ORIGINAL ARTICLE

Enhancement of cardiac autonomic nervous system activity by blood flow restriction in the human leg

N. Kiyohara, T. Kimura, T. Tanaka, T. Moritani

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Correspondence to:
T. Moritani, Ph,D., FACSM, Laboratory of Applied Physiology, The Graduate School of Human & Environmental Studies, Kyoto University, Sakyo-ku, Kyoto 606-8501 Japan
t.moritani@neuro.mbox.media.kyoto-u.ac.jp

See end of article for author's affiliations

The purpose of this study is to develop a unique method to enhance autonomic nervous system (ANS) activity by means of experimental leg occlusion. The effects of blood flow restriction on the activities of the ANS during rest were investigated using a power spectral analysis of heart rate variability. Two patterns of occlusion were randomly assigned to healthy subjects: pattern A, 10 min of 1.4 times of systolic blood pressure; pattern B, 5 min of mean blood pressure followed by 5 min of 1.4 times of systolic blood pressure. Electrocardiogram, blood pressure and cardiac output were continuously monitored during rest and occlusion. During occlusion, cardiac output and stroke volume showed significant decreases, due to modulation of autonomic nervous activity. After releasing from occlusion without blood pooling (A), the high frequency component of R-R interval variability representing vagal activity showed a significant increase ($P<0.05$). However, soon after releasing, the ECG QTc interval temporally prolonged ($P<0.05$) and recovered gradually. Further investigation is recommended to determine blood flow occlusion safety on the cardiac depolarization-repolarization process. In conclusion, the results suggest that blood flow restriction has potential to be a useful method to stimulate the activity of autonomic nervous system, and especially to enhance parasympathetic nervous system activity.
Key words: ANS, HRV, QTc, occlusion, blood flow restriction

INTRODUCTION

The interval time between the beats of the heart (R-R intervals) fluctuate beat by beat. Heart rate variability (HRV) is the amount of heart rate fluctuations around the mean heart rate, and reflects cardiorespiratory control system regulation. Heart rate variability is a valuable marker to investigate the sympathetic and parasympathetic function of the autonomic activity, and autonomic balance (van Ravenswaaij-Arts et al. 1993).

Investigation of ANS activity using frequency domain of HRV began about 2 or 3 decades ago. Early human studies as well as experimental animal studies (Akselrod et al. 1985; Akselrod et al. 1981; Pagani et al. 1986; Rimoldi et al. 1990) have shown that two major frequency components of HRV could provide quantitative markers of SNS and PNS activities respectively. Power spectral analysis of HRV has provided a comprehensive quantitative and qualitative evaluation of neuroautonomic function under various physiological conditions (Hayashi et al. 1994; Moritani et al. 1995; Moritani et al. 1993; Oida et al. 1997).

The high-frequency component (HF, >0.15 Hz) reflects respiration and is associated solely with activity in the parasympathetic nervous system, and the low-frequency component (LF, <0.15 Hz) could provide a quantitative marker of partly of vagal and mainly of sympathetic nervous system, and the balance of these components can represent sympatho-vagal interaction. Saul et al. (1990) showed a significant correlation between LF spectral power of HRV and recorded bursts of muscle sympathetic nerve activity. Paolisso et al. (1997) demonstrated a strong positive correlation between spectral powers and plasma norepinephrine concentration at rest and in response to glucose ingestion.

Reduced HRV has been found in patients with many kinds of diseases; for instance, hypertension (Langewitz et al. 1994; Novak et al. 1994), obesity (Hirsch et al. 1991; Zahorska-Markiewicz et al. 1993), diabetic autonomic neuropathy (Molgaard et al. 1992; Weise et al. 1988), cardiac disease (Casolo et al. 1991; Ue et al. 2000), and depression (Carney et al. 1995). In addition, we have reported that activity in both the sympathetic and parasympathetic nervous system is reduced as age increases (Oida et al. 1999). So, procedures for increasing autonomic nervous activity are now strongly needed. In this study, we focused on blood flow restriction for its possibility to stimulate autonomic nervous system activity by modulating control and peripheral circulatory regulation.

