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Clinical Application of Neuromuscular Electrical Stimulation Induced Cardiovascular Exercise

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Abstract— **We need to find novel ways of increasing exercise participation, particularly in those populations who find it difficult to participate in voluntary exercise. In recent years researchers have started to investigate the potential for using electrical stimulation to artificially stimulate a pattern of muscle activity that would induce a physiological response consistent with cardiovascular exercise. Work to date has indicated that this is best achieved by using a stimulation protocol that results in rapid rhythmical isometric contractions of the large leg muscle groups at sub tetanic frequencies. Studies completed by our group indicate that this technique can serve as a viable alternative to voluntary cardiovascular exercise. Apart from being able to induce a cardiovascular exercise effect in patient populations (e.g. heart failure, COPD, spinal cord injury, obesity), this approach may also have value in promotion of exercise activity in a microgravity environment.**

I. Introduction

We are currently experiencing significant healthcare problems on a worldwide basis that can be traced back to the increasingly sedentary lifestyle that has become a dominant feature of modern society. Any technology advances that can encourage increased participation in physical activity can have a beneficial effect on public health. This is particularly the case in situations in which people find it hard to participate in traditional forms of voluntary exercise due to a variety of reasons such as presence of neurological injury, morbid obesity, degenerative joint disease, or diseases of the cardiovascular or respiratory systems. In recent years investigators have directed attention to the use of neuromuscular electrical stimulation (NMES) technology to elicit a cardiovascular response. This has primarily involved the use of NMES to produce a pattern of functional electrical stimulation that induces leg cycling exercise (FES-LCE), and therefore dissipate energy through a cycle ergometer, in spinal cord injured (SCI) patients. FES-LCE can result in VO2 levels of the order of 0.6-0.8 L/min in SCI subjects [1]. Training with FES-LCE can also result in improvements of 10-35% in aerobic capacity in SCI subjects [2, 3]. Conventional NMES-induced isometric tetanic muscle contractions have a minimal effect on energy consumption, with physiological responses consistent with 2 metabolic equivalents (METS) being observed [4]. These studies have generally involved application of currents at frequencies of 30-70Hz to elicit isometric tetanic contractions in the quadriceps. Such levels of VO2, and the rapid fall-off in VO2 demand due to fatigue, are unlikely to result in therapeutic benefit.

However, more recent advances in NMES technology suggest that it may now be possible to stimulate significant and sustainable levels of oxygen demand which are therapeutically meaningful. We have developed a new form of NMES technology, which we call NMES-EX (exercise), which can generate repeated rhythmical co-contractions of the large muscles in the legs without undue discomfort. This method of NMES-EX involves the delivery of pulse trains at low frequencies (4-6Hz) to the leg muscle groups via very large surface electrodes (total surface area 6-800cm2). The resultant deep rhythmical isometric muscle contractions causes a demand for oxygen in the tissues and results in activation of a cardiovascular response that is consistent with that observed during physical activities such as walking, cycling or running. This paper will incorporate a brief review of initial development and testing that has been carried out on this technique.

II. Application

NMES-EX involves using an electrical current to induce a series of rhythmical 'catch-like' short duration contractions in the large lower extremity muscle groups. The resultant demand for oxygen in the muscles leads to a series of cardiovascular responses that are consistent with an aerobic exercise effect. Initial development of this technique was carried out using a standard 2-channel muscle stimulator on each leg, with separate channels being used to stimulate the quadriceps and hamstring group of muscles at frequencies ranging from 4-8Hz (Neurotech NT2000, Biomedical Research Ltd, Ireland). The resultant pattern of muscle activity did result in significant increases in VO2, however the technique was not well tolerated. Improvements in comfort were achieved by increasing electrode sizes and reducing current density –nonetheless, comfort levels were still not at a

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level where the technique could be tolerated for long periods of time.

