, P < 0.05$] and 69% [$F(1,27) = 60.58, P < 0.05$] of the variance in HR and PEP, respectively, could be accounted for by a linear regression. A complex cosine curve only accounted for 30% of the variation in HR and 55% of the variance in PEP. In contrast, RSA did not change significantly during the high-sleep-pressure condition. Additionally, the variance in RSA could not be significantly accounted for by a linear regression and was only minimally (21%) accounted for by a complex cosine curve.

Sleep pressure influenced the pattern of change in T_c [$F(4,36) = 6.72, P < 0.05$] but had no effect on T_f . During 30 h of wakefulness, a complex cosine curve accounted for 93% of the variance in T_c and 54% of the variance in T_f . The variance in both of these variables could not be accounted for by a linear regression.

Sleep

Figure 4 displays cardiac activity and body temperature during sleep in the two conditions. Compared with wakefulness, sleep lowered HR [$F(1,5) = 19.03, P < 0.05$] and increased both RSA [$F(1,5) = 24.25, P < 0.05$] and PEP [$F(1,5) = 8.39, P < 0.05$]. Furthermore, sleep after extended hours of wakefulness involved a relatively lower level of HR [$F(1,11) = 5.17, P < 0.05$] and relatively higher levels of RSA and PEP [$F(1,11) = 18.74, P < 0.05$ and $F(1,11) = 4.9, P < 0.05$, respectively]. The pattern of change of all variables during sleep was not significantly influenced by sleep pressure. Thus the between-condition differences in HR, RSA, and PEP primarily reflect changes evoked by sleep pressure during preceding wakefulness or sleep onset.

Specifically, RSA was higher during sleep after 30 h of wakefulness, because sleep pressure enhanced the increase in RSA associated with sleep onset [$F(1,5) = 6.64, P < 0.05$]. In contrast, PEP and HR were higher principally because of a continuation of the changes in these variables that occurred during prior wakefulness. Indeed, HR actually declined more with low-compared with high-pressure-sleep onset [$F(1,5) = 17.21, P < 0.05$].

Similarly to wakefulness, the pattern of change in T_c during sleep was significantly influenced by sleep pressure [$F(7,63) = 8.20, P < 0.05$]. T_f did increase during sleep [$F(7,63) = 6.61, P < 0.05$], but this effect was not significantly different between conditions.

SWA

SWA did not correlate highly with HR in either condition ($r = 0.08$ and $r = 0.02$ for the high- and low-sleep-pressure conditions respectively). In the high-sleep-pressure condition, SWA correlated moderately with PEP ($r = 0.48$) but was not associated with changes in RSA ($r = -0.04$). In contrast, in the low-sleep-pressure condition SWA correlated with RSA ($r = 0.45$) and not with PEP ($r = -0.05$).

