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Comparative effect of a 1 h session of electrical muscle stimulation and walking activity on energy expenditure and substrate oxidation in obese subjects

Jean-François Grosset, Louis Crowe, Giuseppe De Vito, Donal O'Shea, and Brian Caulfield

Abstract: It has previously been shown that low-frequency neuromuscular electrical stimulation (NMES) techniques can induce increases in energy expenditure similar to those associated with exercise. This study investigated the metabolic and cardiovascular effects of a 1 h session of lower limb NMES and compared cardiovascular response with that observed during walking in nine obese subjects (three males) (age = 43.8 ± 3.0 years; body mass index (BMI) = 41.5 ± 1.8 kg/m²). The NMES protocol consisted of delivering a complex pulse pattern to the thigh muscles for 1 h. The walking test consisted of five 4-min bouts starting at 2 km/h with 1 km/h increments up to 6 km/h. In both tests, an open-circuit gas analyser was used to assess O₂ consumption ($\dot{V}O_2$), CO₂ production ($\dot{V}CO_2$), respiratory exchange ratio (RER), and heart rate (HR). Rates of fat oxidation (RFO) and carbohydrate oxidation (CHO) were estimated by indirect calorimetry. One hour of NMES significantly increased $\dot{V}O_2$, HR, RER, and mean energy expenditure compared with resting values, reaching 8.7 ± 1.3 mL·min⁻²·kg⁻¹ (47% of $\dot{V}O_{2peak}$), 114.8 ± 7.5 bpm, 0.95, and 318.5 ± 64.3 kcal/h, respectively. CHO, but not RFO, increased during 1 h of NMES. With NMES, CHO was greater and RFO was less than at all walking speeds except 6 km/h. Lactate also increased more with NMES, to 3.5 ± 0.7 mmol versus a maximum of 1.5 ± 0.3 mmol with the walking protocol. These results suggest that NMES can be used in an obese population to induce an effective cardiovascular exercise response. In fact, the observed increase in energy expenditure induced by 1 h of NMES is clinically important and comparable with that recommended in weight management programs.

Key words: obesity, neuromuscular electrical stimulation, oxygen consumption, energy expenditure, substrate oxidation.

Résumé : Selon des études, les techniques de stimulation électrique neuromusculaire à basse fréquence (NMES) peuvent augmenter la dépense d'énergie de façon similaire à celle observée au cours d'un exercice. Cette étude analyse les effets métaboliques et cardiométaboliques d'une séance de 60 min de NMES des membres inférieurs et compare les réponses cardiovasculaires aux ajustements observés au cours d'un exercice de marche chez neuf sujets obèses dont trois hommes (âge = $43,8 \pm 3,0$ ans; IMC = $41,5 \pm 1,8$ kg/m²). Le protocole de NMES consiste en une série complexe d'impulsions dirigées vers les muscles de la cuisse durant 1 h. Le test de marche consiste en une série de cinq séances d'une durée de 4 min commençant à 2 km/h et s'accroissant de 1 km/h pour atteindre 6 km/h. Au cours des deux tests, on évalue au moyen d'un analyseur de gaz en circuit ouvert les variables suivantes : $\dot{V}O_2$, $\dot{V}CO_2$, RER et HR. On évalue par calorimétrie indirecte le taux d'oxydation des graisses (RFO) et des sucres (CHO). Comparativement aux valeurs de repos, les 60 min de NMES augmentent significativement les $\dot{V}O_2$, HR et RER et la dépense énergétique moyenne pour atteindre respectivement $8,7 \pm 1,3$ mL·min⁻²·kg⁻¹ (47% du $\dot{V}O_{2pic}$), $114,8 \pm 7,5$ bpm, 0,95 et $318,5 \pm 64,3$ kcal/h. Au cours des 60 min de NMES, CHO augmente, mais pas RFO. En période de NMES, CHO est supérieur et RFO est inférieur, et ce, à toutes les vitesses à l'exception de 6 km/h. La concentration de lactate augmente plus en période de NMES, soit jusqu'à $3,5 \pm 0,7$ mmol comparativement au maximum de $1,5 \pm 0,3$ mmol observé à la marche. Ces résultats suggèrent l'utilisation de la NMES pour induire une réponse cardiovasculaire manifeste chez une population obèse. De fait, la dépense d'énergie observée au cours des 60 min de NMES est cliniquement importante et comparable aux valeurs recommandées dans les programmes de contrôle du poids. [Traduit par la Rédaction]

Mots-clés : obésité, stimulation électrique neuromusculaire, consommation d'oxygène, dépense énergétique, oxydation des substrats.

Introduction

The World Health Organization (WHO) estimates that globally more than one billion adults are overweight or obese, with increasing obesity rates projected over the next 20 years (WHO 2004). It is well established that in the modern industrialized countries, one of the main reasons for this phenomenon is related to a reduced level of physical activity and therefore energy expenditure among the population across the life span.

The International Association for the Study of Obesity has recommended participation in at least 45–60 min/day and 60–90 min/day

of moderate activity to prevent the transition of overweight to obesity and prevent weight regain in formerly obese individuals, respectively (Saris et al. 2003). However, participating in this quantity of exercise can often prove very difficult for obese adults (Ball et al. 2000), leading to problems with exercise compliance. There is therefore a need to investigate novel intervention strategies that would help to promote increased physical activity and caloric expenditure in obese adults.

One therapeutic modality that has received a lot of attention in this area in recent years is neuromuscular electrical stimulation

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(NMES). Indeed, the clinical use of NMES and transcutaneous electrical nerve stimulation (TENS) in promotion of muscle strengthening and provision of pain relief, respectively, is long established (Lake 1992; Omura 1987). Recent work has demonstrated that an NMES protocol that elicited rhythmical subtetanic isometric contractions of the quadriceps and hamstrings, designed to mimic the pattern of muscle activation associated with shivering, can produce a meaningful increase in energy expenditure in a sedentary adult population (Banerjee et al. 2005b). Furthermore, repeated application of the technique over a period of 6 weeks resulted in a significant improvement in muscle strength and aerobic capacity in a sedentary adult population (Banerjee et al. 2005a). As this protocol was applied in a lying posture, it may have promise as a therapeutic intervention for obese adults as it could offer a means of increasing energy expenditure and improving skeletal and cardiac muscle fitness. In this way, it may help obese adults begin to exercise at moderate intensities in privacy, helping them to progress towards participation in voluntary exercise in the long term.

