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DAYTIME CARDIAC AUTONOMIC ACTIVITY DURING ONE WEEK OF CONTINUOUS NIGHT SHIFT

Alexandra L. HOLMES, Helen J. BURGESS, Kirsty McCULLOCH, Nicole LAMOND, Adam FLETCHER, Jill DORRIAN, Gregory ROACH and Drew DAWSON
Centre for Sleep Research, The University of South Australia, Woodville, Australia

Shift workers encounter an increased risk of cardiovascular disease compared to their day working counterparts. To explore this phenomenon, the effects of one week of simulated night shift on cardiac sympathetic (SNS) and parasympathetic (PNS) activity were assessed. Ten (5m; 5f) healthy subjects aged 18-29 years attended an adaptation and baseline night before commencing one week of night shift (2300-0700h). Sleep was recorded using a standard polysomnogram and circadian phase was tracked using salivary melatonin data. During sleep, heart rate (HR), cardiac PNS activity (RMSSD) and cardiac SNS activity (pre-ejection period) were recorded. Night shift did not influence seep quality, but reduced sleep duration by a mean of 52 ± 29 min. One week of night shift evoked a small chronic sleep debt of 5 h 14 ± 56 min and a cumulative circadian phase delay of 5 h ± 14 min. Night shift had no significant effect on mean HR, but mean cardiac SNS activity during sleep was consistently higher and mean cardiac PNS activity during sleep declined gradually across the week. These results suggest that shiftwork has direct and unfavourable effects on cardiac autonomic activity and that this might be one mechanism via which shiftwork increases the risk of cardiovascular disease. It is postulated that sleep loss could be one mediator of the association between shiftwork and cardiovascular health.

Introduction

While the industrial and consumer benefits of a round-the-clock workforce are self evident, it is generally accepted that, compared to regular day workers, shift workers are more likely to suffer from a variety of health problems including cardiovascular disease (e.g. COSTA, 1997; BOGGILD and KNUTSSON, 1999). That nature of the association between shiftwork and cardiovascular disease remains to be defined. It has been proposed that shiftwork directly reduces cardiovascular health by, for example, disrupting the diurnal pattern of digestive processes (LENNERNÄS et al., 1994) or evoking constant changes in the timing and magnitude of the 24 hour rhythms in cardiac autonomic (ANS) activity (FURLAN et al., 2000). Alternatively, the association between shiftwork and cardiovascular disease may be a product of a more general relationship between socio-economic status and health (GONZÁLEZ et al., 1998). Among lower socio-economic groups, traditional cardiac risk factors such as smoking and a diet high in saturated fats are particularly prevalent. Low socio-economic status might also impact negatively upon cardiovascular health by compromising sleep quality and quantity. In a laboratory setting, chronic sleep loss has been found to increase sympatho-vagal balance (VAN CAUTER and SPIEGEL, 1999), an effect well known to facilitate hypertension and cardiovascular disease.

In order to improve our understanding of the association between shiftwork and cardiovascular disease, the factors that mediate the association, for example sleep loss or socio-economic status, need to be identified. Additionally, the physiological changes that are involved, for example increased cardiac ANS activity, must be realised. The aim of the current study was to explore the possibility that a change in cardiac ANS tone might be one mechanism via which shiftwork increases the risk of cardiovascular disease.

Methods

Ten healthy non-smokers, aged 18-29 years and with regular sleep/wake cycles participated in this study. Subjects attended an adaptation and baseline night before commencing one week of simulated night shift (2300-0700h). During each night shift subjects performed hourly psychomotor performance tests in light levels ranging from 35 to 300 lux. To reproduce the light exposure encountered by shift workers during travel home from a night shift, at the end of each simulated night shift, subjects went outside and were exposed to natural light for 20 minutes. From approximately 0800h subjects slept in dark, quiet, bedrooms maintained at 21°C until they naturally awoke. Throughout the study, napping was not permitted and subjects abstained from caffeine and alcohol.

