Decrease in heart rate variability response to task is related to anxiety and depressiveness in normal subjects

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Aims: Previous studies have shown that heart rate variability (HRV) measurement is useful in investigating the pathophysiology of various psychiatric disorders. The present study further examined its usefulness in evaluating the mental health of normal subjects with respect to anxiety and depressiveness.

Methods: Heart rate (HR) and HRV were measured tonometrically at the wrist in 43 normal subjects not only in the resting condition but also during a task (random number generation) to assess the responsiveness. For HRV measurement, high-frequency (HF; 0.15–0.4 Hz) and low-frequency (LF; 0.04–0.15 Hz) components of HRV were obtained using MemCalc, a time series analysis technique that combines a nonlinear least square method with maximum entropy method. For psychological evaluation of anxiety and depressiveness, two self-report questionnaires were used: State–Trait Anxiety Inventory (STAI) and Self-Rating Depression Scale (SDS).

Results: No significant relation was observed between HR and HRV indices, and the psychological scores both in the resting and task conditions. By task application, HF decreased, and LF/HF and HR increased, and significant correlation with psychological scores was found in the responsiveness to task measured by the ratio of HRV and HR indices during the task to that at rest (task/rest ratio). A positive relationship was found between task/rest ratio for HF, and STAI and SDS scores. Task/rest ratio of HR was negatively correlated with STAI-state score.

Conclusion: Decreased HRV response to task application is related to anxiety and depressiveness. Decreased autonomic responsiveness could serve as a sign of psychological dysfunction.

Key words: anxiety, depressiveness, heart rate variability, parasympathetic activity, responsiveness.

Among various physical changes accompanying psychological disturbances, autonomic symptoms are frequently encountered in clinical practice, including palpitation, sweating, diarrhea and so on, and are incorporated in the diagnosis of mental disorders.1 It is, therefore, reasonable to assume that autonomic measurement can become a useful tool for biologically assessing the psychological state. In the field of cardiac function, in addition to conventional heart rate (HR) measurement, heart rate variability (HRV) is utilized as a convenient and informative way to evaluate autonomic activity by recording electrocardiogram or pulse wave, and has been used frequently in psychiatric research.2 It is clinically applicable because the patients experience little distress on measurement.

HRV was first utilized in the field of fetal health check, and the relationship to intra-uterine condition has been discussed.3 A number of studies were then conducted with regard to ischemic heart disease, and it was found that HRV change was an important risk factor.4 In the field of psychiatry, complication of depression in ischemic heart disease has been noted,5 and HRV was used to analyze this relationship.6,7 Furthermore, a reduction of HRV was observed in depressed patients without cardiac dysfunction.8
Changes in HRV indices were also reported in other psychiatric disorders including post-traumatic stress disorder (PTSD), panic disorder and schizophrenia.9–13
Considering the presence of HRV abnormalities in various mental disorders, it is interesting to examine whether HRV indices can be utilized to assess the psychological state of normal individuals for early detection of mental changes and prevention of the psychiatric disturbances. It has been reported that social isolation, anger and high emotional stress were accompanied with changes in HRV.14,15 Subjects with low HRV reported high anxiety when confronting fearful stimuli.16 HRV is also different depending on pain sensitivity.17 Thus, it is known that HRV is related to various aspects of temperament and behavior.18
The aim of the present study was to further promote the usefulness of HRV in evaluating mental health by focusing on its responsiveness to behavioral or environmental changes, because HRV is profoundly influenced by concurrent physical activity.19 The HRV components respond to the environmental stimuli differently depending on emotional context.20,21 Previous reports have also shown that anxiety and depressed mood are related to low levels of HRV parasympathetic components during exposure to stressors.22–24 Accumulation of data, however, is still necessary to apply HRV responsiveness in evaluating the mental state of normal individuals. Based on this background, we used task application in the present study as a form of stress, and evaluated the responsiveness of HRV to the task in relation to psychological conditions.

METHODS

Subjects

Forty-three normal subjects were recruited from a business company. They had no problems at work and were aged 31.1 ± 4.3 years (mean ± SD; men n = 31; women, n = 12, all right handed). They had no history of psychiatric, neurological, cardiologic, or pulmonary disorders, and showed no signs of mental disorders based on DSM-IV interview by T.S. Those who exhibited hypertension or arrhythmia, and who were under medical treatment were also excluded from the present study.