A significant advance was achieved in terms of efficacy and comfort with the application of a novel method of pulse generation. This method, known as multipath, incorporates a number of characteristics that differentiate it from standard NMES techniques in which current flow occurs between pairs of electrodes arranged over a single target muscle:

- *An array of electrodes is arranged around the target zone*
- *Current flow can be directed between any electrodes in the array, thereby allowing greater numbers of current pathways to be established, for example, directly or diagonally through the target limb, thus targeting neural tissue supplying more than one muscle at a time.*
- *Individual pulses can be divided into multiple phases or sections*
- *Current flow can be switched through multiple pathways in successive pulses or even within a single pulse*
- *Resultant pulse shapes are very complex, and differ amongst electrodes in the array.*

These features, allied to other standard NMES techniques such as using mixed frequency bursts and adjusting the electrode sizes were used to design a new approach to delivering the stimulation protocol required to elicit an aerobic exercise response. The current pathways, electrode combinations per pulse and pulse train characteristics for the standard technique are outlined in Figure 1. It is important to note that modifications have been made to this stimulation protocol in order to apply it effectively to different clinical populations. The electrode arrays are applied to the body via a neoprene 'wrap' garment that is secured to the thigh with Velcro straps.

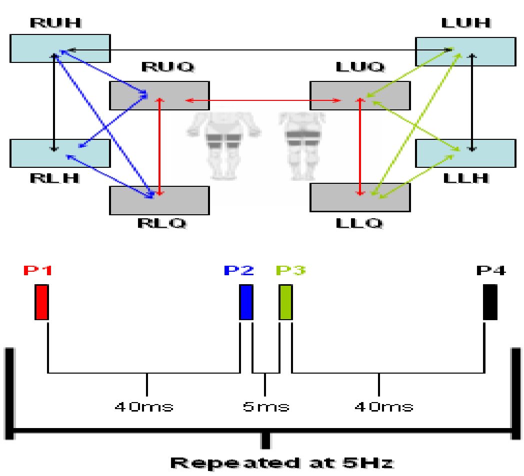

Figure1. Location of Stimulating Electrodes, pulse pathways (color coded), and pulse intervals. RUQ – right upper quadriceps, RUH – right upper hamstring, RLQ – right lower quadriceps etc)

III. Initial NMES-EX Studies

A. NMES-EX in a Healthy Adult Population

The first evaluation of the technique involved a case study on a healthy 31 year old male participant who was a long term user of electrical stimulation and was therefore well habituated to it. He completed an incremental stimulation protocol on 4 separate days to maximal tolerable stimulation intensity [5]. A clear and consistent dose response relationship was observed, with peak energy expenditure levels of the order of approximately 12 metabolic equivalents (Figure 2).

In other work on untrained adults who were unaccustomed to NMES studies, we have demonstrated that this technique can be used to elicit a repeatable physiological response with a clear dose-response relationship that is consistent with cardiovascular exercise with no adverse effects [6]. Furthermore, when these adults have had an opportunity to become accustomed to the NMES-EX, they can typically use it to exercise at a self-reported comfortable intensity that is

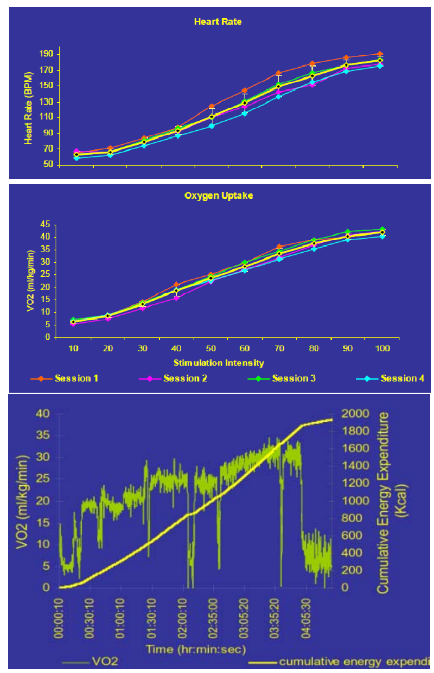

Figure 2. Cardiovascular response to increasing stimulus intensity and during prolonged exposure to NMES-EX in 31yr old male [5].

equivalent to 50-60% of their maximal aerobic capacity [7]. The VO2 response observed is equivalent to an exercise intensity that is sufficient to induce aerobic training effects [8]. This work also demonstrated that Rate of Perceived Exertion and VO2 were very strongly related during NMES-EX (R=0.94) during an incremental protocol suggesting that subjective rating could be used to judge exercise intensity in the absence of HR or VO2 monitoring (Figure 3).

