Enhanced Cardiac Sympathetic Modulations during Sleep in Permanent Nightshift Nurses

Subtitle: Sleep and ANS Changes during Sleep in Nightshift Nurses

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Objectives The most common problem among the many health-related effects of shift work is disturbed sleep, with shift workers clearly having higher rates of cardiac disorders; however, the possible mechanism underlying shift-work-related health effects have yet to be examined. This study therefore set out to explore the influences of long-term nightshift work on the sleep patterns of nurses and on their cardiac autonomic nervous system during sleep.

Methods Our sample was made up of ten permanent nightshift and ten regular morning shift nurses. Nurses slept in their adaptable dormitory where they were allowed to spontaneously sleep and wake. All sleep parameters were digitized using an ambulatory polysomnographic recorder. Using sleep patterns and heart rate variability (HRV), the daytime sleep (P-daytime) and nighttime sleep (P-nighttime) of permanent nightshift nurses were compared to the nighttime sleep (R-nighttime) of regular morning shift nurses.

Results As compared to R-nighttime, P-daytime sleep patterns had significantly lower sleep onset latency, with the latter also having significantly greater proportions of Stage 3 and 4 and arousal index than their recorded levels during P-nighttime shift work. Both the low frequency (LF) and low to high frequency ratio (LF/HF) of P-nighttime nurses were significantly higher during periods of non-rapid eye movement (NREM) sleep than those of the R-nighttime nurses. In addition, the EEG delta-power of P-nighttime

was significantly lower during the first NREM episode (NREM1) sleep than those of both the P-daytime and R-nighttime.

Conclusions Permanent nightshift nurses had higher sympathetic activity during their sleep as compared to that of nighttime sleep of regular morning shift nurses. Night shift working may have effects on the sleeping patterns of nurses in the long run, inducing higher cardiac sympathetic regulation.

Key terms nightshift, nurse, sleep, electroencephalographic delta-power, autonomic nervous system, heart rate variability

Introduction

Permanent nightshift nurses must sleep during the day after working all night, which contradicts the normal diurnal rhythm. As a result, clear indications of physiological desynchronization of circadian rhythms have been found amongst nighttime workers, with this disturbance of biological rhythms potentially resulting in sleep deprivation and acting as a mediator of cardiovascular disease (1). Studies in papermill workers have shown that the quality of daytime sleep is characterized by reduced total sleep and differs from nighttime sleep (2). For temporary nightshift nurses, daytime sleep may be able to compensate for insufficient sleep. However, permanent nightshift nurses may suffer from a long-term sleep reduction when sleeping in the day time. The aim of this study was to examine whether sleep quality and sleep-related cardiac autonomic function differ between nurses working night shifts and those working morning shifts.

Heart rate variability (HRV), which is a measure of the autonomic cardiac control, can be used as markers of cardiac dysfunction (1). High frequency power (HF) mainly indicates cardiac vagal activity, whereas low frequency power (LF) to HF ratio (LF/HF) reflects cardiac sympathetic modulations or sympathovagal balance (3). Reduced cardiac vagal tone or impaired vagal function had an increased risk of hypertension (4) and coronary heart disease (5). In addition, a significant reduction in the LF/HF value is

demonstrated amongst nurses working night shifts as compared to those morning or afternoon shift. This reduction in cardiac sympathetic modulation indicates that nightshift nurses may well have some diminution in alertness during their working hours (6).

There are, however, very few studies which have set out to examine sleep disorders amongst nightshift nurses, as well as the resultant dysfunctions in the automatic nervous system which may be attributed to long-term nightshift working. Various studies have found that chronic insomniacs have an increased risk of coronary artery disease and hypertension (7-9). Shift workers are prone to higher rates of cardiac, gastrointestinal and reproductive disorders (10, 11). Furthermore, shift nurses have greater difficulty falling asleep or staying asleep; they also frequently suffer from severe autonomic disturbances (6, 12). Thus, a relationship is discernible between shift working and autonomic nervous system disturbances among nurses.

Sleep provides an important part of life both human and other mammals; however, several prior studies have demonstrated that the measurement of HRV whilst a person is awake may not reflect their HRV state during sleep (13, 14), since some delicate alternations, such as sympathetic activation accompanied by hypertension, are not readily detected without conducting a sleep study (13, 15). Recent improvements in sleep research techniques (13, 15-18) now allow us to test whether the sleep patterns

and sleep-related cardiac autonomic regulation are influenced by long-term nightshift work in nurses. It therefore seems appropriate to undertake an exploration of the changes in HRV which accompany sleep in order to clarify the pathways between cardiovascular disease and nurses engaged in shift working.

Methods

Participants and Procedures

All of the subjects were recruited from the Medical-Surgical Ward of the Songshan Armed Forces General Hospital. The circadian types could be categorized as Morning-types (M-types), Evening-types (E-types) and in between the Intermediate type (19). The Pittsburgh Sleep Quality Index (PSQI) (20) is a questionnaire which measures self-reported sleep habits over the previous one-month period, with a higher score indicating poorer sleep quality.

