INTRODUCTION

Neuromuscular electrical stimulation (NMES) is a technique used to strengthen muscles, lessen disuse muscle atrophy, and improve neuromuscular function [1-4]. Functional electrical stimulation (FES), which facilitates volitional tasks where normal neural function has been damaged or destroyed, e.g. assisting with walking, standing, and cycling, increases not only local benefit such as increased muscle mass but also whole-body metabolism in persons with spinal cord injury (SCI) [5]. It was shown that FES increases metabolic response and muscle glycogen depletion in healthy subjects[6], and also improves insulin sensitivity in subjects with SCI, [7]. In the same way, therapeutic electrical stimulation is expected to cause not only metabolic change but also structural change. It was shown that NMES could substantially enhance energy consumption, carbohydrate oxidation, and whole body glucose uptake [8]. Moreover, NMES improved insulin sensitivity [9] or glucose metabolism [10] in people with type 2 diabetes.

Electrically Stimulated Eccentric Contractions during Walking Increases Oxygen Uptake

MASAFUMI BEKKI *, HIROO MATSUSE *, RYUKI HASHIDA *, TAKESHI NAGO *, SOHEI IWANAGA *, TAKUMI KAWAGUCHI **, YOSHIO TAKANO † AND NAOTO SHIBA *

* Division of Rehabilitation, Kurume University Hospital,
** Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume 830-0011,
† Department of Physical Therapy, School of Health Sciences at Fukuoka, International University of Health and Welfare, Okawa 831-8501, Japan

Received 12 February 2019, accepted 1 April 2019
J-STAGE advance publication 15 June 2021

Edited by KIMIAKI SATO

Summary: Neuromuscular electrical stimulation (NMES) is used to increase not only muscle strength but also whole-body metabolism. A hybrid training system (HTS) in which NMES is synchronized to voluntary exercise by an articular motion sensor may increase exercise load during aerobic walking exercise. We assessed the metabolic cost during walking exercise (5 minutes at 4 km/h and 5.6 km/h) on a treadmill simultaneously combined with HTS (HTSW) or without HTS (CON). We evaluated oxygen uptake (\( \dot{V}O_2 \)) and heart rate (HR) during HTSW or CON on different days in fifteen subjects. The values of \( \dot{V}O_2 \) during HTSW at 4 km/h and 5.6 km/h were significantly greater than those during CON (16.6 ± 1.85 ml/min/kg vs 15.3 ± 1.48 ml/min/kg; p < 0.05, 21.0 ± 2.17 ml/min/kg vs 19.4 ± 2.13 ml/min/kg; p < 0.01, respectively). The values of HR during HTSW at 4 km/h, 5.6 km/h were significantly greater than those during CON (106.7 ± 8.1 bpm vs 101.7 ± 10.3 bpm; p < 0.05, 126.5 ± 11.1 bpm vs 121.5 ± 12.5 bpm; p < 0.05, respectively). HTS added significantly to the exercise load by 8.3 ± 12.0% or 9.1 ± 9.9% during aerobic walking exercise at 4 km/h or 5.6 km/h, respectively. HTS might be useful for health promotion by increasing metabolic cost during aerobic walking exercise without increasing the perceived difficulty.

Key words aerobic exercise, analysis of expired gas, eccentric, exercise intensity, metabolic cost

Corresponding Author: Hiroo Matsuse, M.D., Ph.D., Division of Rehabilitation, Kurume University Hospital, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan. Tel: +81-942-31-7568, Fax: +81-942-46-6002, E-mail: matsuse_hiroh@kurume-u.ac.jp

