J Occup Health 2001; 43: 32–38

Journal of Occupational Health

24-Hour Heart Rate Variability in Shift Workers: Impact of Shift Schedule

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Abstract: 24-Hour Heart Rate Variability in Shift Workers: Impact of Shift Schedule: L.G.P.M. van AMELSVOORT, *et al.* Department of Epidemiology, Maastricht University—Disturbance of the circadian pattern of cardiac autonomic control by working at night when the physiological system anticipates rest could explain part of the elevated cardiovascular risk in shift workers. Analysis of Heart Rate Variability (HRV) is a non-invasive tool to estimate disturbances of the cardiac autonomic control. To assess the influence of working at night on cardiac autonomic control, HRV levels were determined in shift workers. 24-h ECG recordings were made during a day on morning shift and a day on night shift. Within person differences between a morning and a night shift were calculated. Possible modification of the reported effects by the shift schedule was determined. Significantly elevated mean %LF during sleep was found on a day worked on night shift compared with a day on day shift (%LF + 3.04, P<0.01). Type of shift schedule was found to be a significant modifier of this effect. The difference in %LF between the night and day shift for the different shift schedules apart were: + 0.88% for the workers in the fast forward rotating shift, + 3.06% for the fast backward rotating shift, + 6.15% (P<0.001) for the medium speed backward rotating shift and + 1.18% for the shift workers without a regular shift schedule. The results suggest an increased sympathetic dominance during a night shift sleep, indicating an inferior sleep quality. Optimisation of this schedule might diminish this impact and could contribute to a reduction of the cardiovascular disease risk among shift workers.
(J Occup Health 2001; 43: 32–38)

Key words: Shift work, Work schedules, Heart rate variability

During the last decade the evidence for an elevated cardiovascular risk in people working in shifts has become more convincing[1–4]. However, the mechanisms behind this elevated risk remain unclear. Suggested hypotheses include undesirable changes in eating habits, in physical activity, the involvement of metabolic factors and disturbances in the physiological circadian rhythm[3, 5]. Disturbance of the circadian cardiovascular autonomic control pattern could be a factor in the latter mechanism. A non-invasive technique used for investigating cardiovascular autonomic control is the analysis of heart rate variability. Heart rate variability and its spectral components reflect the dynamics of cardiac parasympathetic and sympathetic outflow[6–8]. In post myocardial infarction patients as well as in the general population heart rate variability measures have been found to be inversely associated with cardiovascular morbidity and mortality[9–11].

Cardiac autonomic control as measured by heart rate variability displays a marked circadian rhythmicity[12, 13]. Circadian rhythmicity of cardiac control could explain part of the reported diurnal distribution of myocardial ischemia and infarction[14]. Possibly, the disturbance of the circadian rhythm of autonomic nervous system activity is also a relevant factor in the elevated cardiovascular risk of shift working. Working at night when the physiological system anticipates rest and recuperation can be regarded as an extra burden on the cardiovascular system due to a mismatch of the work/rest cycle and the output of intrinsic circadian pacemakers. Optimisation of the shift schedule may be a way to relieve this burden. Barton and Folkard[15] reported poorer physical and psychological health among workers in the

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Received July 26, 2000; Accepted Nov. 22, 2000
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Table 1. Structure of the included shift schedules

Shift schedule	Structure
Fast forward	MMEENNNxxMMEEENNxxMMMEENNxxx
Fast backward	NNEEMMMxxNNEEEMMxxNNNEEMMxxx
Medium backward	EEEExxMMMxxNNNNxxxEEExxMMMMxxNNNxxxEEEExxxMMMxxNNNNxxx

M: morning shift, E: evening shift, N: night shift, x: day off.

advancing shift system (that is, rotated in a backward direction: nights-afternoons-mornings) compared with those in the delaying shift system (that is, rotated in a forward direction: mornings-afternoon-nights).