Many studies have already investigated NMES as way to increase physiological response using a high-frequency electrical stimulation protocol designed to elicit tetanic muscle contractions. In healthy humans, Theurel et al. 2007 reported a doubling in cardiovascular demand with high-frequency (70 Hz) NMES applied to the quadriceps. High-frequency NMES has also been used, with some success, as an alternative to cardiovascular exercise in hypoaerobic patients with severe chronic obstructive pulmonary disease (COPD) (Bourjeily-Habr et al. 2002; Neder et al. 2002; Sillen et al. 2008, 2009; Zanotti et al. 2003) and critical illness polyneuropathy (Gerovasili et al. 2009). However, to our knowledge, the application of NMES in obese subjects to induce an increase in physiological response has never been investigated. This may be due to a perception that subcutaneous adipose tissue would result in increased resistance to current flow and reduced tolerance to stimulation in obese subjects. Maffiuletti et al. (2011) recently reported that high-frequency electrical stimulation of quadriceps muscles at motor thresholds is poorly tolerated by obese subjects, particularly women. Half of the obese subjects involved in their study failed to tolerate a level of stimulation sufficient to result in quadriceps contraction that produced a knee extension movement. However, preliminary testing in our laboratory suggests that low-frequency NMES is better tolerated by obese subjects, suggesting that it might offer a potential solution.

Thus, the main aim of the present study was to evaluate, in obese yet otherwise healthy individuals, the effects of a 1 h bout of maximally tolerated low-frequency NMES delivering complex electrical stimulation wave forms and patterns on cardiovascular response and substrate oxidation. A secondary aim was to compare the cardiovascular responses (not substrate oxidation changes) obtained using NMES with those obtained during normal walking at different speeds to investigate any difference or comparative effect of both exercise methods that could justify the preferential use of one training method instead of the other from cardiac output consideration.

It was hypothesized that this 1 h bout of maximally tolerated low-frequency electrical muscle stimulation would be well tolerated by obese adults and would lead to a demand on the cardiovascular system comparable with that obtained during walking at normal to fast speeds.

Methods

Subjects

Nine middle-aged obese subjects (six females, three males; height = 167.0 ± 3.3 cm; body mass = 116.8 ± 8.3 kg; body mass index (BMI) = 41.5 ± 1.8 kg/m² (range = 31–49 kg/m²); age = 43.8 ± 3.0 years) volunteered to participate in the study. The subjects were individually screened and recruited from the Endocrine Ser-

vice of Saint Columcille's Hospital, Dublin, Ireland. For inclusion in this study, the subjects had to be between 20 and 55 years old (we included subjects with age ranging from 30 to 55 years), with a BMI >30 kg/m², and be of steady weight (less than 3% of body mass fluctuation over six months). Subjects were excluded if they had heart, metabolic, or endocrine conditions, were taking medications known to influence energy metabolism, or were smokers. All recruited subjects were sedentary, i.e., not performing regular exercise, and none had physically demanding jobs. Heart rate (HR) behavior during an exercise stress test was monitored for each subject before final inclusion in the present study. This stress test consisted of a submaximal incremental walk test on a treadmill. The experimental design consisted of comparing energy expenditure and substrate oxidation during a 1 h bout of NMES training and treadmill walking at different speeds on two separate days. Each participant also underwent a maximal effort incremental cycle test to establish peak O₂ consumption ($\dot{V}O_{2peak}$), performed at a different session.

The experimental protocol was approved by the Ethics Committee of the University College Dublin, Ireland. The requirements and aims of the study were carefully explained to each participant before the study began. Written informed consent was obtained from all study participants.

Maximal and submaximal exercises

For the three testing sessions (1 h NMES, walking, and $\dot{V}O_{2peak}$), participants were asked to abstain from strenuous exercise and caffeine for at least 24 h preceding data collection. For each subject, testing sessions were randomly assigned and a 48 h interval period between each session was required.

$\dot{V}O_{2peak}$ was determined with an incremental test to voluntary exhaustion on an electrically braked cycle ergometer (Monark 839E, Sweden). A cycle ergometer test protocol, rather than a treadmill walking protocol, was used for this study as it was considered more appropriate for a morbidly obese population, primarily due to safety concerns. Subjects first sat on the cycle ergometer for 4 min at rest. Then, the initial workload was 0 W at 70–80 rpm and increased by 20 W every 3 min, and the test was conducted until volitional exhaustion. Inspired and expired gases were continuously measured, breath by breath, with a metabolimeter (Quark b², Cosmed, Rome, Italy), which was calibrated before each measurement with room air and primary standard span gases. HR was recorded with a chest-strap heart rate monitor (Polar, Finland).

For the walking test, the subject was secured with a safety harness linked to a safety arch and an automatic emergency-stop switch. Once equipped with the safety harness and the facemask, the subject was asked to stay in a standing position on the treadmill (Saturn, h/p Cosmos, Germany) for 4 min to obtain stable standing resting conditions. Then the subject started walking at 2 km/h, which was increased by 1 km/h every 4 min until 6 km/h was reached. For each walking speed, a steady-state was reached within the 4 min. The values over the last 30 s of each 4-min period were used for the analysis (Fig. 1B). For this test, $\dot{V}O_2$, $\dot{V}CO_2$, and HR were also continuously measured as reported above.

A specially designed hand-held muscle stimulator (NT2010, Bio-Medical Research Ltd., Galway, Ireland) was used for the NMES protocol. The 1 h NMES program included 5-min warm-up and 5-min cool-down periods. The pulses were delivered through an array of eight large hydrogel electrodes (17 × 10.3 cm) applied to the skin using two neoprene wrap garments, one applied to each thigh (Fig. 2). The electrodes were initially positioned on the skin over proximal and distal ends of the quadriceps and hamstring muscles prior to securing the neoprene garment around the leg to ensure good electrodes adherence and skin contact to help minimize discomfort during stimulation sequences. The electrodes were prewired and mounted for convenient, rapid, and correct application. The basic NMES pulse pattern is a composite of four

Fig. 1. Energy expenditure (EE) curves obtained in a 50-year-old male participant (BMI = 46.4 kg/m²) during (A) the NMES training session and (B) an incremental walk test (step = 4 min; increment = 1 km/h).

