URINARY EXCRETION OF ADRENALINE, NORADRENALINE, 17-OHCS, 5-HYDROXYTRYPTAMINE AND CERTAIN ELECTROLYTES IN 24-HOUR SHIFT WORKERS TAKING A 4-HOUR NIGHT NAP

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Urinary excretion of adrenaline, noradrenaline, 17-OHCS, 5-hydroxytryptamine and certain electrolytes was measured in 15 male guards engaged in 24-hour shift work containing a 4-hour night nap.

In the night nap, it was found that the urinary output of adrenaline had a significant negative correlation to a self-rated value of feeling about depth of sleep. Based on this finding, it is considered that adrenaline output may be useful as a sleep index.

The urinary level of adrenaline during the night nap was as low as the level during usual normal night sleep. However, the level of adrenaline during a daytime nap after the night work was considerably high compared to those in the night nap and in the normal night sleep. This suggests that the daytime nap was possibly not so deep as night sleep.

According to a report\(^1\) of the Shift Work Committee of the Japan Association of Industrial Health, more than one fifth of workers engaged in mining and manufacturing in Japan are estimated to work at night, mostly on various kinds of shift work schedules. Many of the night workers complain of disadvantages in the abnormal life caused by the night work, especially about disorders of sleep\(^2\). To compensate for the lack of night sleep, the workers usually take a nap in the daytime after the night work. However, such daytime sleep is often disturbed by various kinds of environmental noise\(^3\).

Differences in quality of sleep between that at night and that during the daytime have been demonstrated by EEG measurements. Matsumoto\(^4\) observed in hospital nurses that the percent of stage 1 during sleep in the daytime was significantly higher than that at night, while the percent of stage 2 was smaller in the former than in the latter, and the REM latency and REM cycle were shorter in the former than those in the latter. He also found frequent awakening during daytime sleep. Rutenfranz et al.\(^5\) showed that the duration of sleep in a sound-proof chamber was considerably shorter in the daytime than at night, and that the time course of REM sleep in the daytime was quite different from that at night.
In usual life, men excrete smaller amounts of adrenaline and noradrenaline in the urine in night sleep than during daytime activity\(^4\). According to Fröberg et al\(^5\), the diurnal rhythm of adrenaline excretion was maintained in sleep-deprived men. However, the level of urinary adrenaline in the awake nights in their report appeared to be high compared to the level during normal night sleep given in their later report\(^6\). Excretory rhythm of noradrenaline was not so clear in the sleep-deprivation of their experiment.

The present author et al\(^7\) previously measured the urinary excretion of catecholamines in three-shift workers. In that study, the diurnal rhythm of catecholamine excretion in the day and evening shifts was almost the same as in usual life, although the phase of the rhythm was slightly different. In the night shift, however, the catecholamine level at midnight was markedly high, and the level in the daytime was considerably low compared to those in the former two shifts. These findings are presumed to be related to a reversal of activity and sleep in the night shift. That is to say, the high level of catecholamine excretion in the night shift was probably due to mental and physical activity at night and the low level of the amine excretion in daytime would be attributable to the daytime nap after the night work.

In the present study, the urinary excretion of adrenaline, noradrenaline, 17-OHCS, 5-hydroxytryptamine (serotonin) and certain electrolytes was studied in 24-hour shift workers taking a 4-hour night nap. The relationship between sleep and the variable excretion levels, mainly of catecholamine, is discussed.

**Materials and Methods**

The subjects used were 15 male workers engaged in 24-hour shift work, who had served as guards in an office for 3 to 20 years (average 11 years). Their mean age was 46 years (35 to 58). They were in three groups and worked from 09.00 a.m. to 09.00 a.m. the following morning every 3 days. During the night of the working day, they took a 4-hour sleep in a sleeping room from 22.00 to 02.00, from 00.00 to 04.00 or from 02.00 to 06.00 according to a given schedule. Otherwise, they patrolled around the office buildings for about 40 min every hour. From 08.00 to 09.00 and from 17.00 to 18.00, they were relatively tense, since they had to stand by an entrance of the office and keep watch on the passengers passing through the gate.

