Role of Neuromuscular Electrical Stimulation as an Alternative Exercise Method

Toshiaki Miyamoto*

Department of Physical Therapy, School of Rehabilitation, Hyogo University of Health Sciences

*Corresponding author: Toshiaki Miyamoto, t-miyamoto@huhs.ac.jp

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: The prevalence of chronic diseases, including cardiovascular diseases, type 2 diabetes, and cancer, is escalating at an alarming rate in many countries. These diseases are usually associated with insufficient physical activity since physical activity has beneficial effects on a variety of health outcomes such as decreased mortality and risk of these diseases. Moderate to vigorous physical activity has been recommended to achieve these positive effects. However, many patients cannot perform adequate exercise because of severe diseases, health complications, and/or exercise intolerance. This issue highlights a need for alternative therapies. There is an increasing literature that recognizes the positive effects of neuromuscular electrical stimulation (NMES) on muscle strength, cardiorespiratory fitness, physical performance, and metabolism in healthy adults and clinical settings. The present review introduces the effect of NMES on muscle strength and glucose metabolism as well as NMES-induced physiological responses such as the myokines which are related to preventing dementia and cancer.

Keywords: Neuromuscular electrical stimulation; Skeletal muscle stimulation; Myokine; Prevention

Online publication: March 29, 2024

1. Introduction

With the aging of society, the number of elderly people requiring nursing care is rapidly increasing. The decline in physical function associated with aging is believed to cause chronic neuromuscular and cardiopulmonary function decline [1]. As a result, the elderly become unable to go through their daily lives unassisted due to the diseases [2]. Physical activity such as resistance exercise and aerobic exercise has been shown to inhibit the age-related decline in muscle strength and endurance and is associated with the maintenance of physical function and the ability to perform daily activities [3-4]. The American College of Sports Medicine recommends that healthy adults maintain and improve cardiorespiratory and skeletal muscle function by performing 30 minutes of moderate-intensity exercise five times a day for a total of 150 minutes per week, 20 minutes of high-intensity exercise three times a day, resistance exercise two or three times a week, and a reduction in inactivity time [5]. In addition, for the elderly aged 65 years or older, it is recommended that they engage in 150 minutes of moderate-to-high-intensity physical activity per week and resistance exercise twice per week [6]. However, very few elderly people reach the recommended physical activity. In the aging society of Japan, it is considered difficult
for many to perform these exercises due to aging or co-morbidities [7].

Recently, neuromuscular electrical stimulation (NMES) has been reported to improve neuromuscular function and cardiopulmonary function not only in healthy adults but also in the elderly and patients with certain diseases and is beginning to be considered as an alternative means of exercise without requiring voluntary effort [8–10]. This paper describes the physiological changes induced by NMES and its efficacy on muscle strength and metabolism, as well as its potential to prevent dementia and cancer.

2. Physiological responses induced by neuromuscular electrical stimulation

NMES induces muscle contraction by sending electrical pulses to the target skeletal muscle via surface electrodes and thus does not require voluntary effort for muscle contraction. Therefore, NMES is an effective means for patients who require nursing care to enjoy the benefits of exercise. In voluntary exercise, type I fibers are sequentially mobilized according to the size principle, and type II fibers are mobilized as the intensity increases [11–14]. In other words, the mobilization of type II fibers, which are strongly related to muscle strength, requires high intensity in voluntary exercise, but the non-selective mobilization of type II fibers by NMES makes it possible to mobilize type II fibers even at low intensity. In addition, since type II fibers store a large amount of glycogen in the muscle, it has been shown that the mobilization of type II fibers by NMES enhances the utilization of glycogen in the muscle [15–18]. NMES is used with a variety of electrodes and devices, but it is mainly used to stimulate the quadriceps, hamstrings, and triceps muscles, and it has been suggested that the physiological changes in the body differ depending on the frequency. NMES at relatively high frequencies can induce muscle torsion and is therefore used to increase muscle mass and improve or maintain muscle strength, generally at frequencies between 25–100 Hz [19]. The majority of reports examining the effectiveness of NMES use NMES at these high frequencies. Recently, it has been reported that frequencies between 4 and 7 Hz can induce muscle contraction without complete torsion, therefore improving cardiopulmonary function and exercise tolerance [8, 20–22].