It is reported that under conditions of restricted muscle blood flow, even short-term and low-intensity exercise can induce muscle strength gain, and hypertrophy. Low-intensity resistance training (20-50% of 1RM) combined with a tourniquet restriction of blood flow causes increases in muscular strength and size while exercise with low-intensity (<65% of 1 RM) without blood restriction primarily induces an improvement of muscular endurance capacity without considerable increases in muscular size and strength (Kawada 2005). Training with blood flow restriction was used to improve muscle mass and strength in patients with cardiovascular and orthopedic diseases as well as healthy subjects and athletes (Abe et al. 2005; Takarada et al. 2000a; Takarada et al. 2000b; Takarada et al. 2000c).

Recently, it was reported that blood flow restriction might increase sympathetic nervous system activity (Iida et al. 2005). In this report, the occlusion was performed first at 45 mmHg and following it, at 200 mmHg on both thighs. This study showed: (i) Application of occlusion on both legs caused the pooling of venous blood with pressure-dependent reduction of femoral arterial blood flow; (ii) The pooling of venous blood in the legs by occlusion reduced venous return with a significant decrease in cardiac size and cardiac output, and a compensated increase of total peripheral resistance; and (iii) Application of occlusion on both legs also affects autonomic nervous activities, where an increase in the sympathetic nervous activity was observed. Thus, the authors suggested occlusion to be an effective method to induce venous pooling in the legs like lower body negative pressure. Lower body negative pressure induces the retention of blood flow in lower extremities, and causes subsequent hemodynamic changes including autonomic nervous activities, and has been known to be a useful method to prevent orthostatic intolerance after space flight and bed rest, probably through its effect as orthostatic stimulus.

In this previous study (Iida et al. 2005), blood pooling was used and suggested to be the factor that increases sympathetic nervous activity. Although spectral analysis of HRV has been utilized in the past to document a variety of physiological events, this technique has not been used to examine autonomic variation during and after blood flow restriction without blood pooling.

On the other hand, prolonged ECG QTc interval, which is an adjusted QT interval of the heart rate reflecting cardiac depolarization-repolarization process, has been used as a marker for sudden cardiac death in myocardial infarction patients (Schwartz et al. 1993; Schwartz and Wolf 1978). There is also increasing evidence that a prolonged QTc predicts coronary heart disease mortality in healthy populations as well (Schouten et al. 1991). It has been suggested that QTc prolongation may be a consequence of an unfavorable balance between

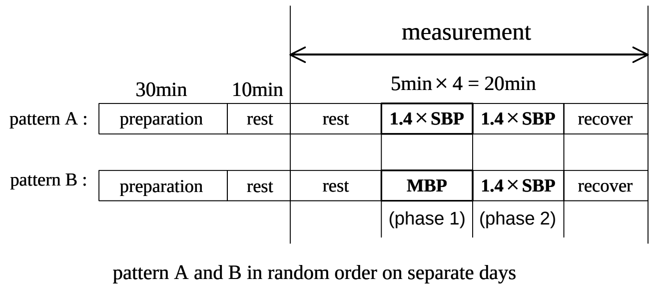

Figure 1. The protocol of occlusion and measurement.

sympathetic and parasympathetic nervous activity. Sympathetic predominance accompanied by dispersion of repolarization reflected in QTc prolongation may result in ventricular electrical instability and increase the risk of fatal myocardial infarction. It can thus be speculated that changes in autonomic nervous system activity, particularly the sympatho-vagal balance contributes to the prolongation of QTc.

The purpose of this study was to examine the effect and the safety of experimental leg occlusion upon hemodynamic systems, aiming to develop a unique method to enhance autonomic nervous system activity.

METHODS

Subjects

Ten healthy male students participated in this study as subjects [age: mean 24.4 (SD 1.1) years, height:172.7 (1.6) cm, weight: 63.6 (2.5) kg]. All subjects had no previous history of cardiovascular disease. They were explained about the purpose of this study and informed consent was obtained from each subject. The study protocol was approved by the Ethical Committee of Kyoto University Graduate School.

