Heart Rate Variation and Urinary Catecholamine Excretion in Response to Acute Psychological Stress in Hand-Arm Vibration Syndrome Patients

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Abstract: Heart Rate Variation and Urinary Catecholamine Excretion in Response to Acute Psychological Stress in Hand-Arm Vibration Syndrome Patients: M. Shawkatuzzaman LASKAR, et al. Department of Hygiene, Yamaguchi University School of Medicine—The aim of this study was to evaluate heart rate variation and urinary catecholamines in response to acute psychological stress in hand-arm vibration syndrome (HAVS) patients and healthy controls. LF% (indicator of both the sympathetic and parasympathetic nervous activity), HF% (indicator of the parasympathetic nervous activity) and their ratio LF/HF (indicator of sympathovagal balance) were calculated from short-term electrocardiographic data from 16 HAVS patients and 14 healthy controls before and immediately after exposure to acute psychological stress. Urinary catecholamines (norepinephrine, epinephrine and dopamine) were analyzed from urine samples collected from every subject during rest and after exposure. The LF% and LF/HF of the patients significantly increased after exposure. The after exposure LF/HF of the patients was significantly greater than that of the controls. The amount of norepinephrine in the patients significantly increased after exposure. The after exposure amount of norepinephrine and epinephrine in the patients were significantly greater than the respective amount of the controls. The results of the present study indicated the predominance of sympathetic tone in the cardiac sympathovagal balance and greater sensitivity of the sympathoadrenal medullary system in response to acute psychological stress in the patients than in the healthy controls. (J Occup Health 2004; 46: 125–131)

Key words: Hand-arm vibration syndrome, Acute psychological stress, Sympathetic response, Noninvasive method, Heart rate variation, Urinary catecholamines

The involvement of the autonomic centers in the brain due to exposure to hand-arm vibration has been under discussion¹, ². It has been suggested in some studies that the autonomic nervous function, besides the peripheral circulation, peripheral nervous and musculoskeletal systems, might be affected due to exposure to hand-arm vibration and was assessed previously in hand-arm vibration syndrome (HAVS) patients by means of time domain analysis of heart rate variation, and measuring levels of plasma catecholamines and cyclic nucleotides³–⁷. It was observed that cold exposure activates the sympathetic nervous system to a higher degree in subjects with HAVS than in controls⁸–¹⁰. Harada et al.¹¹ investigated sympathetic response to noise, vibration and cold exposure in healthy subjects and they observed that combined exposure to multiple stressors was more effective than a single stressor. In a previous study with urinary catecholamine response, we observed that the sensitivity of HAVS patients to acute psychological stress increased¹².

Recently, the frequency domain analysis of R-R intervals has been used to assess the magnitude of individual components of the heart rate power spectrum that usually includes a low frequency (LF) component at 0.04 to 0.15 Hz and a high frequency (HF) component at the respiratory frequency (0.15–0.40 Hz)¹³, ¹⁴. The normalized units of the frequency domain components are used as indices of autonomic nervous activity; LF%, indicator of both sympathetic and parasympathetic nervous activity, HF%, indicator of parasympathetic nervous activity, and LF/HF, indicator of sympathovagal balance or sympathetic activity¹⁵, ¹⁶.
The purpose of the present study was to investigate heart rate variation together with urinary catecholamine excretion in response to acute psychological stress in HA VS patients by using noninvasive methods.

**Materials and Methods**

Sixteen HA VS patients (patients) and 14 healthy subjects (controls) of similar age volunteered for this study. The patients were selected from those under treatment for HA VS at Kochi Seikyo Hospital in Shikoku area, Japan. The patients were chainsaw operators and tunnel construction workers who had been occupationally exposed to hand-arm vibration, and had been officially diagnosed with HA VS by the Japanese Ministry of Labour through examinations of finger skin temperature, nail compression test, vibration perception threshold, pain threshold, gripping power and cold provocation test17). Vibration exposure has been ceased in all of the patients. The job titles of the healthy controls were office worker, fisherman, community cleaner and farmer. They were from healthy residents near the hospital who had never been occupationally exposed to hand-arm vibration.

