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Metabolic and cardiovascular responses during voluntary pedaling exercise with electrical muscle stimulation

Kohei Watanabe · Yoshiki Taniguchi · Toshio Moritani

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Abstract

Purpose We aimed to test the effect of additional electrical muscle stimulation (EMS) during moderate-intensity voluntary pedaling exercise on metabolic and cardiovascular responses.

Methods Eleven healthy male subjects performed moderate-intensity pedaling exercise at a constant workload (80 % of ventilatory threshold) for 20 min while EMS was applied to thigh muscles from 5 to 10 min and from 15 to 20 min during the exercise.

Results A significantly higher oxygen uptake (VO_2), heart rate, and respiratory gas exchange ratio were observed during the exercise periods with EMS despite the constant workload. These changes were accompanied by an elevated blood lactate concentration, suggesting the existence of additional fast-twitch motor unit (MU) recruitment during the exercise with EMS.

Conclusion Our data suggest that the use of intermittent EMS during a constant load exercise mimics the high-intensity interval training, possibly due to additional fast-twitch MU recruitment and co-contractions of the quadriceps and hamstrings muscles, leading to higher anaerobic metabolism and a lower mechanical efficiency.

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Keywords Involuntary exercise · Electrical muscle stimulation · Fast-twitch motor units · Lactate · Interval training

Abbreviations

ECG	Electrocardiogram
EMS	Electrical muscle stimulation
HR	Heart rate
MU	Motor unit
$PETCO_2$	End-tidal CO_2 partial pressure
$PETO_2$	End-tidal O_2 partial pressure
RPE	Rate of perceived exertion
T2DM	Type 2 diabetes mellitus VO_2 oxygen uptake
$\dot{V}E$	Ventilation
$\dot{V}CO_2$	Carbon dioxide production
$\dot{V}O_{2max}$	Maximal oxygen uptake
$\dot{V}O_2$	Oxygen uptake

Introduction

Exercise is strongly recommended for the prevention and management of, and rehabilitation of patients with lifestyle-related disease and/or metabolic diseases such as type 2 diabetes mellitus (T2DM). For these patients, continuous aerobic exercise at a moderate intensity (40–60 % of $\dot{V}O_{2max}$) for 30–60 min has been generally used to enhance the lipid metabolism and to improve aerobic capacity(Colberg et al. 2010). On the other hand, vigorous or high-intensity (>60 % of $\dot{V}O_{2max}$) exercise has also been recommended for T2DM and metabolic disease patients since this type of exercise leads to higher rates of glucose metabolism during exercise and post-exercise facilitation of glucose metabolism, resulting in the greatest improvements in glycemic control and insulin sensitivity (Colberg et al. 2010).

However, high-intensity exercise necessarily imposes quite intense demands upon the musculoskeletal and/or cardiovascular system and, thereby, may lead to orthopedic disorders and/or severe cardiovascular events.