Sleep/wake state was assessed using a regular polysomnographic montage of electrodes connected to a Medilog MPA-2 sleep analysis system (Oxford Medical Limited, Oxton, England). Sleep was scored according to the standard criteria (RECHSTCHAFFEN and KALES 1968). Measures of sleep quality including sleep efficiency, slow wave activity (SWA; 0.33-3 Hz), minutes of REM sleep, Stage 2 sleep and Stage 1 sleep were assessed. The time of nocturnal salivary melatonin onset was used as a marker of circadian phase. For the baseline night and each night shift, saliva samples taken at half hourly intervals (2000h-bedtime) were assayed for melatonin by direct radioimmunoassay. Melatonin onset was defined as the time at which melatonin concentration reached a level at least two standard deviations greater than the mean daytime level.

During each sleep opportunity an electrocardiogram (ECG) and an impedance cardiogram were obtained from a VU-AMS device (version 4.6, TD-FPP, Vrije Universiteit, Amsterdam, the Netherlands). This device measured heart rate (HR) and the activity of the two branches of the ANS. Cardiac sympathetic (SNS) activity was determined from pre-ejection period (PEP), or the isovolumetric contraction time of the left ventricle. PEP is inversely proportional to cardiac SNS activity (e.g. BERNSTON et al., 1997). Cardiac parasympathetic (PNS) activity was determined from the root mean square of the successive differences in R-R intervals (RMSSD; CRAWFORD et al., 1999).

Data from the final sleep period was excluded from all analyses because subjects voluntarily curtailed this sleep period in order to end the experimental week and to return home. To determine the effects of one week of night shift on sleep duration, sleep quality and cumulative phase shift, repeated measures ANOVAs with one within-subject factor (sleep period) were conducted. For every 30-second epoch of sleep, PEP, RMSSD and HR were automatically calculated by the AMS system. For each sleep period, these measures were averaged into consecutive 10% portions of that period. To investigate the effects of one week of night shift on PEP, RMSSD and HR, repeated measures ANOVAs with two-within subject factors (sleep period) and time (10% portions of the sleep period) were conducted. All p-values were based on the Huynh-Feldt corrected degrees of freedom, but the original degrees of freedom are reported when an effect was detected. Significant effects were investigated using planned means comparisons (Greenhouse-Geisser procedure). Significance was determined at $p<0.05$.

Results

The following results are presented in Fig. 1, unless otherwise noted. Compared to baseline (8h 18 ± 9 min), sleep duration was significantly shorter following the second, fourth and sixth night shift ($F(9,6)=3.35$, $p<0.05$). Sleep duration was shorter by an average of 52 ± 29 minutes and by the final night shift a small mean chronic sleep debt of 5h 14 ± 56 minutes had developed ($F(9,5)=7.32$, $p<0.05$). Chronic sleep debt was not significant until following the fourth night shift. One week of night shift had no significant effect on any measure of sleep quality. A significant circadian phase delay was apparent from the second night shift onwards ($F(6,6)=16.41$, $p<0.05$). A mean phase delay of 50 ± 36 minutes occurred per shift and a mean cumulative phase delay of 5h ± 36 minutes was apparent at the end of the week.

