<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Comparative effect of a 1 h session of electrical muscle stimulation and walking activity on energy expenditure and substrate oxidation in obese subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>Grosset, Jean-François; Crowe, Louis; De Vito, Giuseppe; O'Shea, Donal; Caulfield, Brian</td>
</tr>
<tr>
<td><strong>Publication date</strong></td>
<td>2013</td>
</tr>
<tr>
<td><strong>Publication information</strong></td>
<td>Applied Physiology, Nutrition and Metabolism, 38 (999): 57-65</td>
</tr>
<tr>
<td><strong>Publisher</strong></td>
<td>NRC Research Press</td>
</tr>
<tr>
<td><strong>Item record/more information</strong></td>
<td><a href="http://hdl.handle.net/10197/6463">http://hdl.handle.net/10197/6463</a></td>
</tr>
<tr>
<td><strong>Publisher's statement</strong></td>
<td>© Canadian Science Publishing or its licensors</td>
</tr>
<tr>
<td><strong>Publisher's version (DOI)</strong></td>
<td><a href="http://dx.doi.org/10.1139/apnm-2011-0367">http://dx.doi.org/10.1139/apnm-2011-0367</a></td>
</tr>
</tbody>
</table>
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 (V˙ O₂), CO₂ production (V˙ CO₂), 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 V˙ O₂, HR, RER, and mean energy expenditure compared with resting values, reaching 8.7 ± 1.3 mL·min⁻¹·kg⁻¹ (47% of V˙ O₂peak), 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. At the end of the NMES session, 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.

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. There are a number of different NMES protocols that can be used to induce a metabolic response in the muscles, including resistive exercise (RE) and low-frequency NMES (L-NMES). Low-frequency NMES involves the use of low-frequency, high-voltage electrical impulses that are applied to the muscles to induce a muscle contraction. The frequency of the electrical impulses is typically between 10 and 50 Hz, and the voltage is kept low to avoid muscle fatigue. This type of NMES is often used in conjunction with weight training to increase muscle strength and to improve muscle endurance.

NMES has been shown to be effective in inducing a metabolic response in the muscles, with studies showing that it can increase energy expenditure and substrate oxidation. For example, a study by Zehnder et al. (2010) found that NMES increased energy expenditure by up to 40% compared to resting levels. Another study by Zehnder and colleagues (2011) found that NMES was able to increase substrate oxidation in the muscles and improve post-exercise recovery.

The aim of this study was to compare the metabolic effects of a 1 h session of NMES to those of walking in obese subjects. The study involved nine obese subjects (three males) who were asked to participate in a 1 h session of NMES or a 1 h walking protocol. The NMES protocol consisted of delivering a complex pulse pattern to the thigh muscles for 1 h. The walking protocol 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 (V˙ O₂), CO₂ production (V˙ CO₂), 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 V˙ O₂, HR, RER, and mean energy expenditure compared with resting values, reaching 8.7 ± 1.3 mL·min⁻¹·kg⁻¹ (47% of V˙ O₂peak), 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. At the end of the NMES session, 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.
were individually screened and recruited from the Endocrine Service (Bourjeily-Habr et al. 2002; Neder et al. 2002; Sillen et al. 2008, 2009; Zanotti et al. 2003) and critical illness polyneuromyopathy (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 normo- 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 Service 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 (\( V\bar{O}_2\)peak), 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 \( V\bar{O}_2\)peak), 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. \( V\bar{O}_2\)peak 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, \( V\bar{O}_2\), \( V\bar{CO}_2\), 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
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, nontonic 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 μs long; pulse 4 was 857 μs. All pulses are biphasic, symmetrical with an interphase delay of 100 μs. In turn, each pulse is divided into separate segments called time 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):

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

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

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, Arkray, 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 μL 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 \( V_{O_2\text{peak}} \) test \( [La]_{\text{max}} \).

**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 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 ± 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 ± SD. \( \dot{V}O_2, \dot{V}CO_2 \), oxygen consumption; RER, respiratory exchange ratio; EEh, energy expenditure per hour; [La], lactate concentration; 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 \( \dot{V}O_2, \dot{V}CO_2, \) RER, HR, and [La] values or from \( t \) tests for RFO and CHO. For all comparisons, a \( p < 0.05 \) was used to determine statistical significance. Values are means ± SEM.|

<table>
<thead>
<tr>
<th>Condition</th>
<th>( \dot{V}O_2 ) (L/min)</th>
<th>( \dot{V}CO_2 ) (L/min)</th>
<th>RER</th>
<th>EEh (kcal/h)</th>
<th>HR (bpm)</th>
<th>[La] (mmol/L)</th>
<th>RFO (mg/min)</th>
<th>CHO (g/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>2.14±0.2</td>
<td>0.25±0.03</td>
<td>0.82±0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 h NMES</td>
<td>8.7±1.3</td>
<td>1.07±0.21</td>
<td>0.95±0.08</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal test</td>
<td>18.9±1.3</td>
<td>2.11±0.13</td>
<td>0.95±0.08</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Because of the very small number of participants in male and female groups, 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 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 ± SEM.
VO₂ plateau. The subject who did not reach at least two of the four criteria only reached the VO₂ 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 VO₂ was significantly increased with respect to the resting values by 447% ± 72% (p < 0.05) (Table 1). Figure 4A shows that VO₂ 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 VO₂ 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 VO₂ 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% ± 4% (p = 0.02). Figure 4B illustrates the kinetic for RER values calculated every 5 min over the 1 h NMES training. For VO₂, 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% ± 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% ± 5% HRmax 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% ± 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. VO₂, 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·min⁻¹·kg⁻¹ for VO₂; 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 VO₂ reached during the 1 h NMES training session was lower compared with the VO₂ obtained for walking speeds corresponding to either 5 km/h or 6 km/h (p < 0.05). However, the VO₂ value for walking at 6 km/h was close to the VO₂peak 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 VO₂ and EEh data reached during the 1 h NMES session were
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 ± SD. VO$_2$, 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; $p < 0.05$).

In COPD patients, high-frequency NMES resulted in a 129% increase in patients in an intensive care unit due to critical illness polyneuropathy (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, evidenced by a significant increase in HR and oxygen consumption. Mean oxygen consumption reached 50% VO$_{2}$peak 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. 2005) 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 VO$_2$, 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 VO$_2$ 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 VO$_2$ 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 \( V_\text{O}_{2}\text{max} \) 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 \( V_\text{O}_2 \) values up to the steady state reached at the middle of the 1 h NMES protocol.

Though \( V_\text{O}_2 \) 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 served different metabolic and cardiorespiratory responses during the 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, \( V_\text{O}_2 \), 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 60%. 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 Bellfrange 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 during the training session and the significant increase in CHO oxidations (Romijn et al. 1993), and (ii) the increased recruitment of fast twitch, i.e., type II, muscle fibers. This specific recruitment pattern during NMES compared with voluntary muscle contractions may also 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.

\( V_\text{O}_2 \) 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 regimens are insuffciently 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, Maffiuletti 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% HRmax), 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% VO2peak, 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.

**Acknowledgments**

The authors are indebted to the participants who kindly participated in the study and to the medical staff of the endocrine service of Saint Collumcile’s Hospital for patient recruitment and screening. The authors also thank BioMedical Research Ltd. for technical support in this study. This study was supported by grants from Enterprise Ireland and BioMedical Research Ltd.

**References**