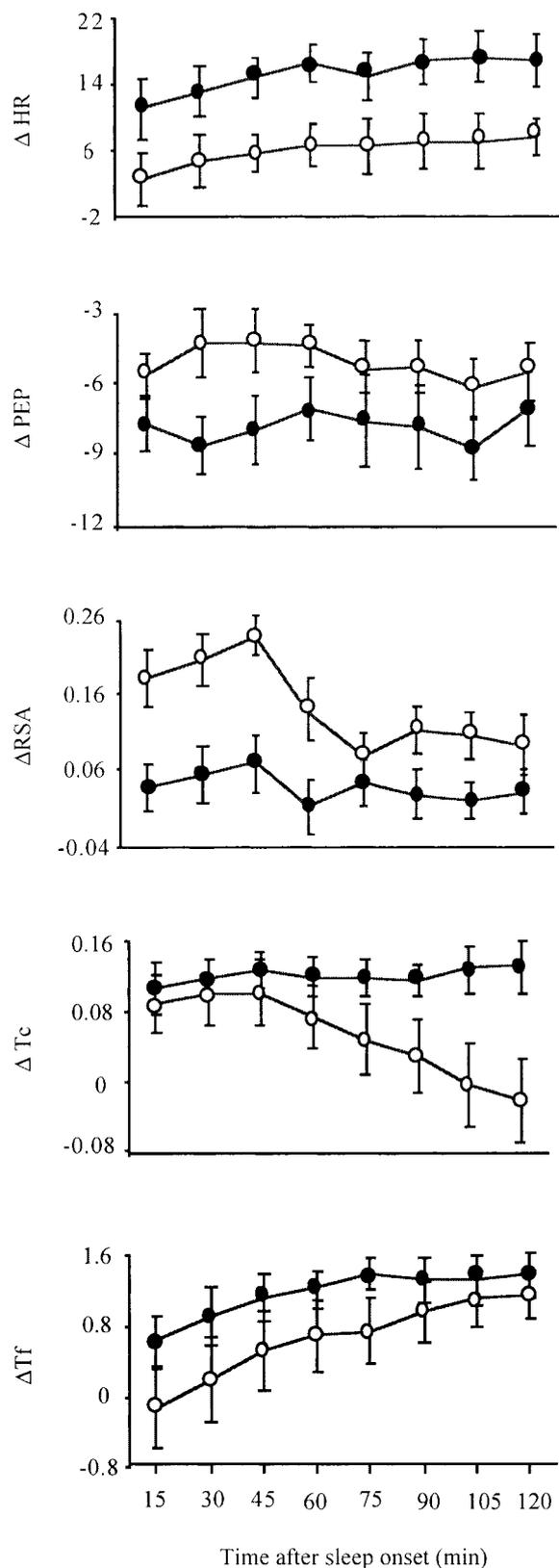


Fig. 4. Change (Δ) in cardiac and thermoregulatory variables during 2 h of sleep after 30 h of wakefulness (\circ) and 6 h of wakefulness (\bullet). Data are ordered according to minutes after sleep onset. HR, PEP, and RSA are averaged over 12 subjects; T_c and T_f are averaged over 10 subjects. Values are means \pm SE (see RESULTS for explanation).

DISCUSSION

This study suggests that increased sleep pressure downregulates cardiac autonomic activity during both wakefulness and subsequent sleep. During extended hours of wakefulness, a reduction in HR was driven by a decline in SNS activity. Ensuing high-pressure sleep amplified PNS activity and reduced SNS activity in a manner negatively correlated with the rebound in SWA. The observed reduction in cardiac autonomic activity during wakefulness and sleep could provide “protective” and “recuperative” value, respectively, and thereby limit the impact of extended hours of wakefulness on the cardiovascular system.

HR declined during 30 h of supine sleep deprivation [reduction of 8.78 ± 1.57 beats/min (mean \pm SD); Fig. 3] by a greater amount compared with during a 30-h sleep deprivation protocol in which the masking effects of posture were not controlled for (~ 3 beats/min decline; Ref. 11). This decline in cardiac activity was driven by a gradual reduction in SNS activity [increase in PEP of 13.21 ± 4.18 ms (mean \pm SD)] during the typical period wakefulness (16 h), and the plateauing of SNS activity as wakefulness extended into the night.

PNS activity was not influenced by increasing hours of wakefulness, instead remaining relatively stable before sleep onset. We did not observe the endogenous 24-h rhythm in RSA or HR previously observed in supine subjects (8) or the circadian variation in HR identified in nearly supine subjects (17). This discrepancy may be accounted for by the slightly elevated posture of subjects in the present study (two pillows behind the head). PNS activity is known to be blocked by higher postures via activation of the sympathetic response that prevents orthostatic hypotension (24), and this response may have limited the detection of circadian rhythmicity in PNS activity and HR. Correspondingly, previous studies have shown variations in RSA across the day in supine but not standing subjects (15).

To our knowledge, the effects of hours of prior wakefulness on cardiac autonomic activity during sleep have not been systematically investigated. High-pressure sleep involved an amplified level of PNS activity and a reduced level of SNS activity and HR and thus may have had enhanced “recovery” value for the autonomic nervous system activity (Fig. 4). PNS activity was higher because, whereas sleep in both conditions elevated PNS activity, high sleep pressure exaggerated this effect. The increment in PNS associated with nighttime sleep onset has previously been suggested to reflect a circadian influence (8). However, these results suggest that PNS activity is responsive to the sleep-wake process, and, in addition, sleep pressure.

SNS activity was lower during sleep after 30 h of wakefulness, primarily because of a continuation of the downregulation of this branch of the autonomic nervous system that occurred during extended prior wakefulness. Additionally, during high-pressure sleep, PEP was associated with SWA, suggesting that the “recovery” of these variables may be driven by the same

process(es). In accordance with this suggestion, slow-wave sleep after 40 h of sleep deprivation has been negatively correlated with plasma cortisol (36). In the low-sleep-pressure condition, no relationship was found between SWA and PEP. Similarly, during normal nighttime sleep, SWA and PEP (7) and SWS and plasma cortisol (36) are reportedly not related. Therefore, the relationship between SWA and PEP appears to be limited to conditions of high sleep pressure. RSA did correlate with SWA in the low-sleep-pressure condition, but this relationship probably reflects the relatively low level of activity in both of these variables after only 6 h of wakefulness.