No significant differences were found between permanent nightshift nurses and regular morning shift nurses in terms of age, body mass index (BMI), years employed in nursing, blood pressure, tea or coffee consumption, sleep quality and circadian type. All of the subjects who choose to work permanently on night shifts were currently unmarried, with such choice having been made mainly for financial reasons and because of the alternatives that such work offered them. The exclusion criteria for these subjects included psychopathology, neurological disease, other cardiovascular disease, and any medication reported to influence sleep, the autonomic nervous system, and cardiovascular fluctuations (such as hypnotics and the subjects' self-reported caffeine or nicotine consumption). Informed written consent was obtained from all participants

and the experimental protocol was approved by the Ethics Committee of Tri-Service General Hospital in Taiwan.

Nurses in the permanent nightshift group worked three consecutive night shifts (from 11:30 PM to 7:30 AM), which was followed by two or three days off, and then a further three or four consecutive night shifts. Nurses in the regular morning shift group worked five consecutive morning shifts per week (from 8:00 AM to 4:00 PM), followed by two days off. After a day of habituation, polysomnographic recordings were performed during nighttime sleep after the second morning shift among regular morning shift nurses (R-nighttime) or daytime sleep after the second night shift among permanent nightshift nurses (P-daytime). We indicated in a prior study that a period of at least two consecutive days off was sufficient for nurses working night shifts to return to the normal nighttime sleep patterns of dayshift workers (21). Therefore, a further recording of permanent nightshift nurses was carried out during their nighttime sleep on their second day off (P-nighttime). The experimental group, which included the P-nighttime and P-daytime samples, was compared with the R-nighttime control group (R-nighttime). All subjects were encouraged to continue to follow their usual sleep habits in their own beds.

Data Recording

The recordings, which were carried out using electroencephalography (EEG, C3/Cz), electro-oculography (EOG), sub-mental electromyography (EMG) and electrocardiography (ECG), were synchronously digitized and stored in a memory card during the night or day using an ambulatory recorder. The filter bandwidths of the signals were using different multipliers, similar to a prior study on data acquisition, as follows: EEG (5,000), EMG (2,000), ECG (5,000), and EOG (1,000) (22).

Both EEG and EMG were filtered with 0.32–40 Hz, the EOG with 0.032–40 Hz and the ECG with 0.64–40 Hz. These bioelectric signals were relayed to an 8-bit analog-digital converter connected to an IBM PC-compatible computer. The EEG, EOG, EMG and ECG signals were synchronously digitized but at different sampling rates (128, 128, 128 and 256 Hz, respectively). The acquired data were analyzed on-line and stored simultaneously on a hard disk for subsequent off-line verification.

Digital Signal Processing

For sleep stage analysis, the data file was converted into European Data Format and then was imported into commercial sleep analysis software (Somnologica 3.1.2, Embla, USA). The computer assisted sleep analysis was carried out according to the criteria defined by Rechtschaffen and Kales (24). The score arousal means that the abrupt shift

of EEG frequency including alpha, theta and/or frequencies greater than 16 Hz (but not spindles) last at least 3 seconds, with at least 10 seconds of stable sleep preceding the change during sleep stages. The Scoring of arousal requires a concurrent increase in submental EMG lasting at least 1 second during REM sleep (24). However, the score of stage wakening has more than 50% of the epoch either reactive alpha or age-appropriate dominant posterior rhythm over the occipital region. Furthermore, arousal index and awaken index indicate that both times of arousals and awakenings were divided into total sleep time (24). The results were verified by a qualified sleep technician. The preprocessing of the ECG signals was designed according to the recommended procedures (3), which are described fully in previous reports (18, 23). In brief, the computer algorithm identified each normal ventricular discharge waveform and rejected each ventricular premature complex or noise according to its likelihood in a standard template. Stationary R-R intervals (RR) were re-sampled and interpolated at a rate of 8 Hz to provide continuity in the time domain. The sampling rate of EEG signals was also reduced to 64 Hz.

Power Spectral Analysis

The sleep periods marked from the first to third non-rapid eye movement sleep (NREM 1-3) and the first to third rapid eye movement sleep (REM 1-3), in addition, the

accompanying autonomic functions were analyzed. The EEG and RR signals analyzed were truncated into successive 64-second time segments (windows) with 50% (32-second) overlapping. A Hamming window was applied to each time segment to attenuate the leakage effect (22). Our algorithm then estimated the power density of the spectral components based on the fast Fourier transformation.

The resulting power spectrum was corrected for attenuation resulting from sampling and the application of the Hamming window (23). They consequently underwent fast Fourier transformation after applying the Hamming window. For each 64-second time segment, we quantified the high-frequency (HF, 0.15–0.4 Hz) and low-frequency power (LF, 0.04–0.15 Hz) of the RR spectrogram (16), and the delta power (0.5–4 Hz) of the EEG spectrogram. The LF to HF ratio (LF/HF) was calculated as well. The HF indicates cardiac vagal activity whereas LF/HF reflects cardiac sympathetic modulations or sympathovagal balance (3). EEG delta-power are a characteristic of NREM and is used to define deep (stage 3 and 4) sleep (24).

Statistical Analysis

The first step of our analyses involved a comparison of the basic characteristics of the study subjects in order to ensure total comparability between the control and experimental groups. The demographic variables of employment, heart rate, blood pressure, tea/coffee consumption, type of morningness/eveningness, and the scores of

sleep quality were presented as mean ± standard deviation (SD) for continuous variables and numbers for categorical factors with proper statistic tests performed.