Subject psychological state was examined on the day of HRV measurement with respect to anxiety and depressiveness using two self-report questionnaires: State–Trait Anxiety Inventory (STAI)25 and Self-Rating Depression Scale (SDS),26 because they are common signs of psychological dysfunction due to stressful events in daily life. The state and trait scores of STAI represent anxiety level at the time of measurement and that in daily life, respectively. SDS was used to evaluate the subject’s depressiveness. The presence of smoking and alcohol drinking was also reported.

Patients were not included in the present study because each mental or physical disturbance may have a different pattern of HRV abnormality, which could make the data complicated. Written informed consent to attend the study was obtained from all subjects, and the study protocol was approved by the Ethics Committee of Tokyo Institute of Psychiatry.

Heart rate variability measurement

On measuring HRV, the subject was seated on a chair with the left arm situated on a soft pad on the desk in front of the subject. The tonometric sensor was placed on the subject’s left wrist over the radial artery, where pulse wave was monitored and its peaks were detected for measuring inter-beat intervals (Jentow-CS, Colin, Tokyo, Japan). The subject’s right hand was free and was used for conducting the task.

HRV was measured both during the resting state (100 s) and the task application (100 s) in order to analyze not only the baseline autonomic activity but also response to behavioral assignment.27 The ratio of the data during the task to that during the resting state was used for evaluating the responsiveness to task (task/rest ratio).

For the task, random number generation was used in the present study because it is simple, is independent of the subject’s educational and intellectual level and is useful in creating moderate mental stress.28 In random number generation the subject was instructed to write a series of digit numbers (0–9) on a matrix sheet (10 cells ¥ 10 rows) at the speed of one digit per second in a random order. The instruction was as follows: ‘Write down the digits from 0 to 9 in Arabic numerals with a pen in a paper matrix, one at a time following the speed of metronome beep sound, from the top left to right bottom, as random as possible, as if you were casting a die’. Metronome beep sounds were delivered at 1 Hz to indicate the writing speed. Randomness of the digit series was checked by scoring the counting bias (CB; tendency to count up) and the random number generation index (RNG; frequency of digit pairs) based on our
previous report.²⁸ In the present study the writing mode of random number generation was used in order to minimize the variation in respiratory cycle, which would occur when the numbers are orally generated and might influence the results.¹⁹

Although various methods of HRV analysis are available, we used MemCalc (GMS, Tokyo, Japan) for measuring the components of inter-beat variation. MemCalc is a method of time series analysis, which is a linearized version of the non-linear least squares method combined with the maximum entropy method.²⁹ In contrast to conventional fast Fourier transform, MemCalc is capable of estimating the power spectrum density from short time series data, and is adequate to examine the changes of HRV in different conditions of short duration.³⁰,³¹

In the present study, inter-beat interval data during the resting period and the random number generation task were used for power spectrum analysis with MemCalc, and the integrated power in the frequency range between 0.04 and 0.15 Hz was designated as the low-frequency component of HRV (LF), and that in the range between 0.15 and 0.4 Hz as the high-frequency component (HF). HF and LF/HF were used as the indices for parasympathetic and sympathetic activity, respectively,⁴,³² and were obtained for both rest and task periods (100 s). Previous studies using MemCalc indicate that a 100-s interval is large enough to analyze HRV.³⁰,³¹ The relationship of HF, LF/HF and HR indices to the psychological scores for anxiety and depressiveness was then assessed.

Statistical analysis

The relationship between HRV indices and psychological scores was analyzed using Spearman correlation coefficients (Prism 4, GraphPad Software, La Jolla, CA, USA). The differences between resting state and task performance, non-smokers and smokers, and non-drinkers and drinkers were checked using Student’s t-test.

RESULTS

HRV and HR indices

Figure 1 shows the changes of HF, LF/HF and HR during the resting state and at the time of random number generation for total subjects. HF was 403.5 ± 300.8 ms² (mean ± SD, n = 43) at rest and significantly decreased to 158.8 ± 138.3 ms² during task performance (t = 7.12, P < 0.0001). LF/HF increased from 1.82 ± 1.31 to 2.73 ± 1.98 (t = 2.82, P < 0.01). Task/rest ratio was 0.45 ± 0.25 for HF and 2.36 ± 3.29 for LF/HF. The HR was 71.1 ± 10.5 b.p.m. at rest and increased to 78.4 ± 12.4 b.p.m. during the task (t = 6.67, P < 0.0001), and its task/rest ratio was 1.10 ± 0.10. Although these changes in HF, LF/HF and HR were significant, there were considerable inter-subject differences. The data in the resting state (men: HF 402.2 ± 335.4 ms², LF/HF 2.05 ± 1.40, HR 71.3 ± 9.8 b.p.m.; women: HF 406.9 ± 196.9 ms², LF/HF 1.23 ± 0.82, HR 70.5 ± 12.5 b.p.m.) and during task performance (men: HF 146.7 ± 129.2 ms², LF/HF 3.03 ± 2.09, HR 78.8 ± 12.9 b.p.m., women: HF 190.1 ± 161.3 ms², LF/HF 1.95 ± 1.48, HR 77.4 ± 11.5 b.p.m.), and the task/rest ratio (men: HF 0.44 ± 0.25 ms², LF/HF 2.25 ± 2.57, HR 1.11 ±
0.10 b.p.m., women: HF 0.47 ± 0.25 ms², LF/HF 2.67 ± 4.82, HR 1.10 ± 0.08 b.p.m.) showed no gender difference (t-test).