Abbreviations: ES, electrical stimulation; FES, functional electrical stimulation; HTS, hybrid training system; HR; heart rate; NMES, neuromuscular electrical stimulation; RER, respiratory exchange ratio; SCI, spinal cord injury; VC, volitional contraction; \( \dot{V}CO_2 \), carbon dioxide output; VE, expired ventilation; \( \dot{V}O_2 \), oxygen uptake; VT, ventilatory threshold
The combined application of electrical stimulation (ES) and volitional contractions (VC) is shown to be more effective than ES or VC alone [11,12]. A hybrid training system (HTS) was developed as a novel technique for creating resistance to the motion of a voluntary contracting agonist muscle by means of the force generated by its electrically stimulated antagonist [13]. HTS was reported effective for muscle strength enhancement and muscle hypertrophy [13-16]. These earlier findings indicated the possibility that HTS could enhance exercise effect more effectively than VC alone. We showed that HTS could enhance exercise induced growth hormone when combined with knee bending exercise or cycling exercise [17,18]. Kawaguchi et al. reported that HTS combined with knee bending exercise twice a week for 12 weeks improved insulin resistance in patients with non-alcoholic fatty liver disease [19]. Recently, we developed an HTS device for use in combination with walking exercise (HTS walking) [20,21]. Walking is the most common physical activity and is effective for health promotion [22-24]. Moreover, the exercise intensity of walking can be adjusted from light to vigorous by changing speed [25]. However, exercise at the moderate or vigorous intensity recommended in various guidelines on health promotion is often not well-tolerated for people with physical disorders. Therefore, HTS combined with walking may be useful for health promotion in such people. To clarify this issue, it is necessary to investigate the exercise characteristics of HTS walking.

The purpose of the present study is to compare the metabolic cost between walking with and without HTS.

METHODS

Subjects

This study protocol was approved by the Ethics Committee of Kurume University. Next, we obtained informed consent from 15 healthy men (age, 37.1 years (SD = 8.6); height, 172.1 cm (SD = 5.3); weight, 77.8 kg (SD = 10.3); and body mass index (BMI), 26.3 (SD = 3.1)) who had reviewed the goals of the study and agreed to participate. Inclusion criteria were as follows: male, age 20 - 64 years, BMI over 22 kg/m² (ideal value of BMI is 22 for Japanese [26]), and had undergone an examination for normal physical fitness, strength, sensation, and range of motion according to the criteria of the Japanese Orthopedic Association. Exclusion criteria were: musculoskeletal problem, adverse medical history affecting cardiorespiratory function, and some kind of ongoing medical treatment. We also instructed the subjects not to participate in any regular sports activities during the study period. We selected subjects who had been recommended to do some kind of exercise for health promotion due to BMI.

Design

We measured the subjects’ height and body weight and performed two cardiopulmonary exercise tests at the clinical laboratory of the rehabilitation center. We performed the exercise test in similar environmental conditions (21 to 24 degrees centigrade, 45 to 55% relative humidity). Subjects were measured for gas exchange during walking exercise on the treadmill (AFW1014, Alinco Incorporated, Tokyo, Japan) using the following protocol after resting for 30 minutes in a reclining position. During the tests, gas exchange data was collected continuously with an automated breath by breath system (AE-100i, Minato Medical Science Co. Ltd., Osaka, Japan) using the standard technique. Heart rates (HR, beats/min) were continuously monitored by electrocardiogram during the tests. VO2 and carbon dioxide output (VCO2) were calculated and recorded during the following tests.

Intervention and Measurements

Walking exercise test protocol

Subjects first rested for five minutes in a reclining position. Next, for the 4 km/h walking test, subjects walked for 5 minutes at 4 km/h on the treadmill after warming up at a slow speed of less than 4 km/h for 3 minutes. Sequentially, for the 5.6 km/h walking test, subjects walked for 5 minutes at 5.6 km/h on the treadmill. We selected the walking speed of 4 km/h as a comfortable speed at light exercise intensity for Japanese subjects (< 3 metabolic equivalents (METs)) and at 5.6 km/h as a useful speed at moderate exercise intensity (3-<6 METs) for health [27-29]. The HTS walking (HTSW), group performed the exercise test (at 4 km/h and 5.6 km/h) with HTS while the CON subjects performed the exercise test without HTS. The sequence of walking tests with or without HTS was performed at random, and on different days. We set the total exercise time for 10 minutes after 3 minutes warm up in consideration of muscle fatigue from electrical stimulation. Subjects were encouraged to maintain a constant stride. At the onset of constant-load exercise, VO2 increases monoeXponentially with a time constant to achieve a steady state within about 3 minutes in healthy individuals below the lactate threshold [30]. Therefore the values of HR, abso-
HTSW protocol

