Modifications of Cardiac Autonomic Profile Associated With a Shift Schedule of Work

Raffaello Furlan, MD; Franca Barbic, MD; Simona Piazza, MD, PhD; Mauro Tinelli, MD, PhD; Paolo Seghizzi, MD; Alberto Malliani, MD

Background—Shift work is associated with an increased rate of cardiovascular diseases and accidents. Discordance between circadian rhythms of stress-related biological variables and the work-sleep schedule might explain the reduced efficiency of work. It is not clear whether a shift schedule of work may induce similar discordance in the 24-hour oscillatory pattern of the cardiac autonomic control in respect to the work-sleep periods.

Methods and Results—Twenty-two healthy male blue-collar shift workers underwent 24-hour ECG recordings during each of the 3 different shifts (first, 6 AM to 2 PM; second, 2 to 10 PM; third, 10 PM to 6 AM). Spectral analysis of heart rate variability over 24 hours provided the normalized markers of cardiac sympathetic (LF nu ) and vagal (HF nu ) modulation of the sinoatrial node activity and of the sympathovagal balance (LF/HF). LF nu and LF/HF exhibited 24-hour oscillations with different times of maximum and minimum in accordance with the working and sleeping periods, respectively. Lower values of LF nu and LF/HF suggestive of a reduced cardiac sympathetic modulation were present when the job task was performed at night compared with the values observed when the work was performed during morning and evening.

Conclusions—Continuous weekly changes of time of maximum and minimum in the cardiac sympathetic and vagal autonomic control may play a role in the excessive rate of cardiovascular diseases in shift workers. The reduced values of the indexes of cardiac sympathetic modulation during night work might be related to the presence of sleepiness or diminished alertness, which in turn could facilitate errors and accidents. (Circulation. 2000;102:1912-1916.)

Key Words: nervous system, autonomic circadian rhythm shift work

There is increasing evidence that rotating shift work over 24 hours is associated with an excessive rate of accidents and errors in both physical and mental tasks during night work. The exact pathophysiology underlying these phenomena is still poorly understood. It has been hypothesized that in most cases of shift work, the job task would be performed in the presence of less favorable biophysical conditions compared with those achieved during habitual diurnal work. Indeed, the stress-related biological variables cortisol and body temperature undergo a circadian pattern characterized by maximum values during the daytime when subjects are active and lower values at nighttime during the sleeping hours. These circadian oscillations seem to be induced by an endogenous clock and synchronized over 24 hours by the daylight alternation and by different cyclical activities of the daily routine. Therefore, the mismatch between circadian rhythms and the work-sleep schedule might explain the reduced efficiency on work.

The autonomic nervous system activity also oscillates over the 24 hours. A multisynaptic pathway between the suprachiasmatic nucleus, responsible for circadian rhythms and daily changes in behavior and physiology, and several sympathetic and parasympathetic outflows has recently been documented in animals by viral transneuronal labeling. Studies based on plasma and urinary catecholamine determinations indicate that sympathetic nervous activity is higher during the day and reduced at night or during sleeping. Similar results have been obtained by direct recording of peroneal sympathetic fibers, although not consistently.

In a study performed on healthy habitual day workers based on spectral analysis of heart rate variability over 24 hours, we previously observed that the index of cardiac sympathetic modulation, LF nu , was reduced during sleeping hours, increased with awakening in the early morning, and was high during the remaining period of the day, particularly during the work period.

In the present study, we hypothesized that a change in working time over 24 hours, as happens with a shifting schedule of work, may modify the 24-hour oscillation of the spectral markers of cardiac sympathetic (LF nu ) and vagal (HF nu ) modu-
lation and might be associated with a different level of cardiac autonomic modulation during the different working periods.

These aspects may be of paramount importance in attempts to better understand maladjustment to shift work and to assess the neural modifications likely to facilitate work accidents. In fact, it is conceivable that a reduction in sympathetic tone during night work might be attended by a decreased alertness and deterioration of working performance, promoting an excess of accidents and errors in the performing of job tasks. In addition, the weekly changes in the time of maximum and minimum of cardiac sympathetic and vagal autonomic control might play a role in the higher rate of cardiovascular diseases described in shift workers.

**Methods**

**Population**

We studied 22 healthy male subjects employed as blue-collar workers in a steel company after a weekly 3-shift system. The week consisted of 5 workdays and 2 rest days, 1 of which was Sunday. The scheduled work time rotated in a counterclockwise direction from the night (10 PM to 6 AM) to the afternoon (2 to 10 PM) to the morning (6 AM to 2 PM) shift.

The mean age of subjects was 39 ± 3 years. Each had 10 years of experience in shift work. At the time of admission to the study, every subject underwent a physical examination and routine laboratory tests. We considered only normotensive subjects who were free of any signs of disease and smoked <15 cigarettes a day. All subjects had similar environmental and working conditions.