Although electrical muscle stimulation (EMS) has undergone a decline in use, mainly because of stimulation discomfort, new technologies now allow the almost painless application of strong contractions (Banerjee et al. 2005, 2009; Hasegawa et al. 2011). It has been suggested that, unlike voluntary exercise, the size-related orderly recruitment of motor units (MUs) should not be induced during EMS since the MU recruitment pattern during EMS is nonselective and/or random (Gregory and Bickel 2005; Hamada et al. 2003, 2004; Jubeau et al. 2007; Maffiuletti et al. 2011; Moritani et al. 2005). Therefore, EMS could activate the MUs which are not recruited during low-moderate intensity voluntary exercise, such as large fast-twitch MUs. This could be of benefit for the prevention and treatment of diabetes and chronic diseases associated with muscle atrophy and heart failure (Banerjee et al. 2009; Hasegawa et al. 2011) that ultimately lead to a bed-ridden state. Accumulated evidence highlights the potential for EMS to have a major impact on these and other lifestyle-related diseases and its role as a useful modality for metabolic enhancement and orthopedic rehabilitation(Clamann et al. 1974; Greenhaff et al. 1993; Hamada et al. 2003, 2004; Miyamoto et al. 2012).We demonstrated that EMS could enhance glucose metabolism more than $\dot{V}O_2$-matched voluntary exercise(Hamada et al. 2004). This new type of involuntary exercise would be useful for improvement and/or management of the blood glucose level in T2DM patients. Miyamoto et al. (2012) applied EMS to control postprandial hyperglycemia in T2DM patients. However, in the case of applying EMS as exercise for patients with lifestyle-related and/or metabolic diseases, both moderate-intensity exercise and EMS are needed for the enhancement of lipid and glucose metabolisms. We thought that the addition of EMS to moderate-intensity exercise may more effectively enhance both types of metabolism by the recruitment of various types of MU, e.g., the size-ranked orderly recruitment of slow-twitch fibers during low-intensity voluntary exercise and the random ordered recruitment of MUs, including both slow- and fast-twitch fibers. On using an electrically braked cycle ergometer, power output could be kept constant regardless of the pedaling cadence as the torque was automatically adjusted depending upon the cadence and vice versa. Therefore, it can be estimated that mechanical output and range of motion for lower extremity joints would also be restricted even if EMS is applied during exercise. This would be important for preventing and minimizing orthopedic problems of the lower extremities. However, precise physiological responses during moderate-intensity voluntary exercise with additional EMS have not been fully clarified. Prior to applying it to patients, physiological responses during this type of exercise should be characterized in healthy subjects.

The purpose of this study was to test the effect of additional EMS during the moderate-intensity voluntary exercise on metabolic and cardiovascular responses. We hypothesized that additional EMS could enhance glucose metabolism.

Methods

Subjects

Eleven healthy male students volunteered as subjects in this study (age 23.7 ± 0.9 years, height 176.4 ± 1.5 cm, body mass 66.5 ± 1.9 kg, body mass index 21.3 ± 0.4 kg/m^2, mean ± SE). No subjects were taking any medication or had a smoking habit. They gave informed consent for the study after receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation. All procedures used were in accordance with the Declaration of Helsinki and approved by the Committee for Human Experimentation of the Graduate School of Human and Environmental Studies, Kyoto University.

Experimental design

Subjects came to our laboratory two times to perform the maximum exercise tolerance test and moderate-intensity voluntary exercise with additional EMS (VE-EMS) trial. These trials were performed with an electrically braked cycle ergometer (75XL II; Combi, Tokyo, Japan).

The exercise tolerance test was performed to determine the exercise intensity of VE-EMS, which was calculated from the maximal oxygen uptake ($\dot{V}O_{2max}$) and ventilatory threshold (VT), at least 7 days before the VE-EMS trial. The workload in the exercise tolerance test was increased by 30 W every 2 min starting from 30 W. We constantly monitored and recorded the heart rate (HR), ventilation ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and the rate of perceived exertion (RPE) using the Borg scale. Detailed measurement methods are indicated below. Subjects were instructed to maintain a pedaling cadence of 60 rpm until reaching a point agreeing with two of three criteria to determine $\dot{V}O_{2max}$. In the present study, $\dot{V}O_{2max}$ was determined in line with following three criteria: (1) HR reached the prospective maximal value [220 − age (bpm)], (2) $\dot{V}O_2$ reached a steady-state despite increasing the load, and (3) subjects could not maintain the pedaling at 60 rpm. VT was estimated using the respiratory gas exchange parameters, e.g., the point of departure from linearity in $\dot{V}E$ and $\dot{V}O_2$, an abrupt increase of expiratory O_2 fraction and

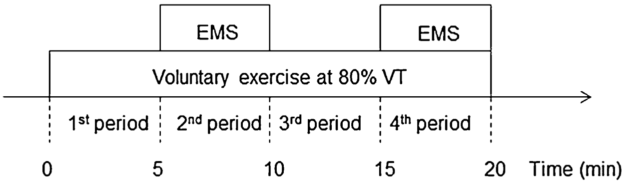

Fig. 1 Schematic representation of the moderate-intensity voluntary exercise with additional electrical muscle stimulation trial. *VT* ventilatory threshold

a systematic increase in the ventilatory equivalent for O_2 ($\dot{V}E/\dot{V}O_2$) without any increase in the ventilatory equivalent for CO_2 ($\dot{V}E/\dot{V}CO_2$), and a systematic increase in the end-tidal O_2 partial pressure ($PETO_2$) without any decrease in the end-tidal CO_2 partial pressure ($PETCO_2$).