Urine was collected from each subject at 3- or 4-hour intervals on 3 consecutive working days. After the workers had returned home, urine was also collected during their daytime nap and night sleep in the first work-off day, and during the morning (9.00 to 12.00) and night sleep in the second off day.

The free adrenaline and noradrenaline contents of the urine samples were determined by the methods described previously\(^8\), and the creatinine content by using the method of Technicon Instrument Co. In addition, 17-OHCS was analyzed with the Cica Ohakit of Kanto Chemical Co., serotonin and histamine by fluorometric methods using o-phthalaldehyde\(^9\), and Na\(^+\), K\(^+\), Ca\(^{2+}\) and Mg\(^{2+}\) by atomic absorption spectrometry.
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After their sleep and naps, the subjects were asked to complete a questionnaire on sleeping hours and subjective feelings of sleep. The subjective feelings of sleep were estimated by a graphic rating-scale method using the following scale: 1, did not sleep at all; 2, slept but not so soundly; 3, slept fairly well; 4, slept very well. The rated values on this scale were tentatively used as the depth of sleep.

The measurements were carried out in November.

RESULTS

1) Diurnal variations in the excretion of catecholamine, 17-OHCS, serotonin, histamine and certain electrolytes in 24-hour shift workers on working days.

The adrenaline and noradrenaline outputs of the 24-hour shift workers on working days are illustrated in Figs. 1 and 2, respectively. The adrenaline value was remarkably high in the morning (06.00-12.00) and in the evening (15.00-18.00) periods. Some of these periods contained busy working hours as described above. At night, the adrenaline level was very low during the night nap, and relatively high during the awake periods. Noradrenaline almost constantly showed a high level during the awake periods throughout the day, and a low level in the night nap periods.

Fig. 1. Diurnal variation of adrenaline excretion in 24-hour shift workers.

- - - O - - - night nap from 22.00 to 02.00
- - - - x - - - night nap from 00.00 to 04.00
- - - - - - - night nap from 02.00 to 06.00
The circadian rhythm of 17-OHCS in the present workers during the working days (Fig. 3) was almost the same as the rhythm in normal life reported previously. There was almost no difference in rhythm among the three types of night nap schedules. Only the level of the working subjects in the early morning (02.00–06.00) was apparently higher than the level of the sleeping subjects during the same period, while the levels...
of the working subjects and sleeping subjects were almost the same at midnight (22.00–02.00). These findings suggest a diurnal variation in responsiveness of 17-OHCS secretion to stress.

The serotonin levels showed a tendency to be higher at midnight and early in the morning, but the time of the serotonin peak did not correspond to the nap time (Fig. 4), in contrast to the results for catecholamine excretion. Histamine excretion did not show any clear diurnal variation. The potassium value was low in the evening and night, and relatively high in the morning, but the other electrolytes appeared to display no distinct diurnal rhythms.

![Fig. 4. Diurnal variation of 5-HT excretion in 24-hour shift workers.](image)

2) Catecholamine excretion in duty days and work-off days.

The mean values of adrenaline and noradrenaline in the morning did not show any remarkable difference between the duty and work-off days (Table 1). However, large intra-individual daily variations in these amine values were observed in the work-off days as compared to the duty days (Fig. 5).

3) Comparison of night nap, daytime nap and normal night sleep.

Table 2 gives a comparison of the results obtained from the three kinds of sleep, i.e. night nap on the working day at the workplace, daytime nap at home and normal night sleep.
The adrenaline value in the normal night sleep (1.03±0.14 ng/mg of creatinine, mean±s.e.) and the value in the night nap (0.95±0.11) were almost the same. However, the value during the daytime nap (3.69±0.81) was significantly larger than these values. The same was true for the noradrenaline excretion, with values of 18.0±1.9, 14.7±1.1 and 22.8±2.6, respectively.

No significant difference in catecholamine excretion was observed between the first
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Table 1. Catecholamine values in the morning of duty days and work-off days.