HTSW was performed during walking exercise on a treadmill with electrical stimulator (HIZA TRAINER, EU-JLM50S, Panasonic Corporation, 1006 Oaza-Kadoma, Kadoma City, Osaka, Japan). This provided a constant voltage stimulus to the skin electrodes (regulated voltage). This stimulator is considered household medical equipment, and includes cloth straps to fix the device in place, and acceleration sensors or electrodes as shown in Figure 1. Acceleration sensors acted as a joint motion sensor (EWTSP9PD, Home Appliances Development Center Corporate Engineering Division, Appliances Company Panasonic Corporation 2-3-1-2 Noji-higashi, Kusatsu City, Shiga, Japan) and were placed on the front of each leg 88 mm above the patellar edge. The sensors analyze the algorithm of each gait pattern, and stimulate the flexor or extensor in accordance with the motion of each bilateral knee joint during walking (Figure 2). ES of the quadriceps started gradually from just before initial contact and stopped with heel off (only during stance phase). Conversely, ES of the hamstring started gradually from just before heel off and concluded with initial contact (swing phase). Therefore, the stimulation produced eccentric contractions. Electrodes (Sekisui Plastics Co., Tokyo, Japan) coated with an oxidation-resistant silver-carbon compound and low impedance gel were placed over the quadriceps on the anterior thigh, and over the hamstrings on the posterior thigh. Size of the electrodes was 15 cm × 5 cm for the quadriceps and 10 cm × 6 cm for the hamstrings (Figure 3). Electrical stimulation parameters were based on a standard Russian waveform in which a 5,000 Hz carrier frequency is modulated at 40 Hz (2.4 ms on, 22.6 ms off) to deliver a rectangular voltage biphasic pulse. Electrical stimulation intensity was set to approximately 80% of the subject’s maximum tolerance. This intensity has been reported to successfully improve muscle strength and mass without causing pain or numbness [16,20,21].

Statistical Analysis

We presented all variables as means ± SD. We assessed values for absolute VO₂ (L/min), relative VO₂ (ml/kg/min), VCO₂ (L/min), VE (L/min), and RER were averaged during the last 2 minutes of the steady state of each test and used for data analysis. Subjects were allowed to see the time display and the treadmill speed.

RESULTS

All subjects completed the walking exercise test with no complaints of pain or fatigue.

Physiological responses to walking exercise

The values of VO₂ during HTSW at 4 km/h and 5.6 km/h were significantly greater than those during CON (16.6 ± 1.85 ml/min/kg vs 15.3 ± 1.48 ml/min/kg; p < 0.05, 21.0 ± 2.17 ml/min/kg vs 19.4 ± 2.13 ml/min/kg; p < 0.01, respectively; figure 4). METs during HTSW at 4 km/h and 5.6 km/h were 4.7 ± 0.53 and 6.0 ± 0.62, respectively. On the other hand, METs during CON at 4 km/h and 5.6 km/h were 4.4 ± 0.42 and 5.5 ± 0.61, respectively. The values of VCO₂ during HTSW at 4 km/h, 5.6 km/h were significantly greater than those during CON (16.0 ± 2.23 ml/min/kg vs 14.4 ± 1.68 ml/min/kg; p < 0.05, 23.1 ± 2.69 ml/min/kg vs 21.2 ± 2.85 ml/min/kg; p < 0.05, respectively; figure 5). The values of HR during HTSW at 4 km/h, 5.6 km/h were significantly greater than those during CON (106.7 ± 8.1 bpm vs 101.7 ± 10.3 bpm; p < 0.05, 126.5 ± 11.1 bpm vs 121.5 ± 12.5 bpm; p < 0.05, respectively; figure 6). The ratio of VO₂ at 4 km/h and 5.6 km/h during HTSW was 8.3 ± 12.0% and 9.1 ± 9.9% of VO₂ during CON.

DISCUSSION

This is the first report to show that HTSW, utilizing electrically stimulated eccentric muscle contractions as a resistance to motion, increased VO₂. We showed here that exercise load was increased by electrical stimulation, and that HTS could augment the metabolic cost of walking exercise.

Walking exercise is one of the most common aerobic exercises and is recommended for all adults with minimal skill and physical fitness because the intensity can easily be modified to accommodate a wide range of physical fitness levels [27]. Absolute VO₂ during exercise is commonly used for measured or estimated measures of absolute exercise intensity. Moreover, VO₂ is used for metabolic calculation in order to estimate energy expenditure. In this study, absolute VO₂ measured while walking at moderate exercise intensity combined with HTSW was larger than without HTS regardless of walking speed. This
showed that there was a difference in exercise intensity between walking with and without HTSW. In other words, utilizing HTS could increase energy expenditure even if physical activity and skill is not increased. Therefore, combining HTS with walking would be useful for improving efficiency in patients who cannot walk fast due to musculoskeletal issues or fatigue.