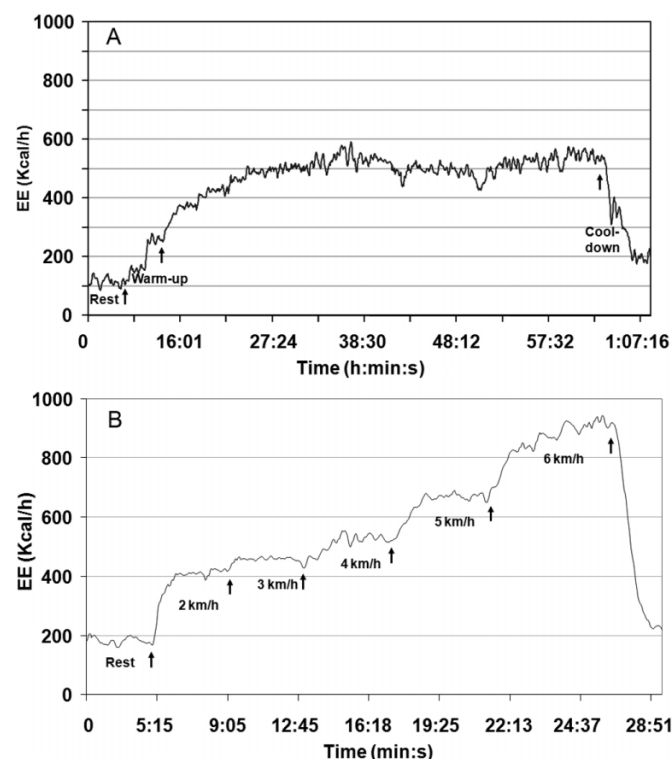
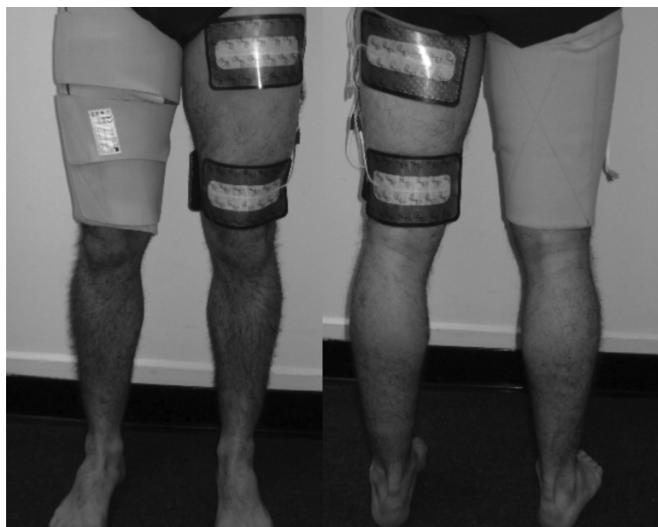


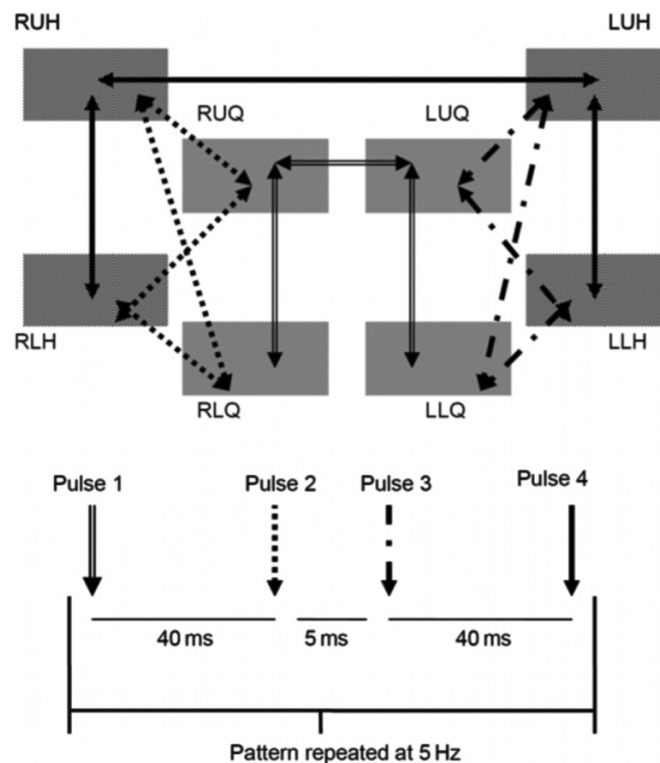
Fig. 2. Wrap and electrode positioning. A wrap, prewired and with mounted electrodes, was applied to the thighs. The model's left leg has no wrap to expose electrode positioning.



pulses shared between the electrode array (Fig. 3). This is repeated either at 4 Hz for the warm-up (5 min) or cool-down (5 min) periods or at 5 Hz for the main part of the NMES treatment session (50 min). This pulse sequence induces a strong nonfused, nontetanic contraction of the large muscle groups in the legs (quadriceps and hamstrings). The maximal unit output is 200 mA.

Pulses 1, 2, and 3 were 760 μ s long; pulse 4 was 857 μ s. All pulses are biphasic, symmetrical with an interphase delay of 100 μ s. In turn, each pulse is divided into separate segments called time

Fig. 3. Simplified diagram of pulse pattern. Each pulse is represented by an arrow type. RUQ, right upper quadriceps electrode; RLQ, right lower quadriceps; RUH, right upper hamstring; RLH, right lower hamstring; LUQ, left upper quadriceps electrode; LLQ, left lower quadriceps; LUH, left upper hamstring; LLH, left lower hamstring. Within a given pulse, the current is shared between electrode subsets at predetermined amplitude and duration ratios.



slots. There were between three and five time slots per pulse phase. For each of the 16 time slots, a subset of the electrode array was designated as source or sink of the current. Furthermore, each time slot can be allocated a percentage of the overall maximum current, set by the user-controlled intensity button. For instance, for user comfort, the time slot targeting vastus medialis is fixed at 60% of the amplitude of those targeting the proximal quadriceps. Using this system, the current densities “seen” throughout the thigh can be optimised. Including the interphase delay, etc., the pattern of four pulses is delivered in 91.4 ms. In the training phase, these groups of four pulses are repeated at a frequency of 5 Hz (for 20 pulses, in total, per second). Thus, the time between the fourth pulse and the first pulse of the next sequence is 108.6 ms.

