Autonomic nervous activity and lipid oxidation postexercise with capsaicin in the humans

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Abstract
This study evaluated the synergistic effects of acute exercise with capsaicin (200mg) upon the restoration of cardiac autonomic functions and depolarization-repolarization interval as well as substrate oxidation. Nine healthy males [21.9(0.8) yrs] volunteered for this study. Cardiac autonomic activity, metabolic responses, and the ECG QT intervals were continuously measured during 5 min at rest and postexercise recovery after 30 min exercise at 50% VO2max on a stationary ergometer with placebo (ECON) or capsaicin intake (ECAP), and no exercise control (NCON) were randomized. Results indicated that the HF power reflecting parasympathetic activity significantly returned to the baseline much faster during ECAP than ECON trial during postexercise [122.1 (23.2) vs. 60.2 (11.7) %, p < 0.05]. The ECAP trial significantly decreased RQ [0.79(0.02) vs. 0.85 (0.03), p < 0.05] with significantly greater fat oxidation [69.3 (6.0) vs. 49.4 (10.8) %, p < 0.05] in comparison to NCON trial during 120 min postexercise recovery without any adverse effects on cardiac electrical stability as determined by trigger-averaged ECG QT interval analyses. We suggest that capsaicin before the exercise may contribute to the improvement of cardio-protective functions and metabolic responses as one of the beneficial supplements accelerating faster restoration of autonomic activity and enhanced lipolysis during postexercise recovery without any adverse effects on cardiac electrical stability.

Key words: Autonomic nervous system, heart rate variability power spectral analysis, cardiac depolarization-repolarization interval, post-exercise recovery, lipolysis.

Introduction
The activity of the human autonomic nervous system (ANS) plays a substantial role in the physiological homeostasis maintenance process, i.e., the regulation of energy balance and body fat storage in the body as well as the control of cardiovascular system under diverse physiological and psychological environments. At rest, the ANS activity of healthy subjects is influenced by parasympathetic activity more than sympathetic activity, whereas during exercise, sympathetic activity predominates and parasympathetic retrieves. These autonomic alterations are mediated by both somatic exercise reflexes and central command mechanisms (Longhurst and Zelis, 1979; Mitchell, 1985).

During postexercise recovery period, the ANS activity is mediated by regain of parasympathetic nervous system activity and withdrawal of sympathetic nervous system activity. Although autonomic mechanisms are unclear, the patients with chronic heart failure are reported to have altered ANS activity, especially impaired vagal activity after exercise (Eckberg et al., 1971; Marin-Neto et al., 1991). Chronic endurance exercise training is associated with increased ANS activity and a shift toward more parasympathetic influence on cardiovascular function during rest (Iellamo et al., 2000; Seals and Chase, 1989), indicating an improved cardiac autonomic environment and improved cardiac health (Berntson et al., 1997). Moreover, Pober et al. (2004) have reported that a single bout of exercise on cardiac ANS function is similar to those seen in investigations of long-term training. Prior study also showed that even a single bout of maximal exercise is able to positively affect the autonomic balance of normal subjects for up to 24 h (Convertino and Adams, 1991; Somers et al., 1985). However, the effect of heart rate variability (HRV) on single bouts of exercise has not been studied widely.

On the other hand, capsaicin is the major pungent principle in various species of capsicum fruits such as hot chili peppers and has long been globally used as an ingredient of spices, preservatives and medicines (Suzuki and Iwai, 1984). There are many animal studies demonstrating that capsaicin activates sympathetic nervous system (SNS) activity associated with thermogenesis. Watanabe et al. (1988) have investigated neurophysiologic functions of capsaicin and have demonstrated that capsaicin increases energy metabolism by catecholamine secretion from the adrenal medulla through sympathetic activation via the central nervous system. Prior work (Matsumoto et al., 2000), capsaicin has reported to increase the thermogenesis and activation of the sympathetic nervous system in young women for 30 min after the meal of capsaicin-containing yellow curry sauce. Shin and Moritani (2007a) have reported that capsaicin increases fat oxidation during low-intensity ergometer exercise. However, these thermogenic sympathetic drives induced by capsaicin may have some adverse effects upon cardiac electrical stability and exaggerated sympathetic drive. As the results of electrical instability in the heart, the risk of sudden death is increased during and immediately after exercise (Albert et al., 2000). This point has not been, at least to our knowledge, previously investigated.