<table>
<thead>
<tr>
<th>No.</th>
<th>Adrenaline</th>
<th>Noradrenaline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duty day</td>
<td>Off day</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>7.3±0.8*</td>
</tr>
<tr>
<td>Cases of high adrenaline in off day</td>
<td>9</td>
<td>6.9±1.2</td>
</tr>
<tr>
<td>Other cases</td>
<td>36</td>
<td>7.5±0.5</td>
</tr>
</tbody>
</table>

a: ng/mg of creatinine (mean±s.e.).
b: The values in this row were calculated from individual mean values.
c: Cases in which the adrenaline value was higher in the work-off day than that of the same worker in the duty day immediately before the work-off day.

**: p<0.01.

Table 2 Comparison of three types of sleep in 24-hour shift workers.

<table>
<thead>
<tr>
<th>Degree of subjective feeling of sleep</th>
<th>Sleeping hours (min)</th>
<th>Adrenaline excretion (ng/mg of creatinine)</th>
<th>Noradrenaline excretion (ng/mg of creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night nap at the workplace</td>
<td>2.8±0.12</td>
<td>254±6 ***</td>
<td>0.95±0.11 ***</td>
</tr>
<tr>
<td>Daytime nap at home</td>
<td>2.7±0.17 **</td>
<td>167±20 **</td>
<td>3.69±0.81</td>
</tr>
<tr>
<td>Normal night sleep at home</td>
<td>3.6±0.11 ***</td>
<td>475±12 ***</td>
<td>1.03±0.14 ***</td>
</tr>
</tbody>
</table>

*: p < 0.05.
**: p < 0.01.

and second work-off days, with values of 1.04±0.13 and 1.03±0.17 for adrenaline, and 17.9±2.0 and 18.1±1.8 for noradrenaline.

The sleeping hours in the normal night sleep, night nap and daytime nap amounted to 475, 254 and 167 min, respectively. The self-rated value of the depth of sleep was larger in the normal night sleep (3.6 on the above-mentioned scale) than in both the night nap and daytime nap (2.8 and 2.7, respectively). This meant that the workers felt a kind of dissatisfaction with the daytime nap at home as well as the night nap at the workplace compared to normal night sleep.

4) Correlation between catecholamine excretion and self-rated value of sleep.

Fig. 6 illustrates the relationship between adrenaline excretion and the self-rated values of sleep for all of the 45 samples obtained from the 15 subjects in the night nap. The adrenaline level was significantly correlated with the rated value (p <0.05). This meant that the sounder sleep the worker felt, the smaller were the amounts of adrenaline found in the urine. Noradrenaline showed more ambiguous findings.
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It was not clear, however, whether the above result indicated an intra-individual correlation or an inter-individual one. This was therefore tested by regression analysis\(^{11}\) considering the individual difference in the urinary levels. Both the adrenaline and noradrenaline values were found to correlate significantly with the rated value of sleep (\(p < 0.05\)). It was indicated therefore that catecholamine excretion correlates intra-individually with the degree of subjective feeling of sleep.

**DISCUSSION**

In the field of work physiology, it is important to establish reliable indices of mental and physical stress in order to evaluate work load or work intensity.

In usual life, men are thought to be active mentally and physically in the daytime and to be at rest at night. Thus, each parameter, if it is to be useful as such a stress index, should show large and reproducible diurnal variations in such normal life. In this sense, the present subjects had an almost normal life during working days, although their sleeping hours were very short. As described above, urinary excretion of electrolytes except K\(^+\) showed no detectable diurnal variation. These parameters may therefore not be so useful as a stress index.

For similar reasons, it is considered that a useful stress index should show a marked difference between activity and sleep periods in the daytime or at night. It was demonstrated in the present study that the urinary excretion of K\(^+\), serotonin and 17-OHCS barely showed such an activity-sleep difference at night, although they did exhibit considerable diurnal variations. The diurnal variations of those variables could thus be attributed to intrinsic diurnal rhythms.

