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 (LFnu) and vagal (HFnu) modulation of the sinoatrial node activity and of the sympathovagal balance (LF/HF). LFnu 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 LFnu 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 increased rate of accidents1-2 and errors3-5 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.6-7 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.8 Therefore, the mismatch between circadian rhythms and the work-sleep schedule might explain the reduced efficiency on work.9,10

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.11 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.12 Similar results have been obtained by direct recording of peroneal sympathetic fibers,13 although not consistently.14

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, LFnu, 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.15

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 (LFnu) and vagal (HFnu) 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 work16 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.1,5 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.17,18

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 day (6 AM to 2 PM) shift.

The experimental protocol was approved by the hospital Review Board in Human Research, and all subjects who participated in the study provided written informed consent.

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 been already described.19,20 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.15 Briefly, from the surface ECG, the computer program calculates the series of consecutive RR intervals.

The Table summarizes the mean values of RR interval, its variance, LFnu, HFn u, and the LF/HF ratio observed during the working periods corresponding to 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 HFn u showed opposite changes (Figures 1 and 2).

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 HFn u showed opposite changes (Figures 1 and 2).

Working Periods and Different Shifts

The Table summarizes the mean values of RR interval, its variance, LFnu, HFn u, 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 HFn u was only slightly higher during

<table>
<thead>
<tr>
<th>Working Periods</th>
<th>First Shift</th>
<th>Second Shift</th>
<th>Third Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep (6±0.3 h)</td>
<td>900±25</td>
<td>953±21</td>
<td>934±24</td>
</tr>
<tr>
<td>Work (8 h)</td>
<td>717±24†</td>
<td>682±22†</td>
<td>775±27†</td>
</tr>
<tr>
<td>Sleep (8±0.2 h)</td>
<td>17 083±1384</td>
<td>21 751±2338</td>
<td>19 266±2409</td>
</tr>
<tr>
<td>Work (8 h)</td>
<td>14 456±1942</td>
<td>11 944±1624†</td>
<td>17 152±2250</td>
</tr>
<tr>
<td>Sleep (5±0.3 h)</td>
<td>1241.6±162.9</td>
<td>1592.5±237.0</td>
<td>1222.9±128.3</td>
</tr>
<tr>
<td>Work (8 h)</td>
<td>1217.3±157.3</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>RR, ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>σRR, ms²</td>
<td>57.8±3.2</td>
<td>64.8±7.0</td>
<td>53.4±14.0</td>
</tr>
<tr>
<td>LFnu, ms²</td>
<td>477.5±101.7</td>
<td>634.8±171.4</td>
<td>151.4±144.0</td>
</tr>
<tr>
<td>HFn u, ms²</td>
<td>24.2±2.6</td>
<td>25.4±1.9</td>
<td>23.8±1.9</td>
</tr>
<tr>
<td>LF/HF</td>
<td>4.0±0.5</td>
<td>3.5±0.5</td>
<td>4.4±1.1</td>
</tr>
<tr>
<td>LF, ms²</td>
<td>19 266±2409</td>
<td>17 152±2250</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>HFn u</td>
<td>10 183±1942</td>
<td>11 944±1624†</td>
<td>17 152±2250</td>
</tr>
<tr>
<td>LF/HF</td>
<td>21 751±2338</td>
<td>11 944±1624†</td>
<td>17 152±2250</td>
</tr>
<tr>
<td>LFnu, ms²</td>
<td>1592.5±237.0</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>HFn u</td>
<td>21 751±2338</td>
<td>11 944±1624†</td>
<td>17 152±2250</td>
</tr>
<tr>
<td>LF/HF</td>
<td>53.4±144.0</td>
<td>523.7±133.6</td>
<td>143±13.3§</td>
</tr>
<tr>
<td>LF, ms²</td>
<td>1217.3±157.3</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>HFn u</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>LF/HF</td>
<td>53.4±144.0</td>
<td>523.7±133.6</td>
<td>143±13.3§</td>
</tr>
<tr>
<td>LFnu, ms²</td>
<td>1592.5±237.0</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>HFn u</td>
<td>11 944±1624†</td>
<td>17 152±2250</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>LF/HF</td>
<td>53.4±144.0</td>
<td>523.7±133.6</td>
<td>143±13.3§</td>
</tr>
<tr>
<td>LF, ms²</td>
<td>1465.9±178.9</td>
<td>1339.4±137.1</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>HFn u</td>
<td>17 152±2250</td>
<td>1339.4±137.1</td>
<td>1339.4±137.1</td>
</tr>
<tr>
<td>LF/HF</td>
<td>53.4±144.0</td>
<td>523.7±133.6</td>
<td>143±13.3§</td>
</tr>
</tbody>
</table>

RR indicates RR interval; σRR indicates RR variance.

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

#P < 0.05 third shift vs first shift during working period; §P < 0.05 third shift vs second shift during working period.
the third shift compared with the others (Figure 1). Conversely, \( LF_{nu} \) 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\(^{24,25} \) and mental\(^{24} \) 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 daily cardiac autonomic control.

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

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.
LF\textsubscript{nu} 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 LF\textsubscript{nu} and HF\textsubscript{nu}. Indeed, in every shift, LF\textsubscript{nu} 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, HF\textsubscript{nu} 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.\textsuperscript{12}

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.\textsuperscript{13} In a study that used power spectral analysis of RR and blood pressure variabilities, LF\textsubscript{nu} and the LF/HF ratio, which reflects the sympathovagal interaction, were lower during sleeping hours, increased at wakening time, and were higher in concomitance with daily activity.\textsuperscript{15} Similar results were obtained in continuously recumbent healthy subjects\textsuperscript{26} and by other studies that used EEG recordings to study circadian oscillations of body temperature and plasma cortisol as observed in different groups of shift workers.\textsuperscript{9,31,32}

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.\textsuperscript{9,31,32}

Finally, the continuous changes over the years of the time of maximum cardiac sympathetic modulation, as suggested by the pattern of the LF\textsubscript{nu} and the LF/HF indexes, might play a role in the excessive rate of cardiovascular disease described in habitual shift workers.\textsuperscript{17,18}

**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 (LF\textsubscript{nu} 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\textsuperscript{33} 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\textsuperscript{34} and train drivers\textsuperscript{35} and in pilots during training sessions\textsuperscript{36} when the appropriate tasks were performed at nighttime. As a consequence, a higher rate of errors\textsuperscript{6,7} or accidents\textsuperscript{1} has been observed compared with day work. Second, the fact that the indexes of cardiac sympathetic modulation, LF\textsubscript{nu} 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 LF\textsubscript{nu} and LF/HF) and the internal, schedule-independent, biological clock. In fact, in accordance with the latter, LF\textsubscript{nu} 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.\textsuperscript{6,7}

**References**

Modifications of Cardiac Autonomic Profile Associated With a Shift Schedule of Work
Raffaello Furlan, Franca Barbic, Simona Piazza, Mauro Tinelli, Paolo Seghizzi and Alberto Malliani

doi: 10.1161/01.CIR.102.16.1912

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/102/16/1912

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/