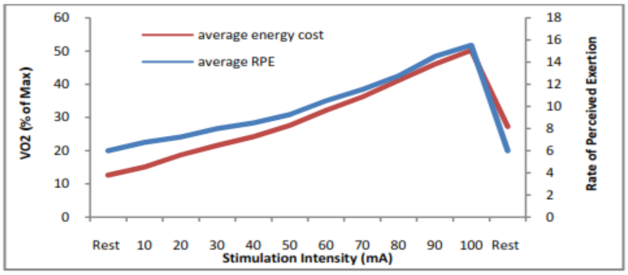

Figure 3. Relationship between Energy Cost and RPE during an incremental NMES-EX protocol [7]

In the first NMES-EX training study a group of 15 healthy subjects (10 men, 5 women) with a sedentary lifestyle completed a 6-wk training program during which they completed an average of 29 1-hour NMES-EX sessions [9]. A crossover study design was employed with subjects undergoing their habitual activity levels during the non-training phase of the study. The training effect was evaluated by a VO2max test, a 6-min walking distance test, and measurement of quadriceps muscle strength. After training, subjects demonstrated statistically significant improvements in all variables (Table 1). These results suggest that NMES-EX can be used in sedentary adults with low baseline fitness to improve cardiovascular exercise capacity and muscle strength.

Table 1. Effects of 6 weeks of NMES-EX Training on aerobic fitness, exercise tolerance and strength in healthy sedentary adults

	Baseline	**Post Training**	**Level of Significance**
Peak VO2 (L/min)	2.46±0.57	2.7±0.55	P<0.05
6 min walk distance (M)	493.3±36.8	529.9±39.2	P<0.005
Quadriceps Torque (N)	360.8±108.7	448.3±123.2	P<0.005

A separate study was carried out to investigate whether these training effects could be seen in a more physically active population with higher levels of baseline fitness [10]. In this study, a group of 19 healthy, physically active adults first underwent a control period to establish a steady baseline. They then underwent a training programme during which they completed 18 NMES-EX training sessions using RPE as a guide to exercise intensity over a 5-6 week period. Measures of aerobic fitness were taken at baseline, and at the end of the control and training periods.

Group mean (±SD) VO2max was 43.9±6.9ml/kg/min at baseline, reflecting the physically active status of the study population. ANOVA F-test analyses revealed highly significant differences in both VO2max and maximal exercise test workloads across the 3 test conditions (P<0.0001). Post hoc analysis indicated that there were no significant differences between group mean VO_2 max levels or maximal exercise test workloads at baseline and at 4 week follow up (P>0.05). However, there were highly significant differences between both VO2max levels and maximal exercise test workloads at 10-week follow up compared to both baseline and 4 week follow up (P<0.005) (Figure 4).

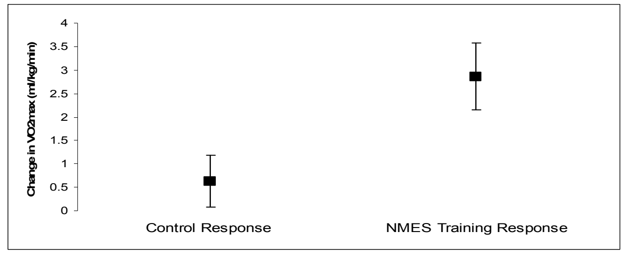

Figure 4. Average (±SE) Control and NMES-EX VO2max training responses in physically active adult population [10].

