Alteration of circadian time structure of blood pressure caused by night shift schedule

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The effects of night shift schedules on circadian time structure of blood pressure were studied in seven healthy young subjects by continuous monitoring of blood pressure every 30 min for 72 h. In the control experiment, subjects were instructed to sleep at regular times with the light off at 00.00 h and the light on at 07.00 h. In the shift experiment, they were instructed to go to bed at 06.00 h and wake up at 11.00 h. The circadian rhythm of blood pressure rapidly phase delayed by 3.5 h in the second night shift day as a group phenomenon. Individual differences in changes in power spectral patterns of blood pressure were found in the night shift schedule. Ultradian rhythmicity of blood pressure was more pronounced in three subjects, whereas the circadian rhythmicity was maintained in four subjects. These findings held when the adaptation to shift work was taken into account.

Key words: Blood pressure; circadian rhythm; ultradian rhythm.

INTRODUCTION

The effects of shift work on circadian time structure in the cardiovascular system have been studied in occupational medicine. Although there is a report that the association between shift work and ischaemic heart diseases or cerebrovascular disease is weak,¹ the altered sleep schedule could affect the development of these work-related diseases by changing cardiovascular function.² It has been reported that the resynchronization of circadian rhythm in blood pressure to a night shift schedule occurs much more rapidly than other circadian parameters such as body temperature.³ This implies that blood pressure circadian rhythm is largely dependent on circadian rhythm in sleep–wakefulness.³⁻⁵ It has also been reported that there are ultradian and circadian rhythm components in the blood pressure of both animals⁶⁻⁷ and humans.⁸⁻¹⁰

The existence of ultradian rhythms in blood pressure suggests the possibility that the oscillation of the biological rhythm of blood pressure is not totally controlled by external synchronizers. The ultradian rhythmic components driven by the endogenous oscillation can contribute to the oscillation of biological rhythms of blood pressure. The ultradian changes in the functions of the autonomic nervous system have been assumed to be responsible for ultradian oscillations of blood pressure.⁷

In order to clarify circadian and ultradian time structures of blood pressure by power spectral analysis, ambulatory blood pressure must be continuously monitored for at least 24 h. The present study was designed to investigate the circadian time structure of blood pressure and its changes caused by night shift schedules by applying power spectral analysis to data recorded continuously for 72 h. Individual differences in the circadian time structure of blood pressure rhythm were studied here because individual differences in the human temporal structure are seldom taken into account in the studies devoted to the effect of shift work although individual differences in the ability to work night shifts have been documented.¹¹⁻¹⁵
METHODS

Subjects and study protocol

Seven healthy young subjects (five males and two females, from 19 to 23 years of age) volunteered to participate in this study. They apparently had no particular health problems, and were classified as neither morning nor evening types according to Horne and Östberg's questionnaire. All subjects were synchronized with a diurnal activity from 07.00 to 24.00 h and sleep from 24.00 and 07.00 h for one week before the experiment. They recorded times going to bed and waking up in a sleep diary during the entire experimental period. After one week's synchronization, the blood pressures of subjects were measured for three consecutive days with sleep time from 00.00 to 07.00 h (control experiment). On the third control day, subjects were ordered to stay in a laboratory room with a neutral thermal for 24 h in order to precisely document circadian rhythm data. Sleep was deprived on the third day in order to document blood pressure circadian rhythm without sleep effects. This procedure, known as the constant routine, is a useful experimental method to validate an endogenous component of human circadian rhythm.

The night shift experiment was conducted for three consecutive days starting one week after the control day experiment (shift experiment). The experimental protocol was the same as that for the control days except that sleep time was from 06.00 to 11.00 h. At night, subjects were instructed to remain awake at a moderate level of activity such as reading or desk work. On the third day of the night shift experiment, subjects were ordered to stay in a laboratory room with a neutral thermal for 24 h, and sleep was deprived. In both experiments, the duration of sleep and the quality of sleep were monitored by a sleep diary every day. Subjects reported to be able to sleep even in the shift experiment, in spite of a decrease in the quality of sleep. Subjects took no pharmacologically active agents in order to facilitate or phase delay their sleep.