During the VE-EMS trial, the subjects continuously performed constant exercise at 80 % of VT, which was previously determined in the exercise tolerance test, with pedaling cadence of 60 rpm for 20 min. EMS was applied to the thigh muscles from 5 to 10 min (2nd period) and from 15 to 20 min (4th period) during the voluntary exercise (Fig. 1).

Electrical muscle stimulation

During the 2nd and 4th periods of VE-EMS, EMS was applied to the thigh muscle group including the quadriceps femoris, hamstrings, and hip adductor muscles, with the stimulator (Auto Tens Pro; Homer ion, Tokyo, Japan) used in our previous studies (Hasegawa et al. 2011; Kimura et al. 2010; Miyamoto et al. 2012). The stimulator current waveform was designed at a frequency of 4 Hz with a pulse width of 250 μs. The stimulation frequency in the present study was very low as compared to our previous studies (Hamada et al. 2003, 2004; Hasegawa et al. 2011; Miyamoto et al. 2012). Because a high frequency induces complete or incomplete tetanic contractions, additional EMS disturbs voluntary pedaling movements. We thus chose a low frequency such as 4 Hz. An exponential climbing pulse was used in the present study. Detailed information on this pulse was provided in our previous study (Hasegawa et al. 2011). Since stimulation cycles for the bilateral thighs were synchronized, both thighs were simultaneously stimulated. Silicon-rubber electrode bands (4.3 × 43.2 cm) were wrapped around proximal and distal parts of the thigh with a special designed Velcrostrap (Fig. 2). Contact areas between the skin and electrodes were covered by a specially designed wet cloth (Wacoal, Kyoto, Japan). Anode (+) and cathode (−) electrodes were set at distal and proximal parts of the thigh, respectively (Fig. 2). Prior to the VE-EMS trial, EMS was applied to the thigh muscle group during the pedaling exercise for the familiarization and determination of EMS intensity which is the highest intensity that the subject could maintain 60 rpm without discomfort. Stimulation intensities were 166.9 ± 26.4 mA (mean and SE) at 9 min for the 2nd period and 168.4 ± 26.4 mA (mean and SE) at 19 min for the 4th period during the VE-EMS trial.

Metabolic and cardiovascular responses analysis

Our methods for measuring online respiratory gas exchange parameters were extensively described in our laboratory's previous studies (Hamada et al. 2003, 2004; Moritani et al. 1993). In brief, $\dot{V}O_2$, VE, and the respiratory gas exchange ratio (RER) were calculated from expired gas using the mixing chamber method with an oxygen and