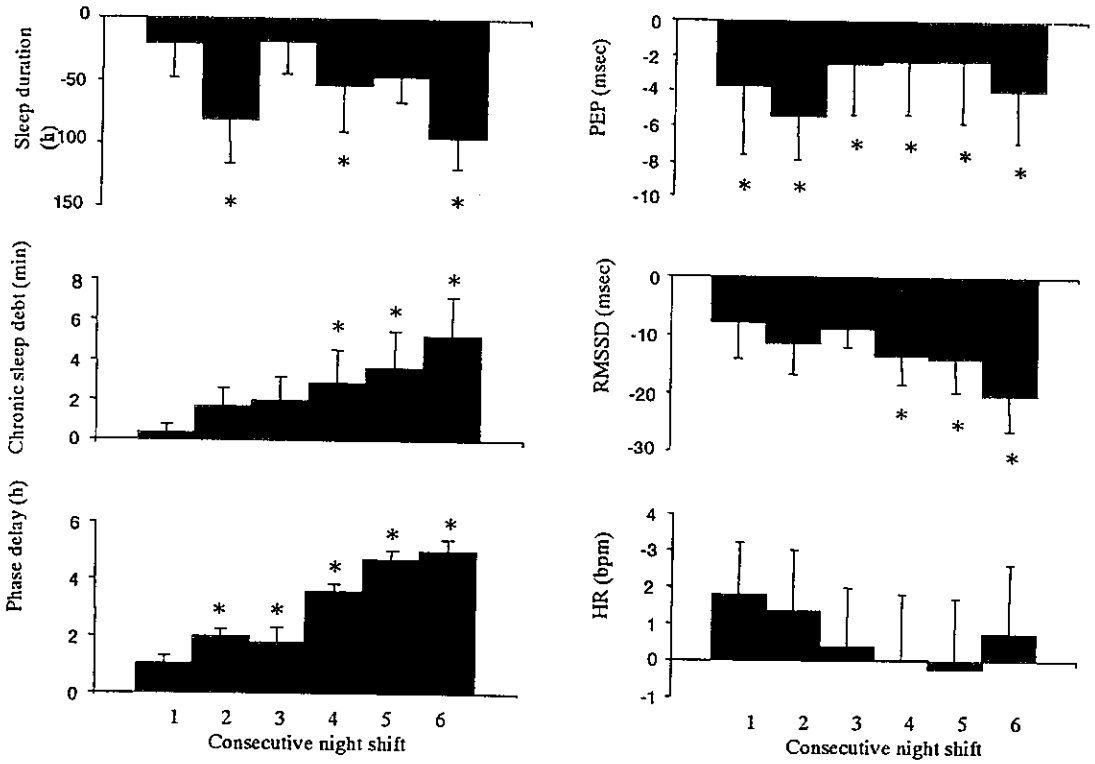

Fig. 1. Mean sleep duration (min), chronic sleep debt (h), cumulative circadian phase delay (h), PEP (msec), RMSSD (msec) and HR (bpm) for each night shift during one week of night shift. Data is displayed relative to that for baseline. Values are means ± SE. * indicates significance from baseline.

During one week of night shift, mean PEP during sleep was consistently lower (cardiac SNS activity was higher) than that during baseline sleep ($F(9,6)=2.57$, $p<0.05$). Specifically, PEP was on average 5.03 ± 2.28 msec lower (mean of 122.91 ± 3.36 msec during baseline sleep). During the 40-70 % portion of sleep, PEP was significantly lower than baseline in at least 5 of the sleep periods (Figure 2). PEP increased (cardiac SNS activity decreased) during sleep in a manner that was not significantly different between sleep periods ($F(9,9)=8.46$, $p<0.05$).

Compared to baseline sleep (mean of 117.24 ± 15.77 msec), mean RMSSD during the 4th, 5th and 6th sleep period was significantly lower ($F(9,6)=2.57$, $p<0.05$). Mean RMSSD was maximally reduced by 20.25 ± 6.16 msec (sixth night shift). Night shift reduced mean RMSSD by lowering RMSSD at the start of the sleep period (Fig. 2). For the first 20% of sleep, RMSSD was lower than baseline in at least 4 of the sleep periods. During sleep, RMSSD increased such that by the last 20% of sleep it was not significantly different between baseline and night shift ($F(9,9)=3.36$, $p<0.05$).

One week of night shift did not significantly influence mean HR (55.58 ± 1.78 bpm during baseline sleep), however it did alter the pattern of change in HR ($F(9, 54)=1.35$, $p<0.05$). During the 40-60 % portion of sleep, HR was significantly higher than baseline in at least 3 sleep periods. During the 80% portion of sleep, HR was significantly lower than baseline in at least 3 sleep periods.

