An Increase in Noradrenaline Excretion during Prolonged Mental Task Load

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Abstract: To investigate the effects of prolonged mental work, urinary excretion of catecholamines and cortisol was measured in 18 human subjects from 9:30 to 17:00. On the ‘task day,’ the subjects performed mental tasks during the morning (10:20-11:45) and afternoon sessions (13:00-17:00), otherwise taking chair rest. On the ‘control day,’ the subjects took chair rest in the afternoon after performing mental tasks in the morning. In the morning session, urinary excretion of adrenaline during mental work increased greatly compared to that before the mental work. Mental work in the afternoon session also caused a marked increase in adrenaline excretion compared to the rest level in the afternoon on the control day. Cortisol levels in the first hour of the afternoon mental work were significantly higher than those during the corresponding time on the control day. Urinary excretion of noradrenaline during mental work in the morning session only increased slightly compared to that before the mental work. In the afternoon session, however, noradrenaline excretion during mental work on the task day was markedly elevated compared to that during the rest condition at the corresponding time on the control day. These findings suggest that prolonged exposure to mental work, but not short-term mental work, produces a marked increase in noradrenaline excretion in human subjects.

Key words: Prolonged mental work, Noradrenaline, Adrenaline, Cortisol, Urine, Questionnaire

Introduction

It is thought that work load or work stress may be responsible for certain health problems, for example, ulcers, high blood pressure and myocardial infarction, in workers2). To protect workers from these problems, it is necessary to evaluate the work load associated with their jobs, and to control the working conditions and environment. To evaluate the work load, several objective measures, such as a Questionnaire on subjective fatigue complaints that was developed by Japan Association of Industrial Health, have been used in experimental and field studies on industrial health.

Urinary excretion and plasma levels of adrenaline and noradrenaline are known to increase under various stressful situations3). Previous experimental studies3-5) have revealed that the performance of mental arithmetic over a 1 hr period induces a marked increase in urinary excretion of adrenaline, but not noradrenaline, in human subjects, while physical exercise over the same time period causes large increases in both adrenaline and noradrenaline excretion. This suggests that excretion of adrenaline, but not noradrenaline is a useful index for the evaluation of mental stress. This notion has been supported by several other studies6,7). However, most of previously published studies dealt with short-term (1 to 2 hr) exposure to mental stress. To our knowledge, little is known about the changes in catecholamine excretion associated with prolonged mental work. In the study reported here, we describe the effects of prolonged mental tasks on urinary excretion of catecholamines, with the emphasis on noradrenaline, in human subjects.
**Experimentals**

The subjects used in this study were 18 healthy college students, 16 male and 2 female, with an average age of 22.3 years (range: 20–25). On their arrival at 9:00, the subjects took rest for one hour and 20 min until the start of the experiment. The time schedule of the experiment is shown in Table 1. On the task day (Day A), the subjects performed 3 kinds of mental task on a visual display unit: an anagram task between 10:20 and 11:45; entry of 4-digit numbers using a keyboard between 13:00 and 15:00; and comparisons of 2 4-digit numbers between 15:15 and 17:00. On the control day (Day B), the subjects performed the anagram task between 10:20 and 11:45, and in the afternoon (13:00–17:00) they spent 5 hr relaxing in a separate room, reading newspapers or magazines, watching TV or listening to CD music. The anagram task used on Day B was supposed to be easier than that used on Day A, because the number of letters used in the anagram task was 3–4 on Day B and 4–8 on Day A. All of the subjects were asked to perform the tasks as quickly and precisely as possible. The subjects were assigned randomly to either the schedule of Day A after Day B or to the schedule of Day B after Day A, and the interval between Days A and B for each subject was usually 7 days. The rationale behind the experiment was explained in advance to the subjects, and informed consent was obtained from all of them.