Each participant controlled the stimulation amplitude him/herself but was encouraged to use it as high as was tolerable. The participants remained in a lying position during the 1 h NMES session to ensure that any cardiovascular responses observed were attributable to the NMES intervention and not to any other form of voluntary exercise. Expired gases were continuously recorded (Quark b², Cosmed, Rome, Italy) for further analysis. Due to interference between the electrical muscle stimulator and the heart rate sensor, HR was recorded after 30 and 55 min during 15 s stimulation breaks.

Substrate oxidation calculation

Indirect calorimetry was used to estimate the rates of fat oxidation (RFO) and carbohydrate oxidation (CHO). Steady-state values were observed at rest, during the second half of the 1 h NMES protocol, and while walking at different speeds. $\dot{V}O_2$ and $\dot{V}CO_2$

were measured as previously shown. Mean $\dot{V}O_2$ and $\dot{V}CO_2$ were calculated from the last 30 s at each walking speed and from the last 10 min of the 50-min NMES exercise phase. RFO and CHO were then calculated according to the following equations (Frayn 1983) and previously used in obese subjects (Dumortier et al. 2005):

$$[1] \quad \text{RFO rate (mg/min)} = 1.6946 \times \dot{V}O_2 - 1.7012 \times \dot{V}CO_2$$

$$[2] \quad \text{CHO rate (mg/min)} = 4.585 \times \dot{V}CO_2 - 3.2255 \times \dot{V}O_2$$

with gas volume expressed in millilitres per minute. These equations are based on the assumption that protein breakdown contributes little to energy metabolism during exercise (Brooks 1987). Energy expenditure was calculated from $\dot{V}O_2$ (L/min) at different times, multiplied by 4.82, which is the average caloric equivalent to O_2 (4.82 kcal are burned to consume 1 L O_2), and then multiplied by 60 to give kcal/h.

Knowing that the respiratory exchange ratio (RER), and then substrate utilization, may be strongly influenced by energy balance and dietary composition, all participants were requested to maintain and replicate their usual dietary habits on the day before each test. For each testing session, participants fasted overnight for approximately 10 h.

Lactic acid concentration

A portable lactate analyser (Lactate Pro, Arkay, KDK Corporation, Kyoto, Japan) was used to assess lactate (La) concentration. A calibration using a "check strip", following manufacturer's guidelines, was performed before each individual test. A finger pulp was pricked with a spring-loaded disposable needle, and 5 μ L of blood was drawn into the strip for analysis. La (mmol/L) was measured at rest and after 30 min (La_{30}) and 55 min of NMES (La_{55}), as well as during the last 30 s of each walk speed (from 2 km/h to 6 km/h). La was also measured immediately at the end of the $\dot{V}O_{2\text{peak}}$ test (La_{max}).

Statistics

Because of the very small number of participants in male and female groups ($n = 3$ and $n = 6$, respectively), it was not possible to investigate gender differences in the present study. Thus, the two groups were pooled together. Statistics were undertaken using SigmaStat 3.1 (Jandel Corporation, San Rafael, California, USA). A one-way repeated measures ANOVA was performed to compare the differences between rest, NMES, and maximal test. Statistical results of this one-way repeated measures ANOVA are presented in Table 1. A second one-way repeated measures ANOVA on time for dependant variables ($\dot{V}O_2$, RER, RFO, and CHO) to assess the time effect throughout the NMES exercise (rest, 5 min, 10 min, ..., 60 min) was performed. Statistical results of this one-way repeated measures ANOVA are reported in Fig. 4. Finally, a third one-way repeated measures ANOVA was applied to evaluate the effect of the six walking speeds on the studied parameters, as well as to compare the different walking speeds with 1 h NMES training intervention. Statistical results of this one-way repeated measures ANOVA are shown in Table 2. A Tukey post hoc test was adopted where appropriate. Paired t tests were used to evaluate differences between resting and 1 h NMES conditions for RFO and CHO. For all comparisons, a $p < 0.05$ was used to determine statistical significance. Values are means \pm SEM.

Results

Maximal exercise

Table 1 reports physiological and substrate oxidation values obtained for the entire population during the maximal test on an electrically braked cycle ergometer. At the end of the maximal test, eight of the nine participants reached at least two of the following criteria: RER > 1.1 , HR $> 90\%$ maximal HR, HR plateau, or

Table 1. Main Physiological and substrate oxidation data recorded at rest, during the 1 h NMES training session, and from the voluntary maximal exercise test in obese participants ($n = 9$). Data are means \pm SD. $\dot{V}O_2$, oxygen consumption; RER, respiratory exchange ratio; EEh, energy expenditure per hour; [La], lactate concentration, 30 min and 55 min refer to [La] evaluated at these specific times during the 1 h NMES training session; HR, heart rate; RFO, rate of fat oxidation; CHO, rate of carbohydrate oxidation. Data were recorded or calculated at rest, during the 1 h NMES training session, and from the maximal test. An asterisk (*) indicates significant differences between conditions from one-way repeated measures ANOVA for $\dot{V}O_2$, RER, EEh, HR, and [La] values or from t tests for RFO, CHO, and PO_x values ($p < 0.05$).