Monitoring of blood pressure

Blood pressure was monitored continuously by a non-invasive ambulatory blood pressure monitoring apparatus, ABPM600 (Nippon Colin, Komaki City, Japan) for 72 h. Systolic and diastolic blood pressure and heart rate were automatically recorded every 30 min. This apparatus recorded blood pressure of the brachial artery by the Korotokoff method and the oscillometric method. In this study the data from the oscillometric method were used for the analysis. The predominant power spectrum of 24 h was observed in both systolic and diastolic blood pressure. An ultradian rhythm with \( T = 8 \) h was also found in the systolic blood pressure. Figure 1 (right) shows a chronogram of blood pressure and the results of power spectral analysis for the three shift days. A circadian rhythm pattern with \( T = 24 \) h was maintained in both systolic and diastolic blood pressures by visual inspection of the chronogram. The highest ultradian power density was 16 h in both systolic and diastolic blood pressure.

Circadian time structure of blood pressure in control days and its alteration in shift days

Figure 1 (left) shows an example of continuous recording of blood pressure and results of power spectral analysis for the three control days (Subject 3). The circadian rhythm of blood pressure with a period \( (\tau) = 24 \) h was confirmed by both visual inspection and power spectral analysis. The predominant power spectrum of 24 h was observed in both systolic and diastolic blood pressure. An ultradian rhythm with \( \tau = 8 \) h was also found in the systolic blood pressure. Figure 1 (right) shows a chronogram of blood pressure and the results of power spectral analysis for the three shift days. A circadian rhythm pattern with \( \tau = 24 \) h was maintained in both systolic and diastolic blood pressures by visual inspection of the chronogram. The highest ultradian power density was 16 h in both systolic and diastolic blood pressure.

Figure 2 (left) shows another example of the continuous recording of blood pressure and results of power spectral analysis in control days (Subject 1). A circadian rhythm with \( \tau = 24 \) h was dominant in both systolic and diastolic blood pressure as confirmed by visual inspection and power spectral analysis. Figure 2 (right) shows a chronogram of blood pressure and results of power spectral analysis for the three shift days. Visual inspection and power spectral analysis showed an ultradian rhythm with \( \tau = 8 \) h was dominant in both systolic and diastolic blood pressure. In this subject, the power spectrum of 24 h decreased during the night shift days.

Figure 3 shows the changes in mean blood pressure of all subjects in both control and shift days. In the second night shift day, the blood pressure trough, estimated by visual inspection on the chronogram, occurred around 3.5 h after that of the second control day in both systolic and diastolic blood pressure. This meant that the
Figure 1. Chronograms and results of power spectral analysis of blood pressure in both control (left) and shift days (right) in a subject with ultradian rhythm dominant type. Three days' data are shown for each experimental schedule. In control days, a circadian rhythm with a period of 24 h was observed by visual inspection of chronograms, and power spectral analysis confirmed a predominant power spectral density of 24 h in both systolic and diastolic blood pressure. In shift days, an ultradian rhythm with a period of 8 h was observed by both visual inspection and power spectral analysis.

Subject 3, Control days
Subject 3, Shift days

8 18 4 14 0 10 20
Time (Clock hour)

24
Period (hr)
Power spectra

12 22 8 18 4 14 0 10
Time (Clock hour)

24
Period (hr)
Power spectra

Figure 2. Chronograms and results of power spectral analysis of blood pressure in both control (left) and shift days (right) in a subject with circadian rhythm dominant type. Three days' data are shown for each experimental schedule. In control days, a circadian rhythm with a period of 24 h was observed by visual inspection of chronograms, and power spectral analysis confirmed a predominant power spectral density of 24 h in both systolic and diastolic blood pressure. In shift days, a circadian rhythm with a period of 24 h was still dominant as confirmed by both visual inspection and power spectral analysis.

Subject 1, Control days
Subject 1, Shift days

24
Period (hr)
Power spectra

32 8 3.55
Period (hr)
Power spectra

8 12 7.38
Period (hr)
Power spectra

32 7.38
Period (hr)
Power spectra

circadian rhythm of blood pressure was rapidly phase delayed by 3.5 h by the night shift schedule as a group phenomenon.

Change in power spectral pattern of blood pressure caused by night shift schedule

Table 1 summarizes changes in power spectral patterns of blood pressure and heart rate caused by the experimental night shift schedules of seven subjects. In control days, the power spectral density of 24 h was dominant in both systolic and diastolic blood pressure and heart rate in all subjects. In shift days, the power spectral density of 24 h was also dominant except in Subject 1. Regarding the highest ultradian power spectral density of blood pressure, four subjects showed the predominance of an ultradian rhythm with \( \tau \geq 12 \text{ h} \) (\( \tau = 16 \sim 19.2 \text{ h} \)), whereas three subjects showed the predominance of an
Figure 3. Changes in mean blood pressure of all subjects in both control (white circles) and shift days (black circles). In the second night shift day, the circadian rhythm of blood pressure phase was delayed by 4.5 h by the night shift schedule.