A prolonged cardiac heart rate-adjusted QT interval (QTc) is associated with a risk for increased cardiovascular mortality in patients with cardiac disease (Algra et al., 1991) and healthy populations (Schouten et al., 1991). The QT interval is the time required to complete myocardial depolarization and repolarization period. It has been suggested that QTc prolongation may be a consequence of an unfavorable balance between sympathetic...
and parasympathetic nervous activity. Our prior work (Ue et al., 2000), we measured cardiac depolarization-repolarization interval and performed the analysis of electrocardiogram (ECG) R-R interval power spectral analysis simultaneously by using CM5 lead ECG in patients with ischemic heart disease (IHD) and with varying degree of diabetic autonomic neuropathy.

With these methods and in consideration of our recent nutritional studies (Shin and Moritani, 2007a; 2007b), the purpose of this study was to determine whether a single bout of aerobic exercise with capsaicin intake (200mg) induces enhancement of cardiac ANS activity and lipolysis without any adverse effects of cardiac depolarization-repolarization process during postexercise recovery period.

Methods

Subjects

Nine healthy college male volunteers (age: 21.9 ± 0.8 yrs, height: 1.72 ± 0.02 m, body mass: 64.9 ± 2.7 kg, BMI: 21.9 ± 1.1 kg·m⁻², body fat: 16.9 ± 1.7 %, VO₂max: 3.1 ± 0.1 l·min⁻¹ and 47.8 ± 2.5 ml·kg⁻¹·min⁻¹) were recruited from the Kyoto University by E-mail and our laboratory homepage notices. We considered as subject for the study if they were not taking any medications, nonsmokers, not performing regular physical exercise at least over 2 times/week and have no cardio-vascular and metabolic diseases as checked by our university general health screening performed prior to this study. The Institutional Review Board of Kyoto University Graduate School approved this study for Use of Human Subjects. All subjects gave written informed consent before taking part in this study.

Maximal oxygen consumption (VO₂max) exercise test

Prior to the progressive exercise test, body composition of each subject was determined by using bioelectrical impedance analyzer (BIA) (BC-118D, Tanita, Japan). After measurement of body composition, VO₂max test of each subject was performed by using a stationary cycle ergometer and assessed by an open-circuit computerized indirect calorimeter (Aero monitor AE 300, Minato Medical Science, Tokyo, Japan). The initial exercise intensity was 30 W for 3-min and increased by 20 W per minute until voluntary exhaustion. Subjects pedaled at frequency of 60 rpm during the test. The progressive exercise test was considered a peak effort, and the highest oxygen consumption value was included in the analysis, if three of the following four criteria were fulfilled: 1) a respiratory gas exchange ratio greater than 1.15, 2) a final RPE score of 17 or greater on the Borg scale, 3) a maximal heart rate within 15 beats·min⁻¹ of age predicted maximum (220 – age), and 4) volitional exhaustion.

Experimental procedures

All subjects came to the laboratory on three occasions for experimental treatments one week after measurement of VO₂max test. The experimental trials of each subject were assigned according to a double-blind design under the following conditions: control without exercise and capsaicin (NCON) trial; placebo with exercise at 50% VO₂max (ECON) trial for 30-min; and capsaicin with exercise (ECAP) trial for 30-min. The NCON trial rested for 30-min at sitting position as a substitute for exercise. Body composition of subjects was measured before the beginning of each trial. Experimental outline of this study is illustrated in Figure 1. The subjects were allowed to read some books or listen to music during resting condition at a table over each trial period. The subjects were instructed to refrain from strenuous physical exercise, alcohol, and any spicy food at least on the day before each experiment trial as well as abstain any beverages except for water after 10:00 PM. Each trial of subjects was made at the same time of separate days by at least one week. All experiment trials were performed from 9:00 AM to 13:00 PM. On the day of each trial, subjects ate a simple breakfast (about energy content 600 kcal) 2 h before visiting to the laboratory. This meal was composed 10, 20, and 70 % of energy as fat, protein, and carbohydrate, respectively.