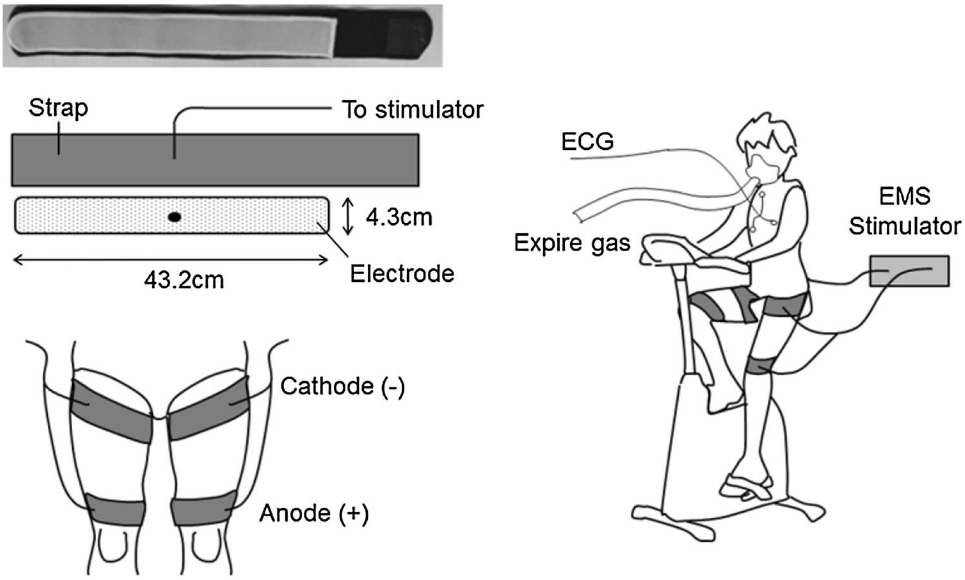

Fig. 2 The stimulation electrodes (*left*) and experimental setting (*right*). *ECG* electrocardiogram, *EMS* electrical muscle stimulation

carbon dioxide analyzer (FC-10 and CA-10A; Sable Systems International, Las Vegas, USA) and a flow transducer (FM-200XB; ARCO SYSTEM, Chiba, Japan). Analog signals from the gas analyzers and flow transducer were continuously recorded after analog-to-digital conversion at a sampling rate of 1,024 Hz (DAQ AD13; Elan Digital Systems Ltd., UK). HR was calculated from the bipolar lead (CM5) electrocardiogram (ECG) (Bio-tex, BBA-8321, Kyoto, Japan) by employing the procedure used in our previous studies (Amano et al. 2001; Fujibayashi et al. 2009; Hamada et al. 2003, 2004).The ECG signal was also collected after analog-to-digital conversion simultaneously with analog signals from the gas analyzers and flow transducer. The blood lactate concentration was measured with the lactate oxidase method using an automated analyzer (Lactate Pro; Arklay, Kyoto, Japan) and 5 μL of blood obtained from the fingertip. During the VE-EMS trial, $\dot{V}O_2$, RER, HR, and the blood lactate concentration were measured at the end of the sample periods: 4–5, 9–10, 14–15, and 19–20 min.

Statistical analysis

All data are presented as the median and interquartile range. We used nonparametric methods for statistical analysis, in accordance with the statistical reporting guidelines of the European Journal of Applied Physiology, because of the small number of subjects. $\dot{V}O_2$, RER, HR, and the blood lactate concentration were analyzed using Friedman's test to determine the differences among the periods and the Dunn's multiple comparison test to compare the variables between the 1st period and other periods. The level of statistical significance was set at $p < 0.05$. For comparison among periods using the Dunn's multiple comparison test, the level of significance was modified by Bonferroni correction, i.e., $\alpha = 0.05$/number of pairs. All statistical analyses were performed using SPSS software (SPSS version 11.5; SPSS, Tokyo, Japan).

Results

The maximum exercise tolerance test

The mean $\dot{V}O_{2\max}$ and VT were 61.6 ± 7.2 and 36.2 ± 7.5 mL/kg/min, respectively. Thus, the intensity of voluntary exercise was approximately 47 % of $\dot{V}O_{2\max}$ in the present study.

VE-EMS trial

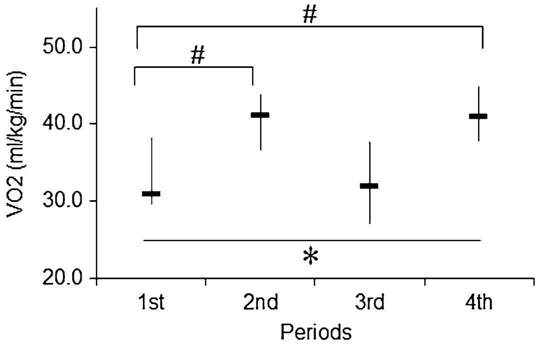

Fig. 3 Oxygen consumption during the moderate-intensity voluntary exercise with and without additional electrical muscle stimulation. Values are shown as the median and interquartile range. $^{*}p < 0.05$ significant change with time, $^{\#}p < 0.05$ significant difference between the periods