B. Evaluation in Patient Populations

The acute and training effects of NMES-EX have also been evaluated in selected patient populations including heart failure, chronic obstructive pulmonary disease, diabetes, and spinal cord injury. Banerjee and co-workers evaluated its effectiveness during a home training programme in 10 patients (age 66.6±6.5 years, 9 male) with chronic heart failure were randomized to 8 weeks of training or habitual activity before crossing over to the other limb after a washout period of 2 weeks [11]. Training consisted of NMES-EX for a minimum of 1 hour, 5 days a week. All training sessions were conducted in the patients' homes without clinical supervision. A clinically and statistically significant treatment effect was observed for peak oxygen consumption, 6-minute walking distance and quadriceps muscle strength (Table 2).

Table 2. Effects of 6 weeks of NMES-EX Training on aerobic fitness, exercise tolerance and strength in Heart Failure Patients

	Baseline	**Post Training**	**Level of Significance**
Peak VO2 (ml/kg/min)	19.5±3.5	21.2±5.1	P<0.05
6 min walk distance (M)	415.1±56.6	454.9±54.5	P<0.005
Quadriceps Torque (N)	377.9±110.4	404.9±108.6	P<0.005

Grossett et al evaluated the acute effects of a modified NMES-EX protocol in 9 morbidly obese adults (3m, 6f) [12]. Average VO2 during a 60 minute NMES-EX session at self selected comfortable stimulation intensity was equivalent to 4.0±0.8 METS or 47.3±4.7% of their maximal aerobic capacity (mean±sd). Men achieved a steady state energy expenditure level of approximately 600Kcal/hr compared to a level of approx 200Kcal/hr for women (Figure 5). These results suggest that rhythmical NMES-EX induced leg muscle contractions can be used to elicit a cardiovascular exercise response at therapeutic intensities in obese adults, though the effect is significantly stronger in men compared to women.

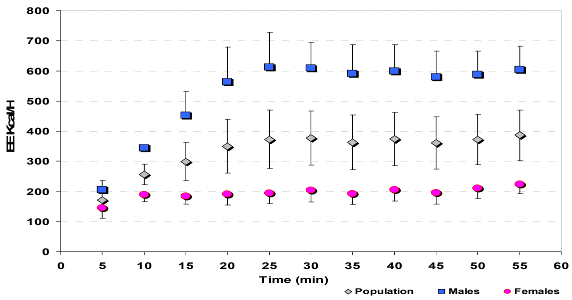

Figure 5. NMES-EX energy expenditure in obese adults [12].

One patient group in which NMES-EX has a potentially critical role is spinal cord injury. A recently completed evaluation in 6 male spinal cord injured volunteers demonstrated that energy cost during a targeted NMES-EX protocol increased by an average of 3 METS from resting levels, with no adverse effects [13]. Furthermore, a 6-week NMES-EX training programme in the same population resulted in significant increases in peak VO2 measured using an incremental treadmill protocol and spasticity using a subjective rating scale (Spinal Cord Assessment Tool) [14].

Initial case reports in other patient groups have also yielded interesting findings. A pilot study in COPD patients who underwent an 8-week home training programme consisting of a hybrid NMES-EX and NMES induced strengthening programme reported very strong improvements in 6 minute walking distance and measures of health related quality of life [15]. An evaluation of the training effects of NMES-EX in 9 males with type 2 diabetes [16] reported significantly increased aerobic fitness and peak isometric torque of the quadriceps, and decreased body fat following an 8-week programme. A small yet non statistically significant decrease in resting blood glucose was also observed.

IV. Conclusion

In summary, the available evidence to date suggests that NMES-EX has the potential to serve as an alternative aerobic exercise modality. It may have an important role to play in scenarios where participation in voluntary exercise is either difficult or not possible. Our initial experience suggests that patients with COPD, heart failure, and spinal cord injury are most likely to benefit from NMES-EX. However, it may also have a benefit for patients with degenerative joint disease as it permits performance of aerobic exercise in a reclined posture without joint loading. Outside of the clinical setting it may be beneficial as an exercise modality in a microgravity environment and in sport when an athlete wishes for a change in exercise modality for variety. However, before these possibilities can be realized there are many questions to be answered and studies to be completed to fully understand the effects and clinical role of NMES-EX.

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