Table 1. Power spectral patterns of blood pressure and heart rate in all subjects. Subjects whose highest ultradian power spectral density was 12 h or higher were classified as A. Subjects whose highest ultradian power spectral density in shift days was less than 12 h were classified as B. Dominant ultradian power spectra in shift days were shown in italic.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Power spectra</th>
<th>Ultrasound rhythm pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Systolic BP</td>
<td>24 &gt; 8 &gt; 12</td>
</tr>
<tr>
<td></td>
<td>Diastolic BP</td>
<td>24 &gt; 19.2 &gt; 16</td>
</tr>
<tr>
<td></td>
<td>Heart rate</td>
<td>12 &gt; 24 &gt; 19.2</td>
</tr>
<tr>
<td>2</td>
<td>Systolic BP</td>
<td>24 &gt; 12 &gt; 6.9</td>
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<tr>
<td></td>
<td>Diastolic BP</td>
<td>24 &gt; 16 &gt; 12</td>
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<tr>
<td></td>
<td>Heart rate</td>
<td>24 &gt; 12 &gt; 10.3</td>
</tr>
<tr>
<td>3</td>
<td>Systolic BP</td>
<td>24 &gt; 12 &gt; 19.2</td>
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<tr>
<td></td>
<td>Diastolic BP</td>
<td>24 &gt; 7.4 &gt; 16</td>
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<td></td>
<td>Heart rate</td>
<td>24 &gt; 19.2 &gt; 7.4</td>
</tr>
<tr>
<td>4</td>
<td>Systolic BP</td>
<td>24 &gt; 19.2 &gt; 16</td>
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<tr>
<td></td>
<td>Diastolic BP</td>
<td>24 &gt; 13.2 &gt; 16</td>
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<tr>
<td></td>
<td>Heart rate</td>
<td>24 &gt; 10.7 &gt; 3.7</td>
</tr>
<tr>
<td>5</td>
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<tr>
<td></td>
<td>Diastolic BP</td>
<td>24 &gt; 12 &gt; 19.2</td>
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<tr>
<td></td>
<td>Heart rate</td>
<td>24 &gt; 12 &gt; 6</td>
</tr>
<tr>
<td>6</td>
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<td>Diastolic BP</td>
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<td></td>
<td>Heart rate</td>
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<tr>
<td>7</td>
<td>Systolic BP</td>
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<td>Diastolic BP</td>
<td>24 &gt; 12 &gt; 9.6</td>
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<tr>
<td></td>
<td>Heart rate</td>
<td>24 &gt; 19.2 &gt; 13.7</td>
</tr>
</tbody>
</table>

A = Predominant ultradian period in a range from 12 to 20 h.
B = Predominant ultradian period less than 12 h.

Figure 4. An example of three days’ data on blood pressure and the levels of physical activity in shift days in a subject with ultradian rhythm dominant type. The categories of levels of physical activities were as follows: asleep (level 1); awake but lying down (level 2); sitting down — relaxed (level 3); sitting down — mentally active (level 4); standing or walking intermittently (level 5) and physically active (level 6). Ultradian peaks of systolic blood pressure corresponding to levels 5 and 6 are shown by the arrow.
ultradian rhythm with $\tau < 12$ h ($\tau = 3.69$ h). The former group was comprised of subjects whose circadian rhythmicity of blood pressure was maintained by visual inspection during the night shift schedule (see Figure 1). The latter group was comprised of subjects whose circadian rhythmicity tended to decrease while the ultradian rhythmicity became dominant by visual inspection during the night shift schedule (see Figure 2).

Physical activity level and ultradian peak of blood pressure

Figure 4 shows an example of three days' data for blood pressure and the level of physical activity in night shift days in one subject with ultradian rhythm dominance (Subject 1). The times of ultradian peaks of blood pressure were compared to those of peak times of physical activity level 6. The ultradian peaks of systolic and diastolic blood pressure corresponding to level 6 of physical activity are shown by the upward and downward arrows, respectively, in Figure 3. The total number of ultradian peaks of systolic and diastolic blood pressure corresponding to level 6 was eight and 10, respectively, during the three days. There were 20 peaks of physical activity level 6. Thus, 40% of the ultradian peaks of systolic blood pressure and 50% of the ultradian peaks of diastolic blood pressure were explained by the physical activity peaks in this subject. The coincidence rate of peak of blood pressure and level 6 of physical activity in the three subjects whose highest ultradian rhythm period was less than 12 h was 31.7 ± 7.6% in systolic blood pressure and 33.3 ± 15.3% in diastolic blood pressure, respectively, in shift days. On the other hand, in control days, the coincidence rate of peak of blood pressure and level 6 of physical activity in the three subjects whose highest ultradian rhythm period was less than 12 h was 22.1 ± 7.5% in systolic blood pressure and 27.2 ± 8.0% in diastolic blood pressure, respectively.