**Experimental Protocol**

Each subject underwent 24-hour ECG recording during the 3 different shifts after 2 days of adaptation to the current shift. All ECG recordings were obtained with a 2-channel Holter recorder (Reynolds, Traker model), starting at about 2 PM. The workers were instructed to maintain a daily routine outside the firm as close as possible to their habitual one. The Table shows the average time of minimum and maximum variability.

**Data Analysis**

Twenty-four-hour Holter recordings were played back offline by an analyzer unit (Cardio Data Holter Analysis System) at 120 × real time. Analog-to-digital conversion was performed at 300 samples per second. The principles of the software for data acquisition and spectral analysis have already been described. In the present study, we used a recursive version of the program, which provided, depending on individual heart rate, >200 consecutive spectra for every 24-hour ECG recording. Briefly, from the surface ECG, the computer program calculates the series of consecutive RR intervals, depending on individual heart rate, and the autoregressive coefficients necessary to define the best estimate of the power spectral density are calculated. Two major oscillatory components can be extracted from RR spontaneous variability: a high-frequency (HF, ~0.25 Hz) component, an accepted marker of vagal modulation of the sinoatrial node activity, and a second low-frequency (LF, ~0.10 Hz) component considered, when normalized, a marker of cardiac sympathetic modulation. In the present study, the power of the oscillatory components is presented both in absolute (ms²) and normalized units (nu). Normalization is obtained by dividing the absolute power of each oscillatory component by total power within 0.04 and 0.5 Hz and multiplying by 100.

**Statistical Analysis**

Data are expressed as mean ± SEM. Student’s t-test for paired observations and 1-way ANOVA for repeated measures with a Newman-Keuls method posttest were used when appropriate. Differences were considered significant at \( P < 0.05 \).

<table>
<thead>
<tr>
<th>RR Interval and Cardiac Autonomic Control Indexes During Sleeping Time and Working Period as Observed in Workers During 3 Shifts</th>
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</thead>
<tbody>
<tr>
<td><strong>First Shift</strong></td>
</tr>
<tr>
<td>Sleep (6±0.3 h)</td>
</tr>
<tr>
<td>RR, ms</td>
</tr>
<tr>
<td>αRR, ms²</td>
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<tr>
<td>LF, ms²</td>
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<tr>
<td>LFnu</td>
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<td>HF, ms²</td>
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<tr>
<td>HFnu</td>
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<tr>
<td>LF/HF</td>
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</tbody>
</table>

RR indicates RR interval; αRR indicates RR variance.

\* \( P < 0.05 \) sleep vs work; † \( P < 0.01 \) sleep vs work, within same shift.

Statistical Analysis

Data are expressed as mean ± SEM. Student’s t-test for paired observations and 1-way ANOVA for repeated measures with a Newman-Keuls method posttest were used when appropriate. Differences were considered significant at \( P < 0.05 \).

**Results**

**Autonomic Circadian Rhythms and Different Shifts**

The Table shows the RR intervals and the spectral indexes of cardiac autonomic modulation observed in 22 shift workers during each of the 3 different shifts. In each shift, RR values were lower during working time compared with the sleeping period. The spectral markers LFnu and LF/HF were higher during the working period than during the sleeping hours, while HFnu showed opposite changes (Figures 1 and 2).

**Working Periods and Different Shifts**

The Table summarizes the mean values of RR interval, its variance, LFnu, HFnu, and the LF/HF ratio observed during the working periods corresponding to each of the 3 different shifts. RR values and RR variance were similar in all shifts. The vagal-related spectral index HFnu was only slightly higher during...
the third shift compared with the others (Figure 1). Conversely, LF\textsubscript{nu} and the LF/HF ratio were lower when working activities had been performed at night time (third shift) compared with the working periods of the first and second shifts (Figures 1 and 2).

Sleeping Periods and Different Shifts
As inferred from the Holter diary, sleeping time was different among the shifts, being longer during the second shift (the Table). Sleeping periods were characterized by similar values of RR interval, RR variance (the Table), and the spectral indexes of cardiac autonomic modulation in the 3 shifts (the Table and Figures 1 and 2).

Discussion
In the present study, we used the model of the 3-shift rotating work schedule to evaluate the potential modifications of the daily cardiac autonomic control induced by the changes in working and sleeping times over 24 hours.

The population of steel shift workers furnished the opportunity to deal with an identical working load because of the standardization and repetition of job tasks in each of the 3 shifts, thus overcoming the potential confounding effects induced by different physical\textsuperscript{24,25} and mental\textsuperscript{24} activities on power spectral components during 24 hours.