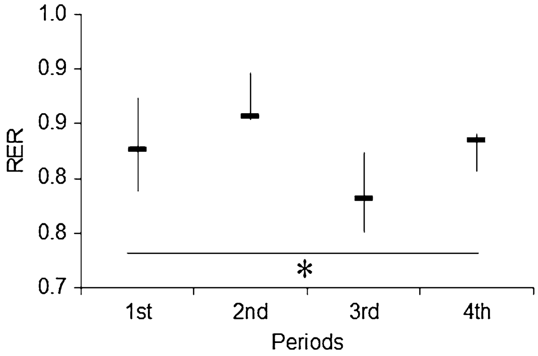

Fig. 4 Respiratory gas change ratio (RER) during the moderate-intensity voluntary exercise with and without additional electrical muscle stimulation. Values are shown as the median and interquartile range. $^{*}p < 0.05$ significant change with time, $^{\#}p < 0.05$ significant difference between the periods

A significant change with time in $\dot{V}O_2$ was observed ($p < 0.05$) and $\dot{V}O_2$ in the 2nd and 4th periods was significantly higher than in the 1st period ($p < 0.05$) (Fig. 3).There was a significant change with time in RER ($p < 0.05$) (Fig. 4). HR and blood lactate concentration significantly changed with time and those in the 4th periods were significantly higher than in the 1st period ($p < 0.05$) (Figs. 5, 6).

Discussion

In the present study, we investigated the effect of EMS during moderate-intensity voluntary exercise on metabolic and cardiovascular responses. This is, to our knowledge, the first study to investigate cardiovascular and metabolic responses during voluntary exercise combined with EMS. Our results demonstrated increases in cardiovascular responses, i.e., $\dot{V}O_2$ and HR, and tendencies toward increases in metabolic responses, i.e., RER and the blood

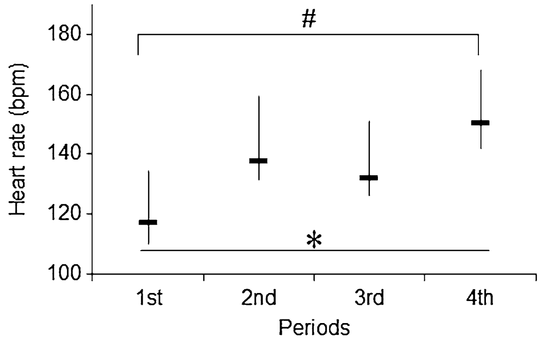

Fig. 5 Heart rate during the moderate-intensity voluntary exercise with and without additional electrical muscle stimulation. Values are shown as the median and interquartile range. $*p < 0.05$ significant change with time, $^{\#}p < 0.05$ significant difference between the periods

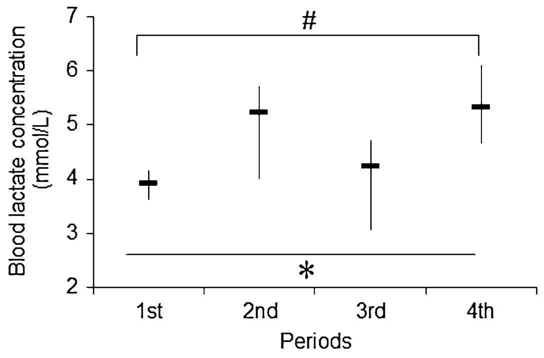

Fig. 6 Blood lactate concentration during the moderate-intensity voluntary exercise with and without additional electrical muscle stimulation. Values are shown as the median and interquartile range. $*p < 0.05$ significant change with time

lactate concentration, during the periods with compared to those without EMS. Although these results do not fully support our hypothesis that EMS enhances glycemic metabolism, the present study clarified that additional EMS during voluntary exercise alters metabolic responses.

The net power output produced by a rider's lower extremities was automatically controlled by the electrically braked cycle ergometer. Thus, we assumed that oxygen consumption would not differ between the moderate-intensity exercise with and without EMS since the same power outputs were given to the subjects on the cycle ergometer between the two conditions theoretically. However, $\dot{V}O_2$ in the periods with EMS was significantly higher than in the period without EMS (Fig. 3). Moreover, HR was also significantly increased during the periods with EMS. There are three potential factors that might explain the difference in the net and gross power output during the voluntary exercise with EMS.