So far only a small-scale study by Freitas *et al.*[16] reported the influence of working at night on heart rate variability by working in shifts. In the twelve monitored subjects he found that the circadian pattern of heart rate variability (HRV) seemed to be predominantly related to the sleep-wake rhythm and was independent of the night-day cycle.

Our study aims at determining, in the 24-h heart rate variability profile, the differential effects of forward and backward rotating shift schedules on circadian cardiac autonomic control. We focussed our study on the night shifts of 110 subjects.

Methods

Population

One hundred ten shift workers on rotating schedules, participating in an ongoing cohort study comparing cardiovascular risk factors among shift workers with controls working in daytime including nights, were asked to undergo two 24-h Holter recordings. Workers from a broad variety of jobs were included in the study, although most work was on industrial production lines. In the cohort study changes in cardiovascular risk factors are being monitored over a one-year period in shift workers and in daytime working controls to identify possible factors that might be responsible for the elevated cardiovascular disease risk among shift workers. The study was approved by the ethical committee of the Wageningen Agricultural University.

The following inclusion criteria were applied:

- Starting in a new job.
- Working at least 32 h a week
- Expecting to work next year in the same job
- No use of medication or previous hospitalisation for cardiovascular disease.
- No insurmountable objections to shift work (see measurements)
- Aged between 18 and 55 yr.

Holter recordings were performed on two 24-h periods: a day with a morning shift and a day with night shift duty. In total 110 respondents were approached for two Holter recordings. Nineteen of the respondents refused to carry a Holter recorder. Seventeen shift workers refused to finish the first measurement or to enrol for the second measurement because “it was to cumbersome” (10) or due to due to skin irritation (7).

Seven recordings could not be used due to a poor signal to noise ratio (4) or technical malfunction of the equipment (3). Two pairs of recordings were not used due to an excessive number of premature beats. This left 65 complete pairs of 24-h Holter recordings for further analysis.

Measurements

Measurements were performed between one week and two months after the start of a new job.

1. 24-h Holter recordings:

The participants had a 24-h Holter recording starting at the beginning of a period of consecutive morning shifts and at the beginning of a period of consecutive night shifts. All participants were instructed to note down start and end time of sleep, work, meals, leisure time, physical activities and other possibly relevant events or activities. These diaries were later coded into a choice out of a list of standard activities. Sleep was defined as 1 h after going to sleep until 1 h before getting up, as recorded in the diary. This one-hour time window was introduced to prevent possible errors due to imprecise diary recordings and a possible time lag between the noted time of “going to sleep” and the actual start of the true sleep.

2. Personal and work characteristics:

All participants completed a questionnaire regarding:

Current job title: We asked for the current job, including company, department, and shift schedule. According to social status and job content all jobs were coded in one of nine different job titles. Shift schedules were coded as backward rotating (nights-afternoons-mornings, advancing schedule) or forward rotating (mornings-afternoon-nights, delaying schedule). We coded rotation as fast when at most three consecutive night shifts were worked. At most five consecutive night shifts on a row were coded as medium rotation. Irregular shift schedules, often made each month after consultation with all workers involved were coded as “irregular”. These schedules did not display a marked direction of rotation. In Table 1 the subsequent time schedules of the rotation schedules are represented.

Personal characteristics: Educational level was coded in seven levels from elementary school to university education (junior, senior, or higher education). The physical activity indexes for work, sport and leisure time were assessed as described by Baecke, Burema and Frijters17). The ranges of the indexes were 1.1–4.3, 1.0–5.2 and 1.3–4.5 respectively. Current and past smoking habits were asked.

HRV Assessment

The 24-h Holter recordings were analysed with a Marquette Series 8000 Holter Analyser (USA) by an experienced Holter analyst. The onset-Q instants of all beats were determined with the CCTOC Marquette Holter research software module. The resulting inter-beat interval series were downloaded from the Holter analyser, and further analysed on a personal computer as described by Janssen *et al.*18)

The complete recording was split into 5-minute segments. Only segments with 5% or less missing values (due to a noisy ECG) were used. Heart rate and HRV parameters were computed for each segment. The 24-h values and the mean values during sleep and work were obtained by averaging. For the normal beats the standard deviation (SDNNi) was calculated as standard deviation during a five-min reference period, with the exclusion of all segments with more than 5% missing values.