The specific design included two comparison scenarios: (i) comparisons between P-nighttime and P-daytime samples in the experimental group; and (ii) the comparison of each P-nighttime and P-daytime sample with the R-nighttime control group. The comparisons of the sleep pattern indices during REM or NREM periods of sleep were carried out using Mann-Whitney U tests for regular morning shift nurses and permanent night shift nurses, and Wilcoxon Sign-Rank test for the experimental group. A similar analysis strategy was then performed for the logarithmically transformed EEG delta-powers, HF, LF and LF/HF of the RR spectrogram in order to correct for the skewness of their distributions (23). All of the statistical analyses in this study were undertaken using the SPSS 13.0 for Windows software package, with the *P*-value of less than 0.05 being considered to be statistically significant.

Results

As shown in Table 1, no significant differences were identified between two groups according to the baseline comparisons, with both of the groups being young and healthy nurses, and therefore providing a solid comparison basis. Based upon a comparison with the R-nighttime sleep patterns, the P-daytime nurses were found to have significantly lower sleep onset latency. Nevertheless, as shown in Table 2, the P-daytime nurses were also found to have significantly greater proportions of Stage 3 and 4 sleep, and arousal index, than their recorded levels during P-nighttime shift work. The EEG delta-power during the first NREM episode (NREM1) and the arousal index of the P-nighttime was significantly lower than the values for the P-daytime and R-nighttime nurses (Figure 1 and Table 2).

As regards cardiac autonomic function, the LF and LF/HF of in the P-nighttime sleep patterns were both found to be significantly higher than those of the R-nighttime sleep patterns. Furthermore, as compared to the P-daytime sample, the P-nighttime exhibited higher LF and LF/HF values during their sleep, albeit with no statistical significance. The HRV analyses from the first to the third REM and NREM, which were summarized in Figure 2, reveal slight, but important, differences between the different shifts. The RR of the P-nighttime during NREM2, REM2, REM3 sleep

periods and the RR of P-daytime during REM3 sleep periods were found to be significantly higher than those of the R-nighttime. The LF of P-nighttime group during NREM1-3, REM1, REM2 sleep periods were significantly higher than that of R-nighttime group, as was the LF of P-daytime during NREM1-3, and REM1, REM3 sleep periods. The LF/HF of P-nighttime during NREM1-3, REM1 sleep periods, and that of P-daytime group during NREM3 sleep periods were also found to be significantly higher than those of R-nighttime. Finally, within the experimental group, the LF/HF during the sleeping periods of the P-daytime nurses was found to be significantly lower than that of P-nighttime nurses during their NREM1 and REM1 sleep periods.

Discussion

This paper indicated that sleep patterns and cardiac autonomic activity during sleep did differ between nurses working only night shifts and those working only morning shifts. We found that nurses working night shifts had significantly higher LF and cardiac LF/HF values, particularly during periods of NREM sleep, as compared to regular morning shift nurses. Furthermore, the daytime sleep of permanent nightshift nurses showed significantly higher proportions of slow wave sleep (Stage 3 and 4), arousal index, and EEG delta-power during the first episode sleep (NREM1), as compared to their nighttime sleep periods. Based upon the different sleep patterns, we found that Cardiac LF was permanently higher amongst permanent nightshift nurses independent of nighttime or daytime sleep. The findings of this study suggested that nighttime workers would seem to have higher cardiac sympathetic regulations attributable to long-term night shift working, a finding which may explain why shift workers were found to have higher rates of cardiac disorders. Sleep assigned according to a predetermined schedule in the laboratory schedule can sometimes fail to reflect the habitual sleeping time (27-29). Our design allowed nurses to spontaneously sleep in their own beds, with accustomed privacy and according to flexible nightshift sleep schedule.

The spectral analysis of R-R intervals assessing HRV was reported a lower LF/HF value during periods of NREM sleep than during periods of REM sleep amongst permanent nightshift nurses; however, this study indicated that there were similar elevations during both NREM and REM sleep. Sleep characterized by autonomic nervous activity were found to be in line with the findings of the prior studies (30, 31), which revealed a sympathetic dominance in the autonomic system during REM sleep. However, this result contradicted the expectation of vagal influence being predominant during NREM sleep.

The present study demonstrated, as compared to regular morning shift nurses, permanent nightshift nurses had higher LF/HF and LF values, especially the LF was shown to be significantly higher, independent of nighttime or daytime sleep. It is now becoming increasing recognized that LF levels are influenced by both sympathetic and vagal modulations (3). This elevation of the LF value may explain the higher sympathetic activity induced; thus, the LF value may prove to be a good marker for night shift nurses.

It has been indicated, in one particular prior study, that a reduction in sympathetic activity, which could preserve the perfusion of the heart though an appropriate reduction in vascular resistance, may be responsible for attenuating the workload on the heart during periods of NREM sleep (32). In this study, the notable increase in

sympathetic activity during periods of NREM sleep was found to lead to an increase in workload on the heart, which may explain the mechanisms linking shift work to cardiovascular events. We argue that there are several reasons why permanent nightshift nurses have higher HRV sympathetic activity during sleep.

Firstly, the shift schedule involved three or four night shifts in a row, followed by two days off between these consecutive shift periods. When nurses are off their work schedules, they return to nighttime sleep. That is, permanent nightshift nurses usually sleep during the day, but sometimes sleep at night. Thus, the nightshift nurses became more biologically adapted to sleeping during the day and working throughout the night. However, no discernible differences were found between the different shift nurses during their waking hours, and this study also found no significant difference in terms of total sleep time and sleep efficiency to support this hypothesis of circadian adaptation (Table 2).