Fig. 1. Components of the HIZA TRAINER. (A) Electrical stimulation unit controller. (B) External appearance of the supporter. (C) An electric stimulation unit is attached inside the supporter.

Fig. 2. Schematic model of HTSW. During walking both lower extremities are electrically stimulated in response to the gait phase of each foot. Electrical stimulation of the quadriceps is gradually initiated from just before heel contact and discontinues with heel off. Conversely, electrical stimulation of the hamstring is gradually initiated from just before heel off and discontinues with heel contact. The result is that both muscles are exercised electrically during the walking exercise. (source: J Phy Fitness Sports Med, 5(2):195-203(2016))

Fig. 3. Placement of electrodes. Electrodes placed over anterior thigh (left side of illustration). Electrodes placed over posterior thigh (right side of illustration).
NMES activates muscles non-selectively and synchronously regardless of the type of motor unit, and it preferentially activates Type II fibers as compared with VC [11,31,32]. Moreover, the recruitment pattern of eccentric exercise is different from that of an equivalent concentric workload [33]. Therefore, physiological costs of NMES or eccentric contraction are different from VC or concentric contractions, respectively. Vanderthommen et al. observed that after low-intensity intermittent exercise corresponding to 10% maximal voluntary torque, ES acidifies more cytoplasm than VC [34]. Therefore, ES strongly activates anaerobic glycolysis. On the other hand, it is reported that oxygen cost per unit of work in eccentric contractions is much less than in concentric contractions [35,36]. In our past study, we showed that agonist contractions that resisted electrically stimulated antagonist contractions increased oxygen uptake by about 5% in cycling activity [37]. Moreover, cycling exercise at moderate intensity combined with HTS increased oxygen uptake at an average of about 20% [38]. In this study, combining HTS with walking exercise at moderate intensity increased oxygen uptake by 8-9%. Therefore, the exercise load added by HTS in walking exercise increases metabolic cost in the same way as for cycling exercise. This is a potential advantage of HTS, which combines VC and ES simultaneously, as metabolic cost consists of both electrically stimulated muscle contractions and VC.

One of the potential advantages of HTS is the use of electrically stimulated eccentric contractions which provide 30-50% greater force than when using identical stimulation intensity to that of concentric or isometric contractions [39]. This characteristic use is thought to contribute to increased muscle strength and mass using HTS with relatively low intensity exercise [13-16]. Moreover, NMES could substantially en-

Fig. 4. Oxygen uptakes during walking.
The values of oxygen uptake during walking exercise simultaneously combined with hybrid training system at 4 km/h and 5.6 km/h, respectively were significantly greater than those during walking exercise without hybrid training system (16.6 ± 1.85 ml/min/kg vs 15.3 ± 1.48 ml/min/kg; * p < 0.05, 21.0 ± 2.17 ml/min/kg vs 19.4 ± 2.13 ml/min/kg; ** p < 0.01, respectively). The ratio of oxygen uptakes at 4 km/h and 5.6 km/h during walking exercise simultaneously combined with hybrid training system was 8.3 ± 12.0% and 9.1 ± 9.9% more than during walking exercise without hybrid training system.

Fig. 5. Carbon dioxide output during walking.
The values of carbon dioxide output during walking exercise simultaneously combined with hybrid training system at 4 km/h, 5.6 km/h, respectively were significantly greater than those during walking exercise without hybrid training system (16.0 ± 2.23 ml/min/kg vs 14.4 ± 1.68 ml/min/kg; * p < 0.05, 23.1 ± 2.69 ml/min/kg vs 21.2 ± 2.85 ml/min/kg; * p < 0.05, respectively).