Samples of urine and saliva from each subject were collected before and after the tasks, as shown in Table 1. Self-rated scores for fatigue, stress and arousal were measured using questionnaire with a 6-point scale. Catecholamines and cortisol in the urine were analyzed by HPLC fluorometric methods, and expressed as pmol/min/kg body weight. Salivary cortisol was also measured by the HPLC method. Urinary outputs of sodium and potassium were measured by the atomic absorption spectrophotometric method. During the performance of tasks, blood pressure and pulse rate were recorded by means of an automatic hemodynamometer (ABPM-630, Nippon Colin Co., Japan) using the Korotokoff Riva-Rocci method. Data are presented as the mean ± SE. Levels of statistical significance were tested by a paired t-test, and differences at the level of p<0.05 were considered to be significant. To test the effects of morning tasks on Days A and B, the data were compared with those before the morning task. To examine the effects of the afternoon task, comparisons were made between the data at corresponding times on Days A and B.

**Results**

Catecholamine and cortisol excretion during mental tasks performed in the morning and afternoon

Urinary excretion of adrenaline, noradrenaline and dopamine during the mental tasks in the morning and afternoon is shown in Table 2. In the morning of Days A

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**Table 1. Time schedule of the experiment**

<table>
<thead>
<tr>
<th>Time of day</th>
<th>Task Day A</th>
<th>Task Day B</th>
<th>Measurement</th>
<th>Urine</th>
<th>Saliva</th>
<th>Questionnaire</th>
<th>Pulse rate &amp; B.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:30</td>
<td>Rest</td>
<td>Rest</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>10:20</td>
<td>Task I</td>
<td>Task I'</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>11:45</td>
<td>Lunch &amp; Rest</td>
<td>Lunch &amp; Rest</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>12:45</td>
<td>Task II</td>
<td>Rest</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>14:10</td>
<td>Task II</td>
<td>Rest</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>15:00</td>
<td>Task III</td>
<td>Rest</td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>17:00</td>
<td></td>
<td></td>
<td></td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>

Task I: anagram task, Task II: entry of 4-digit numbers using a keyboard, and Task III: comparison of two 4-digit numbers. Anagram in task I’ on Day B was easier than that in task I on Day A. The symbol means that the measurements were carried out in the time period indicated.
and B, adrenaline excretion increased significantly during the anagram tasks compared with the pre-task levels, the percentage increase being similar on both days (50% for Day A, 54% for Day B). This result suggests that the task difficulty had no effect on adrenaline excretion. Adrenaline excretion in the afternoon on Day A was significantly higher than that during rest periods in the afternoon on Day B.

Noradrenaline excretion exhibited a slight increase during the anagram tasks in the morning session on both Days A and B. The percentage increase in noradrenaline excretion was 6% and 12% for Days A and B, respectively. This small increase suggests that task difficulty had little effect on this parameter. Noradrenaline levels in the afternoon on Day A were significantly higher (18–36%) than the initial resting level on Day A, and were also higher (29–41%) than the levels at the corresponding time on Day B. On Day B, urinary excretion of dopamine was increased during the task period, compared to that before the task (Table 2). The dopamine level during the last session of task on Day A was higher than during the rest period at the corresponding time of day on Day B. These findings suggest a task-related increase in dopamine excretion.

Cortisol excretion was relatively high in the rest period before the morning tasks on both Days A and B, probably due to its circadian rhythm of secretion. The reduction in cortisol excretion during the mental task on Day A was relatively small (18%) and was not statistically significant (p=0.48). However, the difference in cortisol excretion between the pre-task period and the task period in the morning on Day B (40% decrease) was significant (p=0.012). These findings suggest that the reduction in cortisol levels is less pronounced in response to a difficult anagram task than in response to an easier anagram task. The increase in cortisol excretion in the first 1.5-hr period of the afternoon session on both Days A and B may be partially attributable to an after-meal increase in cortisol secretion.

The ratio of the sodium concentration to the potassium concentration in urine decreased during the task in the morning on both Days A and B. The ratio in the afternoon on Day A was also lower than in the afternoon on Day B.