Related studies have indicated that autonomic activity shows a diurnal pattern and the sympathetic activity is also prevalent during the working time (6); thus, the sympathetic activity may be elevated during the night time, regardless of whether a subject is working or sleeping. Furthermore, the potential effects of the diurnal pattern on the autonomic activity found to be related to higher sympathetic activity during periods of daytime sleep. This study indicated that P-nighttime nurses had significantly

higher LF/HF values than those of the R-nighttime nurses, particularly during periods of NREM1 sleep. According to Endo et al., the rapid REM accumulation may be attributable to circadian influence, with the distribution of REM sleep being reliant upon the circadian phase over consecutive cycles (33). Therefore, we inferred that as night shift nurses sometimes sleep during the day; the sleep pattern had a greater effect on the cardiac autonomic function during the first episode of REM sleep. However, the LF/HF of P-daytime and P-nighttime nurses revealed a significantly higher value during periods of NREM3 sleep, as compared to the LF/HF value for R-nighttime nurses. Parker et al reported that there was a delay when a person normally rises from bed, there will be a delay in the timing of the morning increase in myocardial ischemic episodes (34). This result was in line with this previous study, which indicated that the augmentation of sympathetic activity was induced around 1:00 PM, with this situation proving the elevated risk of cardiovascular disease in the early afternoon.

Secondly, we demonstrated in the present study that as compared to the R-nighttime nurses, nightshift nurses had lower EEG delta-power during both their nighttime sleep and daytime sleep (Table 2); however, the higher EEG delta activity during their daytime sleep was still found to be lower than that of regular morning shift nurses. EEG delta-power is a characteristic of NREM and is used to define deep sleep (Stage 3 and 4) (24). Several prior experimental studies have revealed that slow wave

activity during periods of NREM sleep is reliant on prior waking time (33, 35, 36). We argue that the P-daytime nurses may have longer periods of restlessness and exhaustion before eventually falling asleep, since we find that as compared to their nighttime sleep, daytime sleep has lower sleep onset latency and significantly higher proportions of Stage 3 and stage 4 (deeper sleep) thereby explaining the obvious exhaustion of nurses following periods of nighttime working. Our results also indicated that the total sleep time for daytime sleep was a slightly shorter than that for nighttime sleep, which is consistent with several of the prior studies on healthy men (2, 33, 35, 37). That is, there is a tendency for permanent nightshift nurses to develop worse sleep quality and a small, but cumulative, sleep deficit. It has been known that deeper sleep was accompanied by further suppression of the sympathetic function (16). Thus the higher sympathetic tone could be explained by the lower EEG delta-power and a higher proportion of deeper sleep.

Thirdly, frequent exposure to environmental factors (i.e., light, as well as social factors) may be another important issue; this is because, although permanent nightshift nurses become accustomed to sleeping during the day, the influence of morning light is unavoidable before, during and after their periods of daytime sleep in the nurses' dormitory. The prior studies have indicated that exposure to bright light certainly enhances activity in the sympathetic nervous system (38). It is worth noting that the

morning light (entering through the bedroom windows) appeared to have some effects on the autonomic nervous system of nurses. If this was the case, we may assume that as time progresses, nurses would increasingly grow accustomed to their environment, resulting in subtle changes to activity within their autonomic nervous system; therefore, cumulative enhancement of sympathetic activity may be developed, despite any reduction in competing social and/or domestic factors.

In the current study, none of the participants had children, and many of them had succeeded in minimizing the competing social factors to set sleep as their first priority. Although the participants were encouraged to sleep as long as they could, we found that most permanent nightshift nurses usually slept until afternoon, when they woke for lunch, then they may elect to sleep for a while before their night shift. The effects of this pattern of two periods of sleep in permanent nightshift nurses are worthy of further investigation.

We identified changes in EEG, EMG, EOG and HRV among permanent night nurses for reference purposes; however, consecutive monitoring of sleep over several nights is necessary to produce additional data to provide a more complete picture of possible changes in sleeping pattern. The nurses who participated in the study had approximately 2 years of work experience on the night shift. In a future study, we plan to compare nurses with 2 years of nightshift experience to nurses with 10 years of

nightshift experience and also to nurses with less than 1 year of nightshift experience. These should help to provide a better understanding of how sleep might affect their performance at work.

This study included only a small sample of nurses; thus, it was very low power, particularly in terms of finding differences between various shifts. However, our results clearly indicate that in the long run, night working has effects on sleep-related cardiac autonomic function. This study provided only a brief picture of daytime sleeping patterns in nightshift nurses working three or four consecutive night shifts and then returning to nighttime sleep during their days off. Sleeping patterns over several nights, as well as after long vacations, would seem to be warrant future study.

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References

1.Knutsson A, Boggild H. Shiftwork and cardiovascular disease: review of disease mechanisms. Rev Environ Health 2000;15:359-72.

2. Dahlgren K. Adjustment of circadian rhythms and EEG sleep functions to day and

night sleep among permanent nightworkers and rotating shiftworkers. Psychophysiology 1981;18:381-91.

3. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996;93:1043-65.
4. Grossman P, Brinkman A, de Vries J. Cardiac autonomic mechanisms associated with borderline hypertension under varying behavioral demands: evidence for attenuated parasympathetic tone but not for enhanced beta-adrenergic activity. Psychophysiology 1992;29:698-711.
5. Hayano J, Yamada A, Mukai S, Sakakibara Y, Yamada M, Ohte N, *et al.* Severity of coronary atherosclerosis correlates with the respiratory component of heart rate variability. Am Heart J 1991;121:1070-9.
6. Furlan R, Guzzetti S, Crivellaro W, Dassi S, Tinelli M, Baselli G, *et al.* Continuous 24-hour assessment of the neural regulation of systemic arterial pressure and RR variabilities in ambulant subjects. Circulation 1990;81:537-47.
7. Bonnet MH, Arand DL. Heart rate variability: sleep stage, time of night, and arousal influences. Electroencephalogr Clin Neurophysiol 1997;102:390-6.
8. Schwartz S, McDowell Anderson W, Cole SR, Cornoni-Huntley J, Hays JC, Blazer D. Insomnia and heart disease: a review of epidemiologic studies. J Psychosom Res 1999;47:313-33.
9. Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. J Occup Health 2003;45:344-50.
10. Wilson JL. The impact of shift patterns on healthcare professionals. J Nurs Manag 2002;10:211-9.
11. Muecke S. Effects of rotating night shifts: literature review. J Adv Nurs 2005;50:433-9.

12. Freitas J, Lago P, Puig J, Carvalho MJ, Costa O, de Freitas AF. Circadian heart rate variability rhythm in shift workers. J Electrocardiol 1997;30:39-44.
13. Kuo TBJ, Lai CJ, Shaw FZ, Lai CW, Yang CCH. Sleep-related sympathovagal imbalance in SHR. Am J Physiol Heart Circ Physiol 2004;286:H1170-6.
14. Baharav A, Kotagal S, Gibbons V, Rubin BK, Pratt G, Karin J, *et al.* Fluctuations in autonomic nervous activity during sleep displayed by power spectrum analysis of heart rate variability. Neurology 1995;45:1183-7.
15. Chen HY, Kuo TBJ, Shaw FZ, Lai CJ, Yang CCH. Sleep-related vagotonic effect of zolpidem in rats. Psychopharmacology (Berl) 2005;181:270-9.
16. Yang CCH, Lai CW, Lai HY, Kuo TBJ. Relationship between electroencephalogram slow-wave magnitude and heart rate variability during sleep in humans. Neurosci Lett 2002;329:213-6.
17. Kuo TBJ, Yang CCH. Scatterplot analysis of EEG slow-wave magnitude and heart rate variability: an integrative exploration of cerebral cortical and autonomic functions. Sleep 2004;27:648-56.
18. Kuo TBJ, Shaw FZ, Lai CJ, Lai CW, Yang CCH. Changes in sleep patterns in spontaneously hypertensive rats. Sleep 2004;27:406-12.
19. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. Int J Chronobiol 1976;4:97-110.
20. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
21. Ahasan R, Lewko J, Campbell D, Salmoni A. Adaptation to night shifts and synchronisation processes of night workers. J Physiol Anthropol Appl Human Sci 2001;20:215-26.

22. Kuo TBJ, Chan SH. Continuous, on-line, real-time spectral analysis of systemic arterial pressure signals. Am J Physiol 1993;264:H2208-13.
23. Kuo TBJ, Lin T, Yang CCH, Li CL, Chen CF, Chou P. Effect of aging on gender differences in neural control of heart rate. Am J Physiol 1999;277:H2233-9.
24. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques, and scoring system for sleep stages of Human subjects. Psychopharmacology (Berl) 1968;181:270-9.
25. Yang CCH, Shaw FZ, Lai CJ, Kuo TBJ. Relationship between electroencephalogram slow-wave magnitude and heart rate variability during sleep in rats. Neurosci Lett 2002;336:21-4.
26. Kuo TBJ, Yang CCH. Sleep-related changes in cardiovascular neural regulation in spontaneously hypertensive rats. Circulation 2005;112:849-54.
27. Luoh HF, Kuo TBJ, Chan SHH, Pan WH. Power spectral analysis of electroencephalographic desynchronization induced by cocaine in rats: correlation with microdialysis evaluation of dopaminergic neurotransmission at the medial prefrontal cortex. Synapse 1994;16:29-35.
28. Cajochen C, Brunner DP, Krauchi K, Graw P, Wirz-Justice A. Power density in theta/alpha frequencies of the waking EEG progressively increases during sustained wakefulness. Sleep 1995;18:890-4.
29. Finelli LA, Baumann H, Borbely AA, Achermann P. Dual electroencephalogram markers of human sleep homeostasis: correlation between theta activity in waking and slow-wave activity in sleep. Neuroscience 2000;101:523-9.
30. Somers VK, Anderson EA, Mark AL. Sympathetic neural mechanisms in human hypertension. Curr Opin Nephrol Hypertens 1993;2:96-105.
31. Ako M, Kawara T, Uchida S, Miyazaki S, Nishihara K, Mukai J, *et al.* Correlation between electroencephalography and heart rate variability during sleep. Psychiatry

Clin Neurosci 2003;57:59-65.