Figure 1. Experimental outline of this study.
Figure 2. A computer output from a subject of ECAP trial shows the raw ECG R-R interval and trigger-averaged signals for determining cardiac depolarization-repolarization interval during 120-min postexercise recovery period. RTc: corrected cardiac recovery time, QTc: heart rate corrected QT.

The subjects were then relaxed and at sitting-up condition for at least 30-min before the beginning of the experiment in a room of the temperature of 24–25°C. The ECG and gas exchange parameters of each subject were recorded for 5 minutes as baseline data. At rest, all subjects breathed in synchrony with a metronome at 0.25 Hz to ensure that respiratory-linked variations in heart rate did not overlap with low-frequency heart-rate fluctuations (<0.15 Hz) from other sources during the experiment period. Then, the subject ingested placebo tablets or capsaicin tablets (200 mg, Cerebos Co., Ltd., Taiwan) with 100 ml of water at random 1 h before the exercise, on separated week. After 1 h, the subjects exercised using a stationary cycle ergometer (CB-X 1000, NAPS, Japan) for 30-min at 60 rpm with intensity of 50% VO_{2max}, ranging from 89 to 129 W for each subject. Each subject was measured for 5-min at rest and 5-min per 30-min during total 120-min recovery to collect the ECG and gas sample in all trials. In the present study, the baseline values of each trial were standardized as 100%, and the relative values were compared during preexercise resting condition and postexercise recovery among trials.

ECG R-R interval power spectral analysis

Figure 2 described that the sample of a computer output from a subject of ECAP trial shows the raw ECG R-R interval and trigger-averaged signals for determining cardiac depolarization-repolarization interval during 120-min postexercise recovery. The ECG R-R interval power spectral analysis processes have been fully explained in our previous studies (Moritani et al., 1993; Nagai et al., 2003). Briefly, analog output of the ECG monitor (Life Scope, Nihon Kohden) was digitized via a 13-bit analog-to-digital converter (Trans Era HTB 410) at a sampling rate of 1024Hz. Digitized ECG signal were differentiated the resultant QRS spikes, and the R-R intervals were stored sequentially on a hard disk for later analyses. To evaluate ANS activity, we analyzed low frequency (0.03-0.15 Hz, LF), high vagal component (0.15-0.5 Hz, HF), and total power (0.03-0.5 Hz, TOTAL) by integrating the HRV power spectrum analysis for the respective bandwidth. The TOTAL power reflects over all ANS activity. The LF power reflects the combined sympathovagal activities and the HF power contains with only PNS activity. The index of SNS activity (LF/HF) associates the SNS activity, and the index of the PNS activity (HF/TOTAL) reflects the PNS activity (Saul et al., 1988; Seals and Chase 1989). The baseline values of each trial were standardized as 100%, and the relative values were compared baseline data and postexercise recovery among trials because integrated values of the basal spectral total power differ greatly among individuals. At rest and during recovery period, all subjects breathed in synchrony with a metronome at 0.25 Hz to ensure that respiratory-linked variations in heart rate did not overlap with low-frequency heart-rate fluctuations (<0.15 Hz) from other sources.