DISCUSSION

The circadian rhythm in blood pressure was confirmed in control days. There were individual differences in changes in circadian time structure of blood pressure during the night shift schedule. In shift days, circadian rhythmicity of blood pressure was less dominant than the ultradian rhythmicity in three subjects. The ultradian rhythmicities become apparent by visual inspection when the highest ultradian power spectrum was less than 9 h in these subjects. Subject 1, who showed an apparent ultradian rhythm dominance of 8 h in both systolic and diastolic blood pressure in shift days, was a typical case. In this subject, biological rhythms of blood pressure and sleep-wakefulness were desynchronized internally.12,18 Thus, the subject with ultradian rhythm dominance was apt to have an internal desynchronization between biological rhythms of blood pressure and sleep-wakefulness. In contrast, the blood pressure of the other four subjects maintained a circadian pattern. In these subjects, the highest ultradian power spectrum in shift days was greater than 16 h. The circadian rhythm in blood pressure in shift workers has been reported to adapt to new sleep-wake cycles of night shifts within a few days.2 This rapid adaptation to night shift occurs because circadian rhythm of blood pressure is largely dependent on sleep time.3,4 In past studies, mean blood pressure was presented and analysed in relation to rapid phase shifts of circadian patterns of blood pressure, though there were no further analyses of individual blood pressure data from individuals. Therefore, there is a possibility that mean data of blood pressure masked the information on individual differences in phase transition of blood pressure in response to night shift schedule.

The present study clarified individual differences of blood pressure circadian rhythms to the 6 h phase delay schedule for three days. Three days' data were obtained to provide enough information on blood pressure for power spectral analysis. By using 144 points of time series data, 24 h power spectrum and ultradian power spectra from 3–20 h were separated by power spectral analysis. In the subjects with the highest ultradian rhythm period in a range from 12 to 20 h, circadian rhythm of blood pressure was largely dependent on the sleep time, and their circadian patterns of blood pressure rapidly phase-shifted to night shift schedule, while circadian patterns in shift days did not differ greatly from those of control days. In contrast, in the subjects with the highest ultradian rhythm period equalling less than 12 h, an ultradian rhythm pattern of blood pressure was dominant in shift days by visual inspection. Although physical activity could influence rhythmic patterns of blood pressure, its contribution to blood pressure variation was limited. In the present study, 22–33% of ultradian rhythmic variations in the mean were explained by physical activities in both shift and control days, results which were similar to those of Stewart et al.,19 who reported that ambulatory blood pressure monitoring in hypertensive patients showed that activity accounted for 20% of variations in systolic blood pressure and 26% of variations in diastolic blood pressure. Thus, the remaining variations in blood pressure were probably caused by other factors. In the present study, we cannot clarify whether individual differences in circadian time structure caused by night shift schedules were due to endogenous factors, but the ultradian fluctuation of blood pressure was not fully explained by the physical activity. Since there is a report suggesting that individual differences in the flexibility of human temporal organization can be explained by genetic background,13,14 future studies should be designed to focus on the role of some endogenous factor in the individual difference in circadian time structure of human blood pressure.

The individually different response to night shift schedule could be explained by the degree of flexibility of circadian time structure against the external synchronizer,12,13 although its precise mechanism is unclear. The subjects whose circadian time structure in shift days remained nearly the same as in control days seemed to be those who adapted rapidly to the night shift schedule, and therefore were considered to maintain good health during
the ultradian time structure became dominant in shift days seemed to be those whose health condition deteriorated during the night shift schedule due to a tendency towards internal desynchronization of circadian rhythm. Furthermore, field studies on shift workers are necessary in order to confirm the above-mentioned possibility of predicting the tolerance to shift work from the flexibility of circadian time structure of blood pressure.

In conclusion, circadian rhythm of blood pressure was rapidly phase delayed by 3.5 h by night shift schedules in healthy human subjects as a group phenomenon, and there were individual differences in the circadian time structure of blood pressure during a night shift schedule.

REFERENCES