On the other hand, the urinary levels of adrenaline and noradrenaline showed remarkable diurnal variations in normal life, and clear-cut activity-sleep differences at night. It is considered, therefore, that sympathico-adrenomedullary activity as indicated by the urinary outputs of catecholamines may be useful as indices of stress. Ishizaki et al\(^{14}\) demonstrated previously that increased excretion of adrenaline and noradrenaline was found in physically active states and that only increased adrenaline was observed in mentally active states. In the present study, adrenaline excretion was considerably accelerated when the workers were presumed to be busy, and the adrenaline level was also high immediately after the start of the work. This finding suggests that the workers may be in a keyed-up state for a few hours after the beginning of their duty.

The mean levels of catecholamines in the morning did not show any significant difference between duty days and work-off days in the present workers. However, the distribution of coefficients of intra-individual variations among the three days measured was considerably different between the duty and work-off days (Fig. 6). That is to say, the catecholamine excretion showed a larger intra-individual daily variation in the work-off days than in the duty days. The total 45 cases were tentatively divided into two groups: one comprised the cases in which the adrenaline value in the work-off day was
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higher than that in the duty day immediately before the work-off day, and the other comprised the rest of the cases (Table 1). In the former cases, a significantly higher level of noradrenaline was found in the work-off days than in the duty days. In the latter cases, the adrenaline value in the off days was significantly lower than that in the duty days, but there was no difference in the noradrenaline values. The above results are presumed to suggest that the workers tend to be in physical activity in the work-off days in the former cases and at rest in the latter cases compared to the duty days. These findings probably reflect a large variation in the workers' lives in the work-off days.

On the other hand, the urinary outputs of adrenaline and noradrenaline were expected to be smaller in deeper sleep in men, based on the above hypothesis that sympathico-adrenomedullary activity is increased in various stressful situations. The present study investigated the relationship between a self-rated value of sleep and the excretion of catecholamine, particularly adrenaline. A significant negative correlation was found between these two parameters in the night nap. Such a correlation was not so clear in the case of the daytime nap or night sleep at home, perhaps due to a large variation in sleeping hours in the sleeping period.

The adrenaline value during the night nap at the work-place remained very low, similarly to the value during the usual night sleep at home. The noradrenaline level during the night nap was significantly lower than that in the usual night sleep (p<0.05).

Fig. 6. Relation between adrenaline excretion and degree of subjective feeling of depth of sleep in the night nap.
Similar findings were also observed in another study\textsuperscript{12,13} as described below (Table 3). Thus, no evidence was recognized in the catecholamine data to show poor sleep in the night nap compared to the usual night sleep. The inferiority of the night nap observed from the subjective feeling of depth of sleep possibly derived from the shorter sleeping hours in this nap. Oppositely, the adrenaline and noradrenaline values were large during the daytime nap. It is assumed, therefore, that the night nap taken during night duty was more effective than the daytime nap, in order to make up the deficit of normal night sleep.

Several years ago, the urinary outputs of catecholamines were investigated in two groups of three-shift workers in certain chemical plants\textsuperscript{12,13}. In the night shift, the workers in one group (A) were permitted to have a 2-hour nap and in the other group (B) to have a 3-hour nap during the working hours. The results\textsuperscript{14} of these two investigations and of the present study (C, 4-hour nap) are summarized for comparison in Table 3.

Table 3. Night nap hours and catecholamine excretion in night work.