Salivary levels of cortisol during the mental tasks

Cortisol concentrations (pmol/ml, mean ± SE) in saliva collected at 10:10, 11:45, 12:45, 15:00 and 17:00 were 2.41 ± 0.25, 2.35 ± 0.25, 3.93 ± 0.51, 2.02 ± 0.21 and 1.91 ± 0.23 on Day A and 2.49 ± 0.27, 2.90 ± 0.37, 3.83 ± 0.51, 1.62 ± 0.19 and 2.24 ± 0.21 on Day B, respectively. There were no significant differences between saliva cortisol concentrations at different times, or on different days (A or B).

Self-rated scores of fatigue, stress and arousal during the mental tasks

Subjective scores of fatigue, stress and arousal are given in Table 3. The scores of fatigue during the morning tasks on Days A and B were significantly higher than those before the tasks, and a marked increase in the fatigue score was observed during the afternoon tasks on Day A compared to those on Day B. Stress scores showed a similar result.

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**Table 2. Catecholamines and cortisol and sodium/potassium ratio in urine before and during mental tasks**

<table>
<thead>
<tr>
<th>Day</th>
<th>Time of day</th>
<th>Task</th>
<th>Noradrenaline</th>
<th>Adrenaline</th>
<th>Dopamine</th>
<th>Cortisol</th>
<th>Na/K ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day A</td>
<td>9:30–10:10</td>
<td>rest</td>
<td>2.20 ± 0.16</td>
<td>0.47 ± 0.06</td>
<td>27.2 ± 1.8</td>
<td>1.54 ± 0.22</td>
<td>4.14 ± 0.49</td>
</tr>
<tr>
<td>(Task Day)</td>
<td>10:10–11:45</td>
<td>anagram</td>
<td>2.35 ± 0.18</td>
<td>0.70 ± 0.09**</td>
<td>26.1 ± 1.7</td>
<td>1.26 ± 0.31</td>
<td>3.19 ± 0.41**</td>
</tr>
<tr>
<td></td>
<td>11:45–12:45</td>
<td>rest</td>
<td>2.69 ± 0.23**</td>
<td>0.54 ± 0.06</td>
<td>27.5 ± 1.7</td>
<td>0.90 ± 0.12*</td>
<td>2.36 ± 0.34**</td>
</tr>
<tr>
<td></td>
<td>12:45–14:10</td>
<td>data entry</td>
<td>3.00 ± 0.18**</td>
<td>0.74 ± 0.08**</td>
<td>27.2 ± 1.6</td>
<td>1.81 ± 0.33*</td>
<td>3.80 ± 0.47</td>
</tr>
<tr>
<td></td>
<td>14:10–15:00</td>
<td>data entry</td>
<td>2.92 ± 0.14**</td>
<td>0.88 ± 0.09**</td>
<td>26.3 ± 1.4</td>
<td>0.99 ± 0.13</td>
<td>3.87 ± 0.44**</td>
</tr>
<tr>
<td></td>
<td>15:00–17:00</td>
<td>number comparison</td>
<td>2.61 ± 0.15**</td>
<td>0.87 ± 0.11**</td>
<td>27.1 ± 1.4</td>
<td>1.11 ± 0.26</td>
<td>4.19 ± 0.50*</td>
</tr>
<tr>
<td>Day B</td>
<td>9:30–10:10</td>
<td>rest</td>
<td>2.13 ± 0.16</td>
<td>0.44 ± 0.05</td>
<td>25.5 ± 1.4</td>
<td>1.76 ± 0.34</td>
<td>4.64 ± 1.04</td>
</tr>
<tr>
<td>(Control Day)</td>
<td>10:10–11:45</td>
<td>anagram</td>
<td>2.40 ± 0.15**</td>
<td>0.69 ± 0.07**</td>
<td>26.5 ± 1.6*</td>
<td>1.07 ± 0.21*</td>
<td>3.45 ± 0.50</td>
</tr>
<tr>
<td></td>
<td>11:45–12:45</td>
<td>rest</td>
<td>2.64 ± 0.20**</td>
<td>0.52 ± 0.05*</td>
<td>27.0 ± 1.7**</td>
<td>0.98 ± 0.16**</td>
<td>2.51 ± 0.38*</td>
</tr>
<tr>
<td></td>
<td>12:45–14:10</td>
<td>rest</td>
<td>2.32 ± 0.19*</td>
<td>0.36 ± 0.04</td>
<td>26.7 ± 1.7*</td>
<td>1.28 ± 0.18</td>
<td>4.95 ± 0.70</td>
</tr>
<tr>
<td></td>
<td>14:10–15:00</td>
<td>rest</td>
<td>2.08 ± 0.15</td>
<td>0.43 ± 0.04</td>
<td>25.3 ± 1.5</td>
<td>0.88 ± 0.16*</td>
<td>5.79 ± 0.69</td>
</tr>
<tr>
<td></td>
<td>15:00–17:00</td>
<td>rest</td>
<td>1.88 ± 0.15*</td>
<td>0.59 ± 0.07</td>
<td>25.1 ± 1.3</td>
<td>0.94 ± 0.16*</td>
<td>5.60 ± 0.62</td>
</tr>
</tbody>
</table>