Testing Protocol

The subjects visited the laboratory 3 times in all. On the first day, the study was explained and subjects were accustomed to the environment and equipment of the experiment. On the second and third day, the subjects came to the laboratory 40 minutes before the measurement. Then they performed one of blood flow restriction trials consisting of 2 patterns of occlusion on the separate day in random order. All subjects were asked not to consume any food or beverages containing caffeine after 6:00 pm of the day preceding the study. The subjects were also instructed to abstain from alcohol and excessive physical activity for 24 to 48 h before testing. The room was kept at the quiet condition and the temperature was controlled to 25.7 (0.5)°C [mean

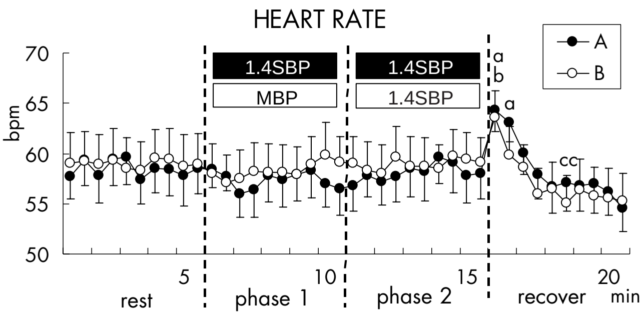

Figure 2. Heart Rate changes during 2 patterns of blood flow restriction (n=10). Black represents pattern A and white is B. A one-way analysis of variance indicated the significant effect of time (P<0.01) in both pattern. "a" indicates P<0.01 in Pattern A, and "b" is P<0.01 and "c" means P<0.05 in Pattern B vs. the first 30-seconds averaged value at rest.

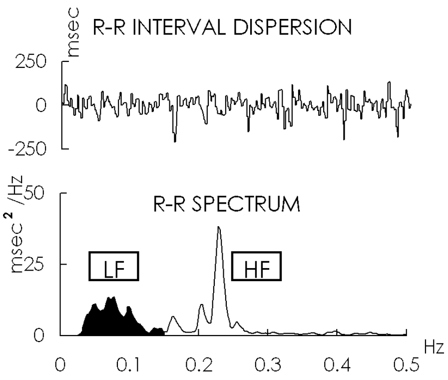

Figure 3. Representative data sets of ECG R-R intervals and the corresponding power spectral data during occlusion without blood pooling. The technique of heart rate variability power spectral analysis used in the present study identifies two separate frequency components, LF (0.03-0.15Hz) and HF (0.15-0.5Hz), which are represented by the black and the white areas, respectively.

(SE)]. All measurements were done from 8:15 am to 12:45 pm.

One experiment was composed of 20 minutes of measurement, which consisted of 5 minutes of rest, 10 minutes of occlusion which consisted of 2 phases of occlusion pressure, and 5 minutes of recovery, all following 30 minutes of preparation and 10 minutes of rest. The occlusion was performed with an automatic pressure cuff (E20, Hokanson, WA, USA) on the left thigh as follows: Pattern A: both phase 1 and 2 were 5 minutes of 1.4 times systolic blood pressure; Pattern B: during phase 1, occlusion is performed with mean blood pressure for 5 minutes, followed by phase 2, occlusion with 1.4 times systolic blood pressure for 5 minutes (Fig. 3);these values of blood pressure were measured after the 30 minute rest. During the test, we measured electrocardiogram, blood pressure, and stroke volume continuously, while subjects were directed to control their breathing 15 times per minutes (0.25 Hz) in synchrony with a metronome to ensure that respiratory-linked variations in the heart rate did not overlap with LF components (<0.15Hz) from other sources.