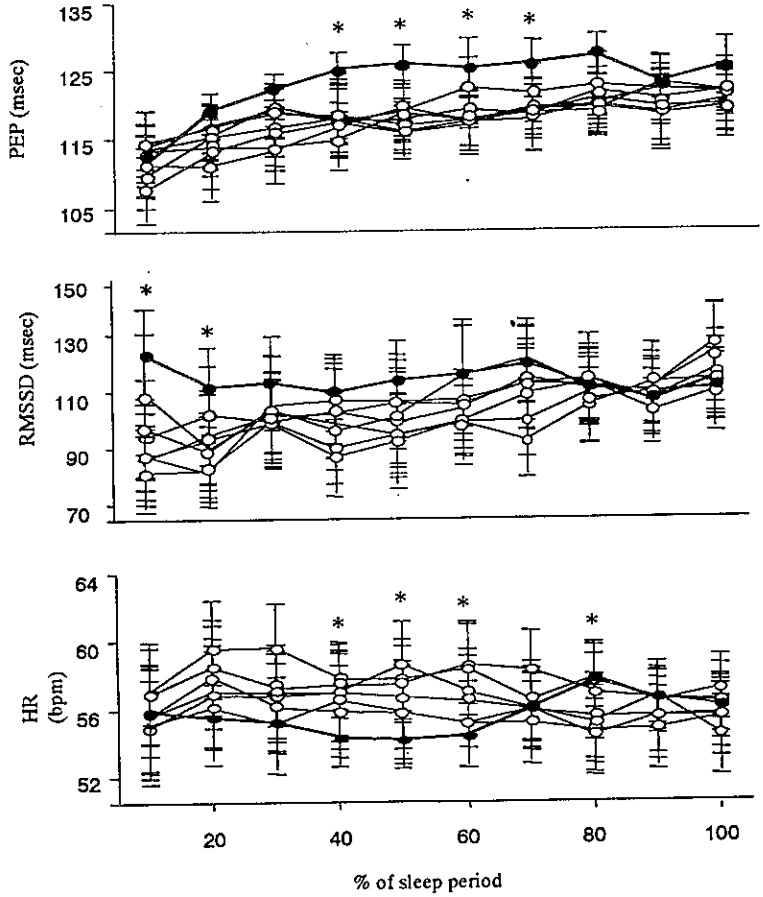

Fig. 2. Mean PEP (msec), mean RMSSD (msec) and HR (bpm) during baseline sleep (•) and for the sleep periods (o) during one week of night shift. Data is presented in 10% portions of each sleep period. Values are means ± SE. * indicates 10% portions during which PEP, RMSSD or HR, in at least 3 sleep periods, was significantly different from baseline sleep.

Discussion

During one week of simulated night shift, mean cardiac sympathetic (SNS) activity during sleep was consistently elevated and from the fourth night shift onwards, mean cardiac parasympathetic (PNS) activity during sleep was reduced. In addition, night shift increased mean HR during the middle portion of sleep. As both increased cardiac SNS activity and reduced cardiac PNS activity are predictors of cardiovascular disease, these results suggest that a change in cardiac autonomic (ANS) tone might be one mechanism via which shiftwork reduces cardiovascular health. During night shift the patterns of change in cardiac SNS and cardiac PNS activity that are typically associated with sleep were altered. As changes in the timing of the diurnal rhythms of cardiac activity have been suggested to promote cardiovascular disease among diabetics (ARONSON, 2001), this may represent an additional mechanism by which shiftwork increases the risk of cardiovascular disease (FURLAN et al., 2000).

A number of researchers have assessed the effects of shiftwork on 24 hour cardiac ANS activity in the applied setting (e.g. FURLAN, 2000; KOBAYASHI et al., 1997). Generally, shiftwork has been found to modify waking cardiac ANS activity, but to have minimal influence on cardiac ANS activity during sleep. It is likely that an effect of night shift on cardiac PNS activity during sleep has not previously been reported because researchers only recorded cardiac activity during the first night shift. In this study night shift did not influence cardiac PNS activity until the

fourth consecutive shift. An increase in cardiac SNS activity during sleep has only been observed in one prior study (VAN AMELSVOORT et al., 2001). The majority of prior work may have failed to reveal such an effect because cardiac SNS activity was measured using the low frequency (LF) component of the cardiac power spectrum. While PEP is a specific index of cardiac SNS activity, a significant body of research has demonstrated that the LF component of the cardiac power spectrum reflects changes in both branches of the ANS (e.g. BERNSTON et al., 1994). In studies utilising the LF component, it is possible that any effects of shiftwork on cardiac SNS activity were masked by a relatively constant degree of cardiac PNS activity.