As for the psychological evaluation, the mean scores of STAI-state, STAI-trait and SDS were 43.0 ± 10.7 (range, 26–77), 42.8 ± 10.5 (range, 24–63) and 37.6 ± 9.0 (range, 23–57). Table 1 lists Spearman correlation coefficients for the relation between HR and HRV indices, and psychological scores. Task/rest ratio of HF was significantly correlated with STAI-state (r = 0.37, P < 0.05), STAI-trait (r = 0.39, P < 0.01) and SDS (r = 0.44, P < 0.01) scores (Fig. 2). Task/rest ratio of HR was negatively related to STAI-state score (r = -0.37, P < 0.05, Fig. 3). Other HR and HRV indices did not have a significant relationship with psychological scores (Table 1).

### Task performance, smoking and alcohol habit

As for the random number generation task performance, the average CB and RNG were 0.05 ± 0.07 and 0.33 ± 0.05, respectively. There was no significant relationship between the randomness scores of the generated digit series in the task and task/rest ratio of HF (CB, r = -0.01, n.s.; RNG, r = -0.02, n.s.) and HR (CB, r = -0.11, n.s.; RNG, r = -0.04, n.s.).

### Table 1. Spearman correlation coefficients

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<td>Task/rest ratio</td>
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</table>

*P < 0.05. **P < 0.01.

HF, high-frequency component of heart rate variability; HR, heart rate; LF, low-frequency component of heart rate variability; SDS, Self-Rating Depression Scale; STAI, State–Trait Anxiety Inventory.

Figure 2. Relationship between task/rest ratio of high-frequency component (HF) and psychological scores. Significant positive correlation was found for State–Trait Anxiety Inventory (STAI) and Self-Rating Depression Scale (SDS) scores (n = 43, r = Spearman correlation coefficient). (a) STAI-state (r = 0.37; P < 0.05); (b) STAI-trait (r = 0.39; P < 0.01); (c) SDS (r = 0.44; P < 0.01). The regression line is shown in each figure.

Figure 3. Relationship between task/rest ratio of heart rate (HR) and psychological scores. Significant negative correlation was found for (a) State–Trait Anxiety Inventory (STAI)-state score (n = 43, r = -0.37; P < 0.05). (b) STAI-trait; (c) Self-Rating Depression Scale. The regression line is presented for STAI-state data.
The numbers of non-smokers and smokers were 27 (men, \( n = 18 \); women, \( n = 9 \)) and 16 (men, \( n = 13 \); women, \( n = 3 \)), and those of non-drinkers and drinkers were 11 (men, \( n = 8 \); women, \( n = 3 \)) and 32 (men, \( n = 23 \); women, \( n = 9 \)), respectively. No significant change in gender distribution was observed between non-smokers and smokers (\( \chi^2 = 1.062 \), n.s.) and non-drinkers and drinkers (\( \chi^2 = 0.003 \), n.s.). No difference in task/rest ratio of HF was found with respect to smoking habit (non-smoker, 0.44 ± 0.24; smoker, 0.47 ± 0.28, \( t = 0.34 \), n.s.) and to alcohol drinking (non-drinker, 0.46 ± 0.19; drinker, 0.44 ± 0.27, \( t = 0.25 \), n.s.). As for HR, task/rest ratio was 1.13 ± 0.10 for the non-smokers and 1.06 ± 0.05 for the smokers, and the difference was statistically significant (\( t = 2.67, P < 0.05 \)), although HR in the resting condition in the non-smokers (70.5 ± 10.6) was not different from that in the smokers (72.1 ± 10.5, \( t = 0.47 \), n.s.). No difference in the task/rest ratio of HR was observed with respect to alcohol habit (non-drinker, 1.07 ± 0.08; drinker, 1.12 ± 0.10, \( t = 1.48 \), n.s.).