Device set-up

Blood Pressure and ECG

Our R-R interval power spectral analysis procedures have been fully described elsewhere (Moritani et al. 1995; Moritani et al. 1993; Nagai et al. 2004; Nishijima et al. 2002; Ue et al. 2000). We obtained electrocardiogram data from CM5 bipolar lead at a sampling rate of 1024 Hz and stored sequentially on a hard disk for later analyses. Arterial blood pressure signal was continuously recorded using an automatic non-invasive sphygmomanometer (NIHON COLIN, JENTOW-7700, Aichi, Japan). The tonometry sensor was fitted to the radial artery of the left hand, while the forearm and the hand were kept at heart level during experiments. Previous to the measurement, the sphygmomanometer was calibrated by the value obtained when using the manchette by itself. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were detected from blood pressure wave and mean blood pressure (MBP) was calculated as DBP+(SBP-DBP) / 3. The averaged results of heart rate, blood pressure, and QTc interval were calculated for every 30 seconds. Before spectral analysis was performed, the R-R interval and blood pressure data were detected, displayed and aligned sequentially to obtain equally spaced samples with an effective sampling frequency of 2 Hz and displayed on a computer screen for visual inspection. Then, the direct current component and trend were completely eliminated by digital filtering for the band-pass between 0.03 and 0.5 Hz. The root mean square value of the R-R interval and blood pressure was calculated as representing the average amplitude. After passing through the Hamming-type data window, power spectral analysis by means of a fast Fourier transform was performed on a consecutive 256-second time series of R-R interval and blood pressure data obtained during the test. We used the last 4 minutes data of every 5 minutes of experimental phase at rest, during blood flow restriction, and during recovery.

We used ECG R-wave trigger averaging technique before calculating cardiac depolarization-repolarization related parameters. The points of QRS onset and the end of T wave were determined automatically by our computer system from CM5 lead ECG. The QT interval was defined as the interval between the QRS onset and the end of T wave. The QT interval time was corrected (QTc) by Bazzett's method.

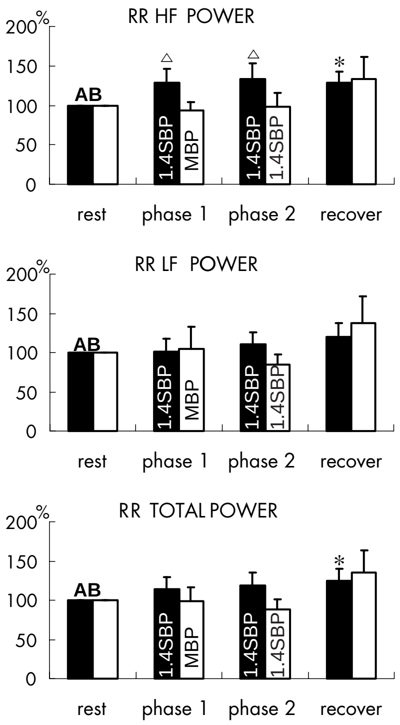

Figure 4. Group data showing the changes in HF, LF, and TOTAL power of R-R interval for each pattern of occlusion (n=10). Black represents pattern A and white is B. * indicates significant difference (P<0.05) vs. rest, and △ indicates difference vs. rest (P<0.1).

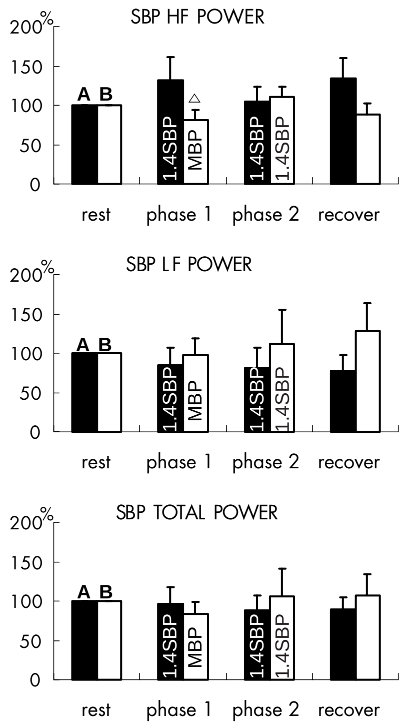

Figure 6. Group data showing the changes in HF, LF, and TOTAL power of SBP for each pattern of occlusion (n=7). (Black represents pattern A and white is B.) △ indicates difference vs. rest (P<0.1).

Stroke Volume Recording

To obtain the data of stroke volume and cardiac output, we used noninvasive impedance cardiography in this study. This noninvasive technique was first described by Kubicek et al. (1966). Stroke volume and cardiac output were calculated for every 16 seconds, and then averaged for every 5 minutes.

Analysis of Data

Since spectral values of R-R interval and systolic blood pressure, stroke volume, and cardiac output individual differences, the values were standardized by dividing each value obtained by spectral analysis by the rest value of each subject for each day respectively.