Cardiac depolarization-repolarization interval

The procedures of measurement of cardiac depolarization-repolarization interval have also been fully explained elsewhere (Benhorin et al., 1990; Ue et al., 2000). We used the ECG waveform averaging technique using a computer algorithm analysis before calculating cardiac depolarization-repolarization related parameters according to our previous studies (Moritani et al., 1993; Nagai et al., 2003). Briefly, analog output of the ECG monitor (Life Scope, Nihon Kohden) was digitized via a 13-bit analog-to-digital converter (Trans Era HTB 410) at a sampling rate of 1024Hz. Digitized ECG signal were differentiated the resultant QRS spikes, and the R-R intervals were stored sequentially on a hard disk for later analyses.
Calculation of substrate oxidation
We measured the gas exchange parameters at rest and recovery periods. The gas exchange data of each subject were averaged over the last 3 min for 5 min measured at rest. After performing the exercise, subjects moved to their seat. And then, the subjects rested for the first 30 min of recovery. During total 120 min of recovery period, expired gas data of each subject were analyzed over the last 3-min of 5 min time point every 30-min.

To calculate respiratory quotient (RQ) and substrate oxidation from expired gas data, we used the table of Lusk (1924). To calculate respiratory quotient (RQ) and substrate oxidation from expired gas data, we used the table of Lusk (1924).

Statistical analyses
All statistical analyses were performed using a commercial software package (SPSS version 11.5 for Windows, SPSS Inc., Chicago, IL). Statistical differences were assessed using two-way ANOVA with repeated measurements for time, treatment, and time x treatment. The one-way ANOVA with repeated measures was used to determine the significant differences over time during rest and postexercise recovery. The p values < 0.05 were considered to be statistically significant. Data are expressed as mean (SE).

Results
Power spectrum of the R-R intervals
Figure 3 demonstrates the alterations of cardiac ANS activities during experimental periods among trials. The ECG R-R interval power spectral results showed that TOTAL power did not reach the statistical significance at baseline data among trials. At RY30 (30min of postexercise recovery), the TOTAL power value of ECON trial was significantly lower than that of NCON trial [73.4 (13.0) vs. 140.1 (27.1) %, means (SE), p < 0.05]. ECON trial on TOTAL value also was lower than ECAP trial, but the difference did not reach the significant difference [73.4 (13.0) vs. 128.3 (30.6) %, p=0.065]. No differences were found between TOTAL power values during the recovery periods except at RY30 among all trials (Figure 3A). In the LF power (Figure 3C), there was no significant difference during baseline condition and postexercise recovery periods among trials. The HF power values showed no significant differences during preexercise resting condition among trials. During postexercise recovery, at RY30 of postexercise recovery, the HF power value of ECON trial was significantly lower than that of NCON and ECAP trials [60.2 (11.7) vs. 120.2 (20.5), 122.1 (23.2) %, means (SE), p < 0.05, respectively] (Figure 3B). In both SNS and parasympathetic nervous system (PNS) indices, there were significant differences at RY120 (120-min of postexercise recovery) time between ECAP and NCON trials. The index of PNS activity of ECAP trial during postexercise recovery was higher than that of NCON trials at RY120 [115.1 (15.4) vs. 83.2 (7.9) %, p < 0.05] (Figure 3C). The index of SNS activity showed lower values in ECAP trial in comparison to NCON trial [89.3 (23.4) vs. 196.2 (53.1) %, P<0.05] (Figure 3D).

Metabolic response
Figure 4 shows the alterations of metabolic responses during experimental periods among trials. The RQ values of both ECON and ECAP trials were significantly decreased during postexercise recovery in comparison to the NCON trial. However, the RQ values of ECON trial significantly decreased [RY30: 0.87 (0.03) vs. 0.81 (0.02), RY60: 0.87 (0.03) vs. 0.8 (0.03), NCON vs. ECON, means (SE), p < 0.05] until RY60 (60-min of postexercise recovery), significant differences of RQ values between ECAP and NCON trials, on the other hand, were found during over postexercise recovery periods [RY30: 0.87 (0.03) vs. 0.8 (0.02), RY60: 0.87 (0.03) vs. 0.8 (0.02), RY90: 0.85 (0.03) vs. 0.8 (0.02), RY120: 0.85 (0.03) vs. 0.79 (0.02), NCON vs. ECAP, means (SE), P=0.05] (Figure 4A). In fat and CHO oxidation, there were no significant differences during baseline resting condition among trials. Similar to the RQ results, fat oxidation of both ECON and ECAP trials significantly accelerated in comparison to NCON trial during postexercise recovery periods (Figure 4B). Additionally, the CHO oxidation significantly decreased both in the ECON and ECAP trials more than the NCON trial at recovery after the exercise (Figure 4C). However, the substrate oxidation of ECON trial only showed significant differences until 60 min of recovery period. On the other hand, the ECAP trial continuously demonstrated significant differences during entire postexercise recovery periods.