3. Effects of neuromuscular electrical stimulation on muscle strength and hypertrophy in the elderly

Sarcopenia is characterized by age-related loss of muscle mass and muscle strength [23]. Sarcopenia is found in 15%–50% of the elderly [24]. Muscle weakness in the elderly is associated with the effects of nerve activity and atrophy of muscle fibers [24]. It has been reported that aging not only decreases muscle strength but also decreases cardiopulmonary function, with a 10% decrease in maximal oxygen uptake every 10 years [25]. Since cardiopulmonary function in the elderly has been shown to influence early mortality, maintaining and improving muscle strength and cardiopulmonary function in old age is an extremely important issue [26]. As mentioned above, 150 minutes of physical activity or resistance exercise per week is recommended for the elderly, but it has been reported that only 5% of the elderly reach this exercise recommendation [27]. Although time, interest, and other factors may contribute to this, many elderly people are unable to reach the recommended exercise duration and intensity due to declining physical function. Kern et al. performed NMES at 60 Hz for 30 minutes per day, 2 to 3 days per week for 9 weeks in elderly subjects, and found that muscle strength and walking speed increased, and type I and type II fiber diameters increased (Figure 1) [28]. In addition, NMES for 60 minutes at a combination of 25 Hz and 4 Hz frequencies for 8 weeks improved muscle strength and endurance in healthy elderly subjects [9]. A systematic review of the effectiveness of NMES for the elderly found that it was generally effective for muscle strength and balance capacity, although there were differences in protocols such as frequency and implementation [29]. These results suggest that NMES can be applied to the elderly who...
are unable to exercise or who are ill, but further validation is needed to determine whether sarcopenia can be prevented and whether it can be applied to the elderly who are less active.

**Figure 1.** Comparison of knee extension muscle strength and gait speed between pre and post-9-week neuromuscular electrical stimulation intervention, \(*P < 0.05\) \([28]\)

4. Effects of neuromuscular electrical stimulation on metabolism

4.1. Basic studies of neuromuscular electrical stimulation on glucose metabolism

Hamada et al. have examined the effects of NMES on glucose metabolism in healthy adult male subjects using the hyperinsulinemic-normoglycemic clamping method \([30]\). They found that oxygen uptake during NMES was increased to twice the resting level and energy consumption was enhanced during 20 minutes of 20 Hz NMES to the thighs. The insulin clamp technique revealed that under physiological conditions in which endogenous 
glucose release was suppressed, the rate of whole-body glucose uptake increased significantly, and the increased glucose uptake was sustained even after NMES was completed. In particular, the glucose metabolic rate after completion of NMES corresponds to the acute effect of glucose metabolism seen during bicycle exercise at 40% of maximal oxygen uptake, which strongly suggests the effectiveness of NMES in controlling blood glucose \([31]\). Furthermore, a comparison of changes in glucose metabolism between NMES and bicycle ergometer exercise at the same oxygen intake using the insulin clamp method revealed that although the rate of glucose uptake increased significantly during both exercises, glucose uptake decreased rapidly after the end of exercise in the bicycle ergometer exercise, whereas the increased rate of glucose uptake continued after the end of the exercise in NMES (Figure 2). In addition, the blood lactate concentration and respiratory flight were significantly higher in NMES than in bicycle ergometer exercise indirectly indicating that NMES induced the mobilization of type II fibers \([32]\).

**Figure 2.** Mean time course changes in plasma glucose and glucose disposal rate during ergometry exercise (solid square) and neuromuscular electrical stimulation (open circle) \([32]\); \(*P < 0.01\) vs pre-exercise condition; \(†P < 0.01\) vs ergometry exercise
4.2. Effects of neuromuscular electrical stimulation on glucose metabolism in diabetic patients

A study examined whether NMES administered after a meal could suppress the increase in postprandial blood glucose levels in patients with type II diabetes mellitus. Subjects performed NMES at 4 Hz for 30 minutes on the thigh and buttock muscle groups, starting 30 minutes after a meal. Oxygen uptake during stimulation was about 2.5 times that at rest, but the increase in blood glucose level 2 hours after a meal was significantly suppressed (Figure 3). This result relates to the acute effect of NMES on glucose metabolism. Since postprandial hyperglycemia in diabetic patients is not only considered a major factor in the progression of diabetic complications but also an independent risk factor for cardiac and cerebrovascular diseases and fatalities, NMES can probably suppress postprandial. Therefore, it is very significant that NMES suppresses the increase in postprandial blood glucose levels.

![Figure 3](image)

The authors also examined the effects of 8 weeks of continuous NMES on body composition and glucose and lipid metabolism in patients with type 2 diabetes. After 8 weeks of NMES on both lower bodies for 40 minutes 5 times a week, body fat percentage and fasting blood glucose significantly decreased in patients with type 2 diabetes (Figure 4). However, HbA1c and blood lipid parameters did not change significantly. HbA1c is considered to indicate average glycemic control over 8 to 12 weeks and voluntary aerobic exercise is considered to be effective in lowering blood glucose levels after a short period of continuous exercise, so HbA1c and lipid metabolism require a relatively long period to improve. Therefore, it is considered that NMES must be performed for 8 weeks or longer to improve HbA1c. At present, NMES has not been shown to improve glucose control in patients with glucose intolerance. Other studies have demonstrated the efficacy of NMES in improving glucose metabolism, so further validation and clinical application of NMES are desirable.

![Figure 4](image)
5. Possibility of alternative methods for the prevention of dementia: Relationship between physical activity and dementia

The number of people suffering from dementia continues to increase, with one new case of dementia occurring every 3.2 seconds worldwide in 2015 [39]. Physical inactivity is considered to be one of the risk factors for dementia, and previous studies have shown that even a single bout of physical activity improves cognitive function and that long-term exercise increases hippocampal capacity [40–43]. Therefore, physical activity, including exercise, is considered to be an effective means of preventing dementia.