First and foremost, it has been suggested that EMS induces the recruitment of MUs which are not recruited during low-moderate-intensity voluntary exercise. Theoretically, during EMS, fast-twitch MUs with glycolytic type 2 fibers are preferentially activated because of their larger nerve axons, which, in turn, have a much lower electrical resistance for a given externally applied electric current (Clamann et al. 1974). On the other hand, recent studies pointed out that this "reversal of the size-related orderly motor unit recruitment" is only imposed by nerve stimulation (Gregory and Bickel 2005; Jubeau et al. 2007; Maffiuletti et al. 2011). They stated that MU recruitment during over-the-muscle stimulation, which was used in the present study, is non-selective or random rather than disorderly (Gregory and Bickel 2005; Jubeau et al. 2007; Maffiuletti et al. 2011). The variable spatial distribution of the motor axonal branches in a non-uniform current field has much greater importance than the excitability threshold of the axonal branches (Maffiuletti et al. 2011). Irrespective of this, EMS activates MUs without size-related orderly MU recruitment which is used during voluntary contraction. This means that at low-moderate force levels, EMS can recruit a relatively higher number of high-threshold MUs, i.e., fast-twitch fibers which have a larger capacity for glycogen utilization, high force production, and low mechanical efficiency (Burke et al. 1973; Greenhaff et al. 1993; Henneman et al. 1965) than voluntary exercise. Thus, it was suspected that EMS potentially induces different metabolic and cardiovascular responses compared with voluntary contraction. We previously demonstrated the concurrent elevation of RER and the blood lactate concentration during EMS-induced intermittent isometric contractions with a 1 s-on 1 s-off duty cycle for the quadriceps femoris muscle group, indicating anaerobic breakdown and the utilization of intramuscular glycogen by the contracting muscle (Hamada et al. 2003). In fact, an EMS-induced decrease in the glycogen content was directly demonstrated in human skeletal muscles (Greenhaff et al. 1993; Hultman and Spriet 1986). Therefore, the significant increases in $\dot{V}O_2$, RER, and lactate during the periods of exercise with EMS strongly suggest enhanced glucose and glycogen utilization in addition to aerobic metabolism accompanied by voluntary exercise, despite the same net physiological burden applied during the periods with and without EMS.

The second is that EMS induces the contraction of muscle showing low-level contribution to the pedaling movement. During pedaling exercise, heterogeneity of activation levels among thigh muscles was reported using electromyography (Hug and Dorel 2009; Watanabe et al. 2009), muscle functional magnetic resonance imaging (Akima et al. 2005; Endo et al. 2007; Hug et al. 2004), and positron emission tomography (Gondoh et al. 2009). For example, a lower activation level was represented in the adductor longus muscle compared with the vastus lateralis muscle which is one of the most activated muscles within the thigh during pedaling exercise (Akima et al. 2005; Watanabe et al. 2009). EMS was applied non-selectively to all thigh muscles in this study. Thus, less activated muscles during voluntary pedaling exercise, such as the adductor longus muscle, could have been activated to a much greater extent during the exercise periods with EMS. Contraction of such muscles could, in turn, lead to a joint torque which has a low or even negative contribution to the pedaling movement and, thus, result in the difference in gross and net power outputs during the voluntary movement.

The third possibility is that EMS might have induced the contraction of a muscle that is normally relaxed during a particular phase of voluntary pedaling movement. In the present study, EMS was applied throughout an entire crank cycle during the periods with EMS. On the other hand, individual lower extremity muscles are functionally activated according to the torque required during voluntary contraction. For instance, quadriceps femoris muscles are mainly activated during the down-stroke to contribute to knee extension joint torque (Hug and Dorel 2009; Watanabe et al. 2009). Thus, EMS-induced contraction of the quadriceps femoris muscles during the up-stroke phase may lead to additional muscle contraction and generate negative torque for pedaling movement. These phenomena would also contribute to the difference between the net and gross physiological loads.