Discussion
This study provides some new findings regarding nutrient aid on autonomic parameters and metabolic responses during postexercise recovery periods. One of the major findings of the present study is that cardiac ANS activity regained as rest condition much faster in ECAP trial than in ECON trial during postexercise recovery. In cardiac ANS activities of the present study, the TOTAL power of ECON trial was significantly lower than that of NCON trial at RY30 after exercise. On the contrary, the TOTAL power of ECAP trial almost regained to control of resting condition at this time. Our results indicated that the recovery of over all ANS activity in ECON trial in comparison to ECAP trial still restrained at this time. In LF power at RY30, although no significant difference, ECON trial [100.45 (17.52) %] was still lower than NCON trial [182.68 (46.91) %] (p > 0.056). The ECAP trial returned
Figure 3A-E. The results of ANS activities by HRV power spectrum analysis among trials. Values represent means (SE): a: NCON trial vs. ECON trial, P<0.05; **: NCON trial vs. ECON trial, ECAP trial vs. ECON trial, P<0.01; *: ECAP trial vs. NCON trial, P<0.05. RY, recovery; ANS, autonomic nervous system; HRV, heart rate variability; TOTAL, total power; HF, high frequency; LF, low frequency, PNS index, parasympathetic nervous system index; SNS index, sympathetic nervous system index.

To similar lever with NCON trial at this time. On the other hand, they showed a significantly large reduction in the HF power at 80% exercise of the AT. In the present study, the HF power of ECON trial was also significantly lower than that of both NCON and ECAP trials at RY30. The results of our ANS activities suggested that capsaicin supplement with aerobic exercise accelerated the recovery of the indices of the SNS and PNS activities. Moreover, we found significant differences during postexercise recovery in the SNS and PNS indices. At RY120 of postex-
exercise recovery, the PNS index of ECAP trial significantly increased in comparison to that of NCON trial. The SNS index of ECAP trial significantly decreased in comparison to that of NCON trial. Although aerobic exercise influences positive ANS activities, our results suggest that physical activity with capsaicin component more than solely physical activity improves relaxation effect and enhances both sympathetic and vagal activities. From these results of cardiac ANS activities, we suggest although there were direct effects of exercise on cardiac ANS balance, capsaicin consumption before exercise has faster regain to resting condition on cardiac autonomic functions during postexercise recovery after 50% of VO₂max exercise. We also suggest that further study needs to confirm the effect of various nutrient aids with exercise.

Second important finding of the present study is related to the alterations of cardiac electrical stability on the effect of capsaicin ingestion and/or exercise. The alterations of cardiac depolarization-repolarization interval during postexercise recovery periods on capsaicin ingestion have not yet been reported. Although capsaicin ingestion with exercise would enhance cardiac autonomic functions, the use of capsaicin supplement must limit if it caused the prolongation of cardiac electrical recovery. For this reason, there is a need to investigate the influence of capsaicin ingestion upon cardiac electrical stability. The cardiac depolarization-repolarization interval has been classically thought to be the duration of electrical systole. Prolongation of cardiac QTc interval has been shown in various cardiac diseases (Schwartz et al., 1993), particularly in patients with ventricular arrhythmias. In our previous study (Ue et al., 2000), cardiac depolarization-repolarization interval was also significantly prolonged in patients with IHD and with varying degrees of diabetic autonomic neuropathy in comparison to control subjects.