During one week of simulated night shift, cardiac SNS activity may have been elevated as the result of stress associated with the protocol or the influence of the circadian pacemaker (discussed later). Alternatively, because cardiac SNS activity declines (PEP increases) during sleep (e.g. TRINDER et al., 2001), a reduction in sleep duration might have been responsible. The mean level of cardiac PNS activity associated with sleep gradually declined during one week of simulated night shift and was significantly lower than baseline from the fourth shift onwards. This pattern of change suggests that cardiac PNS activity declined in relation to the gradual development of a chronic sleep debt (see Fig. 1). Minimal research has attended to the effects of chronic sleep loss on cardiac ANS activity. However, in support of the results of this study, van Cauter and colleagues found that restricting the sleep opportunity to 4 hours (0100-0500h) for 6 consecutive nights increased sympatho-vagal balance (correlation coefficient of the R-R intervals; rRR) the following day (0900-1400h; VAN CAUTER and SPIEGEL, 1999).

The possibility that sleep loss mediated the observed changes in cardiac ANS activity deserves attention because, in comparison to shift workers, subjects in this study experienced a mild degree of sleep loss. In the field night shift generally reduces the length of the major sleep period by between 2 to 4 hours and in simulated shiftwork conditions subjects only lost approximately 52 minutes of sleep per day (e.g. KOGI, 1982). Subjects slept particularly well in this study because, in contrast to shift workers, they slept in ideal conditions and were isolated from the disrupting effects that social and domestic responsibilities can have on daytime sleep. A number of researchers have demonstrated that circadian adaptation to shiftwork increases sleep duration (e.g. EASTMAN et al., 1994). In the current study such an effect was not apparent, probably because subjects were relatively young and therefore *'phase tolerant'* or apt at sleeping and performing at unusual circadian phases (e.g. DIJK et al., 1999). In other words, there was little room for an improvement in sleep duration.

It is interesting to note that simulated night shift increased mean cardiac PNS activity by elevating cardiac PNS activity at the start of sleep (Fig. 2). By the end of each daytime sleep period cardiac PNS activity was not significantly different from that at the end of baseline sleep. This finding suggests that night shift reduced waking cardiac PNS activity during wakefulness and that during the sleep process cardiac PNS activity *'recovered'* from this effect. While cardiac PNS activity during wakefulness was not assessed, we have previously reported that following sleep loss cardiac PNS activity varies in a *'recovery'* function. Specifically, following 30 hours of supine wakefulness, cardiac PNS activity during sleep was significantly higher than that following 6 hours of supine wakefulness (HOLMES et al., 2002).

Night shift also modified the pattern of change in cardiac SNS activity that is typically associated with sleep. Specifically, during one week of night shift, cardiac SNS activity during the middle portion of sleep was significantly greater than that during baseline (Fig. 2). This increase in cardiac SNS activity probably drove the increase in HR that was apparent during a similar portion of the sleep period. The observed pattern in cardiac SNS activity and HR cannot be accounted for by a disruption of sleep quality, as a significant effect of night shift on sleep quality was not observed. It is more likely that cardiac SNS activity and HR were increased as a result of sleep loss (discussed previously). It is also possible that cardiac SNS activity and HR were altered because night shift necessitates that sleep occurs during the day, when the downregulating effects of sleep on cardiac activity are counteracted by the circadian influence on the heart (e.g. KERKHOF et al.,

1998). Nonetheless, as circadian adaptation to night shift did not appear to improve cardiac autonomic tone, a role for the circadian pacemaker is not well supported.

In conclusion, one week of simulated night shift consistently elevated cardiac SNS activity during sleep and cardiac PNS activity during sleep was reduced towards the end of the week. These findings suggest that a change in cardiac autonomic activity might be one mechanism by which shiftwork increases the risk of cardiovascular disease. This study was not designed to address the specific role that sleep loss plays in the cardiovascular consequences of shiftwork. Nonetheless, it is interesting to note that a reduction in sleep length and the development of a chronic sleep debt may be responsible for the observed changes in cardiac SNS activity and cardiac PNS activity, respectively. This proposal highlights the value that good sleep quantity and quality could play in limiting the negative cardiovascular consequences of shiftwork. While circadian adaptation to night shift did not appear to directly benefit cardiac autonomic activity, it is likely that the sleep enhancing effects of circadian adaptation would have indirect value for cardiovascular health.

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