The algorithm used for spectral analysis has been described elsewhere19). Briefly, intervals were normalised to the duration of the mean interval. Then, linear trend removal, and 10% left and right tapering was done. After padding the data with zeros to the nearest power of two, the power density spectrum was computed by means of a Fast Fourier algorithm. We computed the spectral powers within two frequency bands: low frequency power, LF (0.05–0.15 Hz; a marker of fluctuations in either sympathetic or sympathetic plus vagal activity) and high frequency power, HF (0.15–0.40 Hz;, a marker of vagal activity6)). The spectral components were calculated both as absolute units and as normalised units (the latter by dividing LF and HF by their sum, and multiplying this by 100).

Statistical analysis

Because of the skew within and between person distribution of the high and low frequency spectral components of the heart rate variability, log-transformation of these parameters was performed before any averaging was done.

Comparisons of night shift day and morning shift day HRV measures were performed using the paired t-test. For the evaluation of effect modification of the night shift-morning shift differences, analysis of variance (ANOVA) modelling was used, using the SAS program. Least square mean values are shown to enable comparison of mean values between subgroups, adjusted for a covariant. Least square means are the class or subclass means that one would expect for a balanced design involving the class variable with all covariates at their mean value20). For the evaluation of possible modification of the reported effects by the number of successive days worked in the same shift, mixed model analysis was used21).

Results

Table 2 lists general characteristics of the study group. Most participants had industrial work sites with a predominantly male work force (this caused the large proportion of male subjects in our study). Almost all female subjects (except two) worked as nurses. These nurses worked primarily without a fixed shift schedule with approximately 2–4 night shifts per month. All other workers worked an average of 5–7 nights per month.

In Tables 3, 4 and 5 individual differences (night-shift-day minus morning-shift-day values) are presented. In Table 3 the 24 h means of the individual differences are shown. The most prominent differences in heart rates between the night and morning shift day were present in the irregular shift schedule group, where, next to a lower heart rate during night shifts, higher SDNNi and %LF values could also be observed. When correcting for the difference in 24-h heart rate, the difference in SDNNi and %LF between the night and morning shift disappears (For heart rate corrected differences: δSDNNi: 0.5, SE: 2.3; δ%LF − 1.0, SE: 1.4). In the three other groups a change towards dominance of low frequency heart rate variability was observed but only reached statistical significance in the fast forward rotating group.

In Table 4 mean differences of night and morning shift HRV values measured during working hours are presented. Respondents working “irregular shift schedule”, “fast forward shift schedule” or “fast backward shift schedule” exhibited a considerably lower heart rate during work on a night shift compared with a morning shift. The mean log(LF) values for all shift schedules were lower during night shifts but only significant for the irregular shift schedule group and for the data of all workers combined.

Twenty-four hour mean differences between night and morning shift days reflected differences in work and leisure time activities as well as differences due to disturbance of circadian physiological rhythms. Mean values during sleep were probably much less influenced by the differences in work and leisure time activities and therefore might be better indicators of disturbances of the circadian physiological rhythm. In Table 5, the night and morning shift differences in mean values during sleep are presented. The most prominent differences in mean values during sleep were observed in the workers working according to a medium backward rotating shift schedule.