	$\dot{V}O_2$ (mL·min ⁻¹ ·kg ⁻¹)	$\dot{V}O_2$ (L/min)	RER	EEh (kcal/h)	HR (bpm)	[La] (mmol)	RFO (mg/min)	CHO (g/min)
Rest	2.1 \pm 0.2	0.25 \pm 0.03	0.82 \pm 0.06	77.7 \pm 11.1	67.7 \pm 1.7	1.2 \pm 0.1	43.1 \pm 14.0	0.32 \pm 0.12
1 h NMES	8.7 \pm 1.3	1.07 \pm 0.21	0.95 \pm 0.08	318.5 \pm 64.3	114.8 \pm 7.5	3.2 \pm 0.6 (30 min)	85.6 \pm 30.6	1.53 \pm 0.54
	18.9 \pm 1.3	2.11 \pm 0.24	1.13 \pm 0.09	649.1 \pm 73.4	164.9 \pm 2.9	3.5 \pm 0.7 (55 min)	-	-
Maximal test	-	-	-	-	-	5.6 \pm 0.7	-	-

Fig. 4. Oxygen consumption ($\dot{V}O_2$) expressed as (A) percentage of peak oxygen consumption versus time, (B) respiratory exchange rate (RER), (C) rate of fat oxidation, and (D) rate of carbohydrate (CH) oxidation during the NMES training session. Values are mean \pm SEM. Asterisk (*) indicates significant differences between resting and NMES values calculated every 5 min.

$\dot{V}O_2$ plateau. The subject who did not reach at least two of the four criteria only reached the $\dot{V}O_2$ plateau requirement.

Acute effects of the 1 h NMES training

Mean maximal stimulation intensity reached during the 1 h NMES training session was 130 ± 35 mA, with a range of values from 90 to 200 mA. During the 1 h NMES training, the mean $\dot{V}O_2$ was significantly increased with respect to the resting values by $447\% \pm 72\%$ ($p < 0.05$) (Table 1). Figure 4A shows that $\dot{V}O_2$ increases for the first 25 min during the incremental phase of the NMES session, followed by a plateau as participants maintained a constant stimulation intensity or continued slightly increasing it. The steep decline in $\dot{V}O_2$ in the last 5 min corresponds to the period in which the intensity of stimulation and the pulse-pattern frequency was reduced (the cool-down period). Statistical analysis shows that $\dot{V}O_2$ was significantly higher than mean resting value throughout the NMES protocol, i.e., from warm-up to cool-down periods ($p < 0.05$) (Fig. 4A). Table 1 also reports that NMES led to a significant increase in RER with respect to the resting values by $16\% \pm 4\%$ ($p = 0.02$). Figure 4B illustrates the kinetic for RER values calculated every 5 min over the 1 h NMES training. For $\dot{V}O_2$, Fig. 4B shows that mean RER was significantly higher than resting values throughout the NMES session whatever the considered interval ($p < 0.05$). Figure 1A shows typical energy expenditure (EEh) of a subject during the 1 h NMES training session. Mean EEh during 1 h NMES was significantly increased, by $428\% \pm 82\%$, compared with the mean resting value ($p < 0.05$) (Table 1). By subtracting the resting EEh value from the 1 h NMES EEh value reached in the present study, we calculated an average energy consumption of 240.8 ± 60.1 kcal during the 1 h NMES session in the present study. Mean HR value was significantly increased with respect to the resting HR and reached $70\% \pm 5\%$ HR_{max} recorded during the maximal test (Table 1). No significant changes in RFO values were observed over the 1 h NMES session compared with resting values ($p > 0.05$) (Table 1; Fig. 4C). NMES increased mean CHO over resting values, by $601\% \pm 175\%$ ($p < 0.05$) (Table 1; Fig. 4D). Figure 4D also shows that mean CHO was significantly increased from 10 min compared with mean resting CHO ($p < 0.05$). Finally, the mean relative contribution of RFO and CHO during NMES was not significantly different from resting condition ($p > 0.05$).

Comparison between 1 h NMES and treadmill walking

The EEh of a subject during the incremental walking protocol is illustrated in Fig. 1B. $\dot{V}O_2$, RER, EEh, [La], HR, and CHO were significantly increased with increasing walking speed ($p < 0.05$) (Table 2).

Resting values obtained when subjects were in standing position on the treadmill were as follows: 3.3 ± 0.4 mL \cdot min $^{-1}\cdot$ kg $^{-1}$ for $\dot{V}O_2$; 0.86 ± 0.07 for RER; 116.0 ± 19.9 kcal/h for EEh; 86.5 ± 3.0 bpm for HR; 1.3 ± 0.1 mmol for [La]; 0.05 ± 0.2 g/min for RFO values; and 0.3 ± 0.07 g/min for CHO values.

As shown in Table 2, mean $\dot{V}O_2$ reached during the 1 h NMES training session was lower compared with the $\dot{V}O_2$ obtained for walking speeds corresponding to either 5 km/h or 6 km/h ($p < 0.05$). However, the $\dot{V}O_2$ value for walking at 6 km/h was close to the $\dot{V}O_{2peak}$ value, an unsustainable level. Mean EEh reached over the 1 h NMES training session was only significantly lower than the EEh calculated walking at 6 km/h ($p < 0.05$). Interestingly, mean $\dot{V}O_2$ and EEh data reached during the 1 h NMES session were