There is also increasing evidence that a prolonged QTc is predictive of coronary heart disease mortality in healthy populations as well (Schouten et al., 1991). The present study investigated the alterations of cardiac

![Figure 4A-C](image-url)  
**Figure 4A-C.** The results of metabolic responses during preexercise resting and postexercise recovery periods among trials. Values represent means (SE). a: NCON trial vs. ECON trial, P<0.05; b: NCON trial vs. ECAP trial, P<0.05. RY, recovery; RQ, respiratory quotient; FAT, fat; CHO, carbohydrate.
depolarization-repolarization interval on the ECG beat-by-beat during postexercise recovery period by the newly developed method (Ue et al., 2000). Our results showed that the RTC and QTc of both ECAP and ECON trials were not significantly different in comparison to those of NCON trial during postexercise recovery period. These results suggested that both ECON and ECAP trials did not result in the prolongation of the QT and/or RT intervals during postexercise recovery, indicating no adverse effect upon cardiac depolarization and repolarization process.

Last important finding of the present study is related to metabolic response during postexercise recovery. The metabolic effects of exercise have been reported in the energy expenditure (EE) and substrate oxidation. Endurance exercise can also result in higher fat oxidation (Kuo et al., 2005). Only few studies, however, have so far investigated metabolic effects during postexercise recovery (Al Mulla et al., 2000; Bielinski et al., 1985). As well, no study has been reported the metabolic effect of capsaicin during recovery periods after exercise. In the present study, metabolic responses [RQ, Fat(%), CHO(%) of ECON trial were significantly different than that of NCON trial until RY60 (150 min of the recovery). Otherwise, the ECAP trial showed significant difference than that of NCON trial during postexercise recovery period. These results indicated that capsaicin supplement with exercise, but not solely exercise, accelerates the enhancement of fat utilization in recovery after exercise. Physical activity and/or exercise training raise total EE (Brooks and Gladden, 2003) and daily lipid oxidation (Bielinski et al., 1985), even though little lipid is used during physical activity per se (Bergman and Brooks, 1999; Bergman et al., 1999). As well, chronic exercise training is associated with increased HRV and a shift toward more the parasympathetic nerve dominance on cardiovascular function (Iellamo et al., 2000; Seals and Chase, 1989), indicating an improved cardiac autonomic environment and improved cardiac health (Berntson et al., 1997). Prior study (Matsumoto et al., 2000), capsaicin has also reported to increase the thermogenesis and activation of the SNS in young women for 30-min at rest after the meal of capsaicin-containing yellow curry sauce.

Meanwhile, the results of this study were derived from a small number of subjects and non-invasive method. Therefore, the interpretation of our results must be carefully considered until further studies confirm the present findings.

**Conclusion**

In conclusion, our data indicated that capsaicin is a safe nutrient supplement, which enhances cardio protective activities and metabolic responses during postexercise recovery. Therefore, the results of the present study suggest that the exercise with capsaicin ingestion may contribute to the improvement of cardio-protective functions and metabolic responses by enhancing faster recovery of the ANS activity and fat utilization during postexercise recovery period without any adverse effects on cardiac electrical stability.

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**References**

ANS activity and lipid oxidation

• Capsaicin before exercise may contribute to the improvement of cardio-protective functions as one of the beneficial supplements accelerating faster restoration of autonomic activity.
• Capsaicin before exercise enhanced lipolysis during postexercise recovery period
• Capsaicin intake does not influence cardiac electrical stability during recovery period.

QTC prolongation measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest. Circulation 83, 1888-1894

Key points

- Capsaicin before exercise may contribute to the improvement of cardio-protective functions as one of the beneficial supplements accelerating faster restoration of autonomic activity.
- Capsaicin before exercise enhanced lipolysis during postexercise recovery period
- Capsaicin intake does not influence cardiac electrical stability during recovery period.
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