Table 2. Population characteristics

		Males	Females	Total
N		53	12	65
Age (yr)		34.2 (8.1)	25.3 (5.7)	32.5 (8.4)
Smoking (%)	Non smoker	49.0	41.7	47.6
	Smoker	33.3	33.3	33.3
	Ex smoker	17.7	25.0	19.0
Job strain categories (%)				
• High demands, low control		5.9	58.3	15.9
• High demands, high control		9.8	8.3	9.5
• Low demands, low control		31.4	25.0	30.2
• Low demands, high control		52.9	8.3	44.4
Shift schedule (%)				
• Fast forward		35.9	16.7	32.3
• Fast backward		20.8	0.0	16.9
• Medium backward		43.4	0.0	35.4
• Irregular		0.0	83.3	15.4
Heart rate (beats/min)*		73.3 (7.0)	86.0 (9.1)	75.6 (8.8)
%LF*		69.6 (8.4)	66.2 (8.6)	68.9 (8.4)
SDNNi (10^{-3} sec^2)*		76.0 (19.4)	60.2 (19.4)	73.1 (20.2)
Log (LF) (log sec^2)*		−2.78 (0.21)	−2.85 (0.21)	−2.79 (0.21)
Log (HF) (log sec^2)*		−3.19 (0.33)	−3.18 (0.31)	−3.19 (0.32)

Mean values with standard deviation in brackets or %. *24 hr mean during day with morning shift.

Table 3. Night and morning shift differences in 24 h mean values

	All workers	Shift schedule				P-value$^{\#}$ Shift schedule difference
		Fast forward	Fast backward	Medium backward	Irregular shift schedule	
δHeart rate (beats/min)	−0.47 (0.66)	1.25 (0.98)	−1.15 (1.11)	−0.03 (1.19)	−4.50 (1.86)*	0.05
δSDNNi (10^{-3} sec^2)	1.88 (1.33)	0.34 (1.45)	−1.47 (3.83)	2.68 (2.67)	7.0 (2.9)*	0.2
δLog (LF) (10^{-3} log sec^2)	18.4 (13.6)	30.0 (12.4)*	−26.9 (35.7)	51.9 (27.5)	−33.1 (33.9)	0.08
δLog (HF) (10^{-3} log sec^2)	−4.8 (17.9)	−21.7 (23.6)	−65.0 (58.8)	24.5 (32.1)	29.3 (38.9)	0.6
δ%LF	0.96 (0.61)	2.18 (0.89)*	1.44 (1.69)	1.33 (1.07)	−2.97 (1.27)*	0.05

Mean values of difference between a night shift and morning shift day. Standard error of mean between brackets. P values according to the paired t-test: significant difference between night and morning shift values (*$p<0.05$; ** $p<0.01$). $^{\#}$P-value according to F-test (ANOVA).

Table 4. Mean night and morning shift difference during work

	All workers	Shift schedule				P-value$^{\#}$ Shift schedule difference
		Fast forward	Fast backward	Medium backward	Irregular shift schedule	
δHeart rate (bpm)	−3.12 (0.89)**	−3.91 (1.45)*	−3.10 (0.97) **	0.25 (1.59)	−9.22 (2.15)**	<0.001
δSDNNi (10^{-3} sec^2)	1.48 (1.47)	5.44 (2.19)*	−1.46 (3.48)	−3.08 (2.66)	6.91 (3.01)*	0.04
δLog (LF) (10^{-3} log sec^2)	−36.4 (13.1)**	−19.3 (19.4)	−78.4 (35.6)	−18.9 (25.6)	−66.2 (23.0)*	0.05
δLog (HF) (10^{-3} log sec^2)	−36.4 (21.5)	−19.9 (29.8)	−97.2 (82.1)	−39.5 (30.5)	30.2 (55.4)	0.18
δ%LF	−0.29 (0.73)	−0.08 (1.04)	0.11 (2.51)	0.65 (1.07)	−2.97 (1.27)*	0.4

Mean values of difference between a night shift and morning shift day. Standard error of mean between brackets. P values according to the paired t-test: significant difference between night and morning shift values (*$p<0.05$; ** $p<0.01$). $^{\#}$P-value according to F-test (ANOVA).