In the present study, cardiac autonomic activity was necessarily assessed by using indirect measures. The valid use of these measures is based on a number of assumptions. Specifically, to limit the effects of preload and afterload on PEP, subjects should maintain a constant posture and keep movements to a minimum (9). Additionally, RR, tidal volume, central respiratory output, and intrathoracic pressure must remain relatively stable so as not to confound RSA (e.g., Ref. 2). In the present study, although the confounding effects of RR were directly assessed, tidal volume was not recorded because we were concerned that this could have disrupted subject's sleep (22, 28). Additionally, we were concerned that the use of a face mask may have artificially influenced respiration (perhaps providing extra unwanted feedback to the subject on their voluntary breathing pattern), thereby unduly influencing RSA. Because tidal volume and other respiratory variables were not assessed, caution should be taken in inferring that the observed changes in RSA are a direct reflection of PNS activity. During both sleep and sleep deprivation, a number of respiratory changes may have unduly influenced RSA. For example, sleep has been shown to evoke a decrease in tidal volume and the rib cage-abdominal motion ratio (21), and respiratory movement varies with sleep stage (27, 31). Additionally, sleep deprivation has been associated with a reduction in maximal voluntary ventilation (11). Nonetheless, the respiratory modulation of vagal activity during sleep has been reported as “slight” (12) and to account for only 8–15% of the variance in cardiorespiratory transfer (35).

In lieu of the hypothermic effect of nighttime sleep (18), high-pressure sleep appeared to curtail the circadian increase in T_c . This effect may have been mediated by a reduction in heat production alone because heat loss (indirectly measured by $T_{\dot{f}}$; Ref. 20) was similar in both conditions. Although heat production was not directly assessed in the present study, it has been suggested to be modulated by SNS activity (20, 29). Accordingly, the timing of maximal and minimal SNS activity (after 2 and 19 h of wakefulness, respectively) in this study coincides with previously reported times of maximal (0900–1200 h) and minimal (2400–0600 h) heat production, as measured via indirect calorimetry in constant routine conditions (20). HR is presently used as an indirect measure of heat production, but these findings suggest that use of cardiac SNS

activity as a potentially more specific measure deserves attention.

To put the present findings in context, the physiological consequences of an endogenously lowered sympathetic tone during prolonged wakefulness need to be identified. Endogenous lowering of cardiac activity may be adaptive in "protecting" against an increase in cardiac demand when hours of wakefulness are extended. Alternatively, it could necessitate amplification of the cardiac response to stress and/or physical demands and therefore have negative consequences for cardiac health. Additionally, further work could compare the cardiovascular response to acute sleep deprivation with the response to the more commonly experienced chronic sleep debt because these states may have disparate effects on some physiological systems (30).

This work was supported by an Australian Research Council grant awarded to D. Dawson and H. J. Burgess.