Written informed consent was obtained from all subjects. Then they completed a questionnaire about age, height, alcohol and smoking habits, occupation, use of vibrating tools, years of exposure to vibration, time under treatment, past and present medical history, symptoms concerning HAVS, and other health items. There was no statistically significant difference in the mean age, body mass index, and percentage of smokers and drinkers among the groups as shown in Table 1. None of the study subjects had diseases associated with peripheral neuropathy, such as diabetes, rheumatic diseases, chemical- or drug-induced neuropathy, or other neurological diseases, or severe injuries to the upper extremities.

The examination room was kept at $21\pm1$°C. All the subjects were requested to avoid smoking and use of any drug stimulants from 3 h, and alcohol drinking from 12 h prior to the examination. The time from 1 h before or 4 h after food was eaten by the subjects was avoided for setting examination periods. These experiments were carried out between 10:00 and 17:00 on the examination days.

After an initial rest for 1 h, the subjects were exposed to acute stress for about 1 h with stressors- mirror drawing (8 min), watching a horror video (23 min) and arithmetic under intermittent noise at 90 dBA (15 min) (Fig. 1). During the rest period, every subject was allowed to drink 350 ml of soft drink.

Short-term electrocardiographic data were recorded in the supine position during spontaneous breathing before and immediately after exposure, and LF%, HF% and LF/HF were calculated with a fast Fourier transformation program15).

Urine was collected from every subject during the before exposure rest period for 1 h, and also for another 1 h starting from the start of the exposure, after the initial excretion of urine by the subject was discarded. The collected urine was preserved in a refrigerator and urinary catecholamines (norepinephrine, epinephrine and dopamine) were analyzed by HPLC with the ECD method18).

After exposure to the stressors and data recordings, the subjects were asked to rate their subjective complaints to the stressors on a scale from 1 (none) to 5 (extreme). The differences between patients and controls were tested by Student $t$-test or Fisher’s exact probability test. Comparison of parameters within the individual group before and after exposure was performed by paired $t$-test. Pearson correlation analysis was used for simple

**Table 1. Demographic characteristics of the subjects**

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=14)</th>
<th>Patients (n=16)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>56.1 ± 5.2</td>
<td>59.4 ± 6.1</td>
<td>NS$\dagger$</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.7 ± 3.6</td>
<td>23.5 ± 2.6</td>
<td>NS$\dagger$</td>
</tr>
<tr>
<td>Smoker number (%)</td>
<td>0 (0%)</td>
<td>5 (31.3%)</td>
<td>NS$\ddagger$</td>
</tr>
<tr>
<td>Drinker number (%)</td>
<td>11 (78.6%)</td>
<td>11 (68.8%)</td>
<td>NS$\ddagger$</td>
</tr>
<tr>
<td>Years of exposure to vibration</td>
<td>—</td>
<td>21.7 ± 10.4</td>
<td>—</td>
</tr>
<tr>
<td>Time under treatment (yr)</td>
<td>—</td>
<td>2.0 ± 1.5</td>
<td>—</td>
</tr>
</tbody>
</table>

Number (%) or mean ± SD. BMI, body mass index; NS, not significant; $\dagger$: Student $t$-test; $\ddagger$: Fisher’s exact probability test.

Fig. 1. Protocol of the experiment. $\triangle$, voiding of urine from the urinary bladder; $\star$, 1 h rest; $\square$, short-term electrocardiographic recording and urine sampling.
correlation between after exposure variables. Statistical significance was considered when \( p < 0.05 \).

**Results**

Table 2 shows the prevalence of subjective symptoms in the subjects. The patients had higher prevalence rates for most of the subjective symptoms localized and not localized in the upper limbs than the controls had (\( p < 0.05, 0.01, 0.001 \)).

Figure 2 shows the severity of discomfort expressed in scores of subjective complaints regarding the stressors. The mean score of subjective complaints of the patients was greater than that of the controls (\( p = 0.001 \)).

Table 3 shows the LF%, HF% and LF/HF of the subjects before and after exposure to the stressors. The LF% and LF/HF of the patients significantly increased after exposure (\( p = 0.001 \)). The after exposure LF/HF of the patients was significantly greater than that of the controls (\( p = 0.019 \)).