Table 5. Mean night and morning shift difference during sleep

	All workers	Shift schedule				P-value# Shift schedule difference
		Fast forward	Fast backward	Medium backward	Irregular shift schedule	
δHeart rate (bpm)	0.70 (0.71)	0.90 (1.02)	0.43 (1.78)	1.36 (1.38)	−0.93 (1.78)	0.6
δSDNNi (10^{-3} sec^2)	2.81 (2.73)	0.27 (3.00)	−1.56 (6.92)	5.24 (6.26)	7.39 (4.08)	0.6
δLog (LF) (10^{-3} log sec^2)	51.9 (26.4)*	16.9 (35.1)	−10.0 (75.6)	131.3 (52.0)*	10.7 (40.4)	0.06
δLog (HF) (10^{-3} log sec^2)	−10.1 (30.1)	−11.1 (43.7)	−106.0 (95.5)	15.7 (57.7)	38.3 (57.8)	0.8
δ%LF	3.04 (1.11)**	1.25 (1.68)	4.55 (2.93)	5.92 (2.02)**	−1.50 (2.18)	0.02

Mean values of difference between a night shift and morning shift day. Standard error of mean between brackets. P values according to the paired t-test: significant difference between night and morning shift values (*$p<0.05$; ** $p<0.01$). #P-value according to F-test (ANOVA).

Table 6. Age adjusted mean night and morning shift difference during sleep

	Shift schedule				P-value# Shift schedule difference
	Fast forward	Fast backward	Medium backward	Irregular shift schedule	
δHeart rate (bpm)	0.89 (1.29)	0.36 (2.08)	1.38 (1.28)	0.63 (5.67)	0.8
δSDNNi (10^{-3} sec^2)	1.17 (3.52)	0.58 (5.67)	6.41 (3.50)	−1.59 (7.15)	0.3
δLog (LF) (10^{-3} log sec^2)	20.1 (44.6)	−5.8 (71.7)	137.8 (44.3)**	−13.8 (71.6)	0.09
δLog (HF) (10^{-3} log sec^2)	−0.91 (41.5)	−76.4 (66.7)	19.6 (41.2)	−38.4 (66.7)	0.6
δ%LF	0.88 (1.62)	3.06 (2.61)	6.15 (1.64)***	1.18 (2.61)	0.01

Least square mean of difference between a night shift and morning shift day corrected for age; SDNNi, Log (LF), Log (HF) and %LF also corrected for difference of heart rate during sleep. Standard error of mean between brackets. p: significant difference between night and morning shift values (*$p<0.05$; **$p<0.01$; ***$p<0.001$). #P-value according to F-test (ANOVA).

They showed a considerable shift towards low frequency power dominance (elevated %LF and Log LF).

Investigation of possible effect modification by factors other than shift schedule was done by including the possible effect modifiers age, job strain, sex and physical activity at work, one by one in an ANOVA model. Only for age there was an indication for a small, but non-significant effect modification on several HRV parameters. The most prominent effect modification was found for %LF. With each five year increase of age the effect of working on a night shift on mean %LF during sleep increased with 0.9% LF ($p=0.18$).

Because of the correlation between the various HRV measures with heart rate a separate analysis was performed on the mean values during sleep with correction for mean heart rate during sleep. Also differences in age might explain the different effects of the shift schedules as presented in Table 5. Therefore, adjustments for the possible confounding of the effect of shift schedule by age and heart rate, were included in the model presented in Table 6. Adjustment of the results, as presented in Table 6, yielded only small differences, compared with the unadjusted results, as presented in Table 5.

Discussion

Increased levels of 24-h %LF were found during a night shift day compared with a day shift day, except for the participants working an irregular shift schedule. Decreased 24-h mean heart rate values during a night shift day were found in most workers but were most prominent in the nurses working on an irregular shift schedule. Next to other possible sources of bias, differences in tasks during work and leisure time are likely to have influenced the 24-h heart rate and heart rate variability. Especially the respondents working irregular shift schedules seem to have different work tasks at night compared with their daytime task. This is reflected in the considerable differences in heart rate and heart rate variability levels during work. Because the differences during sleep are much less prone to bias due to differences in work and leisure time activities22) we will focus the discussion on these results.