<table>
<thead>
<tr>
<th>Study</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night nap hours (hours)</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>No. of workers investigated</td>
<td>14</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Working hours a day (hours)</td>
<td>10</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>No. of consecutive nightwork days</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Daytime nap hours after night work (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>333.3±21.5</td>
<td>217.7±20.8</td>
<td>167.0±19.9</td>
</tr>
<tr>
<td>1st day</td>
<td>349.2±30.8</td>
<td>250.0±30.3</td>
<td>167.0±19.9</td>
</tr>
<tr>
<td>2nd day</td>
<td>305.3±15.3</td>
<td>172.1±14.7</td>
<td></td>
</tr>
<tr>
<td>Adrenaline excretion (ng/mg of creatinine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night nap (mean)</td>
<td>1.57±0.51</td>
<td>1.51±0.34</td>
<td>0.95±0.11</td>
</tr>
<tr>
<td>Normal night sleep (mean)</td>
<td>0.72±0.16</td>
<td>0.97±0.28</td>
<td>1.03±0.14</td>
</tr>
<tr>
<td>Daytime nap Mean</td>
<td>2.16±0.57</td>
<td>2.73±0.45</td>
<td>3.69±0.81</td>
</tr>
<tr>
<td>1st day</td>
<td>1.16±0.30</td>
<td>2.24±0.49</td>
<td>3.69±0.81</td>
</tr>
<tr>
<td>2nd day</td>
<td>3.16±1.08</td>
<td>3.57±0.81</td>
<td></td>
</tr>
<tr>
<td>Noradrenaline excretion (ng/mg of creatinine)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night nap (mean)</td>
<td>18.4±1.4</td>
<td>15.7±1.7</td>
<td>14.7±1.1</td>
</tr>
<tr>
<td>Normal night sleep (mean)</td>
<td>14.6±0.9</td>
<td>18.3±2.7</td>
<td>18.0±1.9</td>
</tr>
<tr>
<td>Daytime nap Mean</td>
<td>16.9±1.2</td>
<td>19.4±2.8</td>
<td>22.8±2.6</td>
</tr>
<tr>
<td>1st day</td>
<td>16.1±1.3</td>
<td>18.3±2.2</td>
<td>22.8±2.6</td>
</tr>
<tr>
<td>2nd day</td>
<td>17.7±1.6</td>
<td>22.1±4.5</td>
<td></td>
</tr>
</tbody>
</table>

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In studies A and B, which had the shorter durations of night nap, the adrenaline value during the nap was slightly higher than that during the normal night sleep, while the two values were almost the same in the present study with a longer duration of night nap. The noradrenaline value in the night nap showed a high level in study A and a low level in studies B and C, compared to the value in the usual night sleep at home. It seems reasonable to consider, therefore, that a night nap of long duration tends to lead to deep and sound sleep and that the deep sleep results in a smaller amount of catecholamine excretion.

Among the three studies, the hours of daytime nap were the shortest in the present study (C), and the mean values of catecholamine excretion during the nap were the greatest. The workers in studies A and B continued their night work for three and two consecutive days, respectively. In study A, the urinary output of adrenaline during the daytime nap was greater on the second day than on the first day of the night shift. Study B also demonstrated a similar phenomenon; that is to say, the adrenaline and noradrenaline outputs during the daytime nap were larger on the second day than on the first day, and the daytime nap hours were shorter on the second day than on the first. It was found that one of the 15 workers in the present study (C) did not have daytime nap after the night work, and that two of 9 workers in study B also did not have a nap after the second day of the night shift, while all the workers took a nap after the first night duty. These findings perhaps mean that the night workers took only a short nap in the daytime on the day before a holiday. They probably preferred to take night sleep rather than a daytime nap, when possible, in order to compensate for the lack of sleep.

In study A, extremely low levels of adrenaline and noradrenaline (1.16±0.30 and 16.18±1.3 ng/mg of creatinine, respectively) were found in the urine of the workers during the daytime nap after the first day of the night shift. These levels were almost the same as their usual night levels (0.70±0.16 and 14.6±0.9, respectively). In study B, the noradrenaline level during the daytime nap after the first night duty (18.36±2.2) was also as low as the usual night level (18.3±2.7). Mori demonstrated a low level of adrenaline excretion in men during the daytime sleep after they were exposed to a heavy stressor throughout the previous night. The adrenaline level was reported to be as low as the level in their usual night sleep. These results appear to suggest that catecholamine excretion does not have any distinct endogenous circadian rhythm. The high levels of catecholamine excretion during the daytime nap would then be partially attributable to the shorter hours of the daytime nap and workers' motivation.

On the other hand, the present study demonstrated that the adrenaline values during the awake periods showed a day-night difference, as in the results of Froberg et al. and others. These findings suggest a possible day-night difference in susceptibility of the sympathico-adrenomedullary response to various stressors. The high level of adrenaline excretion during the daytime nap may indicate that the nap is unsatisfactory since the human body in the daytime is highly susceptible to various environmental stressors, such as noise and light.
REFERENCES