Fig. 6. Heart rate during walking.
The values of HR during walking exercise simultaneously combined with hybrid training system at 4 km/h, 5.6 km/h, respectively were significantly greater than those during walking exercise without hybrid training system (106.7 ± 8.1 bpm vs 101.7 ± 10.3 bpm; * p < 0.05, 126.5 ± 11.1 bpm vs 121.5 ± 12.5 bpm; * p < 0.05, respectively).
hance energy consumption and whole body glucose uptake [8], and, in people with type 2 diabetes, improved insulin sensitivity [9] and glucose metabolism [10]. In our past study, Kawaguchi et al. showed that knee bending exercise with HTS twice a week for 12 weeks decreased fasting blood glucose in elderly people [40], and improved hepatic steatosis and reduced insulin resistance in non-alcoholic fatty liver disease patients who are resistant to lifestyle counseling [19]. Another potential advantage of HTS is the possibility of its use in concurrence with other continuous exercise types [17,20,21,38,41]. Watanabe et al. showed that moderate-intensity pedaling exercise at a constant workload (80% of ventilatory threshold) with NMES on the thigh muscles led to higher oxygen uptake and blood lactate concentration than without NMES [42]. They considered that the use of intermittent NMES during a constant load exercise mimics high-intensity interval training, possibly due to additional fast-twitch motor unit recruitment and co-contractions of the quadriceps and hamstrings muscles. In our past studies, cycling exercise with HTS at moderate intensity increased oxygen uptake during exercise [38], and blood lactate concentration immediately after exercise [17]. Walking is a superior exercise in terms of both cost and continuance. The effect of high-intensity interval walking for health promotion was reported in middle-aged and older subjects [43-45]. HTS could enhance exercise intensity easily without increasing walking speed. HTSW may contribute to health promotion for people having difficulty adjusting exercise intensity due to problems with cardiorespiratory or musculoskeletal function. A long-term intervention study is necessary to examine its effects in various people.

There are a few potential limitations of this study. All our subjects were male, therefore a study including women is necessary. The objective of this study was to evaluate the basic response of HTS combined with walking exercise on oxygen uptake for people with a relatively high risk of life-style related diseases. For estimating exercise intensity, oxygen uptake reserve or heart rate reserve is preferable [46]. However, we did not evaluate peak oxygen consumption or peak heart rate. For the investigation of clinical response, it is necessary to include clinical patients with some problems of cardiorespiratory and/or musculoskeletal function after evaluating oxygen uptake reserve or heart rate reserve. Additionally, muscle contraction quantity and time influence kinetic oxygen uptake. Therefore various protocols of electrical stimulation (such as modification of frequency, pulse width, or duty cycle) is necessary to evaluate the effect of HTSW.

CONCLUSION

Our findings indicate that walking exercise in combination with HTS was able to increase metabolic cost, and therefore might be useful for health promotion.

AURHORS’ CONTRIBUTIONS:
1. Masafumi Bekki wrote the manuscript and carried out all the experiments.
2. Naoto Shiba and Hiroo Matsuse managed the exercise method and hybrid training system.
3. Takeshi Nago, Sohei Iwanaga, and Yoshio Takano measured and calculated the data.
4. Ryuki Hashida and Takumi Kawaguchi managed this experiment.

DISCLOSURES: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors declare that they have no competing interests in this study.

FINANCIAL DISCLOSURES: All authors have declared that no competing interests exist.

FUNDING/SUPPORT: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

INSTITUTIONAL REVIEW: The study was designed in accordance with the ethical standards of the Helsinki Declaration of 1975 and received the approval of the Ethics Committee of Kurume University.

All procedures were fully explained to the participants who gave their written informed consent to participate.

REFERENCES
1. Balogun JA, Onilari OO, Akeju OA, and Marzouk DK. High voltage electrical stimulation in the augmentation of muscle strength: effects of pulse frequency. Arch Phys Med Rehabil 1993; 74:910-916.
2. Snyder-Mackler L, Delitto A, Bailey SL, and Stralka SW. Strength of the quadriceps femoris muscle and functional recovery after reconstruction of the anterior cruciate liga-
ment. A prospective, randomized clinical trial of electrical stimulation. J Bone Joint Surg Am 1995; 77:1166-1173.
3. Kagaya H, Shimada Y, Ebata K, Sato M, Sato K et al. Restoration and analysis of standing-up in complete paraplegia utilizing functional electrical stimulation. Arch Phys Med Rehabil 1995; 76:876-881.
4. Delitto A, Rose SJ, McKowen JM, Lehman RC, Thomas JA et al. Electrical stimulation versus voluntary exercise in strengthening thigh musculature after anterior cruciate liga-
ment surgery. Phys Ther 1988; 68:660-663.
5. Davis GM, Hamzaid NA, and Formusek C. Cardiorespiratory, metabolic, and biomechanical responses during functional electrical stimulation leg exercise: health and fitness benefits. Artif Organs 2008; 32:625-629.

6. Kim CK, Bangsbo J, Strange S, Karpakka J, and Saltin B. Metabolic response and muscle glycogen depletion pattern during prolonged electrically induced dynamic exercise in man. Scand J Rehabil Med 1995; 27:51-58.