REFERENCES

- Berntson GG, Bigger JT, Eckberg DL, Grossman P, Kaufmann PG, Malik M, Nagaraja HN, Porges SW, Saul JP, Stone PH, and van der Molen MW. Heart rate variability: origins, methods, and interpretative caveats. *Psychophysiology* 34: 623–648, 1997.
- Berntson GG, Cacioppo JT, and Quigley KS. Respiratory sinus arrhythmia: autonomic origins, physiological mechanisms and psychophysiological implications. *Psychophysiology* 30: 183–196, 1993.
- Bliwise DL. Historical change in the report of daytime fatigue. *Sleep* 19: 462–464, 1996.
- Boggild H, Burr H, Tuchsén F, and Jeppesen HJ. Work environment of Danish shift and day workers. *Scand Work Environ Health* 27: 97–105, 2001.
- Boggild H and Knutsson A. Shift work, risk factors and cardiovascular disease. *Scand J Work Environ Health* 25: 85–99, 1999.
- Bonnet MH and Arand DL. We are chronically sleep deprived. *Sleep* 18: 908–911, 1995.
- Burgess HJ, Holmes AL, and Dawson D. The relationship between slow wave activity, body temperature and cardiac activity during night-time sleep. *Sleep* 24: 343–349, 2001.
- Burgess HJ, Trinder J, Kim Y, and Luke D. Sleep and circadian influences on cardiac autonomic nervous system activity. *Am J Physiol Heart Circ Physiol* 273: H1761–H1768, 1997.
- Cacioppo JT, Berntson GG, Binkley PF, Quigley KS, Uchino BN, and Fieldstone A. Autonomic cardiac control. II. Noninvasive indices and basal response as revealed by autonomic blockades. *Psychophysiology* 31: 586–598, 1994.
- Chen HI. Effects of 30-h sleep loss on cardiorespiratory functions at rest and in exercise. *Med Sci Sports Exerc* 23: 193–198, 1991.
- Cooper KR and Phillips BA. Effect of short-term sleep loss on breathing. *J Appl Physiol* 53: 855–858, 1982.
- Crasset V, Mezzetti S, Antione M, Linkowski P, Degaute JP, and van de Borne P. Effects of aging and cardiac denervation on heart rate variability during sleep. *Circulation* 103: 84–89, 2001.
- De Geus EJC, Willemsen GH, Klaver CH, and van Doornen LJ. Ambulatory measurement of respiratory sinus arrhythmia and respiration rate. *Biol Psychol* 41: 205–227, 1995.
- Delamont RS, Julu PO, and Jamal GA. Sleep deprivation and its effect on an index of cardiac parasympathetic activity in early non-REM sleep in normal and epileptic subjects. *Sleep* 21: 493–498, 1998.
- Hayano J, Sakakibara Y, Yamada M, Kamiya T, Fujinami T, Yokoyama K, Watanabe Y, and Takata K. Diurnal variations in vagal and sympathetic cardiac control. *Am J Physiol Heart Circ Physiol* 258: H642–H646, 1990.
- Kato M, Phillips BG, Sigurdsson G, Narkiewicz K, Pesek CA, and Sommers VK. Effects of sleep deprivation on neural circulatory control. *Hypertension* 35: 1173–1175, 2000.
- Kerkhof GA, van Dongen HPA, and Bobbert AC. Absence of endogenous circadian rhythmicity in blood pressure? *Am J Hypertens* 11: 373–377, 1998.
- Kleitman N. *Sleep and Wakefulness* (2nd ed.). Chicago, IL: University of Chicago Press, 1963.
- Knutsson A. Shift work and coronary heart disease. *Scand J Soc Med Suppl* 44: 1–36, 1989.
- Krauchi K and Wirz-Justice A. Circadian rhythm of heat production, heart rate, and skin and core temperature under unmasking conditions in men. *Am J Physiol Regulatory Integrative Comp Physiol* 267: R819–R829, 1994.
- Kreiger J. Breathing during sleep in normal subjects. In: *Principles and Practice of Sleep Medicine*, edited by Kreiger MH, Roth T, and Dement WC. Philadelphia, PA: Saunders, 1994, p. 212–223.
- Kreiger J and Kurtz D. Effects of pneumotachographic recording of breathing on sleep and respiration during sleep. *Bull Eur Physiopath Respir* 19: 641–644, 1983.
- Mahan RP, Carvalhais AB, and Queen SE. Sleep disruption in night-shift workers: is it sleep deprivation or a sleep disturbance disorder? *Percept Mot Skills* 70: 723–730, 1990.
- Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan R, Pizzinelli P, Sandrone G, Malfatto G, Dell'Orto S, Piccaluga E, Turial M, Baselli G, Cerutti S, and Maliani A. Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. *Circ Res* 59: 178–193, 1986.
- Phillips B. Sleep, sleep loss and breathing. *South Med J* 78: 1483–1486, 1985.
- Rechtschaffen A and Kales A. *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. Washington, DC: National Institute of Health, 1968.
- Sako T, Burioka N, Suyama H, Nomura T, Takeshima T, and Shimizu E. Nonlinear behaviour of human respiratory movement during different sleep stages. *Chronobiol Int* 18: 71–83, 2001.
- Smith S and Trinder J. The effect of arousals during sleep onset on estimates of sleep onset latency. *J Sleep Res* 9: 129–135, 2000.
- Snitker S, Macdonald E, Ravussin E, and Astrup A. The sympathetic system and obesity: role in aetiology and treatment. *Obes Rev* 1: 3–15, 2000.
- Spiegel K, Leproult R, and van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 354: 1435–1439, 1999.
- Stradling JR, Chadwick GA, and Frew AJ. Changes in ventilation and its components in normal subjects during sleep. *Thorax* 40: 364–370, 1985.
- Thakor NV, Webster JG, and Tompkins WJ. Optimal QRS detector. *Med Biol Eng Comput* 21: 343–350, 1983.
- Van Amelsvoort LG, Schouten EG, and Kok FJ. Duration of shiftwork related to body mass index and waist to hip ratio. *Int J Obes Relat Metab Disord* 23: 973–978, 1999.
- Van Cauter E and Spiegel K. Sleep as a mediator of the relationship between socioeconomic status and health: a hypothesis. *Ann NY Acad Sci* 896: 254–261, 1999.
- Van de Borne P, Biston P, Paive M, Nguyen H, Linkowski P, and Degaute J. Cardiorespiratory transfer during sleep: a study in healthy young men. *Am J Physiol Heart Circ Physiol* 269: H952–H958, 1995.
- Vgontzas AN, Mastorakos G, Bixler EO, Kales A, Gold PW, and Chrousos GP. Sleep deprivation effects on the activity of the hypothalamic-pituitary-adrenal and growth axes: potential clinical implications. *Clin Endocrinol (Oxf)* 51: 205–215, 1999.
- Willemsen GHM, de Geus EJC, Klaver CHAM, van Doornen LJP, and Carroll D. Ambulatory monitoring of the impedance cardiogram. *Psychophysiology* 33: 184–193, 1996.