Statistical Analysis

All statistical analyses were performed using a commercial software package (SPSS version 11.5J for Windows, SPSS inc., Chicago, Illinois, USA). A Dunnett's post hoc test was used for the stroke volume and cardiac output through the experiment when one-way repeated measures ANOVA indicated a significant effect. In the analysis of heart rate, blood pressure and QTc interval, we used one-way repeated-measurements of ANOVA followed by Dunnett's post hoc test vs. rest. For the comparisons between rest and other phase of experiment in TOTAL, LF, and HF components of R-R interval and blood pressure, as shown in Figure 4 and 6, we used student's t-test. P values of less than 0.05 were considered to be statistically significant. Data are expressed as mean ± S.E., in stead of S.D. for better and easier representation of time series data.

RESULTS

Effect of Blood Flow Restriction on Autonomic Nervous System Activity

Heart Rate

Figure 2 shows changes of heart rate averaged every 30 seconds throughout the measurement. The one-way repeated ANOVA indicated statistically significant effects in both occlusion patterns (P<0.01). The heart rate tended to decrease immediately after occlusion. In both patterns, just after release from occlusion, the heart rate increased (P<0.05, respectively). Later, it smoothly decreased to a significantly lower value than that of rest in occlusion pattern B (P<0.05, 3 and 5 minutes after the releasing).

R-R interval Power Spectral analysis

Figure 3 shows a typical set of data showing raw R-

R intervals and the corresponding power spectrum data. Figure 4 shows group data for changes in HF, LF, and TOTAL power of R-R interval power spectral analysis. In contrast to the rest phase, the HF component showed a marked tendency to increase (P<0.1, t-test) during occlusion pattern A, while no apparent change is noted during occlusion pattern B. After releasing from the occlusion pattern A, the high-frequency components showed significant increase (P<0.05) in contrast to the rest. After releasing from the occlusion pattern B, the high-frequency components also showed a tendency to increase, but was not significant.

During occlusion, we found no significant changes in the LF component. After release from occlusion, the LF component tended to increase in both patterns A and B, but was not significant. With regard to TOTAL power after releasing from occlusion, we found a significant increase in pattern A (P<0.05), while during occlusion we found no significant changes.

Blood Pressure

We obtained the complete data of blood pressure successfully from 7 out of 10 subjects. In the other 3 subjects, entire blood pressure data was not obtained due to recording difficulty. Figure 5 shows the changes of mean blood pressure during blood flow restriction averaged for every 30 seconds. The one-way ANOVA indicated a statistically significant effect in both pattern A (P<0.01) and B (P<0.05). When occlusion pattern A is performed just after the start of occlusion, mean blood pressure rapidly increased and showed a significantly high value (P<0.05, 3minutes from start of occlusion), and then progressively declined. After releasing, mean blood pressure started to increase again, and reached to a significantly high value (P<0.01). Contrastingly, in the case of pattern B, when occlusion phase 1 is performed, mean blood pressure increased comparatively slowly, and kept this high value, but was not significant. Then Pattern B mean blood pressure decreased after blood flow was released.

Blood Pressure Spectral Analysis

HF, LF, and TOTAL power of systolic blood pressure power spectral analysis are shown in Figure 6. In contrast to the rest phase, the systolic blood pressure HF component showed a marked tendency to decrease (P=0.09) during occlusion pattern B. Throughout the experiment in pattern A, the high-frequency components did not show any tendency to change (P>0.1). LF and TOTAL component in systolic blood pressure variability did not change throughout the experiment (P>0.1).

Stroke Volume and Cardiac Output

We obtained complete data of stroke volume and cardiac output successfully from 7 out of 10 subjects. In other 3 subjects, cardiac output could not be obtained due to recording difficulty. Figure 7 shows the group data of changes in stroke volume and cardiac output calculated from the Z value. The one-way ANOVA indicated statistically significant effect in both pattern A and B in stroke volume (A: P<0.01, B: P<0.05), and in cardiac output (A: P<0.05, B: P<0.01). The Dunnet's post hoc test indicated significant differences between rest and phase 2, in