Anagram on Day A was more difficult than on Day B. Urinary excretion of catecholamines and cortisol is expressed as pmol/min/kg BW, and presented as mean ± SE. (n=18). **: p<0.01, *: p<0.05 compared with the pre-task level (9:30–10:10) of each day, and "": p<0.01, "": p<0.05 for Day A vs Day B.
Task-related increases in the fatigue score tended to be greater in the afternoon session (38% at 15:00 and 54% at 17:00, compared to the respective rest-level on Day B) than those in the morning session (26% and 29%, compared to each pre-task level on Day A or Day B, respectively). Stress scores showed similar results, the percentage increases in the scores being 58% at the 15:00 and 62% at 17:00, compared to the rest-level on Day B, and those in the morning session 34% and 22%, compared to each pre-task level on Day A or Day B. It appears that the stress score was greater when performing the difficult anagram task than the easy anagram task. A decrease in the arousal score was observed during the afternoon tasks, and this decrease appeared to be greater, and was significantly greater during the last session of the task.

Pulse rate and blood pressure during the mental tasks
Table 4 shows pulse rates and blood pressures before, during and after the tasks on Days A and B. Although the initial pulse rate before the morning task was higher on Day B than on Day A, the pulse rate and systolic blood pressure tended to be higher on Day A than on Day B, suggesting that the difficulty of the anagram task is related to increases in pulse rate and systolic blood pressure. Pulse rates and blood pressures during tasks in the afternoon on Day A appeared to be higher than those in the rest periods on Days A and B.

Discussion
In the study reported here, we have investigated the urinary
excretion of catecholamines and cortisol, and other physiological and psychological parameters in human subjects performing mental tasks for 1.5 hr in the morning and 4 hr in the afternoon on the task day (Day A). On the control day (Day B), the subjects performed an easier mental task only in the morning. The task in the morning on both Days A and B caused a marked increase in adrenaline excretion, but only a slight increase in noradrenaline excretion. It was found, however, that cortisol excretion, pulse rate, systolic blood pressure and subjective scores of stress tended to be greater on Day A than on Day B, suggesting that the changes in the physiological functions are associated with the psychological effects of the difficulty of the task, or distress, as described by Lundberg and Frankenhaeuser.

The differences between Day A and Day B were no longer observed during lunch rest periods, implying that the task difficulty had almost no influence on the physiological and psychological functions in the afternoon.