Figure 3 shows the percentage of the subjects with an increase in LF% or LF/HF in response to exposure to the stressors. The percentage of the patients with an increase in LF/HF tended to be greater than that of the controls (\( p = 0.071 \)).

Table 4 shows the urinary catecholamines of the subjects before and after exposure to the stressors. The amount of norepinephrine in the patients significantly increased after exposure (\( p = 0.03 \)). The after exposure amounts of norepinephrine and epinephrine in the patients were significantly greater than the respective amounts in the controls (\( p = 0.006 \) and \( p = 0.018 \), respectively).

Figure 4 shows the percentage of the subjects with an increase in urinary catecholamines in response to exposure to the stressors. There was no significant difference between the two groups in the percentage of the subjects with an increase in urinary catecholamines.

When the patients were divided into patients without vibration induced white finger and patients with vibration induced white finger, there was no difference in heart rate variation indices and urinary catecholamines between the two groups (data not shown).

Table 5 shows the coefficients of correlation between variables after exposure to the stressors in the subjects. The after exposure LF% and LF/HF correlated positively and significantly with the after exposure urinary norepinephrine and epinephrine (\( p < 0.05, 0.01 \)). A similar correlation was also observed between the after exposure LF/HF and the after exposure urinary dopamine (\( p < 0.05 \)).
Table 3. LF%, HF% and LF/HF in the subjects before and after exposure to the stressors

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=14)</th>
<th>Patients (n=16)</th>
<th>p value (Student t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF%</td>
<td>12.6 ± 1.6</td>
<td>12.9 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>HF%</td>
<td>24.9 ± 1.7</td>
<td>25.3 ± 3.0</td>
<td>NS</td>
</tr>
<tr>
<td>LF/HF</td>
<td>0.51 ± 0.05</td>
<td>0.51 ± 0.04</td>
<td>NS</td>
</tr>
<tr>
<td><strong>After exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LF%</td>
<td>13.6 ± 1.5</td>
<td>14.1 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>HF%</td>
<td>25.9 ± 2.2</td>
<td>25.6 ± 2.0</td>
<td>NS</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>LF/HF</td>
<td>0.52 ± 0.04</td>
<td>0.55 ± 0.04</td>
<td>0.019</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SD. NS, not significant.

Fig. 3. The percentages (%) of the subjects with an increase in LF% or LF/HF in response to exposure to the stressors. a: p=0.574; b: p=0.071, Fisher’s exact probability test.

Table 4. Urinary catecholamines (µgm/h) in the subjects before and after exposure to the stressors

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=14)</th>
<th>Patients (n=16)</th>
<th>p value (Student t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>2.0 ± 0.3</td>
<td>2.7 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>1.1 ± 0.2</td>
<td>1.5 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Dopamine</td>
<td>16.7 ± 3.0</td>
<td>18.2 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td><strong>After exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>2.1 ± 0.3</td>
<td>3.6 ± 0.5</td>
<td>0.006</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>1.1 ± 0.3</td>
<td>2.1 ± 0.3</td>
<td>0.018</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td>15.2 ± 3.4</td>
<td>19.5 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>p value (paired t-test)</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Mean ± SE. NS, not significant.
Table 6 shows the coefficients of correlation between variables after exposure to the stressors and years of exposure to vibration and time under treatment in the HA VS patients. The correlations were not statistically significant.

Discussion

Various stressors such as mirror drawing test, mental arithmetic, watching a horror video, public speaking, etc., are used to investigate human responses to acute psychological stress\textsuperscript{19, 20}. In previous study, we found that exposure to more than one stressor was adequate to induce stress responses in healthy subjects\textsuperscript{11}. In the present study, mirror drawing test, watching a horror video and arithmetic under intermittent noise were used sequentially, and the response to the stressors should be interpreted as cumulative response to acute psychological stress. If a subject is exposed to a psychological test alone for a long time, the subject may become accustomed to it\textsuperscript{21}. Therefore, we used combined exposure to the tests mentioned in this study. As the severity of discomfort in the patients expressed in scores of subjective complaints to the stressors was greater than in the controls, it is considered that the stressors were adequate to induce responses.