In the present study, we compared physiological responses among the periods during the same trial. Therefore, 2nd, 3rd, and 4th periods may include the history of physiological responses in prior periods. For example, EMS in the 2nd period may influence physiological responses in the 3rd period. Hamada et al. (2003) reported that EMS-induced changes in metabolic responses persist even 90 min after stimulation. However, it is difficult to separate the effect of prior periods on physiological responses on a given period in the present study. This is a key limitation of our experimental design. More detailed work is necessary to resolve this issue.

The present study used a specially designed electrode band which wraps around the circumference of the proximal and distal parts of the thigh as a common electrode pair among the different muscle groups on one side of the thigh. This electrode configuration should induce the co-contraction of thigh muscles. Since the contraction of a limited muscle group leads to a joint torque which may disturb pedaling movement, the co-contraction of various muscle groups would be favorable for additional EMS during voluntary exercise. Also, this electrode design may stimulate larger portions of muscles including deep sites when compared to traditional electrodes which are located on the muscle belly. Adams et al. (1992) demonstrated with muscle functional magnetic resonance imaging that electrodes on muscle belly selectively stimulate superficial regions of the muscle. They also showed that electrodes which are located at the proximal and distal edges of the muscle activate both superficial and deep regions (Adams et al. 1992). We are of the opinion that our electrode design can stimulate larger regions of muscle than traditional electrodes, although we have not quantified this. In the future, it will be necessary to investigate the impact of the electrode design on the results of EMS.

The blood lactate concentration in the 1st period was markedly high for 80 % of VT or 47 % of $\dot{V}O_{2max}$. In the present study, the rise in the blood lactate concentration was seen even during rest periods before the VE-EMS trial (2.0 ± 0.5 m mol/L). We applied EMS for familiarization and determination of the EMS intensity which was the highest intensity at which the subject could maintain 60 rpm without discomfort before the VE-EMS trial. Although we tried to minimize the effect of this process on the main trial, this process could have elevated the blood lactate concentrations at the baseline and in the 1st period.

For patients with lifestyle-related and/or metabolic diseases, moderate-intensity exercise has been strongly recommended to enhance lipid metabolism and improve the aerobic capacity (Colberg et al. 2010). Recently, in addition to this type of exercise, high-intensity exercise has also been recommended for improvements of glycemic control and insulin sensitivity, which are closely related to the glucose metabolism (Colberg et al. 2010). In the present study, we applied EMS, which can enhance glucose metabolism (Clamann et al. 1974; Greenhaff et al. 1993; Hamada et al. 2003, 2004; Miyamoto et al. 2012), during moderate-intensity voluntary exercise. During moderate-intensity voluntary contraction, low-threshold MUs would be mainly recruited according to the size principle (Henneman et al. 1965). Thus, it is reasonable to assume that the addition of EMS during the moderate-intensity voluntary exercise would lead to the recruitment of both high and low-threshold MUs and utilize both lipid and glucose metabolism. However, we should note that the results of the present study were observed in young, healthy subjects. It is debatable whether the same physiological responses are induced by the additional EMS during moderate-intensity voluntary exercise in patients with lifestyle-related and/or metabolic diseases. For example, previous studies suggest that T2DM patients manifest abnormal cardiovascular (Regensteiner et al. 1998), metabolic (Mogensen et al. 2007; Scheuermann-Freestone et al. 2003), and neuromuscular (Watanabe et al. 2012, 2013) responses during exercise. Future studies are needed to investigate physiological responses to voluntary exercise with EMS in patients.

In conclusion, we investigated the effect of EMS on metabolic and cardiovascular responses during the moderate-intensity voluntary exercise. Our results indicated that $\dot{V}O_2$ and HR significantly increased during the exercise periods with EMS. Also, tendencies toward increases in RER and the blood lactate concentration, which means the enhancement of glucose metabolism, during periods with EMS were observed. These results suggest that additional EMS during voluntary exercise enhances cardiovascular and metabolic responses, particularly glucose metabolism, although the net physiological burdens are theoretically the same between moderate-intensity pedaling exercise with and without EMS.

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