Brain-derived neurotrophic factor (BDNF), a hormone-like protein, is thought to be a central mediator of the improvement of cognitive function induced by physical activity. The peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha, a transcriptional coactivator of skeletal muscle induced by physical activity, induces a myocyte membrane protein, fibronectin type III domain containing 5 (FNDC5), which crosses the blood-brain barrier as irisin BDNF has been reported to promote angiogenesis, synaptic connectivity and brain protection [46–48]. It has also been shown that BDNF expression is decreased in patients with dementia, whereas peripheral blood BDNF levels increase during moderate-to-high intensity exercise, whether transient or continuous [43, 49–51].

This study examined the response of plasma BDNF to NMES in healthy adult subjects and found that BDNF concentrations after NMES increased significantly and were equivalent to those after moderate-intensity bicycle ergometer exercise (Figure 5) [32]. NMES non-selectively mobilizes type II fibers and increases lactate production. The results of this study also showed a significant increase in lactate. Since lactate concentration has been suggested to affect peripheral BDNF concentration, it is possible that the glycolytic effect of NMES had an influence, but it is also possible that the decrease in blood glucose level also had an effect [53]. Glucose is a major source of energy for the brain, and it is possible that BDNF increased defensively as a protective effect on the brain when blood glucose levels decreased. The authors also examined whether long-term use of NMES altered BDNF in type 2 diabetic patients, and found that plasma BDNF levels were significantly higher after 8 weeks of NMES [36]. At the same time, fasting blood glucose levels also decreased, strongly suggesting that there is some relationship between glucose metabolism and peripheral BDNF concentrations. The mechanism by which exercise improves cognitive function is not completely clear currently, but research is ongoing. The effectiveness of NMES in preventing dementia and exploring its physiological background may be one piece of the puzzle in unraveling the relationship between exercise and cognitive function.

![Figure 5](image-url). The group data of plasma brain-derived neurotrophic factor, blood lactate, and glucose concentrations on three sessions: control, moderate exercise, and neuromuscular electrical stimulation; *P < 0.05 vs pre-value, †P < 0.05 vs post-value in control; ‡P < 0.05 vs post-value in NMES.
6. Possibility of alternative methods for the prevention of cancer development

6.1 Relationship between physical activity and cancer

Recent epidemiological studies have shown that physical activity is effective in preventing colorectal cancer and breast cancer \[^{54}\]. Although the mechanism by which physical activity prevents cancer is not completely clear, it has been suggested that myokines secreted by skeletal muscle play a central role. Myokines have both autocrine and paracrine actions, and it has recently been shown that skeletal muscle has a role as an endocrine organ. Many previous studies have suggested an endocrine role for myokines and that it is increased or decreased by moderate-to-high intensity exercise \[^{55}\].

6.2. NMES and cancer-related myokines

The authors examined the effect of NMES on secreted protein acidic and rich in cysteine (SPARC), which is considered central to colorectal cancer prevention. They examined the possibility that NMES could be an alternative means of cancer prevention. SPARC was significantly elevated after 30 minutes of NMES in healthy young adults (Figure 6). SPARC is transiently elevated by moderate-to-high intensity exercise and is responsive to NMES \[^{56}\]. SPARC has been suggested to inhibit the formation of aberrant crypt foci (ACF), a precursor lesion of colorectal cancer, by promoting apoptosis via caspase-3 and caspase-8 (Figure 7) \[^{56}\]. It has been reported that regular physical activity can prevent ACF from forming on the mucosal surface of the mouse colon. Furthermore, it has been reported that the expression of SPARC affects the sensitivity of tumors of the colon and rectum to radiation and chemotherapy and that the 5-year survival rate of cancer patients expressing

![Figure 6](image_url)

**Figure 6.** The group data of secreted protein acidic and rich in cysteine (SPARC) on control and neuromuscular electrical stimulation (NMES); \(*P < 0.05\) vs pre-value within a session

![Figure 7](image_url)

**Figure 7.** Schematic of colon cancer prevention induced by exercise via secreted protein acidic and rich in cysteine (SPARC)
high levels of SPARC is significantly better than that of patients not expressing SPARC [57]. The results obtained from epidemiological studies suggest that the physiological response in the body to moderate-to-high-intensity exercise is necessary because moderate-to-high-intensity exercise is recommended for the prevention of colorectal cancer, and that the non-selective mobilization of muscle fibers by NMES causes physiological changes equivalent to those of moderate-to-high intensity exercise. The SPARC response to NMES suggests that NMES may be a tool for the prevention of colorectal cancer. Still, the relationship between physical activity and cancer needs to be clarified, and the long-term effects of NMES need to be examined.

7. Future prospects

NMES is expected to be an alternative to voluntary resistance exercise and aerobic exercise, with many reports showing its effectiveness, but it is necessary to establish an optimal protocol in the future. The physiological mechanisms by which exercise prevents chronic diseases are not fully understood, so further research on physiological changes induced by exercise, including myokinesis, is warranted. As NMES has become more widely used clinically in recent years, the scope of its application is expected to expand further as more evidence is established.

Disclosure statement

The author declares no conflict of interest.

Reference


Publisher’s note
Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.