In the present study, we investigated heart rate variation during spontaneous breathing in the supine posture not during deep breathing, as it may have a contradictory effect on heart rate variation responses to psychological stress\textsuperscript{22}. Nevertheless, a possible limitation that supine posture also may have a contradictory effect on heart rate variation responses to psychological stress remains in this study, but the condition was the same for both groups of subjects. Some studies view LF% as reflecting both the sympathetic and vagal influences and LF/HF is considered by some investigators to mirror the sympathovagal balance or to reflect the sympathetic activity\textsuperscript{13, 16, 23, 24}. The results of the frequency domain analysis of heart rate variation in this study showed that the cardiac autonomic response to acute psychological stress in the patients was different from that in the healthy controls, which indicated a predominance of sympathetic tone in the cardiac sympathovagal balance.

It is well known that circulating catecholamines are rapidly metabolized and levels of plasma catecholamines (norepinephrine and dopamine) are sensitive indicators of the sympatheticmediated response to acute stress\textsuperscript{25–28} and epinephrine is an emotional stress index\textsuperscript{29}. Because a percentage of catecholamines are excreted in the urine, analysis of urinary catecholamines is used as an

\begin{table}[h!]
\centering
\begin{tabular}{|c|c|c|}
\hline
 & LF% & HF% & LF/HF \\
\hline
Norepinephrine & 0.34* & –0.11 & 0.55** \\
Epinephrine & 0.35* & –0.08 & 0.52** \\
Dopamine & 0.25 & 0.00 & 0.31* \\
\hline
\end{tabular}
\caption{Pearson’s correlation of LF%, HF% and LF/HF with urinary catecholamines in the subjects after exposure to the stressors.}
\end{table}

\begin{table}[h!]
\centering
\begin{tabular}{|c|c|c|}
\hline
Years of exposure & p & Time under \begin{tabular}{c} \text{treatment (yr)} \end{tabular} & p \\
\hline
vibration & & value & value \\
\hline
LF% & 0.35 & NS & 0.39 & NS \\
LF/HF & 0.31 & NS & 0.26 & NS \\
Norepinephrine & 0.21 & NS & 0.05 & NS \\
Epinephrine & 0.24 & NS & –0.06 & NS \\
Dopamine & –0.23 & NS & 0.04 & NS \\
\hline
\end{tabular}
\caption{Pearson’s correlation coefficients between variables after exposure to the stressors and years of exposure to vibration and time under treatment in the hand-arm vibration syndrome patients.}
\end{table}
Norepinephrine, secreted primarily by the sympathetic nerves, increases in plasma and urine with standing, volume contraction, cold exposure, physical activity, and exercise. Epinephrine, secreted primarily by the adrenal medulla, is increased in plasma and urine with problem-solving, mood change, and mental stress such as flying a plane, driving in traffic, or speaking in public. As the present study is of a noninvasive character, we used measurements of urinary catecholamines instead of plasma catecholamines. The results for urinary catecholamines in the present study indicated greater sensitivity of the sympathoadrenal medullary system to acute psychological stress in the patients than in the healthy controls.

There were some subjects who had an increase in the variables after exposure. On the other hand, there were some subjects who had a decrease in the variables. The overall direction of responses of both types of variables in the subjects was shown by the correlations between the variables after exposure to stressors using the data from all subjects. Kurita et al. found a significant negative correlation between high-frequency component of heart rate variation and urinary catecholamine levels in healthy volunteers under severe hyperbaric pressure in submarine experimental facilities. In the present study, we found a negative but not significant correlation between HF% and urinary norepinephrine or epinephrine, and a positive and significant correlation between LF% or LF/HF and urinary norepinephrine or epinephrine.

Most correlations between exposure years and after exposure variables in the patients were positive but not significant. The fact that vibration exposure had been stopped in all of the patients and they were under treatment may be the reason for this.

In the present study, the influence of acute psychological stress was evaluated by noninvasive indices (heart rate variation and urinary catecholamines). It could be concluded that the findings of the present study indicated an increased sympathovagal balance and sympathoadrenal medullary responses to acute psychological stress in the HAVS patients.

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References
7) MS Laskar, M Iwamoto, N Toibana, T Morie, T Wakui and N Harada: Heart rate variability in response to psychological test in hand-arm vibration syndrome patients assessed by frequency domain analysis. Ind Health 37, 382–389 (1999)