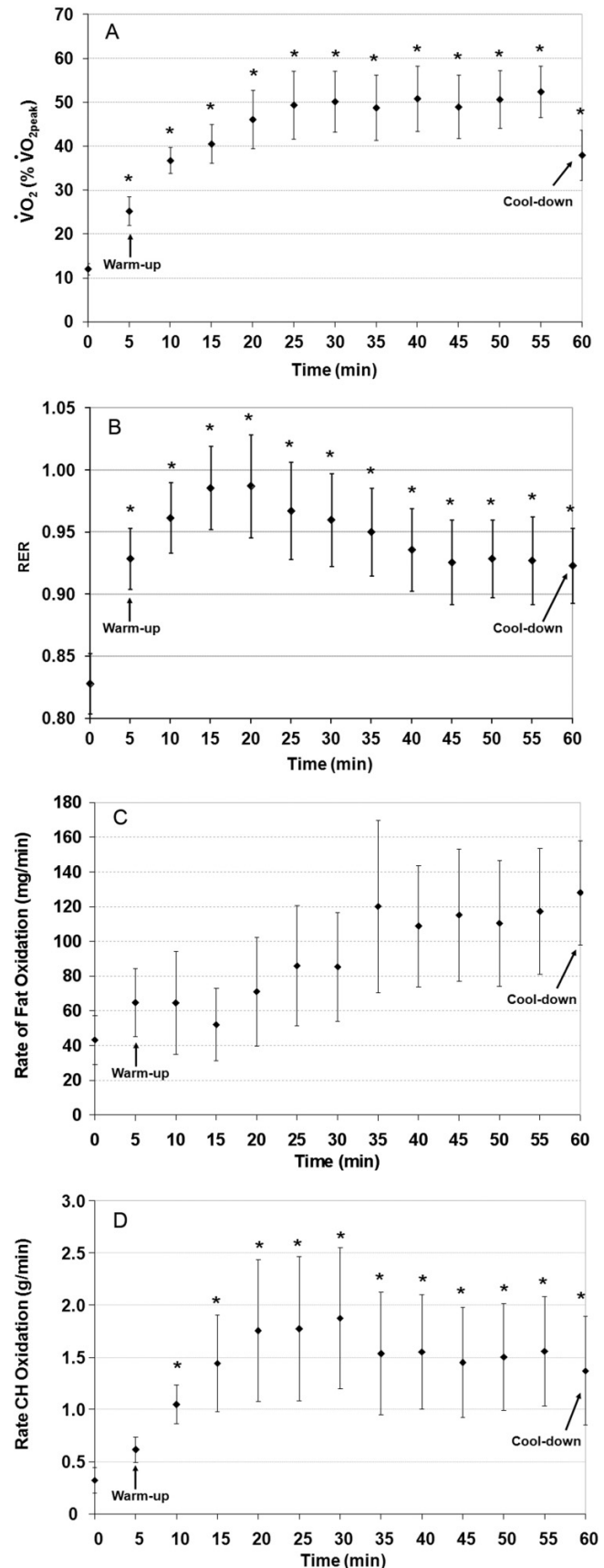


Table 2. Comparison between a 1 h NMES training session and walking at different speeds (from 2 to 6 km/h) in obese participants ($n = 9$). Data are means \pm SD. $\dot{V}O_2$, oxygen consumption; RER, respiratory exchange rate; EEh, energy expenditure per hour; [La], lactate concentration (value taken at 55 min for the 1 h NMES session); HR, heart rate frequency; RFO, rate of fat oxidation; CHO, rate of carbohydrate oxidation. Dagger (†) indicates significant effect of walking speed on the considered parameter ($p < 0.05$). Asterisk (*) indicates significant differences between 1 h NMES training session and walking speed (one-way repeated measures ANOVA; $p < 0.05$).

	$\dot{V}O_2$ (mL·min ⁻¹ ·kg ⁻¹)	RER	EEh (kcal/h)	[La] (mmol)	HR (bpm)	RFO (mg/min)	CHO (g/min)
2 km/h	7.5 \pm 1.9	0.79 \pm 0.06	259.0 \pm 105.1	1.1 \pm 0.1	92.2 \pm 6.7	300.4 \pm 60.7	0.40 \pm 0.12
3 km/h	8.9 \pm 1.5	0.83 \pm 0.07	310.3 \pm 112.1	1.1 \pm 0.1	97.3 \pm 7.0	283.2 \pm 60.3	0.67 \pm 0.18
4 km/h	10.7 \pm 1.5	0.84 \pm 0.06	373.8 \pm 122.9	1.0 \pm 0.1	103.9 \pm 6.4	335.0 \pm 71.8	0.83 \pm 0.19
5 km/h	13.3 \pm 2.1	0.87 \pm 0.05	456.5 \pm 163.0	1.1 \pm 0.1	114.0 \pm 5.9	334.8 \pm 75.5	1.20 \pm 0.24
6 km/h	17.9 \pm 2.8 [†]	0.96 \pm 0.09 [†]	625.2 \pm 219.8 [†]	1.5 \pm 0.3 [†]	136.0 \pm 13.7 [†]	252.4 \pm 56.9	2.58 \pm 0.55 [†]
1 h NMES	8.7 \pm 1.3	0.95 \pm 0.08	318.5 \pm 64.3	3.5 \pm 0.7	114.8 \pm 7.5	85.6 \pm 30.6	1.53 \pm 0.54

comparable with data obtained at a walking speed of 3 km/h regarding the nearest mean values in both activities. The average HR during the 1 h NMES session was not significantly different than that observed at all walking speeds, with the exception of 6 km/h (Table 2). Considering substrate oxidation, as reported in Table 2, the mean RFO value reached during the 1 h NMES training session was significantly lower than mean RFO values obtained during walking activity from 2 to 5 km/h ($p < 0.05$). Finally, even though the mean $\dot{V}O_2$ was 47% \pm 4% of their $\dot{V}O_{2peak}$ during the 1 h NMES session, walking at only 2 km/h leads to a significantly higher RFO value than during the NMES session ($p < 0.05$).

Discussion

To the best of our knowledge, this is the first study showing that NMES is well suited to obese adults and can lead to significant changes in physiological ($\dot{V}O_2$, EEh, RER, HR, and La) and metabolic (CHO) responses. Comparisons with normal walking have shown interesting and promising results.