It has been recognized that noradrenaline output is not as useful a measure of mental stress as adrenaline output, since most laboratory experiments have failed to demonstrate clearly an increase in noradrenaline excretion. In most of previously published experimental studies, the duration of mental work was no longer than 2 hr. In a preliminary experiment, we measured urinary excretion of catecholamines in 6 human subjects before and during 1-hr tasks of 4-digit number comparison both in the morning and in the afternoon. The results of the preliminary experiment (Table 5) showed no significant increase in noradrenaline excretion during the task in the afternoon session, although a significant but only slight (16%) increase in noradrenaline excretion was observed in the morning session.

In this present study, during the afternoon session, a significant and marked increase in noradrenaline excretion was observed during mental tasks on Day A compared to that during resting on Day B.

These results could be interpreted as showing that mental work, if prolonged, produces a considerable increase in noradrenaline excretion in human subjects.

Kurimori et al. examined catecholamine excretion in human subjects during an 11 hr mental task performed throughout the morning and afternoon of an experiment day, and also measured catecholamine excretion during an 11-hr rest period on a control day. These authors did not report differences in urinary catecholamine levels between the experiment day and the rest day. However, according to the data they presented, noradrenaline excretion on the experiment day tended to be higher than that on the rest day, and the difference appeared to be slightly greater in the afternoon than in the morning. Therefore, our present findings are consistent with the findings of our study.

The average score of subjective fatigue symptoms in our experiment increased after tasks in both the morning and afternoon sessions. The percentage increases relative to the respective control in the afternoon session (46%) was considerably higher than that in the morning session (27%). Task-induced changes in the stress score and the arousal score also tended to be greater in the afternoon session than those in the morning session. The coincidence of increases in noradrenaline excretion and the subjective scores suggests that the increase in noradrenaline excretion is related to the fatigue and stress caused by prolonged mental tasks.

It has been reported that the plasma levels or urinary excretion of noradrenaline is elevated in essential hypertension, some heart diseases and depression. The plasma levels of noradrenaline in congestive heart failure appears to be correlated with mortality. Christensen and Jensen described a population study on 1,129 subjects aged 70 years, who were selected from the national register, and

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**Table 5. Urinary excretion of noradrenaline and adrenaline before and during 1-hr tasks on 4-digit number comparison, in the morning session and in the afternoon session**

<table>
<thead>
<tr>
<th>Session</th>
<th>Noradrenaline before task</th>
<th>during task</th>
<th>Adrenaline before task</th>
<th>during task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning session</td>
<td>2.93 ± 0.59</td>
<td>3.41 ± 0.59**</td>
<td>0.57 ± 0.20</td>
<td>0.84 ± 0.23*</td>
</tr>
<tr>
<td>Afternoon session</td>
<td>3.90 ± 0.59</td>
<td>3.95 ± 0.64</td>
<td>0.52 ± 0.15</td>
<td>0.68 ± 0.19*</td>
</tr>
</tbody>
</table>

Six healthy human subjects performed tasks on 4-digit number comparison from 10:30 to 11:30 in the morning session and from 14:30 to 15:30 in the afternoon session, otherwise taking chair rest. Urine was collected during rest periods (9:30–10:30 and 13:30–14:30) and task periods. Urinary excretion of noradrenaline and adrenaline is expressed as pmol/min/kg BW (mean ± SE). **: p<0.01, *: p<0.05, #: p=0.05 compared with the rest level before the task.
from whom blood was drawn for catecholamine analysis. During the following 7 years, 115 male and 63 female subjects had died. Mortality in the male group was positively correlated with plasma noradrenaline, while negatively correlated with plasma adrenaline.

It has been accepted that noradrenaline is a neurotransmitter in postganglionic sympathetic nerves. It is thought that an increase in the plasma levels or urinary excretion of noradrenaline therefore indicates enhanced activity of the sympathetic nervous system. Long-term activation of sympathetic nerves would induce detrimental effects on the circulatory system, possibly resulting in stress-related diseases. Studies on the relationship between noradrenaline secretion and 'ill health' may provide useful information about the health care of workers.

References