Major Findings
The first major finding was that the spectral indexes of cardiac sympathetic and vagal modulation maintain their 24-hour fluctuations with maximum and minimum values in accordance with the different working and sleeping periods. Second, nighttime work was associated with lower values of

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**Figure 1.** The 24-hour variations of spectral indexes of cardiac autonomic modulation during 3 shifts. In every shift, marker of cardiac sympathetic activity, LF\textsubscript{nu}, was higher during working time and lower when subjects were sleeping. Interestingly, night work period (third shift) was characterized by reduced values of LF\textsubscript{nu} compared with morning and evening working periods corresponding to other 2 shifts. Marker of cardiac vagal modulation, HF\textsubscript{nu}, showed circadian opposite pattern.

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**Figure 2.** The 24-hour changes of heart rate and index of cardiac sympathovagal balance LF/HF in 3 shifts. Notice that in every shift circadian oscillation of LF/HF ratio parallels 24-hour fluctuation of heart rate (HR). Lower values of LF/HF during night work (third shift) compared with other 2 shifts indicate reduced cardiac sympathetic modulation to heart rate when subjects were working at nighttime. Heart rate was similar in concomitance with 3 sleeping periods, and same pattern can be observed for LF/HF.
LFnu and the LF/HF ratio, suggesting reduced cardiac sympathetic modulation compared with the morning and evening working periods.

**Autonomic Circadian Rhythms and Different Shifts**

The results of the present study suggest that regardless of the time of day, work activity and sleeping time played a major role in generating the maximum and the minimum of the spectral markers LFnu and HFnu. Indeed, in every shift, LFnu and the LF/HF ratio were higher during working periods and lower at sleeping time, thus paralleling the 24-hour fluctuations of heart rate. Conversely, HFnu was higher during sleeping hours.

The relationship between changes in the autonomic profile and working and sleeping periods has previously been assessed only in habitual day workers, ie, in subjects with a lifestyle characterized by fixed working and sleeping times. In this population, the overall sympathetic activity was found to be higher during the daytime compared with nighttime. In fact, plasma and urinary catecholamine concentrations were higher during the day and lower during sleeping hours. Direct recordings of sympathetic nerve activity have documented a higher rate of sympathetic discharge during wakefulness compared with the non–rapid eye movement phase of sleep at night. In a study that used power spectral analysis of RR and blood pressure variabilities, LFnu and the LF/HF ratio, which reflects the sympathovagal interaction, were lower during sleeping hours, increased at waking time, and were higher in concomitance with daily activity. Similar results were obtained in continuously recumbent healthy subjects and by other studies that used EEG recordings to better define the periods of wakefulness and the different stages of sleep. It is important to point out that normal cardiovascular neural regulation is essential to maintain the 24-hour periodicity. In fact, the autonomic alterations attending diabetes mellitus, coronary heart disease, hypertension, and sleepiness were found to be associated with blunted 24-hour fluctuations of the spectral markers of cardiac autonomic control.

The 24-hour oscillatory patterns of LFnu and LF/HF observed in the present study are synchronous in each shift with working and sleeping periods and seem to differ from the circadian oscillations of body temperature and plasma cortisol as observed in different groups of shift workers. Indeed, morning peak levels of temperature and cortisol tend to move only slightly toward early afternoon values when work is performed at nighttime, thus showing a time lag between their maximum and the working period.

Finally, the continuous changes over the years of the time of maximum cardiac sympathetic modulation, as suggested by the pattern of the LFnu and the LF/HF indexes, might play a role in the excessive rate of cardiovascular disease described in habitual shift workers.

**Different Working Periods and Cardiac Autonomic Control**

An important aspect of the present study is the observation that the spectral indexes of cardiac sympathetic modulation (LFnu and the LF/HF ratio) were lower when subjects worked at night compared with morning and evening periods of work, despite the fact that job assignments were similar during the 3 shifts. This finding is corroborated by the concomitant observation of slightly increased values of RR interval during night work compared with the other 2 shifts.

A previous study by Freitas et al did not observe any variation in the low-frequency component of RR variability in a group of security shift workers of an oil refinery considered during morning and night work. Differences in the experimental design and in the intensity of physical activity during working periods may account for the discrepancies with our results.

In the present study, the finding of a decrease in the cardiac sympathetic modulation when work was performed at nighttime entails 2 major considerations. First, it might reflect the presence of periods of sleepiness or reduced alertness. It must be emphasized that for security reasons we could not assess the consciousness state directly by continuous EEG recordings. Nonetheless, a reduction in alertness or periods of sleepiness have been previously reported in truckers and train drivers and in pilots during training sessions when the appropriate tasks were performed at nighttime. As a consequence, a higher rate of errors or accidents has been observed compared with day work. Second, the fact that the indexes of cardiac sympathetic modulation, LFnu and LF/HF, were reduced during night work compared with the other diurnal working periods may reflect the likely opposite influences exerted by the work-sleep schedule (according to which the physical and mental activity attending job execution would increase LFnu and LF/HF) and the internal, schedule-independent, biological clock. In fact, in accordance with the latter, LFnu and the LF/HF ratio would have been reduced at night as happens in habitual diurnal workers for a stress marker such as cortisol and for body temperature.

**References**

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