

Electromyostimulation to fight atrophy and to build muscle: facts and numbers

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Abstract

In recent years, electrical myostimulation (EMS) is becoming more and more popular to increase muscle function and muscle weight. Especially it is applied in healthy individual after injury to rebuild muscle mass and in severely atrophic patients who are not able or willing to perform conventional exercise training programs. Studies in experimental models as well as in human subjects confirmed that EMS can increase muscle mass by around 1% and improve muscle function by around 10–15% after 5–6 weeks of treatment. Despite a severe increase in circulating creatine kinase during the first session, EMS can be regarded as a safe therapeutic intervention. At the molecular level, EMS improves the anabolic/catabolic balance and stimulates the regenerative capacity of satellite cells. EMS intensity should be as high as individually tolerated, and a minimum of three sessions per week [large pulses (between 300–450 μ s), high frequency (50–100 Hz in young and around 30 Hz in older individuals)] for at least 5–6 weeks should be performed. EMS improved functional performances more effectively than voluntary training and counteracted fast type muscle fibre atrophy, typically associated with sarcopenia. The effect of superimposing EMS on conventional exercise training to achieve more muscle mass and better function is still discussed controversially. Nevertheless, EMS should not be regarded as a replacement of exercise training per se, since the beneficial effect of exercise training is not just relying on building muscle mass but it also exerts positive effects on endothelial, myocardial, and cognitive function.

Keywords Muscle atrophy; muscle function; electrical stimulation; exercise training; molecular mechanisms

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In recent year, conventional exercise programs have become one important cornerstone in the management of patients with cardiovascular disease. It is clearly documented that these exercise training programs exert beneficial effects on exercise capacity and quality of life.^{1,2} Even in healthy adults, there is a relation between fitness and the incidence of cardiovascular disease (reviewed in Lee *et al.*³) and the sedentary time is directly associated with the sarcopenic risk—for each 1 h increment in overall daily sitting time, there is a 33% increased risk of having sarcopenia in adults aged ≥ 60 years regardless of their physical activity, lifestyle, and other confounding factors.⁴ Furthermore, in chronic heart failure (CHF) or cancer patients, the loss of skeletal muscle mass and function is associated with exercise intolerance, dyspnoe, and prognosis.^{5–8} Therefore, reducing muscle wasting and improving exercise capacity as therapeutic

intervention has the potency to modulate quality of life and even mortality. Unfortunately, often time constraints or the inability of a patient to perform exercise are often reported as the main hindrance for frequent exercise. Therefore, new attractive and effective but also time-saving alternatives have to be put forward for people seeking to increase their exercise performance and muscle mass. One such option would be electromyostimulation (EMS) or whole-body electrostimulation (WB-EMS), which is becoming increasingly popular during the last years. Do we have evidence in the current literature supporting this EMS hype for increasing muscle mass and treating severely diseased patients and if yes what is the molecular mechanism behind the positive effect of EMS? To answer this question, it is interesting to shortly review data available in cell culture and animal experiments and finally in human trails.

Cell culture experiments

Already in 1994, Wehrle and colleagues established myotube cultures from satellite cells of three rat muscles of different fibre-type composition, slow-twitch soleus, diaphragm, and fast-twitch tibialis anterior.⁹ The electrical stimulation of these cultures for up to 13 days (250 ms impulse trains of 40 Hz, repeated every 4 s) led to an isoform switch, as indicated by an increase in slow myosin expression. In recent years, several researchers have used C2C12 skeletal muscle myotubes electrically stimulated in cell culture allowing contraction-inducible cellular responses to be explored.^{10,11} Using these models, contraction-inducible myokines potentially linked to the metabolic alterations, immune responses, and angiogenesis induced by exercise could be identified.¹² It became clearly evident that electrical stimulation of cells resulted in an upregulation and activation of AMPK, JNK, Akt, eNOS, GLUT4, and PGC1.¹¹ Furthermore, it seems that the EMS-stimulated Glut4 translocation to the cell membrane is mediated via Rac1-Akt signaling¹⁰ and that electrically stimulated cells are protected against lipid-induced insulin resistance.¹³ Taken together, the electrical stimulation of cells in culture at least partially mirrors effects of exercise training seen in experimental models or human subjects.

Animal experiments

Hindlimb suspension in rats is a very powerful tool to induce muscle atrophy, and several studies were performed using this model to study the effect of electrical stimulation on muscle mass/function and the corresponding molecular mechanisms.^{14–17} For example, Guo and colleagues¹⁵ performed electrical stimulation (20 Hz frequency, twice a day for 3 h with 2 h rest in between) in one leg of hindlimb suspended mice, whereas the other leg served as control. The electrically stimulated suspended soleus muscle exhibited significant improvement in muscle mass, cross sectional area, and peak tetanic force.¹⁵ This improvement was probably due to the increase in satellite cell proliferation and a reduction of apoptotic cell death. This effect on satellite cell activity and muscle atrophy was already described earlier by Zhang *et al.* during a 28 days hindlimb suspension in rats and the use of low-frequency electrical (2 × 3 h at a 20 Hz) stimulation.¹⁶ Also in other atrophy models, electrical muscle stimulation seems to be effective. In recent studies, Nakagawa *et al.*¹⁷ and Xing *et al.*¹⁸ documented in a denervation model that low-frequency electrical muscle stimulation resulted in attenuation of muscle atrophy, muscle function, and capillary-to-fibre (C/F) ratio of the tibialis anterior muscle. An important question with regard to electrical stimulation, which is still not completely solved, is the optimal stimulation frequency and duration. To partially answer this

question, Wan and colleagues used again a hindlimb suspension model and tested different electrical stimulation protocols.¹⁴ They concluded that at least in this experimental setting, electrical stimulation at 2 Hz for 2 × 3 h per day is the optimal protocol for counteracting muscle disuse atrophy, reduced muscle function, impaired satellite cell proliferation, and enhanced cell apoptosis.