Measurements during sleep on either night or morning shift days are considered to be less susceptible to differences in leisure time or work activities. Elevated values of %LF during sleep were found on night shift days compared with morning shift days for all respondents. When taking effect modification by shift schedule into account, the elevation was largest in the workers working in a medium backwards rotating shift schedule whereas the workers working in the irregular shift schedule did not show this elevation.

Because we compared night and morning shift differences within subjects, variation between individuals is not considered a major source of bias. Effect modification, due to differences in sensibility between individuals, however cannot be ruled out. From the factors considered as possible effect modifiers, the type of shift schedule was the most important and the only one to reach statistical significance. In our study, gender and number of nights worked per month were highly correlated (p chi-square: <0.001) with type of shift schedule and both factors could therefore not be assessed separately as a possible effect modifier. One could argue that the deviant results in the group of workers working with “irregular shift schedule” are caused by a difference in gender, or a smaller number of nights worked per month, rather than a different shift schedule. Extrapolation of the presented results to female workers and to workers in irregular shift schedules needs further research.

Differences between days on night shift and morning shift within individuals are a likely source of bias of the presented results. Eating habits, coffee consumption, alcohol consumption, medication use and physical activity are all likely to differ on night shift compared with morning shift days. These factors could also influence heart rate variability, and might therefore be intermediary factors between shift work and HRV. Nevertheless, we do not consider it likely that the difference between the shift schedules is explained by differences in these factors.

Because the measurements during the different shifts were not all on the same day from the start of a new rotation cycle, bias or effect modification could be present due to differences between the number of the day in a row of days on the same shift. Mixed model analysis was used to evaluate possible effects of the number of days worked in the same shift. No significant influence of the number of consecutive shifts in a row was found.

The effect of working at night is on average larger during sleep than measured during 24 h. This indicates that a part of the elevated %LF values during sleep is compensated elsewhere during the day. Because the differences during work did not show considerable differences between a night and day shift day a change during leisure time is therefore considered the most likely explanation. Unfortunately, because of the large variation in leisure time mean values it was not possible to assess this in the current data.

Only one other study has been found reporting 24-h heart rate variability differences during night and morning shift days was found[16)]. No differences in HRV levels during sleep and work, between the night and morning shifts, were reported. However, in this study, only 12 observations were included and no shift rotation schedule was given.

When comparing the different shift schedules included in this study, the ordered levels of differences in %LF during sleep for the different shift systems coincides with the basis of theoretical health considerations ordered shift systems (i.e. forward rotation favoured above backward, fast rotation favoured above slow rotation). A forward rotation is considered more healthy because in the absence of external cues the sleep-wake and other circadian rhythms run with a period of approximately 25 h so sleep occurs later and later[23, 24)]. Sleeping when working in a forward rotation is considered to be less disruptive because the shift in relation to the internal circadian clock is smaller. The elevation of %LF during night could be an indication of unfavourable sleep. This effect was largest in the group working in a medium speed backward rotating shift schedule so one might hypothesise that this shift schedule causes a larger disruption in the normal wake-sleep cycle and therefore leads to a decreased sleep quality.

In conclusion, our study provides empirical data that support the hypothesis that working nights causes a shift of the autonomic balance towards sympathetic dominance. This effect was most pronounced during sleep, but was also found in 24-h averages. This is especially true for workers with an anti-clockwise (or backward) rotating shift schedule.

One might hypothesise that the less favourable shift in the autonomic balance towards sympathetic predominance, as found in this study, might lead to an increased cardiovascular burden. An increased cardiovascular burden might be a component in the elevated cardiovascular disease risk of shift workers. Additional evidence for the involvement of the cardiovascular regulation in this elevated risk comes from a study by Murata *et al.*[25, 26)] who reported a shift work related QTc prolongation. Because the type of shift was related to the reported effect, type of shift schedule has to be considered as a possible factor for the reduction of the adverse impact of shift work on cardiovascular health.

Acknowledgments: This study was supported by grant 94.101 from the Netherlands Heart Foundation.

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