As shown in this study, a 1 h NMES session led to a significant increase in metabolic demand, evidenced by a significant increase in HR and oxygen consumption. Mean oxygen consumption reached 50% $\dot{V}O_{2peak}$ during NMES. Moreover, the mean HR reached during NMES was 65% HR_{max} (calculated from HR_{max} predicted: $HR_{max} = 220 - \text{age}$). This mean HR value is in the middle range of the training intensity zone recommended by the American College of Sports Medicine (55%–90% of HR_{max}) (Pollock et al. 1998). The average stimulating intensity selected by the participants in this study (130 mA) is very similar to that selected by participants in two other studies performed by our group on sedentary adults (Banerjee et al. 2005a) and on heart failure patients (Banerjee et al. 2009); in both cases, the average stimulation intensity was 138 mA. However, the average HR response in the present investigation, expressed as a percentage of maximal HR, was higher (70%) than that observed in the previous studies (57% in both cases). These discrepancies could be partially explained by the increased stimulating frequency in the current study compared with the two previous studies (5 Hz versus 4 Hz), leading to the potential for increased muscle activation and associated energy cost. Another potential contributing factor is the chronic sympathetic nervous system overactivity that is associated with obesity (Smith and Minson 2012). However, we have not directly measured this in the present study cohort. The present results obtained in an obese population are consistent with previously reported data showing a substantial increase in metabolic demand using new NMES techniques in healthy adults (Banerjee et al. 2005a, 2005b; Moritani et al. 2005). As mentioned in the Introduction, many studies have already been conducted to investigate physiological response to high-frequency NMES. Indeed, Theurel et al. (2007) reported a mean increase by 22% and 93% for heart rate frequency and $\dot{V}O_2$, respectively, following 17.5 min of maximally tolerated NMES of the quadriceps muscles in healthy young males. High-frequency NMES has also been extensively used in hypoactive patients as an alternative form of exercise. Gerovasili et al. (2009) reported a significant 5% increase in heart rate frequency after a 45-min NMES program of lower extremities in patients in an intensive care unit due to critical illness polyneuropathy. In severe chronic obstructive pulmonary disease (COPD) patients, high-frequency NMES resulted in a 129% increase in $\dot{V}O_2$ following a 21-min intervention (Sillen et al. 2008). In the present study, using a low-frequency NMES protocol in obese subjects, mean HR and $\dot{V}O_2$ were increased by 70% and 447%, respectively. This suggests that the low-frequency NMES technique used in this study leads to higher physiological responses than the high-frequency NMES protocol classically used and would thus lead to higher physiological adaptations following short- or long-term training programs. The higher physiological response reported in the present study compared with the high-frequency

NMES protocol could be related to the low stimulation frequency protocol used but also could be influenced by the stimulated muscle mass involved. Indeed, high-frequency NMES studies only stimulated quadriceps muscle (Sillen et al. 2008; Theurel et al. 2007), whereas our protocol stimulated simultaneously both knee flexors and extensors. A larger contracting muscle mass should lead to a larger physiological response. Furthermore, in the present study, the significant increase in mean lactate up to 3.2 mmol after 30 min of NMES and the stabilization at this value until the end of the 1 h NMES session indicates that a steady state that is consistent with moderate physical activity was probably reached. These results are of interest particularly in the present population. Indeed, severe obesity generally leads to a diminution in physical activity that will automatically lead to an important decrease in cardiovascular capacities. Thus, the main step in the retraining phase for the current population is to use new NMES techniques to stimulate cardiac muscle through peripheral striated muscle electrical stimulation, which seems relevant regarding the previously mentioned data. Furthermore, our results on energy expenditure are in line with the recommendations of a weight management program with regard to exercise duration (Saris et al. 2003). It has been shown that increasing physical activity by just ~100 kcal/day (500–1500 kcal/week) can help to prevent gradual weight gain and improve weight maintenance (Andersen et al. 1999; Hartman et al. 1993; Hill and Wyatt 2005; Hill et al. 2003; Jakicic et al. 1999). In the present study, we found that a regular 1 h low-frequency NMES session consuming 240.8 ± 60.1 kcal would comfortably meet these requirements.

Study volunteers were instructed to increase the stimulation intensity throughout the initial phase of the 1 h NMES protocol to reach their maximally tolerated level of current. This gradual increase to maximally tolerated intensity explains the observed pattern of an initial increase in $\dot{V}O_2$ followed by a steady state. Unfortunately, the kinetics of individual subjects' patterns of increase in stimulation intensity was not recorded throughout the NMES protocol in the present study. Only the maximal intensity reached at the end of the protocol was noted. Thus a limitation is that it is not possible to investigate any correlation between stimulation intensity and other physiological variables in this study. However, issues such as pain and (or) discomfort that are associated with application of NMES mean that it is difficult to rapidly increase intensity to produce high levels of muscle contraction force early during a session (Theurel et al. 2007; Zory et al. 2005). A gradual increase in intensity is required to accommodate the current. This phenomenon explains the initial increase in $\dot{V}O_2$ values up to the steady state reached at the middle of the 1 h NMES protocol.

Though $\dot{V}O_2$ values obtained in the present study during the maximal cycling test and the 4-min walk were similar, we observed different metabolic and cardiorespiratory responses during the two modes of exercise. HR, lactate, and RER values were higher during cycling compared with treadmill walking at any given submaximal $\dot{V}O_2$. It has already been shown in different populations that cycle ergometer exercise leads to a higher heart rate compared with treadmill walking at any given submaximal $\dot{V}O_2$ (Faulkner et al. 1971; Hermansen 1973; Hermansen et al. 1970; Hilloskorpi et al. 1999). It has been hypothesized that the higher HR value during cycle ergometer exercise may be due to lower stroke volume induced by a reduced venous return derived from compression of vessels (Faulkner et al. 1971; Hermansen 1973; Hermansen et al. 1970) as observed in cycling (Hoes et al. 1968). Moreover, blood lactate has also been reported to be higher during cycle ergometer exercise compared with treadmill walking at comparable metabolic rates, and this has been attributed to the smaller muscle size involved during cycling compared with during treadmill walking (Hermansen 1973; Koyal et al. 1976; Miles et al. 1980). More recently, Lafortuna et al. (2008) investigated cardiovascular response in obese and normal-weight women in treadmill walking and cycle ergometer exercise and confirmed

our present results, observing higher heart rate and blood lactate values during cycle ergometer exercise than in treadmill exercise, at any given submaximal $\dot{V}O_2$. To explain these differences, Lafortuna et al. (2008) also hypothesized that in obese participants, the different body position required for cycling and walking may influence venous return by fat mass impeding venous flow at the abdominal level. Finally, higher RER values during the cycling maximal test compared with treadmill walking at any similar submaximal $\dot{V}O_2$ could be due to the choice of a cycling incremental test with shorter steps (3 min) compared with the 4-min walking test, which facilitated the obtainment of a steadier metabolic response. Thus, the different exercise modes used are a limitation of the present study when comparing maximal and submaximal data.