Taken together, electrical stimulation seems to be effective in counteracting muscle atrophy and muscle dysfunction in experimental atrophy models. The activation of satellite cell proliferation and prevention of cell apoptosis seems to be important mechanisms initiating these beneficial effects.

Human data

What evidence is available from human clinical studies supporting the therapeutic effect of electrical stimulation? As outlined by many studies, neuromuscular electrical stimulation (NMES) may be an effective alternative approach to enhance lower limb muscle mass and force in numerous diseases associated with muscle atrophy (summarized in Paillard¹⁹). A cohort profiting probably most from EMS are sarcopenic individuals, unable or unwilling to perform regular exercise. As reported in several studies,^{20–22} EMS improves muscle mass and muscle function without altering abdominal and total body fat content, thus enhancing gait and quality of life.²³ For example, a 4 month EMS intervention period (in total 48 sessions) in subjects >75 years resulted in an increase of rectus femoris cross-sectional area by around 30%.²⁴ Molecular wise EMS stimulates not only anabolic pathways (e.g. secretion of IGF-1) but also negatively modulates catabolic metabolism (expression of MafBx or MuRF1), thereby increasing muscle mass (reviewed in Paillard¹⁹). In addition, EMS effectively downregulated myostatin mRNA,²⁵ decreased the production of reactive oxygen species,²⁶ and increased the regenerative capacity of satellite cells.²⁶

Is electrical stimulation as effective as conventional exercise training? In a recently performed study by Zampieri *et al.*, sedentary seniors with a normal life style were recruited and randomized either to leg press (LP) exercise or EMS for 9 weeks.²⁷ Before and at the end of both training periods, mobility functional tests were performed and muscle biopsies from the Vastus Lateralis muscles were taken. Altogether, the results demonstrate that EMS improved functional performances more effectively than voluntary training and counteracted fast type muscle fibre atrophy, typically associated with sarcopenia.

Is it beneficial to add EMS to conventional exercise training? Already 1998, Willoughby and Simpson²⁸ concluded that supplementing dynamic contractions with EMS appears more effective than EMS only, or weight training only, for increasing knee extensor strength in female track and field athletes.

This finding was corroborated 2010 by Herrero and colleagues²⁹ who documented that superimposed EMS onto voluntary contractions (superimposed technique: application of an electrical stimulus during a voluntary muscle action) increased muscle strength more effectively in healthy individuals. Nevertheless, this beneficial effect of superimposed EMS is still discussed controversially since not all studies could confirm these findings.³⁰ When adding EMS to voluntary contraction in patients already exhibiting muscle atrophy, like CHF, a recently published multicentre randomized prospective study in 91 CHF patients reported no additional improvement in exercise capacity and quality of life when adding EMS to an exercise training program.³¹ Additional current clinical trials are performed in different patients cohort (NCT03306056, NCT03020693), and their results will add additional information to this topic.

With respect to stimulation modalities, a broad variation has been reported. Based upon several review articles, Pailard¹⁹ concluded that following criteria with respect to efficiency and comfort should be taken into account: the stimulation current should be biphasic, large pulses (between 300–450 μ s), high frequency (50–100 Hz in young and around 30 Hz in older individuals), the electricity should be applied using surface electrodes, the relaxation time between the pulses should be at least equal the stimulation time, intensity should be as high as individually tolerated, and a minimum of three sessions per week for at least 5–6 weeks. Following these principles, a significant gain in muscle mass and function can be expected. With respect to safety of EMS application, extremely high creatine kinase concentrations (117-fold above baseline at 3–4 days post) were reported as sign of severe rhabdomyolysis.^{32,33} Despite these high CK values, no rhabdomyolysis-induced complications were reported. Nevertheless, the authors concluded that WB-EMS should be carefully increased during the initial sessions, because the CK rise was blunted

after several sessions and averaged in the area of conventional resistance training.

Conclusion

Based on the evidence available in the current literature, we may conclude that EMS is safe and would limit or reverse the sarcopenic process and its structural alterations by modulating molecular processes involved in atrophy development. EMS seems to increase muscle mass and functional properties of limb muscles, but adding EMS to conventional exercise training programs is still discussed controversially. Therefore, EMS may be a valuable tool to treat sarcopenic or CHF patients who do not qualify (comorbidities, or advanced or end-stage heart failure) or comply with conventional exercise training programs. EMS may also be seen as a bridge to conventional training in case the physical status of the patient is too poor to start with conventional training. Nevertheless, EMS should not be regarded as a replacement of exercise training per se, since the beneficial effect of exercise training is not just relying on building muscle mass but it also exerts positive effects on endothelial, myocardial, and cognitive function.

Acknowledgements

The author certify that he comply with the ethical guidelines for authorship and publishing in the Journal of Cachexia, Sarcopenia, and Muscle.³⁴

Conflict of interest

None declared.

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