7. Mohr T, Dela F, Handberg A, Biering-Sorensen F, Galbo H et al. Insulin action and long-term electrically induced training in individuals with spinal cord injuries. Med Sci Sports Exerc 2001; 33:1247-1252.

8. Hamada T, Sasaki H, Hayashi T, Moritani T, and Nakao K. Enhancement of whole body glucose uptake during and after human skeletal muscle low-frequency electrical stimulation. J Appl Physiol (1985) 2003; 94:2107-2112.

9. Joubert M, Metayer L, Prevost G, Morera J, Rod A et al. Neuromuscular electrostimulation and insulin sensitivity in patients with type 2 diabetes: the ELECTRODIAB pilot study. Acta Diabetol 2015; 52:285-291.

10. van Buuren F, Horstotte D, Mellwig KP, Frund A, Vlachojannis M et al. Electrical Myostimulation (EMS) Improves Glucose Metabolism and Oxygen Uptake in Type 2 Diabetes Mellitus Patients—Results from the EMS Study. Diabetes Technol Ther 2015; 17:413-419.

11. Dehail P, Duclos C, and Barat M. Electrical stimulation and muscle strengthening. Ann Readapt Med Phys 2008; 51:441-451.

12. Paillard T. Combined application of neuromuscular electric stimulations and voluntary muscular contractions. Sports Med 2008; 38:161-177.

13. Yanagi T, Shiba N, Maeda T, Iwasa K, Umezu Y et al. Agonist contractions against electrically stimulated antagonists. Arch Phys Med Rehabil 2003; 84:843-848.

14. Matsuse H, Shiba N, Umezu Y, Nago T, Tagawa Y et al. Muscle training by means of combined electrical stimulation and volitional contraction. Aviat Space Environ Med 2006; 77:581-585.

15. Iwasaki T, Shiba N, Matsuse H, Nago T, Umezu Y et al. Improvement in knee extension strength through training by means of combined electrical stimulation and voluntary muscle contraction. Tohoku J Exp Med 2006; 09:33-40.

16. Takano Y, Haneda Y, Maeda T, Sakai Y, Matsuse H et al. Increasing muscle strength and mass of thigh in elderly people with the hybrid-training method of electrical stimulation and volitional contraction. Tohoku J Exp Med 2010; 221:77-85.

17. Omoto M, Matsuse H, Hashida R, Takano Y, Yamada S et al. Cycling Exercise with Electrical Stimulation of Antagonist Muscles Increases Plasma Growth Hormone and IL-6. Tohoku J Exp Med 2015; 237:209-217.

18. Matsuse H, Nago T, Takano Y and Shiba N. Plasma Growth Hormone Is Elevated Immediately after Resistance Exercise with Electrical Stimulation and Voluntary Muscle Contraction. Tohoku J Exp Med 2010; 222:69-75.

19. Kawaguchi T, Shiba N, Maeda T, Matsugaki T, Takano Y et al. Hybrid training of voluntary and electrical muscle contractions reduces steatosis, insulin resistance, and IL-6 levels in patients with NAFLD: a pilot study. J Gastroenterol 2011; 46:746-757.

20. Matsuse H, Hashida R, Takano Y, Omoto M, Nago T et al. Walking Exercise Simultaneously Combined With Neuromuscular Electrical Stimulation of Antagonists Resistance Improved Muscle Strength, Physical Function, and Knee Pain in Symptomatic Knee Osteoarthritis: A Single-Arm Study. J Strength Cond Res 2017; 31:171-180.

21. Hashida R, Matsuse H, Takano Y, Omoto M, Nago T et al. Walking exercise combined with neuromuscular electrical stimulation of antagonist resistance improved muscle strength and physical function for elderly people: A pilot study. J Phys Fitness Sports Med 2016; 5:195-203.

22. Lee IM and Buchner DM. The importance of walking to public health. Med Sci Sports Exerc 2008; 40:S512-S518.

23. Suzuki Y and Miyashita M. Exercise walking for prevention and improvement in life-style related diseases. Nihon Rinsho 2000; 58(Supplement 5):231-234. (in Japanese)

24. Centers for Disease Control and Prevention. Vital signs: walking among adults—United States, 2005 and 2010. Morb Mortal Wky Rep 2012; 61:595-601.

25. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM et al. Compendium of Physical Activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000; 32(9):S498-S504.