Concerning substrate oxidation, the mean rate of fat oxidation was not significantly modified during a 1 h NMES session. Taking this result alone into account, it could be concluded that this NMES protocol does not have any potential role in obesity management as it does not appear to have any influence on fat oxidation and thus body composition. However, the method seems capable of inducing a significant increase in HR, $\dot{V}O_2$, and VE (pulmonary ventilation). Thus, long-term beneficial effects could be expected in obese individuals from a cardiorespiratory fitness point of view, which is one of the main parameters that will limit physical activity participation in this population. Encouraging people to replace their sedentary lifestyle with additional physical activity has been, and is still, a major challenge, particularly in this patient population. Long-term training with this form of NMES could help to facilitate engagement in a voluntary physical activity throughout a significant improvement in cardiorespiratory fitness in obese people.

Although the mean rate of fat oxidation was not affected by a 1 h NMES session, the mean rate of carbohydrate oxidation was increased by 601%. Many factors play important roles in the progressive rise with increasing exercise intensity in the proportion of total energy provided by carbohydrate oxidation such as (i) the reduction in the amount of fatty acids released from adipose tissue (Romijn et al. 1993; Rosell and Belfrage 1979), (ii) increased activation of glycogenolysis (Romijn et al. 1993), and (iii) an increased recruitment of fast twitch, i.e., type II, muscle fibers. It is well established that for low-intensity exercise, the work is predominantly performed by slow-twitch (type I) fibers, which have a high capacity for fat oxidation and a low capacity for glycogenolysis–glycolysis. As the exercise intensity increases, progressively more fast-twitch (type II) fibers, which have a high capacity for and obtain much of their energy from glycogenolysis–glycolysis, are recruited (Gollnick et al. 1974). However, during muscle contractions induced by NMES, the motor unit recruitment follows a different pattern. Indeed, NMES recruits motor units in a nonselective, spatially fixed, and temporally synchronous pattern (Feiereisen et al. 1997; Vanderthommen et al. 2003). Thus, the recruitment of type II fibers with NMES, even at low intensity, may largely explain the comparative stability of the RFO over the training session and the significant increase in CHO (Fig. 4). The specific fibre recruitment pattern during NMES compared with voluntary muscle contractions may also partly explain the higher blood lactate values reported during our 1 h NMES protocol in comparison with walk test values. Indeed, as outlined above, fast-twitch fiber recruitment during NMES, even at low intensity, will activate glycogenolysis–glycolysis pathway energy production (Gollnick et al. 1974) and will thus lead to higher blood lactate production than during walking activity.

$\dot{V}O_2$ responses during the 1 h NMES session were similar to those observed during walking at a speed of about 3.5 km/h. In obese participants, it has been reported that ground reaction forces during walking are greatly increased and that, as a result, sagittal-plane net muscle moments and joint loads at the hip, knee, and ankle are also greater for obese participants compared

with normal-weight adults (Browning et al. 2006, 2007; Browning and Kram 2007). Thus, in extremely obese people, the load on the skeletal system could be a deterrent from using weight-bearing forms of exercise. For a long-term exercise program in obese participants, walking, even at 3.5 km/h, may lead to musculoskeletal pathology due to the overload imposed on the muscles and joints. In this context, our NMES protocol seems to be a safe and adequate alternative to voluntary physical activity because it elicits an exercise response, within the range of the recommendations for obese population (as discussed previously), without loading the limbs and thus does not involve performance of external work. Additionally, many obese persons could but will not exercise sufficiently, perhaps due to the time commitment required or a host of psychological issues as well reported in Ball et al. (2000). Thus, standard exercise regimes are insufficiently appealing to the many who could but do not regularly exercise (Varo et al. 2003) and the present NMES protocol could be an alternative. Moreover, it has recently been shown that an NMES protocol may also attenuate postprandial hyperglycemia in obese male participants (Kimura et al. 2010). Thus NMES techniques may emerge as a potential alternative exercise method for overweight participants and people with diabetes.

It is established that NMES is uncomfortable and even painful at high or near maximally tolerated intensities. Recently, Maffuletti et al. (2011) reported that after high-frequency electrical stimulation of quadriceps muscles, obese subjects showed lower motor excitation (higher threshold) than nonobese subjects and that women demonstrated greater sensory excitability (lower thresholds) but lower motor excitability (higher thresholds) than men. These authors also reported that four subjects failed to attain the first motor threshold (minimal visible muscle contraction without force production) (4 of 16 obese women), and 14 subjects failed to attain the second motor threshold (minimal knee extension visually assessed) (9 of 16 obese women, 4 of 16 obese men, and 1 of 17 nonobese women). These results suggest that high-frequency NMES may not be suitable for a large proportion of obese subjects as they cannot reach stimulation intensity high enough to induce a minimal knee extension. Considering the dose relationship between the stimulation intensity (and by extension, the current tolerance) and physiological responses (Banerjee et al. 2005b) and that six women were included in this study, one could assume that NMES would be a suitable tool in obese subjects only if the subjects are able to reach high stimulation intensity. The present protocol is thus promising for obese subjects as it facilitates muscle contractions at high levels (as attested by the high heart rate reached during our 1 h NMES protocol (~70% HR_{max}), as well as the current intensity reached (130 ± 35 mA with a range of values from 90 to 200 mA)) and in a total duration that would not be reached during voluntary activities in obese subjects. As mentioned above, for obese individuals, voluntary physical activities can also lead to musculoskeletal or joint pathologies due to overload imposed on these structures. Thus, muscle contraction level, total duration of muscle contractions, and protection from musculoskeletal injuries and pathologies are in favour of our 1 h NMES intervention for obese subjects as opposed to voluntary physical activity. Moreover, all of the participants of the present study applied the 1 h NMES protocol for 6 months (unpublished data), which means that pain induced by NMES can be acceptable even for a long-term training program. Knowing that many obese persons will not exercise with other people anyway, the NMES intervention, which can be done at home, seems a good alternative to voluntary physical activity for these subjects, at least in the early phase of physical activity engagement.

Conclusions

The severely obese may benefit from advances in NMES techniques that were found to be safe and acceptable. The participants

were able to exercise for 1 h at close to 50% $\dot{V}O_{2peak}$, with raised lactate and carbohydrate oxidation levels normally associated with moderate to intense exercise, which could contribute towards calorie expenditure for weight management. NMES can be done unsupervised, at home, and does not load the joints in the same way as much voluntary exercise, e.g., walking. It may be a beneficial complement to a voluntary exercise program or an alternative exercise for those obese who have physical or psychological barriers to voluntary exercise.

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