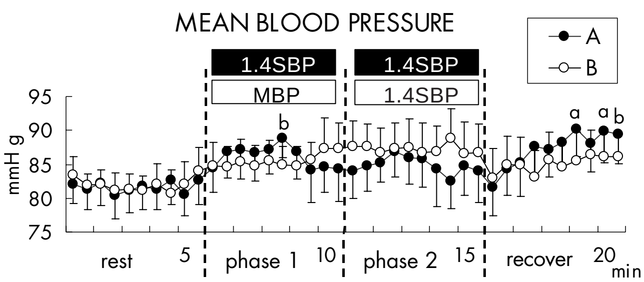

Figure 5. Group data of Mean Blood Pressure (MBP). The black circle represents the MBP during pattern A. The white circle represents the changes of MBP during pattern B. The one-way ANOVA indicated statistically significant effect in both pattern A (P<0.01) and B (P<0.05). "a" indicates P<0.01 and "b" is P<0.05 in Pattern A vs. the first minute of rest.

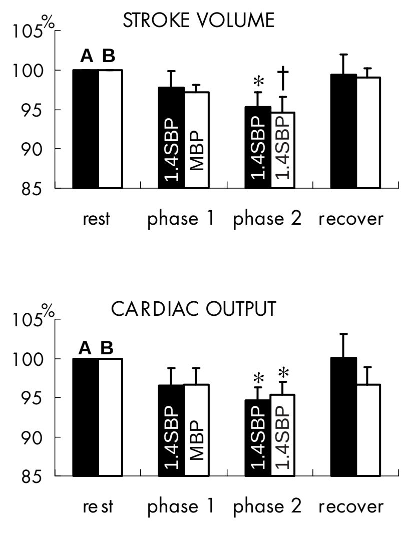

Figure 7. Group data of stroke volume calculated from Z value (n=7) and cardiac output. To standardize the data because of differences between subjects, the value was divided by the value at rest. (Black represents pattern A and white is B). A one-way analysis of variance indicated the significant effect of time in both A (P<0.01) and B (P<0.05) in stroke volume, and in A (P<0.05) and B (P<0.01) in cardiac output. † indicates significant difference vs. rest (P<0.01) and * indicates significant difference (P<0.05) vs. rest.

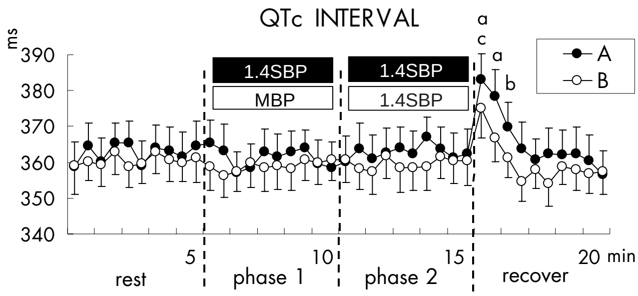

Figure 8. QTc interval changes during blood flow restriction (n=10). Black represents pattern A and white is B. A one-way analysis of variance indicated the significant effect of time (P<0.01) in both pattern. "a" indicates P<0.01 and "b" is P<0.05 in Pattern A, and "c" represents P<0.01 in Pattern B ,vs. the value of first 30-seconds at rest.

both pattern, in both stroke volume and cardiac output, respectively (stroke volume in Pattern B: P<0.01, others: P<0.05). After the release from occlusion, cardiac output returned nearly to the value at rest in pattern A, but in pattern B, the value tended to be still lower than rest (P<0.1, t-test), while stroke volume returned nearly to that of rest both in A and B.

QTc interval

We successfully obtained QTc interval that was averaged every 30 seconds in each individual from all the subjects. Figure 8 shows the changes in QTc interval during occlusion. The one-way repeated measures of ANOVA showed significant change in both pattern (P<0.01). QTc interval was almost stable during the occlusion in both patterns, and showed significantly high value just after the releasing from occlusion in both patterns (P<0.05) and soon returned near to the normal value.

DISCUSSION

In occlusion pattern A, occlusion was performed with pressure of 1.4 times systolic blood pressure throughout the occlusion trial. Because the pressure was higher than systolic blood pressure, it is assumed that there was no blood flow into leg through vessels under the cuff, and so no blood pooling was occurred. In pattern B, occlusion was performed with mean arterial blood pressure in the first 5 minutes, followed by 5 minutes of 1.4 times of systolic arterial blood pressure. Because the pressure was lower than systolic blood pressure, it is suggested that there was blood flow into leg through vessels under the cuff, and so blood pooling might have occurred in this pattern B trial.