26. Tokunaga K, Matsuzawa Y, Kotani K, Keno Y, Kobatake T et al. Ideal body weight estimated from the body mass index with the lowest morbidity. Int J Obes 1991; 15(1):1-5.

27. Pescatello LS, Arena R, Riebe D, and Thompson PD. ACSM’s Guidelines for Exercise Testing and Prescription. American College of Sports Medicine 2014:177-178.

28. Saito N, Takei K, and Kurosawa K. Relationship between Gait Speed and Physical Activity at Preferred Gait Speeds on Flat Ground and Treadmill. Rigakuryoho Kagaku 2008; 23:653-657. (in Japanese)

29. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011; 43(8):1575-1581.

30. Gaesser GA and Poole DC. The slow component of oxygen uptake kinetics in humans. Exerc Sport Sci Rev 1996; 24:35-71.

31. Gregory CM and Bickel CS. Recruitment Patterns in Human Skeletal Muscle During Electrical Stimulation. Phys Ther 2005; 85(4):358-364.

32. Hainaut K and Duchateau J. Neuromuscular electrical stimulation and voluntary exercise. Sports Med 1992; 14(2):100-113.

33. Enoka RM. Eccentric contractions require unique activation strategies by the nervous system. J Appl Physiol (1985) 1996; 81(6):2339-2346.

34. Vanderthommen M, Duteil S, Wary C, Raynaud JS, Leroy-Willig A et al. A comparison of voluntary and electrically induced contractions by interleaved 1H- and 31P-NMRS in humans. J Appl Physiol (1985) 2003; 94(3):1012-1024.

35. Knutgen HG, Petersen FB, and Klausen K. Oxygen uptake and heart rate responses to exercise performed with concentric and eccentric muscle contractions. Med Sci Sports 1971; 3(1):1-5.

36. Clarkson PM and Newham DJ. Associations between muscle soreness, damage, and fatigue. Adv Exp Med Biol
1995; 384:457-469.
37. Matsuse H, Shiba N, Takano Y, Yamada S, Ohshima H et al. Cycling exercise to resist electrically stimulated antagonist increases oxygen uptake in males: pilot study. J Rehabil Res Dev 2013; 50(4):545-554.
38. Omoto M, Matsuse H, Takano Y, Yamada S, Ohshima H et al. Oxygen Uptake during Aerobic Cycling Exercise Simultaneously Combined with Neuromuscular Electrical Stimulation of Antagonists. J Nov Physiother 2013; 3(6):185.
39. Seger JY and Thorstensson A. Electrically evoked eccentric and concentric torque-velocity relationships in human knee extensor muscles. Acta Physiol Scand 2000; 169(1):63-69.
40. Kawaguchi T, Shiba N, Takano Y, Maeda T, and Sata M. Hybrid training of voluntary and electrical muscle contractions decreased fasting blood glucose and serum interleukin-6 levels in elderly people: a pilot study. Appl Physiol Nutr Metab 2011; 36(2):276-283.
41. Hashida R, Takano Y, Matsuse H, Kudo M, Bekki M et al. Electrical Stimulation of the Antagonist Muscle During Cycling Exercise Interval Training Improves Oxygen Uptake and Muscle Strength. J Strength Cond Res 2021; 35(1):111-117.
42. Watanabe K, Taniguchi Y, and Moritani T. Metabolic and cardiovascular responses during voluntary pedaling exercise with electrical muscle stimulation. Eur J Appl Physiol 2014; 114(9):1801-1807.
43. Morikawa M, Okazaki K, Masuki S, Kamiyo Y, Yamazaki T et al. Physical fitness and indices of lifestyle-related diseases before and after interval walking training in middle-aged and older males and females. Br J Sports Med 2011; 45(3):216-224.
44. Sawashita J, Onitsuka S, Gen-no H, Ishikawa S, Iino F et al. Effects of mild calorie restriction and high-intensity interval walking in middle-aged and older overweight Japanese. Exp Gerontol 2009; 44(10):666-675.
45. Nemoto K, Gen-no H, Masuki S, Okazaki K, and Nose H. Effects of High-Intensity Interval Walking Training on Physical Fitness and Blood Pressure in Middle-Aged and older People. Mayo Clin Proc 2007; 82(7):803-811.
46. Swain DP and Leutholtz BC. Heart rate reserve is equivalent to %VO2 reserve, not to %VO2max. Med Sci Sports Exerc 1997; 29(3):410-414.