32. Mancia G. Autonomic modulation of the cardiovascular system during sleep. N Engl J Med 1993;328:347-9.
33. Endo S, Kobayashi T, Yamamoto T, Fukuda H, Sasaki M, Ohta T. Persistence of the circadian rhythm of REM sleep: a variety of experimental manipulations of the sleep-wake cycle. Sleep 1981;4:319-28.
34. Parker JD, Testa MA, Jimenez AH, Tofler GH, Muller JE, Parker JO, *et al.* Morning increase in ambulatory ischemia in patients with stable coronary artery disease. Importance of physical activity and increased cardiac demand. Circulation 1994;89:604-14.
35. Borbely AA, Baumann F, Brandeis D, Strauch I, Lehmann D. Sleep deprivation: effect on sleep stages and EEG power density in man. Electroencephalogr Clin Neurophysiol 1981;51:483-95.
36. Dijk DJ, Brunner DP, Beersma DG, Borbely AA. Electroencephalogram power density and slow wave sleep as a function of prior waking and circadian phase. Sleep 1990;13:430-40.
37. Akerstedt T, Kecklund G, Knutsson A. Spectral analysis of sleep electroencephalography in rotating three-shift work. Scand J Work Environ Health 1991;17:330-6.
38. Saito Y, Shimizu T, Takahashi Y, Mishima K, Takahashi K, Ogawa Y, *et al.* Effect of bright light exposure on muscle sympathetic nerve activity in human. Neurosci Lett 1996;219:135-7.
39. Dijk DJ, Brunner DP, Borbely AA. EEG power density during recovery sleep in the morning. Electroencephalogr Clin Neurophysiol 1991;78:203-14.
40. Ito H, Nozaki M, Maruyama T, Kaji Y, Tsuda Y. Shift work modifies the circadian patterns of heart rate variability in nurses. Int J Cardiol 2001;79:231-6.

41. Stauss HM, Mrowka R, Nafz B, Patzak A, Unger T, Persson PB. Does low frequency power of arterial blood pressure reflect sympathetic tone? J Auton Nerv Syst 1995;54:145-54.
42. Friberg P, Karlsson B, Nordlander M. Sympathetic and parasympathetic influence on blood pressure and heart rate variability in Wistar-Kyoto and spontaneously hypertensive rats. J Hypertens Suppl 1988;6:S58-60.
43. Lucini D, Mela GS, Malliani A, Pagani M. Impairment in cardiac autonomic regulation preceding arterial hypertension in humans: insights from spectral analysis of beat-by-beat cardiovascular variability. Circulation 2002;106:2673-9.
44. Galinier M, Pathak A, Fourcade J, Aloun JS, Massabuau P, Curnier D, *et al.* Left ventricular hypertrophy and sinus variability in arterial hypertension. Arch Mal Coeur Vaiss 2001;94:790-4.

Table 1. The basic characteristics for comparisons of experimental and control groups

Variable	Control group (n = 10)	Experimental group (n = 10)	p value^
Age, yr	29.00 ± 2.91	26.90 ± 2.60	0.11
Years employed in Nursing, yr	3.10 ± 2.03	4.30 ± 1.70	0.17
Body mass index	20.00 ± 1.14	20.34 ± 1.83	0.62
Heart rate, bpm	76.70 ± 7.89	77.40 ± 4.55	0.81
Diastolic blood pressure, mmHg	71.40 ± 5.17	71.30 ± 7.51	0.97
Systolic blood pressure, mmHg	117.6 ± 6.38	111.60 ± 5.13	0.33
Tea consumption			
Never	4	2	0.62
< 1 per week	1	1	
1-2 per week	3	2	
3-4 per week	1	4	
5-7 per week	1	1	
Coffee consumption			
Never	5	4	0.38
< 1 per week	1	2	
1-2 per week	2	0	
3-4 per week	0	0	
5-7 per week	2	4	
Global PSQI	8.80 ± 2.86	7.10 ± 2.33	0.32
Diurnal type (morningness / eveningness)			
Morningness	1	2	0.23
Neither	9	6	
Eveningness	0	2	

^ Mann-Whitney U tests for continuous variables and Chi-square tests for categorical variables; the data are expressed as mean ± SD of 10 nurses per group.

Note: control group (regular morning shift nurse); experimental group (permanent night-shift nurses); Pittsburgh Sleep Quality Index (PSQI)

Table 2. The differences of sleep patterns between shifts

Variable	Control group (R-nighttime) (n = 10)	Experimental group (n = 10)	
		P-nighttime	P-daytime
Total sleep time, min	359.89 ± 43.39	362.55 ± 97.53	330.15 ± 136.84
Wake after sleep onset, min	31.48 ± 28.62	25.74 ± 12.82	21.32 ± 17.48
Sleep onset latency, min	15.50 ± 12.92	14.45 ± 20.06	4.65 ± 1.73 *
Sleep efficiency, %	0.89 ± 0.08	0.90 ± 0.07	0.92 ± 0.07
Stage l, %	9.35 ± 3.77	8.39 ± 4.18	7.40 ± 5.11
Stage 2, %	62.17 ± 7.90	61.44 ± 8.17	60.44 ± 10.84
Stage 3+4, %	4.81 ± 7.17	1.54 ± 2.24	7.39 ± 5.92†
REM , %	23.67 ± 6.96	28.63 ± 7.46	23.17 ± 5.76
REM latency from sleep onset , min	97.60 ± 64.52	61.60 ± 21.68	63.35 ± 26.50
Number of sleep stage transitions/hour	15.78 ± 4.84	14.54 ± 3.71	16.12 ± 5.49
Awakening index, times/hr	4.02 ± 1.49	4.53 ± 1.42	3.22 ± 1.26
Arousal index, times/hr	3.91 ± 1.61	2.69 ± 0.65 *	3.71 ± 1.24†
Delta power, ln(μV^2)	3.82 ± 0.75	3.41 ± 0.78	3.74 ± 0.63