Pattern A

A tendency to increase HF power was observed during the occlusion pattern A. This suggests that blood flow restriction by pattern A enhance vagal tone, and it might have a beneficial effect on the cardiovascular system. In the present study, we found a tendency to reduce heart rate during occlusion pattern A. In general, reduced heart rate usually results from the decreased sympathetic activity and/or increased parasympathetic activity. The present data suggest that blood flow restriction enhances vagal activity.

In this study, blood pressure rapidly increased and showed a significantly higher value than rest (P<0.01) when blood flow restriction was performed with the pressure of 1.4 times systolic blood pressure and then decreased. In this pattern, heart rate and cardiac output decreased during blood flow restriction. These are explained as follows: when occlusion is performed, blood pressure increases as the direct result of occlusion, and the barorecepter would work on the vagal nerve to decrease blood pressure, and then results in an increase of the HF component of the R-R interval spectrum, and a decrease in cardiac output and blood pressure.

After releasing, blood pressure decreased but soon after rose smoothly. And, in contrast, heart rate elevated and then decreased. Those things may not be able to be explained by only activity of autonomic nervous system, though HF and TOTAL component of R-R interval increased (P<0.05), which indicate activated parasympathetic nervous activity and total autonomic nervous system activity, while the spectral analyses were made during the last 4 minute of recover phase. It could be suggested that, blood pressure acutely decreased as a direct effect of releasing from occlusion, and that caused the low blood pressure. Then, the low blood pressure caused a heart rate increase, through withdraw of vagal nerve activity or activated sympathetic nervous system activity. Following this, it is possible that sympathetic nervous system activity was stimulated by hypotension, blood pressure was forced to increase, and that stimulated parasympathetic nervous system activity, caused heart rate decrease, and is represented by both a HF and TOTAL component increase. But the reason of blood pressure rise is unknown, and more research is needed.

Pattern B

In this occlusion pattern, blood pressure was kept elevated and kept high during blood flow restriction. Cardiac output significantly decreased (P<0.05), which is in agreement with a previous report (Iida et al. 2005), pooled blood by using pressure of 45mmHg for 4minutes and then 200 mmHg for 4 minutes. It is suggested that when occlusion is performed, cardiac output decreased by blood pooling in leg, and the autonomic system might have had to raise the blood pressure.

During occlusion, we could not find any significant change on components of R-R interval power spectral analysis. After release, we found that heart rate decreased and HF component tended to increase. This result is different from a previous report (Iida et al. 2005). A possible explanation is that we applied the cuff on only one leg while the previous work applied the cuff on both legs. So, the magnitude of blood pooling in our study was less than the previous study.

In occlusion pattern B, the HF component of systolic blood pressure tended to decrease in occlusion phase 1. The presence of HF respiratory components in arterial pressure recordings has been traditionally interpreted as a mechanical consequence of respiration, which could act directly on intrathoracic vessels or indirectly through changes in stroke volume (Dornhorst et al. 1952; Schweitzer 1945) and heart period (Akselrod et al. 1985). Sympathetic modulation of arterial smooth muscle is probably too slow to follow the 0.25 Hz respiratory frequency. Obviously, these beat-to-beat pressure changes could affect R-R interval through complex reflex adjustments, among which baroreflex could have a paramount importance (Pagani et al. 1986). In this experiment with blood pooling, HF component showed tendency to decline. This might represent a decrease of mechanical consequence of respiration, due to decrease in circulating blood, stroke volume, and cardiac output caused by blood pooling in leg.

In pattern B, we found a decrease in heart rate, normal value of blood pressure, and increase in autonomic nervous system activity when occlusion was released. This suggested that when circulating blood rapidly increased, stroke volume increased not by the work of any modulation system but by increasing blood volume, and the autonomic nervous system worked to keep homeostasis in body, so vagal nerve activity increased through barorecepter activation, and heart rate decreased.