DISCUSSION

Responsiveness of HRV and HR to task application

The present study found that HRV and HR responsiveness is related to the psychological scores of anxiety and depressiveness, and could be useful for biologically assessing mental health in normal population, and for detecting changes. If we assume that application of the task was a form of stress, decreased autonomic responsiveness to stress would be related to anxiety and depressive feeling. In addition to the data for at rest, assessment of responsiveness should add information for psychological analysis using HRV.

Because HRV depends on age, the present results for the subjects aged mainly in the 20s and 30s may not be applied to other age groups. Future studies using children as well as subjects in old age will be necessary to generalize the present findings. Gender difference in HRV and HR indices was not noted in the present study, therefore the present findings would apply to both men and women.

In the present study the random number generation task was used for applying stress, and the changes in HRV indices due to the task were analyzed. The scores of random number generation were not related to HRV indices, indicating that the present finding on the relationship between HRV and mental state was not due to the differences in task performance. Other tasks would also be utilized in future studies for examining the effect on HRV to consolidate the present results.

HF component significantly decreased and LF/HF and HR increased with task application, indicating the tilt of autonomic balance toward sympathetic activation. As in the resting state, HF, LF/HF and HR during the task were not related to STAI and SDS scores (Table 1). Because there was considerable inter-subject variation in these indices with respect to magnitude of the change (Fig. 1), response to the task was analyzed as task/rest ratio, and that of HF and HR had significant correlation with mental state (Table 1). In HF, correlation was significant for both STAI and SDS scores (Fig. 2). When there was less change in HF by task application, the subject had more anxiety and depressiveness in daily life. For HR, significant relation was found only with STAI-state score (Fig. 3). When HR showed little elevation during the task, the subject tended to be anxious at that moment. These results could suggest that HR responsiveness is more influenced by the present state of anxiety. The future studies with different psychological scales may enable the use of HRV and HR indices on differentially assessing anxiety and depressive states.

The present study also suggests that decreased responsiveness of parasympathetic activity would be reflected in the diminished changes in HF and HR, and may be related to appearance of anxiety and depressiveness. Parasympathetic reactivity could be important in maintaining healthy mental state through the control of the arousal level. Future studies are necessary to assess the underlying mechanism.

Clinical implications of decreased HRV responsiveness

It was reported that PTSD patients manifested a decrease in responsiveness of HRV to traumatic stimulation, possibly due to the increased arousal level at the baseline state. The HR increase in response to startle sound was related to PTSD severity. We have also shown that HRV sympathetic indices are useful in monitoring the emotional response and habituation to trauma in the prolonged exposure therapy for PTSD. In the acute psychotic
condition, decreased capacity of reaction to external stimuli was observed for HF during psychological tasks, such as oddball tasks.\textsuperscript{27} HRV responses to emotional condition can also predict antidepressant responses in depressed patients.\textsuperscript{36}

The present study further indicates that HRV of normal individuals with high anxiety or depressiveness may not respond when the task is applied, although it is not altered during the resting state, in contrast to that in PTSD. It is also possible to assume that other mental conditions than anxiety and depressiveness may be related to the decreased HRV responsiveness. Future studies are necessary to further delineate its significance in clinical practice.

**HRV indices at rest**

HF, LF/HF, and HR at the resting condition did not have a significant relationship with STAI and SDS scores (Table 1). Although various studies on anxiety and depression have indicated that HRV, especially HF component, is reduced when the subjects are in an anxious or depressive mood, and the association between mental state and HRV components has been suggested,\textsuperscript{14,37} the present study did not support this association for the resting state of normal individuals due to large inter-subject variations. Absence of this relationship could also be due to the healthy state of the subjects in the present study, whose social activities were well maintained in contrast to the that of psychiatric patients.\textsuperscript{2} Because it is reported that HF component at rest increased after a period of daily exercise,\textsuperscript{38} baseline HRV indices can be used as long-term markers for mental health.

**Effects of smoking and alcohol**

It is known that smoking and alcohol drinking affect HRV. Smoking reduces parasympathetic activity and increases LF/HF index.\textsuperscript{39,40} Alcohol intake also diminishes HRV.\textsuperscript{41} In the present study no definite effect of smoking or alcohol habit was found for the HF data. Many kinds of physical and psychological factors were present for each subject in the present study, and these influenced the HRV parameters and lessened the effect of smoking and alcohol. As for the HR data, diminished responsiveness was related to smoking habit. It may be reasonable to assume that the subjects with a high anxiety state tend to smoke, although there is a possibility that smoking directly affected the parasympathetic activity and reduced the HR responsiveness. Future studies with larger samples are necessary to further examine this possibility.

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