* : Pairs with statistical differences for shifts in experiment group comparing to control group by Mann-Whitney U tests;

† : Statistical significance within experiment group by Wilcoxon Sign-Rank test;

* P< .05 vs R-nighttime, † P< .05 vs P-nighttime; The data are expressed as mean ± SD of 10 nurses per group.

Note: the nighttime sleep of regular morning shift (R-nighttime); the nighttime sleep of night shift (P-nighttime); the daytime sleep of night shift (P-daytime).

Table 3. Comparisons of cardiac autonomic functions between different shifts

Variable	Control group (R-nighttime) (n = 10)	Experimental group (n = 10)	
		P-nighttime	P-daytime
Awake			
RR, ms	829.88 ± 49.85	858.37 ± 83.06	750.85 ± 267.23
HF, ln(ms^2)	6.05 ± 0.71	6.30 ± 0.84	6.38 ± 0.79
LF, ln(ms^2)	6.68 ± 0.67	7.08 ± 0.57	7.17 ± 0.60
LF/HF, ratio	0.66 ± 0.45	0.79 ± 0.44	0.79 ± 0.75
NREM sleep			
RR, ms	914.99 ± 52.42	990.40 ± 86.39 *	963.95 ± 97.26
HF, ln(ms^2)	6.22 ± 0.66	6.35 ± 0.90	6.44 ± 0.79
LF, ln(ms^2)	6.18 ± 0.58	7.01 ± 0.61*	6.84 ± 0.47*
LF/HF, ratio	-0.04 ± 0.40	0.61 ± 0.56*	0.40 ± 0.58
REM sleep			
RR, ms	882.89 ± 63.32	963.50 ± 73.76*	926.96 ± 91.93
HF, ln(ms^2)	5.91 ± 0.56	6.30 ± 0.92	6.34 ± 0.74
LF, ln(ms^2)	6.71 ± 0.44	7.45 ± 0.63 *	7.34 ± 0.41*
LF/HF, ratio	0.79 ± 0.35	1.14 ± 0.48	1.01 ± 0.50

* : Pairs with statistical differences for shifts in experiment group comparing to control group by Mann-Whitney U tests;

† : Statistical significance within experiment group by Wilcoxon Sign-Rank test;

*P< .05 vs R-nighttime; the data are expressed as mean ± SD of 10 nurses per group.

Note: the nighttime sleep of regular morning shift (R-nighttime); the nighttime sleep of night shift (P-nighttime); the daytime sleep of night shift (P-daytime); R-R intervals (RR), high-frequency power (HF), low-frequency power (LF) and the LF-to-HF ratio (LF/HF).

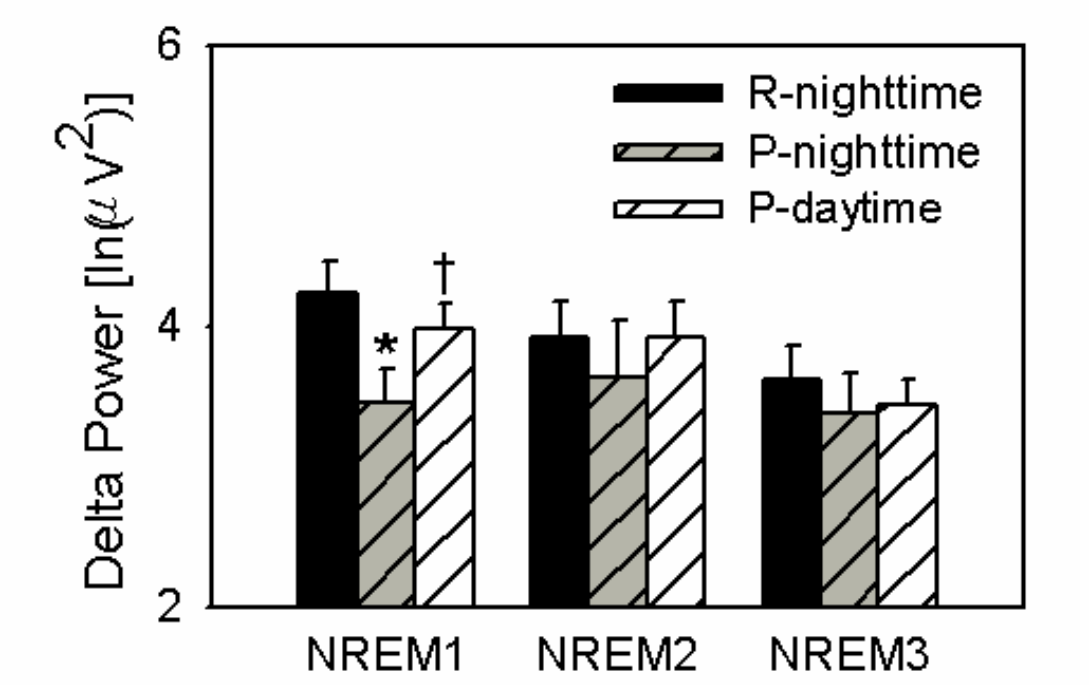

Figure1. Electroencephalographic delta-power *during periods of NREM and REM sleep*Notes:

The figure illustrates Electroencephalographic delta-power magnitude during 1-3 periods of non rapid eye movement (NREM) and rapid eye movement (REM) nighttime sleep for the nighttime sleep of regular morning shift (R-nighttime); the nighttime sleep of night shift (P-nighttime); the daytime sleep of night shift (P-daytime) nurses. The data are expressed as mean ± SEM of 10 nurses per group. Superscripts indicate p-values as follows: $^{*}P < .05$ vs R-nighttime, $^{\dagger}P < .05$ vs P-nighttime.

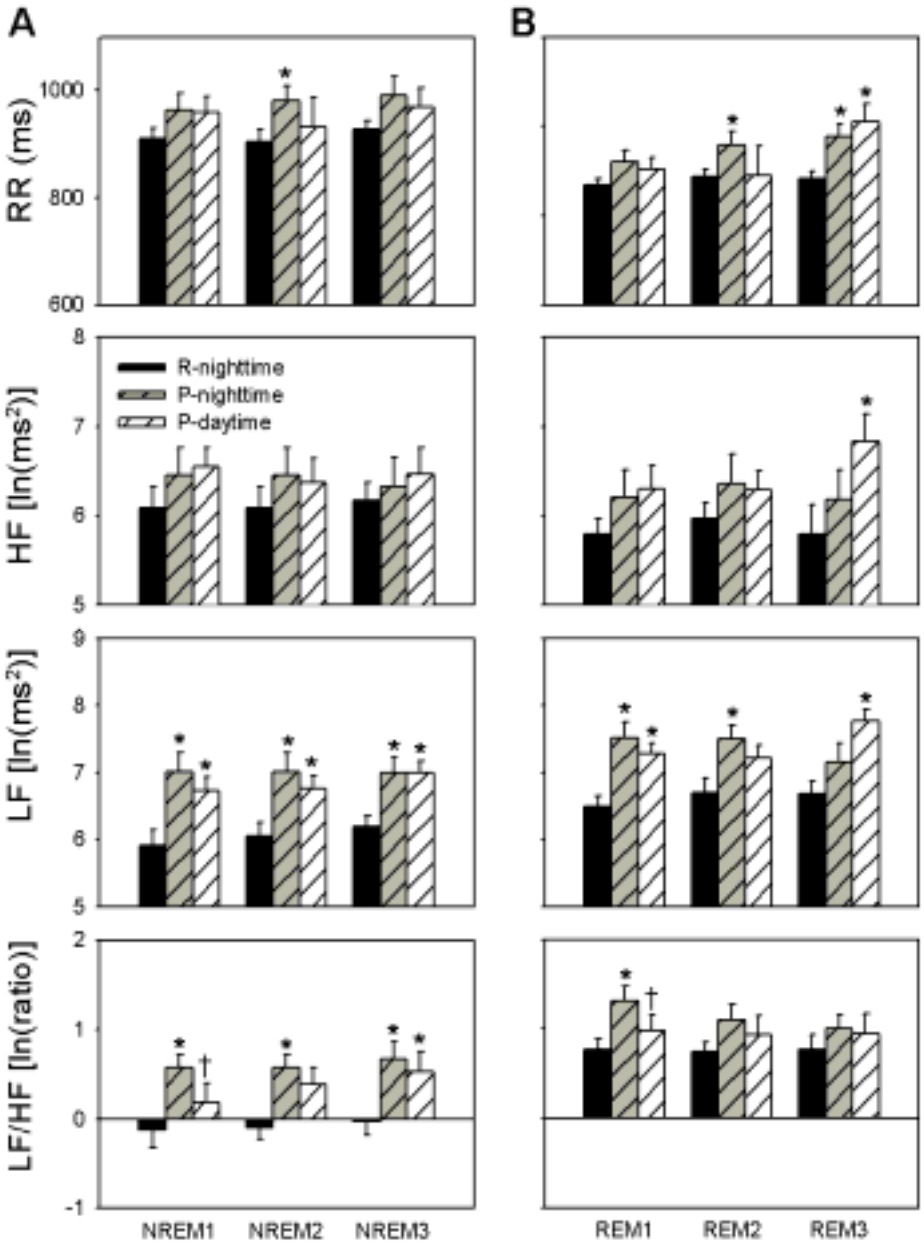

FIGURE 2 *R-R intervals and heart rate variability during periods of NREM and REM sleep*
Notes:
The figure illustrates R-R intervals (RR), high-frequency power (HF), low-frequency power (LF) and the LF-to-HF ratio (LF/HF) of heart rate variability among rotating three-shift nurses during 1-3 periods of non rapid eye movement (NREM) and rapid eye movement (REM) nighttime sleep for the nighttime sleep of regular morning shift (R-nighttime); the nighttime sleep of night shift (P-nighttime); the daytime sleep of night shift (P-daytime) nurses. The data are expressed as mean ± SEM of 10 nurses per group. Superscripts indicate p-values as follows: $^{*}P< .05$ vs R-nighttime, $^{\dagger}P< .05$ vs P-nighttime.