Autonomic Nervous System Activity

Measurement of the HRV integrates pre-synaptic and post-synaptic end-organ response and provides a comprehensive quantitative and qualitative evaluation of neuro-autonomic function under various physiological conditions and clinical settings (Davy et al. 1998; Hayano et al. 1990; Hayashi et al. 1994; Liao et al. 1998; Matsumoto et al. 1999). Although quantification and interpretation of HRV remain an intricate issue (Conny et al. 1993; Eckberg 1997), the efficacy and applicability of the technique utilized in the present study have been shown in the previous research: The findings from a pharmacological blockade experiment with atropine, a parasympathetic muscarinic antagonist and propranolol, a β-adrenoceptor antagonist, in our laboratory(Hayashi et al. 1994; Matsumoto et al. 1999; Oida et al. 1997) supported the classic studies(Akselrod et al. 1981; Pagani et al. 1986) and confirmed: (1) HF power is associated solely with the parasympathetic nerve activity, and the LF power is jointly mediated by the parasympathetic and sympathetic nervous system activity; and (2) R-R interval variability and the integrated values of all the components of power spectra could reflect overall autonomic nervous system activity.

It is suggested that a decrease in the power of HF component was a significant risk factor for coronary atherosclerosis (Hayano et al. 1991). Their observations suggest that an increase in the cardiac vagal tone may help to prevent heart disease. A number of studies have also demonstrated that coronary artery occlusion elicits reflex increases in cardiac sympathetic activity, often accompanied by reductions in parasympathetic tone (Billman 1992; Corr et al. 1986). These studies suggest that activation of the sympathetic nervous system tends to reduce the electrical stability of the heart, whereas parasympathetic nerve stimulation can protect against malignant arrhythmias (Corr et al. 1986).

The LF components correspond to the well-known Mayer waves, a phenomenon that, although described in quite artificial experimental conditions, seems to pertain to normal human subjects as well. Various theories, including myogenic oscillations, central rhythms, feedback mechanisms, and "resonance" disturbances, have been advanced for their interpretation (Pagani et al. 1986). In this experiment, no significant change of LF was found in both occlusion patterns, in both R-R interval and arterial blood pressure. It is thus suggested that blood flow restriction does not have a major impact on such suggested underlying mechanisms.

Parasympathetic predominance may be the neuroautonomic feature that helps to protect against cardiovascular disease, so the augmented HRV during and after blood flow restriction may have cardio-preventive impact.

QTc interval

We found that QTc interval was stable during the occlusion, while it temporally showed significantly higher value soon after releasing from occlusion in both patterns. As QT interval itself did not show so large change (data not shown) and QTc interval is corrected by heart rate, the change can be said to have happened along with the temporal increase in heart rate. Generally, it is said that a prolonged QTc is predictive of sudden cardiac death in myocardial infarction patients and coronary heart disease mortality in healthy populations. To the best of our knowledge, effects of temporal QTc prolongation have not got studied during experimentally-induced occlusion. There are some studies suggesting that exercise stress testing (Eggeling et al. 1992; Shimizu et al. 1991), isoproterenol infusion, Valsalva maneuver and cold pressure test (Rubin et al. 1979) are helpful in unmasking a prolonged QTc interval. In these studies, people of "borderline QTc prolongation" are detected from control subjects, by measuring QTc interval after these autonomic stimulations. This temporal rapid prolongation in QTc interval must be paid attention in taking training with blood flow restriction.

CONCLUSION

The purpose of this study is to develop a unique method to enhance autonomic nervous system activity by means of experimental leg occlusion. The effects of blood flow restriction on the activities of the autonomic nervous system during rest condition were investigated using a power spectral analysis of heart rate variability.

Our results suggested that when applied in normal healthy subjects, blood flow restriction could stimulate autonomic nervous system, possibly through the input from the barorecepter to regulate blood pressure against external perturbations. A possible prolongation of QTc after cuff pressure release may require further investigation.

In conclusion, the results suggest that blood flow restriction have a potential to be a useful method to stimulate the activity of autonomic nervous system, especially to enhance parasympathetic nervous system activity.

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Authors' affiliations

N. Kiyohara, **T. Kimura**, **T. Tanaka**, **T. Moritani**, Laboratory of Applied Physiology, The Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan.