WHOLE-BODY ELECTROMYOSTIMULATION: A TRAINING TECHNOLOGY TO IMPROVE HEALTH AND PERFORMANCE IN HUMANS?

EDITED BY: Wolfgang Kemmler, Michael Fröhlich and Heinz Kleinöder
PUBLISHED IN: Frontiers in Physiology

frontiers Research Topics

ISSN 1664-8714
ISBN 978-2-88963-837-6
DOI 10.3389/978-2-88963-837-6

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Citation: Kemmler, W., Fröhlich, M., Kleinöder, H., eds. (2020). Whole-body Electromyostimulation: A Training Technology to Improve Health and Performance in Humans?. Lausanne: Frontiers Media SA.
doi: 10.3389/978-2-88963-837-6

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frontiers in Physiology

EDITORIAL
published: 26 May 2020
doi: 10.3389/fphys.2020.00523

Editorial: Whole-Body Electromyostimulation: A Training Technology to Improve Health and Performance in Humans?

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Keywords: whole-body electromyostimulation, exercise, health, performance, training technology

Editorial on the Research Topic

Whole-Body Electromyostimulation: A Training Technology to Improve Health and Performance in Humans?

Originally created and commercially launched in Germany in 2009, whole-body electromyostimulation (WB-EMS) is a promising training technology with rapid and widespread dissemination particularly in Europe and the Far East. Even though there are more than 2,000 commercial WB-EMS providers with about 250,000 clients in Germany alone, research on WB-EMS is still limited. Symptomatically, there is not even a mandatory definition of WB-EMS. Thus, we would suggest defining WB-EMS as "simultaneous application of electric stimuli via at least six current channels or participation of all major muscle groups, with a current impulse effective to trigger muscular adaptations." This concurrent stimulation of large muscle areas, each with dedicated impulse intensity, delivers the "time effectiveness" of WB-EMS, a key feature of this training method. However, apart from its "efficiency," EMS technology applied locally or globally enables a supramaximal workload without high voluntary effort (Paillard; Watanabe et al.). This unique feature of efficiency and high workload with low voluntary effort may explain the steadily growing attractiveness of WB-EMS for health, fitness, and performance professionals. The present Research Topic on WB-EMS thus aimed to stimulate incentivize dedicated research in all these disciplines.

Since completion of the present Research Topic, 15 of 24 submitted articles have been accepted. Simplified, five contributions (Berger et al.; Ludwig et al.; Paillard; Watanabe et al.; Zart et al.) focus on basic EMS research, predominately to derive optimized WB-EMS protocols. While the German research group (Berger et al.; Ludwig et al.; Zart et al.) focused on dedicated strain parameters, Watanabe et al. and Paillard addressed the interaction of WB-EMS and voluntary contraction in humans. Apart from other important findings highly relevant for practical application, one key message can be derived from both basic research and the performance studies listed below: Evidence suggests that simultaneously applied WB-EMS did not increase the effects of maximum voluntary contractions. Thus, when exercising with WB-EMS, impulse parameters and not high voluntary effort are the decisive effectors.

With seven studies, the majority of projects address the fitness and performance domain. In summary, the trials included recreational runners (Amaro-Gahete et al.; Amaro-Gahete et al.), sports students (Dörmann et al.; Wirtz et al.), amateur ice-hockey players (Schuhbeck et al.), and professional soccer players (Filipovic, DeMarees et al.; Filipovic, Bizjak et al.). Apart from functional

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *12 March 2020*
Accepted: *29 April 2020*
Published: *26 May 2020*

Citation:
Kemmler W, Kleinöder H and Fröhlich M (2020) Editorial: Whole-Body Electromyostimulation: A Training Technology to Improve Health and Performance in Humans? Front. Physiol. 11:523. doi: 10.3389/fphys.2020.00523

outcomes e.g., sprint and jump performance, shoot speed, strength, and power (Amaro-Gahete et al.; Amaro-Gahete et al.; Dörmann et al.; Filipovic, DeMarees et al.; Schuhbeck et al.; Wirtz et al.) amenable to resistance-type WB-EMS, Amaro-Gahete et al. and Amaro-Gahete et al. reported WB-EMS induced improvements in running performance after volume reductions in recreational runners. This finding on endurance capacity was not confirmed by Filipovic, Bizjak et al., however, who found no relevant WB-EMS effects on VO_2max and various blood parameters related to oxygen supply in professional soccer players.

Reviewing the present literature on WB-EMS, with only three contributions that addressed health related issues (Schink et al.; Willert et al.; Teschler and Mooren), the "WB-EMS and health" domain was considerably underrepresented in our Research Topic. While Teschler and Mooren reviewed negative side-effects of WB-EMS, a topic that will be addressed in more depth later, two research groups from Erlangen, Germany (Schink et al.; Willert et al.) addressed interactions of WB-EMS and dietary supplements. While Schink et al. determined the effect of combined WB-EMS and dietary support on body composition, physical function, quality of life, and blood parameters in patients with hematologic malignancies, Willert et al. evaluated effects of WB-EMS and protein supplementation on energy-restriction-induced loss of muscle mass during intended weight reduction.

Although it is far from clear which composition of exercise and/or impulse parameters might be optimum or even appropriate for a given outcome (Berger et al.; Ludwig et al.; Paillard; Watanabe et al.; Zart et al.), in essence most of the studies indicated that WB-EMS can be indeed be considered an effective training technology for improving health- and performance-related parameters. Transferred into clinical practice, WB-EMS might thus be an option for people with low time resources and inability or unwillingness to exercise conventionally. This also includes athletes looking for time-efficient exercise protocols to impact secondary training aims related to strength and power.

However, beside effectiveness, other less positive aspects of WB-EMS fall short in the present Research Topic. Based on its artificial application, physiological mechanisms that protect against overloading during conventional training do not come into play during EMS. Thus, considering that even local EMS application might induce severe rhabdomyolysis (Johannsen and Krogh, 2019), it is obvious that a technology able to stimulate up to 2,600 cm^2 of muscular area simultaneously entails a high risk of triggering unintended effects (Teschler and Mooren)—at least when inappropriately applied (Kemmler et al., 2016). Indeed, severe rhabdomyolysis was frequently reported (e.g., Stollberger and Finsterer, 2019) in particular after improper i.e., too intense, first WB-EMS sessions. Of note, these negative side effects led to a temporary ban of WB-EMS in Israel in 2015. As a result many researchers call for stronger regulation of WB-EMS (e.g., Malnick et al., 2016). In Germany, several recommendations for safe and effective WB-EMS (Kemmler et al., 2016, 2019) have been launched. In 2018, DIN (German Industry Norm) 33961-5, a German standard regulating the application of WB-EMS in commercial, non-medical settings in depth, was released. In parallel, the German "Federal Ministry for the Environment, Nature Conservation, and Nuclear Safety (BMU)" published the revised German Radiation Protection Statutes, a mandatory guideline that includes WB-EMS ("applications of non-ionizing radiation to humans"; NISV) (BMU, 2019). The NISV cover in particular aspects of operation, information, documentation, and the mandatory requirements for qualification as EMS trainer. However, apart from the latter aspect, we are not convinced that the formal requirements specified by the NiSV will contribute to fewer adverse effects and increased effectiveness of WB-EMS. Thus, we would like to take the opportunity to clearly state our position on aspects of WB-EMS application under ongoing discussion.

Firstly, we strongly support DIN 33961-5 (Kemmler et al., 2019) with its relative and absolute contraindications for commercial, non-medical WB-EMS application. Nevertheless, we are aware of the problem that people falling within the absolute or relative contraindications have been excluded from or not allowed to apply WB-EMS due to their physicians' unjustified concerns, although WB-EMS might be the most suitable training option for them. Generating scientific evidence might lead to a revision of the contraindications in the nearest future, allowing more people to use this time-efficient, joint friendly and tailored exercise intervention. Further, as mentioned, DIN 33961-5 covers commercial, non-medical providers; medical providers with an even more individualized WB-EMS application under medical supervision were not addressed. However, as physicians will still act as gatekeepers for questionable WB-EMS application, and considering their crucial role during instructor education (BMU, 2019), at least training programs for sports medicine and physical rehabilitation should include aspects of WB-EMS application.

Second, we consider very close support by attentive, well-trained, and mandatorily licensed instructors as the key factor of safe and effective WB-EMS application. The close interaction and narrow distance between instructor and participant necessary to ensure especially (1) frequent feedback from the participant about perceived exertion for each area of stimulation, (2) permanent visual monitoring of the participant and eye contact to check participant strain, avoid overload, and to react immediately to the first signs of cardiorespiratory or metabolic side effect, and (3) verbal and haptic movement corrections and rapid assistance in cases of emergency, particularly cutting off power supply of the device, leads us to strongly advise a 1:1 instructor-participant ratio; although a 1:2 ratio is also considered tolerable for non-medical WB-EMS application with less critical participants.

We feel that this Research Topic provides additional evidence for the health, fitness and performance aspects WB-EMS application. We are aware that a plethora of research questions with respect to the most optimum WB-EMS protocol for given outcomes and varying target populations remained to be addressed. However, we conclude that some key aspects of WB-EMS should be addressed with particular emphasis in the nearest future. From a sport scientific point of view, intensity regulation by objective strain parameters based on advanced biomarkers might further increase the safety and effectiveness of WB-EMS. In parallel, the evaluation of progression models is essential for ensuring the sustainability of WB-EMS effects. To date, only few studies exceed a period of 6 months, thus longer trials have to monitor WB-EMS effectiveness and safety. Considering the time effectiveness, joint friendliness, low voluntary effort and customization of WB-EMS; from a health perspective, further research should particularly focus on diseases (e.g., multiple sclerosis, diabetes mellitus, selected types of cancer, hypertonia, arthritis) with limited potential or perspective for conventional exercise. The permissive, additive or synergistic effect of other low-threshold interventions (e.g., dietary supplements) combined with WB-EMS should also be addressed more forcefully. However, apart from health issues, the feasibility and effectiveness in settings with low time and spatial resources but high physical demands (e.g., Naval and Special Forces, Fire Fighters) will be challenging.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 13 June 2018
doi: 10.3389/fphys.2018.00720

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Functional Exercise Training and Undulating Periodization Enhances the Effect of Whole-Body Electromyostimulation Training on Running Performance

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OPEN ACCESS

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Specialty section:
This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 19 April 2018
Accepted: 24 May 2018
Published: 13 June 2018

Citation:
Amaro-Gahete FJ, De-la-O A,
Sanchez-Delgado G,
Robles-Gonzalez L, Jurado-Fasoli L,
Ruiz JR and Gutiérrez A (2018)
Functional Exercise Training and
Undulating Periodization Enhances the
Effect of Whole-Body
Electromyostimulation Training on
Running Performance.
Front. Physiol. 9:720.
doi: 10.3389/fphys.2018.00720

The popularity of whole-body electromyostimulation is growing during the last years, but there is a shortage of studies that evaluate its effects on physical fitness and sport performance. In this study, we compared the effects of a periodized and functional whole-body-electromyostimulation training on maximum oxygen uptake (VO_2max), ventilatory thresholds (VT1 and VT2), running economy (RE), and lower-body muscle strength in runners, vs. a traditional whole-body-electromyostimulation training. A total of 12 male recreational runners, who had been running 2–3 times per week (90–180 min/week) for at least the previous year and had no previous experience on WB-EMS training, were enrolled in the current study. They were randomly assigned to a periodized and functional whole-body-electromyostimulation training group (PFG) ($n = 6$; 27.0 ± 7.5 years; 70.1 ± 11.1 kg; 1.75 ± 0.05 m) whose training program involved several specific exercises for runners, or a traditional whole-body-electromyostimulation training group (TG) ($n = 6$; 25.8 ± 7.4 years; 73.8 ± 9.8 kg; 1.73 ± 0.07 m), whose sessions were characterized by circuit training with 10 dynamic and general exercises without external load. The training programs consisted of one whole-body electromyostimulation session and one 20-min running session per week, during 6 weeks. The PFG followed an undulating periodization model and a selection of functional exercises, whereas the TG followed a traditional session structure used in previous studies. Both groups were instructed to stop their habitual running training program. VO_2max, VT1, VT2, RE, and lower body muscle strength (vertical jump) were measured before and after the intervention. The PFG obtained significantly higher improvements when compared with the TG in terms of VO_2max (2.75 ± 0.89 vs. 1.03 ± 1.01 ml/kg/min, $P = 0.011$), VT2 (2.95 ± 1.45 vs. 0.35 ± 0.85 ml/kg/min, $P = 0.005$), VO_2max percentage at VT2 (5.13 ± 2.41 vs. 0.63 ± 1.61%), RE at VT1 (−7.70 ± 2.86 vs. −3.50 ± 2.16 ml/kg/km, $P = 0.048$), RE at 90% of VT2 (−15.38 ± 4.73 vs. −3.38 ± 4.11 ml/kg/km, $P = 0.005$), and vertical jump in

Abalakov modality (2.95 ± 0.94 vs. 0.52 ± 1.49 cm, $P = 0.008$). Therefore, we conclude that running performance improvements were better after a 6-week program following an undulating periodization and consisting on functional exercises when compared with a 6-week traditional WB-EMS program.

Keywords: WB-EMS, VO_2max, running economy, VT2, training periodization

INTRODUCTION

Running has become increasingly popular in recent decades, and numerous novice runners start to practice this activity each year all over the world (Lee et al., 2017). Aerobic running performance is determined by different physiological parameters such as (i) maximum oxygen consumption (VO_2max), (ii) ventilatory threshold 1 (VT1), (iii) ventilatory threshold 2 (VT2), (iv) running economy (RE) (Jones and Carter, 2000; Barnes and Kilding, 2015), and (v) muscular strength, among others (Tucker et al., 2013). Strength training is able to increase all of them (Paavolainen et al., 1999; Jones and Carter, 2000; Beattie et al., 2014). Local electromyostimulation training seems to be an alternative to traditional strength training (Filipovic et al., 2012), yet there is a lack of studies evaluating its effects on running performance-related parameters.

Whole-body electromyostimulation (WB-EMS) has recently emerged as an innovative training modality, and enables the simultaneous exogenous muscle activation of up to 18 regions with a total area of 2,800 cm^2 covered by electrodes. It allows the configuration of different intensities in each region. To note, WB-EMS improves muscle strength in elite soccer players (Filipovic et al., 2016), in postmenopausal women (Kemmler et al., 2010), and in healthy untrained middle-aged men (Kemmler et al., 2016). WB-EMS training has some advantages: (i) training sessions are relatively short (<20 min), (ii) training frequency is low (3 sessions in 2 weeks) (Kemmler et al., 2016), (iii) sessions are dynamic and entertaining, (iv) it is a novel training stimulus, and (v) it could be used in training cessation situations such as injuries. However, to our knowledge, there are no intervention trials studying the effects of WB-EMS on aerobic performance parameters in runners.

WB-EMS intervention studies commonly use a pre-determined configuration of the electrical parameters, which is not modified during the training sessions. Moreover, the selection of exercises applied only includes motor patterns with a short range of motion and isometric actions (Kemmler et al., 2010, 2012, 2014, 2016; Kemmler and von Stengel, 2013). It is well-known that the application of a periodized training is more effective than non-periodized programs in resistance training programs (Harries et al., 2015). In addition, the application of exercise tasks involving specific running action (functional and transference task) enhance aerobic performance in endurance athletes (Balsalobre-Fernández et al., 2016). Thus, although it seems plausible that a WB-EMS training program including periodization (stimuli variation applied to achieve a specific training goal) and transference (specificity in exercise selection) as principles of sport training would result in additional benefits to those exerted by traditional WB-EMS training, empirical evidence is needed to confirm this hypothesis.

The purpose of the current study was to compare the effects of a 6-week periodized and functional WB-EMS training on VO_2max, VT1, VT2, RE, and lower-body muscle strength in runners, vs. a traditional whole-body-electromyostimulation training. Our hypothesis is that the periodized and functional WB-EMS training will improve running performance when compared with traditional WB-EMS.

METHODS

Participants

We recruited 15 healthy male recreational runners, who had been running 2–3 times per week (132.7 ± 28.6 min/week) for at least the previous year and had no previous experience on WB-EMS training. Three participants did not complete the study (due to job and family reasons) and were excluded from further analysis. The participants signed an informed consent. The study was approved by the Human Research Ethics Committee of the University of Granada (200/CEIH/2016) and complied with the revised ethical guidelines of the Declaration of Helsinki.

Design

A randomized controlled trial design (ClinicalTrials.gov ID: NCT03425981) was applied following CONSORT statements. The participants were randomized into two groups: (i) the PFG ($n = 6$) and (ii) the TG ($n = 6$). Participants were instructed to do one supervised WB-EMS training session and one RE test per week, and to stop their training routines while the WB-EMS program was performed. Both WB-EMS programs sessions had the same total duration.

WB-EMS Training Program

The WB-EMS training programs were designed considering different electrical parameters: (i) frequency; number of electrical pulses per time unit; it has been shown that there is not a selectively activation of muscle fibers using low or high frequencies, but fast fibers are predominantly recruited independently of the frequency applied (Gregory and Bickel, 2005), (ii) impulse width; which could influence the intensity of muscle contraction and is specific for each muscle group (Filipovic et al., 2011), (iii) impulse intensity; percentage of maximum voluntary contraction; in spite no data about it was provided in WB-EMS studies, several studies that applied local EMS showed a stimulation intensity of >50% maximum voluntary contraction is required to produce physiological improvements (Filipovic et al., 2011), and (iv) duty cycle; ratio between time receiving electrical stimuli and the total cycle time (Filipovic et al., 2011).

The WB-EMS training program consisted on six training sessions (1 per week). Before starting the program, the participants went through a familiarization session to learn movement patterns and to be adapted to the electrical stimuli. An experienced National Strength and Conditioning Association Certified Personal Trainer (NSCA-CPT) supervised all training sessions. Specific exercises of each training program modality are collected in Supplementary Material.

WB-EMS Periodized and Functional Running Training Group (PFG)

The PFG followed an undulating periodization model (understanding periodization as a systematic planning of athletic or physical training). The training sessions were divided into four parts (the participants only did movements when receiving electrical impulse in all cases): warm up (A), strength training (B), high intensity interval power training (C), and high intensity interval training (D). The electrical parameters, except impulse intensity, were modified across different parts of the session (see **Table 1**) in order to follow the recommendations for each exercise modality to improve strength and aerobic performance improvements (Kemmler et al., 2014; Amaro-Gahete et al., 2017). The impulse intensity was individually adjusted by RPE every 2 min. We applied a circuit training methodology (no rest between exercises) in all phases and we did not use any external load. In phase A, the participants performed 7–10 repetitions (1 set) of 3 exercises; both concentric and eccentric phases took 2 s each in every repetition. In phase B, the participants did 1–2 sets of 5–10 repetitions of 6 exercises; the concentric phase took 1 s and the eccentric phase duration was 3 s. In phase C, the participants performed 1 set of 8 exercises; they were instructed to do as many repetitions as possible in 10 s with a 10-s rest between exercises. In phase D, the participants did 1–2 interval sets with two different intensities: moderate intensity (65% VO_2max speed) and high intensity (>85% VO_2max speed) running on a treadmill (30 s each set at both intensities).

The exercises selected were functional and specific for the running discipline in order to comply with the principle of specificity. The exercises used in phase A (see Figure S1) were: (i) ½ squat and arm curl, (ii) ½ squat and bench flies, and (iii) ½ squat and horizontal push. The exercises used in phase B (see Figures S2.1, S2.2) were (i) lunge and knee-hip flexion, (ii) American swing, (iii) push-up, (iv) Bulgarian squat and vertical press, (v) sumo squat and lateral raises, and (vi) dead lift and horizontal pull. We used explosive and plyometric exercises in phase C (see Figures S3.1, S3.2, e.g. step jump, arms and leg frequency and cadence, climber, side step jump, skipping etc.). Finally, in phase D, the participants performed running intervals at different intensities.

The rationale of our periodization was based on the principle of progression, because it is not well-determined the best combination of electrical parameter in WB-EMS training for improve running performance.

Traditional WB-EMS Training Group (TG)

The TG program was based on training interventions applied in previous WB-EMS studies (Kemmler et al., 2010, 2012, 2014, 2016; Kemmler and von Stengel, 2013). The electrical impulse and training load were increased along the program (see **Table 1**). The impulse intensity was individually adjusted by RPE (Borg, 1982) every 2 min during all sessions.

The sessions were structured in a circuit format and consisted on 10 dynamic and general exercises without external load (see Figures S4.1, S4.2): (i) ½ squat and arm curl, (ii) dead lift and horizontal pull, (iii) ½ squat and trunk flexion, (v) ½ squat and vertical push, (v) ½ squat and lateral raises, (vi) ½ squat and horizontal push, (vii) squat and frontal raises, (viii) dead lift and triceps kick, (ix) squat and lateral flies, and (x) trunk rotation. The participants performed six to 10 sets (1 exercise repetition per set) depending on the total session duration, and both concentric and eccentric phases took 2 s in every repetition (a 4-s rest between exercises and 30 s between sets).

Performance-Related Variables

Two assessment days took place before and after the intervention. An anthropometric evaluation and a maximal treadmill exercise test were performed on day 1, and a vertical jump test and a RE test were performed on day 2. The participants were instructed not to consume alcohol, caffeine, and not to do vigorous-intensity exercise on the 48 h prior to the assessment days. Both assessment days were separated by 48 h.

Anthropometry

Body mass was determined by a scale (SECA, Hamburg, Germany) and height was determined by stadiometer (SECA, Hamburg, Germany); body mass index was also calculated (kg/m^2).

VO_2max

VO_2max was assessed in a maximum treadmill (H/P/Cosmos Pulsar treadmill, H/P/Cosmos Sport & Medical GMBH, Germany) exercise test with a progressive incremental protocol (Noakes et al., 1990; Machado et al., 2013). In brief, after a warm-up consisting on walking at 5 km/h for 3 min, the incremental protocol started with an initial speed of 8 km/h (1% grade), which was increased 1 km/h every minute until the participants reached their volitional exhaustion. Thereafter, the participants performed a cooling-down period (4 km/h and 0% grade during 5 min). O_2 consumption and CO_2 production were measured with a gas analyzer (Oxycon Pro; Jaeger, Höchberg, Germany). The gas analyzer was calibrated with a known gas mixture (0% O_2 and 5.5 CO_2) and environmental air (20.9% O_2 and 0.03% CO_2) immediately before each test. Consistently across assessments, the participants were strongly encouraged to invest maximum effort. The participants were previously familiarized with the 6–20 Borg scale (Borg, 1982), which was used to measure the RPE during the last 15 s of each stage and at exhaustion. Heart rate was recorded every 5 s (Polar RS300, Kempele, Finland). We also registered respiratory, RPE, and heart rate parameters during the cooling-down period. The gas

TABLE 1 | Electric parameters description in WB-EMS-PFG and WB-EMS-TG sessions (proposed progression).

WB-EMS-PFG	Session 1				Session 2				Session 3				Session 4				Session 5				Session 6			
	W	S	HP	HT	W	S	HP	HT	W	S	HP	HT	W	S	HP	HT	W	S	HP	HT	W	S	HP	HT
Total duration (min)	2	6	2	2	4	6	3	3	4	8	3	3	4	8	4	4	4	8	4	4	4	8	4	4
Frecuency (Hz)	12	55	60	20	12	65	70	25	12	75	80	35	12	85	90	40	12	85	90	40	12	85	90	40
Impulse width (μs)	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350
RPE impulse intensity (6-20)	10	12	13	13	10	12	13	13	10	14	15	15	10	16	17	17	10	16	17	17	10	16	17	17
Duty cycle (%)	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
	4:4	4:4	10:10	30:30	4:4	4:4	10:10	30:30	4:4	4:4	10:10	30:30	4:4	4:4	10:10	30:30	4:4	4:4	10:10	30:30	4:4	4:4	10:10	30:30

WB-EMS-TG	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6
Total duration (min)	12	16	18	20	20	20
Frecuency (Hz)	85	85	85	85	85	85
Impulse width (μs)	350	350	350	350	350	350
Impulse intensity (mA)	60	60	60	60	60	60
RPE (6–20)	12–14	13–15	14–16	15–17	15–17	15–17
Duty cycle (%)	50% (4:4)	50% (4:4)	50% (4:4)	50% (4:4)	50% (4:4)	50% (4:4)

WB-EMS-PFG, Whole-Body Electromyostimulation Periodized and Functional Running Training group; WB-EMS-TG, Traditional Whole-Body Electromyostimulation training group; W, Warm-up phase; S, Strength phase; HP, High Intensity Interval Power Training phase; HT, High Intensity Interval Training phase; RPE, Rated Perceived Exertion; Hz, Hertz; μs, Microseconds; mA, Milliamps.

exchange data was averaged every 10 s and was downloaded for later analysis.

Ventilatory Thresholds

In the maximum treadmill exercise test, VT1 and VT2 were estimated from gas exchange data through different respiratory variables: minute ventilation (VE) and equivalents for oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2) by two independent researchers (FA and AG), and a third researcher opinion was sought when they disagreed (AO). VT1 and VT2 were determined following a validated methodology applied in previous studies (Lucía et al., 2000).

Running Economy

RE was determined during a treadmill protocol following a specific protocol used in previous studies (Guglielmo et al., 2009; Shaw et al., 2014; Holmes et al., 2015). The treadmill test consisted of two 10-min stages at two different intensities; (i) speed at VT1 and (ii) speed at 90% of VT2. The first 2-min record of each stage were discarded in order to ensure that the participants reached the steady-state criteria. RE (oxygen cost of running a kilometer at a specific velocity) was calculated using the following equation: RE = VO2 (ml/kg/min)/[speed (km/h)/60] (Guglielmo et al., 2009; Shaw et al., 2014; Holmes et al., 2015). RE was assessed before, during (once per week), and after the training program considering pre-intervention VT1 and 90% VT2 speed.

Lower Body Muscular Strength

Vertical jump performance was assessed using the countermovement (CMJ) and Abalakov jump (ABJ) tests. In standing position, with legs straight and both hands on hips, the participant performs a vertical jump with an earlier fast counter movement. The Abalakov jump is similar to the CMJ, but now the participants is allowed to freely coordinate the arms and trunk movements to reach the maximum height (Bosco et al., 1983). The jumping height was calculated from the flight time using kinematic equations (Lehance et al., 2005) estimated by Ergo Jump Bosco System® (Globus, Treviso, Italy). Before carrying out the tests, a standardized warm-up was performed which included a 5-min run at 50% of heart rate reserve, and mobility and muscle activation exercises.

Statistical Analyses

All outcome variables were checked for normality with a graphical test (QQ-Plots) and results are expressed as mean and SD or median and ranges. The baseline and post intervention data were compared using Student's paired t-test. One-way analysis of covariance (ANCOVA) was used to examine the effect of group (fixed factor) on VO_2max change, i.e., post-VO_2max minus pre-VO_2max (dependent variable), adjusting for baseline value. The same analyses were used for maximal aerobic speed, oxygen uptake at VT1 and VT2, VO_2max percentage in VT1 and VT2, VT1 and VT2 speed, RE at VT1 speed and 90% of VT2 speed, and vertical jump (countermovement jump and Abalakov jump). Multiple comparisons were adjusted by Bonferroni. Two-way ANOVA (Time x Group) was used to determine changes in RE during the intervention study; we applied an adjustment by Greenhouse-Geisser when the Mauchly test of sphericity was significant ($p < 0.05$). We conducted all statistical analyses using SPSS Statistics (version 20, IBM, Ehningen, Germany) software, setting level of significance at $p < 0.05$.

RESULTS

There were no WB-EMS-related adverse effects. The baseline characteristics by training group are shown in **Table 2**. We observed no statistically significant differences at baseline (**Table 3**). The participants reported similar values of the impulse intensity (measured by RPE) than the pre-established ranges (mean difference ± *SD*, 0.71 ± 0.24 and 0.64 ± 0.34). This fact confirmed that participants of WB-EMS group adhered to the protocol designed in term of impulse intensity.

Anthropometry

BMI significantly decreased in a similar fashion in the PFG and the TG (from 22.6 ± 2.8 to 22.1 ± 2.6 kg/m^2, and from 24.5 ± 3.3 to 24.1 ± 3.2 kg/m^2, $P = 0.022$ and $P = 0.021$, respectively).

VO_2max

There were no changes in absolute VO_2max (ml/min^{-1}) levels in the TG, whereas changes were border on significance ($P = 0.082$) in the PFG (**Figures 1A,B**). VO_2max in relative terms (ml/kg/min) increased in PGF group and a tendency were observed in TG after training ($P < 0.001$ and $P = 0.053$ for the PFG and the TG respectively, **Figure 1C**), being the pre-post changes higher in the PFG group than in the TG (mean difference: 1.72 ml/kg/min, $P = 0.011$, **Figure 1D**). Similarly, maximal aerobic speed increased in the PFG ($P = 0.041$, **Figure 1E**), whereas no changes were observed in the TG (**Figure 1E**). Between group changes comparisons were border of significance for maximal aerobic speed (mean difference: 1.01 vs. −0.17 km/h for the PFG and the TG, respectively, $P = 0.065$, **Figure 1F**).

TABLE 2 | Descriptive parameters.

	Total (n = 6)	WB-EMS-PFG (n = 6)	WB-EMS-TG (n = 6)
BODY MASS (kg)	71.9 ± 10.2	70.1 ± 11.1	73.8 ± 9.8
HEIGHT (cm)	174.7 ± 6.3	175.7 ± 5.5	173.8 ± 7.4
BMI (kg/m^2)	23.6 ± 3	22.6 ± 2.7	24.5 ± 3.3
VO_2max (ml/min)	3855.7 ± 615.5	3790.8 ± 812.4	3920.5 ± 404.4
VO_2max (ml/kg/min)	53.7 ± 4.6	53.9 ± 5.3	53.5 ± 4.4
VO_2VT1	27.7 ± 3.2	28.2 ± 3.4	27.2 ± 3.3
VO_2 VT2	40.8 ± 4.4	40.8 ± 4.6	40.7 ± 4.5
%max VO_2 VT1	51.6 ± 4.4	52.2 ± 2.7	51.1 ± 5.9
%max VO_2 VT2	73.4 ± 4.8	72 ± 3.9	74.8 ± 5.4
SPEEDpeak (km/h)	16.7 ± 1.4	16.7 ± 1.6	16.7 ± 1.2
VT1s (km/h)	9.3 ± 1	9.3 ± 1.2	9.2 ± 0.8
VT2s (km/h)	13.8 ± 1.1	14 ± 1.1	13.5 ± 1
RE VT1 (ml/kg/km)	213.5 ± 12.6	210.1 ± 12	216.9 ± 13.2
RE VT2 (ml/kg/km)	246.1 ± 24.4	248.5 ± 26.3	243.7 ± 24.6
CMJ (m)	0.31 ± 0.06	0.32 ± 0.07	0.31 ± 0.05
ABJ (m)	0.36 ± 0.06	0.36 ± 0.06	0.36 ± 0.07

BMI, Body Mass Index; VO_2max, Maximum Oxygen Uptake; %max VO_2 VT1, Oxygen uptake percentage in aerobic threshold relative of maximum oxygen uptake; %max VO_2 VT2, Oxygen uptake percentage in anaerobic threshold relative of maximum oxygen uptake; VT1s, Aerobic Threshold Speed; VT2s, Anaerobic Threshold Speed; CMJ, Countermovement Jump; ABJ, Abalakov Jump; RE VT1, Running Economy Aerobic Threshold; RE VT2, Running Economy at 90% of Anaerobic Threshold; WB-EMS-PFG, Whole-Body Electromyostimulation Periodized and Functional Running Training group; WB-EMS-TG, Traditional Whole-Body Electromyostimulation training group.

Ventilatory Thresholds

There were no significant pre-post changes in VO2 at VT1, VO_2max percentage in VT1, and VT1 speed in the TG (all $P > 0.076$), yet, significant pre-post differences in VO_2 at VT1, and VT1 speed were observed in the PFG. There were no significant between groups differences when comparing pre-post changes (all $P > 0.094$, **Table 3**).

Regarding VT2, there were significant pre-post differences in VO_2 at VT2, VO_2max percentage in VT2, and VT2 speed in the PFG (all $P < 0.004$), but not in the TG (all $P > 0.360$). Changes in VO_2 at VT2, VO_2max percentage in VT2, and VT2 speed were significantly different in the PFG and the TG (all $P < 0.008$) (see **Figure 2**).

Running Economy

RE at VT1 speed and 90% VT2 speed improved in the PFG ($P < 0.001$) (**Figures 3A,C**, respectively), but it did not in the TG ($P > 0.111$), and significant differences were found when comparing pre-post changes between groups ($P < 0.05$ and $P < 0.01$ for VT1 speed and 90% VT2, respectively). Repeated measures analysis showed that between-group differences in RE at VT1 speed appeared after 6 weeks of intervention ($P < 0.05$), whereas differences in RE at 90% of VT2 speed appeared in the fourth week ($P < 0.05$) and continued until the post-intervention assessment ($P < 0.01$) (**Figures 3B,D**).

Lower Body Muscle Strength

The levels of CMJ increased after the intervention in both the PFG and the TG ($P < 0.05$ in both cases), being pre-post changes similar between groups ($P = 0.203$) (**Figures 4A,B**). The pre-post changes in ABJ were, however, different between the PFG vs. the TG ($P < 0.01$, **Figures 4C,D**), and we observed no pre-post differences in the TG ($P = 0.724$).

DISCUSSION

This study shows that the effects of a 6-week periodized and functional WB-EMS training program on running performance-related parameters including VO_2max, VT2, RE, and ABJ in recreational runners are better than those observed after following a traditional WB-EMS training program. These findings reinforce the fact that the effects of WB-EMS training on running performance can be greatly improved if it is correctly designed. To our knowledge, this is the first study analyzing the effect of WB-EMS on running performance-related parameters in recreational runners.

VO_2max

VO_2max is considered one of the best predictor of running performance (Tucker et al., 2013). We observed an increment of 2.75 ml/kg/min in the PFG. These findings do not concur with an intervention program consisting on two combined strength

TABLE 3 | Results for principal and secondary outcomes over time.

	WB-EMS-PFG		WB-EMS-TG		Test of change over time		Test of treatment effects
	M±SD	CI	M±SD	CI	WB-EMS-PFG	WB-EMS-TG	*P*-value
BODY MASS (kg)	−0.48 (1.12)	−2.66, −0.31	−0.13 (0.89)	−2.07, −0.20	**0.023**	**0.027**	0.443
BMI (kg/m^2)	−0.52 (0.39)	−0.93, 0.07	−0.39 (0.29)	−0.62, 0.10	**0.022**	**0.021**	0.395
VO_2max (ml/min)	104.01 (117.38)	−227.18, 19.18	21.67 (56.80)	−81.27, 37.94	0.082	0.393	0.182
VO_2max (ml/kg/min)	2.75 (0.89)	−3.69, −1.81	1.03 (1.01)	−2.09, 0.02	**<0.001**	0.053	**0.011**
MAS (km/h)	1.01 (0.89)	−1.94, −0.06	−0.17 (0.98)	−0.87, 1.20	**0.041**	0.695	0.065
VO_2VT1	1.43 (0.87)	−2.34, −0.51	0.67 (1.14)	−1.87, 0.53	**0.010**	0.209	0.257
VO_2 VT2	2.95 (1.45)	−4.47, −1.42	0.35 (0.85)	−1.24, 0.55	**0.004**	0.368	**0.005**
%max VO_2 VT1	−0.02 (1.87)	−1.94, 1.98	0.13 (2.39)	−2.63, 2.38	0.98	0.900	0.843
%max VO_2 VT2	5.13 (2.41)	−7.66, −2.60	0.63 (1.61)	−2.32, 1.06	**0.003**	0.379	**0.008**
VT1s (km/h)	0.83 (0.75)	−1.62, −0.04	0.5 (0.55)	−1.08, 0.08	**0.042**	0.076	0.094
VT2s (km/h)	1.17 (0.41)	−1.60, −0.74	0.08 (0.38)	−0.48, 0.31	**<0.001**	0.611	**<0.001**
RE VT1 (ml/kg/km)	−7.70 (2.86)	4.70, 10.70	−3.5 (2.16)	1.24, 5.76	**<0.001**	**0.011**	0.257
RE VT2 (ml/kg/km)	5.38 (4.73)	10.42, 20.35	−3.38 (4.11)	−0.93, 7.70	**<0.001**	0.100	**0.005**
CMJ (cm)	1.47 (1.16)	−2.68, −0.25	0.70 (0.63)	−1.36, −0.04	**0.027**	**0.042**	0.203
ABJ (cm)	2.95 (0.94)	−3.93, −1.97	0.52 (1.49)	−2.08, 1.04	**<0.001**	0.434	**0.008**

Changes in variables (Final-Baseline) for the WB-EMS-PFG and WB-EMS-TG groups over time. Change scores are Mean (SD), and confidence interval (CI). Reported p-values are for tests of an overall change over time among all subjects, and for tests of a treatment effect between MIT and HIIT groups over time. Boldface values indicate significance differences ($P < 0.05$). Only participants with complete intervention program were included in the complete analysis. BMI, Body Mass Index; VO_{2max}, Maximum Oxygen Uptake; MAS, Maximal Aerobic Speed; VO_2VT1, Oxygen uptake Ventilatory Threshold 1; VT2, Ventilatory Threshold 2 VT1s; %max VO_2 VT1, Oxigen uptake at Ventilatory Threshold 1; VO_2 VT2, Oxigen uptake at Ventilatory Threshold 2; %max VO_2 VT1, Oxygen uptake percentage in Ventilatory Threshold 1 relative of maximum oxygen uptake; %max VO_2 VT2, Oxygen uptake percentage in Ventilatory Threshold 2 relative of maximum oxygen uptake, VT1s, Ventilatory Threshold 1 Speed; VT2s, VT1s, Ventilatory Threshold 2 Speed; RE VT1, Running Economy at Ventilatory Threshold 1 Speed; RE VT2, Running Economy at 90% of the Ventilatory Threshold 2 Speed; CMJ, Countermovement Jump; ABJ, Abalakov Jump; WB-EMS-PFG, Whole-Body Electromyostimulation Periodized and Functional Running Training group; WB-EMS-TG, Traditional Whole-Body Electromyostimulation training group.

sessions per week which lasted for 11 weeks while maintaining its endurance training volume in trained athletes, which increased several strength parameters and muscle fiber cross sectional area of both fiber type I and fiber type II, but no changes in VO_2max were found (Vikmoen et al., 2016). However, a meta-analysis (Sloth et al., 2013) evaluated the effects of high intensity interval training interventions (lasting 2–8 weeks) on VO_2max in healthy sedentary or recreationally active adults, and showed a similar VO_2max increase (ranged between 4.2 and 13.4%). These improvements are similar to those observed in the PFG.

Traditionally, WB-EMS training programs do not vary electrical frequency, electrical intensity, width impulse, and duty cycle, within the training sessions. Moreover, the selection of exercises usually consists on a set of non-functional movements (i.e., not motor related with the competition movement) (Filipovic et al., 2011; Amaro-Gahete et al., 2017). We designed a training intervention that followed (i) an undulating periodization training model, and (ii) a functional selection of exercises to improve running performance. We observed that absolute VO_2max increased by 2.78% after the 6-week intervention program in the PFG compared with the TG. When expressed in relation to body mass (ml/kg/min), an improvement on VO_2max could be explained either by a reduction on body mass and/or an increase in VO_2max itself (ml/min). Our data suggest that improvements obtained in VO_2max relative to body mass were determined only by body mass loss in the TG; however, VO_2max in relative terms were strongly influenced by VO_2max in absolute terms ($P = 0.08$) in the PFG.

Periodized resistance training programs result on higher benefits over muscle strength compared to non-periodized training programs, which also seems to be the case in WB-EMS training programs (Williams et al., 2017). On the other hand, Nuhr et al. reported that a local electromyostimulation training program (10 weeks, 4 h per day, 7 days per week) at low frequency (15 Hz) applied in quadriceps and hamstring muscles of both legs in healthy men improve maximal aerobic-oxidative capacity (Nuhr et al., 2003). Interpreting our results, despite the fact that both WB-EMS training programs had the same time exposure (same number of sessions and duration), we cannot discard that differences in overall training load (e.g., different muscular tension) explain the observed differences.

Ventilatory Thresholds

It is well-known that VT1 and VT2, especially the latter, have an important role in long-distance running performance (Jones and Carter, 2000; Barnes and Kilding, 2015). The effect of concurrent training on VT1 and VT2 is controversial. Two studies reported little changes on VT2 in runners (Mikkola et al., 2011; Støren et al., 2013), which concur with our findings in the TG. In contrast, others observed substantial improvements in VT2 (Guglielmo et al., 2009; Taipale et al., 2013) after following resistance training program in trained athletes. In our study, the

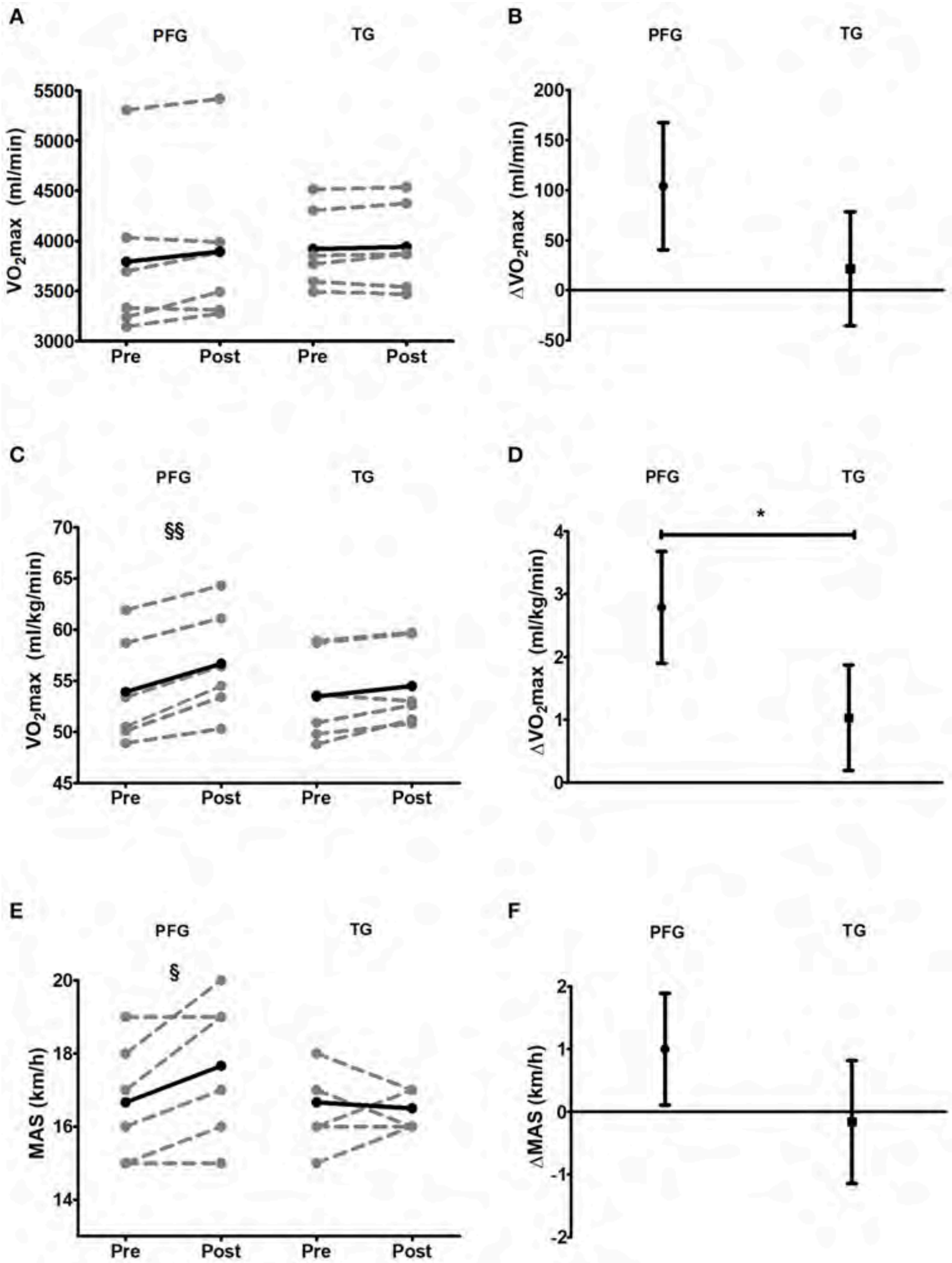

FIGURE 1 | Pre and post 6-week intervention values and mean change (95% CI) in maximal oxygen uptake (absolute and relative values), and maximal aerobic speed after the intervention program. **(A,B)** Maximal oxygen uptake in absolute values [VO_2max (ml/min)]; **(C,D)** Maximal oxygen uptake in relative values [VO_2max (ml/kg/min)]; **(E,F)** Maximal Aerobic Speed [MAS (km/h)]. §$P < 0.05$, §§$P < 0.01$, §§§$P < 0.001$ (analysis pre-post; Student's paired *t*-test). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (analysis between groups; analysis of covariance). PFG, Periodized, and Functional group; TG, Traditional Whole-Body-Electromyostimulation training.

PFG experienced an increase of 7% in VO_2 at VT2. Of note is that an improvement in VT1 and VT2 speed, and VO_2 at VT1 and VT2, could be an indirect effect of an improvement on VO_2max and/or RE (see below). However, the increase of VO_2max percentage at which VT2 is achieved suggest that a direct improvement of VT2 was observed in the PFG.

Running Economy

RE, defined as the oxygen consumption required at a given absolute submaximal exercise intensity, is considered critical for running performance in trained individuals with homogenous VO_2max (Saunders et al., 2004). Our findings concur with those of Taipale et al. who reported substantial improvements in RE

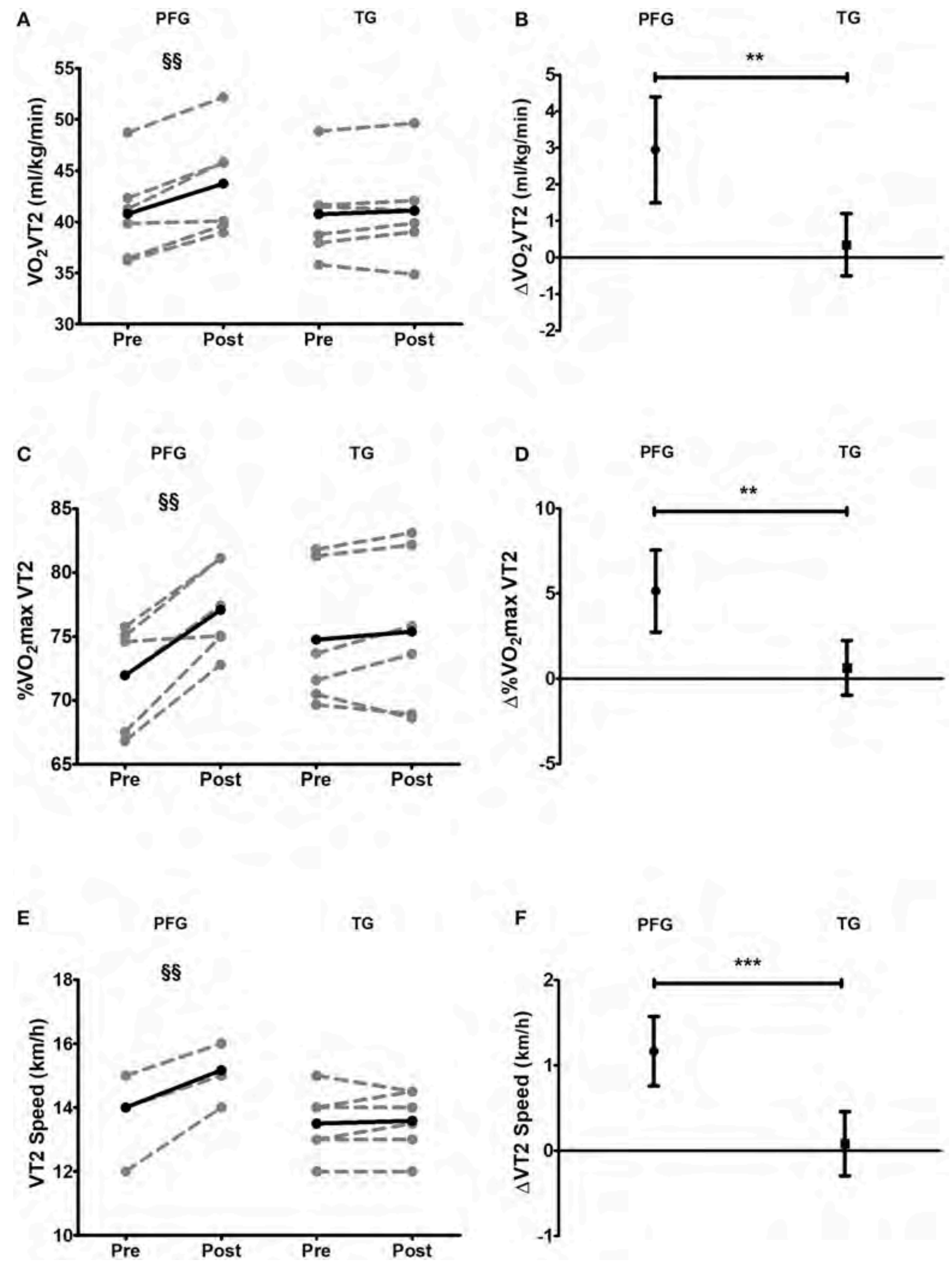

FIGURE 2 | Pre and post 6-week intervention values and mean change (95% CI) in oxygen uptake at ventilatory threshold 2, maximal oxygen uptake percentage in ventilatory threshold 2, and ventilatory threshold 2 speed. **(A,B)** Oxygen uptake at ventilatory threshold 2 [VO_2VT2s (ml/kg/min)]; **(C,D)** Maximal oxygen uptake percentage in ventilatory threshold 2 [$\%VO_2$max VT2]; **(E,F)** Ventilatory Threshold 2 Speed [VT2 speed (km/h)]. §$P < 0.05$, §§$P < 0.01$, §§§$P < 0.001$ (analysis pre-post; Student's *t*-test). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (analysis between groups; ANCOVA). PFG, Periodized and Functional Whole-Body-Electromyostimulation training; TG, Traditional Whole-Body-Electromyostimulation training.

after 8 weeks of combined explosive strength and endurance training in runners (Taipale et al., 2013).

Although we cannot know whether the periodization or the use of functional exercises are the main cause of the improvement in RE, the performance of functional exercises with running actions at maximal speed with superimposed electromyostimulation could be an important factor to improve RE. The PFG included a period of high intensity short run intervals with superimposed electromyostimulation; this fact could determine some advantages over the TG inasmuch this

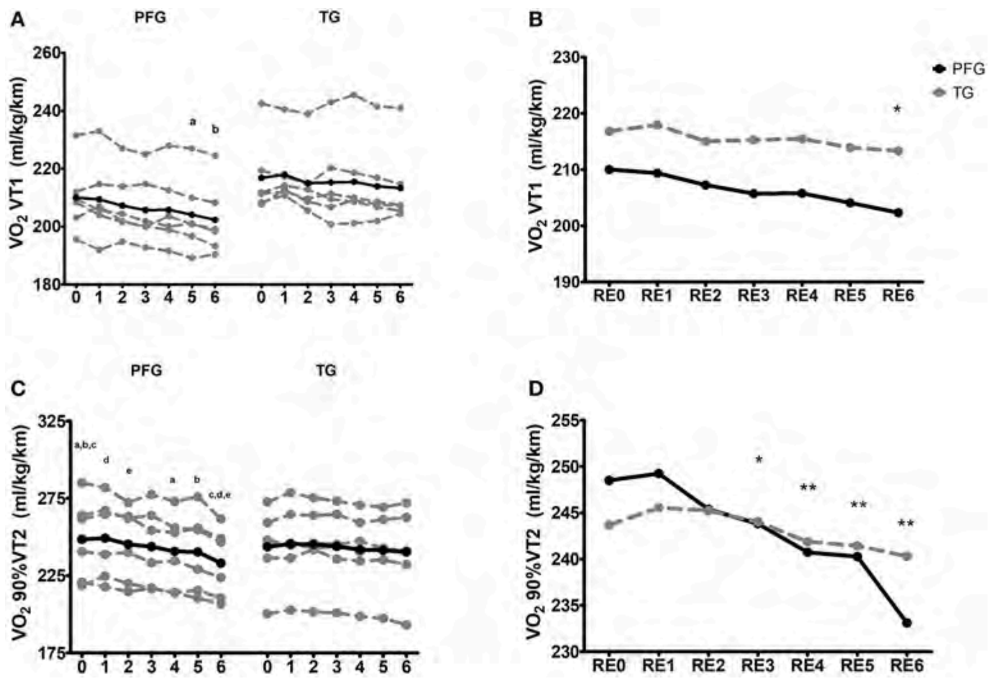

FIGURE 3 | Running economy (RE) kinetics at ventilatory threshold 1 speed, and 90% of ventilatory threshold 2 speed after the intervention program. **(A,B)** Running economy at ventilatory threshold 1 speed [VO_2 VT1 (ml/kg/km)], **(C,D)** running economy at 90% of ventilatory threshold 2 speed [VO_2 90%VT2 (ml/kg/km)]. RE0 corresponded to the first running economy test (pre-test); RE1 corresponded to the running economy test performed in week 1; RE2 corresponded to the running economy test performed in week 2; RE3 corresponded to the running economy test performed in week 3. RE4 corresponded to the running economy test performed in week 4; RE5 corresponded to the running economy test performed in week 5; RE6 corresponded to the running economy test performed in week 6 (post-test). Repeated letters (a–a; b–b, etc.) indicate $P < 0.05$ in different weeks (analysis throughout time; Repeated ANOVA measures). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ (analysis between groups of the pre-test differences; ANCOVA). PFG, Periodized and Functional Whole-Body-Electromyostimulation training; TG, Traditional Whole-Body-Electromyostimulation training.

training modality did not include running actions. Therefore, this fact could contribute to maximize performance at high speed intensity. On the other hand, we cannot discard that following a periodization training model could increase the improvements obtained (Harries et al., 2015).

Lower Body Muscle Strength

Several studies have shown the importance of lower body muscle strength in running performance, especially in RE (Dumke et al., 2010). Our findings concur with those observed by other studies using WB-EMS and local electromyostimulation training (12–28 sessions) on the lower body muscles in trained athletes (Babault et al., 2007; Filipovic et al., 2011, 2016). Filipovic et al. (2016) applied a WB-EMS intervention twice a week, which consisted on 3 × 10 maximal squat jumps with a set pause of 60 s. They found significant increases in squat jump, CMJ, and drop jump (all $P < 0.05$), which concur with our findings. Our study showed an increase in CMJ in both training groups, whereas significant improvement in ABJ was only observed in the PFG. This fact could be explained by differences in the exercises used and the electrical parameters applied in both intervention groups (e.g., the inclusion of several plyometric exercises in the PFG). Since the main difference between CMJ and ABJ is the contribution of interlimb coordination, the improvement obtained in ABJ in the PFG when compared to the TG, suggest that a periodized and functional WB-EMS training program could have a considerable impact on inter-limb coordination (Dal Pupo et al., 2013). However, more studies are needed to elucidate which physiological or biomechanical mechanism may explain the differences reported between groups.

Possible reasons which could explain the physiological improvements observed are: (i) a better efficiency of mitochondrial metabolism, what is related with an increase in the rate of lipid utilization [it is well-known that this fact produces an important descent in rate of glycogen depletion (Esfarjani and Laursen, 2007)], (ii) an increased capillary density after an specific training program, yet we applied low frequencies in different parts of PFG sessions and it is well-known that low frequencies produce a development of capillarization process (Miyamoto et al., 2016), and (iii) positive changes in neurological process related to lower limb coordination, recruitment and synchronization of motor units, and co-activation of muscles, which could results in a greater leg stiffness and muscular strength (Barnes and Kilding, 2015); only PFT include an wide values spectrum of the different electrical parameters manipulated, and specific functional task (plyometric or explosive strength exercises) oriented to improve these facts. All of the previous items could produce a delay in local and peripheral fatigue resulting in a decrease of oxygen uptake for

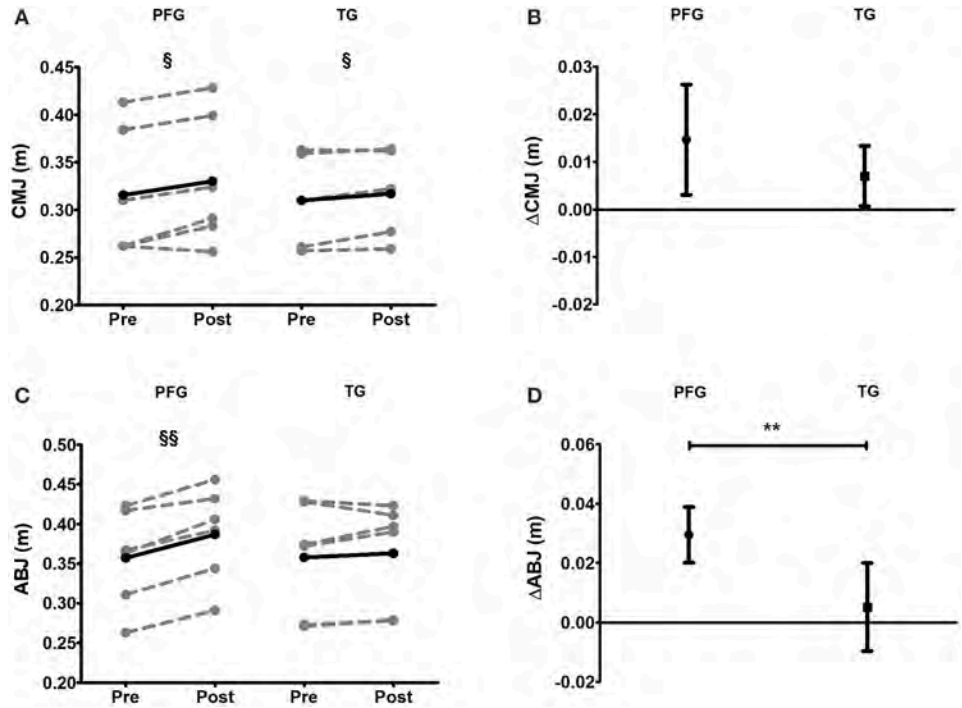

FIGURE 4 | Pre and post 6-week intervention values and mean change (95% CI) countermovement jump and Abalakov jump after the intervention program. **(A,B)** Countermovement jump [CMJ (m)], **(C,D)** Abalakov jump [ABJ (m)]. §$P < 0.05$, §§$P < 0.01$, §§§$P < 0.001$ (analysis pre-post; Student's paired *t*-test). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (analysis between groups; ANCOVA). PFG, Periodized and Functional Whole-Body-Electromyostimulation training; TG, Traditional Whole-Body-Electromyostimulation training.

a specific speed and, consequently, getting a better running performance.

Limitations

The results of this study should be considered with caution as there are some limitations. The main limitation of this study (as all WB-EMS previous studies) is the lack of information about the total electrical impulse magnitude applied. Indeed, the best methodology to control WB-EMS training load is currently unknown. Moreover, the low sample size and the inexperienced participants in WB-EMS training may have influenced the results, since improvements produced by the application of a novel stimulus are expected. In addition, we cannot know whether these results extend to longer training programs, and or to not professional athletes or patients. We did not confirm VO_2peak by checking VO_2max plateau with a constant work rate test (110% of the maximal intensity reached after the ramp protocol test) because our participants were recreational runners and this validation is not necessary in this population (Poole and Jones, 2017). One of the strengths is that we included a positive control group which allowed to avoid the existence of false positive cases.

CONCLUSION

A 6-week periodized and functional WB-EMS training program produces considerable higher on VO_2max, VT2, RE, and ABJ in recreational runners compared with a traditional WB-EMS training program. Our findings indicate that WB-EMS training, as a novel stimulus, could complement or even modify the common training methods in runners. In addition, our results strongly support that WB-EMS training must be carefully designed and supervised, not only for safety reasons, but also for efficiency issues. This concept is particularly relevant in the commercial context where this type of technology could be understood as a completely autonomous training methodology. More studies are needed to better understand the practical applications of this new training methodology in other populations, to elucidate whether the improvements obtained are due to the exercises selected, or to the electrical parameters, or to its combination, and also to elucidate whether a traditional strength program get higher improvements in running performance than WB-EMS training.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

AUTHOR CONTRIBUTIONS

FA-G, AD-l-O, LR-G, and AG conceived and designed research. FA-G, AD-l-O, LR-G, and LJ-F conducted experiments. FA-G and

JR analyzed data. FA-G wrote the manuscript. AG and JR revised the manuscript. All authors read and approved the manuscript.

FUNDING

The study is supported by the Spanish Ministry of Education (FPU 13/04365, FPU14/04172, and FPU15/03960). The study was partially supported by the University of Granada, Plan Propio de Investigación 2016, Excellence actions: Units of Excellence; Unit of Excellence on Exercise and Health (UCEES). This study is part of a Ph.D. Thesis conducted in the Biomedicine Doctoral Studies of the University of Granada, Spain.

ACKNOWLEDGMENTS

The authors would like to thank all the runners who participated in this study for their time and effort. We are grateful to Ms. Carmen Sainz Quinn for assistance with the English language, and to Manuel Castillo for constructive scientific discussions.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphys.2018.00720/full#supplementary-material

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

OPINION
published: 12 October 2018
doi: 10.3389/fphys.2018.01428

Training Based on Electrical Stimulation Superimposed Onto Voluntary Contraction Would be Relevant Only as Part of Submaximal Contractions in Healthy Subjects

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Keywords: muscle, electrical stimulation, training, voluntary contraction, superimposed stimulation, submaximal intensity, exercise, performance

OPEN ACCESS

Edited by:
Wolfgang Kemmler, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany

Reviewed by:
Andre Filipovic, German Sport University Cologne, Germany

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: 22 June 2018
Accepted: 20 September 2018
Published: 12 October 2018

Citation:
Paillard T (2018) Training Based on Electrical Stimulation Superimposed Onto Voluntary Contraction Would be Relevant Only as Part of Submaximal Contractions in Healthy Subjects. Front. Physiol. 9:1428. doi: 10.3389/fphys.2018.01428

Voluntary (VOL) and electrically stimulated (ES) muscular contractions engender differences in activation of muscle fibers and metabolism (Vanderthommen and Duchateau, 2007). During submaximal VOL actions, even if the muscle fibers activated are distributed in the whole muscle, they are progressively recruited in an orderly fashion from small to large according to the intensity of the contraction considered (Henneman et al., 1965), i.e., from the viewpoint of distribution of muscle fibers in quadriceps femoris mainly from the depth of the muscle to the surface since small fibers (slow-twitch fibers, tonic fibers, or type I fibers) are mainly located in the depth of the muscle while large fibers (fast-twitch, phasic fibers, or type II fibers) are mainly located in the surface (Lexell et al., 1983). In turn, the muscle fibers recruitment through ES depends on the current density and it mainly involves muscle fibers located directly beneath the stimulation electrodes since the current density decreases with increasing depth of muscle. Muscle fibers are recruited from the surface of the muscle to the depth according to the current intensity. The higher the intensity, the deeper the fibers are recruited independently of the type of fibers (and the excitability threshold linked to their size) which means that the muscle fibers recruitment is random and spatially fixed (Feiereisen et al., 1997; Vanderthommen et al., 2003; Gregory and Bickel, 2005). Moreover, ES can enhance energy consumption, carbohydrate oxidation, and whole body glucose uptake at low intensity of exercise substantially more than VOL (Hamada et al., 2004). Overall, VOL and ES can be considered as complementary stimuli of a different nature, inducing different acute physiological effects.

Theoretically, the simultaneous superimposition of ES onto VOL (VOL + ES) should augment the produced force through additional muscle fibers recruitment in acute application, and should constitute a potential accumulation (possible additional gains) of the physiological effects induced by each contraction in terms of improvement of muscular power, strength or endurance in the context of chronic application.

Practically, acute application of VOL + ES in pathological (e.g., injured) or over-trained (e.g., chronically fatigued) subjects presenting incomplete voluntary (central) activation levels (i.e., unable to fully activate their muscle) indeed facilitates additional muscle fibers recruitment or muscle fibers firing rates and thus enables an increase in production force in comparison with VOL (Koutedakis et al., 1995). In return, with healthy subjects who are able to fully activate their muscles, VOL + ES does not generate any enhancement of the force production in comparison with VOL (e.g., Hortobágyi et al., 1992). Chronic application of VOL + ES, with pathological subjects following post-traumatic rehabilitation programs (e.g., related to arthroplasty, arthroscopy, ligamentoplasty), is more effective than VOL to facilitate recovery of injuries (e.g., Drapper and Ballard, 1991). VOL + ES compensates for volume and muscle strength deficit with more efficiency than programs using VOL or ES separately (Paillard et al., 2005). With healthy subjects, VOL + ES does not reveal significant benefits in comparison with programs performed only with VOL or ES (e.g., Paillard et al., 2004). In fact, most of muscle fibers are already activated with VOL and superimposed electrical stimulation does not enable the supplementary recruitment of muscle fibers and cannot induce greater long-term training adaptations (Wirtz et al., 2015). Whether in acute or chronic application, VOL + ES does not result in any advantage in comparison with VOL or ES when subjects are healthy and their central nervous system (CNS) fully activates their skeletal muscles and their locomotor apparatus is devoid of any pathology (Paillard et al., 2005).

Since the publication of the review article by Paillard et al. (2005), the understanding of VOL + ES as a training technique has only slightly evolved. Indeed, there is still a certain consensus according to which VOL + ES would be not more efficient than VOL (with or without additional weight/load) or ES alone in order to improve motor and/or sport performance in chronic application whether with isometric, dynamic or plyometric movements (Paillard et al., 2005; Herrero et al., 2010; Park et al., 2016; Wirtz et al., 2016; Gomes da Silva et al., 2018). Yet, some recent papers showed that VOL + ES could bring some advantages in comparison with VOL and ES practiced alone as part of training programs aiming at improving motor performance in healthy subjects (Wahl et al., 2012, 2014, 2015; Matsuse et al., 2013; Mathes et al., 2017). Hence, it seems relevant to analyze why some studies reported benefit effects of VOL + ES in chronic application in comparison with VOL and ES in healthy subjects.

In fact, for regularly repeated maximal tasks (maximal resistance/strength exercises), it was confirmed that VOL + ES does not enable the force produced to be increased after a training period (e.g., Park et al., 2016). In turn, as part of regularly repeated submaximal tasks (submaximal resistance/strength exercises), VOL + ES could improve motor performance more than VOL or ES alone after a training period. Evidence suggests that submaximal tasks engender greater muscle fibers recruitment with VOL + ES than with VOL or ES (**Figure 1**) and would be likely to generate greater gains in terms of motor output after a training period.

To this end, as part of the VOL + ES application, on the one hand, the voluntary contraction should be relatively remote from maximal effort (submaximal intensity) and on the other hand, the intensity of the current related to electrical stimulation should be relatively low (e.g., 15–25 mA $<$) in order to allow any well-coordinated movements. Only submaximal contractions enable an efficient movement control with VOL + ES (Bezerra et al., 2011). If the intensity of the current applied to motor muscles is too high, no free and accurate segmental displacement of limbs is achievable since the resistance exerted on joints is too strong, which impedes or limits movement. The intensity value requires to render possible motor/sport activity of subject while being electrically stimulated. Moreover, the VOL + ES application in submaximal condition (i.e., submaximal contraction) would induce greater metabolic activation and energy consumption as well as greater muscle fibers recruitment and motor output during exercise in comparison with the VOL application. All these different physiological changes would not occur in maximal motor tasks i.e., maximal contractions (Paillard et al., 2005).

From a metabolic viewpoint, some studies showed that acute metabolic changes (e.g., some respiratory, cardiac, biological and biochemical blood parameters) induced by exercise as well as energetic and mechanical output are greater during cycling with superimposed ES than during cycling alone (Wahl et al., 2012, 2014, 2015; Matsuse et al., 2013; Mathes et al., 2017). Hence, one can infer that ES during cycling exercise might be an enhancing stimulus for skeletal muscle metabolism and induced adaptations. Wahl et al. (2014) concluded that at low exercise intensities, VOL + ES characterizes a high stimulus by provoking greater hormonal secretions (e.g., cortisol, Growth Hormone). This high stimulus would entail adaptations related to metabolic endurance (e.g., expression of aerobic enzymes via cortisol, erythropoiesis via Growth Hormone). These favorable enzymatic and hormonal responses were not observed at high intensities in comparison with VOL (Wirtz et al., 2015). Moreover, VOL + ES at submaximal intensity would enhance glucose metabolism through additional fast-twitch muscle fibers recruitment in comparison with VOL (Watanabe et al., 2014). Overall, long-term training adaptations induced by VOL + ES at submaximal intensity contribute to positive effects, similar to those of VOL intense trainings (Wahl et al., 2014) provided that the training period is sufficiently long e.g., more than 4 weeks (Mathes et al., 2017).

From a motor output viewpoint, other authors reported that at submaximal intensity, VOL + ES would be also more efficient than VOL (Valli et al., 2002). They indeed showed that the superimposition of ES onto submaximal contractions (60% of maximal voluntary contraction) induced better strength gains than the same exercise performed without ES superimposition. Theses authors hypothesized that the superimposition of ES with submaximal contractions induced a neurogenic facilitatory effect enabling greater strength development thanks to the recruitment of supplementary muscle fibers. This type of training would be relevant not only for the ipsilateral limb but also for the contralateral limb. Indeed, Bezerra et al. (2009) observed that VOL + ES would cause additional training effects and greater cross-education compared with VOL training, because it would activate the same neural pathways that are used normally in voluntary exercise, with additional afferent inputs (centrally integrated) provoked by the electrostimulation. The review article by Frazer et al. (2018) linked to neural adaptations as part of the cross-education would reinforce this assumption.

Moreover, the quality of a training program depends on its intensity (knowing that the quantity of a training program depends on its amount). It is well-known that the intensity is fundamental in order to improve motor performance. However, it is not always possible to constantly train sportsmen at high intensity because they would risk overtraining and chronic fatigue (Lehmann et al., 1992; Anish, 2005; Purvis et al., 2010). Hence, the intensity should be regularly reduced to avoid the harmful consequences of excess stimulation of the CNS (Kellmann, 2010; Schaun et al., 2018). Based on this data, in order to apply a certain intensity, regularly or occasionally,

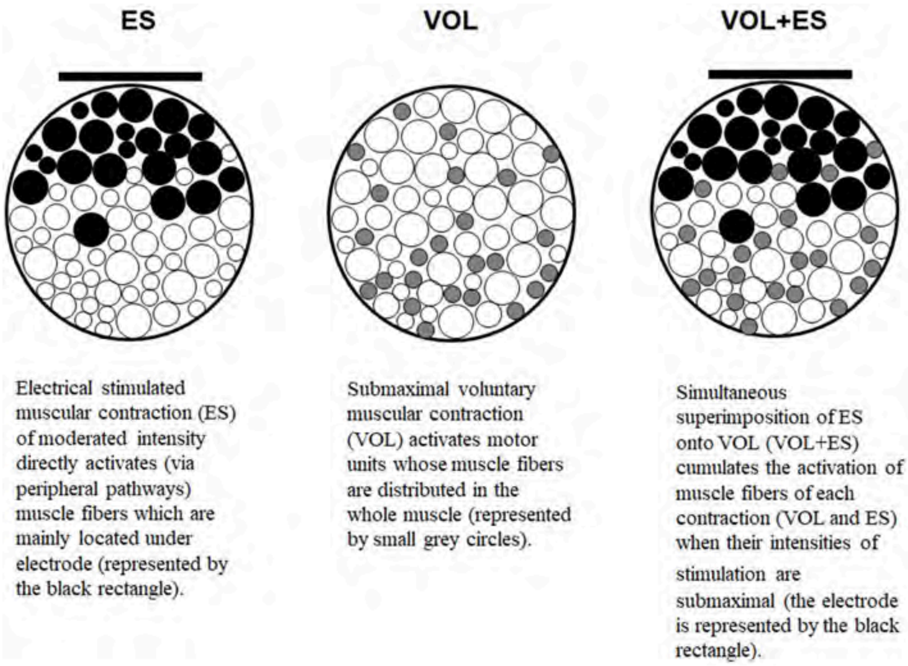

FIGURE 1 | When VOL and ES are applied in submaximal condition (i.e., submaximal intensity), the superimposition of ES onto VOL enables a greater muscle fibers recruitment than the completion of VOL or ES alone.

by limiting the involvement of the CNS (i.e., central factors) while maintaining a strong stimulation of motor muscles (i.e., peripheral factors), the superimposition of ES onto VOL can be used as part of training aiming the improvement/maintaining of muscle strength or endurance. Indeed, even if the ES exercise affects the CNS (i.e., corticospinal excitability) in acute application (Chaubet et al., 2013; Kotan et al., 2015) a VOL + ES fatiguing exercise impaired motor output (e.g., muscle strength) and motor control (e.g., postural control) less than did a VOL fatiguing exercise (Paillard et al., 2010). These authors suggested that the contribution of VOL + ES would limit the changes in muscle activation and then the central fatigue during a fatiguing exercise performed with submaximal contraction. In practice, besides its beneficial effects generating greater physiological adaptations compared to VOL, VOL + ES may limit muscle fatigue in acute application which may reduce the risk of overtraining in chronic application.

VOL + ES would present few if any advantage as part of motor/sport performance when it is applied at maximal intensity. In return, at submaximal intensity, VOL + ES could constitute an interesting and complementary training technique to traditional training in terms of improvement of motor/sport performance as well as reduction of residual fatigue. Other works should be achieved in order to confirm or invalidate these hypotheses.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of Interest Statement: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 13 November 2018
doi: 10.3389/fphys.2018.01576

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Whole-Body Electromyostimulation Improves Performance-Related Parameters in Runners

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The aim of this study was to study the effects of a 6-session (one per week) WB-EMS training intervention on maximum oxygen uptake, aerobic and gas exchange thresholds, running economy, and muscular power in male recreational runners. Twelve men were randomized into WB-EMS intervention (n = 6; 27.0 ± 7.5 years; 70.1 ± 11.1 kg; 1.75 ± 0.5 m) or control (n = 6; 27.0 ± 6.1 years; 73.6 ± 3.4 kg; 1.77 ± 0.3 m). The WB-EMS group reduced the running training frequency to one per week and followed one WB-EMS training session per week during 6 weeks. Participants in the control group maintained their usual running endurance training. Each participant completed four assessments: physiological parameters [(i) VO_2max, aerobic and gas exchange threshold values, and (ii) running economy at two intensities], muscular power (vertical jump), and anthropometric parameters both at baseline and after the intervention. Participants in the WB-EMS group improved VO_2max, aerobic and gas exchange threshold values, running economy, and vertical jump (p < 0.05) compared to the control group. There, WB-EMS seems to be an effective training methodology leading to improvements in performance during endurance training volume reduction in male recreational runners.

Keywords: WB-EMS, VO_2max, running economy, detraining, recreational runners, endurance

OPEN ACCESS

Edited by:
Wolfgang Kemmler, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany

Reviewed by:
Pedro Jiménez Reyes, Universidad Rey Juan Carlos, Spain
Nicolas Wirtz, German Sport University Cologne, Germany

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *31 July 2018*
Accepted: *22 October 2018*
Published: *13 November 2018*

Citation:
Amaro-Gahete FJ, De-la-O A, Sanchez-Delgado G, Robles-Gonzalez L, Jurado-Fasoli L, Ruiz JR and Gutierrez A (2018) Whole-Body Electromyostimulation Improves Performance-Related Parameters in Runners. Front. Physiol. 9:1576. doi: 10.3389/fphys.2018.01576

INTRODUCTION

Long-distance running performance depends on the interaction of physiological, biomechanical, and psychological factors (Bassett and Howley, 2000). Physiological attributes include (i) high cardiac output and high rate of oxygen availability and delivery to working muscles reflected on maximum oxygen consumption (VO_2max) and dependent of muscle capillary density, stroke volume, maximal heart rate, and hemoglobin content; (ii) capacity to sustain a high VO_2 fraction for long periods of time [i.e., ventilatory threshold 1 (VT1) and ventilatory threshold 2 (VT2), which depend on aerobic enzyme activity, and distribution of power output]; (iii) capacity to produce movement with the minimum energy cost [i.e., running economy (RE), which depends on the percentage of slow twitch muscle fibers, anthropometry, and elasticity] (Bassett and Howley, 2000; Foster and Lucia, 2007; Joyner and Coyle, 2008); and (iv) capacity to develop muscular power (Nuhr et al., 2003).

Detraining has been characterized as a partial loss of training-induced physiological and performance adaptations, as a consequence of various weeks of training cessation (Maldonado-Martín et al., 2016). However, detraining periods are frequent and, in many cases, uncontrollable in most sport disciplines (injuries, transition periods, discharge micro-cycle, etc.). It has been shown that detraining periods produce several decrements in VO_2max after 3 and 8 weeks (7% and 16%, respectively) (Costill et al., 1985; Mujika and Padilla, 2001). Therefore, it is necessary to seek for other alternatives to prevent or reduce the large decreases in physiological and performance-related parameters induced by training cessation (Mujika and Padilla, 2001; Berryman et al., 2018).

Strength training has emerged as an effective strategy to improve aerobic running performance (Mujika, 2017; Berryman et al., 2018). Although local electromyostimulation training seems an alternative to traditional strength training (Filipovic et al., 2012), there are no studies that evaluate its effects on physiological parameters related physical fitness in recreational runners.

Whole-body electromyostimulation (WB-EMS) is becoming increasingly popular as a novel training technology. While local electromyostimulation produces an external stimulation of single specific muscle groups, WB-EMS is able to simultaneously stimulate up to 14–18 regions or 8–12 different muscle groups with up to 2.800 cm^2 electrode area (Filipovic et al., 2015). Positive effects of WB-EMS on health biomarker parameters have been shown. WB-EMS improves body composition in elderly women (≥60 years) with sarcopenic obesity or at risk of sarcopenia (Kemmler et al., 2014, 2016c), in postmenopausal (Kemmler et al., 2010) and in healthy untrained middle-aged men (Kemmler et al., 2016b). Secondly, WB-EMS increases resting metabolic rate in postmenopausal women (Kemmler et al., 2010), and increases energy expenditure during exercise in moderately trained men (Kemmler et al., 2012). WB-EMS also improves strength levels in elite football players (Filipovic et al., 2016), in postmenopausal women (Kemmler et al., 2010), and in healthy untrained middle-aged men (Kemmler et al., 2016b), as well as bone mineral density in osteopenic women (>70 years) (Von Stengel et al., 2015). Finally, WB-EMS training seems to improve human red blood cell deformability in elite football players (Filipovic et al., 2015). Whether WB-EMS is able to improve running performance parameters is unknown, and whether it is able to prevent or reduce performance-related detraining after a period of training volume reduction remains to be investigated. However, considering that previous studies have demonstrated that WB-EMS can enhance muscular strength (Kemmler et al., 2010, 2014; Filipovic et al., 2016) and body composition (Kemmler et al., 2010, 2014, 2016b,c) by an increment of total muscle contraction during a training session, and that the development of muscular strength and body composition are related to endurance performance (Mujika, 2017; Berryman et al., 2018), it seems plausible that a well-designed WB-EMS training program can induce an improvement of endurance performance-related parameters. A possible physiological explanation that support this idea could be that the extra activation produced by WB-EMS may induce better neural function, peripheral changes such as a shift in muscle-fiber distribution (from fast twitch type IIb toward fatigue-resistant type IIa) and increases in muscle–tendon stiffness improving endurance performance.

To note, most of the intervention programs applied in scientific studies using WB-EMS consisted of a set of non-functional exercise tasks (i.e., not considering the motor requirements of specific sport or functional movements). Moreover, these programs did not modify electrical or training parameters across sessions. This lack of stimuli variation could lead to a decrease in training efficiency (Harries et al., 2015), and poor sport performance (Kiely, 2012). Thus, there is a need to study whether a WB-EMS intervention based on functional exercises (considering the motor requirements of specific sport) and with electrical parameters following a periodization improves running performance.

The aim of this study was to determine the effects of a 6 weeks (once session per week) WB-EMS training program on VO_2max, VT1, VT2, RE, and vertical jump in recreational runners, while participants reduced the running frequency training to once per week. Our hypothesis, is that WB-EMS training program could keep and even improve running performance despite a relative running frequency training reduction.

MATERIALS AND METHODS

Experimental Approach

The present study is part of a parallel randomized controlled trial that followed the CONSORT statements (ClinicalTrials.gov ID: NCT03425981). The first part of this project that studied the effects of a periodized and functional WB-EMS training on VO_2max, VT1, VT2, RE, and vertical jump in runners compared with a traditional WB-EMS was published recently (Amaro-Gahete et al., 2018). The present study investigated the effects of the periodized and functional WB-EMS training modality on running performance with a control group. Participants in the WB-EMS group were instructed to reduce their running training program volume, whereas the CG continued with their running training in term of volume and intensity: two or three times per week (45–60 min per day) at an intensity of 60–70% heart rate reserve, which was controlled by heart rate monitor (Polar RS300X, POLAR, Kempele, Finland), and with 24–48 h of rest between sessions. Nevertheless, there is some overlap between the two publications with respect to participants and general methodology.

Participants

Fourteen healthy male recreational runners (26.6 years; BMI = 23.5 kg/m^2) participated in the study. Participants were frequent runners (running frequency of two to three times per week, at least 90–180 min/week) and none had received WB-EMS training. Two out of fourteen participants did not complete the study and were excluded from the analysis. Participants signed an informed consent to participate in the study and no ethical issues were raised in relation to the type of measurements to be performed in the study. The study was approved by the Human Research Ethics Committee of the University of Granada

(200/CEIH/2016) and complied with the ethical guidelines of the Declaration of Helsinki, last modified in 2013. Participants were instructed not to modify their nutrition habits.

WB-EMS Training Program

The WB-EMS device used (Miha Bodytec, Augsburg, Germany) allows to modify several electrical parameters: (i) frequency, defined as the number of electrical pulses per time unit. Several studies shown that slow and fast fibers are not selectively activated with local electromyostimulation at low or high frequencies, but it is well known that it preferentially recruits fast versus slow motor units independently of the frequency applied (Gregory and Bickel, 2005), (ii) impulse width, which could influence the intensity of muscle contraction when combined with other stimulation parameters in the recommended range (Filipovic et al., 2012; Amaro-Gahete et al., 2017); (iii) impulse intensity, which was adjusted (at the subject's maximum tolerance levels) because of the increasing tolerability of the current intensity, following the guided and supervised low-intensity resistance protocols recently described (Kemmler et al., 2016a) every 3–5 min in close cooperation with the participants (Kemmler et al., 2010, 2012, 2014, 2016b,c; Kemmler and von Stengel, 2013; Von Stengel et al., 2015); and (iv) duty cycle, which is defined as the ratio between time receiving electrical stimuli and the total cycle time (in relation to the frequency selected, as high duty cycle need to be used with low frequencies to be feasible) (Filipovic et al., 2012; Amaro-Gahete et al., 2017).

The WB-EMS equipment enables the simultaneous activation of sixteen different muscle groups (e.g., upper legs, upper arms, gluteals, abdomen, chest, lower back, upper back, shoulder; total size of electrodes: at least 2,800 cm^2). The WB-EMS training program consisted of six WB-EMS training sessions (one per week) and six running training sessions (also one per week). All WB-EMS training sessions were short (<20 min) and a high intensity training approach was applied. Participants went through a familiarization session (prior to the exercise program) aiming to learn movement patterns (i.e., proper techniques of the exercises) and adapt to the electric stimuli. Electrical parameters (frequency, impulse intensity, and duty cycle), volume (training session time and work-recovery time), and perceived intensity (RPE) were gradually increased along the 6 weeks of intervention. Despite several reviews have provided information about efficacy ranges of most common electrical parameters in local electromyostimulation (Gregory and Bickel, 2005; Maffiuletti, 2010; Filipovic et al., 2011), the rationale of our periodization was based on the principle of progression, because it is not well known which are the best specific values of each electrical parameter in WB-EMS training for improving running performance. Participants were asked to report the intensity of the electric impulse training and the perceived intensity by using the RPE scale (Borg, 1982).

Running training sessions consisted in 20 min running at two different intensities; 10 min at VT1 speed and 10 min at 90% of VT2 speed, and these running sessions were also performed by the control group as a part of its running training volume per week. All WB-EMS sessions were supervised by

TABLE 1 | Electric parameters description in WB-EMS sessions (periodization).

WB-EMS/SESSION	1				2				3				4				5				6			
	W	**S**	**HP**	**HT**	**W**	**S**	**HP**	**HT**	**W**	**S**	**HP**	**HT**	**W**	**S**	**HP**	**HT**	**W**	**S**	**HP**	**HT**	**W**	**S**	**HP**	**HT**
Total duration (min)	2	6	2	2	4	6	3	3	4	8	3	3	4	8	4	4	4	8	4	4	4	8	4	4
Frequency (Hz)	12	55	60	20	12	65	70	25	12	75	80	35	12	85	90	40	12	85	90	40	12	85	90	40
Impulse width (µs)	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350
RPE impulse intensity (6–20)	10	12	13	13	10	12	13	13	10	14	15	15	10	16	17	17	10	16	17	17	10	16	17	17
Duty cycle (%)	50 4:4	50 4:4	50 10:10	50 30:30	50 4:4	50 4:4	50 10:10	50 30:30	50 4:4	50 4:4	50 10:10	50 30:30	50 4:4	50 4:4	50 10:10	50 30:30	50 4:4	50 4:4	50 10:10	50 30:30	50 4:4	50 4:4	50 10:10	50 10:10

WB-EMS, whole-body electromyostimulation training; W, warm-up phase; S, strength phase; HP, high intensity interval power training phase; HT, high intensity interval training phase; RPE, rated perceived exertion; Min, minutes; Hz, hertz; µs, microseconds; mA, milliamps.

an experienced National Strength and Conditioning Association Certified Personal Trainer (NSCA-CPT).

This intervention program followed a within-day undulating periodization model. The training sessions were divided into four parts: warm up (phase A), strength training part (phase B), high intensity interval power training part (phase C), and high intensity interval training part (phase D). In all cases, participants only did movements when receiving electrical impulse. Electrical parameters were modified throughout different parts of the training program and throughout the session (see **Table 1**). A circuit training methodology was applied (with no rest between exercises) in all phases and no external load was used. In phase A, participants performed 7–10 repetitions (one set) of three exercises (e.g., ½ squat and arm curl); both concentric and eccentric phases lasted 2 s each in every repetition. In phase B, participants performed one to two sets of 5–10 repetitions of six exercises (e.g., Bulgarian squat and military press); concentric phase lasted one second and eccentric phase duration was three seconds. In phase C, participants performed one set of eight exercises (e.g., climber); they were instructed to do as many repetitions as possible in 10 s with a 10-s rest between exercises. In phase D, participants did one to two interval sets running on a treadmill with two different intensities: moderate intensity (65% VO_2max speed, 30¨) and high intensity (>85% VO_2max speed, 30¨). Specific exercises of each training session have been largely described in a previous study (Amaro-Gahete et al., 2018).

Assessments of Dependent Variables

Before and after the intervention, participants were examined during 2 days. On day 1, an anthropometric assessment and a maximal treadmill exercise test were performed; on day 2, a vertical jump test and a running economy test were conducted (**Figure 1**). Assessments were performed at the same time of day (midmorning) to avoid diurnal variation in performance and changes in laboratory conditions (19–22°C temperature; 45–55% relative humidity). Subjects were asked to consume their habitual diet and to avoid alcohol, caffeine, and vigorous-intensity exercise in the 48 h prior to assessments days. Day 1 and day 2 were separated by 48 h.

Anthropometry

Body mass was determined with an accuracy of 100 g on a SECA scale (SECA, Hamburg, Germany) and height was determined with an accuracy of 0.100 cm with a SECA stadiometer (SECA, Hamburg, Germany); and body mass index was calculated (kg/m^2).

Maximal Oxygen Consumption

Maximal oxygen consumption was assessed using a maximum treadmill (H/P/Cosmos Pulsar treadmill, H/P/Cosmos Sport and Medical GMBH, Germany) exercise test with a progressive incremental protocol that has been extensively used and validated (Machado et al., 2013). In brief, after a warm-up consisting in walking at 5 km/h for 3 min, protocol started with an initial speed of 8 km/h, which was increased 1 km/h every minute until participants reached their volitional exhaustion. Thereafter, participants underwent a cooling-down period (4 km/h during 5 min). O_2 uptake and CO_2 production were measured with a gas analyzer (Oxycon Pro; Jaeger, Höchberg, Germany). The gas analyzer was calibrated with a known gas mixture (0% O_2 and 5.5% CO_2) and environmental air (20.9% O_2 and 0.03% CO_2) immediately before each test. Participants were strongly encouraged to invest maximum effort consistently across assessments. Participants were previously familiarized with the 6–20 Borg scale (Borg, 1982), which was used to measure the RPE during the last 15 s of each stage and at exhaustion. Heart rate (HR) was recorded every 5 s (Polar RS300, Kempele, Finland) and maximum heart rate (HRmax) was defined as the highest recorded HR value (Tanaka et al., 2001). We also registered respiratory, RPE, and heart rate parameters during cooling-down period. Serum lactate was measured by a Lactate Pro analyzer (Fact Canada, Quesnel, BC, Canada) 3 min after the volitional exhaustion was reached. The electrocardiogram was continuously monitored. Gas exchange data was averaged each 10 s and was downloaded for later analysis. Poole and Jones

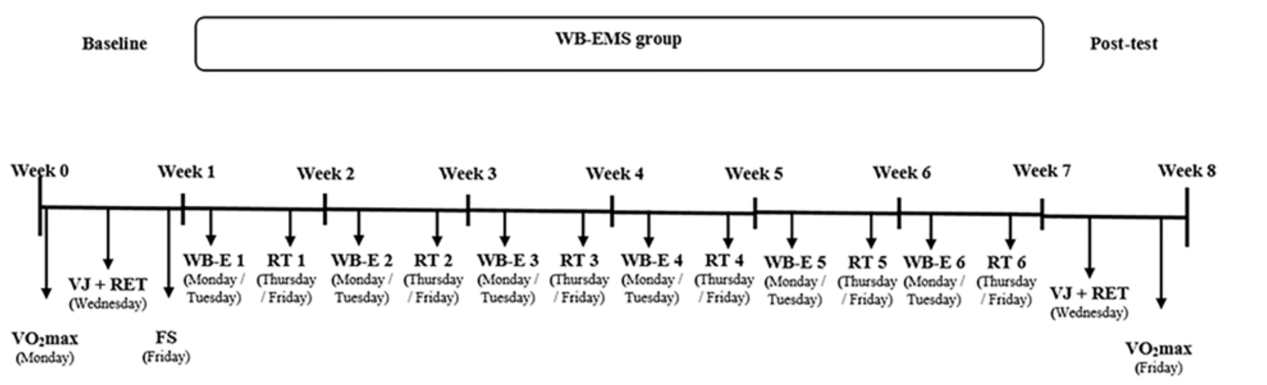

FIGURE 1 | Experimental timeline: Testing period in week 0 and week 7, training and running economy from week 1 to week 6. WB-EMS, whole-body electromyostimulation; VO_2max, maximal treadmill exercise test; VJ, vertical jump test; RET, running economy test; FS, familiarization session; WB-E, whole-body electromyostimulation training session; RT, running training session.

(2017) recommended to check VO_2max plateau with a constant work rate test performed at 110% of the work rate achieved after ramp protocol test. However, we decided not to include it because our participant were recreational runners and this validation is important specially in sedentary people or patients (Poole and Jones, 2017).

Ventilatory Thresholds

VT1 and VT2 were estimated from gas exchange data through different respiratory variables: minute ventilation (VE) and equivalents for oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2) by two independent researchers (FAG and AGS). A third researcher opinion was sought when they disagreed (AOP). VT1 was determined at the first point where an increase in VE/VO_2 with no increase in VE/VCO_2 and the departure from linearity of VE occurred (Lucía et al., 2000). VT2 was determined at the first point where an increase in both the VE/VO_2 and VE/VCO_2 occurred (Lucía et al., 2000). Speed at VT1 and VT2 was determined and VO_2max percentage in VT1 and VT2 were also calculated.

Running Economy

Running economy was determined during a treadmill test following a specific protocol used in previous studies (Foster and Lucia, 2007; Shaw et al., 2014). The treadmill test consisted of two 10-min stages at two different intensities. The two stages were performed at the speed where VT1 and the 90% of VT2 were reached in the pre-intervention maximum treadmill exercise test. The first 2 min of each stage were discarded. RE (oxygen cost of running a kilometer at a specific velocity) was calculated using the following equation: VO_2 (ml/kg/min)/[speed (km/h)/60] (Foster and Lucia, 2007; Shaw et al., 2014).

Muscular Power

Vertical jump performance was assessed using the countermovement jump (CMJ) and Abalakov jump (ABJ) tests. Jumping height was calculated from flight time using kinematic equations (Lehance et al., 2005) estimated by Ergo Jump Bosco System® (Globus, Treviso, Italy). Before carrying out the tests, a standardized warm-up was performed which included 5 min run at 50% of heart rate reserve, mobility and muscle activation exercises.

To perform the CMJ, participants were instructed to start in a standing position without arm swing; they performed a 2-leg CMJ consisting in a fast-downward movement to a freely chosen angle, immediately followed by a fast-maximal vertical thrust. Any jump that was perceived to deviate from the required instructions was repeated. Two trials separated by 1 min of passive recovery were performed. The highest jump was considered for further analysis. For the ABJ, participants did the same actions than CMJ, but including arm swing.

Statistical Analyses

All outcome variables were checked for normality with a graphical test (QQ-Plots) and results expressed as mean and SD. Baseline and post intervention data were compared using Student's paired t-test. One-way analysis of covariance (ANCOVA) was used to examine the effect of treatment group (fixed factor) on performance-related parameters. Multiple comparisons were adjusted according to Bonferroni. We conducted all statistical analyses using SPSS Statistics (version 20, IBM, Ehningen, Germany) software, setting level of significance at $p < 0.05$.

RESULTS

Participants completed 95.83% training sessions in WB-EMS. No WB-EMS related adverse effects were reported by any participant. Baseline characteristics, post-intervention values, and mean change of study performance-related variables and body composition parameters in WB-EMS and control groups are listed in **Table 2**. There was no difference between groups before the intervention program. The impulse intensity reported by the participants for each session (measured by RPE) was similar to the impulse intensity pre-established (mean difference ± SD, 0.84 ± 0.24). This fact confirmed that participants of WB-EMS group adhered to the protocol designed in term of impulse intensity. Detailed information of the training performed by control group during the intervention study is listed in **Table 3**.

Figure 2 shows changes (post–pre) on maximal performance-related parameters by group. Student's paired t-test showed no statistical changes in absolute values of VO_2max in WB-EMS and CG, but clinically relevant in WB-EMS (104.01 ± 41.22 ml/kg/min, $P = 0.082$) (**Figure 2A**). However, relative values of VO_2max significantly increased in WB-EMS (2.79 ± 0.89 ml/kg/min, $P = 0.001$), while no significant changes were registered in CG (−0.36 ± 1.08 ml/kg/min, $P = 0.821$) (**Figure 2C**). We observed significant changes when comparing WB-EMS with CG ($P < 0.001$) only in relative terms (**Figures 2B,D**).

ANCOVA revealed significant differences in maximal aerobic speed and VT2 speed when comparing changes of WB-EMS with CG ($P < 0.05$ for maximal aerobic speed and $P < 0.001$ for VT2 speed) (**Figures 2E,F**, **3E,F**) but no differences were found in VT1 speed ($P = 0.243$).

Student's paired t-test also showed significant increases in VO_2 at VT2 in WB-EMS ($p = 0.01$) (**Figure 3A**). When compared mean change in WB-EMS with CG, we also observed significant differences ($P < 0.001$) (**Figure 3B**). Changes of the VO_2max percentage reached in VT2 were also higher in WB-EMS when compared with CG ($P < 0.001$) (**Figures 3C,D**) and no changes were observed in VO_2max percentage reached in VT1 ($P = 0.517$).

Running economy at VT1 speed significantly increased in WB-EMS (−9.99 ± 3.80 ml/kg/min) compared with CG ($P < 0.001$; **Figures 4A,B**). Running economy at 90% of VT2 speed (**Figures 4C,D**) was also increased in WB-EMS (−15.38 ± 4.72 ml/kg/min, $P = 0.01$).

Muscular power, assessed by vertical jump (CMJ and ABJ), improved in WB-EMS (0.02 ± 0.02 m in CMJ and 0.03 ± 0.01 m in ABJ, respectively), while no changes were observed in CG

TABLE 2 | Descriptive parameters and changes in primary and secondary outcomes following a 6-week training program.

	WB-EMS (*n* = 6)			**CONTROL GROUP (*n* = 6)**		
	PRE	**POST**	***P*-value**	**PRE**	**POST**	***P*-value**
Body mass (kg)	70.1 ± 11.1	68.6 ± 11.0	0.023*	73.6 ± 2.1	74.1 ± 1.9	0.083
BMI (kg/m^2)	22.6 ± 2.8	22.2 ± 2.6	0.031*	23.4 ± 0.8	23.5 ± 0.7	0.060
VO_2max (ml/min)	3790.8 ± 812.4	3894.8 ± 802.4	0.082	3905.8 ± 480.2	3905.0 ± 412.6	0.983
VO_2max (ml/kg/min)	53.9 ± 5.3	56.7 ± 5.2	0.001**	53.1 ± 6.4	52.7 ± 5.6	0.442
VO_2 VT1	28.2 ± 3.4	29.6 ± 3.4	0.010**	27.0 ± 3.6	26.8 ± 3.4	0.399
VO_2 VT2	40.8 ± 4.6	43.7 ± 5.1	0.004**	40.6 ± 3.3	40.1 ± 3.7	0.325
%max VO_2 VT1	56.3 ± 8.5	58.8 ± 12.1	0.336	54.2 ± 5.4	54.9 ± 2.8	0.797
%max VO_2 VT2	84.2 ± 5.4	87.2 ± 7.1	<0.001***	85.2 ± 4.5	83.9 ± 3.5	0.101
SPEEDpeak (km/h)	16.7 ± 1.6	17.5 ± 1.8	0.041*	15.5 ± 1.6	15.5 ± 0.8	1.000
VT1s (km/h)	9.3 ± 1.2	10.3 ± 1.4	0.042*	8.3 ± 0.5	8.5 ± 0.5	0.611
VT2s (km/h)	14.0 ± 1.1	15.2 ± 0.8	0.001**	13.2 ± 1.2	13.2 ± 1.2	0.511
RE VT1 (ml/kg/km)	210.1 ± 12.0	202.4 ± 12.5	0.001**	220.5 ± 20.5	219.8 ± 19.6	0.465
RE VT2 (ml/kg/km)	248.5 ± 26.3	233.1 ± 22.6	0.001**	258.7 ± 21.2	260.1 ± 23.7	0.340
CMJ (m)	0.32 ± 0.06	0.33 ± 0.06	0.027*	0.32 ± 0.04	0.32 ± 0.03	0.967
ABJ (m)	0.36 ± 0.06	0.38 ± 0.06	0.001**	0.37 ± 0.01	0.37 ± 0.01	0.789

**$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, Student's paired t-test. BMI, body mass index; VO_2max, maximum oxygen uptake; %max VO_2 VT1, oxygen uptake percentage in ventilatory threshold 1 relative of maximum oxygen uptake; %max VO_2 VT2, oxygen uptake percentage in ventilatory threshold 2 relative of maximum oxygen uptake; VT1s, ventilatory threshold 1 speed; VT2s, ventilatory threshold 2 speed; CMJ, countermovement jump; ABJ, Abalakov jump; RE VT1, running economy ventilatory threshold 1; RE VT2, running economy at 90% of ventilatory threshold 2; WB-EMS, whole-body electromyostimulation group.*

TABLE 3 | Detailed information of the training performed by control group during the intervention study.

	Training session (session/weeks)	**Session duration (min)**	**Session intensity (%HRres)**
Week 1	2.7 ± 0.3	51.7 ± 6.2	64.8 ± 3.1
Week 2	2.6 ± 0.4	48.3 ± 8.0	61.4 ± 7.8
Week 3	2.7 ± 0.5	53.1 ± 4.6	62.8 ± 4.7
Week 4	2.5 ± 0.4	49.5 ± 5.2	66.7 ± 5.7
Week 5	2.8 ± 0.3	50.3 ± 7.3	67.1 ± 3.8
Week 6	2.4 ± 0.5	54.4 ± 5.7	65.7 ± 4.3

Results are expressed as mean ± SD. HRres, heart rate reserve.

(**Figures 5A,C**). Significant differences were found in CMJ and in ABJ changes between WB-EMS and CG ($P < 0.05$ and $P < 0.01$, respectively) (**Figures 5B,D**).

DISCUSSION

The major findings of this study were that 6 weeks of WB-EMS training (coupled to a reduction in running endurance training) improved: (i) VO_2max (5.2%); (ii) speed and VO_2max percentage at which VT2 is reached (Δ = 8.6% and Δ = 4.6%, respectively); (iii) running economy at speeds where VT1 and 90% of VT2 were reached (−3.3% and −6.2%, respectively); and (iv) muscular power in CMJ and ABJ (Δ = 4.4% and Δ = 8.4%, respectively). These results suggest that, in recreational runners, WB-EMS training increased performance in spite of the significant reductions in endurance training, provided that WB-EMS training program follows a specific periodization of electrical parameters and is based on functional exercises.

Maximal Oxygen Consumption

VO_2max is not only an excellent marker of running performance (Bassett and Howley, 2000) but also a marker of health and quality of life (Kodama et al., 2009; McKinney et al., 2016). Available evidence suggests that aerobic endurance training, at an intensity of at least 65% of VO_2max is an adequate stimulus to improve VO_2max in individuals with baseline aerobic capacities below 40 ml/kg/min (Swain and Franklin, 2002). This finding was confirmed by a meta-analysis which revealed that the training effect of this modality was greater for less fit runners and with longer duration interventions (Milanović et al., 2015). On the other hand, it has been shown that other fitness training programs, such as HIIT, improved cardiovascular fitness and other fitness parameters (strength, body composition, or physical appearance) applying lower volume but higher intensity training. For this reason, HIIT is suggested to be a viable alternative to the traditional approach of continuous endurance training (Milanović et al., 2015). There are no plausible studies examining the effect of WB-EMS on cardiorespiratory fitness. However, Nuhr et al. (2003) found that the chronic application of local electromyostimulation (10 weeks, 4 h per day, 7 days per week) at low frequency (15 Hz) of the knee extensor and hamstring muscles of both legs in healthy volunteers improve maximal aerobic-oxidative capacity and VO_2 at the anaerobic threshold 26% and 20%, respectively. In our study, we expected a decrease in VO_2max as a result of the reduction applied in running training session; paradoxically an increase of 5.2% in relative values of VO_2max was observed after 6 weeks of WB-EMS. This effect was similar to an intervention program consisting of 24 sessions of HIIT in people with cardiometabolic disorders (2–5 min at 80% VO_2max with active recovery at 60% VO_2max) and a bit smaller than the effects determined by 4 weeks of HIIT

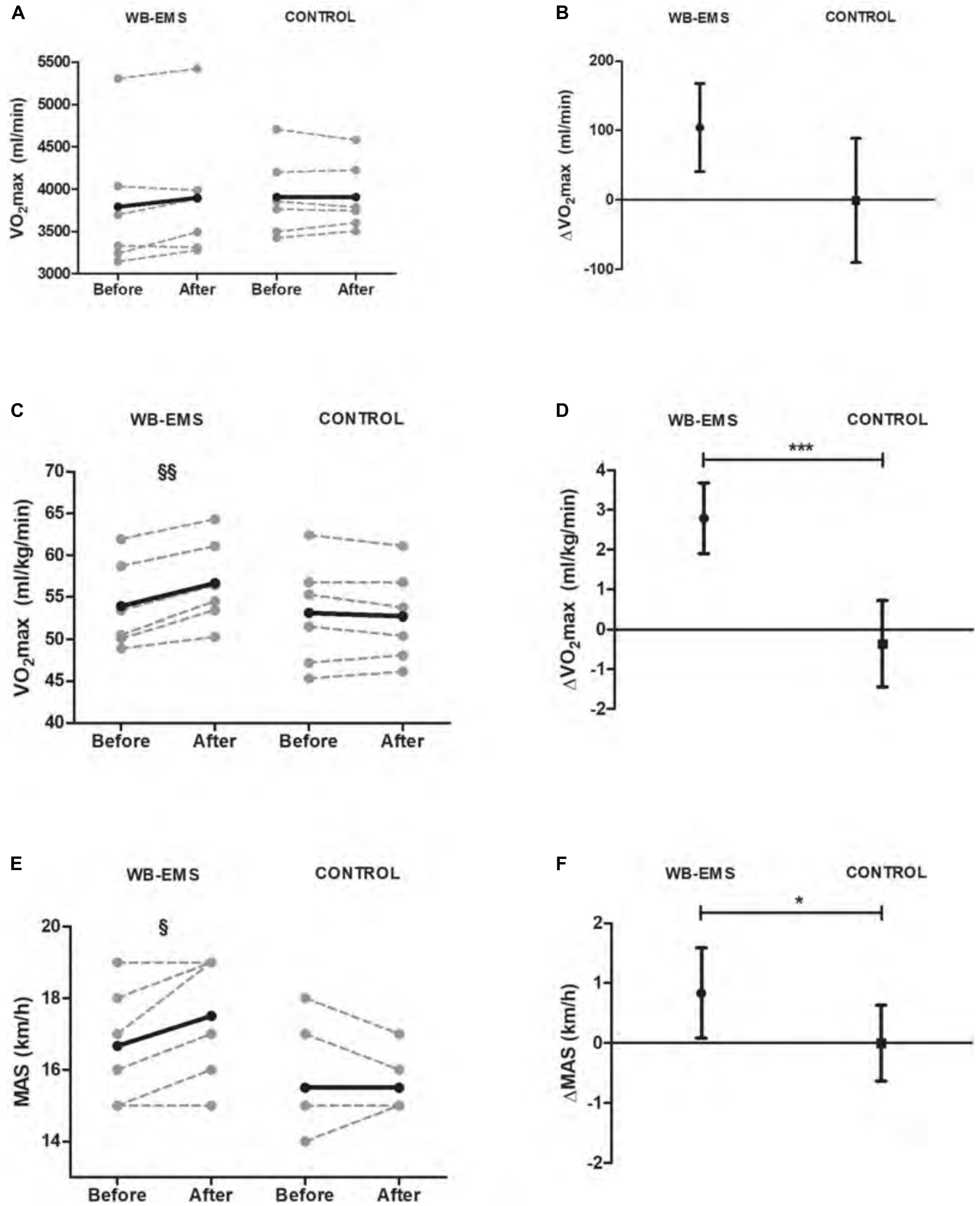

FIGURE 2 | Pre and post 6-week intervention values and mean change (95% CI) in maximal oxygen uptake (absolute and relative values), and maximal aerobic speed after the intervention program. **(A,B)** Maximal oxygen uptake [VO_2max (ml*min^{-1})]; **(C,D)** maximal oxygen uptake [VO_2max (ml*kg^{-1}*min^{-1})]; **(E,F)** maximal aerobic speed [MAS (km*h^{-1})]. § $P < 0.05$, §§ $P < 0.01$, §§§ $P < 0.001$ (analysis pre–post; Student's paired *t*-test). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (analysis between groups; ANCOVA).

(4 × 4-min interval training at 90–95% HRmax with 3 min of active resting periods at 70% HRmax between each interval) in adults that elevated VO_2max by 7.5% (Adamson et al., 2014).

Ventilatory Thresholds

VT1 and VT2 speed performance is associated with muscle respiratory capacity, and the ability to produce less lactate at a given running speed is a determinant of prolonged running performance. It has been suggested that the submaximal blood lactate response to exercise is associated with peripheral factors including muscle fiber type, capillary density, and mitochondrial volume density (Esfarjani and Laursen, 2007). In the present study, speed at which VT1 and VT2 are reached were increased in WB-EMS (8.9% and 8.3%, respectively) compared with baseline values. These results are slightly smaller than those obtained in a specific HIIT intervention [high-intensity running

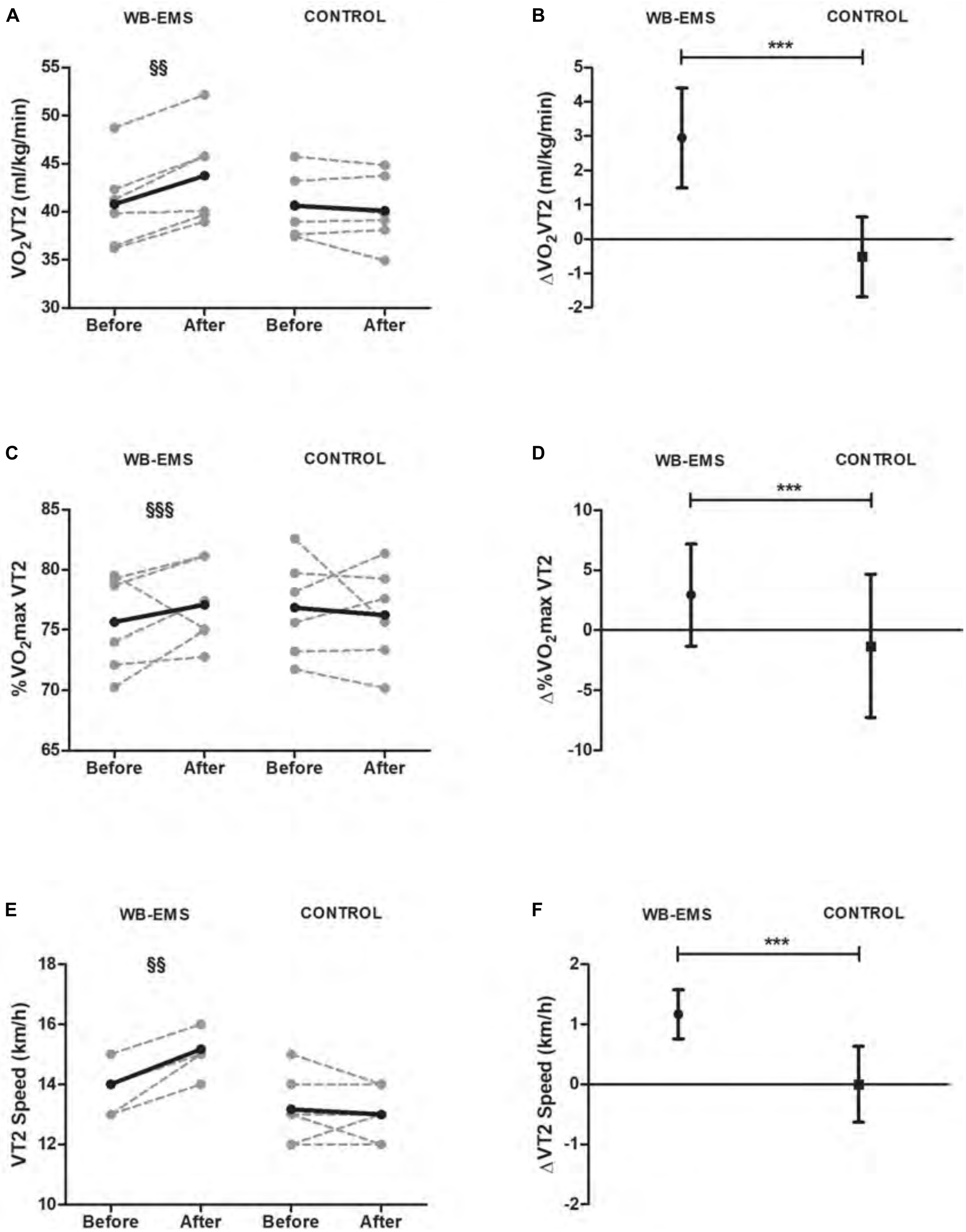

FIGURE 3 | Pre and post 6-week intervention values and mean change (95% CI) in oxygen uptake at ventilatory threshold 2, maximal oxygen uptake percentage in ventilatory threshold 2, and ventilatory threshold 2 speed. **(A,B)** Oxygen uptake at ventilatory threshold 2 [VO_2 VT2s (ml*kg^{-1}*min^{-1})]; **(C,D)** maximal oxygen uptake percentage in ventilatory threshold 2 [%VO_2max VT2]; **(E,F)** ventilatory threshold 2 speed [VT2 speed (km*h^{-1})]. $^{\$}$ $P < 0.05$, $^{\$\$}$ $P < 0.01$, $^{\$\$\$}$ $P < 0.001$ (analysis pre–post; Student's *t*-test). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (analysis between groups; ANCOVA).

bouts at 15.7 (0.7) km/h for 3.5 (0.7) min followed by low intensity recovery runs at 7.8 (0.3) km/h for 3.5 (0.7) min] in moderately trained young males (improvement of 11.7% in VT2 compared to baseline) (Esfarjani and Laursen, 2007). The increased mitochondrial enzyme content, which is associated with an increase in the rate of lipid utilization and consequently a decrease in rate of glycogen depletion and increased capillary density after endurance training, could also increase the exchange area and decrease the distance between the site of lactate production and the capillary wall, which could improve the

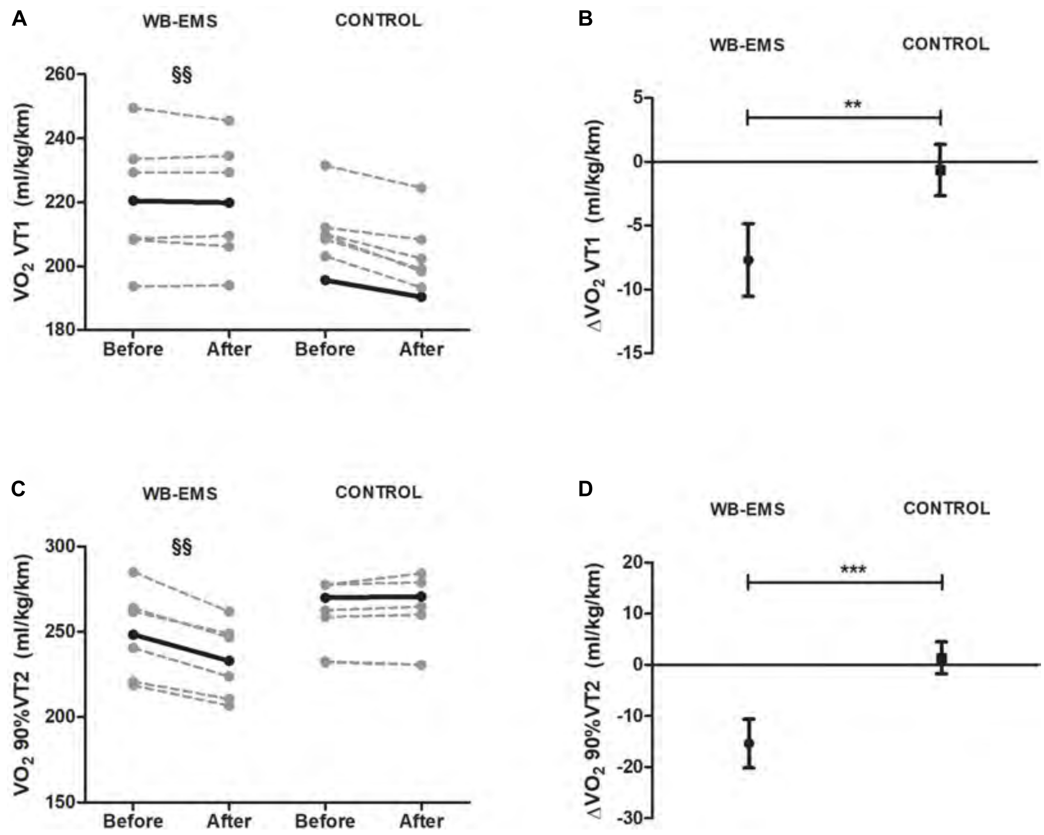

FIGURE 4 | Pre and post 6-week intervention values and mean change (95% CI) in running economy at ventilatory threshold 1 and 90% of ventilatory threshold 2 speed after the intervention program. **(A,B)** Running economy at ventilatory threshold 1 speed [VO_2 VT1s (ml/kg/km)]; **(C,D)** running economy at 90% of ventilatory threshold 2 speed [VO_2 VT2s (ml/kg/km)]. § $P < 0.05$, §§ $P < 0.01$, §§§ $P < 0.001$ (analysis pre–post; Student's paired *t*-test). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ (analysis between groups; ANCOVA).

lactate exchange ability (Esfarjani and Laursen, 2007). These are possible explanations for the increase of speed at which VT1 and VT2 is reached, after the application of WB-EMS training. Other possible reasons that could explain the increase of VT2 speed are the improvement of (i) running economy, (ii) VO_2max, and (iii) maximal oxygen uptake percentage in VT2. Our results suggest that if we examined WB-EMS parameters, we could remark that improvements in VT2 speed could be the consequence of the sum of the three previous factors.

Running Economy

Running economy refers to the oxygen uptake required at a given absolute exercise intensity (Barnes and Kilding, 2015). We have not found previous studies analysing the effects of WB-EMS in RE. However, it is well known that other training methodologies produce improvements in running economy. A traditional 14-week strength training protocol (six exercises, three to five sets, three to five reps, % 1RM) added to typical endurance training (concurrent training) produced a significant improvement in RE (5.6%) in middle-level young athletes (Guglielmo et al., 2009). In addition, explosive strength based on sprints (20–100 m) and plyometric training during 9 weeks also induced a significant improvement in RE (8.0%) comparing with a control group (no exercise) (Guglielmo et al., 2009). On the other hand, a HIIT protocol (3 min at 60–65% of maximal heart rate followed by four bouts alternating 4 min at 90–95% maximal heart rate and 3 min at 60–65% maximal heart rate, during 3 weeks) produced improvements in running economy at VT2 speed (8.8%) in healthy, physically active adults (Holmes et al., 2015). In our study, RE improved after the implementation of an intervention program with WB-EMS in two levels: VT1 speed and 90% of VT2 speed. The differences in both cases were a decrease of 3.3% VO_2 in the VT1 speed and 6.2% in the 90% of VT2 speed intensity. Possible reasons for these results could be: (i) improvement of lower limb coordination and co-activation of muscles, increased leg stiffness and decreased stance phase contact times, allowing a faster transition from the braking to the propulsive phase through elastic recoil; (ii) changes in the nervous system increasing the activation capacity of the working muscles, thus producing a greater net force with each stride; (iii) increasing motor unit recruitment and motor unit synchronization that could improve mechanical efficiency and motor recruitment patterns; (iv) that greater muscular strength following strength and electromyostimulation training could produce a delay in muscular fatigue, resulting in a smaller increase in oxygen uptake (increased RE) at any given speed

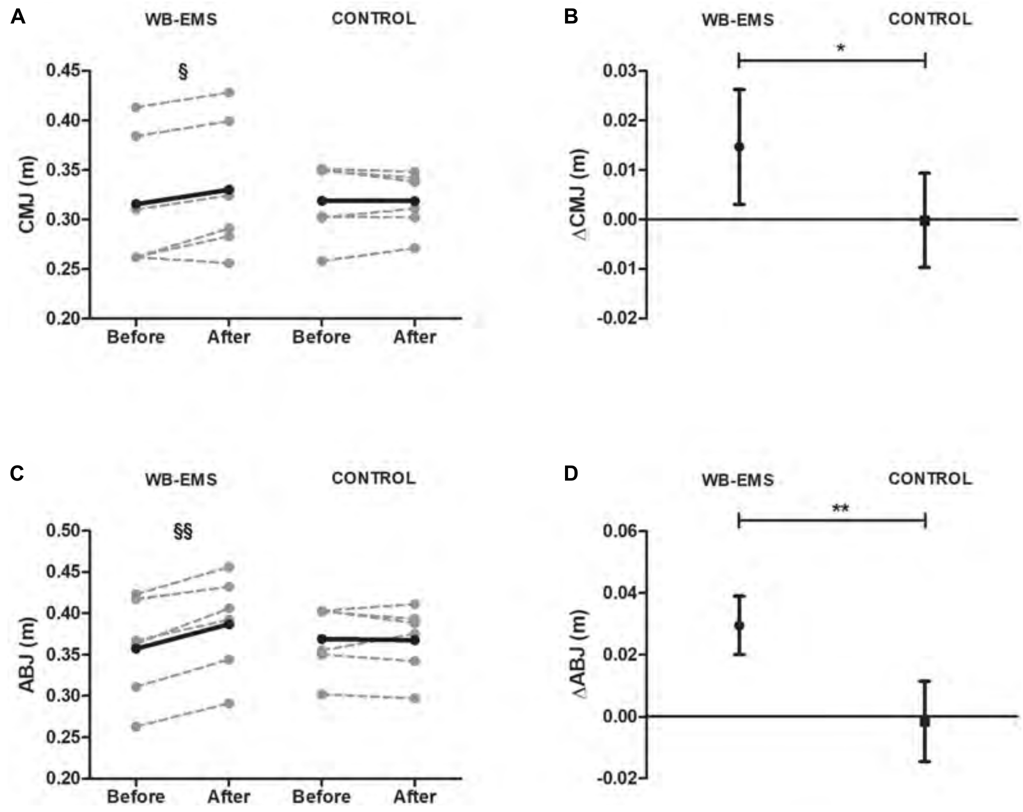

FIGURE 5 | Pre and post 6-week intervention values and mean change (95% CI) countermovement jump and Abalakov jump after the intervention program. **(A,B)** Countermovement jump [CMJ (m)], **(C,D)** Abalakov jump [ABJ (m)]. $^{\$}$ $P < 0.05$, $^{\$\$}$ $P < 0.01$, $^{\$\$\$}$ $P < 0.001$ (analysis pre–post; Student's paired *t*-test). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ (analysis between groups; ANCOVA).

during sustained running (Foster and Lucia, 2007; Barnes and Kilding, 2015).

Muscular Power

Muscular power is considered a critical element for carrying out daily activities and occupational tasks, as well as successful athletic performance and usually it is measured by vertical jump (Markovic, 2007). In our study, we analyzed the effects on two types of jump that allow differentiation between the elastic muscle component (CMJ) and coordinative jump component (ABJ). Both CMJ and ABJ improved after WB-EMS (4.4% and 8.4%, respectively). These results were similar to those showed in a meta-analysis, which concluded that plyometric training improved vertical jump performance, with CMJ improvements between 7 and 10.4% and ABJ improvements between 6.2 and 10.8% (Markovic, 2007). On the other hand, a 4-week local electromyostimulation in quadriceps combined with plyometric training program [16 sessions, four times per week: eight electromyostimulation training sessions (two each week) and eight plyometric training sessions (two each week)] increased CMJ (8.7%) (Herrero et al., 2006). The results of our study could be explained by neuromuscular adaptations, such as increased neural drive to the agonist muscles, improved intermuscular coordination, changes in the muscle–tendon mechanical-stiffness characteristics, changes in muscle size or architecture, and changes in single-fiber mechanics produced for the training protocol (de Villarreal et al., 2009). Of note, WB-EMS included a strength phase (thought to improve muscular power), HIIT which include plyometric exercises (thought to improve biomechanical parameters such us elastic muscular component), HIIT (thought to improve ventilatory and metabolic parameters), being all of them accompanied by WB-EMS (thought to improve neural activation of the trained muscles).

LIMITATIONS

Our study has some limitations: (i) lack of food intake control; (ii) we cannot extrapolate the study results to well-trained athletes or sedentary population because our sample only includes male recreational runners; (iii) the absence of an additional group which includes WB-EMS while maintaining previous endurance training prevents us from knowing if these effects are equal or better when the WB-EMS is added to the habitual running training; (iv) we cannot measure health biomarkers which confirm the absence of high values of creatine kinase levels and/or rhabdomyolysis, yet participants did not report muscle pain or fatigue; (v) participants had no previous experience with WB-EMS training and we do not know whether these results extent to athletes with previous WB-EMS experience; (vi) the small sample size and therefore the low statistical power; (vii) the assignment of a WB-EMS effects in our study is difficult since we combined a variation of multiple stimuli (strength, power and HIIT training modalities); (viii) we did not use belts and cable to ensure speed actions like power-training. However, we strongly encouraged participants to perform each power action as fast as possible.

CONCLUSION

In conclusion, our results suggest that a 6-week WB-EMS training program (six training sessions) combined with a significant reduction in endurance training, improved VO_2max, VT1, VT2, RE, and vertical jump, which are related to running performance in recreational runners. Therefore, WB-EMS could be an effective training methodology to produce improvements in performance of recreational runners despite reductions in endurance training and to avoid detraining when aerobic training is reduced for certain reasons.

WB-EMS once per week combined with a relatively low volume of endurance training can be used to improve physiological performance attributes and muscular power capacities within a relatively short time period in male recreational runners. This study shows that a functional running structure of WB-EMS programming is able to improve VO_2max, VT1, VT2, RE, and vertical jump over a 6-week period. For optimal adaptation and development of endurance and muscular power qualities, WB-EMS sessions should be carefully programmed considering the load, volume, and intensity of other training sessions without WB-EMS. In addition, it could be interesting to evaluate whether a combined WB-EMS and other training program produce extra improvements when controlling for confounders variables (physical activity, nutrition, rest, etc.). Inasmuch, when training cessation are superimposed (muscle discomfort, injuries, environmental conditions, etc.), WB-EMS could be a feasible and effective training alternative to prevents not only detraining consequences, but even to increase performance. We do not know whether these results can be extended to elite athletes, since the scope of performance in these individuals are lower. However, the fact that the application of WB-EMS is a novel stimulus could derive in an increment of running performance of the same magnitude as in recreationally runners. Moreover, further studies are needed to examine the physiological mechanisms that produce these improvements, and to well-understand if the improvement of endurance performance-related parameters observed in our study, are dependent of the exercises selected, the electrical parameters, or their combination.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

AUTHOR CONTRIBUTIONS

FA-G, AD-l-O, LR-G, JR, and AG conceived and designed the study. FA-G, AD-l-O, LR-G, and AG designed the tests and did the intervention training. FA-G, GS-D, and JR elaborated the statistical section. FA-G drafted the manuscript. AG and JR revised the manuscript. All authors read and approved the final manuscript.

FUNDING

The study was supported by the Spanish Ministry of Education (FPU 13/04365, FPU14/04172, and FPU15/03960). The study was partially supported by the University of Granada, Plan Propio de Investigación 2016, Excellence actions: Units of Excellence; Unit of Excellence on Exercise and Health (UCEES). This study was also partially supported by Wiemspro, Spain.

ACKNOWLEDGMENTS

We would like to thank all the runners who participated in this study for their time and effort. We are grateful to Ms. Carmen Sainz Quinn for assistance with the English language, and to Manuel Castillo, and Alejandro Romero for constructive scientific discussions. This study is part of a Ph.D. Thesis conducted in the Biomedicine Doctoral Studies of the University of Granada, Spain.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 18 December 2018
doi: 10.3389/fphys.2018.01808

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Whole-Body Electromyostimulation Combined With Individualized Nutritional Support Improves Body Composition in Patients With Hematological Malignancies – A Pilot Study

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OPEN ACCESS

Edited by:
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Reviewed by:
Christoph Zinner, Hessische Hochschule für Polizei und Verwaltung, Germany
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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *09 October 2018*
Accepted: *30 November 2018*
Published: *18 December 2018*

Citation:
Schink K, Reljic D, Herrmann HJ, Meyer J, Mackensen A, Neurath MF and Zopf Y (2018) Whole-Body Electromyostimulation Combined With Individualized Nutritional Support Improves Body Composition in Patients With Hematological Malignancies – A Pilot Study. Front. Physiol. 9:1808. doi: 10.3389/fphys.2018.01808

Patients undergoing the complex treatment for hematological malignancies are exposed to a high physiological and psychological distress inducing fatigue and physical inactivity. In line with cancer-related metabolic changes patients are predisposed for skeletal muscle mass loss that leads to a functional decline, affects therapeutic success, and quality of life. Benefits of physical exercise and nutritional interventions on muscle maintenance are observed in solid cancer patients, but marginally investigated in patients with hematological cancer. We here studied the effects of a combined supportive exercise and nutrition intervention using whole-body electromyostimulation (WB-EMS) training and individualized nutritional support in patients actively treated for hematological malignancy. In a controlled pilot trial, 31 patients (67.7% male; 58.0 ± 16.7 years) with various hematological cancers were allocated to a control group (n = 9) receiving nutritional support of usual care regarding a high protein intake (>1.0 g/kg/d) or to a physical exercise group (n = 22) additionally performing WB-EMS training twice weekly for 12 weeks. Bodyweight and body composition assessed by bioelectrical impedance analysis were measured every 4 weeks. Physical function, blood parameters, quality of life and fatigue were assessed at baseline and after 12 weeks. No WB-EMS-related adverse effects occurred. Patients attending the exercise program presented a higher skeletal muscle mass than controls after 12-weeks (1.51 kg [0.41, 2.60]; p = 0.008). In contrast, patients of the control group showed a higher fat mass percentage than patients of the WB-EMS group (−4.46% [−7.15, −1.77]; p = 0.001) that was accompanied by an increase in serum triglycerides in contrast to a decrease in the WB-EMS group (change ± SD, control 36.3 ± 50.6 mg/dl; WB-EMS −31.8 ± 68.7 mg/dl; p = 0.064). No significant group differences for lower limb strength, quality of life, and fatigue were detected. However, compared to controls the WB-EMS group significantly improved in physical functioning indicated by a higher increase in the 6-min-walking distance (p = 0.046). A combined therapeutic intervention of WB-EMS and protein-rich nutritional support seems to be safe and effective in improving skeletal muscle mass and body composition in hematological cancer patients during active oncological treatment.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier NCT02293239.

Keywords: body composition, physical function, whole-body electromyostimulation, exercise, nutrition, skeletal muscle mass, hematological malignancies, cancer

INTRODUCTION

With an increasing trend, 40,000 newly diagnosed cases of malign hematological diseases were registered and accounted for approximately 19,000 deaths in Germany in 2013 (Robert-Koch-Institut, 2016). The main malignant neoplasms comprise leukemia, Hodgkin and Non-Hodgkin lymphoma and multiple myeloma. Treatment regimens for affected patients are complex involving high-dose chemotherapy and total-body irradiation probably before or followed by hematopoietic stem cell transplantation. Even though improved therapy modalities had increased the survival of the patients in the past years, adverse therapy effects are still responsible for many deaths in hematological patients (Copelan, 2006; Othus et al., 2014; Buckley et al., 2015). Side effects linked to the disease as well as therapy complications such as anemia, a high susceptibility for infections, fatigue or Graft-versus-Host-Disease (GvHD) lead to a decreased physical activity – especially in patients with a long inpatient treatment (Danaher et al., 2006; Morishita et al., 2012a; Wiskemann et al., 2014). As a consequence of physical inactivity, the catabolic effects of cytotoxic and immunosuppressive therapies, as well as the metabolic changes and myopathy induced by a long-term glucocorticoid treatment (Gupta and Gupta, 2013; Macedo et al., 2016), hematological cancer patients undergo unfavorable body composition changes during the active treatment period (Greenfield et al., 2014). While fat mass increases during and after the oncological therapy, muscle mass declines. Those alterations are hardly reversible into the pre-illness and pre-treatment status and may result in sarcopenic obesity that may predispose patients for other metabolic diseases in future (Morishita et al., 2012b; Orgel et al., 2016; Xiao et al., 2016). Treatment-associated muscle weakness also leads to functional declines that can be still observed in survivorship (Inaba et al., 2012; Hung et al., 2013). Muscle wasting and physical deconditioning thereby not only enhance symptoms of fatigue, but also substantially impair patients' quality of life, reduce therapy options and worsen prognosis (Danaher et al., 2006; Mosher et al., 2009; Morishita et al., 2012a,b; Lanic et al., 2014; Chu et al., 2017).

Adverse disease and treatment effects such as nausea, vomiting, diarrhea and mucositis can impair nutritional intake and are responsible for the high numbers of hematological patients that are at nutritional risk – particularly in patients who received stem cell transplantation (Liu et al., 2016). Thus, an adequate individual nutritional support is highly emphasized for hematological cancer patients as malnutrition could increase mortality (Calleja Fernandez et al., 2015).

Previous studies clearly suggest the feasibility of exercise intervention in hematological cancer patients to stabilize muscular status, body composition and improve physical activity (Liu et al., 2009). However, most studies were conducted as post-treatment rehabilitation interventions. A primary investigation of clinically relevant outcomes such as changes in skeletal muscle mass during treatment has been neglected so far. Treatment-related effects including fatigue and physical discomfort, but also bone lesions as a complication of multiple myeloma, may hinder actively treated patients to enter time-consuming and strenuous physical exercise programs. We therefore tested the feasibility of the innovative strength training method of whole-body electromyostimulation (WB-EMS) in hematological cancer patients undergoing treatment. The WB-EMS technology enables a simultaneous muscle contraction of all large muscle groups that is additionally supported by easy-to-perform dynamic exercises, as we described in detail previously (Schink et al., 2018). Observed benefits of a dual intervention of WB-EMS and individualized nutritional support on muscle mass in patients with advanced solid cancers (Schink et al., 2018), led us to the primary hypothesis that this combined approach is also feasible in hematological patients and may show better effects on stabilizing or even increasing skeletal muscle mass than a dietary support alone. Within this multimodal approach we also investigated the effect of the exercise and nutrition therapy on objective outcomes including bodyweight and body composition, physical functioning, hematological and blood chemistry parameters as well as on patient-reported quality of life and fatigue.

MATERIALS AND METHODS

Patients

Adult patients ($\geq$18 years) with confirmed diagnosis of a malignant hematological disease undergoing active treatment at initial evaluation were considered eligible for the study. This included patients with or without prior or subsequent hematopoietic stem cell transplantation (HSCT) and patients who were treated for acute GvHD as an adverse effect of HSCT. To enable the conduction of exercises patients had to display a Karnofsky performance status $\geq$60 at baseline.

Patients were excluded from study participation when they already participated in other nutritional or physical exercise trials and consumed anabolic drugs, recently. An study exclusion was also necessary if patients experienced acute cardio-vascular events, suffered from epilepsy, severe neurological diseases or skin lesions within the area of electrodes, underwent surgery in the last 3 months, presented acute vein thrombosis, a cardiac pace-maker or conductive implants or in case of pregnancy as those conditions would exclude a WB-EMS application and bioelectrical impedance analysis measurement (Schink et al., 2018).

The declaration of the written informed consent to participate was obtained from every patient before his inclusion into the study. The study was conducted according to the guidelines of the Declaration of Helsinki. The protocol of this study was approved by the ethics committee of the Friedrich–Alexander University Erlangen–Nürnberg (Reg.Nr.155_13B) and registered at clinicaltrials.gov (NCT02293239). Participants of the present trial were recruited from the Department of Medicine 5 – Haematology and Oncology at the University Hospital Erlangen during November 2013 and March 2017. All baseline and outcome assessments, the WB-EMS exercise program, dietary counseling and data collection were performed at the Department of Medicine 1 – Gastroenterology, Pneumology and Endocrinology, Hector-Center for Nutrition, Exercise and Sports at the University Hospital Erlangen.

Study Design

The pilot study was conducted as a two-armed prospective controlled clinical trial. After baseline assessment patients were either allocated to a physical exercise group regularly performing a WB-EMS training (WB-EMS group) or to a control group without any exercise intervention. Both groups received the same nutritional support during the study. Allocation to the study group was limited by the patients' ability to attend the exercise program twice weekly, as described previously (Schink et al., 2018). In case of inability due to logistical aspects, patients were allocated to the control group resulting in an approximately 2:1 partition favoring the WB-EMS group. For each patient the duration of the study intervention was 12 weeks. Patients and outcome assessing personnel were not blinded.

Dietary Support

The nutritional risk of the recruited study patients was assessed at baseline and documented by the nutritional risk screening (NRS-2002) (Kondrup et al., 2003). Patients who scored greater or equal three points were assumed to be at nutritional risk caused by low body mass index, decreased food intake and/or prior involuntary weight loss (Kondrup et al., 2003). The dietary support and monitoring of the nutritional intake by weekly 24 h-dietary records (Freiburger Ernährungsprotokoll; Nutri-Science GmbH, Freiburg) during the study have been described previously (Schink et al., 2018). Briefly, dietary intake was analyzed by Prodi®6 (Nutri-Science GmbH, Freiburg) and a certified dietician instructed/motivated patients by face-to-face conversation to achieve a daily protein intake of >1.0 g/kg and caloric intake of at least 25 kcal/kg bodyweight in regard to current dietary recommendations for patients with malignant diseases (Arends et al., 2015, 2016). As a precautionary measure, patients suffering from renal insufficiency or displaying high serum creatinine concentrations (women, >1.0 mg/dl; men, >1.2 mg/dl) were instructed not to exceed a daily protein intake of 1.0 g/kg in acute or 1.2 g/kg in chronic renal disease (Arends et al., 2016). Supplemental nutrition in form of protein/amino acid-rich oral supplements or parenteral nutrition (Olimel 5.7% E, Baxter Germany, Munich) was provided to patients with insufficient or impaired nutrient intake.

To assess the compliance to the dietary recommendations proportions of patients who achieved only a normal (<25 kcal/kg/d; ≤1.0 g/kg/d) or an increased (≥25 kcal/kg/d; >1.0 g/kg/d) protein and energy intake were calculated.

Physical Exercise Program

Study intervention included a physical exercise program in the form of a regular WB-EMS training over a period of 12 weeks. The conduction of the WB-EMS training and exercises were detailed described previously (Schink et al., 2018). Electrical muscle stimulation was applied by bipolar impulses at a frequency of 85 Hz and pulse width of 350 μs mediating a stimulation for 6 s followed by a 4 s stimulation rest. Here, muscles of the upper legs, upper arms, bottom, abdomen, chest, lower back, upper back, and latissimus dorsi have been stimulated. The supervised WB-EMS training was conducted twice a week for 20 min/session and comprised a sequence of light dynamic and easy-to-perform physical exercises that supported the activation of the mentioned muscle groups (Schink et al., 2018). WB-EMS equipment was purchased from Miha bodytec (Miha bodytec GmbH, Gersthofen).

Study Outcomes

Assessments

Demographic data were collected by an anamnesis questionnaire and medical records. Assessments of study outcomes on body composition were performed at baseline, in week 4, week 8 and at study end after 12 weeks of study intervention. Blood parameters, physical functioning and patient-reported quality of life and fatigue were assessed at baseline and study end.

The adherence of the patients to the WB-EMS training was registered by the supervising physiotherapists at each exercise session. Exercise adherence rate of the patients who completed the 12-week period of the study was calculated by the number of performed trainings from a total of 24 WB-EMS trainings.

Body Composition, Physical Function, and Quality of Life

The primary outcome was the change of skeletal muscle mass assessed by bioelectrical impedance analysis – BIA (seca mBCA 515; Seca GmbH & Co., KG, Hamburg) (Bosy-Westphal and Jensen, 2017). Secondary endpoints of bodyweight and body composition including fat mass percentage and phase angle were also assessed by BIA.

Physical functioning and endurance were assessed by the 6-min-walk test (Schmidt et al., 2013). Functioning and strength of the lower limbs was indirectly determined by the 30 s sit-to-stand (STS) test (Jones et al., 1999). Physical performance status was determined by Karnofsky-Index (Karnofsky and Burchenal, 1949).

Patient-reported quality of life was evaluated by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – C30 (EORTC QLQ-C30) (Aaronson et al., 1993). Here, a higher score in global health and functional scales indicate a better quality of life while high scores in symptom scales hint toward a higher symptomatic burden. An additional assessment of fatigue was done by the use of the Functional Assessment of Chronic Illness Therapy – Fatigue Scale that indicates less fatigue and better function by a higher score (13-item FACIT Fatigue Scale) (Lai et al., 2003).

Analysis of Blood Samples

Blood samples were collected at baseline and after 12 weeks of intervention by puncture of the arm vein or blood values were extracted from the documented routine blood sampling undertaken during the oncological treatment. The analysis of nutritional and inflammatory blood markers (normal values: C-reactive protein, CRP <5 mg/l; albumin 35–55 g/l; total protein 66–83 g/l; triglycerides 50–200 mg/dl; creatinine 0.51–1.17 mg/dl; lactate dehydrogenase, LDH <250 U/l) and hematological parameters (leukocytes 4.4–11.3 $\times$ $10^3/\mu$l, thrombocytes 150–300 $\times$ $10^3/\mu$l, hematocrit 35–48%, hemoglobin 11.5–18.0 g/dl, erythrocytes 4.1–6.0 $\times$ $10^6/\mu$l) was carried out by the diagnostic laboratories of the University Hospital Erlangen.

Statistical Analysis

Descriptive data are presented as means $\pm$ standard deviations (SD) for continuous variables and count and percentages for categorical variables. Laboratory variables are expressed as median with range. Normal distribution of data was tested by Shapiro–Wilk test. Baseline differences between study groups were analyzed by Pearson's chi-squared test and Fisher's exact test, where appropriate, for categorical variables. Continuous variables were analyzed by independent-samples t-test, Welch-test or Mann–Whitney U-test, where appropriate. Similarly, comparisons between patients who completed and not completed the study were conducted.

To evaluate the effect of WB-EMS intervention on skeletal muscle mass, bodyweight, and body composition throughout the study course, linear mixed models (LMM) were generated. LMM allow the analysis of longitudinal data with missing samples that is common for clinical trials including serious ill patients with expected high dropout rates and thus follows the intent-to-treat approach (Chakraborty and Gu, 2009; West, 2009; Peters et al., 2012). The LMM were fitted for each outcome using a patient-specific random intercept. To control for baseline differences, the baseline value of each outcome was included in the models. Time and a time-group interaction to estimate the intervention effect on the study outcome over time were included as fixed effects. As part of a sensitivity analysis, we also assessed fixed effects adjusted for age, gender, diagnosis of the hematological malignancy and glucocorticoid intake. Results are presented as parameter estimates with 95% confidence intervals (95% CI). To assess an association between protein intake and changes in skeletal muscle mass a Pearson correlation analysis was carried out for both study groups with patients presenting skeletal muscle mass data after 12 weeks. Secondary outcomes only assessed at baseline and after 12 weeks were analyzed for all patients with pre- and post-intervention data. Pre- to post-test changes were compared by the use of independent-samples t-test or Mann–Whitney U-test, where appropriate, and presented as mean $\pm$ SD.

Statistical analysis was conducted using SPSS version 21 (IBM SPSS Statistics, Ehningen, Germany) and Prism 7.00 (GraphPad Software Inc., La Jolla, CA, United States). Two-sided p-value <0.05 was considered as statistically significant. Due to the exploratory character of this pilot study, no correction for multiple testing was applied.

RESULTS

Participants

Baseline Characteristics

Thirty-one patients undergoing active treatment for acute myeloid leukemia (AML), Hodgkin lymphoma, Non-Hodgkin lymphoma (NHL), multiple myeloma and/or associated acute GvHD were recruited for the trial (**Figure 1**).

Participants' baseline characteristics are presented in **Table 1**. Study groups were well balanced in demographic and anthropometric baseline variables with a higher percentage of male participants in both study groups. No significant group differences between body composition parameters and functional status were observed at study entry. Patients of both groups showed a high mean body mass index ($>$25.0 kg/m^2) and 61.3% of all recruited patients were defined as overweight or obese regarding the WHO classification of the nutritional status (World Health Organization [WHO], 2000). The obese phenotype of the patients was underlined by a high fat mass percentage ($>$27.0% fat mass) and increased metabolic risk factors indicated by higher serum triglyceride concentrations ($>$170 mg/dl). Nevertheless, approximately two-third of the study patients in both groups were at nutritional risk (NRS score $\geq$3) due to decreased food intake or unintended disease- or treatment-related weight loss indicating the demand of nutritional support at baseline. However, only one patient of the control and three patients of the WB-EMS group had to be supported by artificial nutrition in addition to the support by nutritional counseling. Patients of both study groups reported comparable quality of life (p = 0.286) and fatigue severity (p = 0.284) at the beginning of the study. Disease characteristics including diagnosis and current oncological treatment of the hematological cancer were not significantly different at baseline except of a significantly lower median leukocyte count in the control group compared to the WB-EMS group. Approximately one-third of the study patients of each group exhibited osteolytic lesions as a consequence of myeloma bone marrow infiltration.

Nutritional Intake

During the study the nutritional goals regarding a high daily caloric ($\geq$25 kcal/kg) and protein ($>$1.0 g/kg) intake were

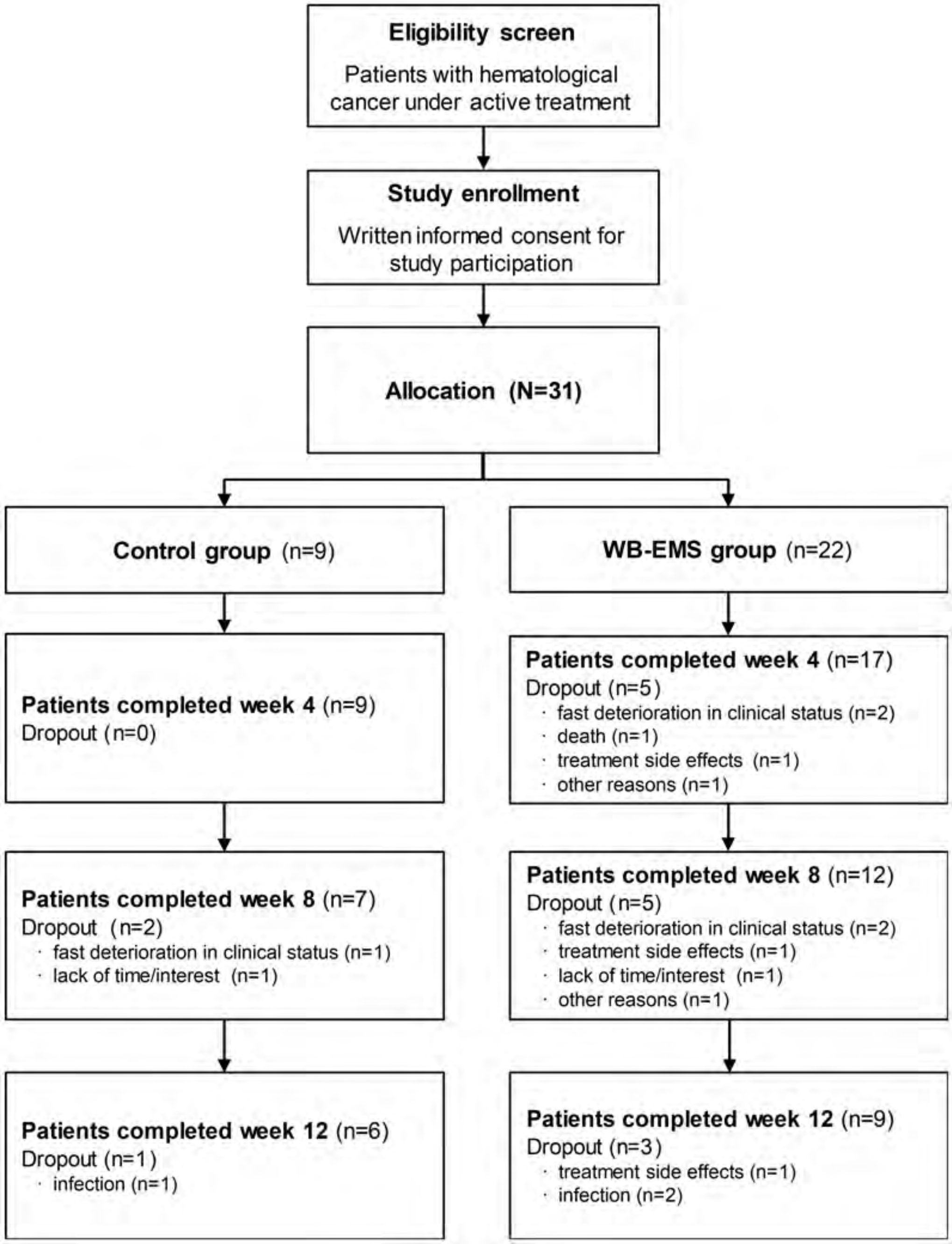

FIGURE 1 | Patient flowchart. The flowchart shows the number of the allocated patients and the number of patients who dropped out during study course with dropout reasons and the number of patients who completed the whole intervention period of 12 weeks. During the study, body composition analysis was missed by 1 patient of the WB-EMS group at week 4 and 1 control and 2 WB-EMS patients at week 8. WB-EMS, whole-body electromyostimulation.

achieved by approximately 90% of all recruited patients of the control and the WB-EMS group (**Table 2**). Both study groups exceeded the minimum aimed dietary intake by a mean daily protein intake of 1.4 g/kg and a mean daily caloric intake more than 30 kcal/kg. Of note, two patients of the WB-EMS group and one control patient failed to document dietary intake and were therefore unavailable for the nutritional analysis.

Feasibility and Exercise Adherence

Patients' flow chart and dropout reasons are presented in **Figure 1**. During the trial, 3 patients of the control and 13 patients of the WB-EMS group prematurely withdrew from the study leading to a dropout rate of 33.3% for the control and 59.1% for the WB-EMS group (p = 0.252). Reason for study dropout in the WB-EMS group was mainly due to treatment-related

TABLE 1 | Demographic and disease characteristics of the included patients.

Parameter	Control (*n* = 9)	WB-EMS (*n* = 22)	*p*-Value[a]
Gender			1.000
Male	6 (66.7)	15 (68.2)	
Female	3 (33.3)	7 (31.8)	
Mean age	57.2 ± 14.1	54.8 ± 17.9	0.881
Functional status			
Karnofsky-Index	73.3 ± 8.7	75.9 ± 11.4	0.548
6-min walking distance (m)	504.7 ± 66.1	494.0 ± 142.2	0.832
Sit-to-stand repetitions	12.7 ± 3.7	12.6 ± 5.1	0.953
Anthropometry			
BMI [kg/m^2][2]	25.8 ± 3.1	25.4 ± 4.1	0.810
Underweight (<18.5 kg/m^2)	0 (0.0)	2 (9.1)	0.479
Normal weight (18.5–24.9 kg/m^2)	4 (44.4)	6 (27.3)	
Overweight/Obesity (≥25.0 kg/m^2)	5 (55.6)	14 (63.6)	
Fat mass index (kg/m^2)	7.1 ± 2.1	7.4 ± 3.1	0.829
Fat free mass index [kg/m^2]	18.6 ± 2.1	18.3 ± 2.4	0.741
Body composition			
Skeletal muscle mass [kg]	25.7 ± 6.6	24.7 ± 6.3	0.704
Fat mass [%]	27.4 ± 6.1	27.6 ± 9.7	0.578
Hydration [%; ECW:ICW]	87.6 ± 15.1	86.6 ± 10.3	0.823
Phase angle [°]	4.4 ± 1.1	4.2 ± 0.9	0.625
Nutritional status			
Nutritional risk screening (NRS-2002)			1.000
<3	3 (33.3)	8 (36.4)	
≥3	6 (66.7)	14 (63.6)	
Weight loss [%]	5.2 ± 4.0	4.3 ± 4.5	0.334
≤5%	4 (44.4)	16 (72.7)	0.217
>5%	5 (55.6)	6 (27.3)	
Nutritional therapy			1.000
Only dietary counseling	8 (88.9)	19 (86.4)	
Oral supplementation	1 (11.1)	3 (13.6)	
Parenteral nutrition	0 (0.0)	0 (0.0)	
Quality of life			
EORTC QLQ-C30 global health	45.3 ± 16.5	54.5 ± 20.0	0.286
FACIT-fatigue scale	27.3 ± 10.4	32.6 ± 11.1	0.284
Disease characteristics			
Diagnosis			0.272
Acute myeloid leukemia	3 (33.3)	2 (9.1)	
Hodgkin lymphoma	2 (22.2)	3 (13.6)	
Non-Hodgkin-lymphoma	1 (11.1)	7 (31.8)	
Multiple myeloma	3 (33.3)	10 (45.5)	
Oncological treatment[1]			
Chemotherapy	7 (77.8)	9 (40.9)	0.113
Radiotherapy	1 (11.1)	2 (9.1)	1.000
Targeted/immunotherapy	6 (66.7)	15 (68.2)	1.000
Glucocorticoid intake	6 (66.7)	17 (77.3)	0.660
Immunosuppression	5 (55.6)	15 (68.2)	0.683
Previous HSCT	1 (11.1)	6 (27.3)	0.639
Osteolytic lesion	3 (33.3)	7 (31.8)	1.000
Number of medications	5.9 ± 3.6	7.2 ± 6.0	0.881

(Continued)

TABLE 1 | Continued

Parameter	Control (*n* = 9)	WB-EMS (*n* = 22)	*p*-Value[a]
Comorbidities[1]			
Cardiovascular disease	3 (33.3)	6 (27.3)	1.000
Pulmonary disease	0 (0.0)	2 (9.1)	1.000
Liver disease	1 (11.1)	1 (4.5)	0.503
Renal failure	2 (22.2)	1 (4.5)	0.195
Thyroid disease	2 (22.2)	4 (18.2)	1.000
Diabetes mellitus	0 (0.0)	1 (4.5)	1.000
Hypertension	4 (44.4)	6 (27.3)	0.417
Hyperlipidemia	1 (11.1)	3 (13.6)	1.000
Acute GvHD	0 (0.0)	2 (9.1)	1.000
Laboratory values			
Leukocytes [$\times 10^3/\mu l$]	3.60 (1.30–11.40)	5.45 (2.10–27.90)	**0.016**
Thrombocytes [$\times 10^3/\mu l$]	137.0 (56.0–367.0)	183.5 (26.0–383.0)	0.676
Erythrocytes [$\times 10^6/\mu l$]	3.77 (2.93–4.97)	3.77 (2.71–4.85)	0.996
Hematocrit [%]	32.9 (26.9–41.7)	34.1 (27.8–43.3)	0.607
Hemoglobin [g/dl]	12.1 (9.2–13.9)	11.8 (8.7–14.3)	0.769
Albumin [g/l]	40.6 (35.5–43.6)	39.1 (24.7–46.2)	0.290
C-reactive protein [mg/l]	1.9 (0.6–16.7)	3.4 (0.2–82.9)	0.749
Creatinine [mg/dl]	0.94 (0.60–1.77)	0.86 (0.61–3.11)	0.334
Lactate dehydrogenase [IU/l]	220.0 (48.0–1101.0)	233.5 (103.0–638.0)	0.593
Triglycerides [mg/dl]	174.0 (51.0–695.0)	187.0 (79.0–319.0)	0.377

Data are presented in numbers and proportions (%) and as mean ± standard deviation. Laboratory values are expressed as median and range (min to max). [a]Baseline comparison between WB-EMS and control group assessed by Pearson's chi-squared and Fisher's exact test, respectively, for categorical variables and independent-samples t-test, Welch's test or Mann–Whitney U-test for continuous variables. Statistically significant differences are indicated by $p < 0.05$ and marked in bold type. [1]Numbers of patients for comorbidities and oncological treatment include also patients with several comorbidities and combined anticancer therapies. [2]WHO categories to determine nutritional status (World Health Organization [WHO], 2000). WB-EMS, whole-body electromyostimulation; BMI, body mass index; ECW, extracellular water; ICW, intracellular water; GvHD, Graft-versus-Host-Disease; HSCT, hematopoietic stem cell transplantation.

toxicities and clinical deterioration. Two patients of the WB-EMS group who prematurely terminated the study suffered from acute GvHD. However, reasons were not significantly different between study groups ($p = 0.686$). Patients who were not able to continue the study had a significantly higher drug intake (8.9 ± 6.0 vs. 4.7 ± 3.7; $p = 0.026$) as well as a higher leukocyte count ($9.0 \pm 7.2 \times 10^3/\mu l$ vs. $4.6 \pm 2.4 \times 10^3/\mu l$; $p = 0.033$) in line with lower albumin concentrations (37.7 ± 5.1 g/l vs. 40.7 ± 3.5 g/l; $p = 0.073$) than patients who completed the study. Further, they showed a less social functioning assessed by the EORTC QLQ-C30 (44.9 ± 19.8 vs. 65.5 ± 21.2; $p = 0.015$). No significant differences of the patients who dropped out between the two study groups were detected. Remarkably, no WB-EMS related side-effects or discomfort appeared despite a small muscular aching comparable to other strength training methods. Patients of the WB-EMS group who completed the 12-week intervention period attended in average 18.6 ± 3.5 from a total of 24 training sessions leading to a mean exercise adherence rate of 77.3 ± 14.5%.

TABLE 2 | Nutritional intake during study course of the included patients[a].

	Study group		
	Control (*n* = 8)	**WB-EMS (*n* = 20)**	***p*-Value[b]**
Mean daily nutrient/caloric intake [per kg bodyweight]			
Carbohydrates (g)	3.4 ± 0.8	3.6 ± 1.2	0.650
Fat (g)	1.4 ± 0.5	1.4 ± 0.5	0.636
Protein (g)	1.4 ± 0.3	1.4 ± 0.2	0.733
Energy (kcal)	32.8 ± 8.7	34.2 ± 7.5	0.669
Achievement of dietary goals			
Energy group			1.000
<25 kcal/kg	1 (12.5)	2 (10.0)	
≥25 kcal/kg	7 (87.5)	18 (90.0)	
Protein group			1.000
≤1.0 g/kg	1 (12.5)	2 (10.0)	
>1.0 g/kg	7 (87.5)	18 (90.0)	

Data are presented in numbers and proportions (%) and as mean ± standard deviation. [a]Dietary data of two patients of the WB-EMS group and one patient of the control group were unavailable. [b]Categorical variables were analyzed by Fisher's exact test and continuous variables by independent-samples t-test. WB-EMS, whole-body electromyostimulation.

Body Composition

During the study course of 12 weeks patients of the WB-EMS group showed an increase in skeletal muscle mass, while a reduction in muscle mass was observed for control patients (**Figure 2A**). This resulted in a significant estimated mean difference between the groups of 1.21 kg [0.32, 2.10] at week 4, 1.49 kg [0.41, 2.57] at week 8, and 1.51 kg [0.41, 2.60] at the end of the 12-week intervention period favoring the combined exercise and nutrition intervention ($p < 0.01$; **Table 3**). In line with this, fat free mass index (FFMI) was significantly higher in the WB-EMS group compared to controls after 12 weeks ($p < 0.001$; **Figure 2D** and **Table 3**). Both study groups tended to increase in bodyweight (**Figure 2C**), but in contrast to the WB-EMS group, the bodyweight gain in controls was characterized by an increase in fat mass indicated by an increase of the body fat percentage (**Figure 2B**) and fat mass index (FMI; **Figure 2E**). This led to an estimated negative effect of the WB-EMS group on body fat percentage and FMI ($p < 0.01$ at week 12; **Table 3**). No significant mean group differences were observed for the parameter of phase angle over time ($p > 0.05$; **Table 3**). A trend toward an increased phase angle in controls (**Figure 2F**) is suggested to be rather a result of treatment-related changes in body water distribution of the extracellular water (ECW) to the intracellular water (ICW) (Hydration, **Table 3**) than in body cell mass. Of note, an additional sensitivity analysis adjusting the LMM's for age, gender, cancer diagnosis, and glucocorticoid treatment did not reveal appreciable alterations of the estimated treatment effects and significances (**Table 3**).

Pearson correlation analysis yielded a significant strong positive correlation between an increase in skeletal muscle mass and the amount of protein intake in the WB-EMS group ($r = 0.682$; $p = 0.043$), while no significant relationship between protein intake and muscle mass gain was observed for the control group ($r = -0.609$; $p = 0.275$; **Figure 3**). The significant correlation for the WB-EMS group was also observed for muscle mass changes in week 4 and week 8 ($r > 0.600$), but not in the control group (data not shown).

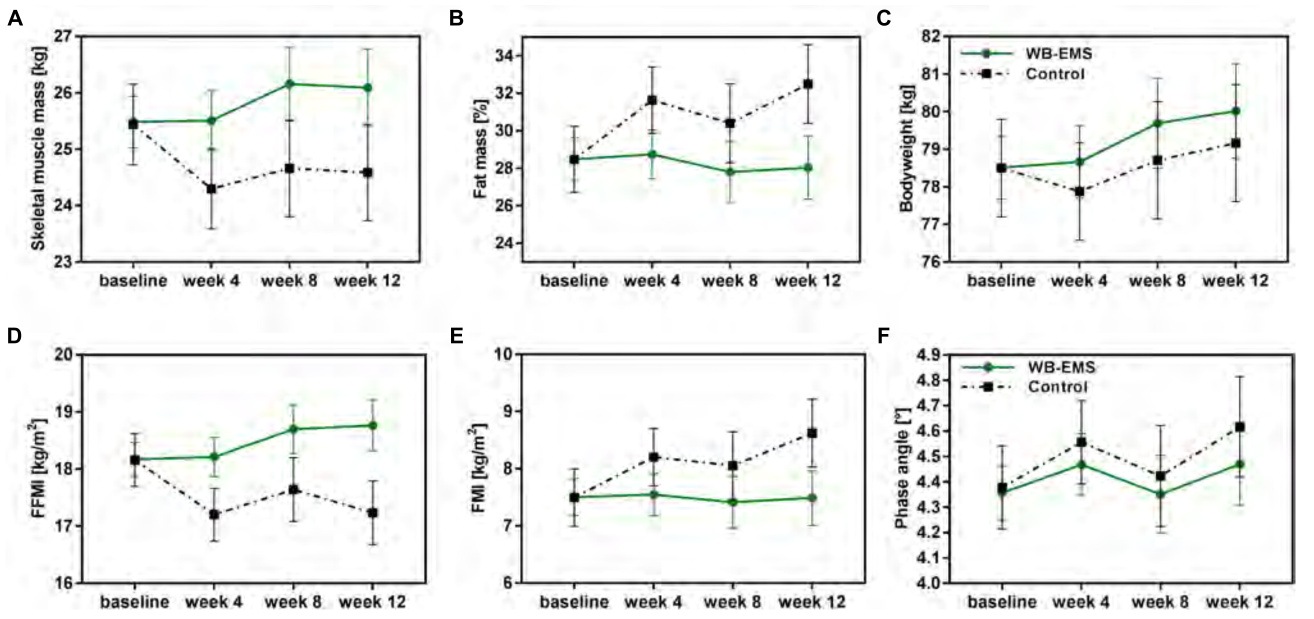

FIGURE 2 | Changes in body composition during the 12-week intervention period. Unadjusted estimated marginal means with 95% confidence intervals of the body composition parameters **(A)** skeletal muscle mass, **(B)** fat mass percentage, **(C)** bodyweight, **(D)** FFMI, **(E)** FMI, and **(F)** phase angle are illustrated for the control group and the WB-EMS group over the 12-week study course. WB-EMS, whole-body electromyostimulation; FMI, fat mass index; FFMI, fat free mass index.

TABLE 3 | Linear mixed model analysis estimating the unadjusted and adjusted[a] effect (group × time) of the combined WB-EMS and nutrition intervention on anthropometry, and body composition over the 12-week study course compared to the usual care control group.

		Estimated effect of WB-EMS intervention compared to controls[b]					
		Estimate [95% CI]	*p*-Value	Estimate [95% CI]	*p*-Value	Estimate [95% CI]	*p*-Value
Outcome measure	**Model**	**Week 4**		**Week 8**		**Week 12**	
Anthropometry							
Bodyweight [kg]	Unadjusted	0.78 [−0.83, 2.40]	0.336	0.99 [−0.98, 2.95]	0.321	0.85 [−1.15, 2.85]	0.399
	Adjusted[a]	0.80 [−0.80, 2.41]	0.320	1.08 [−0.88, 3.03]	0.276	0.94 [−1.04, 2.93]	0.347
FMI [kg/m^2]	Unadjusted	−0.66 [−1.28, −0.04]	**0.039**	−0.64 [−1.39, 0.10]	0.091	−1.13 [−1.89, −0.38]	**0.004**
	Adjusted[a]	−0.75 [−1.42, −0.07]	**0.030**	−78 [−1.57, 0.01]	**0.054**	−1.21 [−2.02, −0.41]	**0.004**
FFMI [kg/m^2]	Unadjusted	1.00 [0.43, 1.59]	**0.001**	1.06 [0.35, 1.76]	**0.004**	1.53 [0.82, 2.25]	**0.000**
	Adjusted[a]	1.10 [0.53, 1.66]	**0.000**	1.22 [0.53, 1.91]	**0.001**	1.70 [1.01, 2.41]	**0.000**
Body composition							
SMM [kg]	Unadjusted	1.21 [0.32, 2.10]	**0.008**	1.49 [0.41, 2.57]	**0.007**	1.51 [0.41, 2.60]	**0.008**
	Adjusted[a]	1.36 [0.48, 2.24]	**0.003**	1.75 [0.68, 2.81]	**0.002**	1.77 [0.68, 2.85]	**0.002**
FM [%]	Unadjusted	−2.89 [−5.08, −0.70]	**0.011**	−2.60 [−5.25, 0.05]	0.054	−4.46 [−7.15, −1.77]	**0.001**
	Adjusted[a]	−3.30 [−5.59, −1.01]	**0.006**	−3.27 [−6.00, 0.53]	**0.020**	−4.91 [−7.68, −2.13]	**0.001**
PhA [°]	Unadjusted	−0.09 [−.29, 0.12]	0.396	−0.07 [−0.32, 0.18]	0.572	−0.15 [−0.40, 0.11]	0.256
	Adjusted[a]	−0.10 [−0.32, 0.13]	0.389	−0.07 [−0.33, 0.20]	0.614	−0.14 [−0.41, 0.13]	0.294
Hydration [%, ECW: ICW]	Unadjusted	0.88 [−1.51, 3.26]	0.466	1.30 [−1.57, 4.17]	0.371	2.95 [0.02, 5.88]	**0.049**
	Adjusted[a]	0.94 [−1.37, 3.25]	0.419	1.06 [−1.74, 3.86]	0.454	2.93 [0.08, 5.78]	**0.044**

[a]Models were adjusted for age, gender, diagnosis of hematological malignancy and glucocorticoid intake. [b]Data are presented as estimated mean difference between study groups and 95% confidence intervals [95% CI]. Statistically significant effects are marked in bold type. WB-EMS, whole-body electromyostimulation; FMI, fat mass index; FFMI, fat free mass index; SMM, skeletal muscle mass, FM, fat mass; PhA, phase angle; ECW, extracellular water; ICW, intracellular water.

Physical Function and Quality of Life

Analysis of physical function, quality of life and fatigue were based on available pre- and post-assessment data measured at baseline and after 12 weeks (**Table 4**). Patients of the WB-EMS group significantly increased their 6-min-walking distance after 12 weeks (48.4 ± 51.5 m; p = 0.032), while walking performance was kept stable in controls, leading to a significant difference between the study groups (p = 0.046; **Table 4**). Though significance level between groups was not reached (p = 0.181), an increased performance status was reported by the patients of the WB-EMS group (Karnofsky-Index, 11.1 ± 17.6; p = 0.095). A comparable increase in patient-reported physical functioning was observed for both study groups (controls, 11.5 ± 18.3; WB-EMS group 10.8 ± 22.7; p = 0.957). Interestingly, controls reported a non-significant decline in social functioning after 12 weeks (−16.6 ± 27.3; p = 0.311), while exercising patients remained stable (2.0 ± 19.3; p = 0.764), and thus tended to function better socially (p = 0.183). Both study groups improved their fatigue symptoms (FACIT and C30 scale), whereby only the within-group difference of the controls for the FACIT-Fatigue scale reached statistical significance (11.3 ± 6.6; p = 0.042). However, no significant inter-group differences between changes in fatigue were revealed. Global health tended to improve within the WB-EMS group (10.4 ± 15.6; p = 0.080), but no significant differences between the groups were detected. Moreover, symptoms of insomnia significantly declined (−37.0 ± 35.2; p = 0.014) and nausea/vomiting tended to decrease in the WB-EMS group (−14.9 ± 22.8, p = 0.066).

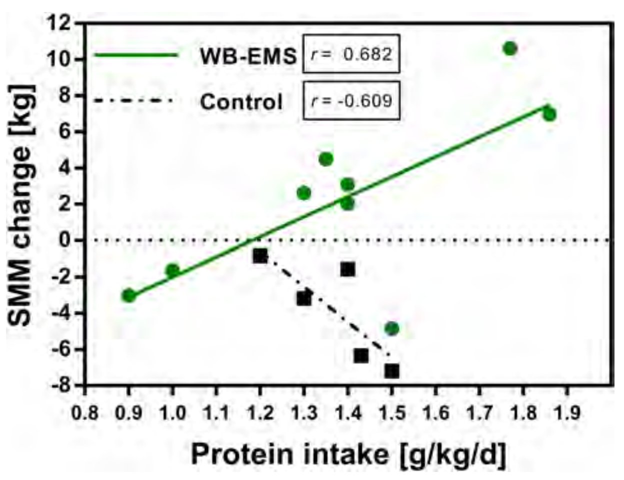

FIGURE 3 | Relationship between daily protein intake and change in skeletal muscle mass. Pearson correlation between daily protein intake (g/kg bodyweight) and change in skeletal muscle mass (kg) of the control (n = 6) and the WB-EMS group (n = 9) after 12 weeks. SMM, skeletal muscle mass; WB-EMS, whole-body electromyostimulation.

Hematological and Biochemical Parameters

No significant within- and between-group differences were detected for hematological blood parameters (**Table 5**). However,

TABLE 4 | Physical function and quality of life at baseline and after 12 weeks[1].

Outcome measure	Study group	*n*	Baseline	Week 12	Difference	*p*-Value[a]	*p*-Value[b]
Physical function							
SMWT distance [m]	Control	6	519.5 ± 66.7	512.1 ± 76.7	−7.4 ± 38.7	0.658	**0.046**
	WB-EMS	8	534.1 ± 76.0	582.6 ± 82.6	48.4 ± 51.5	**0.032**	
STS repetitions	Control	5	14.2 ± 3.0	13.4 ± 2.1	−0.8 ± 1.8	0.336	0.429
	WB-EMS	6	13.7 ± 2.7	13.5 ± 3.9	−0.2 ± 1.7	0.822	
Karnofsky-Index	Control	6	73.3 ± 10.3	75.0 ± 5.5	1.7 ± 7.5	0.611	0.181
	WB-EMS	9	75.6 ± 15.9	86.7 ± 14.1	11.1 ± 17.6	0.095	
Quality of life							
FACIT-fatigue scale	Control	4	25.5 ± 12.4	36.8 ± 8.8	11.3 ± 6.6	**0.042**	0.147
	WB-EMS	9	35.0 ± 12.5	39.8 ± 11.6	4.8 ± 7.0	0.075	
EORTC QLQ-C30							
Functional scales							
PF	Control	4	63.5 ± 32.7	75.0 ± 21.9	11.5 ± 18.3	0.299	0.957
	WB-EMS	9	66.0 ± 20.9	76.8 ± 23.4	10.8 ± 22.7	0.192	
RF	Control	4	60.8 ± 25.7	50.1 ± 19.5	−10.8 ± 18.3	0.570	0.261
	WB-EMS	9	49.9 ± 30.1	62.9 ± 20.1	13.0 ± 33.2	0.274	
EF	Control	4	66.6 ± 26.6	62.3 ± 24.8	−4.3 ± 33.8	0.818	0.710
	WB-EMS	9	64.8 ± 35.9	71.2 ± 23.4	6.4 ± 31.3	0.553	
CF	Control	4	60.4 ± 25.0	66.9 ± 0.2	6.5 ± 25.2	0.641	0.833
	WB-EMS	9	81.4 ± 21.1	90.8 ± 14.6	9.3 ± 20.5	0.208	
SF	Control	4	75.1 ± 9.3	58.5 ± 34.6	−16.6 ± 27.3	0.311	0.183
	WB-EMS	9	61.0 ± 25.1	63.0 ± 35.2	2.0 ± 19.3	0.764	
Symptom scales							
Pain	Control	4	29.0 ± 20.9	12.5 ± 15.4	−16.5 ± 13.5	0.092	0.928
	WB-EMS	9	44.4 ± 40.7	25.8 ± 35.3	−18.7 ± 45.2	0.250	
Dyspnea	Control	4	41.5 ± 42.0	41.5 ± 42.0	0.0 ± 0.0	1.000	0.598
	WB-EMS	9	36.9 ± 31.0	29.6 ± 42.3	−7.3 ± 40.1	0.598	
Insomnia	Control	4	58.3 ± 50.1	24.8 ± 16.5	−33.5 ± 38.7	0.157	0.940
	WB-EMS	9	48.1 ± 37.8	11.1 ± 23.6	−37.0 ± 35.2	**0.014**	
Appetite loss	Control	4	24.8 ± 16.5	16.5 ± 19.1	−8.3 ± 16.5	0.317	0.825
	WB-EMS	9	22.2 ± 29.0	18.4 ± 33.8	−3.8 ± 20.0	0.414	
Constipation	Control	4	33.3 ± 27.4	33.5 ± 38.7	0.3 ± 47.6	0.992	0.414
	WB-EMS	9	11.1 ± 23.6	3.7 ± 11.0	−7.4 ± 14.8	0.180	
Diarrhea	Control	4	8.3 ± 16.5	0.0 ± 0.0	−8.2 ± 16.5	0.317	0.825
	WB-EMS	9	11.1 ± 23.6	3.7 ± 11.0	−7.4 ± 27.8	0.414	
Financial difficulties	Control	4	16.8 ± 33.5	0.0 ± 0.0	−16.8 ± 33.5	0.317	0.503
	WB-EMS	9	14.8 ± 24.2	14.8 ± 24.2	0.0 ± 17.0	1.000	
Nausea/vomiting	Control	4	16.5 ± 19.1	8.3 ± 16.5	−8.3 ± 16.5	0.317	0.710
	WB-EMS	9	18.6 ± 25.7	3.7 ± 11.0	−14.9 ± 22.8	0.066	
Fatigue	Control	4	66.8 ± 24.1	44.3 ± 27.4	−22.5 ± 45.3	0.394	1.000
	WB-EMS	9	46.9 ± 23.0	36.9 ± 35.6	−10.0 ± 25.8	0.114	
Global Health	Control	4	45.8 ± 10.7	64.5 ± 14.2	18.8 ± 21.8	0.184	0.448
	WB-EMS	9	61.8 ± 24.0	72.2 ± 18.3	10.4 ± 15.6	0.080	

[1]Includes patients with pre- and post-assessment data. [a]Paired-sample t-test for parametric or Wilcoxon-signed-rank test for non-parametric values for comparison of pre- and post-intervention values. [b]Independent-samples t-test for parametric or Mann–Whitney U-test for non-parametric values for comparison of pre- to post-test changes. Statistical significance is indicated by $p < 0.05$ and marked in bold type. SMWT, 6-min-walking test; STS, 30 s sit-to-stand test; PF, physical functioning; RF, role functioning; EF, emotional functioning; CF, cognitive functioning; SF, social functioning; WB-EMS, whole-body electromyostimulation.

a distinct decrease in triglyceride concentrations was noticed in the WB-EMS group (−31.8 ± 68.7; p = 0.232) in contrast to an increase in the control group (36.3 ± 50.6; p = 0.139), albeit differences between the groups did not reach level of statistical significance (p = 0.064).

DISCUSSION

This study is the first study, by our knowledge, that investigated the impact of a combined physical exercise and nutrition program on patients actively treated for hematological malignancies.

TABLE 5 | Hematological and blood biochemistry parameters at baseline and after 12 weeks[1].

Outcome measure	Study group	*n*	Baseline	Week 12	Difference	*p*-Value[a]	*p*-Value[b]
Hematological parameters							
Leukocytes [$\times 10^3/\mu$l]	Control	6	4.27 ± 3.63	3.86 ± 1.86	−0.41 ± 2.83	0.739	0.607
	WB-EMS	9	4.85 ± 1.44	4.68 ± 2.23	−0.17 ± 3.21	0.878	
Thrombocytes [$\times 10^3/\mu$l]	Control	6	144.3 ± 99.5	155.0 ± 98.5	10.7 ± 23.4	0.316	0.902
	WB-EMS	9	183.0 ± 89.1	196.6 ± 85.1	13.6 ± 52.2	0.458	
Erythrocytes [$\times 10^6/\mu$l]	Control	6	3.96 ± 0.65	4.30 ± 0.75	0.34 ± 0.74	0.311	0.564
	WB-EMS	9	3.79 ± 0.50	3.93 ± 0.44	0.15 ± 0.32	0.206	
Hemoglobin [g/dl]	Control	6	12.1 ± 1.4	13.3 ± 2.2	1.1 ± 2.3	0.374	0.391
	WB-EMS	9	12.1 ± 1.2	12.5 ± 1.0	0.4 ± 0.9	0.225	
Hematocrit [%]	Control	6	36.1 ± 4.1	39.0 ± 6.0	2.9 ± 6.4	0.312	0.422
	WB-EMS	9	35.5 ± 3.8	36.5 ± 2.9	1.0 ± 2.7	0.325	
Clinical chemistry							
CRP [mg/l]	Control	6	3.7 ± 4.1	6.1 ± 12.3	2.4 ± 9.3	0.600	0.388
	WB-EMS	9	5.7 ± 5.1	5.2 ± 9.0	−0.5 ± 10.3	0.892	
Albumin [g/l]	Control	6	40.3 ± 3.3	41.2 ± 4.0	0.9 ± 4.9	0.676	0.896
	WB-EMS	8	41.0 ± 3.9	42.2 ± 2.5	1.2 ± 3.0	0.303	
Total protein [g/l]	Control	6	62.2 ± 6.0	64.0 ± 7.6	1.8 ± 6.2	0.510	0.382
	WB-EMS	8	65.5 ± 7.7	64.4 ± 5.2	−1.1 ± 5.7	0.602	
Triglycerides [mg/dl]	Control	6	130.5 ± 49.6	166.8 ± 58.8	36.3 ± 50.6	0.139	0.064
	WB-EMS	8	179.0 ± 54.5	147.3 ± 46.3	−31.8 ± 68.7	0.232	
LDH [IU/l]	Control	6	183.0 ± 97.2	187.0 ± 48.1	4.0 ± 92.0	0.919	0.657
	WB-EMS	9	289.0 ± 112.2	269.7 ± 66.3	−19.3 ± 100.4	0.579	
Creatinine [mg/dl]	Control	6	0.91 ± 0.19	0.95 ± 0.29	0.04 ± 0.12	0.446	0.916
	WB-EMS	9	0.92 ± 0.23	0.97 ± 0.28	0.05 ± 0.10	0.174	

[1]Includes patients with pre- and post-assessment data. [a]Paired-samples t-test for parametric or Wilcoxon-signed-rank test for non-parametric values for comparison of pre- and post-intervention values. [b]Independent-samples t-test for parametric or Mann–Whitney U-test for non-parametric values for comparison of pre- to post-test changes. Statistical significance is indicated by $p < 0.05$ and marked in bold type. WB-EMS, whole-body electromyostimulation; CRP, C-reactive protein; LDH, lactate dehydrogenase.

We demonstrated that supervised WB-EMS training seems to be a safe and feasible strength training method for this patient group. Our results showed a significantly higher skeletal muscle in the patients additionally trained by WB-EMS compared to the usual care patients during the 12-week study course. This strengthens our primary hypothesis that a combined exercise and nutrition intervention may be more efficient in maintaining muscle mass during the oncological treatment in hematological cancer patients than a solely nutritional support. The dual therapeutic approach also seemed to induce benefits on the physical functioning and metabolic risk factors with regard to the lipid metabolism of the patients.

Body Composition

Patients suffering from cancer are faced to a broad range of physiological and psychological symptoms resulting in a decline of physical activity that detrimentally affects body composition and functional status. The causes are multifactorial and include disease- and treatment-related toxicities on the cardiopulmonary, gastrointestinal, neurological and hematopoietic system. As a consequence of inflammation-mediated metabolic changes, increased catabolic processes trigger muscle protein breakdown as a hallmark of cancer cachexia that is mostly prominent in patients with solid tumors (Fearon et al., 2013). In hematological cancer, cytotoxic effects of chemotherapeutic agents, radiation, and immunosuppressive agents may be the main contributors to the prognostic process of muscle wasting (Blauwhoff-Buskermolen et al., 2016; Guglielmi et al., 2017). Synthetic glucocorticoids are widely used within the chemotherapeutic treatment of lymphoproliferative diseases (Lin and Wang, 2016). Disadvantageously, glucocorticoids induce a broad range of catabolic actions and dysregulate anabolic signaling leading to a loss in skeletal muscle mass and function (Gupta and Gupta, 2013). Deficits in health-related physical fitness are therefore common (Persoon et al., 2017b). Increasing the physical activity of cancer patients during active treatment could be a key approach to overcome those deficits and preserve muscle mass. We here provided an novel strength training method in form of WB-EMS that is time-efficient, gentle for the patient and was already shown to increase muscle mass in sarcopenic elderly and patients suffering from chronic heart failure (Fritzsche et al., 2010; Kemmler et al., 2014). With the present pilot trial we could emphasize the muscle-building effect of the WB-EMS training for patients actively treated for different hematological malignancies. Our results demonstrated that an additional regular WB-EMS training can improve skeletal muscle mass with a superior effect to a sole nutritional support even after 4 weeks of study intervention. The benefit of this combined 12-week intervention on muscle mass maintenance is in line with the results of our previous study in advanced-stage solid cancer patients (Schink et al., 2018). Studies evaluating the effect of physical exercise on skeletal muscle mass as a primary outcome in hematological cancer patients during active treatment are quite rare. Evidence of the effectiveness of physical exercise to improve skeletal muscle mass in hematological cancer was provided by a study of Coleman et al. (2003), demonstrating a higher muscle mass for multiple myeloma patients after a 12-week aerobic/resistance exercise program compared to a control group who only received advices for an active lifestyle (Coleman et al., 2003). In contrast, a mixed exercise program consisting of home-based, gym-based and group-based exercises showed no effect on fat-free mass index in myeloma patients (Groeneveldt et al., 2013). Likewise, resistance exercise three or five-times a week showed no superior impact on arm muscle area compared to control patients in acute leukemia patients undergoing bone marrow transplantation and total parenteral nutrition (Cunningham et al., 1986). Overall, it would be of great interest to prospectively investigate, if WB-EMS combined with the high protein nutritional support may be more efficient in improving the muscle mass status than conventional strength training methods.

In fact, we observed a strong positive correlation of the amount of protein intake with an increase in skeletal muscle mass after 12 weeks in the WB-EMS group. This observation may suggest that the known hypertrophic effect of physical exercise, especially in form of resistance training (Schoenfeld, 2010), can be supported and probably enhanced by the additional anabolic stimuli of a regular high protein/amino acid intake that helps to efficiently overcome increased catabolic processes (Willoughby et al., 2007). Tieland et al. (2012) demonstrated that an additional protein supplementation of 15 g 2×/day showed a stronger effect on muscle mass gain in older men performing a progressive resistance training for 24 weeks compared to the exercising placebo-group. Contrary, no effect of an additional protein supplementation (40 g/d) on muscle mass gain during a resistance training program was observed in a study with breast cancer survivors (Madzima et al., 2017). In this study, however, patients reached only a mean daily protein intake of 1.2 g/kg/d in contrast to a mean daily protein intake of 1.4 g/kg/d in our trial and calorie restriction resulted in a net gain of the protein intake of only 17 g/d. This may have affected results. However, due to the small sample size and the lack of an exercise group that was not intended to increase protein intake, a definitive conclusion about a valid impact of the amount of protein intake on muscle build up in our patient population cannot be drawn. Nonetheless, although our correlation analysis should be interpreted cautiously, it emphasizes a further investigation of the exact amount of dietary protein that is needed for muscle build-up in lager-scaled randomized controlled trials.

In addition to skeletal muscle mass, we also monitored changes in bodyweight and other body compartments. At baseline, approximately 60% of our patients were classified as overweight or obese. Unfavorable body composition characterized by overweight/obesity as a result of a high body fat percentage and reduced muscle mass is frequently observed in patients treated for hematological cancer and hints toward the presence of the so called sarcopenic obesity (Xiao et al., 2016; Persoon et al., 2017b). High body fat promotes the secretion of inflammatory mediators by the adipose tissue leading to a systemic inflammation and higher oxidative stress level that trigger the development of metabolic diseases (Nanayakkara et al., 2012; Ellulu et al., 2017). Thus, sarcopenic obesity can negatively impact the overall life expectancy (Yip et al., 2015). Considering this, avoiding deterioration of manifestation of metabolic disorders of long-term cancer patients should be goal in a multimodal cancer care. Studies also provide evidence that high body fat can be predictive for greater dose-independent side-effects and a worse treatment response (GroDelta et al., 2017). Our results showed that even though both study groups tended to increase in bodyweight, this increase was due different tissues changes. While patients of the WB-EMS group increased in muscle mass and were balanced in body fat percentage, control patients were further shifted toward sarcopenic obesity, underlined by a decrease in muscle mass and an increase in body fat that was significantly higher at study end. Interestingly, a trial of Kemmler et al. (2017) demonstrated comparable results. Older men receiving WB-EMS training and high protein supplementation (1.7–1.8 g/kg/d) showed a higher reduction of total body fat and increase of muscle mass than men with isolated protein supplementation or no intervention. The increase in body fat during treatment of hematological cancer might be a result of glucocorticoid treatment affecting the lipid metabolism (Peckett et al., 2011) in line with low physical activity levels induced by fatigue (Coleman et al., 2011). Our results therefore suggest that exercise in form of WB-EMS combined with a high protein intake could be efficient to attenuate treatment-related unfavorable body composition changes and may therefore also be helpful to improve treatment response and avoid metabolic diseases in the post-treatment period. Underlining this thesis, we observed changes in serum triglycerides. The lipid profile of patients with hematological malignancies was shown to be negatively altered. Concentrations in cholesterol fractions are suggested to be inversely associated with the incidence of hematological cancer, while triglycerides can be elevated in those patients, especially in the active disease period (Naik et al., 2006; Kuliszkiewicz-Janus et al., 2008). After 12 weeks we recognized a strong trend toward a decrease in serum triglycerides in the WB-EMS group in contrast to an increase in the control group.

During the study course BIA measurements revealed no statistically significant differences in the nutritional and health-predicting parameter of phase angle (Lee et al., 2014). Different glucocorticoid treatments and antidiuretic drugs may have probably influenced body water distribution that highly affects phase angle values.

We assessed body composition and thus skeletal muscle mass by BIA as it was demonstrated to correlate with the results obtained from Dual Energy X-ray Absorptiometry and magnetic resonance tomography (Bosy-Westphal et al., 2008; Bosy-Westphal and Jensen, 2017), but is much easier and faster to apply, as previously described (Schink et al., 2018).

Physical Function

Functional disabilities after treatment for hematological cancer are common and can be observed even years after the initial therapy (Battaglini, 2011; Tuchman et al., 2015). Several reviews suggest that muscle strength and physical functioning can be improved by different exercise interventions in these patients (Bergenthal et al., 2014; Gan et al., 2016). Our results support these findings. A significantly higher 6-min-walking distance and improved patient-reported performance status (Karnofsky-Index) suggest the effectiveness of WB-EMS to stabilize and ameliorate the whole muscular status of the patients by improving functional capacity. In a study with various hematological cancer patients an exercise program did not stabilize 6-min-walking distance during HSCT (Takekiyo et al., 2015), even though exercise was conducted 5 days a week each time for 40 min. In contrast, Mello et al. (2003) showed a significant increase in muscle strength 6 weeks after allogenic bone marrow transplantation. So, either scheduling of exercise programs or the appropriate intensity and application type of exercise may be important to relevantly improve physical function in patients with hematological malignancies. Compared to the conventional exercise programs the less time-consuming exercise schedule of our ambulant WB-EMS training program (2×/week á 20 min) may offer a great advantage to efficiently sustain physical function in hematological patients even during active treatment.

Quality of Life

Maintaining of the quality of life is an important goal in a multimodal cancer care concept. A review of Allart-Vorelli et al. (2015) demonstrated that different dimensions of quality of life including physical and psycho-social well-being are detrimentally affected by hematological malignancies and treatment side-effects. Fatigue is thereby one of the most burdening symptoms in these patients (Miltenyi et al., 2010). Physical exercise was shown to improve physical well-being and to potentially reduce fatigue-symptoms (Oldervoll et al., 2003; Groeneveldt et al., 2013). Both of our study groups improved in fatigue, whereby a greater improvement in the control group was most likely due to a higher fatigue burden at baseline of the analyzed patients. However, a recent study with myeloma and lymphoma patients also showed a decrease in fatigue in the exercising as well as in the usual care control group, probably a result of exercise contamination in controls (Persoon et al., 2017a). Besides physical exercise, also the nutritional support covering patients' energy and nutrient requirements may have relieved fatigue symptoms. The small sample size makes it difficult to interpret the results conclusively. However, although there are no significant differences between the groups, patients of the physical exercise group showed greater improvements for their psychosocial functioning, indicating improved social and role functioning. These patients showed also a distinct increase in global health/overall quality of life after 12 weeks of WB-EMS training. Moreover, intra-group analysis revealed a significant amelioration of insomnia, a frequent symptom in hematological cancer patients (Johnsen et al., 2009; Coleman et al., 2011). Exercise was previously suggested to be a potent treatment against insomnia (Passos et al., 2012). Further, a strong trend toward decreased nausea during anti-cancer treatment was revealed for the WB-EMS group that could also be demonstrated in exercising breast cancer patients undergoing adjuvant chemotherapy (Lee et al., 2008) and hints toward a decreased treatment-related toxicity and adequately adapted nutrition.

Overall Training Adherence

The implementation of exercise interventions into the clinical routine, especially for actively treated hematological cancer patients, is not easy. Many exercise studies were conducted with solid cancer patients, especially breast and prostate cancer patients that are relatively fit. However, treatment toxicities including anemia-induced fatigue, insomnia, and psychological distress hinders hematologic patients from regular exercise (Coleman et al., 2003). The high dropout rate in our physical exercise group of 59.1% underlines this difficulty. Deterioration in clinical status and treatment toxicities (worsening of acute GvHD) were the main reasons for study dropouts. Poor state of health was underlined by the significantly higher daily drug intake and leukocyte count as well as lower serum albumin hinting toward decreased nutritional status. Only visiting the monthly intermediate measurement may have been therefore less burdening for patients than regularly attending the WB-EMS exercise sessions that could interfere with disease-related complications (Oldervoll et al., 2011; Schink et al., 2018). Nonetheless, patients who completed the 12-week intervention period of our study showed a good exercise adherence attaining in mean 77.3% of the scheduled exercise sessions underlining the good acceptance of the WB-EMS training method. Moreover, it has to be mentioned that no WB-EMS related adverse events occurred and that approximately one-third of our patients suffered from osteolytic lesions, as a complication of myeloma infiltration. Those patients might not have been able to undergo a strenuous high intensity apparatus training that is necessary to build up muscles but can be too risky due to possible bone fractures. The innovative technology of WB-EMS to activate almost all large muscle groups simultaneously in line with gentle, easy-to-perform mild exercises removes those concerns.

Study Limitations

Even though, baseline characteristics were well balanced between study groups, the results may be limited by the lack of randomization and blinding of study patients and assessors, respectively, as well as by the small sample size that could have induced bias (Schink et al., 2018). Outcome differences between the study groups may have been a result of a higher percentage of more motivated patients in the WB-EMS group, albeit allocation to study groups was associated to the journey way to the study center to mostly rule out this problem (Schink et al., 2018). Hence, randomized controlled trials are now necessary to confirm our promising results.

CONCLUSION

Summarizing the results of our pilot study we could demonstrate that physical exercise in form of WB-EMS seems to be a feasible and safe strength training method for patients with hematological malignancies. In combination with individual nutritional support high in dietary protein WB-EMS potentially improves skeletal muscle mass and prevents treatment- and disease-related unfavorable changes in body composition and fat metabolism. The clinical relevance of our findings may be emphasized by the observed improvement and preservation of the physical function by the combined therapeutic approach. Our preliminary results now encourage the conduction of further randomized controlled trials with longer follow-up periods to verify these findings and to investigate the maintenance of muscle mass und function after the active treatment period of hematological cancer patients.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

AUTHOR CONTRIBUTIONS

KS, HH, and YZ substantially contributed to the study conception, design, and conduction. KS was responsible for the data acquisition and wrote the manuscript. KS and JM analyzed the data. HH, DR, AM, MN, and YZ revised the manuscript critically for important intellectual content. KS and YZ had primary responsibility for final content. All authors read and approved the final manuscript.

FUNDING

The study was supported by grants from H.W. & J. Hector Foundation, Manfred Roth Foundation, Forschungsstiftung Medizin am Universitätsklinikum Erlangen, Baxter Germany, and Bürgerstiftung Erlangen.

ACKNOWLEDGMENTS

Special thanks to the patients who participated in this study.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 20 March 2019
doi: 10.3389/fphys.2019.00291

Effect of the Combination of Whole-Body Neuromuscular Electrical Stimulation and Voluntary Exercise on Metabolic Responses in Human

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Purpose: Since neuromuscular electrical stimulation (NMES) can recruit high-threshold motor units and enhance glucose metabolism, the combination of NMES and voluntary low-intensity exercise would induce both anerobic and aerobic energy consumptions and this type of exercise could be more efficient and effective than conventional exercise regimens. We aimed to investigate metabolic responses and muscle fatigue during whole body NMES (WB-NMES), voluntary exercise, and their combination.

Methods: The blood lactate concentration and maximal voluntary contraction were measured before and after specified exercises: WB-NMES (E), voluntary exercise (V), and their combination (VE), and expired gas was sampled during the exercises in thirteen healthy young men. Each exercise was conducted for 15 min and interval between exercise was $>$ 48h.

Results: Energy expenditure and $\dot{V}O_2$ relative to the body mass during VE were significantly higher than during V and E ($p < 0.05$). The Respiratory gas exchange ratio (RER) during both E and VE was higher than during V ($p < 0.05$), and the blood lactate concentration after VE was significantly higher than after V and E ($p < 0.05$). Although $\dot{V}O_2$ relative to the body mass was 18.6 $\pm$ 3.1 ml/min/kg and the metabolic equivalent was 5.31 $\pm$ 0.89 Mets, the blood lactate concentration reached 7.5 $\pm$ 2.7 mmol/L after VE.

Conclusion: These results suggest that the combination of WB-NMES and voluntary exercise can enhance the metabolic response to a level equivalent to high intensity exercise under the net physiological burden of low-middle intensity exercises.

Keywords: electrical muscle stimulation, electrical myostimulation, sarcopenia, life-style-related diseases, lactate, high-intensity interval training

OPEN ACCESS

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *04 November 2018*
Accepted: *05 March 2019*
Published: *20 March 2019*

Citation:
Watanabe K, Yoshida T, Ishikawa T, Kawade S and Moritani T (2019) Effect of the Combination of Whole-Body Neuromuscular Electrical Stimulation and Voluntary Exercise on Metabolic Responses in Human. Front. Physiol. 10:291. doi: 10.3389/fphys.2019.00291

Abbreviations: MVC, maximal voluntary contraction; NMES, neuromuscular electrical stimulation; RER, respiratory gas exchange ratio; $\dot{V}O_2$ oxygen uptake; WB-NMES whole body neuromuscular electrical stimulation.

INTRODUCTION

It is well known that exercise is essential for the prevention and management of metabolic diseases, such as type 2 diabetes mellitus (Sigal et al., 2006). Aerobic exercise for conditioning metabolic and cardiovascular systems and resistance exercises for strengthening skeletal muscles are major component of the exercise regimen recommended for such patients. Also, since high-intensity exercise like resistance training can enhance glucose metabolism, this type of exercise should be applied for not only the prevention and management of metabolic diseases but also for improvements in muscle mass or strength (Colberg et al., 2010). However, resistance training may lead to high-impact stress on joints and ligaments or orthopedic disorders.

Neuromuscular electrical stimulation (NMES) could be a useful alternative method of resistance training for people unable to perform high intensity exercise (Lake, 1992; Banerjee et al., 2005; Hortobagyi and Maffiuletti, 2011). It has been shown that the motor unit recruitment pattern during NMES is random and does not follow the size principle, NMES can activate motor units or muscle fibers with a high recruitment threshold even during low intensity electrical stimulation (Gregory and Bickel, 2005; Jubeau et al., 2007; Bickel et al., 2011). This physiological response can enhance glucose metabolism (Hamada et al., 2003, 2004a) and/or muscle hypertrophy (Hasegawa et al., 2011). Recently, the combined regimen of whole-body NMES (WB-NMES) and voluntary exercise was developed (Kemmler et al., 2012, 2014), since this type of regimen is both time-saving and orthopedically gentle. In fact, positive effects of WB-NMES on the muscle mass and function and cardio-metabolic risk factors have been reported (Kemmler and von Stengel, 2013; Wittmann et al., 2016). However, physiological responses during WB-NMES have not been fully clarified. While some studies measured physiological responses such as cardiovascular and/or metabolic responses during NMES application to local muscles (Hamada et al., 2003, 2004a), few studies have quantified physiological responses during WB-NMES. For example, Kemmler et al. (2012) showed energy expenditure during low-intensity resistance training with WB-NMES of 17% higher than that without WB-NMES (Kemmler et al., 2012). Although this previous study quantified energy consumption during the combination of voluntary exercise and WB-NMES, the detailed metabolic response was not investigated to clarify the physiological implication of combining the two types of exercises.

The purpose of the present study was to investigate metabolic responses and muscle fatigue during WB-NMES, voluntary exercise, and their combination. When NMES is applied to pairs of agonist-antagonist muscles on voluntary contraction, it should induce eccentric contraction of antagonist muscles and co-contraction between agonist muscles and NMES-elicited contraction of antagonist muscles (Lepley et al., 2015). This could increase physiological burdens on the muscles and energy expenditure. We thus hypothesized that 1) energy expenditure during the combination of voluntary exercise and WB-NMES is greater than during WB-NMES, voluntary exercise, and their summation, 2) muscle fatigue after the combination of voluntary exercise and WB-NMES is greater than those of WB-NMES and voluntary exercise, and 3) the addition of WB-NMES to voluntary exercises enhances glucose metabolism. These hypotheses were tested by comparing the energy expenditure, oxygen consumption, blood lactate concentration, and maximal voluntary contraction (MVC) during and after WB-NMES, voluntary exercise, and their combination, respectively. We set hypothesis 1 as the primary one to answer the main question of whether the combination of WB-NMES and voluntary exercise induces greater energy consumption.

MATERIALS AND METHODS

Subjects

Thirteen healthy young men (age: 20.7 ± 0.9 years, height: 172.5 ± 5.5 cm, body mass: 63.1 ± 7.6 kg) volunteered for the present study. They did not participate in regular endurance/strength training or competitive athletic events. All subjects gave written informed consent for the study after receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation. They were healthy with no history of any musculoskeletal or neurological disorders. All study procedures were conducted in accordance with the Declaration of Helsinki and research code of ethics of Chukyo University, and were approved by the Committee for Human Experimentation of Chukyo University (2017-002 and -057).

Study Design

Subjects came to the laboratory three times, separated by at least 48 h intervals (2 of 26 cases were separated by only 24 h). On all three days, the blood lactate concentration and MVC were measured before and after a given exercise, i.e., WB-NMES (E), voluntary aerobic exercise (V), or their combination (VE), and expired gas was sampled during a given exercise. On the first day, subjects performed V and familiarization with and determination of the stimulation intensity in WB-NMES were conducted after its completion (**Figure 1**). On the second or third days, E or VE were randomly applied. Each exercise program was conducted for 15 min (**Figure 1**).

Measurements

We measured expired gas from mask covering the mouth and nose during exercise using the breath-by-breath method (AE310S, Minato Medical Science Co., Ltd., Osaka, Japan). $\dot{V}O_2$ relative to the body mass and the respiratory gas exchange ratio (RER) were calculated from sampled gas. The energy expenditure and metabolic equivalent were also calculated from $\dot{V}O_2$ and the body weight of each subject for each exercise. To test hypothesis 1, summation of $\dot{V}O_2$ relative to the body mass for V and E exercises was performed. The basal metabolism (3.5 ml/min/kg) for an exercise was subtracted from the summed V and E in $\dot{V}O_2$ relative to the body weight for comparison with that in VE.

The blood lactate concentration was measured just after exercise with the lactate oxidase method using an automated analyzer (Lactate Pro; Arkray, Kyoto, Japan) and 5 μL of blood

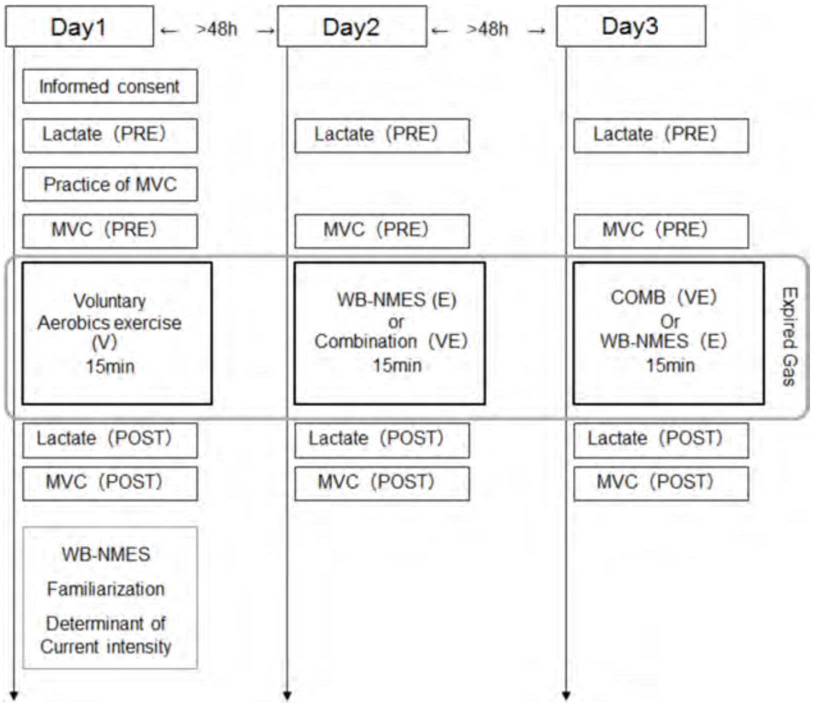

FIGURE 1 | Experimental protocols in this study.

obtained from the fingertip before and after exercise (Watanabe et al., 2014). Subjects sat in a chair during blood sampling. The mean value of two samples for one measurement was used for further analysis.

Maximal voluntary contraction during isometric knee extension and elbow flexion was measured before and after exercise to assess muscle fatigue of the knee extensor (quadriceps femoris) and elbow flexor (biceps brachii) muscles. The subjects were asked to gradually increase their isometric contraction force from the baseline to maximum in 2-3 s and then sustain it maximally for 2 s. Two MVCs were performed before the given exercise and the highest MVC value was used for analysis. After the specified exercise, the subjects performed one MVC. For knee extension, the subjects sat in a custom-made dynamometer and their ankle was fixed to the force transducer with a 90° knee joint angle and a 120° hip joint angles (Watanabe, 2018). For elbow flexion, the subjects sat in a chair and their forearm and wrist were fixed to the force transducer with a 120° elbow joint angle (Watanabe et al., 2015).

TABLE 1 | Electrode size and inter-electrode distance for each muscle group.

	Electrode size (mm)	Inter-electrode distance (mm)
Anterior upper arm	37 × 63	71
Posterior upper arm	37 × 63	71
Chest	37 × 63	53
Back	37 × 63	125
Abdominal	52 × 90	50
Abdominal oblique	37 × 63	40
Gluteus	52 × 90	51
Anterior thigh	51 × 144	102
Posterior thigh	51 × 144	64

Voluntary Exercise

The subjects performed voluntary exercise like body weight resistance training for the whole body during V and VE. This exercise program includes 60 s of stepping as warm-up, 96 s of horizontal squat with pec deck fly (16 reps), 180 s of pec deck fly (30 reps), 198 s of lunge with twist (32 reps), 96 s of horizontal squat with arm curl (16 reps), 5 sets of knee-to-elbow as much as possible in 5 s with 10 s of inter-rest, and resting phases between these exercises (Total: 15 min.). During V and VE, the experimenters showed the subject the specified exercise and instructed them on it.

WB-NMES

NMES was applied to the anterior and posterior upper arm, chest, back, abdominal, abdominal oblique, gluteus and anterior and posterior thigh muscles using the custom-made stimulator based on a commercially developed NMES device (SIXPAD, MTG Ltd., Nagoya, Japan) (Watanabe et al., 2017). Silicon-rubber electrodes covered by wet clothes were used as stimulation electrodes. Pairs of electrodes were placed on the individual muscle groups, with the details of each electrode shown in **Table 1**. These electrodes were set on the inside of an arm band, vest, and shorts that can be tightened by adjustor belts (**Figure 2**) and were connected to small wireless stimulators

FIGURE 2 | Arm band, vest, and shorts for whole-body neuromuscular electrical stimulation (Left panel) and their inside electrode locations for each muscle group (Right panel).

(48.4 x 36.5 x 15.0 mm, 27 g) that are synchronized among stimulators by a control unit. The fundamental duty cycle of NMES was a 4 s stimulation with a 4 s pause and the stimulation frequency was 20 Hz (Moritani et al., 1985). We also applied 2 Hz stimulation during the warm-up and resting phases. Biphasic square current pulses with a 100 μs duration were applied. The maximal electrical potential and current intensity of this device were 50 V and 4.85 mA, respectively. The current intensity was determined as the highest intensity that the subject could perform voluntary exercise without discomfort in each muscle group. The subjects chose 20∼80% of the maximal current intensity of the device. Familiarization with and determination of the stimulation intensity for each subject for WB-NMES were performed after measurements of V on Day1 (**Figure 1**). During VE and E, the current intensity for each muscle group was dynamically changed between 70−100% of the maximal tolerant current intensity for each subject following joint movement in voluntary exercise. For example, current intensities for the chest, back, gluteus, and posterior thigh muscle groups were 100% of the maximal tolerant current intensity for each subject and those for arms, abdominal, and abdominal oblique muscles were 70% of the maximal tolerant current intensity for each subject during the horizontal squat with pec deck fly (E1, **Table 2**).

TABLE 2 | Stimulation frequency and intensity during whole body neuromuscular electrical stimulation.

	W-up	E1	E2	E3	E4	E5	Rest
Frequency (Hz)							
	2	20	20	20	20	20	2
Stimulation intensity (% of maximum for each subject)							
Anterior upper arm	100	70	0	50	100	100	30∼100
Posterior upper arm	100	70	0	50	100	100	30∼100
Chest	100	100	100	70	70	100	30∼100
Back	100	100	100	70	70	100	30∼100
Abdominal	100	70	100	100	70	100	30∼100
Abdominal oblique	100	70	70	100	70	100	30∼100
Gluteus	100	100	70	100	100	100	30∼100
Anterior thigh	100	100	70	100	100	100	30∼100
Posterior thigh	100	100	70	100	100	100	30∼100

W-up, stepping as warm-up; E1: horizontal squat with pec deck fly; E2, Pec deck fly (30 reps), E3, Lunge with twist; E4, Horizontal squat with arm curl; E5, Knee-to-elbow.

During VE, contraction and relaxation times of NMES were synchronized with voluntary exercise, i.e., NMES was applied during muscle lengthening or shortening by joint movements. For E, the same WB-NMES program with VE was applied while the subjects were in a supine position on a bed without performing any voluntary contractions.

Statistics

All data are presented as the mean and standard deviation. To test the effect of the exercise type, one-way ANOVA was applied to $\dot{V}O_2$ relative to the body mass, RER, blood lactate concentration after exercises, and MVC after exercise relative to that before exercise. When there was a significant effect of the exercise type based on ANOVA, the parameters among V, E, and VE were compared by *post hoc* tests such as Tukey HSD. We also compared $\dot{V}O_2$ relative to the body mass between the summation of V and E that were separately performed and VE using the paired *t*-test. The level of significance was set at 0.05. The epsilon-squared estimate of effect size (ε^2) was additionally calculated and this value from 0 to 1 indicates no relationship to a perfect relationship (Tomczak and Tomczak, 2014). Statistical power was calculated in *post hoc* tests for energy expenditure, VO2 relative to the body mass, RER, blood lactate concentration, and MVC after exercise for knee extension and elbow flexion (Vincent, 2005). Statistical analyses were performed using SPSS software (version 15.0; SPSS, Tokyo, Japan).

RESULTS

There were significant effects of the exercise type on energy expenditure ($n = 13$, df = 2, $p < 0.0001$, $F = 843.479$, ES = 0.986), $\dot{V}O_2$ relative to the body mass ($n = 13$, df = 2, $p < 0.0001$, $F = 881.063$, ES = 0.987), RER ($n = 13$, df = 2, $p < 0.0001$, $F = 3471.804$, ES = 0.997), and blood lactate concentration after exercise ($n = 13$, df = 2, $p < 0.0001$, $F = 142.849$, ES = 0.923) (**Figures 3**, **4**). Energy expenditure during VE was significantly higher than during V and E and that during V was significantly higher than during E ($n = 13$, $p < 0.001$, $F = 39.687$, $ES = 0.878$) (**Figure 3**). $\dot{V}O_2$ relative to the body mass during VE was significantly higher than during V and E, and that during V was significantly higher than during E ($n = 13$, $p < 0.001$ for VE vs. E and V and E, $p < 0.001$ for VE vs. V, F = 39.037, ES = 0.877) (**Figure 3**). RER during E and VE was significantly higher than during V ($n = 13$, $p = 0.001$, $F = 11.73$, ES = 0.681) (**Figure 3**). The blood lactate concentration after VE was significantly higher than after V and E ($n = 13$, $p = 0.001$, $F = 13.873$, ES = 0.716)

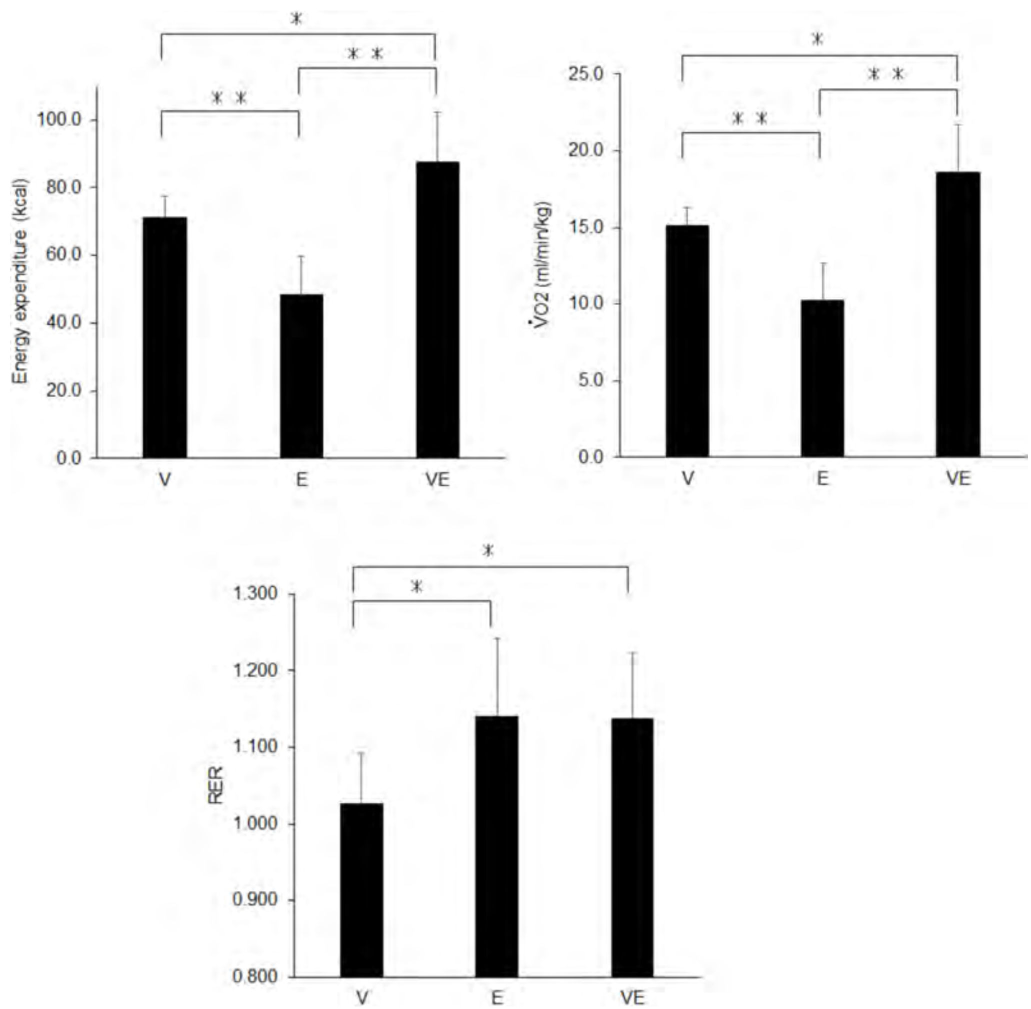

FIGURE 3 | Energy expenditure (Left upper panel), $\dot{V}O_2$ relative to the body mass (Right upper panel), and the respiratory gas exchange ratio (RER) (Bottom panel) during voluntary aerobic exercise (V), whole-body neuromuscular electrical stimulation (E), and their combination (VE). *$p < 0.05$, **$p < 0.01$.

(**Figure 4**). There were no significant differences among the exercises in MVC after exercise for knee extension and elbow flexion ($p > 0.05$) (**Figure 4**). The metabolic equivalents for V, E, and VE were 4.31 ± 0.35, 2.93 ± 0.71, and 5.31 ± 0.89 Mets, respectively. Statistical power in *post hoc* tests for energy expenditure, VO2 relative to the body mass, RER, blood lactate concentration, and MVC after exercise for knee extension and elbow flexion were 87.1 ± 12.4 (67.1-100.0).

$\dot{V}O_2$ relative to the body mass of VE exercise (18.6 ± 3.1 ml/min/kg) was significantly lower than the summation of $\dot{V}O_2$ relative to the body mass of V and E (21.8 ± 3.3 ml/min/kg) ($n = 13$, df = 12, $p = 0.007$).

DISCUSSION

We investigated metabolic responses and muscle fatigue during WB-NMES, voluntary exercise, and their combination. The main findings of the present study were 1) $\dot{V}O_2$ relative to the body mass during VE was greater than during V and E ($p < 0.05$) (**Figure 3**) and was lower than the summation of those during V and E, 2) RER during E and VE was higher than during V ($p < 0.05$) (**Figure 3**) and the blood lactate concentration after VE was markedly higher than after V and E ($p < 0.05$) (**Figures 3**, **4**) there were no significant differences in MVC after the exercises ($p > 0.05$) (**Figure 4**). The results support the former part of hypothesis 1 that energy expenditure during the combination of voluntary exercise and WB-NMES is greater than during WB-NMES and voluntary exercise, but not the latter part of the hypothesis that energy expenditure during the combination of exercise and WB-NMES is greater than their summation. While hypothesis 2 was not supported, hypothesis 3 whereby the addition of WB-NMES to voluntary exercise enhances glucose metabolism was supported by the results of the present study.

Greater energy expenditure during the combination of voluntary exercise and WB-NMES (VE) compared with the separately performed voluntary exercise (V) and WB-NMES (E), as shown in the present study (**Figure 3**), is reasonable,

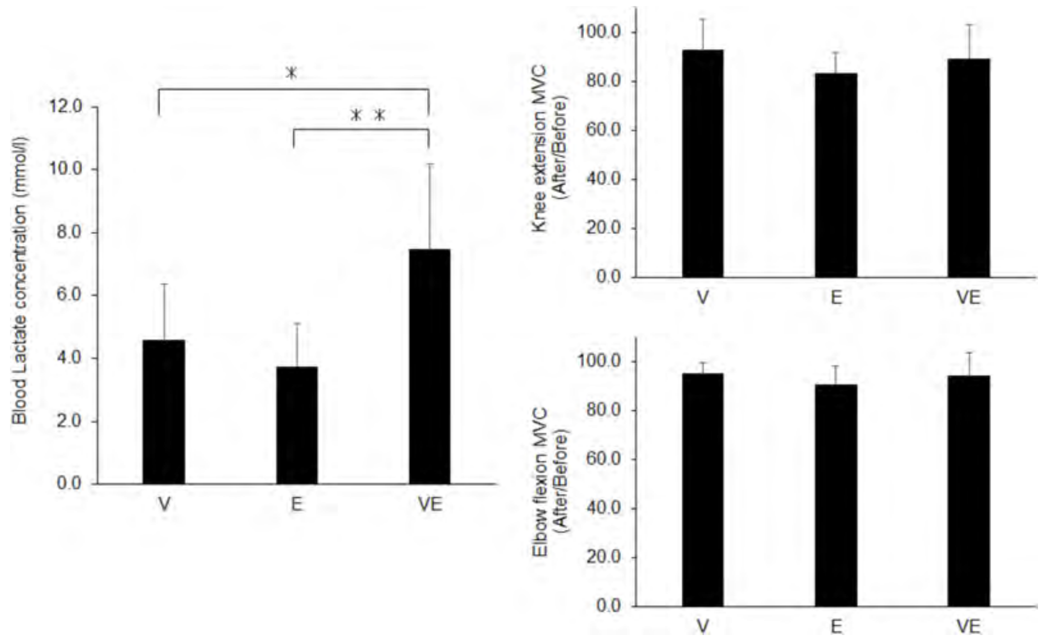

FIGURE 4 | Blood lactate concentration (Left panel) and maximal voluntary contraction (MVC) after the exercises normalized by that before exercises (Right panels) for voluntary aerobic exercise (V), whole-body neuromuscular electrical stimulation (E), and their combination (VE). $^{*}p < 0.05$, $^{**}p < 0.01$.

since NMES can enhance energy expenditure by itself (Hamada et al., 2004a). We already demonstrated an increase in energy expenditure by the addition of NMES to leg muscles during aerobic pedaling exercise on a cycle ergometer (Watanabe et al., 2014). Another study also reported that the addition of WB-NMES leads to a 20% increase in energy expenditure during voluntary exercise (Kemmler et al., 2012). Since the increase in energy expenditure by the addition of WB-NMES was approximately 23% in the present study (**Figure 3**), VE was comparable to the combined program of voluntary exercise and WB-NMES used in a previous study by another research group (Kemmler et al., 2012). Thus, we suggest that the addition of WB-NMES increases energy expenditure during voluntary exercise. On the other hand, we found that this increase in energy expenditure due to the addition of WB-NMES could not be simply explained by the summation of energy expenditures from performing the two exercises. Our results showed that $\dot{V}O_2$ relative to the body mass during the combination of WB-NMES and voluntary exercise (VE) (18.6 $\pm$ 3.1 ml/min/kg) was significantly lower than those for WB-NMES (E) and voluntary exercise (V) that were separately performed (25.3 $\pm$ 3.3 ml/min/kg) ($p < 0.05$). We consider that wearing the suits with electrodes and the muscle contraction elicited by NMES may restrict the range of motion for voluntary exercise. While our study did not measure joint kinematics during the exercises, the range of motion during VE may be more restricted than that during V. This should be noted when the combination of WB-NMES and voluntary exercise is applied as an exercise tool.

The present study showed characteristic metabolic responses during the combination of WB-NMES and voluntary exercise compared with separately performed voluntary exercise and WB-NMES. RER during VE were significantly higher than V exercise ($p < 0.05$) (**Figure 3**). This finding is consistent with our previous study that NMES to leg muscles was applied during pedaling exercise (Watanabe et al., 2014). Also, RER during E, which did not involve any voluntary contractions has greater compared with that of V. Greater RER means an increase in the CO_2 concentration in expired gas, which occurs with the enhancement of anaerobic energy metabolism. It is well-known that NMES can enhance anaerobic energy metabolism due to the recruitment of high-threshold motor units or muscle fibers associated with glucose metabolism (Hamada et al., 2004a,b; Gregory and Bickel, 2005; Jubeau et al., 2007; Bickel et al., 2011). Thus, our results suggest that WB-NMES can increase anaerobic energy metabolism irrespective of whether or not aerobic voluntary exercise is simultaneously applied.

The blood lactate concentration which is also indicator of the metabolic response, was significantly greater in VE than in V and E ($p < 0.05$) (**Figure 4**). This could also be due to NMES-induced recruitment of high-threshold motor units and muscle fibers (Hamada et al., 2004a,b; Gregory and Bickel, 2005; Jubeau et al., 2007; Bickel et al., 2011). On the other hand, there was a significant difference in the blood lactate concentration between VE and E ($p < 0.05$) (**Figure 4**), while RER was not significantly different between them ($p > 0.05$) (**Figure 3**). The blood lactate concentration is determined by both the production and consumption of lactate in metabolic systems. Lactate can be utilized as an energy source by skeletal muscles under high tissue-oxygen conditions, i.e., during voluntary exercise, while it cannot be consumed and accumulates in the blood under low tissue oxygen conditions, i.e., during anaerobic exercise (Brooks, 1986).

A greater blood lactate concentration in VE compared with E may be explained by a decrease in lactate consumption during VE due to low tissue-oxygen conditions induced by the combination of voluntary exercise and WB- NMES. Also, it should be noted that the blood lactate concentration after VE was markedly increased in the present study, i.e., 7.5 ± 2.7 mmol/l (**Figure 4**). The metabolic cost during VE in this study was 5.31 ± 0.89 Mets, calculated from $\dot{V}O_2$, and this metabolic cost corresponds to that during brisk walking (Jette et al., 1990). Since blood lactate concentration of 7.5 mmol/l is observed during high-intensity exercise such as high-intensity interval training (Faude et al., 2009), the combination of voluntary exercise and WB-NMES can enhance the characteristic metabolic response, which cannot be explained by the relationship between the metabolic cost and blood lactate concentration during voluntary exercise.

We estimated energy expenditure, oxygen consumption, and metabolic characteristics by the method of spirometry. As shown in the result of blood lactate concentration, more than 7 mmol/l was observed in VE in the present study (**Figure 4**), indicating that a high anaerobic fraction during metabolism were recruited during this type of exercise. Under the exercise with anaerobic metabolism is enhanced, measurements of metabolic responses with the method of spirometry may underestimates the actual energy consumption, because anaerobic metabolism could be a delayed effect on the respiratory gases (Green and Dawson, 1993). Therefore, energy consumption may be underestimated in VE that recruited anaerobic metabolism in the present study. This would be limitation of this study and it should be noted that our results include this methodological issue in the calculation of metabolic responses and energy expenditure, in particular VE exercise. Significant lower oxygen consumption in VE comparing with the summation of V and E may be partly explained by the underestimation due to the methodology. In the future studies, we need to measure the metabolic responses after exercises to quantify the oxygen required to eliminate the "oxygen debt" for a better approximation of the actual energy consumption.

We assessed local neuromuscular fatigue using a comparison of MVC before and after the exercises. MVC decreased by approximately 10% after all exercises (**Figure 4**), and so all would induce muscle fatigue. However, there were no significant differences among the exercise types in MVC after the exercises for knee extensor and elbow flexor muscles ($p > 0.05$) (**Figure 4**). Considering that the blood lactate concentration was significantly higher in VE compared with V and E ($p < 0.05$) (**Figure 4**), a greater decrease in MVC after VE should be observed. This difference in results between local muscle fatigue assessed by MVC and blood lactate concentration could be mainly explained in two ways. First, while we applied NMES to nine muscle groups of the upper body, trunk, and lower extremities, MVC was measured for only two muscle groups. We thus estimated that differences in local neuromuscular fatigue among the exercises may occur in other muscle groups. Second, as stated above, both the production and consumption of lactate in metabolic systems contribute to the blood lactate concentration (Brooks, 1986). The greater blood lactate concentration in VE compared with V and E under similar local neuromuscular fatigue among the three exercises assessed by MVC may be explained by differences in lactate consumption between VE and V and E, as discussed above.

CONCLUSION

The present study revealed that the found that combination of aerobic exercise and WB-NMES leads to greater energy expenditure, an increase in RER in expired gas, and a marked increase in the blood lactate concentration when comparing with those of separately performed aerobic exercise and WB-NMES. These results suggest that the combination of voluntary exercise and WB-NMES can enhance the metabolic response to a level equivalent to that of high-intensity exercise under the net physiological burden of low-middle-intensity exercise. This type of exercise would be useful for individuals who are unable to perform high-intensity exercise requiring anerobic metabolism or the recruitment of high-threshold motor units/muscle fibers such as type 2 diabetes mellitus patients and/or older adults.

DATA AVAILABILITY

All datasets generated for this study are included in the manuscript and/or the supplementary files.

AUTHOR CONTRIBUTIONS

KW, SK, and TM planned the research. KW, SK, TY, and TI conducted the experiments. KW, TY, and TI analyzed the data. KW, SK, TY, TI, and TM discussed the results. KW wrote the manuscript. KW and TM edited and reviewed the manuscript.

FUNDING

This research was partly supported by the grant from MTG Co., Ltd., Nagoya, Japan.

ACKNOWLEDGMENTS

The authors gratefully acknowledge Miki Sakai from MTG Co., Ltd. for assistance with the experiments.

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Conflict of Interest Statement: SK is employed by company MTG Co., Ltd. All other authors declare no competing interests.

frontiers in Physiology

ORIGINAL RESEARCH
published: 09 May 2019
doi: 10.3389/fphys.2019.00548

Influence of Whole-Body Electrostimulation on the Deformability of Density-Separated Red Blood Cells in Soccer Players

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Edited by:
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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *11 March 2019*
Accepted: *18 April 2019*
Published: *09 May 2019*

Citation:
Filipovic A, Bizjak D, Tomschi F, Bloch W and Grau M (2019) Influence of Whole-Body Electrostimulation on the Deformability of Density-Separated Red Blood Cells in Soccer Players. Front. Physiol. 10:548. doi: 10.3389/fphys.2019.00548

Red blood cell nitric oxide synthase (RBC-NOS) dependent NO production positively affects RBC deformability which is known to improve oxygen supply to the working tissue. Whole-body electrostimulation (WB-EMS) has been shown to improve maximum strength, sprinting and jumping performance, and to increase deformability in elite soccer players during the season. The aim of the present study was to investigate whether WB-EMS affects RBC turnover which might affect overall deformability of circulating RBC by rejuvenation of the RBC population and if this might be related to improved endurance capacity. Thirty male field soccer players were assigned in either a WB-EMS group (EG, *n* = 10), a training group (TG, *n* = 10), or a control group (CG, *n* = 10). EG performed 3 × 10 squat jumps superimposed with WB-EMS twice per week in concurrent to 2–4 soccer training sessions and one match per week. TG only performed 3 × 10 squat jumps without EMS in addition to their soccer routine and the CG only performed the usual soccer training and match per week. Subjects were tested before (Baseline) and in week 7 (wk-7), with blood sampling before (Pre), 15–30 min after (Post), and 24 h after (24 h post) the training. Endurance capacity was determined before and directly after the training period. The key findings of the investigation indicate an increase in young RBC in the EG group along with improved overall RBC deformability, represented by decreased SS1/2:EImax Ratio. Analysis of the different RBC subfractions revealed improved RBC deformability of old RBC during study period. This improvement was not only observed in the EG but also in TG and CG. Changes in RBC deformability were not associated to altered RBC-NOS/NO signaling pathway. Endurance capacity remained unchanged during study period. In summary, the effect of WB-EMS on RBC physiology seems to be rather low and results are only in part comparable to previous findings. According to the lower training volume of the present study it can be speculated that the soccer specific training load in addition to the WB-EMS was too low to induce changes in RBC physiology.

Keywords: electrostimulation, soccer, RBC, VO_2peak, NO-oxidation, deformability

INTRODUCTION

Electromyostimulation (EMS) has been used to complement rehabilitation programs for many years. Lately, EMS is increasingly combined with strength training in high performance sports. Modern whole-body EMS (WB-EMS) systems (e.g., miha bodytec, Augsburg, and Germany) allow athletes to simultaneously stimulate several muscle groups, to train a whole muscle chain and thus to dynamically train specific movements, e.g., jumping movement. A recent study with professional soccer players revealed an increase in maximal strength, jumping, and sprinting ability after WB-EMS training (Filipovic et al., 2016). The study further showed that two sessions of dynamic WB-EMS a week can be sufficient to significantly influence the functional parameters of the red blood cells (RBC) (Filipovic et al., 2015).

Within the body, RBC deliver oxygen to the muscle tissues via the blood flow through the vessel system. To do so, RBC have to deform their shape in order to pass the smallest capillaries of the microcirculation. This RBC deformability is a unique cell characteristic and is, among others, influenced by nitric oxide (NO) (Bor-Kucukatay et al., 2003; Suhr et al., 2012; Grau et al., 2013). In RBC, NO is actively produced by RBC-NO synthase (RBC-NOS) (Kleinbongard et al., 2006; Grau et al., 2013). The phosphorylation status of RBC-NOS has been used as a marker of enzyme activation. Activation occurs through different stimuli such as inflammatory cytokines, growth factors, and hormones, etc (Forstermann and Sessa, 2012) or exercise induced shear stress through activation of Akt kinase (Suhr et al., 2012). Biomechanical stimulation in the form of increased shear stress stimulates the phosphorylation of the RBC-NOS epitopes serine 1177 (Serine^{1177}) via the PI3 Kinase/Akt Kinase pathway (Dimmeler et al., 1999; Suhr et al., 2012). The activated RBC-NOS generates NO, which is a precondition for increasing RBC deformability (Suhr et al., 2012; Grau et al., 2013). In contrast, phosphorylation of RBC-NOS residues threonine 495 (Thr^{495}) or serine 114 (Ser^{114}) were associated to decreased RBC-NOS activation (Grau et al., 2016). RBC-NOS produced NO binds to reactive cysteine thiols, a reaction termed S-nitrosylation. Grau et al. (2013) identified α- and β-spectrin as potential targets for S-nitrosylation in the RBC with increasing S-nitrosylation of the spectrins being associated to increased RBC deformability.

Connes et al. (2004) indicated that increased RBC deformability might improve the blood oxygen content due to an increased oxygen diffusion from alveoli to pulmonary capillaries. This might suggest that an increase in RBC deformability might favour performance capacity.

Soccer match play is characterized by high intensity repeated sprint actions that require a high muscle oxygenation. Higher muscle oxygen-level can positively influence the re-oxygenation of the muscles and thus phosphocreatine re-synthesis for a faster recovery. Due to the high demand of muscle oxygenation during match play, improved RBC deformability could be advantageous for the specific endurance capacity of soccer players such as repeated sprint ability (c.f. Brun et al., 2010).

An increase in RBC deformability after WB-EMS stimulation was associated – at least after acute application – via RBC-NOS activation and increased NO production, respectively (Filipovic et al., 2015). However, the observed chronic increase in RBC deformability occurred in the absence of a further RBC-NOS activation and it was speculated whether WB-EMS might affect RBC turnover. RBC are a heterogeneous cell population consisting of RBC of different ages. RBC aging was associated to a progressive decrease in RBC deformability, paralleled by increasing RBC-NOS activation and NO production (Bizjak et al., 2015).

The purpose of the present study thus was to investigate whether a 7 week dynamic WB-EMS program affects RBC deformability through shift in RBC age distribution, and to examine whether these changes are sustained 3 weeks after the last intervention session. Further, it is unknown if an increased RBC deformability through WB-EMS-Training can positively influence the endurance capacity which was thus also aim of the present study.

MATERIALS AND METHODS

Participants

Only healthy participants were included which means no cardiovascular or metabolic diseases and no preinjury in the tested muscle groups. Participants needed to compete on a national level for the last 3 years and train 2–4 session per week and play one soccer match per week. Experience in strength training was mandatory. Thirty soccer players were randomly assigned into three different groups. The EMS groups (EG, $n = 10$) performed dynamic whole-body strength training with EMS twice a week accompanied by 3×10 squat jumps in addition to the daily soccer routine over a period of 7 weeks. To differentiate between the effects caused by EMS and by the squat jumps and soccer training, respectively, two control groups were included. A jump training group (TG, $n = 10$) performed the same number of squat jumps without EMS stimulus on the same days as the EG and a control group (CG, $n = 10$) that only performed the daily soccer routine.

Basal anthropometric parameters of the participants are presented in **Table 1**. All subjects abstained from alcohol consumption for 24 h prior to and during the training intervention and were non-smokers.

This study was carried out in accordance with the recommendations of the Ethics Committee of the German Sports University Cologne. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the German Sports University Cologne [06-02-2014].

Definition of Daily Soccer Routine

The participants were soccer players and performed 3.2 ± 1.0 training sessions per week and competed once a week in the championships. The standard training sessions lasted approximately 90 min including technical skill activities, offensive and defensive tactics, athletic components with various intensities, small-sided game plays, and continuous play. In a normal training week during season with a match on Sunday

TABLE 1 | Anthropometric data (mean ± SD) and total training load (arbitrary units) during the 7-week intervention period calculated by Polar Team-2 Software according to training time spent in defined heart rates (see section "Materials and Methods").

Group	Age (Year)	Height (m)	Weight (kg)	Bodyfat (%)	relVO$_2$peak (ml/kg*min^{-1})	Sessions/week	Total training load (a.u)
EG	24.4 ± 4.2	1.82 ± 0.03	81.4 ± 5.3	12.9 ± 2.1	52.1 ± 3.4	3.4 ± 1.2	3430.6 ± 910.7
TG	21.1 ± 1.9	1.83 ± 0.06	79.7 ± 5.5	10.8 ± 2.8	56.3 ± 5.7	3.4 ± 1.3	3478.6 ± 1722.8
CG	23.6 ± 3.9	1.82 ± 0.05	79.7 ± 7.5	14.1 ± 3.6	54.3 ± 7.2	2.6 ± 0.7	2644.4 ± 1437.3

training was scheduled on Tuesdays, Wednesdays (optional), Thursdays, and Fridays. Number of training sessions and the training days varied according to the game schedule playing Sunday-Sunday or Sunday-Saturday. The number of training sessions and the total training minutes were documented. The training load was measured according to the training time spent in defined heart rate zones during soccer training or match via Polar Team-2 Software (Polar Electro, Büttelborn, Germany) (see **Table 1**). The training load provided by the Polar-Software aims to determine internal training load based on background variables [sex, training history, metabolic thresholds, and maximal oxygen consumption (VO$_2$max)] and parameters measured during training sessions (exercise mode, and energy expenditure) (c.f. Schumann et al., 2017). The heart rate zones (100–90%, 89–80%, 79–70%, 69–60%, and 59–50%) were defined according to the individual maximum heart rate measured in the maximal ramp test (see endurance test).

The players were asked to maintain their usual food intake und hydration according to the recommendations for soccer players (García-Rovés et al., 2014) and no nutrition supplementation was used. Additional strength training was not allowed during the study.

All players had a constant training volume during the first half of the season (July till December) and were in a well-trained condition with a relative VO$_2$peak of 54.2 ± 5.9 ml/kg*min^{-1}. All players regularly conducted strength training during first half of the season and had experience in strength training of 5.4 ± 3.9 years. The intervention period started after the 3 week mid-season break from end of December till mid of January. During these 3 weeks the training load was relatively low (moderate endurance training twice per week) in order to maintain fitness level and not negatively affect baseline testing.

Exercise Protocol

Whole-body electrostimulation training was conducted on Tuesdays and Fridays in order to obtain a rest interval of 48 h between the two sessions and the championship game on Sunday. The WB-EMS training was conducted using a WB-EMS-system by "*miha bodytec*" (Augsburg, Germany). WB-EMS was applied with an electrode vest to the upper body including the chest, upper and lower back, latissimus, and the abdominals and with a belt system to the lower body including the muscles of the glutes, thighs, and calves. Biphasic rectangular wave pulsed currents (80 Hz) were used with an impulse width of 350 μs (c.f. Filipovic et al., 2016). The stimulation design has been shown to be effective for enhancing strength and performance parameters and to also positively influence RBC deformability (Filipovic et al., 2015, 2016). The squat jumps were only included to integrate specific movement patterns to support strength transfer into jumping and sprinting ability (Requena-Sanchez et al., 2005) and for a better regulation of stimulation intensity to a sub-maximal level. The stimulation intensity (0–120 mA) was determined and set separately for each muscle group by using a Borg Rating of Perceived Exertion (c.f. Tiggemann et al., 2010). The training intensity was defined for each players in a familiarization session 2 weeks before and set at a sub-maximal level that still assures a clean dynamic jump movement (RPE 16–19 "hard to very hard") and was saved on a personalized chip card. The EG performed 3 × 10 maximal squat jumps with a set pause of 60 s (no currents) per session. Every impulse for a single jump lasted for 4 s (range of motion: 2 s eccentric from standing position to an knee angle of 90° – 1 s isometric – 0.1 s explosive concentric – 1 s landing and stabilization) followed by a rest period of 10 s (duty cycle approx. 28%). The players started with a 2–3 min standardized warm-up with movement preparations including squats, skipping and jumps in different variations (squat jumps, jumps out of skipping, or double jumps) at a light to moderate stimulation intensity. The players were told to slowly increase the intensity every few impulses. The training started when the players reached the defined training intensity that was saved on the chip card from the last session according to the RPE 16–19 ("hard to very hard"). The stimulation intensity was constantly increased individually every week (Tuesdays) controlled by the coaches in order to maintain a high stimulation intensity. The intensity was increased after the warm-up during the first and the second set of 10 squat jumps starting from calves up to the chest electrodes.

The TG conducted the same standardized warm-up and performed the same amount of jumps with identical interval and conduction twice per week without EMS. The CG only performed the 2–4 soccer training session plus one match per week.

Experimental Protocol

Endurance Test

For determination of relative maximum oxygen uptake (VO$_2$ peak), spirometry was performed on a WOODWAY treadmill (Woodway GmbH, Weil am Rhein, Germany) 1 week before (Baseline) and within 7 days after the 7-weeks intervention period (Posttest) and again after a detrain period of 3 weeks (Retest) (**Figure 1**). Endurance tests were conducted three days after the soccer match to assure adequate recovery and not negatively influence performance. Spirometry was analyzed with the ZAN600-System and ZAN-Software GPI 3.xx (ZAN Austria e.U., Steyr-Dietach, Austria). To calibrate the device, a gas mixture consisting of 5% CO_2, 16% O_2, and rest nitrogen was used (*Praxair Deutschland GmbH,* Düsseldorf,

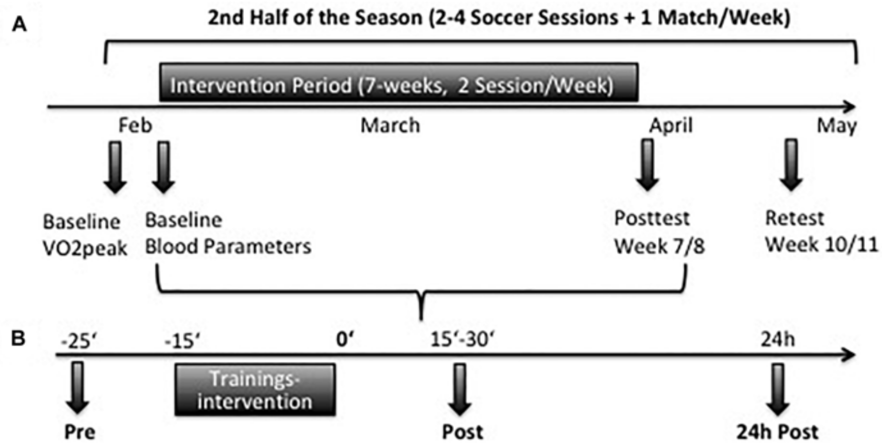

FIGURE 1 | (A) Timeline of endurance testing and blood samples during the study in the second half of the season. **(B)** Timeline of blood samples collection at Baseline and in week 7. At each testing samples were taken before (pre), after 15–30 min (post), and 24 h (24 h post) after the training interventions.

Germany). To measure VO_2 peak, the subjects performed an endurance ramp test according to a protocol of the Institute of Cardiovascular Research and Sports Medicine (German Sport University Cologne).

The players performed a warmup with moderate speed (3 m/s) at 1% incline for 3 min. In the last 30 s the incline was increased to 2.5%. Running speed was then increased every 30 s by 0.3 m/s till subjective exhaustion. Heart rate was documented in the last 10 s of a ramp stage. The VO_2peak was determined as average maximum oxygen uptake of the first 20 s after completion of the test. Additionally, maximum heart rate (HF_{max}), time to exertion (TTE), maximum lactate production and respiratory quotient ($RQ = V\,CO_2/V\,O_2$) was documented by the ZAN-system.

Blood Sampling

At Baseline and at wk-7, blood samples were taken from the vena mediana cubiti of EG and TG before (Pre), 15–30 min after (Post) and 24 h after the interventions (24 h Post), respectively. Blood samples of the CG were taken at the same day time as the intervention groups. For CG samples were only taken before (Pre) because no training sessions were performed between pre and 24 h post sampling (**Figure 1**). A third sampling was scheduled 3 weeks after the end of the intervention period (Retest). Blood was anticoagulated using ethylenediaminetetraacetic acid (EDTA) vacutainer (BD, United States) to measure basal blood parameters or using sodium heparin vacutainer (BD, United States) to measure RBC deformability of RBC in general and of RBC separated according to RBC age (young, main fraction, old, and very old) and related RBC-NOS/NO parameters such as S-nitrosylation and nitrite.

Basal Blood Parameters

Ethylenediaminetetraacetic acid anticoagulated blood was used for the determination of reticulocytes and basal blood parameters (RBC count, white blood cell count, platelet count, hemoglobin concentration, hematocrit, mean cellular volume, mean cellular hemoglobin, and mean cellular hemoglobin concentration). Reticulocytes were analyzed by laboratory Dr. Wisplinghoff, Cologne, Germany. Determination of the hematological profile was obtained using hematology analyzer Sysmex Digitana KX-21N (Sysmex, Horgen, Switzerland).

RBC Subpopulation

Red blood cell were isolated and fractioned to separate young, main fraction old and very old RBC using percoll density centrifugation according to a modified protocol of Bizjak et al. (2015).

Whole blood samples were centrifuged for 1 min at 3500 g at room temperature and plasma and buffy coat were removed. Isolated RBC were washed 10:1 with GASP-buffer (9 mmol/L $Na_2HPO_{4,1.3}$ mmol/L NaH_2PO_4, 140 mmol/L NaCl, 5.5 mmol/L glucose, 0.8 g/L BSA) and centrifuged as described above. The supernatant was discarded and RBC were diluted 1:1 with SAH-buffer (26.3 g/L BSA, 132 mmol/L NaCl, 4.6 mmol/L KCl, 10 mmol/L HEPES).

Percoll solutions with a density of 1.064, 1.066, 1.068, 1.072, and 1.076 g/mL in SAH buffer (Amersham Biosciences, Sweden) were prepared from a Percoll stock solution (1.131 g/mL; VWR). Solutions were layered into a 15 ml tube one on top of the other with the densest layer being right at the bottom. 600 μl of washed and diluted RBC were cautiously given on top of the layers centrifuged at 3000 rpm for 25 min at room temperature to receive young (1.064 g/ml), main fraction (1.065–1.068 g/ml), old (1.072 g/ml), and very old (1.076+ g/ml) RBC. RBC fractions were washed 1:1 with GASP and centrifuged as described above. The supernatant was discarded and the RBC fractions were used for deformability and age distribution analysis. The proportion of each fraction was determined and expressed as percentage of whole RBC.

RBC Deformability

Red blood cell deformability was directly measured after blood sampling and after separation of RBC according to cell age by ektacytometry using the Laser-assisted-optical-rotational cell analyzer (LORCA; RR Mechatronics, Netherlands) described in detail by Hardeman et al. (2001). Briefly, 10 μl of RBC were solved in 2.5 ml of isotonic 0.14 mM polyvinylpyrrolidone (PVP) (osmolarity 300 mOsmol/L, viscosity 28.7 mPa*sec at 37°C). The samples were sheared in a Couette system at nine shear stresses between 0.3 and 50 Pa. A laser beam was directed through the samples and deformation of RBC affected diffraction pattern of the laser beam. The LORCA software used and width (W) and length (L) of the diffraction pattern to calculate an elongation index (EI): EI = (L-W)/(L+W) for the nine shear stresses. EI_{max}, representing maximal deformability at infinite shear stress, and SS ½, representing shear stress necessary for one-half of EImax, were calculated from the curves according to Baskurt et al. (2009). Finally, the ratio of SS1/2:EImax was calculated as described by Baskurt and Meiselman (2013).

Immunohistochemistry

For immunohistochemistical staining, RBC was fixed with 4% formaldehyde in a 1:2 ratio for 20 min at room temperature and washed using 0.1 M PBS. Washed RBC were dispersed on a slide and heat fixed. Immunostaining was performed according to the detailed protocols of Grau et al. (2013) and Bizjak et al. (2015) with primary antibody dilutions of 1:150 for Rabbit anti – phospho-eNOSSerine^{1177} (Merck, Darmstadt, Germany, 07–428), 1:500 for Rabbit anti-phospho-eNOS Serine^{116} (Merck, Darmstadt, Germany, 07–357), 1:400 for Rabbit anti-phospho-eNOS Threonine^{495} (Cell Signaling, Leiden, Netherland, 9574S), 1:700 for Rabbit anti eNOS (BD Biosciences, NJ, United States, 610299), 1:500 for Rabbit anti Human AKT1/PKBα (Merck, Darmstadt, Germany, 07–416), 1:500 for Rabbit anti-phospho AKTSerine^{473} (Cell Signaling, Leiden, Netherlands, 9271). Primary antibody was incubated for 1 h (for Serine^{1177}: overnight at 4°C). A control area, located on the same slide, was incubated in the absence of primary antibodies. After rinsing with TBS and an incubation step with 3% Normal Goat Serum (Dako Agilent Technologies, Germany), both areas were incubated with the secondary goat-anti-rabbit antibody (biotinylated, dilution 1:400; Dako Agilent Technologies, Germany) for 1 h at RT. A streptavidin-horseradish-peroxidase complex (Sigma-Aldrich, United States) was applied as detection system (dilution 1:400) for 30 min at room temperature. The staining was developed using 3,3-diaminobenzidine-tetrahydrochloride solution (Sigma-Aldrich, United States) in 0.1 mol/L TBS.

The stained slides were dehydrated in raising alcohol solutions, mounted with Entellan® (Merck, Darmstadt, Germany) and covered.

Pictures were taken using a Leica microscope coupled to a CCD-camera (DXC-1850P, Sony, Germany) with a magnification of 400-fold. Gray value determination was used for staining intensity analysis. The mean gray values of the edge of 50 RBC on at least 4 different visual fields of the test area and 10 RBC on at least 2 visual fields of the control area were measured with the software "Image J" (National Institutes of Health, United States).

Total immunostaining intensity was calculated as the mean of measuring RBC gray value minus mean background gray value which was obtained on three different cell free areas of the slide. Mean gray values of the control area were subtracted from mean gray values of the test area to yield net gray value representing staining of the RBC.

RBC S-Nitrosylation

For S-nitrosylation analysis of α- and β-spectrin, whole blood was separated by centrifugation (5000 g, 1 min, 4°C). Plasma was removed, RBC pellet was washed using 0.1 mol PBS and again centrifuged. RBC pellet was stored at −20°C until measurement.

S-nitrosylation was determined using S-Nitrosylated Protein Detection Kit (Cayman Chemicals, Ann Arbor, United States) which employs the Biotin-Switch Assay after Jaffrey and Snyder (2001). The protocol has been described in detail elsewhere (Grau et al., 2013). Using the kit buffer and solutions, RBCs were first lysed. Then, free thiol groups were blocked and S-nitrosothiols were cleaved. The newly formed thiols were biotinylated. The samples were then separated by gelelectrophoresis using 4–12% Bis-Tris gel (BioRad, Munich, Germany) and appropriate 1 × MOPS running buffer (BioRad). 60 μg of total protein were separated for 1 h under constant 90 mA and transferred to a polyvinylidene fluoride membrane (0.45 mm pore size). The background of the membrane was blocked in 2% bovine serum albumin (in 1 × TBS with 0.1% Tween 20) overnight at 4°C and incubated with a horseradish peroxidase (dilution 1:2000). The reaction was developed using an enhanced chemiluminescence kit containing peroxidase substrate (Thermo Fisher Scientific). S-nitrosylated protein bands at 240 and 220 kDa, previously identified as α-spectrin and β-spectrin, respectively (Grau et al., 2013), were examined for different "Integrated densities" using the (National Institutes of Health, Bethesda, Maryland, United States) software (Grau et al., 2013).

Nitrite Measurement

Whole blood was centrifuged (1000 g, 4°C, 10 min) and plasma samples were stored at −80°C for nitrite analysis.

For RBC nitrite determination, RBC were immediately mixed with preservation solution (800 mM $K_3[Fe(CN)_6]$, 100 mM NEM, 10 V-% Igepal, 90 V-% aqua dest) in a 5:1 ratio and stored at −80°C until measurement (Pelletier et al., 2006). For plasma

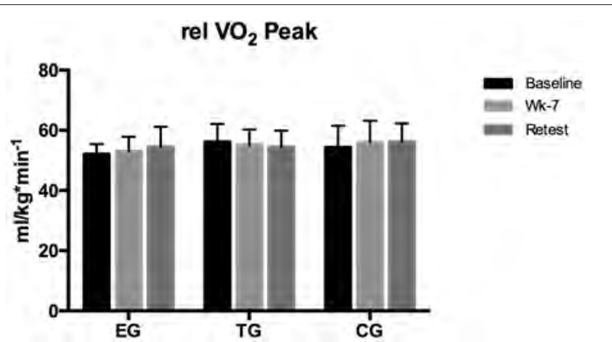

FIGURE 2 | Relative maximum oxygen uptake ($relVO_2peak$) at the endurance ramp-test on the treadmill in EMS-Group (EG), training-group (TG), and control-group (CG) measured before (Baseline) after week 7 (Posttest), and again after 3 weeks (Retest). Values are presented in means ± SD.

TABLE 2 | Basal blood parameters (mean ± SD).

		Baseline			Wk-7			Retest
		Pre	**Post**	**24 h Post**	**Pre**	**Post**	**24 h Post**	**Pre**
Erythrocytes	EG	5 ± 0.25	4.98 ± 0.25	5.06 ± 0.26	5.09 ± 0.23	5.03 ± 0.25	4.97 ± 0.29	4.97 ± 0.24
(10^6/μl)	TG	5.19 ± 0.61	5.10 ± 0.59	5.19 ± 0.66	5.31 ± 0.58	4.83 ± 1.15	5.18 ± 0.66	5.16 ± 0.47
	CG	5.2 ± 0.37			5.19 ± 0.27			5.18 ± 0.35
Thrombocytes	EG	253.2 ± 56.7	258.8 ± 52.6	253.75 ± 55.9	258.67 ± 49.5	266.78 ± 44.2	257.67 ± 54.8	262.7 ± 46.4
(10^3/μl)	TG	217.5 ± 42.3	219.5 ± 46.4#	223.8 ± 44.7	218.4 ± 40.4#	209.9 ± 40.9##	216.3 ± 43.5#	212.5 ± 47.2#
	CG	256.3 ± 63.5			255.44 ± 59.8			271.0 ± 63.4
Leukocytes	EG	5.9 ± 1.7	6.14 ± 2.46	6.39 ± 1.81	6.26 ± 1.85	5.87 ± 1.57	5.77 ± 1.49	6.23 ± 1.41
[10^3/μl]	TG	5.64 ± 1.28	5.2 ± 0.94	5.81 ± 1.29	6.13 ± 1.28	5.46 ± 1.41	5.67 ± 1.48	5.4 ± 1.21#
	CG	7.57 ± 2.24#			6.74 ± 1.48			6.46 ± 1.62
Reticulocytes	EG	9.36 ± 2.94	9.91 ± 3.14	9.65 ± 3.59	8.14 ± 2.18	8.59 ± 2.31	10.01 ± 2.03*	8.39 ± 1.45
(%o)	TG	12.47 ± 4.64	11.94 ± 5.0#	12.09 ± 4.67	11.75 ± 4.13##	9.73 ± 2.67	13.11 ± 3.67	10.15 ± 5.37
	CG	10.87 ± 3.01			9.81 ± 2.55#			9.63 ± 2.04
Hemoglobin	EG	14.86 ± 0.67	14.78 ± 0.66	15.01 ± 0.73	15.11 ± 1.03	14.91 ± 0.90	14.61 ± 0.91	14.69 ± 0.86
(g/dl)	TG	14.56 ± 0.96	14.38 ± 1.09	14.71 ± 1.03	14.96 ± 1.13	14.29 ± 1.11	14.49 ± 1.11	14.645 ± 1.07
	CG	15.27 ± 1.05			15.05 ± 0.89			15.11 ± 1.0
Hematocrit	EG	43.44 ± 1.94	43.22 ± 1.98	44.13 ± 1.80	44.56 ± 2.60	43.78 ± 2.11	43.89 ± 2.42	43.11 ± 2.32
[%]	TG	42.73 ± 2.28	42.18 ± 2.52	43.18 ± 2.89	43.9 ± 3.07	42.4 ± 2.59	43.4 ± 2.99	42.91 ± 2.63
	CG	45.00 ± 2.96			44.75 ± 1.49		44.57 ± 2.64	44.44 ± 2.74
MCV	EG	87.11 ± 3.69	86.89 ± 4.04	87.00 ± 3.51	87.44 ± 3.68	87.33 ± 3.57	87.89 ± 3.44	87.22 ± 3.7
(fl)	TG	83.74 ± 8.21	82.82 ± 7.65	83.81 ± 8.16	83.8 ± 8.64	83.1 ± 8.5	84.4 ± 8.49	83.55 ± 8.17
	CG	86.56 ± 2.74			86.78 ± 2.33			86.22 ± 2.22
MCH	EG	29.89 ± 1.69	29.78 ± 1.56	29.43 ± 1.81	29.67 ± 1.66	29.67 ± 1.66	29.56 ± 1.59	29.67 ± 1.66
(pg)	TG	28.45 ± 3.08	28.36 ± 3.07	28.73 ± 3.10	28.4 ± 2.24	28.1 ± 3.11	28.3 ± 3.23	28.64 ± 3.17
	CG	29.33 ± 0.87			29.22 ± 0.83			29.33 ± 0.87
MCHC	EG	34.22 ± 0.83	34.33 ± 1.00	34.29 ± 1.25	34.0 ± 0.87	34.33 ± 0.71	33.67 ± 0.87	34.0 ± 0.71
(g/dl)	TG	33.91 ± 0.83	34.27 ± 0.9	34.09 ± 0.83	33.8 ± 0.79	33.4 ± 1.65	33.0 ± 1.25	34.18 ± 1.17
	CG	33.78 ± 0.67			33.78 ± 1.09			34.0 ± 0.71

*$P < 0.05$ vs. Pre; #$P < 0.05$ vs. EG; ##$P < 0.01$ vs. EG.

nitrite measurements, samples were thawed on ice and directly measured. For measurement of RBC nitrite, frozen samples were thawed on iced while mixed with methanol in a 1:2 ratio for protein precipitation and centrifuged at 21000 g for 10 min at 4°C. The supernatant was collected in new reaction tubes. Plasma nitrite, nitrite of the supernatant (=RBC nitrite) and nitrite levels of prepared standards were determined using an ozone-based chemiluminescence NO detector (CLD 88e, EcoPhysics, Switzerland) as described by Grau et al. (2007). Samples (100 μl) were injected into an acidified tri-iodide solution that reduces nitrite to NO gas at 60°C. The reduction solution was gas-flushed using helium as NO inert gas. The Helium-NO mix was purged in a NaOH trap and NO concentration of the samples was analyzed by the CLD system. The Chart FIA software (EcoPhysics, Switzerland) was used to analyze the area under the curve and the nitrite/NO concentrations of the samples and standards were calculated. All samples were measured in triplicate. Plasma nitrite concentrations did not require correction. Total RBC nitrite concentration of the sample was corrected for nitrite levels of methanol and preservation solution (Pelletier et al., 2006).

Statistical Analysis

All descriptive and inferential statistical analyses were conducted using SPSS 25® (IBM®, Armonk, NY, United States). To determine the effect of the training interventions on RBC deformability, endurance parameters, and nitrite parameters, a separate 3 × 3 (time*group) mixed ANOVA with repeated measures was conducted. ANOVA assumption of homogenous variances was tested using Maulchy-test of Sphericity. Greenhouse-Geisser correction was used when a violation of Mauchly's test was observed. Partial eta-square ($\eta^2{}_p$) values are reported as effect size estimates. If 3 × 3 mixed ANOVA revealed a significant time-point*treatment or time*group interaction effect on any variable, this effect was further investigated carrying out Bonferroni corrected *post hoc* pairwise comparison. Due to a lower number of samples ($n < 10$), the effect of the training interventions on RBC-NOS activation and S-Nitrosylation and the acute effect (pre, post, 24 h post) on RBC deformability was determined with the help of a student t-test or Wilcoxon test for dependent variables. Kolgomorov-smirnov test was applied to test for normal distribution.

Group differences were determined by a one-way ANOVA. Bonferroni *post hoc*-test was used to calculate significant differences between the tested groups.

For all inferential statistical analyses, significance was defined as p-value less than 0.05. Results were presented as means and standard deviations (SDs). Figures were created with Prism 6 (La Jolla, United States).

RESULTS

Endurance Capacity

Relative VO_2peak did not differ between the groups nor was a within group*time effect observed (**Figure 2**).

Basal Blood Parameters

The analysis of the training based influences on basal blood parameters revealed a significant acute increase in the number of reticulocytes from pre to 24 h post at wk-7. Group comparison showed scattered differences between the three groups. However, the differences cannot be attributed to an effect of the training interventions (**Table 2**).

RBC Proportion

Analysis of the proportion of young RBC, main fraction, old RBC and very old RBC of EG, TG and CG during the study period revealed a slight increase in young RBC in EG from Baseline

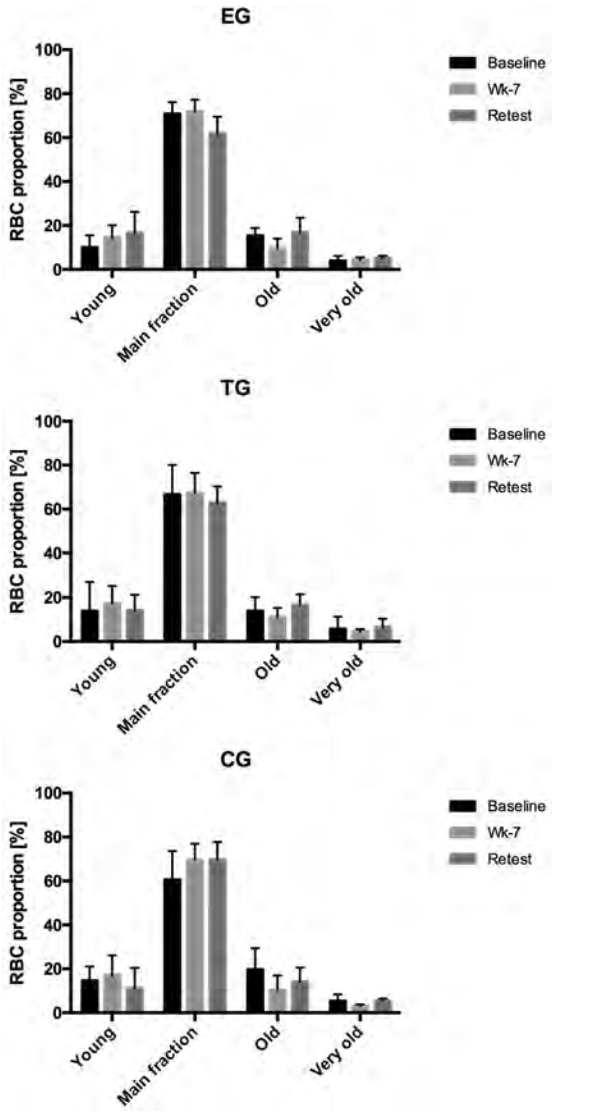

FIGURE 3 | Changes (%) in the RBC proportion of the different RBC subfractions (Young, Main fraction, Old, and Very old) at rest (Pre-values) in EG, TG, and CG measured at Baseline in week 7 (Wk-7) and again after 3 weeks (Retest). Values are presented in means ± SD.

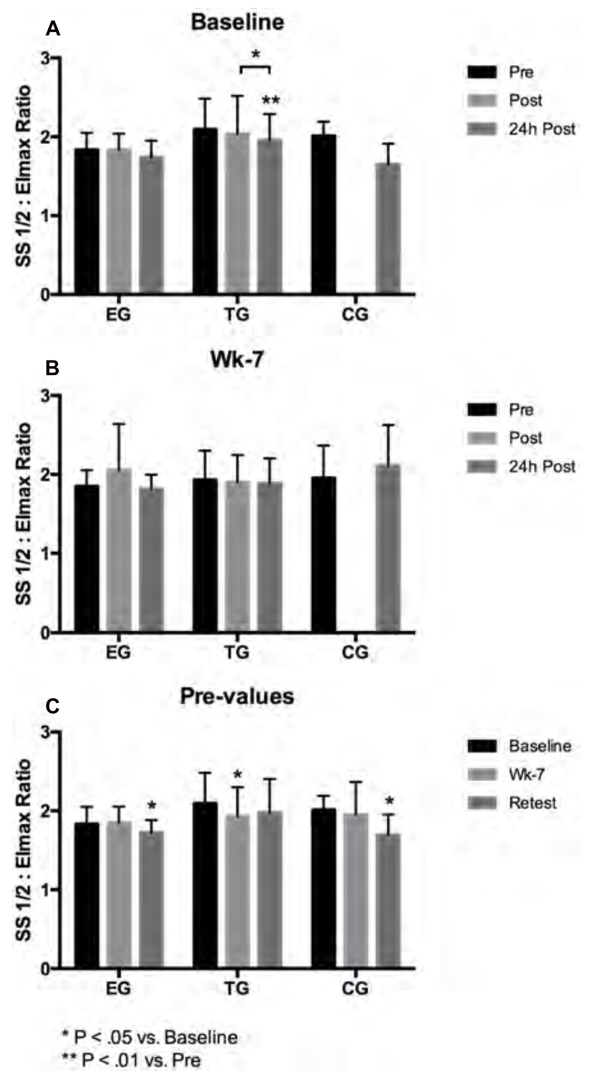

FIGURE 4 | Acute changes in RBC deformability presented as SS1/2: Eimax Ratio in EG, TG, and CG measured before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at **(A)** Baseline and **(B)** in week 7 (Wk-7). Chronic changes of the Pre values over time at **(C)** Baseline, Wk-7 and after 3 weeks without intervention (Retest). Values are presented in means ± SD.

to Retest. In parallel, proportion of main fraction decreased from Baseline to Retest in EG. No changes were observed for the old and very old RBC fraction of this study group. In TG and CG, RBC proportion remained unaltered during the study period (**Figure 3**).

RBC Deformability

Total RBC

The analysis of the acute effects of WB-EMS on RBC deformability revealed a significant decrease in deformability Ratio for TG from pre to 24 h post (p = 0.005) and from post to 24 h post (p = 0.028). No significant changes were shown at wk-7 within the groups (**Figure 4**).

The 3 × 3 mixed ANOVA on total RBC pre-values revealed a significant main effect over time (F = 8.420, d = 2, p = 0.001, η^2_p = 0.260) but no time*group effect. Significant interaction effect on total RBC deformability Ratio was further analyzed by *post hoc* comparisons revealing a significant decrease of the Ratio from Baseline to Retest for EG (p = 0.019) and for CG (p = 0.017), and for TG from Baseline to wk-7 (p = 0.033).

Group comparison showed no differences between the three groups within the study period.

Young RBC

At Baseline, statistical analysis revealed no acute changes between pre, post, and 24 h post in the RBC deformability Ratio of young RBC and no difference between the groups. At wk-7, Ratio significantly decreased from post to 24 h post in TG (p = 0.028). Data remained unaltered in EG and TG, respectively (**Figure 5**). Pre value comparisons revealed no significant time or time*group effects.

Main Fraction

At Baseline and wk-7, Ratio showed no significant differences between the three tested groups. Analysis of pre-values revealed a significant main effect over time for the three groups (F = 15.807; d = 1,324, p < 0.001, η^2_p = 0.397) but no group*time effect. A significant chronic decrease in RBC deformability Ratio was observed in the TG (p = 0.005) from Baseline to Retest and for CG from Baseline to Retest (p > 0.001) and from wk-7 to Retest (p = 0.05), respectively (**Figure 5**).

Old RBC

Red blood cell deformability Ratio of old RBC showed no differences between the groups at Baseline. At wk-7, Ratio significantly decreased from pre to 24 h post in EG (p = 0.015).

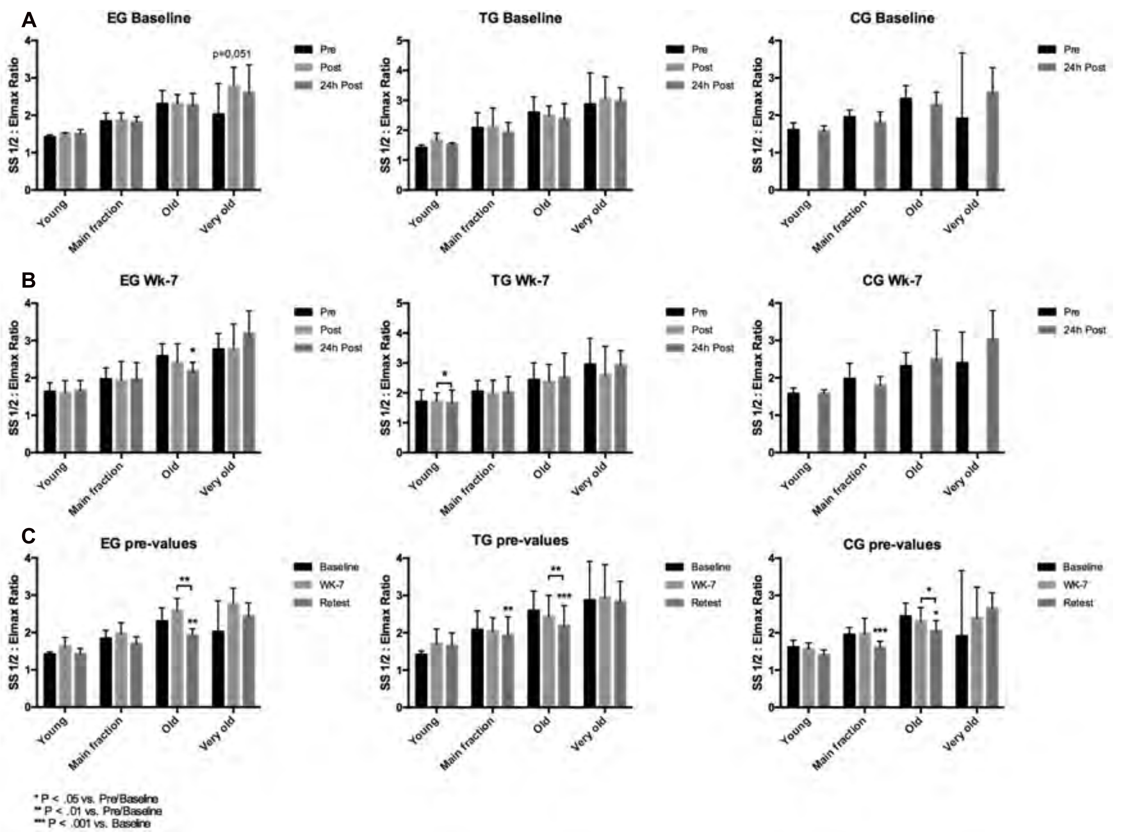

FIGURE 5 | Acute changes in RBC deformability presented as SS1/2: Eimax Ratio in on the different subfractions (Young, Main fraction, Old, and Very old) in (horizontal) EG, TG, and CG measured before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at **(A)** Baseline and **(B)** in week 7 (Wk-7). Chronic changes of the Pre values of the different subfractions over time **(C)** at Baseline, Wk-7, and after 3 weeks without intervention (Retest). Values are presented in means ± SD.

Comparison of pre values of the three time points showed a significant time effect from Baseline to Retest (F = 30.521, d = 2, p < 0.001, η^2_p = 0.560) and a significant time*group effect (F = 3.612, d = 4, p = 0.012, η^2_p = 0.231). *Post hoc* analysis showed a significant decrease from Baseline to Retest for EG (p = 0.001) and TG (p < 0.001) and a significant decrease in all three groups from wk-7 to Retest (EG: p = 0.004; TG: p = 0.002; CG: p = 0.019), respectively. Values did not significantly differ between the groups at the different tests and time points (**Figure 5**).

Very Old RBC

Red blood cells deformability ratio remained unaffected during intervention, time or time*group effect were not observed (**Figure 5**).

RBC Protein Activation State

Akt Kinase

Total Akt kinase

Statistical analysis revealed a significant decrease in total Akt at Baseline for EG from pre to 24 h post (p = 0.02). Values significantly decreased in EG from Baseline to wk-7 (p = 0.006) and for TG from Baseline to Retest (p = 0.022). No changes were observed for CG. Group comparison showed no differences between the groups over time (**Figure 6**).

pAkt threonine^{473}

Staining intensity did not differ between pre, post, or 24 h post test of Baseline and wk-7 in each of the tested groups. The comparison of the pre values over time showed a significant decrease for EG from wk-7 to Retest (p = 0.02). No group differences were detected at the different tests nor within the study period (**Figure 6**).

RBC-NOS Phosphorylation Sites

Total RBC-NOS

Total RBC-NOS showed no acute alternation in EG and TG at Baseline or wk-7, respectively. Also, total RBC-NOS signal remained unchanged during the study groups for each of the tested groups (**Figure 7**).

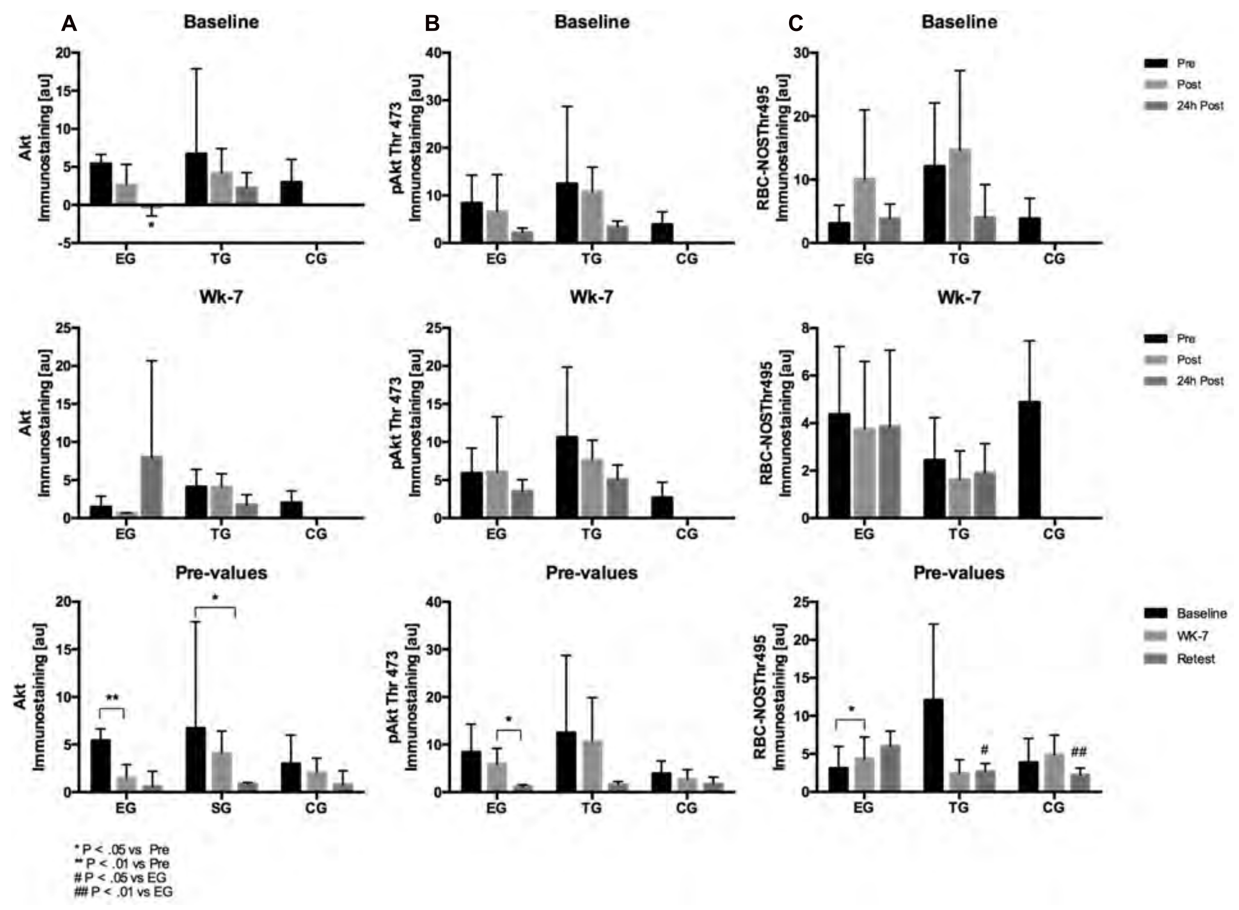

FIGURE 6 | Acute activation of **(A)** Akt, **(B)** pAKtThr473, and **(C)** RBC-NOSThr495 in EG, TG, and CG before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at (vertical) Baseline and in week 7 (Wk-7) and changes of the Pre-values over time at Baseline, Wk-7, and after 3 weeks without intervention (Retest). Values are presented in means ± SD.

RBC-NOS serine[1177]

Statistical analysis revealed a significant increase in RBC-NOS serine 1177 staining intensity of EG at Baseline from pre to post ($p = 0.04$) and pre to 24 h post ($p = 0.003$) and of TG from pre to 24 h post ($p = 0.007$), respectively. At wk-7, RBC-NOS serine 1177 signal increased in EG from pre to post ($p = 0.048$). A significant increase in staining intensity was observed for EG from Baseline to Retest ($p = 0.034$). No chronic changes were shown for TG or CG (**Figure 7**).

RBC-NOS threonine[495]

Statistical analysis revealed no significant acute effects at Baseline and wk-7 for EG and TG. Comparison of pre-values over time revealed a significant increase in EG from Baseline to wk-7 ($p = 0.014$) but not for TG or CG, respectively. Group comparison revealed significant differences in the pre-values at Retest between EG and TG ($p = 0.009$), and between EG and CG ($p = 0.004$), respectively (**Figure 6**).

RBC-NOS serine[114]

Red blood cell nitric oxide synthase serine 114 signal remained unchanged at Baseline and wk-7 for EG and TG, respectively. Comparison of pre values suggest a significant increase in RBC-NOS serine 114 signal in EG from Baseline to wk-7 ($p = 0.043$). Group comparison revealed significant differences between the pre-values ($p = 0.025$) and 24 h post values ($p = 0.0001$) of EG and TG at Baseline (**Figure 7**).

RBC Nitrite

The 3 × 3 mixed ANOVA on RBC nitrite revealed no acute effects within subjects factor time or group*time effect at Baseline or wk-7, respectively. Regarding the chronic effects, the analysis of the pre-values showed a significant effect within subjects factor time ($F = 35.728$, df = 1.60, $p < 0.001$, $\eta^2_p = 0.608$) and a significant group*time effect ($F = 4.373$, df = 3.20, $p = 0.009$, $\eta^2_p = 0.276$). The *post hoc* analysis showed a significant increase in RBC nitrite from Baseline to Retest for TG ($p = 0.022$) and CG ($p = 0.006$), respectively and from wk-7 to Retest for CG ($p = 0.004$). Group comparison revealed a significant difference at Retest between CG and EG ($p = 0.043$) and CG and TG ($p = 0.009$), respectively (**Figure 8**).

S-Nitrosylation

α-*spectrin (240 kDa)*

Students *t*-test revealed no significant acute effects for α-spectrin at Baseline and wk-7 in EG and TG, respectively. Group comparison revealed significantly lower

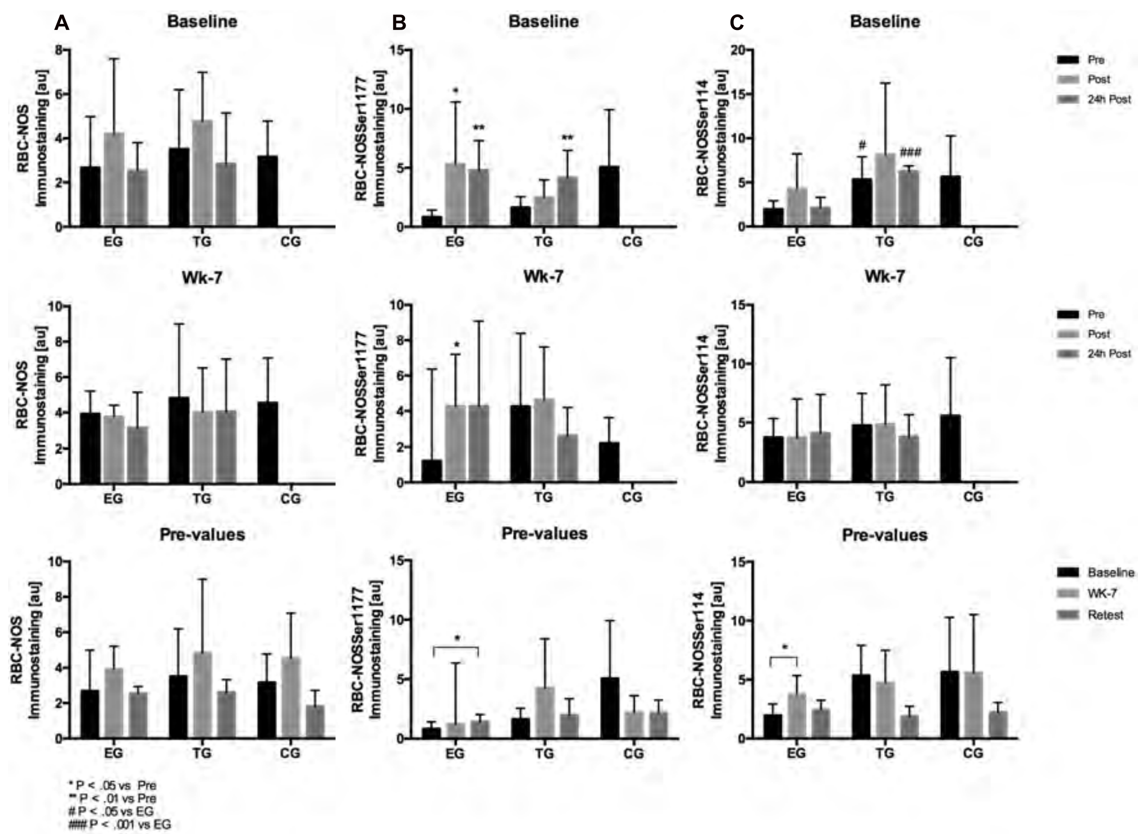

FIGURE 7 | Acute activation of **(A)** RBC-NOS, **(B)** RBC-NOSSer1177, and **(C)** RBC-NOSSer114 in EG, TG, and CG before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at (vertical) Baseline and in week 7 (Wk-7) and changes of the Pre-values over time at Baseline, Wk-7 and after 3 weeks without intervention (Retest). Values are presented in means ± SD.

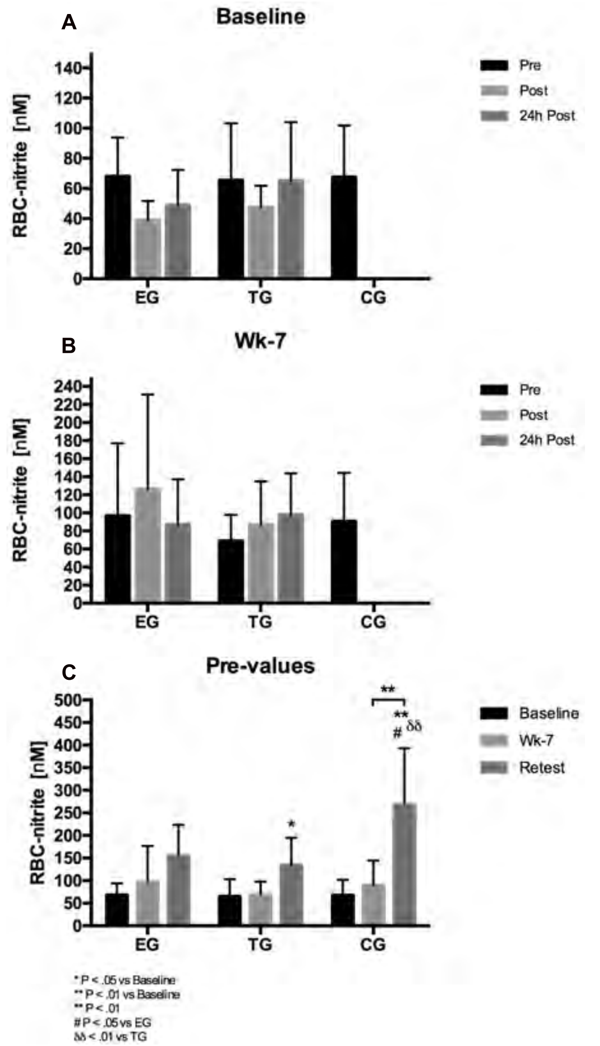

FIGURE 8 | Acute changes in RBC-nitrite in EG, TG, and CG measured before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at **(A)** Baseline and **(B)** in week 7 (Wk-7). Chronic changes of the Pre values over time at **(C)** Baseline, Wk-7, and after 3 weeks without intervention (Retest). Values are presented in means ± SD.

α-spectrin S-nitrosylation for CG at Retest compared to EG ($p = 0.04$) (**Figure 9**).

β-*spectrin (220 kDa)*

Similar to α-spectrin, S-nitrosylation of ß-spectrin showed no significant acute changes at Baseline and wk-7. A significant decrease in β-spectrin S-nitrosylation was observed in all three groups at Retest compared to Baseline (EG, $p < 0.001$; TG, $p = 0.001$; CG, $p = 0.003$) (**Figure 9**).

DISCUSSION

The aim of the present study was to investigate whether WB-EMS affects RBC turnover which might affect overall deformability of circulating RBC by rejuvenation of the RBC population and if this might be related to improved endurance capacity. The key findings of the investigation indicate an increase in young RBC in the EG group along with improved overall RBC deformability, represented by decreased SS1/2:EImax ratio. Detailed observation of the different RBC subfractions revealed improved RBC deformability of old RBC during study period. This improvement was not only observed in the EG but also in TG and CG. Changes in RBC deformability were not associated to altered S-nitrosylation of the spectrins. Endurance capacity remained unchanged during study period.

RBC deformability changes have been associated to influence endurance capacity (Koliamitra et al., 2017) and WB-EMS in turn has been described to affect RBC deformability. Thus, it was assumed that WB-EMS derived improvement in RBC deformability might affect endurance capacity. The results presented herein do not reflect this assumption and are thus in contrast to the findings by Amaro-Gahete et al. (2018) who describe a positive effect of WB-EMS application on runner's VO_2max. All tested participants were experienced soccer players and performed on a competitive level. Training volume and training intensity were not significantly altered during the intervention period and all participants showed a comparable training status to the runners (VO_2max: 53 ml/kg^{*-1}) described by Amaro-Gahete et al. (2018). This might be explained by differences in current frequency, higher training duration and higher intensities of exercises with superimposed EMS in the cited study (Amaro-Gahete et al., 2018).

Red blood cell deformability is an important cell characteristic allowing RBC to pass the microcirculation for gas exchange. RBC deformability has been shown to be affected by a variety of factors with NO being one of them (Kleinbongard et al., 2006; Grau et al., 2013). Within RBC, NO availability depends on RBC-NOS activity (Kleinbongard et al., 2006) under normoxic conditions and nitrite reduction by deoxygenated hemoglobin under hypoxic conditions (Gladwin, 2006; Gladwin and Kim-Shapiro, 2008). RBC-NOS dependent NO generation was described to be affected by shear stress conditions, e.g., exercise, through activation of PI3-Akt kinase pathway (Suhr et al., 2012) or pharmacological stimuli such as insulin (Kleinbongard et al., 2006; Grau et al., 2013). RBC NO reaction routes include the oxidation to nitrite and nitrate, binding to hemoglobin or active cysteine thiol groups also referred to as S-nitrosylation (Ozüyaman et al., 2008). RBC-NOS generated NO was shown to increase S-nitrosylation of the cytoskeletal proteins α- and β-spectrin which was associated to increased RBC deformability (Grau et al., 2013). These reaction routes are well described for mechanical stimulation (Ulker et al., 2009, 2010; Kuck et al., 2019), endurance sports (Suhr et al., 2012; Koliamitra et al., 2017; Tomschi et al., 2018b; Bizjak et al., 2019), but also other types of sport were shown to affect RBC-NOS/NO pathway and RBC deformability (Bizjak et al., 2018). The impact of WB-EMS stimuli on the RBC-NOS/NO signaling pathway has been first shown by Filipovic et al. (2015) suggesting that WB-EMS affects RBC deformability with acute changes being explained

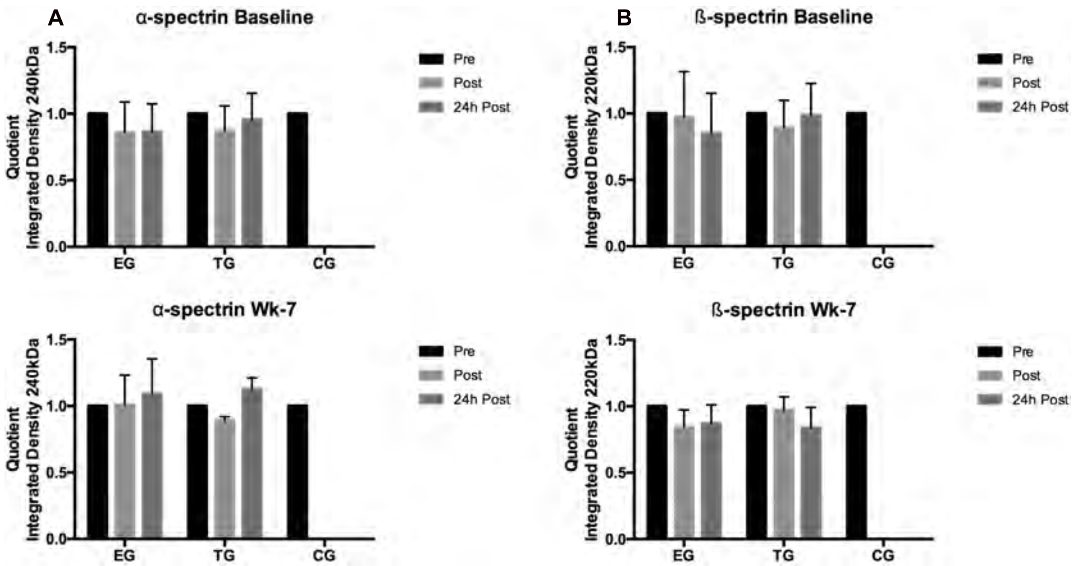

FIGURE 9 | Acute changes in **(A)** α-spectrin and **(B)** β-spectrin in EG, TG, and CG measured before (Pre) 15–30 min after (Post), and 24 h after (24 h Post) the intervention at (vertical) Baseline and in week 7 (Wk-7). Values are presented in means ± SD.

by increased RBC-NOS activation while chronic changes in RBC deformability did not involve RBC-NOS activation. Thus, it was hypothesized for the recent study that WB-EMS affects RBC turnover and that an increase of the proportion of young RBC affects overall RBC deformability. The results of the study in part confirm the hypothesis. Proportion of young RBC increased by trend from Baseline to Retest by 65% ($p = 0.07$) while an increase of young RBC was not observed in the other tested groups. In parallel, proportion of main fraction decreased in EG by 13% ($p < 0.05$) and proportion of very old RBC increased by 30% from Baseline to Retest. Similar changes were not detected in CG and TG. The described changes were not related to possible changes of the measured blood parameters because number of measured blood cells and also RBC associated parameters, e.g., hemoglobin concentration, MCV, MCH and MCHC, remained unaltered throughout the study period. RBC deformability has been shown to be affected by RBC age with old RBC showing lowest RBC deformability values (Bizjak et al., 2015). A shift in RBC age distribution thus affects RBC deformability of overall circulating RBC pool. A recent study indicated that WB-EMS positively affects RBC deformability of professional soccer players (Filipovic et al., 2015). The recent findings indicate no acute effect of WB-EMS on RBC deformability but a significant improvement of overall circulating RBC deformability during the study period. However, an increase in overall RBC deformability was also detectable in TG and CG suggesting that the start of training and competition phase accompanied with higher training load and volume might be responsible for the changes in RBC deformability (Nader et al., 2018; Tomschi et al., 2018a). These data are thus in contrast to the findings of Filipovic et al. (2015).

Compared to the study by Filipovic et al. (2015) the soccer players in the present study had a significantly lower training volume (2–4 vs. 6–7 session/week) per week and thus had a lower fitness level. Studies have shown that moderate exercise increases deformability (Tripette et al., 2010), but intensive exercise can reduce it (Yalcin et al., 2003). As in previous studies shown EMS can be a very intense training method that can produce high metabolic and muscular stress (Jubeau et al., 2008; Nosaka et al., 2011; Filipovic et al., 2016). The applied WB-EMS stimulus might have been too intense for the players due to a lower level of fitness. Furthermore, Filipovic et al. (2015) suggested that the combination of WB-EMS stimulus and soccer specific endurance training load positively affected deformability. Accordingly, the results reveal that the training volume of only 2–4 sessions per week might have been too low to positively influence RBC deformability with two WB-EMS sessions per week.

Red Blood Cells deformability of the sub-fractions support data of the literature that RBC deformability decreases with increasing RBC age (Bizjak et al., 2015). RBC deformability of the RBC sub-fractions remained unaltered at Baseline which supports data of overall RBC suggesting that WB-EMS does not acutely affect RBC deformability. RBC deformability of the main fraction and very old RBC remained unaltered in all three study groups while RBC deformability of old RBC increased during study period. This increase was observed for all three study groups and might thus explain increased RBC deformability of overall circulating RBC. RBC-NOS activation state and RBC-NOS dependent NO production were shown to affect RBC deformability through S-nitrosylation of cytoskeletal spectrins (Grau et al., 2013). Thereby, RBC-NOS activation is affected by Akt kinase activation (Suhr et al., 2012). Total Akt kinase and activation of Akt kinase remained unaffected by the intervention. Total RBC-NOS content was not affected by the intervention but RBC-NOS phosphorylation at its activate residue serine 1177 increased from pre to post WB-EMS and thus support findings of Filipovic et al. (2015). Acute increases in RBC-NOS serine 1177 phosphorylation were also observed at wk-7 and comparisons of pre values suggests that WB-EMS increases RBC-NOS activation. These findings are in contrast to published data of Filipovic et al. (2015). Given the high heterogeneity of the data, it is speculated whether the documented statistical significances would have a physiological effect. Similar findings were observed for RBC-NOS phosphorylation sites serine 114 and threonine 495 which were associated to decreased RBC-NOS activation (Suhr et al., 2012; Heiss and Dirsch, 2014). Values remained unaltered during the study. RBC NO production showed no acute changes at Baseline or at wk-7. But comparisons of pre values revealed increasing values in TG and CG at wk-7 and Retest compared to Baseline, respectively. Since alterations were not found in EG, it seems unlikely that the applied WB-EMS program affects RBC-NO levels. In accordance, S-nitrosylation of the spectrins also remained unaffected.

Limitations of the present study include the lower training volume compared to our previous investigation with professional soccer players (Filipovic et al., 2015). This might have a major influence on deformability because RBC deformability is affected by exercise with increasing training load resulting in increased deformability. Thus, the results of the two studies are difficult to compare. Regarding training load in soccer, the differences in playing time, high intensity running, and/or sprint distances during soccer match and training might show high deviations between the players that might affect adaptive processes. Further, the players were only advised to maintain usual food intake but nutrition was not controlled. An unbalance diet of some players also could have influenced adaptations or performance.

In summary, the effect of WB-EMS on RBC physiology seems to be rather low and results are only in part comparable to previous findings (Filipovic et al., 2015). Because performance parameters also remained unaltered in the recent study, it can be speculated that the combination of WB-EMS and soccer specific training load were lower compared to previous studies and thus too low to induce changes in RBC physiology.

DATA AVAILABILITY

The datasets for this manuscript are not publicly available because of legal reasons. Requests to access the datasets should be directed to the corresponding author.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the Ethics Committee of the German Sports University Cologne. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the German Sports University Cologne [06-02-2014].

AUTHOR CONTRIBUTIONS

AF, MG, and WB conceived and designed the research. AF conducted the experiments. DB and FT prepared, processed, and measured the parameters. AF and MG analyzed the data and wrote the manuscript. DB, FT, and WB revised the manuscript. All authors read and approved the manuscript.

FUNDING

This study was funded by the Bundesministerium für Sportwissenschaft (BISp: ZMVI4-070101_16-17) and supported by the German Sport University Cologne.

ACKNOWLEDGMENTS

The authors would like to thank Bianca Collins, Anika Voß, Benedikt Seeger, and Thomas Dietz for their excellent technical assistance.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ORIGINAL RESEARCH
published: 27 June 2019
doi: 10.3389/fphys.2019.00728

The Effects of Superimposed Whole-Body Electromyostimulation During Short-Term Strength Training on Physical Fitness in Physically Active Females: A Randomized Controlled Trial

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The aim of this study was to compare the effects of short-term strength training with and without superimposed whole-body electromyostimulation (WB-EMS) on straight sprinting speed (SSS), change of direction speed (CODS), vertical and horizontal jumping, as well as on strength and power in physically active females. Twenty-two active female participants (n = 22; mean ± SD: age: 20.5 ± 2.3 years; height: 171.9 ± 5.5 cm; body mass: 64.0 ± 8.2 kg; strength training experience 5.1 ± 3.6 years) were randomly assigned to two groups: strength training (S) or strength training with superimposed WB-EMS (S+E). Both groups trained twice a week over a period of 4 weeks and differed in the application of free weights or WB-EMS during four strength (e.g., split squats, glute-ham raises) and five sprinting and jumping exercises (e.g., side and box jumps, skippings). The WB-EMS impulse intensity was adjusted to 70% of individual maximal sustainable pain. SSS was tested *via* 30-m sprinting, CODS by a T-run, vertical and horizontal jumping using four different jump tests at pre-, post-, and retests. Maximal strength (F_{max}) and power (P_{max}) testing procedures were conducted on the Leg Press (LP), Leg Extension (LE), and Leg Curl (LC) machine. Significant time × group interaction effects revealed significant decreases of contact time of the Drop Jump and split time of CODS ($p \leq 0.043$; $\eta_p^2 = 0.15–0.25$) for S ($\leq$ 11.6%) compared to S+E ($\leq$ 5.7%). Significant time effects ($p < 0.024$; $\eta_p^2 = 0.17–0.57$) were observed in both groups for SSS (S+E: ≤6.3%; S: ≤8.0%) and CODS (S+E: ≤1.8%; S: ≤2.0%) at retest, for jump test performances (S+E: ≤13.2%; S: ≤9.2%) as well as F_{max} and P_{max} for LE (S+E: ≤13.5%; S: ≤13.3%) and LC (S+E: ≤18.2%; S: ≤26.7%) at post- and retests. The findings of this study indicate comparable effects of short-term strength training with and without superimposed WB-EMS on physical fitness in physically active females. Therefore, WB-EMS training could serve as a reasonable but not superior alternative to classic training regimes in female exercisers.

Keywords: linear sprint, change of direction speed, electrical stimulation, power, isoinertial, plyometrics

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Specialty section:
*This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology*

Received: *29 January 2019*
Accepted: *27 May 2019*
Published: *27 June 2019*

Citation:
Dörmann U, Wirtz N, Micke F, Morat M, Kleinöder H and Donath L (2019) The Effects of Superimposed Whole-Body Electromyostimulation During Short-Term Strength Training on Physical Fitness in Physically Active Females: A Randomized Controlled Trial. Front. Physiol. 10:728. doi: 10.3389/fphys.2019.00728

INTRODUCTION

The importance of resistance training in order to enhance sprinting and jumping performance is generally accepted. The relevance of maximal strength and power training has been repeatedly underlined, especially in competitive sports for women and men (Reilly, 2007; Sander et al., 2013; Stojanović et al., 2017; Sommi et al., 2018). Sprinting and jumping performance such as straight sprinting speed (SSS) and change of direction speed (CODS) as well as vertical (VJ) and horizontal jumping (HJ) are basic abilities for successful participation in a variety of sports (Sheppard and Young, 2006; Young, 2006; Brughelli et al., 2008; Perez-Gomez and Calbet, 2013). The lack of incorporating such strength and conditioning approaches into training routines in female athletes compared with their male counterparts is still apparent (Sommi et al., 2018). The transfer of well-developed strength and power variables on sport-specific movement patterns is mostly not as clear as presumed (Sheppard and Young, 2006; Young, 2006; Brughelli et al., 2008). Relatively large gains in strength and power output can lead to meaningful increases in jumping but considerably less in sprinting performance (Young, 2006; Brughelli et al., 2008). Therefore, Young (2006) and Brughelli et al. (2008) highlighted the role of specific exercise movement patterns and contraction velocities in strength training exercises. Additionally, they recommended to perform plyometrics, horizontal jumps, lateral jumps, and loaded vertical jump training including bilateral and unilateral exercises as well as SSS- and CODS-specific skill training in order to adhere to specific movement requirements and directions to develop sprinting performance.

Electromyostimulation (EMS) is known as an effective complementary training method to improve athletic performance surrogates (Filipovic et al., 2011). The application of EMS beneficially affects several physiological pathways that induce adaptations: A higher number of motor units are recruited during exercises with superimposed EMS compared with dynamic voluntary contractions (VCs) alone (Kots and Chwilon, 1971). EMS activates fast-twitch fibers at relatively low force levels (Gregory and Bickel, 2005), and squat exercise with superimposed EMS can potentially induce an increase in recruitment of high-threshold motor units (Dudley, 1992). Moreover, EMS increases activation levels at different muscle length and during different contraction modes, e.g., during eccentric work phases (Willoughby and Simpson, 1998) and possibly reduces the difficulty to achieve sport-specific movement velocities within resistance training (Young, 2006) by a higher firing rate and a synchronization of motor units (Gregory and Bickel, 2005). Further advantages could be achieved by whole-body EMS (WB-EMS) devices that are able to stimulate several muscle groups simultaneously, e.g., muscle chains or agonist/antagonist during a multi-joint movement. WB-EMS triggers a counterproductive firing of the agonist and antagonist. This requires voluntary contractions to reduce co-activation of antagonistic muscles, in order to continue the required dynamic exercise (Wirtz et al., 2016). Most recent evidence suggests that EMS, superimposed onto VCs in a submaximal task, could result in greater muscle fibers recruitment than voluntary or electrical stimulation alone and would be likely to generate greater gains of motor output after a training period (Paillard, 2018). A low voluntary movement control exists at maximum stimulation intensities (Babault et al., 2007), and only submaximal contractions enable an efficient movement control with superimposed EMS (Bezerra et al., 2011). Submaximal dynamic WB-EMS is in accordance with the guidelines for a safe and effective WB-EMS training (Kemmler et al., 2016a). These guidelines consider that WB-EMS features many factors known to be associated with muscle damage, due to the ability to innervate large muscle areas simultaneously with individually tailored intensity per muscle group. For example, Malnick et al. (2016) reported diagnosis of rhabdomyolysis if EMS training was supervised inadequately. Due to the aforementioned background, the question arises whether submaximal WB-EMS during dynamic strength and/or sport-specific exercises over the entire muscle length and muscle chains leads to greater improvements in both jumping and sprinting as well as strength and power performance.

Up to now, there is a lack of studies dealing with submaximal superimposed WB-EMS on sprinting and jumping performance, especially using dynamic strength exercises in combination with jump-, SSS-, or CODS-specific skill training. Most interestingly, there are no available WB-EMS studies in female athletes. Only two studies dealt with the transfer into sprinting and jumping performance with male athletes (Filipovic et al., 2016; Wirtz et al., 2016). Both used squat exercises with superimposed WB-EMS as a strength training intervention. No further exercises for sprinting or jumping performance were conducted. Both studies enhanced CODS (2.4 and 5.5%) and jumping performance (8.1 and 8.7%). SSS only increased for the WB-EMS group in comparison with the control group during 14-week intervention with elite soccer players at 5-m split time (2.9%) (Filipovic et al., 2016).

Therefore, the aim of this study was to compare the effects of short-term strength training with and without superimposed WB-EMS on (1) SSS and CODS, on VJ and HJ, as well as on (2) strength and power parameters in female strength trained sport students. It was hypothesized that short-term strength training with submaximal superimposed WB-EMS improves physical fitness in physically active females more than short-term strength training without superimposed WB-EMS.

MATERIALS AND METHODS

Study Design

This study was designed as a two-armed randomized controlled trial with a parallel-group design comparing effects of submaximal, superimposed dynamic WB-EMS (S+E) with effects of dynamic athletic training without WB-EMS (S) on sprinting and jumping performance as well as on strength and power. S+E and S completed eight training sessions in 4 weeks. To determine training effects, the sprint, jump, strength, and power diagnostics were intra-individually conducted on three occasions at the same time of the day under constant and stable lab conditions: directly before, directly after the training period

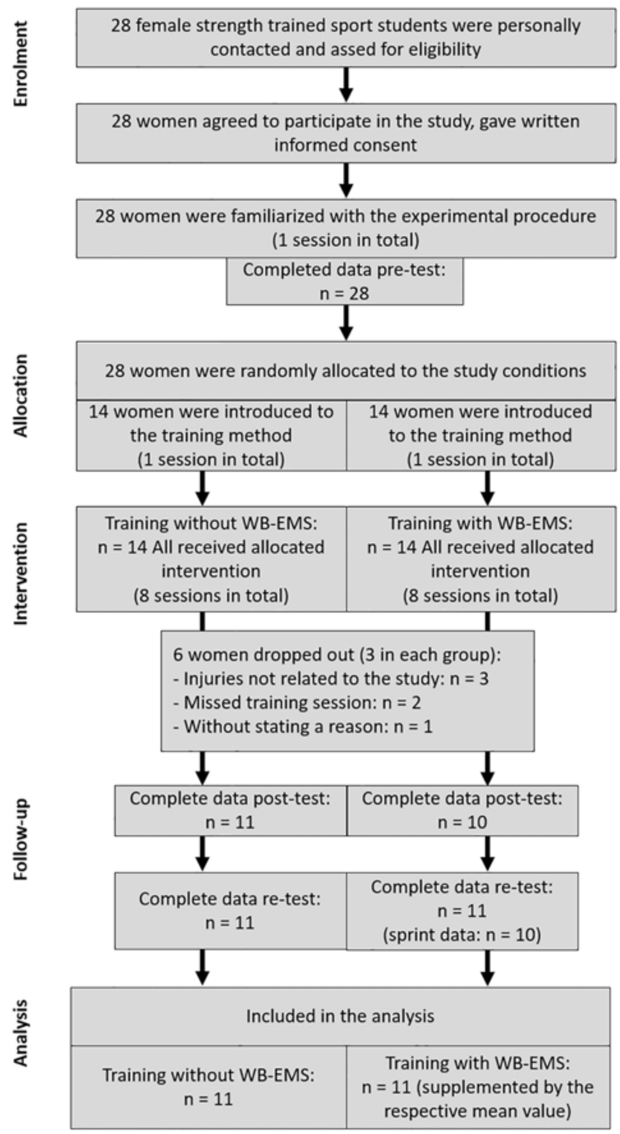

FIGURE 1 | Participants flow through the study [adapted from Moher et al. (2010)].

(pre- and post-tests), and after a 2-week follow-up (retest) (**Figure 1**). The timing of the retest was derived from several EMS studies with delayed strength adaptations after a detraining period of 2–6 weeks (Filipovic et al., 2011). After pretesting, the subjects were randomly assigned to either S+E or S. In order to minimize influences of unspecific training loads, both groups were asked to refrain from any changes of their habitual physical activity behavior. Furthermore, all participants were instructed to maintain their normal dietary intake before and during the study.

Participants

Twenty-eight female strength trained sport students participated in the study. According to Araújo and Scharhag (2016), they can be classified as exercisers and not as athletes. They were medically examined with regard to the musculoskeletal and the cardiovascular systems (exercise electrocardiogram) and signed a consent document about the possible risks and benefits of the study. Exclusion criteria were planned absences during the whole study period, a missed training session, any training experience in WB-EMS, current training programs focusing on sprinting and jumping, as well as inadequate technique in the strength exercises used. One week before the pretests, the participants were familiarized with the experimental procedure. Jump and strength diagnostics were practiced in a sample session until the participants showed a technically correct execution in jumping as well as a variation between the trials smaller or equal to the typical error examined in test–retest procedures of our strength diagnostics lab. After the randomization, the training methods were introduced in a sample session (**Figure 1**). It also included the verification of the individual eight to 10 repetition maximum for the strength exercises for S as well as fitting of the electrodes and familiarization to the electrical stimulus during the exercises for S+E. Six participants, three in each group, terminated their participation. Three suffered injuries that were not related to the study. Two missed a training session. One left the study at her own request without stating a reason. Finally, 22 participants completed all training sessions and were included in the analysis of the results with a 100% attendance rate for both groups ($n = 22$; participants characteristics are presented in **Table 1**). One person from S+E failed the complete posttest. One person from S+E was absent for the sprint testing at retest. The data were supplemented by the respective mean value of the group. The study protocol was approved by the Ethics Committee of the German Sport University Cologne in December 2013 and complied with the Declaration of Helsinki.

Training Procedure

Both groups completed eight training sessions over a 4-week period. The length of the training period and the number of training sessions were derived from numerous EMS studies with an average period of 4–6 weeks with one to seven sessions per week (Filipovic et al., 2012). The two sessions per week were methodologically different. One was focused on strength exercises lasting 25 min and one on jumping and sprinting exercises lasting 20 min. The participants of both groups similarly performed the training sessions with the only difference that S+E performed all exercises superimposed by WB-EMS and S the strength exercises with additional loads (ALs).

The WB-EMS intervention complied with the guidelines for a safe and effective WB-EMS training (Kemmler et al., 2016a). The miha bodytec system (Augsburg, Germany) was selected as EMS device (Kemmler et al., 2012; van Buuren et al., 2013). It was an application unit that was connected *via* electrical cords to a stimulation vest and belts (see **Supplementary Figure S1**). Bilaterally paired surface electrodes were integrated. Thus, eight muscle areas could be stimulated synchronously with freely selectable impulse intensities (0–120 mA) for each pair of electrodes. In our study, three paired electrodes were applied around the muscle belly of the lower legs (27 cm length × 4 cm width), the thighs (44 × 4 cm) and at the buttocks (13 × 10 cm).

TABLE 1 | Anthropometric data (mean ± SD).

	N	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Strength Training Experience (years)
S+E	11	20.4 ± 2.8	172.7 ± 7.3	65.5 ± 10.7	21.8 ± 2.4	6.5 ± 3.9
S	11	20.5 ± 1.8	170.3 ± 3.8	62.0 ± 4.7	21.4 ± 1.6	3.9 ± 3.2

TABLE 2 | Strength training exercises with characteristics about repetitions, sets, rest between the sets, contraction mode (ecc = eccentric, iso = isometric, con = concentric) per repetition, range of motion per repetition and time under tension (TUT) per exercise for both groups as well as on/off ratio of WB-EMS impulse (70% of the individual pain threshold) for the strength training group with superimposed WB-EMS (S+E) and additional load (individual 8–10 repetition maximum) for the strength training group (S).

	S+E Group and S Group						S+E Group	S Group
Strength Training Exercises	**Repetition (n)**	**Set (n)**	**Rest (s)**	**ECC: ISO: CON (s)**	**ROM# (°)**	**TUT (s)**	**On/Off Ratio (s)**	**Additional Load**
(1) Bulgarian Split Squat	10	3 per leg*	60	2: 1: 2	170–90	300	50/5	≤20 kg Barbells
(2) Nordic Curl	8	3	60	2: 0: 2	90–135	96	32/0	Softer Rubber Band
(3) Knee Tuck	8	3	60	2: 0: 2	180–70	96	32/0	–
(4) Side Abs	8 per side	3	60	0.5: 0: 0.5	–	48	16/0	≤4 kg Medicine Ball

*#Range of motion (ROM) of the interior knee or interior hip angle. *The front position of the legs was changed alternately after each set.*

TABLE 3 | Jumping and sprinting training exercises with characteristics about repetitions, sets, rest between the sets, range of motion per repetition and time under tension (TUT) per exercise for both groups as well as on/off ratio of WB-EMS impulse (70% of the individual pain threshold) for the strength training group with superimposed WB-EMS (S+E) and additional load (individual 8–10 repetition maximum) for the strength training group (S).

	S+E Group and S Group					S+E Group	S Group
Jumping and Sprinting Training Exercises	**Repetition or Duration (n or s)**	**Set (n)**	**Rest (s)**	**ROM# (°)**	**TUT (s)**	**On/Off-Ratio (s)**	**Additional Load**
(1) Skipping	8 s	3	30	180–90	24	8/0	–
(2) Heeling	10	3 per leg*	30	180–90	60	10/5	–
(3) Side Jump	5 per side	3	30	–	36	12/0	–
(4) Box Jump	5	3 per leg*	30	–	90	3/5	–
(4) Drop Jump	5	3	30	–	45	3/5	–

*#Range of motion (ROM) of the interior hip angle. *Legs were changed alternately after each set.*

Additionally, the upper body was stimulated with two bilaterally paired electrodes that were integrated in the stimulation vest at the lower back (14 × 11 cm) and at the abdominal (23 × 10 cm). This simultaneous stimulation was used for all exercises, and the application of the electrodes took 5 min for each S+E participant before each session.

The intensity of WB-EMS was adjusted to 70% of the individual pain threshold (iPT = maximum tolerated amperage, 0–120 mA). The iPT was verified separately for each pair of electrodes before each session and lasted 2 min for each S+E participant. The participants stood with an interior knee angle of 170° while tensing their lower limbs muscles. The verification of iPT began with the electrodes at the buttock, followed by the thigh, the lower leg, the abdominal, and the lower back electrodes. Then, the intensity was subsequently downregulated with the main controller at the WB-EMS device to an intensity of 70% to enable dynamic movements. The impulse frequency was set at 85 Hz, the impulse width at 350 μs, the impulse type as bipolar and rectangle (Filipovic et al., 2016; Kemmler et al., 2016b; Wirtz et al., 2016). On/off-time was adjusted for each exercise (see **Tables 2**, **3**). In general, EMS was applied during all the execution time of each exercise and stopped during the rest period.

The strength sessions involved four exercises for both groups: (1) Bulgarian split squat: single leg split squat with heel raise, elevated rear foot, and hands remaining in the akimbo position, (2) Nordic curl: two-legged hamstring curl with supporting rubber bands at chest height, (3) knee tuck: knee pull to the chest while feet hang in loops and upper body remain in push-up position, as well as (4) side abs: side-to-side medicine ball crunch with raised legs (exercise characteristics are presented in **Table 2**; pictures of each exercise are presented in the **Supplementary Table S1**).

During each exercise, temporal distribution of contraction modes was standardized per repetition by an acoustical signal at start and end positions of the exercise. The intensity of each exercise set was controlled by Borg rating of perceived exertion (RPE) (Tiggemann et al., 2010). If a set was no longer exhaustive (RPE < 16 "hard"), the impulse intensity was raised for S+E during the training period. S enhanced the intensity for (1) Bulgarian split squat by adding free weights ≤20 kg, for (2) Nordic curl by adding softer rubber bands (gold to black, Gymstick; Ludwig Artzt GmbH, Dornburg, Germany), and for (4) side abs by adding a heavier medicine ball (Fitness-Mad, Worcestershire, United Kingdom; ≤4 kg). A TRX (Fitness Anywhere, San Francisco, United States) was used as sling system for (3) knee tucks. The intensity could have been increased by stabilizing only one instead of two legs in the TRX. There was no need for this variation during the training period (RPE > 16).

The sessions focusing on sprinting and jumping involved five exercises for both groups: (1) skipping: knee lever runs against a rubber band fixed around the hips, (2) heeling: single leg heels with fore-swinging of the lower leg and active foot attachment when returning the swing leg and hands remaining in the akimbo position, (3) side jumps: single leg side jump from one leg to the other about a 20-cm hurdle, (4) box jumps: single leg box jump after a two-step start on a 38-cm box with 1-m jump distance, as well as (5) drop jumps: drop jumps from a 38-cm box with hands remaining in the akimbo position (exercise characteristics are presented in **Table 3**, pictures of each exercise are presented in the **Supplementary Table S2**). These exercises followed the recommendations of Young (2006), Brughelli et al. (2008), and Stojanović et al. (2017) to increase SSS and CODS as well as VJ and HJ. The intensity of each sprinting and jumping exercise set was controlled by RPE, too. Both groups enhanced the intensity by a maximum movement frequency or an explosive movement speed. The impulse intensity for S+E had been adjusted at 70% of the iPT.

The warm-up consisted of 5-min cycling before each session. The rest between the exercises was 2.5 min. Thus, the total contact time for S lasted 30 min for the strength sessions as well as 25 min for the jumping and sprinting sessions. S+E had a 7-min (5-min application of the electrodes plus 2-min verification of impulse intensity) longer total contact time for each session.

Testing Procedure

Sprint Testing

Sprint testing involved a T-run for CODS (**Figure 2**) and a 30-m sprint for SSS. Both tests were performed with a self-initiated standing start with no hopping or backward movement before the start. The split times were measured for 30-m sprint at 5, 10, and 20 m. The split time values for T-run were measured after the first change of direction at cone A (**Figure 2**). Double infrared photoelectric barriers (DLS/F03, Sportronic, Leutenbach-Nellmersbach, Germany) were used to measure time. The sprinting time as the best of two attempts was used for subsequent analysis. The participants had 2-min rest between the trials.

Moreover, a tapping test about 5 s was conducted with the OptoJump system (Microgate, Bolzano, Italy). It is based on measurements of optical light emitting diodes. The participants were instructed to complete as many steps as possible in 5 s and to start on their own. The system automatically counted the total number of steps for 5 s from the first step. The parameter as the best of two trials was total steps (n). The participants had 2 min rest between the trials.

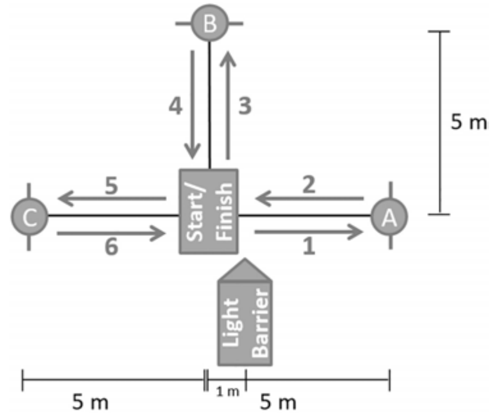

FIGURE 2 | T-run: Cone A, B, and C had to be reached after one another by a forward sprint (1–5). Marks on the floor must be crossed at each corner. After cone C (6), participants could run as fast as possible across the finish line [adapted from McBride et al. (2002) and Reiman and Manske (2009)].

Jump Testing

After one familiarization jump trial, the participants performed three trials of each jump variation in a fixed order: (1) standing long jump (SLJ), (2) counter movement jump (CMJ), (3) squat jump (SJ), as well as (4) drop jump (DJ). For the SLJ (1), the participants were instructed to start jumping from an upright standing position, squatting down to an adequate momentum in order to jump as long as possible. The jump distance was measured from the start line to the participants' heel. The attempts were invalid if the participant stepped back or forward after landing. For the CMJ (2), participants were instructed to start jumping from an upright standing position, squatting down to a knee angle of approximately 90° in order to jump as high as possible. For the SJ (3), participants were instructed to start jumping from a static semi-squatted position holding the knees at 90° without any preliminary movement. The DJ (4) started from a 38-cm box. The participants were instructed to drop down from the box and then to jump as high as possible after a short contact time on the ground. The OptoJump system (Microgate, Bolzano, Italy) was used to verify jump height and contact time using the flight time method. Thereby, hands remained in the akimbo position for the entire movement of each jump to minimize the influence of arm swing. The jump with the greatest height or distance for each variation was subsequently used for analysis. The DJ performance was evaluated by the highest reactive strength index (RSI) (Flanagan and Comyns, 2008; Prieske et al., 2018; Ramirez-Campillo et al., 2018), which was calculated by dividing the jump height by the corresponding ground contact time (Healy et al., 2018).

Strength and Power Testing

Strength and power diagnostics took place on the leg curl (LC), the leg extension (LE), and the leg press (LP) machine (Edition-Line, gym80, Gelsenkirchen, Germany). Those were equipped with the digital measurement equipment Digimax (mechaTronic, Hamm, Germany). It enabled the measurement of the peak force F_{max} and the peak power P_{max} (5-kN strength sensor type KM1506, distance sensor type S501D, megaTron, Munich, Germany) employing the software IsoTest and DynamicTest 2.0. The sensors were installed in line with the steel belt of the machines that lifts the selected weight plates.

Diagnostic procedures consisted of three isometric trials for each machine. Isometric attempts were conducted at an interior knee angle of 120° for LE and LP as well as of 150° for LC. The instruction was to press as forcefully and as fast as possible against the fixed lever arm. This enabled to determine knee joint angle-dependent force–time curve during explosive maximum VC and to calculate the parameter F_{max} (N) as the isometric peak force. Moreover, diagnostic procedures consisted of six isoinertial trials for LE and LC as well as three isoinertial trials for LP. The isoinertial test attempts were conducted with an additional load (AL). AL was individually calculated as a percentage of F_{max} in a further isometric test with the same angle as the starting position of the isoinertial test (LE and LP 90°; LC 170°). Three attempts were conducted with 40% AL for LE and LC as well as three attempts with 60% AL for LP, LE, and LC. Concerning isoinertial tests, the participants were introduced to move the lever arm as forcefully and as fast as possible over the complete concentric range of motion. This enabled to examine knee joint angle-dependent power–load curve during explosive maximum voluntary LE for LP, knee extension for LE, or knee flexion for LC and to calculate the parameter P_{max} as the concentric dynamic peak power. The concentric range of motion corresponded to 90–180° for LP and LE as well as to 170–80° for LC (interior knee angle). The rest design was 60 s between the trials and 3 min between the strength machines, respectively. The parameters F_{max} (N) and P_{max} (W) were calculated for statistical analysis and data presentation as the best of three trials.

Statistical Analysis

The data of the 22 participants were reported as mean value ± SD. All data were normally distributed for all groups except for F_{max} for LC at posttest ($p = 0.010$), P_{max} with 40% AL for LE at retest ($p = 0.050$), P_{max} with 60% AL for LP ($p = 0.033$), SSS 10-m split time ($p = 0.032$) and SJ ($p = 0.002$) at pretest for S+E as well as P_{max} with 40% for LC at pretest ($p = 0.050$) for S, as assessed by Kolmogorov–Smirnov test ($p > 0.05$). With a closer look at the quantile–quantile plots and according to Berkovits et al. (2000), the data were continued without applying measures. There was homogeneity of the error variances, as assessed by Levene test ($p > 0.05$). To determine the effect of the training interventions, a separate 3 × 2 (time × group)-mixed ANOVA with repeated measures was conducted. ANOVA assumption of homogenous variances was tested using Maulchy test of sphericity. If a violation of Mauchly's test was observed, Greenhouse–Geisser correction was used. Partial eta-square (η_p^2) values were reported as effect size for significant main effects of the ANOVA with $\eta_p^2 \geq 0.01$ indicating small, ≥ 0.059 medium, and ≥ 0.138 large effects (Cohen, 1988). If 3 × 2-mixed ANOVA revealed a significant time or time × group interaction effect on any variable, this effect was further investigated carrying out Bonferroni-corrected *post hoc* pairwise comparison ($p < 0.05$). In this context, standardized mean differences (SMD) were calculated between pre-, post-, and retests. Thresholds for small, moderate, and large effects were 0.20, 0.50, and 0.80, respectively (Cohen, 1988). SPSS 25.0 (IBM®, Armonk, NY, United States) was used for all statistical procedures.

Reliability was determined by the coefficient of variation (CV) and the intraclass correlation coefficient (ICC) for F_{max} (CV < 8%; ICC 0.95–0.97) and for P_{max} (CV < 9%; ICC 0.84–0.97) during a week-long test–retest procedure. Previously, measures of CODS, SSS, and jump performance have been shown to be highly reliable (CV 1–9%; ICC 0.80–0.99) (Markovic et al., 2004; Brughelli et al., 2008; Casartelli et al., 2010; Glatthorn et al., 2011; Green et al., 2011; Ball and Zanetti, 2012).

RESULTS

Sprint Testing

Sprint values for both groups are provided in **Table 4**. A statistically significant and large interaction between time × group was observed for split time of CODS ($p = 0.002$; $\eta_p^2 = 0.25$). Only S showed a significantly higher performance for T-run split time between pre- and retests following *post hoc* analyses ($p = 0.001$).

Significant main effects of time were found for SSS for total time ($p < 0.001$; $\eta_p^2 = 0.32$), 5-m ($p < 0.001$; $\eta_p^2 = 0.55$), 10-m ($p < 0.001$; $\eta_p^2 = 0.48$), and 20-m split time ($p < 0.001$; $\eta_p^2 = 0.41$) as well as for CODS for total time ($p = 0.008$; $\eta_p^2 = 0.22$). Total steps of tapping test showed significant main effects of time ($p = 0.005$; $\eta_p^2 = 0.31$), too. Bonferroni-adjusted *post hoc* analysis revealed a significant improvement for both groups between pre- and retests, respectively.

Jump Testing

Jump values for both groups are provided in **Table 5**. There was a significant and large interaction between time × group for contact time of DJ ($p = 0.043$; $\eta_p^2 = 0.15$). Only S showed a significantly higher performance for contact time of DJ between pre- and posttests ($p = 0.007$) as well as pre- and retests ($p = 0.004$).

Significant main effects of time were observed for SLJ ($p < 0.001$; $\eta_p^2 = 0.57$), SJ ($p < 0.001$; $\eta_p^2 = 0.35$) and CMJ ($p < 0.001$; $\eta_p^2 = 0.42$), and RSI ($p = 0.011$; $\eta_p^2 = 0.20$). Bonferroni-adjusted *post hoc* analysis revealed a significantly higher SLJ and CMJ performance between pre- and posttests as well as pre- and retests for both groups. Both groups showed a significantly higher SJ performance between pre- and retests and a significantly higher RSI between pre- and posttests in the *post hoc* comparison.

Strength and Power Testing

Strength and power values for both groups are provided in **Tables 6**, **7**.

Significant main effects of time were found for LC for F_{max} ($p < 0.001$; $\eta_p^2 = 0.38$), P_{max} with 40% ($p < 0.001$; $\eta_p^2 = 0.56$) and 60% ($p < 0.001$; $\eta_p^2 = 0.42$) AL, for LE for F_{max} ($p < 0.001$;

TABLE 4 | Changes in 30-m linear sprint (LS) and in T-run for total time (TT) and split time (ST) as well as in tapping test for total steps in group S (strength training) and S+E (strength training with superimposed WB-EMS) during pre-, post-, and retests.

	Parameter	Group	Pretest	Posttest	Pre–Post		Retest	Pre–Re		ANOVA p (η_p^2)		
					% Delta	SMD		% Delta	SMD	Time	Group	Time* Group
Straight Sprinting Speed	LS TT	S+E	4.80 ± 0.23	4.75 ± 0.19	–1.0	0.24	4.69 ± 0.24	–2.3*	0.47	**<0.001 (0.323)**	0.336 (0.046)	0.954 (0.002)
	(s)	S	4.73 ± 0.20	4.67 ± 0.21	–1.3	0.29	4.60 ± 0.21	–2.8*	**0.63**			
	LS 5-m ST	S+E	1.11 ± 0.05	1.09 ± 0.04	–1.8	0.44	1.04 ± 0.05	–6.3*	**1.40**	**<0.001 (0.548)**	0.666 (0.009)	0.620 (0.024)
	(s)	S	1.12 ± 0.05	1.07 ± 0.06	–4.5	**0.91**	1.03 ± 0.03	–8.0*	**2.18**			
	LS 10-m ST	S+E	1.92 ± 0.10	1.92 ± 0.07	0.0	0.0	1.85 ± 0.09	–3.7*	**0.74**	**<0.001 (0.480)**	0.527 (0.020)	0.705 (0.013)
	(s)	S	1.92 ± 0.07	1.90 ± 0.09	–1.0	0.25	1.82 ± 0.07	–5.2*	**1.43**			
	LS 20-m ST	S+E	3.40 ± 0.16	3.37 ± 0.12	–0.9	0.21	3.30 ± 0.17	–2.9*	**0.61**	**<0.001 (0.408)**	0.392 (0.037)	0.863 (0.007)
	(s)	S	3.36 ± 0.13	3.32 ± 0.15	–1.2	0.29	3.24 ± 0.13	–3.6*	**0.92**			
Tappings	Total Steps in 5 s	S+E	45.00 ± 6.05	46.82 ± 5.31	+4.0	0.32	49.27 ± 5.29	+9.5*	**0.75**	**0.005 (0.306)**	0.419 (0.033)	0.506 (0.025)
	(n)	S	45.09 ± 8.41	49.18 ± 4.45	+9.1	**0.61**	51.64 ± 3.85	+14.5*	**1.00**			
Change of Direction Speed	T-run TT	S+E	8.72 ± 0.36	8.67 ± 0.25	–0.6	0.16	8.56 ± 0.33	–1.8*	0.46	**0.008 (0.215)**	0.426 (0.032)	0.816 (0.010)
	(s)	S	8.62 ± 0.33	8.62 ± 0.23	0.0	0.00	8.45 ± 0.19	–2.0*	**0.63**			
	T-run ST	S+E	2.40 ± 0.11	2.35 ± 0.09	–2.1	**0.50**	2.39 ± 0.12	–0.4	0.09	**0.024 (0.170)**	0.400 (0.036)	0.002 (0.247)
	(s)	S	2.38 ± 0.10	2.39 ± 0.06	+0.4	0.12	2.28 ± 0.06°	–4.2	**1.21**			

Values are presented as mean ± SD. Moderate to large standardized mean differences (SMD) have been highlighted in bold. Significance level for time effects for both groups to pretest was set at $p \leq 0.05$. Significance level for group*time interaction effects was set at $p \leq 0.05$°.*

TABLE 5 | Changes in standing long jump (SLJ), squat jump (SJ) and counter movement jump (CMJ), as well as in drop jump (DJ) for length, height, contact time, and reactive strength index (RSI) in group S (strength training) and S+E (strength training with superimposed WB-EMS) during pre-, post-, and retests.

	Parameter	Group	Pretest	Posttest	Pre–Post		Retest	Pre–Re		ANOVA p (η_p^2)		
					% Delta	SDM		% Delta	SDM	Time	Group	Time* Group
SLJ	Length	S+E	148.82 ± 17.13	159.30 ± 14.67	+7.0*	**0.66**	158.64 ± 13.24	+6.6*	**0.64**	**<0.001 (0.574)**	0.333 (0.047)	0.145 (0.092)
	(cm)	S	155.55 ± 8.78	161.55 ± 14.71	+3.9*	**0.50**	166.64 ± 13.91	+7.1*	**0.95**			
SJ	Height	S+E	25.25 ± 3.79	27.17 ± 3.59	+7.6	**0.52**	27.58 ± 4.66	+9.2*	**0.55**	**<0.001 (0.345)**	0.140 (0.106)	0.245 (0.068)
	(cm)	S	28.59 ± 4.03	28.98 ± 4.72	+1.4	0.09	30.46 ± 4.65	+6.5*	0.43			
CMJ	Height	S+E	27.36 ± 3.83	28.89 ± 3.14	+5.6*	0.44	30.97 ± 4.70	+13.2*	**0.84**	**<0.001 (0.423)**	0.099 (0.130)	0.746 (0.015)
	(cm)	S	30.54 ± 3.89	32.08 ± 4.72	+5.0*	0.36	33.36 ± 5.05	+9.2*	**0.63**			
DJ	Height	S+E	25.21 ± 2.66	27.04 ± 3.03	+7.3	**0.64**	27.53 ± 3.35	+9.2	**0.77**	0.486 (0.035)	0.241 (0.068)	0.163 (0.087)
	(cm)	S	24.85 ± 4.69	24.60 ± 6.53	−1.0	0.01	24.21 ± 5.34	−1.5	0.04			
	Contact Time	S+E	0.177 ± 0.02	0.167 ± 0.01	−5.7	**0.63**	0.177 ± 0.02	+0.0	0.0	**0.001 (0.284)**	0.218 (0.075)	**0.043 (0.146)**
	(s)	S	0.199 ± 0.03	0.176 ± 0.02°	−11.6	**0.90**	0.178 ± 0.03°	−10.6	**0.70**			
	RSI	S+E	1.46 ± 0.31	1.63 ± 0.24	+11.6*	**0.61**	1.59 ± 0.32	+8.9	0.41	**0.011 (0.202)**	0.149 (0.101)	0.969 (0.002)
		S	1.28 ± 0.32	1.43 ± 0.43*	+11.7*	0.40	1.39 ± 0.35	+8.6	0.33			

Values are presented as mean ± SD. Moderate to large standardized mean differences (SMD) have been highlighted in bold. Significance level for time effects for both groups to pretest was set at $p \leq 0.05$. Significance level for group*time interaction effects was set at $p \leq 0.05$°.*

TABLE 6 | Changes in maximal strength (F_{max}) and power (P_{max}) with 40 and 60% additional load for leg curl (LC) and leg extension (LE) in group S (strength training) and S+E (strength training with superimposed WB-EMS) during pre-, post-, and retests.

	Parameter	Group	Pretest	Posttest	Pre-Post		Retest	Pre-Re		ANOVA p (η_p^2)		
					% Delta	SDM		% Delta	SDM	Time	Group	Time* Group
LC	F_{max}	S+E	725 ± 116	843 ± 177	+16.3*	**0.79**	857 ± 168	+18.2*	**0.91**	**<0.001 (0.376)**	0.886 (0.001)	0.560 (0.029)
	(N)	S	722 ± 243	859 ± 161	+19.0*	**0.67**	813 ± 195	+12.6*	0.41			
	P_{max} 40%	S+E	339 ± 81	400 ± 100	+18.0*	**0.67**	392 ± 94	+15.6*	**0.60**	**<0.001 (0.564)**	0.910 (0.001)	0.139 (0.098)
	(W)	S	333 ± 107	390 ± 102	+17.1*	**0.55**	422 ± 103	+26.7*	**0.85**			
	P_{max} 60%	S+E	405 ± 81	445 ± 94	+9.9*	0.46	449 ± 95	+10.9*	**0.50**	**<0.001 (0.424)**	0.701 (0.008)	0.769 (0.013)
	(W)	S	382 ± 98	433 ± 106	+13.4*	**0.50**	441 ± 88	+15.5*	**0.63**			
LE	F_{max}	S+E	1507 ± 202	1657 ± 330	+10.0*	**0.55**	1697 ± 337	+12.6*	**0.68**	**<0.001 (0.475)**	0.509 (0.022)	0.899 (0.005)
	(N)	S	1445 ± 255	1566 ± 277	+8.4*	0.45	1622 ± 258	+12.2*	**0.69**			
	P_{max} 40%	S+E	691 ± 150	768 ± 171	+11.1*	0.48	784 ± 204	+13.5*	**0.52**	**<0.001 (0.379)**	0.716 (0.007)	0.711 (0.017)
	(W)	S	717 ± 193	812 ± 199	+13.3*	0.49	795 ± 173	+10.9*	0.43			
	P_{max} 60%	S+E	663 ± 143	707 ± 154	+6.6	0.30	684 ± 145	+3.2	0.15	0.091 (0.113)	0.391 (0.037)	0.105 (0.106)
	(W)	S	714 ± 185	720 ± 131	+0.8	0.04	777 ± 128	+8.8	0.40			

Values are presented as mean ± SD. Moderate to large standardized mean differences (SMD) have been highlighted in bold. Significance level for time effects for both groups to pretest was set at $p \leq 0.05$.*

TABLE 7 | Changes in maximal strength (F_{max}) and power (P_{max}) with 60% additional load for leg press (LP) in group S (strength training) and S+E (strength training with superimposed WB-EMS) during pre-, post-, and retests.

	Parameter	Group	Pretest	Posttest	Pre–Post		Retest	Pre–Re		ANOVA p (η_p^2)		
					% Delta	SDM		% Delta	SDM	Time	Group	Time* Group
LP	F_{max}	S+E	2905 ± 565	3087 ± 706	+6.3	0.29	2719 ± 781	−6.4	0.27	0.127 (0.098)	0.315 (0.050)	0.546 (0.030)
	(N)	S	2616 ± 656	2737 ± 667	+4.6	0.18	2619 ± 448	+0.1	0.01			
	P_{max} 60%	S+E	742 ± 161	837 ± 140	+12.8	**0.63**	804 ± 158	+8.4*	0.39	**0.010 (0.204)**	0.480 (0.025)	0.113 (0.103)
	(W)	S	820 ± 250	837 ± 231	+2.1	0.07	897 ± 205	+9.4*	0.34			

Values are presented as mean ± SD. Moderate to large standardized mean differences (SMD) have been highlighted in bold. Significance level for time effects for both groups to pretest was set at $p \leq 0.05$.*

$\eta_p^2 = 0.48$) and P_{max} with 40% AL ($p < 0.001$; $\eta_p^2 = 0.38$) as well as for LP for P_{max} with 60% AL ($p = 0.010$; $\eta_p^2 = 0.20$). The significantly higher performances were shown for both groups for LE and LC between pre- and posttests as well as pre- and retests in the *post hoc* comparison. The significant increases for LP exclusively occurred between pre- and retests.

DISCUSSION

This study compared the effects of short-term strength training with and without superimposed WB-EMS on (1) SSS and CODS, on VJ and HJ, as well as on (2) strength and power parameters in female strength trained sport students. It was hypothesized that short-term strength training with submaximal superimposed WB-EMS improves physical fitness in physically active females more than short-term strength training without superimposed WB-EMS.

There is a lack of studies dealing with submaximal superimposed WB-EMS on sprinting and jumping performance, especially using dynamic strength exercises in combination with sprinting and jumping exercises. Moreover, there are no available WB-EMS studies in female athletes.

Against the hypothesis, the findings of this study indicated no advantageous effects for short-term strength training in favor to submaximal superimposed WB-EMS (S+E) in comparison with strength training alone (S) on physical fitness in physically active females. Both groups, S as well as S+E, significantly increased the parameters F_{max} for LC and LE as well as P_{max} for LC, LE, and LP over time. Moreover, both groups transferred these strength and power gains into a significantly greater performance of the primary endpoints like total time of CODS, split and total time of SSS, as well as VJ height, RSI, and HJ length over time. Thus, both training methods, S and S+E, confirmed the results of existing meta-analyses in this context (Perez-Gomez and Calbet, 2013; Seitz et al., 2014). According to Young (2006) and Seitz et al. (2014), the transfer of the strength increases (S: 19.0%; S+E: 18.2%) into jumping performance (S: 11.7%; S+E: 13.2%) was higher than into sprinting performance (S: 2.8%; S+E: 2.3%), too. Moreover, the findings of S+E are in line with the two dynamic WB-EMS studies with males. They improved sprint time with change of directions by 5.5% at 15 m (Filipovic et al., 2016) and 2.4% at 30 m (Wirtz et al., 2016) as well as SJ performance by 8.1% (Filipovic et al., 2016) and 8.7% (Wirtz et al., 2016), respectively. Following Kots and Chwilon (1971), a higher number of motor units are recruited during exercises with superimposed EMS in comparison with dynamic VC alone. Moreover, EMS increases the activation levels at different muscle length and during different contraction modes, especially during eccentric work phases as Willoughby and Simpson (1998) hypothesized. According to Paillard (2018), EMS superimposed onto VCs in a submaximal task could result in greater muscle fibers recruitment than with voluntary stimulation alone. However, no greater gains of motor output could be generated in comparison with the present strength training regime (S) after the short-term training period, in particular for DJ ground contact time and CODS split time.

In contrast, the main findings of this study revealed a significant time × group interaction effect on split time of CODS and contact time of DJ for S in *post hoc* analysis. The split time significantly decreased at 5 m for S (4.2%) in comparison with S+E (0.4%) between pre- and retests ($p < 0.002$) and the contact time of DJ for S (11.6%; 10.6%) in comparison with S+E (5.7%; 0.0%) between pre-, post-, and retests ($p < 0.043$) in *post hoc* analysis. The two available WB-EMS studies investigated CODS at 15 m (Filipovic et al., 2016) and at 30 m (Wirtz et al., 2016) but no split time at 5 m. Moreover, Filipovic et al. (2016) analyzed RSI with positive effects for the WB-EMS intervention group but no height or contact time of DJ performance. Therefore, the present result cannot be placed in a larger context of WB-EMS. However, these initial results offer a practical recommendation. Concerning a large effect size (SMD = 1.21) for CODS at 5 m and a moderate to large effect size (SMD = 0.70–0.90) for contact time of DJ, dynamic strength training combined with jumping and sprinting exercises without superimposed WB-EMS (S) is currently to be preferred for physically active females. Perez-Gomez and Calbet (2013) reviewed training methods to improve vertical jump performance. In comparison with local EMS, vibration training or strength training alone, the combination of strength and plyometric training seemed to be the most effective method. It likely took advantage of the enhancement of maximal dynamic force through strength training and the positive effects of ploymetric training on speed and force of muscle contraction through its specific effect on type II fibers and high-threshold alpha-motoneurones. However, the present S+E intervention showed a moderate effect size (SMD) for CODS at 5 m (0.50) and for contact time of DJ (0.63) at posttest. As mentioned before, both interventions, S and S+E, significantly improved the overall performance like the total time of CODS at 15 m and RSI of DJ as well as the height of CMJ and SJ. On the one hand, these results do not suggest negative consequences by the artificial muscle activation by submaximal WB-EMS. EMS does not facilitate learning the specific coordination of complex movement like jumping or sprinting, especially during maximal local isometric stimulation (Perez-Gomez and Calbet, 2013; Paillard, 2018). According to Babault et al. (2007) and Bezerra et al. (2011), a low voluntary movement control exists at maximum stimulation intensities, and only submaximal contractions enable an efficient movement control with superimposed EMS. Perez-Gomez and Calbet (2013) also recommend applying EMS concomitantly with plyometric training or practice of sports. This confirms the approach of the present study by a submaximal WB-EMS superimposed on strength, sprinting, and jumping exercises. On the other hand, the observation of Bezerra et al. (2009) could not be confirmed. VC + EMS caused no additional training effect compared with VC training. They hypothesized that it would activate the same neural pathways that are normally used in voluntary exercise, with additional afferent inputs (centrally integrated) provoked by the electrostimulation.

With a closer look at the results of SSS and the training method EMS, the present dynamic strength training intervention with sprinting and jumping exercises superimposed by submaximal WB-EMS significantly decreased total time (2.3%) of a 30-m linear sprint as well as 5-m (6.3%), 10-m (3.7%), and 20-m (2.9%) split time between pre-, post-, and retests. So far, SSS performance over distances ≥ 30 m could not be improved, neither by the two WB-EMS studies (Filipovic et al., 2016; Wirtz et al., 2016) nor by local EMS studies in male athletes (Herrero et al., 2006, 2010a; Babault et al., 2007; Billot et al., 2010). The diagnostics of force and power parameters as secondary endpoints of this study supported the results of SSS. Superimposed WB-EMS during the Bulgarian split squat and the Nordic curl resulted in increases of 18.2% of biceps femoris force to 12.6% of quadriceps femoris force. According to Mero et al. (1992) and Delecluse (1997), biceps femoris showed the highest EMG activation during the maximum speed of SSS and quadriceps femoris showed the highest EMG activation during the acceleration phase of SSS. Ebben et al. (2009) demonstrated a < 0.5 EMG activation ratio between biceps femoris and quadriceps femoris for the exercises squat and split squat. The 2 dynamic WB-EMS studies used the squat exercise as strength training intervention. Wirtz et al. (2016) applied ALs during superimposed WB-EMS. They showed increases of 8% of biceps femoris force, but they enhanced quadriceps femoris force by 28.6% without a transfer to SSS. Filipovic et al. (2016) used an explosive movement velocity during superimposed WB-EMS. They showed a significant decrease for 5-m split time after 7 weeks. Thus, the acceleration phase was influenced by an improved quadriceps femoris force of 19.9% but not the maximum speed phase of SSS. Moreover, Herrero et al. (2010a) who applied local EMS at quadriceps femoris during knee extension showed no effects on 20-m sprint time, too. This exercise reached 8.6% of maximum VC of biceps femoris instead of 86.9% of quadriceps femoris during EMG analysis (Ebben et al., 2009). On the contrary, three local EMS studies showed positive effects on SSS over distances ≤20 m (0.8–2.3%) (Herrero et al., 2006, 2010b; Voelzke et al., 2012). They used isometric EMS of quadriceps femoris in combination with plyometrics. Plyometrics reached a higher biceps femoris to quadriceps femoris activation ratio of 1.01 in precontact and 0.55 in post-contact (Ebben et al., 2010). Thus, a strength exercise selection superimposed by WB-EMS with a high biceps femoris activation and a positive activation ratio to quadriceps femoris like the Nordic curl appear reasonable to enhance SSS, especially over distances ≥ 30 m. Moreover, in contrast to CODS, SJ or CMJ performance, additional jumping and sprinting exercises or an explosive movement velocity during strength exercises seem to be crucial in the application of EMS or WB-EMS to improve SSS.

Some limitations of the present study have to be mentioned for further research on WB-EMS. Six dropouts, three in each group without a coherent statement of reasons, occurred. Thus, it seemed to be independent of the intervention with or without WB-EMS. The final 22 participants, sufficient according to the *a priori* power analyses, improved strength, power, and jumping performance without a detraining phase. This indicated that strength trained female sport students were able to cope with the physical requirements. In particular, the WB-EMS training at 70% iPT seemed to be a beneficial compromise to achieve strength and power adaptations as well as to have an appropriate exertional tolerance. A detraining period of 2 to 6 weeks is common in several EMS studies (Filipovic et al., 2011). However, this should be further verified with additional physiological parameters like creatine kinase, questionnaires about physical habits, and recovery–stress states. Moreover, a control, blinding, or placebo intervention group could verify the attribution of environmental influences, expectations, or learning effects on performance gains. With reference to Sommi et al. (2018), a broad acceptance of superimposed WB-EMS by female athletes is decisive for further development of athletic programs. Due to the lack of WB-EMS studies in female athletes, the results of this study were often compared with studies in male athletes. Although Maffiuletti et al. (2008) demonstrated that supramotor thresholds were significantly lower in women than in men, contrary to the expected constitutional differences like subcutaneous fat thickness, women showed no significant differences at motor threshold. However, the subjective tolerance to current intensity remains a key limiting factor of EMS, regardless of sexes (Reed, 1997).

Finally, the conclusion of our investigation is that superimposed submaximal WB-EMS during dynamic strength, sprinting, and jumping exercises could serve as a reasonable but not superior alternative to classic training regimes to improve CODS and SSS, VJ and HJ, as well as strength and power parameters in physically active female. The present WB-EMS approach at 70% of iPT seems to intensify dynamic strength exercises equal but not higher than ALs corresponding to the 8 to 10 repetition maximum. Thus, against the hypothesis, it leads to comparable but no greater improvements in physical fitness. Therefore, it remains to be considered whether the effort of a submaximal superimposed WB-EMS short-term intervention is remunerative. Whether it provides perspectives for female athletes with little experiences or insufficient technique to incorporate strength routines without using moderate to high AL, which is necessary to improve sprinting performance or to provide injury prevention and joint stability, has to be verified in further studies. Moreover, training regimes concentrating on contact time of DJ or CODS at 5 m should be executed without superimposed WB-EMS in physically active females concerning to the present results and has to be verified in further WB-EMS studies, too. Additionally, an improvement of SSS performance over a distance of $\geq$30 m occurs for the first time for superimposed local EMS or WB-EMS. To improve SSS at maximum speed by superimposed WB-EMS, our results offer a combination of jumping and sprinting exercises with strength exercises that have a high biceps femoris activation and a positive activation ratio to quadriceps femoris. In this context, a higher transferability of physically active females than males and the adaptations of WB-EMS over time need to be further researched, as well as concepts for periodization in high-performance sports need to be developed.

ETHICS STATEMENT

The study protocol was approved by the "Ethics Committee of the German Sport University Cologne" in December 2013 and complied with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

UD, NW, and FM conceived and designed the research. UD, NW, FM, and MM conducted the experiments. UD analyzed the data and wrote the manuscript. HK, NW, FM, and LD revised the manuscript. All authors read and approved the manuscript.

ACKNOWLEDGMENTS

The authors would like to acknowledge the time and effort of Nicole Hiermayr, Jens Müller, and Christopher Born as well as of all the participants involved in this investigation.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphys.2019.00728/full#supplementary-material

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 24 July 2019
doi: 10.3389/fphys.2019.00920

Adjustment Effects of Maximum Intensity Tolerance During Whole-Body Electromyostimulation Training

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OPEN ACCESS

Edited by:
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Reviewed by:
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Luis Manuel Rama, University of Coimbra, Portugal
Conor M. Minogue, University College Dublin, Ireland

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: 21 January 2019
Accepted: 08 July 2019
Published: 24 July 2019

Citation:
Berger J, Becker S, Backfisch M, Eifler C, Kemmler W and Fröhlich M (2019) Adjustment Effects of Maximum Intensity Tolerance During Whole-Body Electromyostimulation Training. Front. Physiol. 10:920. doi: 10.3389/fphys.2019.00920

Intensity regulation during whole-body electromyostimulation (WB-EMS) training is mostly controlled by subjective scales such as CR-10 Borg scale. To determine objective training intensities derived from a maximum as it is used in conventional strength training using the one-repetition-maximum (1-RM), a comparable maximum in WB-EMS is necessary. Therefore, the aim of this study was to examine, if there is an individual maximum intensity tolerance plateau after multiple consecutive EMS application sessions. A total of 52 subjects (24.1 ± 3.2 years; 76.8 ± 11.1 kg; 1.77 ± 0.09 m) participated in the longitudinal, observational study (38 males, 14 females). Each participant carried out four consecutive maximal EMS applications (T1–T4) separated by 1 week. All muscle groups were stimulated successively until their individual maximum and combined to a whole-body stimulation index to carry out a possible statement for the development of the maximum intensity tolerance of the whole body. There was a significant main effect between the measurement times for all participants ($p < 0.001$; $\eta^2 = 0.39$) as well as gender specific for males ($p = 0.001$; $\eta^2 = 0.18$) and females ($p < 0.001$; $\eta^2 = 0.57$). There were no interaction effects of gender × measurement time ($p = 0.394$). The maximum intensity tolerance increased significantly from T1 to T2 ($p = 0.001$) and T2 to T3 ($p < 0.001$). There was no significant difference between T3 and T4 ($p = 1.0$). These results indicate that there is an adjustment of the individual maximum intensity tolerance to a WB-EMS training after three consecutive tests. Therefore, there is a need of several habituation units comparable to the identification of the individual 1-RM in conventional strength training. Further research should focus on an objective intensity-specific regulation of the WB-EMS based on the individual maximum intensity tolerance to characterize different training areas and therefore generate specific adaptations to a WB-EMS training compared to conventional strength training methods.

Keywords: adjustment effects, familiarization, intensity tolerance plateau, specific adaptations, whole-body electromyostimulation

INTRODUCTION

Electromyostimulation training (EMS training) has been used since the early 1970s as a high-intensity training technology in high-performance sports, physical therapy, and rehabilitation (Selkowitz, 1985, 1989; Duchateau and Hainaut, 1988; Binder-MacLeod and McDermond, 1992; Filipovic et al., 2011, 2012; Kemmler et al., 2018). Electrodes attached to the skin lead to involuntary contraction of the muscles underneath the electrodes while in conventional strength training, voluntary muscle contraction against a resistance takes place. In conventional strength training, differentiated intensities are derived to control training and generate specific adaptations of the musculature to athletic exercise. These intensities are often based on the one-repetition-maximum (1-RM). The 1-RM has been established as a simple, economic, and adequately valid option to determine training intensity levels. It is considered the gold standard of muscle strength evaluation in non-laboratory conditions (LeSuer et al., 1997; Ritti-Dias et al., 2005; Levinger et al., 2009; Kenney et al., 2015). Due to the complexity of movement and neuronal adaptation mechanisms, strength training beginners are often not able to exploit their absolute maximum capabilities the first time they exercise. Only after repeated units, the personal best may be reached at all (Rutherford and Jones, 1986; Mayhew et al., 1989; Braith et al., 1993; Ritti-Dias et al., 2005, 2011; Wirth et al., 2012). This means that athletes require consecutive stimuli until they are able to reach a certain plateau or their individual maximum. This individual learning and familiarization phase is said to be unexplored in EMS training. Furthermore, there is insufficient knowledge in the fields of deriving percentage training intensities and determining individual maximum intensity tolerances or an equivalent to the 1-RM.

The individual training fields for EMS training are usually specified by assessing the degree of perceived exertion based on the Borg RPE (rating of perceived exertion) scale (Borg, 1998; Kemmler et al., 2012, 2016b,c,d; Kemmler and von Stengel, 2012; Amaro-Gahete et al., 2018). To date, objectified training intensities have not been measured. In their work, Alon and Smith already examined the adaptation to an EMS application after several consecutive sessions and found that the maximum intensity tolerance continuously increases (Alon and Smith, 2005). However, they focused on one muscle only (m. quadriceps femoris) and the combination of an EMS application and maximum voluntary isometric contraction (MVC). Familiarization and adaptation effects regarding a whole-body EMS training have not been identified yet. Training guidelines recommend an 8- to 10-week adaptation phase in order to avoid unwanted metabolic effects. This, however, does not allow any statement on the individual maximum intensity tolerance (Kemmler et al., 2016a).

Therefore, the aim of this study is to determine whether a maximum intensity tolerance plateau occurs after multiple consecutive whole-body electromyostimulation (WB-EMS) application sessions.

MATERIALS AND METHODS

Study Design and Subjects

A total of 59 test subjects participated in the longitudinal, observational analysis in a panel design. Four consecutive tests were performed at the same time of day with a 1-week interval. Due to health complications and further personal reasons (not related to the WB-EMS application), seven persons did not perform four consecutive tests, so that in the end, 38 male and 14 female participants (n = 52) were entered in the study. Participants' characteristics are shown in **Table 1**.

All participants were EMS beginners, recruited via e-mail distribution lists, flyers, and personal contact. Exclusion criteria were acute or chronic diseases, infections or limitations to the musculoskeletal system, EMS experience in the past, and open skin lesions, which would have inhibited EMS application. The subjects had to be between 18 and 40 years of age with a BMI < 30 kg/m^2, and they were not allowed to take any medication that might have affected the examination (pain medication, beta blockers, etc.). Before study start, a detailed anamnesis questionnaire had to be completed in order to exclude any relative and/or absolute contraindications for EMS training (Vatter et al., 2016; Kemmler et al., 2016a). Furthermore, the course of the study, the testing design, and potential risks were explained in detail. Before entering the study, all participants provided written informed consent to the experimental procedure and written consent pertaining to data use. The study was conducted based on the current Declaration of Helsinki guidelines (World Medical Association, 2013) and approved by the ethics commission of the German University of Applied Sciences for Prevention and Health Management (project number 02/17).

Materials

The WB-EMS application was carried out with the miha bodytec 2 EMS device from Miha Bodytec. The device includes one main controller to manage the possible maximal output of the device and 10 subcontrollers to dose the specific muscle groups (**Figure 1**). In this investigation, we just used the eight prepared muscle groups with no additional muscle groups using the canals 9 and 10. The muscle groups were stimulated using an electrode vest including five pairs of electrodes (lower back, latissimus, upper back, abdomen, and chest), a hip belt to stimulate the glutaeus muscle and one

TABLE 1 | Anthropometric data for the entire group (n = 52) and the gender subgroups, shown in mean value ± standard deviation; BMI = body mass index.

	N	Height [cm]	Weight [kg]	Age [years]	Body fat [%]	BMI [kg/m^2]
General	52	177.9 ± 8.9	76.76 ± 11.06	24.13 ± 3.28	18.14 ± 7.67	24.20 ± 2.31
Women	14	167.8 ± 5.1	65.84 ± 7.94	23.84 ± 3.00	28.29 ± 4.48	23.35 ± 2.28
Men	38	181.6 ± 6.6	80.79 ± 9.21	24.93 ± 3.95	14.40 ± 4.56	24.52 ± 2.27

belt pair each for the thighs and the upper arms. To avoid the direct contact of the electrodes to the skin, a special functional EMS lingerie was used. All the electrodes (vest and belts) were moistened before use to guarantee a better conductivity from the electrodes to the participants' body. The EMS application and the way of using the workout clothes were in line with the manufacturer's instructions (Miha Bodytec, Augsburg, Germany). Body fat was determined using the Tanita BC-418 body composition analyzer with the software GMON v.3.2.3. 10. The participants were instructed to drink 1 litre of water up to 60 min before the bioimpedance analysis to reduce the variability of the results.

Tests

The tests were conducted based on common EMS application stimulation parameters, i.e., a frequency of 85 Hz, an impulse width of 350 μs, and a bipolar impulse without impulse increase (rectangular impulse) with interchanging 4-s load and 4-s break intervals (Filipovic et al., 2011; Kemmler et al., 2012, 2018).

Each muscle group was strained in intervals up to their individual, subjective maximum. The maximum was determined by the point at which the test person gave the signal to stop the strain due to the highest degree of strain that could be endured. The last stimulation value output by the EMS device was therefore recorded as the maximum intensity tolerance. This is, however, just a numerical value that cannot be equated with a specific value in milliamperes (mA). All maximum intensity tolerances refer to the stimulation of a specific muscle. The device was set up so that a maximum output and thus maximum device load were possible [maximal value of the main level controller (99)]. All muscle groups were strained consecutively in this way. During the tests, the test persons were never informed about the stimulation value or the maximum intensity tolerances of any of the previous tests. This resulted in a maximum intensity tolerance range of 0–99 (device-specific unit, 0–75 mA) for each muscle group. For a better understanding, **Figure 1** shows the miha bodytec 2 device including the main level controller as well as the specific muscle groups. The individual muscle groups were combined into an unweighted, additive index in order to come to a statement on the development of the entire body and not only a specific muscle group. After a preceding impulse adaptation, each test person took part in four consecutive tests in 1-week intervals. Four tests were selected for better comparability with the approach to the determination of 1-RM in conventional strength training. A separation of 1 week was used to guarantee complete regeneration after each session. In order to exclude time-of-day effects, the tests were performed at the same time of day for each test person. In addition, the participants were always examined by the identical research staff. Before each test, a new anamnesis questionnaire on the current condition was completed in order to exclude spontaneously occurring contraindications (intake of pain medication or alcohol, muscle aches, liquid receptive before the training, etc.).

Statistics

Sample size was calculated using G*power 3.1.9.4 (university of Düsseldorf, Germany). With an effect size of 0.25, total sample size was calculated by 36 participants (Faul et al., 2007). With regard to possible drop-outs, more participants were admitted to the study. Statistical evaluation and graphics generation were executed using IBM SPSS (SPSS Version 25.0, Chicago, IL, USA). The normal distribution was verified by means of the Shapiro-Wilk test. Because of this criteria, to check the maximum intensity tolerance index development, the four test times T1–T4 were analyzed by means of

FIGURE 1 | WB-EMS device miha bodytec 2.

repeated-measures analysis of variance. Since ANOVA is known to be robust when it comes to infringements of the normal distribution, it was applied every time (Schmider et al., 2010). *Post hoc* comparisons including Bonferroni correction were performed to detect differences between the measurement times. As the Mauchly test indicated a violation of sphericity, the degrees of freedom corrected according to Huynh-Feldt were used for the further calculation of p [because epsilon by Greenhouse Geiser >0.75 (Girden, 1992; Field, 2009)]. Furthermore, the effect size η^2 was calculated (Cohen, 1988). The significance level was set to $p < 0.05$.

RESULTS

Since the device-specific maximum was reached for eight test persons during the four test dates, the number of valid data records was reduced to 44. **Table 2** represents the index values of the individual test days. Between the measurement times, a significant main effect F (2.46; 105.96) = 26.95, $p < 0.001$, $\eta^2 = 0.39$ was identified, which categorizes the effect size as large according to Cohen. To differentiate between genders, the degrees of freedom corrected according to Greenhouse Geiser were applied. For the male test persons, a significant main effect was identified F (2.21; 77.41) = 7.66, $p = 0.001$, $\eta^2 = 0.18$. Also for the female test persons, a significant main effect was found between the measurement times with F (1.84; 22.07) = 15.82, $p < 0.001$, $\eta^2 = 0.57$. Significant main effects were also identified pertaining to the gender factor: [F (1; 45) = 12.09, $p = 0.001$, $\eta^2 = 0.21$]. There were no significant interaction effects for gender multiplied by measurement time [F (3; 135) =1.00, $p = 0.394$, $\eta^2 = 0.02$].

There were significant differences between the measurement times T1 to T2 and T2 to T3. There were no significant differences between T3 and T4. The maximum intensity tolerance index values for the various measurement times (including confidence interval for men and women) as well as the percentage increases over the measurement times are included in **Tables 2** and **3**. For improved understanding, the boxplots for all test person data and gender specifics are shown in **Figure 2**.

DISCUSSION

The results of this study show that a plateau develops after the third test session of consecutive measurements of the maximum intensity tolerance. A possible reason could be the habituation to the external electrical stimulation on the one hand and the muscular-coordinative adaptations on the intramuscular level on the other hand. Also neuronal adaptation caused by the maximal stimulation could be important. Therefore, the maximum intensity tolerance should be determined based on several consecutive test units in order to exclude the named influencing factors in the interpretation of results. This approach seems to be similar to that pertaining to the determination of the 1-RM, for which a certain number of familiarization and adaptation sessions is required to reach the individual maximum (Reynolds et al., 2006; Ritti-Dias et al., 2011). In conventional strength training, usually 2 weeks of learning and adaptation training with four measurement sessions precede the actual 1-RM determination so that the training intensity can be derived based on the 1-RM. Similarly, the determination of the individual maximum intensity tolerance through preceding adaptation sessions could serve as a preparation for the whole-body EMS training (Ritti-Dias et al., 2011). So far, one habituation session to an EMS training is recommended, which seems not sufficient to account all habituation and learning effects to a maximaum electrical intensity.

Previous analyses did not identify any intensity tolerance adaption in consecutive tests. For example, Alon and Smith (2005) conducted six NMES (neuromuscular electrical stimulation) sessions with 21 test persons within 2 weeks to see whether an adaptation of the maximum intensity tolerance would occur. During these examinations, they did not identify any adaptations. This could have been due to the isolated stimulation of the right-hand side m. quadriceps femoris in contrast to our whole-body index of maximum intensity tolerance (Alon and Smith, 2005). It remains to be clarified with more test persons whether there is a difference between beginners and experienced subjects at the point of plateau like in the 1-RM bench pressing and squats tests by Ritti-Dias et al. (2011). First studies by Hortobágyi et al. (1992) with 12 test persons point to a difference in maximum intensity tolerance between trained and untrained subjects. The trained persons exhibited a strength value for the m. biceps brachii that was up to 29% higher than that of the untrained participants. With 31.3 mA measured for the trained and 21.9 mA for the untrained subjects, the tolerated intensity strength was clearly higher in the trained subjects (Hortobágyi et al., 1992). The difference of the sensory threshold between males and females, i.e., the response to

TABLE 2 | Maximum intensity tolerance as mean value ± standard deviation and 95% confidence interval [CI] of the measuring times T1–T4 for the entire collective and men and women.

Time of measuring	Maximum intensity tolerance of all participants [CI]	Maximum intensity tolerance of men [CI]	Maximum intensity tolerance of women [CI]
T1	61.03 ± 11.71 [57.59–64.47]	64.67 ± 10.15 [61.13–68.22]	51.49 ± 10.31 [45.25–57.72]
T2	64.57 ± 10.50 [61.48–67.65]	67.02 ± 9.62 [63.65–70.37]	58.18 ± 10.35 [51.92–64.42]
T3	68.97 ± 10.97 [65.75–72.19]	71.25 ± 9.42 [67.96–74.54]	63.03 ± 12.83 [55.27–70.78]
T4	70.46 ± 13.62 [66.46–74.46]	73.50 ± 13.03 [68.95–78.04]	62.51 ± 12.26 [55.10–69.92]

an external impulse, also seems to have been confirmed in previous tests. Maffiuletti et al. (2008) analyzed this with the help of 20 men and 20 women. They identified gender differences at the sensory threshold: the values of the female test persons were 41% lower than those of the male test persons (Maffiuletti et al., 2008). This is a result that we were able to corroborate based on the gender-specific differences in the maximum intensity tolerance (men were 13% higher than women). The results by Alon and Smith are thus confirmed. They found a significantly higher intensity tolerance in males (31.5 ± 8.6 μC) than in females (16.9 ± 8.0 μC). However, the percentage increase between the first and last unit conducted turned out to be mostly identical (male: 47.2%; female: 50.8%) (Alon and Smith, 2005). Similar gender-specific differences were observed by Fehr in pilot studies, with a difference of the maximum intensity tolerance of 35.9 mA in males and 22.3 mA in females (Fehr, 2011). These studies support our results because the intensity tolerance when developing the plateau is also higher in males in our tests. The course beyond the testing times, however, does not seem to be subject to any gender-specific differentiation.

TABLE 3 | Comparison of pairs of testing sessions including significance and increase in %.

Comparison of pairs	*p*	Increase (%)
T1–T2	0.001	6.4
T2–T3	0.000	8.1
T3–T4	1.000	0.4

In order to be able to perform the training studies with the appropriate intensity in the future and to derive conclusions from conventional strength training for EMS, it may be useful to specify a 1-RM equivalent to establish objective intensity ranges. The key question as to the extent to which percentage values of the individual intensity tolerances actually represent individual training areas such as maximum strength training, muscle hypertrophy, or rather strength-endurance training also remains to be clarified in future studies. Since strain intensity (i.e., the intensity in WB-EMS training) is just a control parameter for training adaptations, the methodology to be applied to WB-EMS training itself still needs to be defined. Due to a methodology's essential influence on intensity perception and perceived exertion, it may actually represent a key factor in the establishment of training intensity based on its individual maximum.

CONCLUSION

In summary, after multiple consecutive EMS application sessions with EMS beginners, a maximum intensity tolerance plateau was reached after three adaptation sessions. Therefore, future studies should plan for at least three adaptation sessions preceding the actual whole-body EMS training. We recommend that follow-up studies take the maximum intensity tolerance findings as a basis for defining percentage training areas in order to enable objective training control in the future. It is also recommended that the increase of the individual maximum intensity tolerance over a prolonged period of time and its potential changes caused by training adaptation should

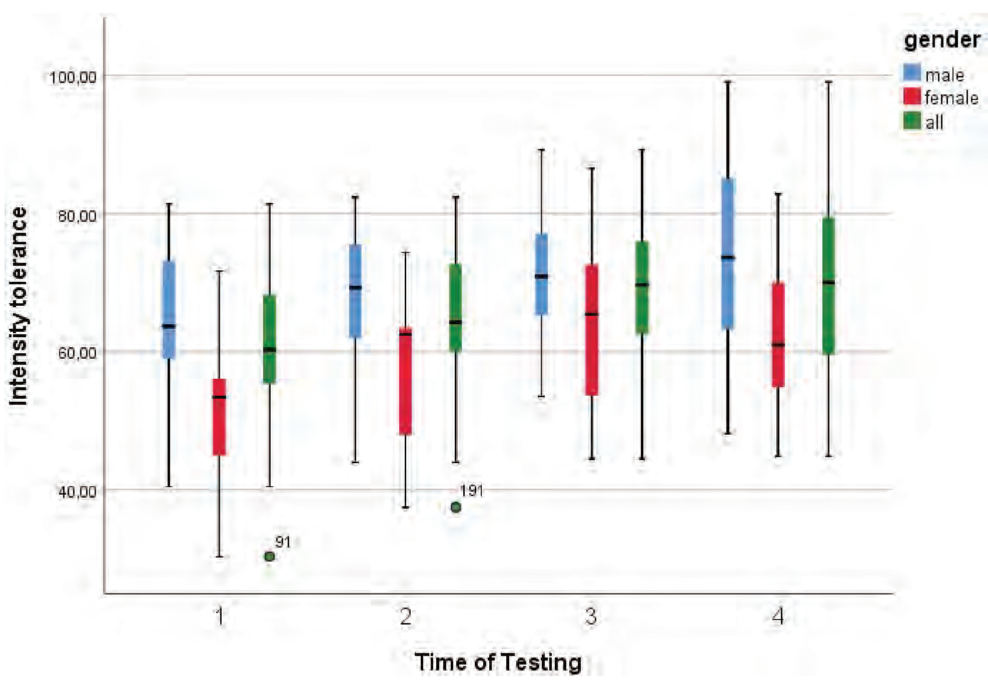

FIGURE 2 | Boxplots of intensity tolerance with 95% confidence interval for all four times of testing.

be verified. Also at a sub-maximum level, training intensity development should be observed in order to be able to derive relevant conclusions. Even if intensity is only one of several measures of training control in EMS training, it could be a key value to define training intensity, similar to 1-RM.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the Declaration of Helsinki with written informed consent from all subjects. The protocol was approved by the ethics commission of the German University of Applied Sciences for Prevention and Health Management (project number 02/17).

AUTHOR CONTRIBUTIONS

JB, SB, and MB participated in the design of the study, carried out the experiments, and performed data analyses. JB wrote the manuscript. MF and SB helped write the manuscript and supervised statistical analysis. MF, CE, and WK contributed to the study design and supervised the entire project. All authors read and approved the final manuscript.

ACKNOWLEDGMENTS

The authors wish to thank their students for their help with data acquisition and Monika Schutz for translating the manuscript.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ORIGINAL RESEARCH
published: 12 August 2019
doi: 10.3389/fphys.2019.01012

Effects of Whole-Body Electromyostimulation on the Energy-Restriction-Induced Reduction of Muscle Mass During Intended Weight Loss

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OPEN ACCESS

Edited by:
Yurdagül Zopf,
University Hospital Erlangen,
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Reviewed by:
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University of Foggia, Italy
Emiliano Cè,
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Specialty section:
This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 25 February 2019
Accepted: 23 July 2019
Published: 12 August 2019

Citation:
Willert S, Weissenfels A, Kohl M, von Stengel S, Fröhlich M, Kleinöder H, Schöne D, Teschler M and Kemmler W (2019) Effects of Whole-Body Electromyostimulation on the Energy-Restriction-Induced Reduction of Muscle Mass During Intended Weight Loss. Front. Physiol. 10:1012. doi: 10.3389/fphys.2019.01012

Purpose: Overweight and obesity are an increasing problem worldwide. However, most studies that focus on weight reduction by energy restriction and/or aerobic exercise reported considerable loss of muscle mass as well. Increased protein intake and/or resistance exercise might inhibit this detrimental effect during a negative energy balance. Whole-body electromyostimulation (WB-EMS), a time effective, joint-friendly, and highly customizable training technology, showed similar hypertrophic effects compared with high-intensity resistance training. The aim of this study is to evaluate the effect of WB-EMS on body composition during negative energy balance with maintained/increased protein intake in overweight premenopausal women.

Patients and Methods: Ninety premenopausal, 25–50-year-old, overweight women were randomly assigned to three groups ($n = 30$ each). (1) Negative energy balance (–500 kcal/day) by energy restriction with compensatory protein intake (CG). (2) Negative energy balance (–500 kcal/day) by energy restriction (–250 kcal/day) and increased physical activity (–250 kcal/day) with increased protein intake (PA). (3) Negative energy balance (–500 kcal/day) due to energy restriction and increased physical activity with increased protein intake plus WB-EMS. The duration of the intervention was 16 weeks. Participants underwent restrictions in kcal per days and supplementation of protein (CG: 1.2 or PA/WB-EMS: 1.7 g/kg body mass/day) where needed. Bipolar WB-EMS was applied 1.5× week for 20 min (85 Hz; 350 μs; intermittent 6 s impulse, 4 s rest; rectangular). The primary study endpoint "lean body mass" (LBM) and secondary endpoint body fat mass (BFM) were assessed by bio-impedance analysis (BIA).

Results: LBM decreased in the CG and PA group (CG: –113 ± 1,872 g; PA: –391 ± 1,832 g) but increased in the WB-EMS group (387 ± 1,769 g). However, changes were not significant ($p > 0.05$). Comparing the groups by ANOVA, no significant differences were observed ($p = 0.070$). However, pairwise adjusted comparisons determined significant differences between WB-EMS and PA (p = 0.049). BFM decreased significantly (p < 0.001) in all groups (CG: −2,174 ± 4,331 g; PA: −3,743 ± 4,237 g; WB-EMS: −3,278 ± 4,023 g) without any significant difference between the groups (ANOVA: p = 0.131).

Conclusion: WB-EMS is an efficient, joint-friendly, and highly customizable training technology for maintaining muscle mass during energy restriction and can thus be considered as an alternative to more demanding resistance exercise protocols.

Keywords: electromyostimulation, energy restriction, weight loss, lean body mass, body composition, protein supplementation

INTRODUCTION

Overweight and obesity represent an increasing problem worldwide. According to newer statistics, more than 2.1 billion people worldwide are overweight or even obese (Smith and Smith, 2016). This development is of course primarily a health problem for the person affected: overweight and obesity are crucial risk factors for hypertension, fat metabolism disorders, diabetes mellitus type 2, cardiovascular diseases, and some types of cancer (Wilson et al., 2002; Villareal et al., 2005; Renehan et al., 2008). Further, the direct and indirect health costs for the treatment of secondary diseases, for example, and the higher risk of inability to work constitute an immense burden for the healthcare system (Lehnert et al., 2015). Smith and Smith (2016), for example, report several hundred billion dollars in costs caused by obesity in the United States.

Different strategies for generating a negative energy balance promise sustainable success in the fight against overweight and obesity. As has been proved, energy restriction leads to a loss of body mass. For health reasons, however, this reduction of body mass should focus on the loss of body fat, not muscle mass (Biesalski and Grimm, 2007). Creating a negative energy balance *via* pure restriction of calorie intake without looking at the macronutrients seems to result in a loss of lean body mass of up to one third of the total loss of body mass (Miller et al., 1997). However, there is evidence that supplementation with protein might reduce the loss of muscle mass during energy restriction (Pasiakos et al., 2013, 2015).

In addition to energy restriction alone, an increase in energy turnover through greater physical activity in daily life, particularly exercise training, also contributes to a negative energy balance. Endurance- and resistance-exercise training (RT) generate a sharp increase in energy consumption and thus contribute to a loss of body fat (Wilmore et al., 1999; Dietz et al., 2012). Apart from the acute effect of exercise, particularly intense bouts of resistance exercise affect energy demands through two further mechanisms. Adaptation and repair processes significantly increase energy demands up to 48–72 h post-exercise (Melby et al., 1993; Gillette et al., 1994; Paschalis et al., 2010). Furthermore, in contrast to endurance or mixed exercise protocols, hypertrophic effects induced by adequate resistance exercise increase the resting metabolic rate (RMR; Byrne and Wilmore, 2001; Hunter et al., 2008). Correspondingly, retention of lean body mass and consequently RMR in periods of weight reduction (Goran and Poehlman, 1992; Hunter et al., 2008) is of high relevance.

Thus, the combination of strength training and high protein intake during phases of energy restriction might be a reasonable intervention for decreasing body mass predominately or even exclusively by a reduction in body fat mass (Wycherley et al., 2010).

However, a lack of time might be the primary obstacle to start conventional exercise programs that focus on weight loss (Rütten et al., 2009). In addition, orthopedic problems due to overweight or simple aversion to heavy exercise might prevent a subject's participation in exercise programs. Thus, time efficiency, joint friendliness, and high customization should be considered as a crucial aspect for effective interventions particularly for cohorts with low experience with or enthusiasm for physical exercise.

Whole-body electromyostimulation (WB-EMS), a novel time-saving, joint-friendly, and highly customizable training technology, might be a perfect candidate for cohorts with low time resources and/or low propensity for exercise (Kemmler et al., 2018). Recent studies have confirmed that WB-EMS has a comparable effect on hypertrophy, muscle strength, and fat loss as high intensity resistance training. Of interest, WB-EMS-induced reductions of body fat regularly increase the hypertrophic effect of this technology (Kemmler et al., 2016).

With regard to a personal-effective approach, the digital monitoring of training targets for increased physical activity in everyday life with the help of so-called activity trackers is of key importance. With the help of these trackers and the corresponding online training diary, a single trainer would thus have the opportunity to support his clients simultaneously without direct and prolonged contact with them and to check the activity specification. This combination of time-saving WB-EMS training, protein supplementation, and digital monitoring could be an effective, useful, and elegant solution in the setting of weight loss programs.

In summary, the aim of this study is to evaluate the effects of WB-EMS on body composition during energy restriction, increased physical activity in everyday life, and increased protein intake.

Our primary hypothesis is that WB-EMS, applied under energy restriction (ER), increased habitual physical activity in everyday life (PA) and high protein intake (PI), generates significantly more favorable changes on lean body mass than (1) isolated ER with moderate PI or (2) ER, high PI, and increased habitual physical activity in everyday life. Our secondary hypothesis is that (1) all three study arms generate significant reductions in absolute body fat mass (2) without significant group differences.

MATERIALS AND METHODS

Trial Designs

The **W**eight-**R**eduction and **E**lectromyostimulation **P**lus **P**rotein (WREPP) project is a randomized, controlled, clinical intervention study (RCT) with three study arms in a parallel group design. The study was designed and conducted by the Institute of Medical Physics (IMP), Friedrich-Alexander University Erlangen-Nuremberg (FAU). The study follows the Helsinki Declaration "Ethical Principles for Medical Research Involving Human Subjects" and was approved by the Ethical Committee of the FAU (ethics application no. 19_16b). The project was fully registered under NCT03746977. All women participating were intensively informed about the study procedures. Written informed consent was obtained before each subject's participation in the trial. We strictly followed the CONSORT 2010 guideline for randomized studies with a parallel group design (Moher et al., 2010).

Participants

Using citizen registers provided by the municipality, 1,000 women, 25–50 years old, living in the area of Erlangen-Nuremberg, Germany, were contacted by personal letters that already included the most important eligibility criteria. Two hundred women responded and were informed in more depth *via* a hotline and successive joint information events. Based on the eligibility criteria (1) 25–50 years old; (2) premenopausal status; (3) no diseases or pharmacological therapy with relevant influence on muscle mass and body fat (e.g., glucocorticoids >5 mg/day); (4) no pregnancy or acute breastfeeding period; (5) no conditions that exclude WB-EMS application (e.g., cardiac pacemaker); (6) no cardiovascular events (e.g., stroke, coronary infarction); and (7) no absence of more than 2 weeks during the study period, the eligible women (n = 110) were invited to determine obesity criteria by BIA (total body fat rate > 28%). Finally, 90 women fulfilled these criteria and agreed to participate in the study. Stratified according to body fat rate (%), participants were randomly allocated to three balanced intervention groups: (1) negative energy balance due to energy restriction with compensatory protein intake (CG: n = 30); (2) negative energy balance due to energy restriction and increased habitual physical activity in everyday life with increased protein intake (PA: n = 30); and (3) negative energy balance due to energy restriction and increased physical activity in everyday life with increased protein intake plus whole-body electromyostimulation (WB-EMS: n = 30). The flow chart of the study is shown in **Figure 1**, and the baseline characteristics of all the participants are illustrated in **Table 1**.

Intervention

The interventions were applied for 16 weeks in all the groups (February 2018 until July 2018).

Group CG: Negative Energy Balance Due to Energy Restriction With Compensatory Protein Intake

Based on individual nutritional analysis (Freiburger Nutrition Protocol, Nutri-Science, Hausach, Germany) and nutrition consultations, participants had to achieve the 500 kcal/day energy reduction through a corresponding reduction of carbohydrates (i.e., ≈125 g/day). Multi-component protein powder (Hansepharm, Roth, Germany) was supplemented to ensure a total protein intake of 1.2 g/kg body mass/day. Women in the CG were asked to maintain their normal daily activity and exercise habits.

Group PA: Negative Energy Balance Due to Energy Restriction and Increased Habitual Physical Activity With Increased Protein Intake

As with the CG, participants had to reduce the amount of carbohydrates by 250 kcal/day (i.e., ≈62.5 g/day). Based on the dietary protocol, multi-component protein powder (Hansepharm, Roth, Germany) was supplemented to ensure a total protein intake of 1.7 g/kg body mass/day. In order to generate a negative energy balance of −500 kcal/day, the women were asked to increase their normal daily activity by 250 kcal/day by executing more daily steps at their habitual gait speed. For this purpose, a specific individual target of steps was calculated. Therefore, the mean value of pedestrian cadence (115.2 steps/min) under natural conditions (Tudor-Locke and Rowe, 2012) and the body mass of each participant were taken as a reference. Steps were monitored by a fitness tracker (Polar Loop 2, Polar Electro Oy, Kempele, Finland). The information, transmitted electronically to the study management, was checked regularly to ensure compliance with the training target. Nutritional and exercise guidelines should accordingly result in a reduction of energy balance of 500 kcal/day.

Group Whole-Body Electromyostimulation: Negative Energy Balance Due to Energy Restriction and Increased Habitual Physical Activity With Increased Protein Intake Plus Whole-Body Electromyostimulation

In addition to the treatment of the PA group, we applied a WB-EMS training 1.5 × 20 min/week (every Tuesday and every second Friday) using devices from miha bodytec (Gersthofen, Germany). Eight muscle groups (upper arms, chest, abdomen, latissimus, upper back, lower back, buttocks, thighs) were addressed by the WB-EMS (standard) application (85 Hz; 350 μs; intermittent; 6 s impulse phase, 4 s rest; rectangular; bipolar). Two sets of six to eight repetitions of easy movements with a small range of motion such as moderate squats, butterfly movements, and trunk flexions were carried out during the impulse phase. Sessions were supervised and guided by two certified instructors each responsible for two participants. In order to gradually guide the participants to the intended training load, the duration of the

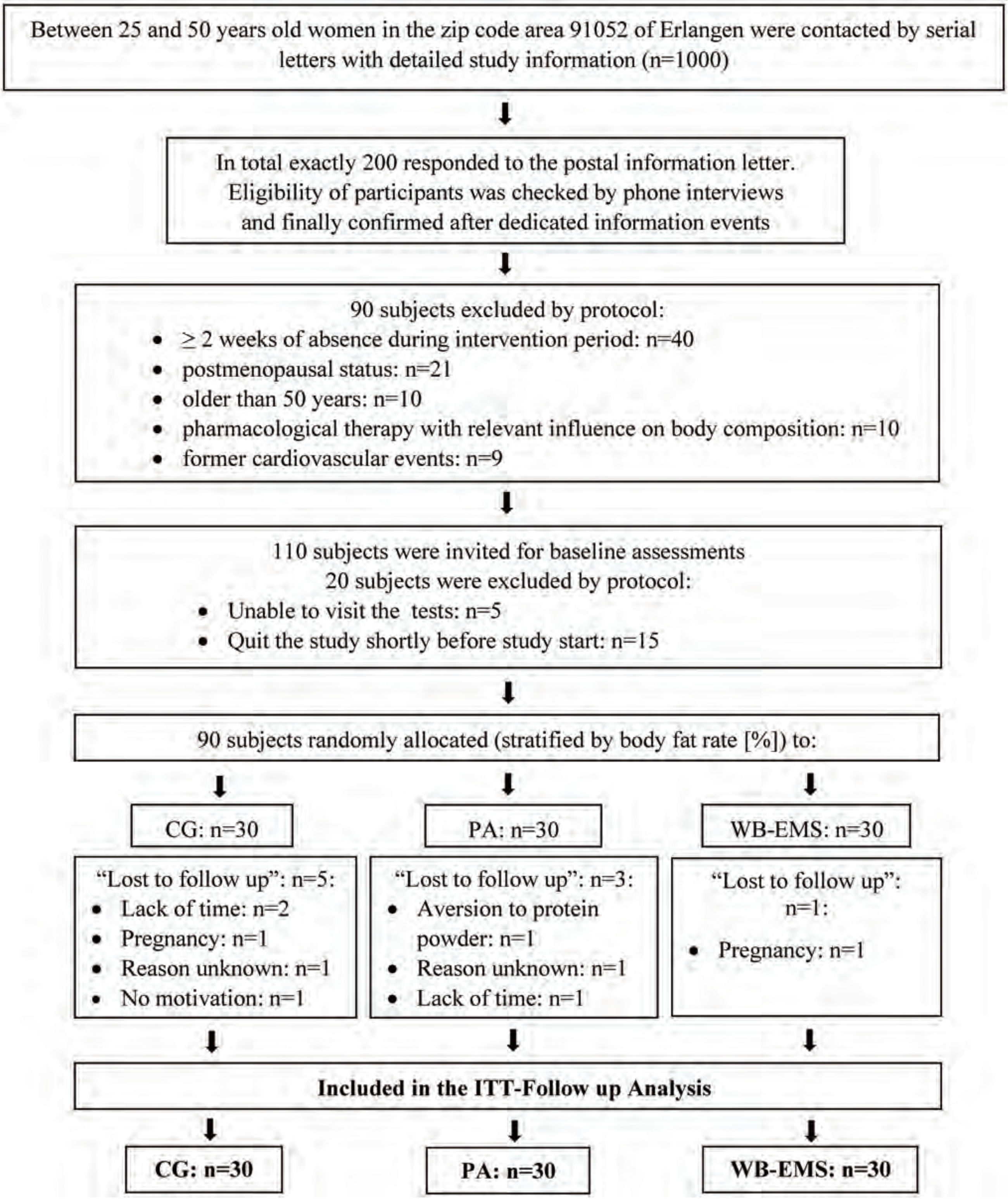

FIGURE 1 | Flow diagram of the study intervention. *n*, numbers; CG, pure energy restriction with compensatory protein intake; PA, energy restriction and increased physical activity with increased protein intake; WB-EMS, energy restriction and increased physical activity with increased protein intake plus whole-body electromyostimulation; ITT, intention-to-treat.

TABLE 1 | Baseline characteristics of all groups (WB-EMS, PA, and CG; *n* = 30 per group).

Variable	WB-EMS MV ± SD	PA MV ± SD	CG MV ± SD	*p*
Age (years)[a]	38.4 ± 8.0	34.4 ± 8.3	35.3 ± 7.4	0.136
Body height (cm)[b]	167.6 ± 4.9	166.3 ± 5.6	167.5 ± 6.9	0.658
Body mass (kg)[c]	92.3 ± 17.6	84.8 ± 15.4	86.0 ± 17.8	0.195
BMI (kg/m^2)	32.8 ± 6.8	30.5 ± 6.1	30.7 ± 6.2	0.327
Total body fat (%)[c]	42.0 ± 6.6	40.1 ± 7.2	39.2 ± 7.7	0.317
Energy consumption/d (kcal)[d]	2,299 ± 831	2,292 ± 555	2,178 ± 579	0.732
Protein intake/d (g)[d]	96 ± 33	88 ± 23	90 ± 22	0.506
Carbohydrate intake/d (g)[d]	240 ± 92	258 ± 59	231 ± 73	0.376
Total fat intake/d (g)[d]	94 ± 47	91 ± 30	89 ± 30	0.850
Hypertension (*n*)[a]	4	3	1	0.423
Smoking (*n*)[a]	4	3	4	0.896
Sport/week (min)[a]	74 ± 67	61 ± 68	91 ± 60	0.226
Steps/week (*n*)[e]	70,283 ± 21,105	65,302 ± 14,119	–	0.287
Physical condition (*n* of items)[f]	5 ± 1	5 ± 1	5 ± 1	0.901
Mental constitution (*n* of items)[f]	3 ± 2	3 ± 2	3 ± 1	0.683
Physical stress in daily life (*n* of items)[f]	3 ± 1	3 ± 1	3 ± 1	0.421

WB-EMS, energy restriction and increased physical activity with increased protein intake plus whole-body electromyostimulation; PA, energy restriction and increased physical activity with increased protein intake; CG, pure energy restriction with compensatory protein intake; p, significance; d, day; kcal, kilocalories; g, gram; n, number; min, minutes.
[a]Assessed by baseline questionnaire.
[b]Measured by stadiometer.
[c]Measured by bio-impedance analysis (DSM-BIA, InBody 770, Seoul, South Korea).
[d]Analyzed by Freiburger Nutrition Protocol (Nutri-Science, Hausach, Germany).
[e]Measured by fitness tracker (Polar Loop 2, Polar Electro Oy, Kempele, Finland).
[f]Assessed by baseline questionnaire with a scale from 1 "very satisfied"/"very low" to 7 "very dissatisfied"/"very high."

WB-EMS session was successively increased by 2 min from the first unit of 12 min until the full 20 min were reached in the fifth session. The intensity of training was based on the Borg CR 10 scale (Borg and Kaijser, 2006). The participants were instructed to realize a perceived exertion of between "5" (hard) and "7" (very hard). Trainers asked every 2 or 3 min, if they could raise the intensity of stimulation to adjust for the accustoming effect. The energy turnover of a single bout of WB-EMS (120 kcal/20 min session) (Kemmler et al., 2012) was considered in the calculation of the energy restriction (−225 kcal/day).

Outcomes

Primary endpoint:

- Changes in lean body mass from baseline to 16-week follow-up.

Secondary endpoint:

- Changes of total body fat mass from baseline to 16-week follow-up.

Assessments

All measurements were conducted at the IMP, FAU by dedicated researchers and research assistants. To ensure adequate standardization, the same test assessor using the same procedure carried out the dedicated baseline and follow-up measurement. All measurements were performed at similar times of the day (±1 h).

Calibrated devices were used for all assessments. Body height was measured barefoot using a stadiometer (Holtain Ltd., Crymych Dyfed, Great Britain). Body mass was assessed using bio-impedance technique (InBody 770, Seoul, South Korea), described in detail below. Body mass index (BMI) was calculated body mass (kg)/body height (m^2).

All participants recorded their habitual diet as accurately as possible for 5 representative days (four weekdays and one weekend day) before and during the last week of the intervention. Using the corresponding evaluation software (Freiburger Nutrition Protocol, Nutri-Science, Hausach, Germany), the average volume of carbohydrate, fat, protein, and alcohol intake per day was calculated. Corresponding dietary changes and specification were discussed in detail with the participants by the principal investigator (SW). Based on the dietary analysis, the amount of carbohydrate intake was limited, by 56, 62.5, and 125 g/day, respectively, in order to generate a negative balance of 225 kcal/day (WB-EMS), 250 kcal/day (PA), and 500 kcal/day (CG). On the other hand, the intake of all the other macro-nutritional components was maintained. In parallel, protein supplements were provided to ensure a daily protein uptake of 1.2 g/kg body mass/day in the CG and 1.7 g/kg body mass/day in the PA and WB-EMS groups. We used a multicomponent protein powder (Hansepharm Power Eiweiß Plus, Roth, Germany), i.e., a mix of a whey, casein, soy, and egg protein blend with a high leucine (10.3%) and carnitine (1.7%) content. The same protocols and analysis were applied to check participants' compliance with the dietary requirements, during the sixth and the last week of the intervention.

The calculation of the daily step target was based on the habitual walking volume of participants as determined by a fitness tracker (Polar Loop 2, Polar Electro Oy, Kempele, Finland). Trackers were worn for 2 weeks prior to the start of the intervention. Participants were instructed to maintain their normal daily activity and use representative days for the monitoring of their physical activity in everyday life. Considering the body mass of the participants, the daily walking volume in minutes required to consume 250 kcal of energy was calculated using an online calculator. Using the average number of steps per minute (115 steps/min) reported for "adult pedestrians" (Tudor-Locke and Rowe, 2012), the number of steps per day equivalent to an energy expenditure of 250 kcal/day was calculated. Of importance, all the tracked information were transmitted every fifth day to an online platform and submitted to the principal investigator (SW) who checked compliance of the participants and, if necessary, asked participants to increase (or decrease) their daily step number in order to properly comply with the physical activity protocol.

Direct segmental, multi-frequency BIA-technique (Inbody 770, Seoul, South Korea) was applied to evaluate body composition including the primary (LBM) and secondary (BFM) study outcome. The device separately measures trunk, arms, and legs using a tetrapolar eight-point tactile electrode system by means of six different frequencies (1, 5, 50, 250, 500, and 1,000 kHz). Among the participants of the present study, intra class correlation (ICC, test-retest) of LBM as assessed by the Inbody 770 was 0.90, and ICCs for percent body fat was comparably high (0.88).

Sample Size

Based on a 5% difference in lean body mass between the WB-EMS group and the PA group (MV, SD: 6.5%), 27 persons/group had to be included to generate at least a power of 80% based on an $\alpha = 0.05$ (t test based sample size calculation). Anticipating a "loss to follow-up" rate of 10%, we included 30 women/group in order to perform an adjuvant per protocol analysis.

Randomization

Stratified for body fat rate (%) and consistently supervised by the principal investigator (SW), the participants drew lots and allocated themselves to the three conditions. Lots were put in opaque plastic shells and were drawn by the participants from the same bowl in the order of their appearance. Of importance, neither participants nor researchers knew the allocation beforehand. After the assignment into three equal groups ($n = 30$/each), each woman was informed in detail by the principle investigator (SW) about dos and don'ts.

Blinding

Due to the study design, we were unable to properly blind participants with respect to their allocation. However, researchers conducting the tests or analysis were not aware of the participants' group status and were not allowed to ask, either.

Statistical Analyses

Analyses were carried out using the statistical software R (R Development Core Team, 2018) and SPSS 25 (SPSS Inc., Chicago, IL, USA). Data were reported using mean values (MV) and standard deviation (SD). We applied an intention to treat analysis with multiple imputation for missing values, using Amelia II, which is implemented in the R package "Amelia" (Honaker et al., 2011). Following the recommendations of Honaker et al. (2011), the complete data set was used for imputation. In order to obtain stable results, 100 imputed data sets were generated. The "overimpute" plot was used to control the imputations. The plots showed that the imputations for the variables to the primary and secondary endpoints had worked very well. Statistical (Shapiro-Wilk test) and graphical (QQ plots) tests indicated a normal distribution for the measured endpoints. To evaluate intra-group changes dependent t test were applied. Inter-group differences were analyzed using ANOVA. In case of relevant differences ($p < 0.150$), pairwise differences between the groups were checked using independent t tests, adjusted for multiple testing according to the method of Barnard and Rubin (Barnard and Rubin, 1999). Nominal scaled data, reported in **Table 1**, were analyzed by χ^2 tests. All tests were two tailed, and statistical significance was accepted at $p < 0.05$.

RESULTS

Baseline characteristics are given in **Table 1**. As stated, no significant between-group differences were determined (**Table 1**).

Nine participants (WB-EMS: $n = 1$ vs. PA: $n = 3$ vs. CG: $n = 5$) were lost to follow-up. Reasons given for withdrawal were (1) lack of motivation ($n = 2$); (2) pregnancy ($n = 2$); (3) lack of time ($n = 2$); and (4) aversion to protein powder ($n = 1$). Two women apparently lost interest and did not give reasons for their withdrawal.

Due to the possibility to catch up missed sessions, the attendance rate in the WB-EMS group was 100% (i.e., 24 sessions). None of the participants reported any adverse effects or complaints caused by the training. Further, based on our logs, compliance with the prescribed protein (powder) dose was high. Personal interviews with the participants (SW) showed a strict compliance with the protein supplementation protocol and confirmed this finding. However, slight decreases in dietary protein intake were observed, thus none of the study groups fully realized the intended total protein intake (WB-EMS: 1.67 ± 0.11 vs. PA: 1.62 ± 0.12 vs. CG: 1.16 ± 0.13 g/kg body mass/day).

Five-day dietary intake protocols conducted by all the participants indicated that average energy reduction by carbohydrate restriction, i.e., 500 kcal/day in the CG, and 225 and 250 kcal/day for the WB-EMS and PA group, respectively, was significantly exceeded ($p \leq 0.007$) in all the groups. However, considerable differences among the participants of all three groups were observed. Energy reduction reported by participants in the CG averaged 678 ± 505 kcal/day (range: 110 to −1,433 kcal); corresponding energy reduction was 528 ± 477 kcal/day (range: 301 to −1,261 kcal/day) in the PA and 462 ± 399 kcal (range: 97 to −1,177 kcal/day) in the WB-EMS group. We further observed that the WB-EMS

(198 ± 40 kcal/day) and the PA (180 ± 38 kcal/day) groups failed to generate the intended physical activity level corresponding to 225/250 kcal/day. Thus, overall reductions of net energy balance were 678 ± 505 kcal/day in the CG, 708 ± 519 kcal/day in the PA, and, considering the energy cost of the WB-EMS application, 660 ± 501 kcal in the WB-EMS group. Using ANOVA, significant between-group differences were not observed for the latter parameter (p = 0.660).

The primary study endpoint "lean body mass" (**Table 2**) decreased in the CG (−0.2 ± 2.9%) and PA groups (−0.8 ± 1.8%) but increased in the WB-EMS group (0.5 ± 2.5%). However, none of these intra-group changes ($p \geq 0.11$) were statistically significant. In parallel, no significant differences between the three groups were determined by ANOVA (p = 0.070) (**Table 2**). However, pairwise comparisons adjusted for multiple testing indicated a borderline significant difference between WB-EMS and PA (p = 0.049), while other comparisons, i.e., CG vs. PA (p = 0.424) or CG vs. WB-EMS (p = 0.390) were far from being significant (**Table 2**). Thus, we confirm our primary hypothesis (2) that WB-EMS generated significantly more favorable changes on lean body mass than a similar intervention, however without EMS-application (i.e., PA group). However, we have to reject our primary hypothesis (1) that WB-EMS, PA (250 kcal/day), energy restriction (225 kcal/day), and high protein intake (1.7 g/kg body mass/day) generated significantly more favorable changes on LBM than a control group with isolated energy restriction (500 kcal/day) and moderate protein intake (1.2 g/kg/body mass/day).

Total body fat mass decreased significantly ($p < 0.001$) in all the groups (CG: −6.3 ± 7.8%; PA: −10.7 ± 8.7%; WB-EMS: −8.3 ± 7.4%) without significant group differences (p = 0.131) as determined by ANOVA (**Table 2**). After adjusting for multiple testing, pairwise comparisons did not result in significant differences between the groups (CG vs. PA: p = 0.142; CG vs. WB-EMS: p = 0.331; PA vs. WB-EMS: p = 0.578). Thus, we fully confirm our secondary hypothesis that (1) all three groups generated significant reductions in total body fat mass (2) without significant group differences.

Changes in parameters that might confound our results were not detected. None of the participants reported any new disease or change of relevant medication or smoking habits during the study period. Physical activity and exercise outside the study increased in all the groups (CG: p = 0.034 vs. PA: p = 0.257 vs. WB-EMS: p = 0.076), however, without significant between-group differences (p = 0.800).

DISCUSSION

The general purpose of the study was to evaluate the effect of WB-EMS on body composition, under specific consideration of LBM changes, during negative energy balance, but increased protein intake in overweight 25- to 50-year-old premenopausal women. In summary, all of the interventions favorably affect LBM (<10%). Compared with the 25–30% LBM contribution to total weight loss reported by others (Ballor et al., 1988; Miller et al., 1997; Weinheimer et al., 2010), WB-EMS in combination with high protein intake seems to be the most suitable method for maintaining muscle mass during intended, mild decreases of net energy balance by caloric restriction and/or increased physical activity. Addressing changes in total body fat mass, all the groups significantly reduced fat mass during the 16-week intervention period (−6.3 ± 7.8 to −10.7 ± 8.7%).

This study is the first trial to determine the effect of WB-EMS on body composition during intended and structured negative energy balance. In summary, the present study provided evidence for introducing WB-EMS in treating overweight and obesity. Considering the hypertrophic effects of WB-EMS, a recent study demonstrates positive effects in the range of a high-intensity resistance training (HIT-RT). Applying both types of exercise for 16 weeks in untrained men, 30–50 years old (n = 46), Kemmler et al. (2016) reported comparable (p = 0.395), highly significant increases in LBM in the WB-EMS (0.63 ± 0.77 kg) and HIT (0.86 ± 0.97 kg) study arm of its randomized controlled trial (RCT). Of importance for the present topic, most WB-EMS studies reported reductions in fat mass that considerably exceeded the increases in muscle mass, resulting in a net weight loss (Kemmler et al., 2018). However, in contrast to HIT-RT, WB-EMS is a joint friendly and safe training method (Kemmler et al., 2016) feasible for all people unable or unwilling to join conventional (resistance) exercise programs. Due to the lack of other WB-EMS studies in this field, however, we now discuss results of RT trials to allow the reader to consider the relevance of our results.

Reviewing the literature, several studies indicated that isolated energy restriction protocols reduce body fat mass and LBM

TABLE 2 | Baseline value, changes (i.e., pre-post difference per group) of primary and secondary study endpoints, and significance levels.

	WB-EMS MV ± SD	PA MV ± SD	CG MV ± SD	p
Lean body mass (g)				
Baseline	52,707 ± 6,319	49,883 ± 4,799	51,250 ± 6,063	0.172
Difference	387 ± 1,769	−391 ± 1,832	−113 ± 1,872	0.070
Absolute body fat mass (g)				
Baseline	39,580 ± 13,428	34,953 ± 12,309	34,733 ± 13,878	0.282
Difference	−3,278 ± 4,023***	−3,743 ± 4,237***	−2,174 ± 4,331***	0.131

*WB-EMS, energy restriction and increased physical activity with increased protein intake plus whole-body electromyostimulation; PA, energy restriction and increased physical activity with increased protein intake; CG, pure energy restriction with compensatory protein intake; p, significance; MV, mean value; SD, standard deviation. ***p < 0.001.*

(Ballor et al., 1988; Miller et al., 1997; Weinheimer et al., 2010). Applying a hypocaloric diet in 40 obese people, Ballor et al. (1988) reported that 25% of total body mass loss can be attributed to LBM reductions. This result was confirmed by the systematic review of Weinheimer et al. (2010) that included trials examining overweight postmenopausal women under caloric restrictions of 9–52 weeks and calculated an average decrease in fat-free mass of about 25% of weight loss. In the "diet only" study arm of their meta-analysis (493 studies) with overweight adults, 2–90 weeks long, Miller et al. (1997) reported a body-mass reduction that constituted two thirds fat and one third fat-free mass.

Revisiting promising methods to stop or attenuate the loss of LBM during energy restriction, the current state of research suggests resistance exercise training. In their systematic review and meta-analysis, Sardeli et al. (2018) observed that RT, particularly when applied in multiple sets over 12–24 weeks, stops the decline of LBM in obese elderly people during a phase of caloric restriction (472 and 800 kcal/day; Sardeli et al., 2018). Hunter et al. (2008) investigated the effect of RT on fat-free mass in premenopausal overweight women during a diet-induced (800 kcal/day, 21 weeks) weight loss of approximately 12 kg. Compared with participants without exercise training (47.9 ± 4.7 to 46.4 ± 5.1 kg) or aerobic training (45.4 ± 4.2 to 44.4 ± 4.1 kg), RT maintained fat-free mass (46.9 ± 5.2 to 47.2 ± 5.0 kg) to a similar degree as in the present study (Hunter et al., 2008). Monitoring 40 obese premenopausal females in an eight-week weight-loss study, Ballor et al. (1988) draw a similar conclusion. Following a daily deficit of 1,000 kcal and supplementing protein to ensure a protein intake of ≥1.0 g/kg body mass/day, the exercise group conducting RT 3 days per week preserved and even significantly increased LBM compared with the "diet only" group (0.43 ± 0.26 vs. −0.91 ± 0.28 kg; $p < 0.05$).

Another possibility to protect LBM during a phase of negative energy balance might be a higher daily protein intake. In their meta-analysis of 27 RCTs, Stonehouse et al. (2016) compared the effects of dairy products (including whey protein) on body composition during energy restriction in 18–50-year-old predominately overweight to obese adults (n = 1,278) (Stonehouse et al., 2016). The daily energy restriction of the trials was usually 500 kcal or more for the average of 16 weeks. In summary, intervention groups with increased protein intake lost (non-significantly) less LBM than control groups (−0.12 ± 1.57 vs. −0.56 ± 1.54 kg). Of importance, the authors observed the most favorable effects on LBM maintenance using a protein intake of >1.2 g/kg body mass/day and additional RT. Similar findings were provided by another meta-analysis or meta-regression (Krieger et al., 2006; Wycherley et al., 2012). The comparison of 24 RCTs by Wycherley et al. (2012) with adults (mean study duration 12.1 ± 9.3 weeks) under energy restriction (exact amount not specified) demonstrated that diets with high protein intake (1.25 ± 0.17 g/kg body mass/day) resulted in significantly lower reductions in fat-free mass than diets with standard protein consumption (0.72 ± 0.09 g/kg/day). However, differences were significant for interventions longer than 12 weeks only. Krieger et al. (2006) reported that the degree of FFM retention during energy-restricted weight loss tended to increase with each successive quartile of dietary protein intake and that protein intake of 1.05 g/kg body mass/day or more might improve FFM retention. A 12-week RCT with 46, 28–80-year-old overweight and obese women on energy deficit (750 kcal/day) compared the effect of normal versus higher (0.92 vs. 1.52 g/kg body mass/day) protein intake (Leidy et al., 2007). In summary, the high protein group lost less LBM than the lower protein group (−1.5 ± 0.3 vs. −2.8 ± 0.5 kg; $p < 0.05$). This finding confirmed the results of an earlier trial (Farnsworth et al., 2003) with 43 overweight and obese women, 20–65 years old, on a 12-week energy restrictive diet (≈−500 kcal/day). Again, participants with higher protein intake (1.4 g/kg body mass/day) lost less LBM (−0.1 ± 0.3 kg vs. −1.5 ± 0.3 kg, $p = 0.02$) than their peers' standard protein consumption (0.8 g/kg body mass/day). Summing up the results in his systematic review, Pasiakos et al. (2013) recommend a daily protein intake twice (1.6 g/kg body mass) or three times (2.4 g/kg body mass) as high as the usual standard recommendation (0.8 g/kg body mass) to preserve lean body mass.

Although a recent meta-analysis (Stonehouse et al., 2016) did not fully confirm this strategy, a combination of strength training and increased protein intake during energy restriction might promise additive effects on LBM retention. Closest to our study, Layman et al. (2005) provided a high protein (1.6 g/kg body mass/day) reduced carbohydrate diet (400–500 kcal/day) combined with RT twice a week for 16 weeks for 48 overweighed women, 40–56 years old. In summary, this protocol resulted in more favorable changes in LBM (−0.9%) and fat mass (−22%) than a low protein (0.8 g/kg body mass/day) high carbohydrate diet (−5.4 and −12%) or an isolated high protein diet (−4.0 and 18%). The authors (Layman et al., 2005) applied a single set RT to fatigue of 30 min, a protocol with similar effects on body composition compared with WB-EMS (Kemmler et al., 2016).

Apart from effectiveness, adherence to the exercise protocol is a crucial aspect of weight loss (Acharya et al., 2009). In summary, a recent systematic review on WB-EMS reported low dropout (<10%) and high attendance (>90%) rates without any injuries (Kemmler et al., 2018). Even excluding studies with a high dropout (i.e., >30%), in their systematic review addressing early postmenopausal women, Asikainen et al. (2004) reported less favorable findings for RT, aerobic, or mixed protocols (Asikainen et al., 2004).

Summing up, we conclude that WB-EMS combined with high protein intake is an effective and feasible option for maintaining LBM under negative net energy balance and thus preventing a decrease of RMR with negative consequences on further weight management. However, some features and study limitations might decrease the evidence of the present trial or at least aggravate its proper interpretation. (1) One may argue that the study design with three groups and a mix of energy restriction, protein supplementation with different dose, physical activity, and WB-EMS might be too sophisticated and complex for a single study. Retrospectively, we partially agree with this criticism; however, the aim of the study was to determine the specific effect of WB-EMS on LBM retention applying a "state of the art" weight loss protocol[1]. As discussed in detail above, this includes adequate protein supplementation, which was provided in all the groups, albeit in different doses (1.7 vs. 1.2 g/kg/body mass/day). The reason for the latter strategy was the increased demand for protein due to RT- (or WB-EMS-) induced negative muscle protein balance (Phillips et al., 1997). (2) Considering the rather modest decreases in fat mass (−6.3 ± 7.8 to −10.7 ± 8.7%) in this cohort of overweight to obese women, it is unlikely that net energy deficiency truly fell within the range of about 650–700 kcal/day (i.e., ≈75.000 kcal/16 weeks). While physical activity was tracked by calibrated, valid devices and can be thus considered as a reliable outcome (Bunn et al., 2019), results on energy restriction as reported by the participants were dubious. Although we strictly emphasized a practicable protocol that focused on carbohydrate reduction only, extensively discussed the dietary protocol with the participants and contacted participants every second week to check compliance with the dietary recommendations, the majority of participants obviously "over-reported" their caloric restriction. (3) We applied multi-segmental multi-frequency bio-impedance analysis (BIA) to determine body composition of our cohort. However, the more common way of assessing body composition in research is dual-energy X-ray absorptiometry (DXA) – considered as the gold standard in body composition assessment. Recent comparisons, however, report that BIA appears to be an adequate alternative - not only because of its easier handling in the clinical setting and the lack of x-rays (Fosbol and Zerahn, 2015; Gomez-Arbelaez et al., 2017). Fosbol and Zerahn (2015) and Gomez-Arbelaez et al. (2017) compared different methods of measurement for body composition and concluded that there is no general recommendation for any type of measurement, since every single method has its advantages and disadvantages. Our own research has confirmed this conclusion. In studies with different cohorts (Von Stengel et al., 2013; Kemmler et al., 2017), we observed a high agreement for lean and fat mass between the Inbody 770 used in this trial and a Hologic 4500a DXA Scanner with a narrow limit of agreement. Even more important, the reliability of the BIA device to determine muscle mass determined by a test-retest approach with 25 participants resulted in high intra class correlation (ICC) of 0.86–91 (95% CI: 84–94) for LBM (Kemmler et al., 2017). (4) Although physical activity is frequently listed as a component of weight reductions programs (PA & WB-EMS), its transfer to everyday practice is problematical. With respect to our aim of 250/225 kcal energy consumption by physical activity in everyday life, the increase of daily walking ranged from 6,000 to 10,000 additional steps. Since all the women are employed and the predominant majority of them has to manage their families including younger children, it is understandable that most of them failed to realize their daily step specification. The latter aspect might further hinder the generality of our result. Additionally, the wide range of overweight and obesity (28–55% body fat rate) within our study might limit the proper transfer to dedicated premenopausal cohorts. Thus, more dedicated eligibility criteria for the present study might have generated more meaningful and transferable results.

In summary, the combination of WB-EMS and higher protein intake is an effective tool for favorably affecting body composition in overweight premenopausal women following a moderate energy deficit. Considering the time efficiency, joint friendliness and high degree of customization of this novel training technology, WB-EMS might be a feasible alternative to RT at least in people unmotivated or unable to join demanding resistance exercise protocols during their weight loss programs. However, further WB-EMS studies are needed to overcome the limitations of the present study and to check transferability on other cohorts.

[1]Considering that LBM reduction in all of the study groups averaged below 10% of total weight loss we obviously realized this aim….

DATA AVAILABILITY

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of "Declaration of Helsinki", with written informed consent from all subjects. The protocol was approved by the "Ethics Commission of the Friedrich-Alexander University Erlangen-Nürnberg" (number: 19_16b).

AUTHOR CONTRIBUTIONS

SW, AW, SS, DS, MT, and WK designed the study, completed the data analysis on each location and/or interpretation, and drafted the manuscript. MF and HK contributed to study conception and design and contributed to revise the manuscript. MK performed the statistical analysis of the data. SW accepts responsibility for the integrity of the data sampling, analysis, and interpretation.

FUNDING

The study was exclusively funded by own resources of the Institute of Medical Physics (IMP), University of Erlangen-Nuremberg (FAU). We acknowledge support by Deutsche Forschungsgemeinschaft and Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) within the funding program Open Access Publishing.

ACKNOWLEDGMENTS

The present work was performed in (partial) fulfillment of the requirements for obtaining the degree "Dr. rer. biol. hum." We would like to take this opportunity to thank Hansepharm (Roth, Germany), which provided the protein powder for the study participants.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The handling editor declared a past co-authorship with several of the authors WK and MK.

frontiers in Physiology

ORIGINAL RESEARCH
published: 20 August 2019
doi: 10.3389/fphys.2019.01020

The Impact of Whole-Body Electromyostimulation on Body Posture and Trunk Muscle Strength in Untrained Persons

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Muscular imbalances of the trunk muscles are held responsible for changes in body posture. At the same time, whole-body electromyostimulation (WB-EMS) has been established as a new training method that enables simultaneous stimulation of many muscle groups. This study was aiming to analyze if a 10 weeks WB-EMS training changes posture-relevant parameters and/or improves isometric strength of the trunk extensors and flexors, and if there are differences based on stimulation at 20 Hz and 85 Hz. Fifty eight untrained adult test persons were divided into three groups (control, CON; training with 20 Hz stimulation, TR20; training with 85 Hz, TR85). Anthropometric parameters, trunk extension and flexion forces and torques, and posture parameters were determined before (n = 58) and after (n = 53: CON: n = 15, TR20: n = 19, TR85: n = 19) a 10 weeks WB-EMS training program (15 applications, 9 exercises). Differences between the groups were calculated for pre- and post-tests using univariate ANOVA and between the test times using repeated (2 × 3) ANOVA. Comparisons of pairs were calculated *post hoc* based on Fisher (LSD). No differences between the groups were found for the posture parameters. The *post hoc* analysis of both trunk flexion and trunk extension forces and torques showed a significant difference between the groups TR85 and CON but no difference between the other group pairs. A 10 weeks whole-body electrostimulation training with a stimulation frequency of 85 Hz in contrast to training with a stimulation frequency of 20 Hz improves the trunk muscle strength of an untrained group but does not significantly change posture parameters.

Keywords: WB-EMS, muscle training, trunk flexion, trunk extension, posture training

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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *08 February 2019*
Accepted: *24 July 2019*
Published: *20 August 2019*

Citation:
Ludwig O, Berger J, Becker S, Kemmler W and Fröhlich M (2019) The Impact of Whole-Body Electromyostimulation on Body Posture and Trunk Muscle Strength in Untrained Persons. Front. Physiol. 10:1020. doi: 10.3389/fphys.2019.01020

INTRODUCTION

Basically, body posture is based on the interaction of muscles, tendons, and bones. Changes of the habitual posture develop as the body adapts to routine daily postures (Harrison et al., 1999; Prins et al., 2008; Claus et al., 2009; Roussouly and Pinheiro-Franco, 2011; Drzal-Grabiec and Snela, 2012; Jung et al., 2016). It is assumed that permanent poor posture in daily routines leads to muscular and articular overload, which in turn results in physical problems (Bruno et al., 2012; Araujo et al., 2017; Jentzsch et al., 2017). Particularly posture issues such as hyperlordosis and a hunched back are considered to be the reasons for back problems (Jentzsch et al., 2017; Murray et al., 2017). Current studies show an interrelationship between individual posture parameters and the occurrence of lower back pain (Kim et al., 2006; Dolphens et al., 2012; Aggarwal et al., 2013).

Poor posture is currently assumed to be caused by muscular imbalances and dysfunctional body perception (Kim et al., 2006; Buchtelová et al., 2013). Muscular imbalances are understood to be an imbalance of strength between agonist and antagonist, which moves a joint's resting position from its neutral position (Nadler et al., 2001; Frank et al., 2009; Buchtelová et al., 2013). The position of the pelvis in the sagittal plane is particularly important in this case (Schwab et al., 2006; Sorensen et al., 2015). Functionally, the pelvis is considered a seesaw that is kept in equilibrium by muscular activity (Buchtelová et al., 2013). The abdominal muscles (*Musculus rectus abdominis*, *Musculus transversus*), the gluteal muscles (*Musculus gluteus maximus*), and the hamstrings (*Musculus biceps femoris*, *Musculus semitendinosus*, *Musculus semimembranosus*) all seem to influence the position of the pelvis by lifting the anterior pelvic rim and thus reduce anterior pelvic tilt (Bridger et al., 1992; Nourbakhsh and Arab, 2002; López-Miñarro et al., 2012; Jeong et al., 2015). Preventive recommendations include strengthening the pelvis-straightening muscles (Kim et al., 2006; Ludwig et al., 2016). Physical therapy to correct poor posture starts with practicing targeted muscle activation and improving muscular strength, joint flexibility, as well as body perception (Pope et al., 1985; Calvo-Muñoz et al., 2012; Laird et al., 2014; Barczyk-Pawelec et al., 2015; Kim et al., 2015; Szczygiel et al., 2018).

A proven therapeutic option to strengthen muscles is neuromuscular electrical stimulation (NMES) (Doucet et al., 2012). This method is based on the application of electrodes to the skin, which generate an electric field that changes membrane potentials and thus results in muscle fiber contractions (Filipovic et al., 2012). Depending on the frequency of the voltage pulse applied, the efferent nerve is usually not involved (Gondin et al., 2005; Maffiuletti, 2010). Particularly in physical therapy, NMES can help to rebuild muscles atrophied due to an injury or after immobilization (Adams, 2018). In contrast to NMES, functional electromyostimulation (FEMS) means the combination of electrical stimulation with functional movements such as walking or lifting objects. Some studies have shown that FEMS is able to increase muscle strength (Coupaud et al., 2008), retard muscle atrophy (Gargiulo et al., 2011), and reduce pain (Koyuncu et al., 2010).

Whole-body electromyostimulation (WB-EMS) has been established as a new training method that enables simultaneous stimulation of many muscle groups, for example by means of electrode vests (Kemmler and von Stengel, 2013). In contrast to the electromyostimulation known from physical therapy, newer WB-EMS concepts promote the idea to perform active movements during stimulation, i.e., to add an active central-nervous muscle activation to the passive electric stimulation (Herrero et al., 2010; Amaro-Gahete et al., 2018). Therefore, the application of WB-EMS has to be grouped under FEMS, because movements are carried out at the same time as voltage is applied. Studies have shown that WB-EMS improves strength in elite soccer players (Filipovic et al., 2016) and in untrained middle-aged men (Kemmler et al., 2016b) by increasing the number of muscle fibers brought to contraction during an exercise movement (Kemmler et al., 2010).

A number of stimulation parameters, such as impulse amplitude, impulse type, and impulse frequency can be modified to control EMS training. Research is not in agreement in this context, though. Most working groups describe a frequency range between 20 and 110 Hz to stimulate as many muscle fibers as possible (Moreno-Aranda and Seireg, 1981; Binder-Macleod and Barrish, 1992; Jones, 1996; Dreibati et al., 2010; Weissenfels et al., 2018). Certain frequencies are said to elicit a stronger stimulation of specific muscle fibers (Dreibati et al., 2010). Stimulation frequencies of up to 50 Hz appear to activate mainly the slower type-I muscle fibers, while frequencies between 50 and 120 Hz seem to stimulate the faster type-II fibers. However, there is no scientific consensus (Kemmler and von Stengel, 2013; Weissenfels et al., 2018), and this means that studies examining the effect of WB-EMS on specific muscle groups must observe the presumable effects of different stimulation frequencies.

Studies on the influence of WB-EMS training on body posture do not exist to date. Considering the high prevalence of poor posture (Bansal et al., 2014) and the time-consuming physical therapy treatments required, the research demand concerning new intervention methods is substantial. Therefore, the question arises whether an unspecific WB-EMS training might contribute to an improvement of posture parameters. This could be the case if the neuromuscular balance of the trunk muscles connected to the pelvis could be changed by WB-EMS training. Strengthening the lumbar parts of the back extensor also appears to be useful from a therapeutic point of view because this is already a proven form of therapy to treat lower back pain (Kahanovitz et al., 1987; Mannion et al., 2001; França et al., 2010). It has already been shown that conventional EMS training is able to achieve an improvement of muscular strength of *Musculus erector spinae* to prevent lower back pain (Kahanovitz et al., 1987; Kemmler et al., 2017; Weissenfels et al., 2018). Based on the seesaw model of the pelvis WB-EMS training could, however, also have a negative effect on the pelvis position through unspecific strengthening of the lumbar back muscles by increasing the pelvic tilt and thus leading to a more pronounced lumbar lordosis. On the other hand, strengthening the thoracic sections of *M. erector spinae*, which acts as a trunk extensor, WB-EMS training could result in a reduced forward body tilt and reduced spinal column curvatures, thus having a posture-improving effect.

In the light of the above, any potential influence of WB-EMS training on posture-constituting muscle groups and thus on body posture in general is unclear. In gyms, WB-EMS training is usually performed unspecifically, i.e., many superficial muscle groups in trunk and gluteus are activated during a training session. General strengthening of the trunk muscles does not necessarily have to have an effect on body posture, because muscular relationships often seem to be more important than absolute muscle force (Buchtelová et al., 2013). For this reason and since this training method spreads very quickly, research has a very strong interest in delimiting potential preventive and curative effects from potentially posture-damaging effects. As WB-EMS training is less time-consuming compared to conventional strength training (usually, a complete whole-body workout only takes 20 min), it could become interesting for large target groups in both prevention and therapy.

This study is therefore aiming to analyze the following questions:

(1) Can a 10 weeks WB-EMS training change the posture parameters *flèche cervicale, flèche lombaire* and trunk anteversion?
(2) Does a 10 weeks WB-EMS training change the isometric strength of the trunk extensors and flexors?
(3) Is there a difference in the change of posture parameters *flèche cervicale, flèche lombaire* and trunk anteversion based on stimulation at 20 Hz and 85 Hz?

MATERIALS AND METHODS

Test Persons

The sample size was calculated using G*Power 3.1 (University of Kiel, Germany). For a repeated (2 × 3) ANOVA (within and between interactions, $f = 0.3$, $\alpha = 0.05$) a minimum group size of 48 persons was calculated (power 0.958), which we increased due to the expected drop outs. Finally, 58 test persons participated in the study. They were recruited by means of flyers distributed on the university campus. Five test persons did not complete the 10 weeks training and were removed from the study. In the end, the data from 53 test persons was included in the evaluation (see **Table 1** and flowchart **Figure 1**). All participating test persons did not have any previous experience or knowledge concerning EMS training. The test persons had to be between 18 and 40 years old, were not to perform any regular athletic activity, and needed to be free of internal and orthopedic limitations. Muscle stretchability and joint mobility were not explicitly examined before the start of the study. However, since all participants were able to perform all movements in the required range of motion (ROM) during the dynamic exercises, we assume that there was no movement restriction relevant for our study. All test persons were informed about the process and objectives of the study and gave their written consent before the study started. In order to exclude any risks associated with EMS training, a comprehensive anamnesis questionnaire had to be completed (Kemmler et al., 2016a). The study was approved by the ethics commission of the Technical University Kaiserslautern (ref. no. 02/17) and was conducted based on the Declaration of Helsinki (World Medical Association [WMA],, 2013).

TABLE 1 | Anthropometric data of the three groups (means ± standard deviation).

	CON	TR20	TR85
N (total/men/women)	15/4/11	19/8/11	19/10/9
Age [years]	25.60 ± 2.80	24.84 ± 3.82	24.50 ± 4.40
Height [m]	168.22 ± 7.07	174.26 ± 7.87	176.72 ± 9.78
Weight [kg]	67.06 ± 19.93	74.04 ± 16.26	73.32 ± 15.14

Measurements

In both the initial and the final examination, the following anthropometric parameters were determined: body weight, height, and body fat percentage. The static trunk extension and flexion forces were measured by means of the isometric force testing device Back Check 607 (Dr. Wolff GmbH, Arnsberg, Germany). This required the test persons to stand with their arms hanging loosely and with slightly bent knee joints, fixated in the sagittal plane at the iliac crest area by one dorsal and one ventral pad. The flexion in the knee joints served to reduce the influence of the iliopsoas, since we only wanted to measure the strength of the trunk muscles. Two pads with force transducers were placed without pressure at the sternum and between the shoulder blades at an individual height (**Figure 2**). Alternatingly, three maximum strength measurements of the trunk flexion and the trunk extension were performed for 5 s each and 30 s breaks in between the measurements. The test persons were instructed to press against the pads as strongly as they could. If the isometric strength value of the last measurement was the largest, the sequence was continued after 30 s breaks until the value decreased. The highest values for extension and flexion were included in the evaluation. The flexion and extension torques were calculated as M = F*(vertical distance between force transducer pad and pelvis fixation pad).

The reliability of this measurement system was analyzed in other studies and found to be in a good range [intraclass correlation coefficient 0.76–0.89 (Scheuer and Friedrich, 2010)].

To evaluate posture, surface scans of the entire body were performed using the Paromed 4D Sanner (Paromed GmbH, Neubeuern, Germany). For those scans, the test persons stood barefoot and shirtless or wearing a sports bra about 2.5 m away from the scanner. They were instructed to stand at ease (habitual posture), let their arms hang loosely, look straight ahead, and breathe normally. Anatomic landmarks such as C7, S1, and the PSIS (posterior superior iliac spines) were marked by means of adhesive stickers on the skin (Patias et al., 2010). The PSIS markers were not used for further calculations but are required by the software used. By projecting a coded light stripe grid on to the body, the system reconstructed the three-dimensional contours of the body's back. Three scans were averaged. The total measurement itself took about 10 s. The following parameters were calculated based on the 3D representation (**Figure 3**):

(1) *Flèche cervicale*: horizontal distance between the point of strongest thoracic kyphosis and the point of the lowest neck lordosis in the sagittal plane.
(2) *Flèche lombaire*: horizontal distance between the point of strongest thoracic kyphosis and the point of the lowest lumbar lordosis in the sagittal plane.
(3) Trunk anteversion: angle between the connecting line C7-S1 against the vertical axis in the sagittal plane.

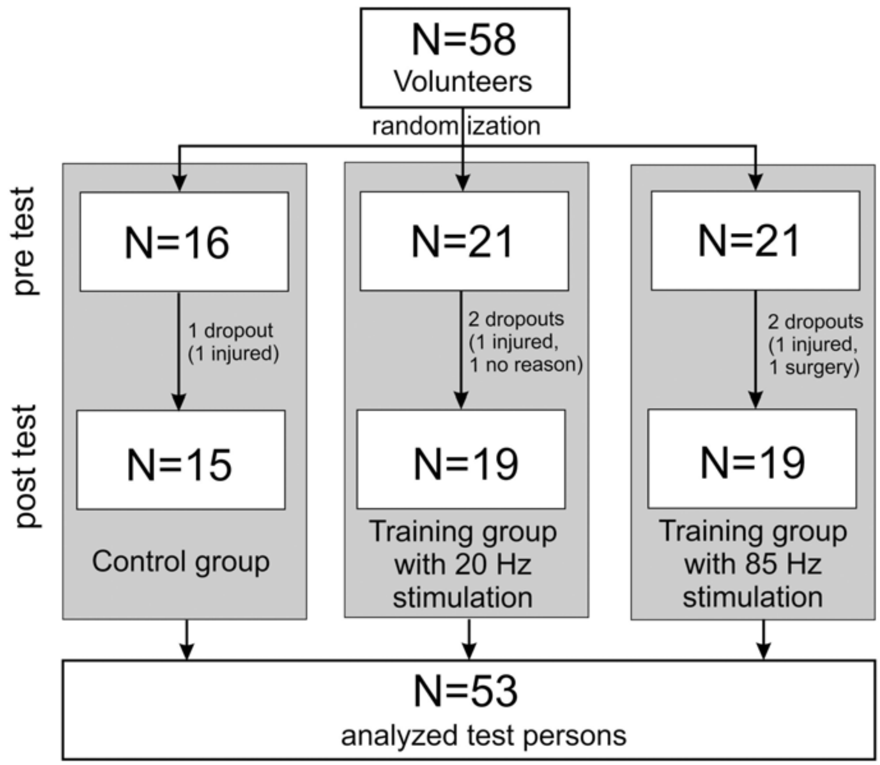

FIGURE 1 | Flowchart according to the CONSORT recommendation (Schulz et al., 2010).

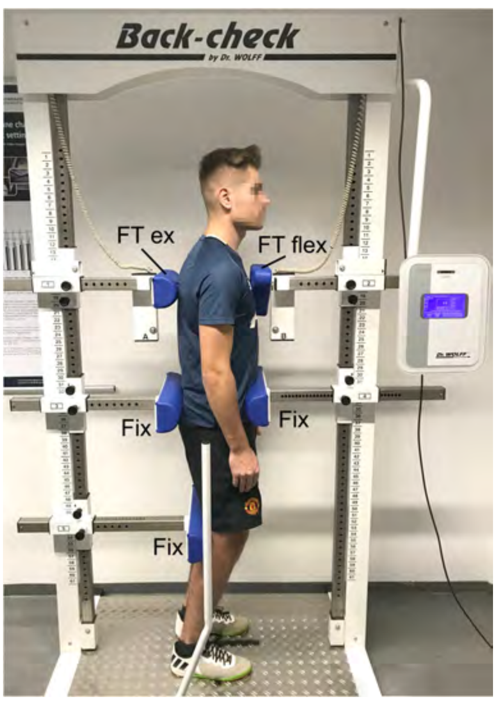

FIGURE 2 | Placement and fixation of a test person in the isometric force measurement device. FT ext, force transducer extension; FT flex, force transducer flexion; Fix, fixation pads.

Flèche cervicale and *flèche lombaire* are orthopedic measurements that show the depth of the curvature of the spine by using the distance of the extreme points of the lordosis and the thoracic kyphosis. Increased values suggest posture deficits (Stagnara et al., 1982; Vrtovec et al., 2009; Allier and Monnet, 2013). Both parameters were additionally calculated as percentage values by having been relativized to the vertical distance between C7 and S1.

Training

The participating test persons were randomly assigned to two training groups (TR20, TR85) and the control group (CON) by lots. At no time during the study were the members of the training groups or the investigators informed about this assignment (training groups were double-blinded).

The CON did not perform any athletic activity during the 10 weeks training phase. In all, the training groups performed a total of 15 WB-EMS training sessions. They alternatingly exercised once or twice a week, so that an average of 1.5 training sessions was performed per week (Kemmler et al., 2016b, 2018). Before the training phase started, all test persons took part in a familiarization session in order to get used to the imminent WB-EMS application (Jee, 2018). The familiarization session took 12 min and was characterized by reduced voltage intensity to avoid muscular overload (Kemmler et al., 2016a). At the same time, the test persons were taught the proper exercise techniques and learned about the RPE (rating of perceived

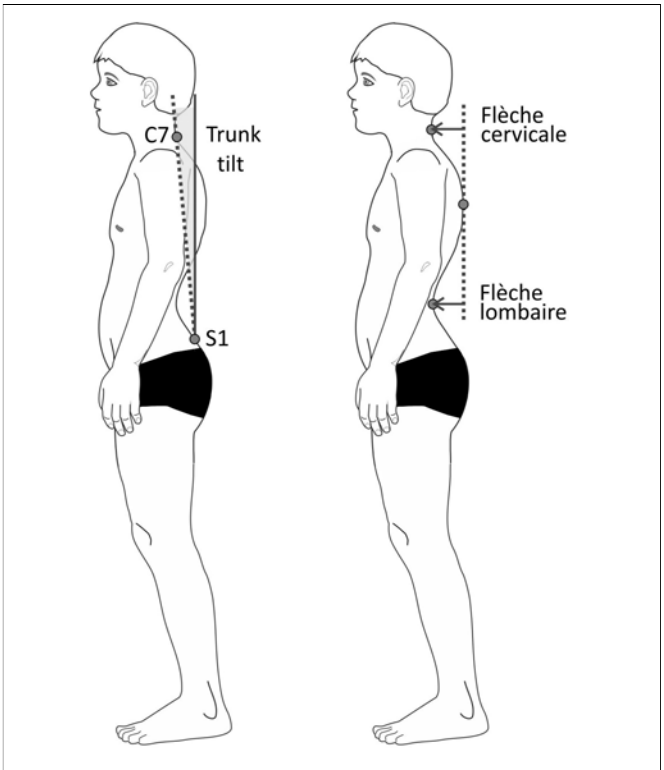

FIGURE 3 | Schematic drawing of the posture parameters trunk tilt (left) and flèche cervicale and lombaire (right).

exertion) scale [0 = no exertion, 10 = maximum exertion (Borg and Kaijser, 2006)].

Stimulation was applied in line with common parameters: impulse width of 350 μs, bipolar impulse without impulse increase, 4 s load and 4 s break intervals, overall training duration 20 min (Kemmler et al., 2016a). Both training groups differed only in the stimulation frequency applied, i.e., 20 Hz (TR20) and 85 Hz (TR85), respectively. The test persons were instructed to exercise with an intensity of 6 ("hard") on the modified Borg scale, while maintaining the entire ROM during the exercise. In order to ensure adequate exertion, the intensity of the electric impulses both during the sessions and between the sessions was adapted by the investigator. Every 2–3 min, the participants provided feedback and the intensity for each muscle group was changed in a way that the participant felt the exertion to be "hard". The devices produce a maximal peak output voltage of 75 V at 1 kOhm (corresponding to a current of 75 mA), but do not display the actual intensity in absolute voltage. The output is only displayed in device-specific units from 0–100, in proportion to the initial voltage. The intensity data was noted at the end of each training session for each muscle group.

The training times were kept at a constant level for each test person in order to avoid influences caused by the time of day. Before each training session, a new anamnesis questionnaire on the current condition was completed. This was to exclude potential contraindications (e.g., dizziness, nausea, and pain) and to ensure safe training for the test persons. The test persons were instructed to drink sufficient liquids before the training started (at least 500 ml). During the course of the study, the test persons were instructed not to perform any additional physical training. This was asked repeatedly at the beginning of each training session. They were also requested not to physically exert themselves in the preceding 24 h by everyday activities. Furthermore, the questionnaire was used to make sure that medication or pain killers had not been taken, so that overexertion due to a missing ability to assess the extent of exertion was avoided.

Devices and Exercises

A Miha Bodytec 2 WB-EMS (Miha Bodytec, Augsburg, Germany) was used. This system consists of an impulse transmitter with control panel and optical feedback. A 2 m cable connects the training vests including the integrated electrodes to the system. The training vests were available in various sizes, which were tightly attached to the upper body. The cranial tip of the sternum served as an anatomical reference for the correct placement of the vest. Caudal, the vest reached up to the iliac crests. The electrode surfaces and arrangement of all vests were proportional in all sizes (**Figure 4**). Upper arms and thighs were also equipped with additional circular electrodes that were attached with velcro at the level of the muscle bellies. The gluteus was stimulated by flat electrodes integrated into a belt that was closed at the abdomen. All electrodes and accessories were provided by the same manufacturer (Miha Bodytec, Augsburg, Germany). The system allows free programming of the stimulation parameters, whereas the stimulation parameters, except the applied voltage, are the same for all electrodes. The device settings were saved on a chip card for each test person.

Exercises were selected based on the exercises integrated in the WB-EMS device used. They were therefore representative of a typical exercise program performed in a gym, targeting as many stimulated muscle groups as possible. These exercises were performed:

(1) Dynamic squats (15 repetitions).
(2) Dynamic trunk flexion with retracted arms (12 repetitions).
(3) Static knee presses against own resistance (12 repetitions).

FIGURE 4 | Positioning of the electrodes in a typical training vest. Only the largest target muscles below the electrodes are mentioned. Pect. – *M. pectoralis*, Trapezius – *M. trapezius*, Latiss. – *M. latissimus dorsi*, Rect. abdom. – *M. rectus abdominis*, Erect. spinae lumb. – *M. erector spinae* pars lumbalis.

(4) Dynamic side lunge, left and right (10 repetitions each).
(5) Dynamic crunches, diagonal, left and right (10 repetitions each).
(6) Dynamic squats, wide stand (15 repetitions).
(7) Dynamic one-leg stand with lifting one leg, elbow to contralateral knee, left and right (10 repetitions each).
(8) Dynamic overextension of the trunk (12 repetitions).
(9) Static forward lunge, left and right (12 repetitions).

Active movements were initiated just before the electrical impulse was applied and continued to be performed during the entire impulse duration. Between impulses, the participants adopted a resting position.

The training was conducted exclusively under supervision of trained investigators with a support ratio of 1:2. Both safety and accurate exercising were ensured by the permanent supervision by the investigator (Moreno-Aranda and Seireg, 1981).

Statistics

Differences between the groups (TR20, training at 20 Hz stimulation; TR85, identical training at 85 Hz stimulation; CON, untrained control group) were calculated for pre- and post-tests using univariate ANOVA (XLSTAT 2018.4, Addinsoft, Paris, France). Group differences between the test times were calculated using repeated (2 × 3) ANOVA. Comparisons of pairs were calculated *post hoc* based on Fisher (LSD). A possible influence of sex on the percentual increase of flexion and extension torques was calculated using (2 × 3) ANOVA. The significance level was set at 5%.

RESULTS

A significant difference between the three groups was not found for any of the posture parameters measured, neither at the beginning nor at the end of the study. Only the upper body anteversion decreased over time, but for all groups including the control group with no significant differences between the groups (TR85 vs. CON: $p = 0.14$, TR85 vs. TR20: $p = 0.96$; TR20 vs. CON: $p = 0.16$). All other posture parameters did not change. **Table 2** shows the results of the statistic tests.

The **trunk flexion force** values were not significantly different between the groups at the beginning of the study ($df = 2$, $F = 1.44$, $p = 0.25$). At the end of the study, significant differences were identified for the factor *time* ($df = 1$, $F = 36.97$, $p < 0.0001$) and for the interaction *group*time* ($df = 2$, $F = 3.92$, $p = 0.02$). The *post hoc* analysis showed a significant difference between the groups TR85 and CON ($p = 0.02$). There was no difference between the other group pairs (TR85 vs. TR20: $p = 0.31$; TR20 vs. CON: $p = 0.16$).

The **trunk flexion torque** values showed comparable results: they were not significantly different between the groups at the beginning of the study ($df = 2$, $F = 1.61$, $p = 0.21$). At the end of the study, we found significant differences for the factor *time* ($df = 1$, $F = 31.90$, $p < 0.0001$) and for the interaction *group*time* ($df = 2$, $F = 3.45$, $p = 0.04$). The *post hoc* analysis showed a significant difference between the

TABLE 2 | Temporal development (pre = base line, post = after 10 weeks) of the posture parameters. CON, control group; TR20/TR85, training groups with stimulation frequencies of 20 Hz/85 Hz. The lower rows show the results of the repeated (2 × 3) ANOVAs.

	Trunk tilt pre#	Trunk tilt post#	Flèche cervicale pre	Flèche cervicale post	Flèche cerv. % pre	Flèche cerv. % post	Flèche lombaire pre	Flèche lombaire post	Flèche lombaire % pre	Flèche lombaire % post
CON	−3.47 ± 2.59	−3.17 ± 1.66	6.44 ± 1.76	6.13 ± 1.40	13.86% ± 3.56	13.15% ± 2.48	4.43 ± 1.16	3.96 ± 0.78	9.52% ± 2.39	8.54% ± 1.65
TR20	−3.19 ± 2.57	−2.29 ± 1.34	5.98 ± 1.59	5.45 ± 1.28	12.32% ± 3.21	11.19% ± 2.45	3.48 ± 1.71	3.22 ± 1.51	7.15% ± 3.50	6.63% ± 3.13
TR85	−3.67 ± 2.08	−2.55 ± 1.68	6.33 ± 1.73	6.12 ± 1.72	12.96% ± 3.05	12.50% ± 2.89	3.85 ± 1.10	3.96 ± 1.01	7.97% ± 2.38	8.14% ± 2.03
ANOVA (time)	df = 1; F = 6.56 p = **0.01***		df = 1; F = 3.00 p = 0.09		df = 1; F = 3.30 p = 0.07		df = 1; F = 2.20 p = 0.14		df = 1; F = 2.40 p = 0.12	
ANOVA (group* time)	df = 2; F = 1.14 p = 0.33		df = 2; F = 0.23 p = 0.79		df = 2; F = 0.23 p = 0.79		df = 2; F = 1.51 p = 0.23		df = 2; F = 1.44 p = 0.24	

*# Trunk tilt: negative values indicate anterior upper body tilt. Significant differences at p = 0.05 are marked in bold and with *.*

groups TR85 and CON (p = 0.03), but no difference between the other group pairs (TR85 vs. TR20: p = 0.42; TR20 vs. CON: p = 0.14).

There were also no group differences at the beginning of the study for the **trunk extension force** (df = 2, F = 1.38, p = 0.26). After the treatment, significant effects were identified for the factor *time* (df = 1, F = 56.59, $p < 0.0001$) and for the interaction *group*time* (df = 2, F = 4.27, p = 0.02). The *post hoc* analysis showed a significant difference between the groups TR85 and CON (p = 0.04). There was no difference between the other group pairs (TR85 vs. TR20: p = 0.49; TR20 vs. CON: p = 0.15).

For the **trunk extension torque** we could not find a significant difference between the groups at the beginning of the study (df = 2, F = 1.46, p = 0.24). At the end of the study, significant differences for the factor *time* (df = 1, F = 44.84, $p < 0.0001$) and for the interaction *group*time* (df = 2, F = 4.37, p = 0.02) could be found. The Fisher *post hoc* analysis showed a significant difference between the groups TR85 and CON (p = 0.04), and no difference between the other group pairs (TR85 vs. TR20: p = 0.55; TR20 vs. CON: p = 0.13).

The percentage improvement in the training groups did not differ between men and women (extension torque increase in %: men: 20.18% ± 16.64 vs. women 19.2% ± 17.5; flexion torque increase in %: men: 18.1% ± 12.03 vs. women 16.2% ± 15.9). A 2 × 3 ANOVA (sex, group) did not provide significant results; based on the Type III sum of squares, the variable sex did not bring any additional significant information (flexion: df = 1, F = 0.20, p = 0.66, extension: df = 1, F = 0.06, p = 0.80).

Body mass index did not change significantly during the study (*group*time*: $F(2)$ = 0.68, p = 0.52). This applied to all groups.

DISCUSSION

The objective of this study was to find out the extent to which unspecific WB-EMS training over a period of 10 weeks would achieve an improved body posture and increased trunk muscle strength in untrained persons, and whether any differences exist in terms of stimulation frequency.

Trunk Muscle Strength

In the training group stimulated with 85 Hz, we were able to prove a significant improvement of the isometric strength and torque of trunk extension and flexion compared to the control group. The strength increases identified were on average between 15.0 and 21.4% (force) and between 15.9 and 26.6% (torque) for the groups in training (**Table 2**) and were of a similar size as increases found in other studies (Kemmler et al., 2016b, 2018). In the WB-EMS training, large electrodes in the areas of *M. rectus abdominis* (flexion), the lumbar and thoracic *M. erector spinae*, and the *Mm. multifidii* (flexion) induced contractions, so that an adequate training stimulation and corresponding muscle strengthening over the 10 weeks of the study can be assumed (Ng and Richardson, 1994). However, we also found force increases between 4.8 and 7.4% and torque increases between 4.4 and 9.2% in the control group. We interpret this finding as test habituation, i.e., that familiarity with the task of isometric maximal strength exercises was higher in the post-test and had a positive effect on the initially unfamiliar isometric strength development.

No significant difference was identified in the group stimulated at 20 Hz (**Table 3**). This difference between the groups was unexpected because the back musculature (*M. erector spinae*), which is important for posture control, consists of mainly slow type-I fibers [men 62.0 ± 9.3%, women 67.8 ± 10.5% (Mannion et al., 2001)]. We had actually expected a higher strength increase in the TR20 group, though, because the lower stimulation frequency presumably stimulates rather the slow muscle fibers (Cabric et al., 1988; Sillen et al., 2013; Kemmler et al., 2016b). The straight abdominal muscles, on the other hand, consist of a slightly higher percentage of type-II fibers [type I 46.1%, type II 53.9% (Johnson et al., 1973)] and should therefore be more susceptible to an 85 Hz stimulation. However, Gregory and Bickel found that an EMS-induced recruitment of motor units does not always proceed selectively. Type I and type II fibers seem to be recruited by EMS without adhering to any specific sequence (Gregory and Bickel, 2005). We therefore assume that muscle fibers were activated independently of the stimulation frequency, and that this fiber activation did not primarily depend on the fiber type, but rather on the physical location of the electrodes. Since the tetanic contraction of muscle fibers increases from a stimulation frequency of 20 Hz and more (Smith et al., 1985), we assume that the applied training stimulus was too low in the group training at 20 Hz. In addition, the duty cycle (on-off ratio) of the muscle fibers was more than four times lower with the lower stimulation frequency than with the 85 HZ stimulation. However, the duty cycle seems to play an important role in generating a training stimulus (Lloyd et al., 1986). In a comprehensive review, Filipovic et al. (2012) recommend a stimulation frequency greater than 50 Hz in order to generate a stimulation intensity that is sufficient to activate strength adaptation. Collins et al. (2007) were additionally able to prove that higher EMS stimulation frequencies (50–100 Hz) lead to electrically evoked sensory potentials, which induce the spinal motor neurons via reflex circuits to activate additional motor units. This contribution to muscle contraction, which is generated by the central nervous system, does not develop with frequencies < = 20 Hz and seems to max out at frequencies > = 80 Hz (Dean et al., 2007). Dean et al. (2007) were able to achieve an additional strength increase of 10.2% of the maximum voluntary contraction by applying four two-second stimuli. For this study, the stimulation was applied in 4 s stimuli, i.e., they were similar in intensity. We therefore assume that the lack of additional central-nervous contractions at an applied frequency of 20 Hz resulted in a lower training stimulus and thus in lower strength increases.

Posture

A classification of the test persons based on the average *flèche lombaire* percentage of 8.06% (see **Table 2**) shows that all test persons together constitute a group with poor posture. Proprietary, unpublished data of 724 test persons showed a *flèche lombaire* percentage of 6.92% ± 3.06 (95% confidence interval 6.63–7.21%) for a normally pronounced lumbar lordosis and

TABLE 3 | Temporal development (pre = base line, post = after 10 weeks) of the trunk extensor (Ext) and flexor (Flex) forces and torques, the percentual improvement (Delta), and the ratio "extension/flexion" (Ext/Flex). CON, control group; TR20/TR85, training groups with stimulation frequencies of 20 Hz/85 Hz.

	Force Flex pre [N]	Force Flex post [N]	Force Delta [%]	Torque Flex pre [Nm]	Torque Flex post [Nm]	Torque Delta Flex [%]	Ext pre [N]	Ext post [N]	Delta [%]	Torque Ext pre [Nm]	Torque Ext post [Nm]	Torque Delta Ext [%]	Ext/Flex pre [-]	Ext/Flex post [-]
CON	419.2 ± 173.4	439.2 ± 196.2	4.8%	12.6 ± 7.5	13.2 ± 8.3	4.4 ± 12.7	558.5 ± 206.5	599.6 ± 205.0	7.4%	16.9 ± 9.0	18.0 ± 9.0	9.2 ± 12.5	1.4	1.4
TR20	478.6 ± 175.7	550.3 ± 197.5	15.0%	15.7 ± 7.6	18.1 ± 9.2	15.9 ± 10.8	590.3 ± 180.4	716.3 ± 175.3	21.4%	19.2 ± 8.0	23.3 ± 9.4	26.6 ± 18.7	1.3	1.4
TR85	533.9 ± 207.7	624.0 ± 170.9	17.1%*	16.9 ± 7.5	19.9 ± 9.3	18.3 ± 17.2*	672.1 ± 228.3	762.90 ± 258.98	13.5%*	21.3 ± 8.4	24.3 ± 9.8	14.4 ± 13.3*	1.3	1.3

Significant difference to CON at $p = 0.05$.

a mean value of 9.17% ± 3.59 (95% confidence interval 8.76–9.58%) for a hyperlordosis. Accordingly, we had expected that all our test persons would notably benefit from a strengthening of the posture-straightening muscle groups. However, changes in posture parameters were identified only for trunk anteversion, which improved for all groups including the control group. We think that this improvement was caused by a learning process, more specifically with an increased familiarity with the testing procedure, because upper body anteversion is easy to consciously improve by activating the dorsal muscle chain. We assume that the test persons unconsciously straightened their body posture due to the familiarity with the testing situation during the post-tests. In contrast to the sagittal tilt of the body, the depth of the lordosis of the cervical and the thoracic spine are more difficult to change deliberately and require an excellent body awareness (Singla and Veqar, 2017). The WB-EMS training activated the muscle groups of the trunk, the pelvis and the legs unspecifically. This means that the simultaneous stimulation by large surface electrodes activated all muscle fibers underneath. Agonists and antagonists were simultaneously activated and, depending on the exercise, the muscles actively involved in the movement were additionally activated by the central nervous system. Therefore, it is plausible that both the dorsal and the ventral muscle chains were exercised to the same extent. Looking at the isometric strength ratio of extension and flexion (extension/flexion quotient), the values found in this study correspond to the values determined in other studies (Smith et al., 1985; Beimborn and Morrissey, 1988; Kim et al., 2006). For the isometric strength and torque ratios among the groups, no significant differences were determined, even if the absolute values in some instances significantly increased (**Table 3**).

The reduction of a pronounced lumbar lordosis is considered an important therapeutic approach because interrelationships with increased degeneration are known, in particular in the facet joints (articulationes processuum articularium) (Murray et al., 2017). It is also known that the position of the pelvis in the sagittal plane plays a key role in the reduction of lumbar lordosis (*flèche lombaire*) (Buchtelová et al., 2013). Analyses of adolescents with poor posture came to the conclusion that targeted training of the pelvis-straightening musculature (*M. rectus abdominis*, *M. gluteus maximus*, *M. biceps femoris*, *M. semitendinosus*) improved the habitual position of the pelvis (Ludwig et al., 2016). We suspect that the simultaneous training of the pelvis-straightening muscles (see above) and the pelvis-flexing muscles (*M. erector spinae lumbalis*, *M. quadriceps femoris*) counterbalanced the influence of both muscle groups on the pelvis position. In addition, the correction of pelvis or spinal column curvatures works best when the test persons exercise their body perception (Bansal et al., 2014; Ludwig et al., 2016). This, however, was not part of the WB-EMS training. Paillard emphasizes that EMS is not able to improve the coordination between agonist and antagonist muscles and therefore does not support the coordination of complex movements (Paillard, 2008). Even if the training did strengthen the muscles, the awareness of how to utilize specific muscle groups for posture correction was apparently not improved. However, this awareness seems to be a key factor in conscious posture correction (Woollacott and Shumway-Cook, 1990; Ludwig et al., 2016).

We consider this a limitation of the WB-EMS training because this shows that merely (and demonstrably) strengthening the muscles does not have any direct effect on processes controlled by the central nervous system, such as body posture. The interaction of sensory information and motor activity in the form of a regulation process (Feldman et al., 2014; Chiba et al., 2016) can probably not be improved easily. Even if movements were actively performed during stimulation, it remains unclear which central-nervous learning processes run when conscious muscle activity overlaps with externally triggered muscle activity. Some studies even suspect a negative effect of EMS training on central-nervous learning processes in this context (Paillard, 2012).

Although we did not determine any improvement of body posture through WB-EMS training, we need to point out that a decline was not determined, either. Possible reasons that might have caused an increase in the forward tilt of the pelvis by changing the muscular balance of the muscle groups connected to the pelvis have already been discussed. To sum it up, we can say that while unspecific training was able to result in a strength increase of the trunk muscles, it did not have any direct effect on habitual posture.

Limitations

Our study has some limitations. Firstly, we tested healthy test persons only. On average, the test persons exhibited a relative lumbar lordosis depth of 8°, meaning they were close to poor posture, but symptom-free. Therefore, the results cannot be transferred directly to patients with extensive poor posture and low back pain. Secondly, the WB-EMS training was unspecific. This means that the specific muscle groups required for posture corrections were not trained exclusively and selectively. However, we deliberately decided to apply an exercise program as it is preset by device manufacturers and used in many gyms. We must also note that the forces of trunk extension and flexion were measured only summarily. We were not able to measure the forces of other, possibly relevant muscle groups (e.g., gluteal muscles, thigh muscles, neck muscles). However, these muscle groups may influence the position of the pelvis and thus, under certain circumstances, the *flèche lombaire* or the position of the thoracic spine and thus the *flèche cervicale*. Furthermore, our test persons were all inexperienced in WB-EMS training and not actively involved in sports. Even though we see this as one of the strengths of our study, we cannot transfer the results directly to athletes.

CONCLUSION

A 10 weeks whole-body electrostimulation training with a stimulation frequency of 85 Hz in contrast to training with a stimulation frequency of 20 Hz improves the trunk muscle strength of an untrained group but does not significantly change posture parameters.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the ethics commission of Fachbereich Sozialwissenschaften, Technische Universität Kaiserslautern, Germany with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the ethics commission of Fachbereich Sozialwissenschaften, Technische Universität Kaiserslautern, Germany under No. 02/17.

AUTHOR CONTRIBUTIONS

OL was involved in the design and implementation of the study, and wrote the manuscript. JB was involved in the design and implementation of the study, and helped in the writing of the manuscript. SB was involved in the implementation of the study. WK and MF was involved in the design of the study and helped in the writing of the manuscript.

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World Medical Association [WMA], (2013). Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 310, 2191–2194.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
published: 10 September 2019
doi: 10.3389/fphys.2019.01136

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The Influence of WB-EMS-Training on the Performance of Ice Hockey Players of Different Competitive Status

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Edited by:
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Specialty section:
This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 28 February 2019
Accepted: 19 August 2019
Published: 10 September 2019

Citation:
Schuhbeck E, Birkenmaier C, Schulte-Göcking H, Pronnet A, Jansson V and Wegener B (2019) The Influence of WB-EMS-Training on the Performance of Ice Hockey Players of Different Competitive Status. Front. Physiol. 10:1136. doi: 10.3389/fphys.2019.01136

Purpose: The aim of this study was to examine the influence of long-term whole-body electromyostimulation (WB-EMS) training in addition to standard ice hockey training in the following areas: shot speed, counter-movement-jump (CMJ) height and power, 10 m-sprint, isokinetic maximum force at 60 and 300°/s of the knee extensor muscle and subjective performance. The purpose was further to check, whether competitive status influenced the extent of response to WB-EMS and whether WB-EMS would hypothetically be a suitable method to reduce injury rate.

Methods: Thirty male amateur ice hockey players participated in this study. They were divided into two cross-over groups (Group A and Group B). EMS sessions were carried out once a week for 12 weeks for each group with a subsequent 4 week EMS pause. The sessions consisted of 20 min electromyostimulation with 150 contractions (4 s duration, 85 Hz). Shot speed of slap shot was measured with Sportradar 1503. Jumping ability was determined with a ground reaction force platform (GRFP). Sprint time for 10 m skate was recorded using an infrared photo sensor. Isokinetic force of the knee extensor muscle was detected with Isomed 2000 at two different angular velocities (60 and 300°/s) and the subjective performance was collected using a questionnaire.

Results: After 12 weeks of WB-EMS training jumping power increased significantly for the WB-EMS groups by 5.15%, 10 m skating time decreased significantly by 5%, and maximum isokinetic force at 300°/s increased significantly by 7% (all $p < 0.05$). In contrast post training shot speed showed no significant change. Isokinetic torque at 60°/s and vertical jump height were collected as secondary variables and showed increases of 5.45 and 15.15%, respectively. After finishing the WB-EMS and continuing the normal training, it was shown that the training effect regressed.

Conclusion: This study demonstrated that WB-EMS training significantly decreased 10 m skating time and increased jumping power and maximum isokinetic force at

300°/s. We conclude that with additional WB-EMS training, an increase in performance might also be achieved for athletes in lower leagues. Due to the higher training potential of leisure athletes, the effect is probably even more pronounced than would be expected for competitive athletes.

Keywords: WB-EMS, slap shot, shot speed, counter-movement-jump, isokinetic strength, knee extensor, subjective performance, ice hockey

INTRODUCTION

In medicine electromyostimulation has long been an established method for supplementing rehabilitation concepts. It is utilized to increase the functional efficiency of patients with gonarthrosis (Banzer, 2016; Klimkiewicz et al., 2016), to reduce back pain (Kemmler et al., 2017) and to serve as a well-documented procedure for rehabilitation of paresis in stroke patients (Bock, 2018). Furthermore is was shown that whole-body electromyostimulation (WB-EMS) improves body composition in patients with hematological malignancies (Schink et al., 2018) and increases muscle mass in patients at risk for sarcopenic obesity (Kemmler et al., 2016).

During the last years, WB-EMS has found its way into strength training. Several studies on professional athletes of various kinds of sport have shown that complimentary training with WB-EMS can achieve efficient results in strength gains. Those ranged up to 19.5% in terms of jumping ability and up to 35.2% in terms of maximum force respectively, as seen in volleyball (Malatesta et al., 2003), basketball (Maffiuletti et al., 2000) and soccer players (Billot et al., 2010; Filipovic et al., 2016), swimmers (Pichon et al., 1995) as well as rugby (Babault et al., 2007) and tennis players (Maffiuletti et al., 2009).

In Filipovic et al.'s (2012) systematic review regarding EMS training on trained and untrained athletes maximum force, high-speed force, vertical jump height and sprint time were examined. The training period amounted to 3–6 weeks. Results showed an increase of maximum isokinetic strength in eccentric (37.1%) and concentric condition (41.3%) and counter-movement-jump (CMJ) performance (19.2%), such as a decrease of sprint time (4.8%). The effect on untrained athletes however, was not discussed in detail. Brocherie et al. (2005) published an EMS study on French division II ice hockey players which revealed a 41% increase of maximum power at an angular velocity of 60°/s and 49% at 300°/s and a 4.8% decrease of sprinting time and 6% decrease of jumping height. However, many of those studies show diverging not comparable results due to a smaller number of cases and shorter lengths of training periods, aberrant stimulation modes, testing procedures, and individual conditions of the subjects. Moreover nearly all of these studies discuss the effect of EMS on professional athletes.

To the best of our knowledge, no WB-EMS study has previously been published on leisure ice hockey players. We were interested in the question whether this fairly new training concept may also benefit athletes of amateur leagues. This constitutes an interesting group of athletes, as especially the pool of district league players represents a possible way to recruit young professional athletes. Since most studies have only stimulated individual muscle groups, we wanted to investigate the effect of WB-EMS training on amateur ice hockey players and investigate whether athletes' competitive status as an indicator of their fitness level influenced the magnitude of their response to WB-EMS. Due to the greater training potential of hobby athletes we expect them to gain higher effects on the performance increase through additional WB-EMS training.

Lastly training with WB-EMS and strength training show similar effects (Simpson and Willoughby, 1988; Colson et al., 2009). Furthermore there is a correlation between range of maximum power, body control and injury rate. In addition to equipment and fair play, specific strength training and proprioceptive training are methods to prevent injury to hip and core muscles (Weisskopf, 2010). A minimum of 6 weeks specific strength program and proprioceptive training decreases the injury rate of adductors and inguinal structures (Tyler et al., 2002). Therefore, a reduction of the injury rate could be expected from an improvement of strength and proprioception.

MATERIALS AND METHODS

Subjects

The present study included 30 male ice hockey players aged 18–48 years (on average 27.5 ± 7.9 years) from two amateur ice hockey leagues (70% district league players and 30% hobby league players). Anthropometric data were collected (height: 1.81 ± 0.07 m; weight: 80.2 ± 12.5 kg, circumference of thigh: 58.5 ± 6 cm; upper arm: 35.6 ± 3 cm, and waistline: 88.9 ± 9 cm). The players' average begin with ice hockey was at child's age, their training frequency ranged from 2 trainings and 1 game per week for hobby league players to 3 trainings plus 1–2 games per week for district league players.

Before training, differences were observed between Group A and Group B. Group A athletes weighed an average of 12.98 kg more, their circumferences of thigh and upper arm were 4 and 2 cm bigger, as well as their average waistline (5 cm). Group A athletes showed higher baseline values in jump power (0.29 kW), shot speed (11.55 km/h), maximum force at 300°/s (13.11 Nm), and maximum force at 60°/s (9.12 Nm), whereas Group B athletes reached higher baseline values in jump height (3.56 cm) and lower values in sprint time (0.06 s). The athletes were assigned randomly and in equal parts to the two groups, also in terms of their league affiliation. They participated voluntarily and signed an informed consent prior to beginning with the training. The study was approved by the Ethics Committee of the Ludwig Maximilian University of Munich. It was registered with the German clinical trials register (ID: DRKS00012249) and is therefore listed in the International Clinical Trials Registry of the World Health Organization. Over the period of our study, ice hockey training continued in the same manner for all participants as usual. The players performed their hobbies the same way as before and equally in both study periods. Four athletes had to resign from the study because of injuries sustained during ice hockey training, but unrelated to WB-EMS training.

WB-EMS-Training

In a randomized cross-over design, one group was first trained with WB-EMS in addition to normal training for 12 weeks, followed by a phase without WB-EMS for 4 weeks. During the first 6 weeks, WB-EMS training was performed in static mode, followed by a further 6 weeks of dynamic training. The second group performed WB-EMS in exactly the same fashion. The WB-EMS period consisted of a total of 12 sessions in 12 weeks, one session per week, with a duration of 20 min each. The full number of sessions was completed by every participant in the predetermined time. Training times were set in adequate time distance from ice hockey training and matches to create a sufficient recovery period. Ordinarily, the training was held separately from ice hockey training, and was set at always the same days of the week. The training plan targeted every big muscle group. Training time was divided into different sections in which specific exercises for the respective disciplines were carried out. As overview:

Sprint: Abductor training, side steps, static, dynamic and plyometric lunges – straight forward and diagonal, butterfly, sprinter arms, explosive steps, step jumps, diagonal sprint steps.

Shooting and stability: Torso rotations, crunches, bench press without weights, shot pose, upswing pose, various types of shots and slap shots in static, dynamic and explosive motion, as well as different types of planking exercises.

Jumping ability: Squats with different ranges of motion, squats with pulses, straight jumps, squat jumps, jumps over box, CMJs.

Isokinetic force: Static and dynamic squats, explosive squat pushes, high skips – squat – jump squat combinations, slow and fast squats, tap the floor, alternating lunge jumps.

Electrode-straps were attached to upper arms, upper legs and buttocks and a vest was done to stimulate back and abdominal muscles. Pulse currents of 85 Hz frequency with a pulse width of 350 μs were used. A duty cycle of 50% with a contraction time of 4 s was applied. At the beginning of each session the individual daily maximum tolerated pain intensity was adjusted and a consecutive increase throughout the training period was sought. The minimum level was set to be at least 75% of last session's intensity score.

Testing

Shot speed, jumping ability, 10-m sprint time, maximum isokinetic force at 60 and 300°/s and the subjective performance according to a questionnaire was recorded. The measurements were taken at baseline, after 6 and after 12 weeks. The results after the WB-EMS pause phase were tested 16 weeks after the start of the training as a follow up measure. All data were collected in accordance to the training- and match time table of the subjects. Additionally, the appointments were scheduled in adequate distance to previous WB-EMS sessions to achieve equivalent physiological initial conditions for all players.

According to the cross-over strategy chosen for this trial, there were two study periods of equal length, divided by a wash-out phase. Group A had WB-EMS in addition to regular ice hockey training during period 1 and regular training only in period 2, whereas the schedule for Group B was arranged in reverse.

Period 1 started with the initial physical examination and testing on T1 corresponding baseline-results. After a 6 week WB-EMS training phase in Group A and exclusive ice hockey training in Group B, the second data collection followed at T2. Re-measurement of the variables took place after 12 weeks. The final measurement T4 after 16 and 4 weeks of WB-EMS pause respectively, was a follow-up measurement to evaluate the retention of training effects. After a wash-out phase of 3 months, period 2 ensued analog with Group B undergoing training with EMS (**Figure 1**).

T1 and T3, such as T5 and T7 were used as reference measurements. T2 and T6 were used to illustrate the value development. T4 and T8 were collected to assess the degree of retention of any training effects. Data of all participants of both groups were collected at each measurement.

Since fewer athletes participated in measurement T6 than in the other measurements, this measurement is not considered representative.

Shot Speed

The shot speed in km/h was measured by means of an unmodulated continuous wave sport radar "Ballspeedometer 1503." This sensor was centrally located just behind the net of the goal and all shots were targeted at the sensor. For the test, subjects performed three slap shots from a distance of 10 m and the average shot speed was calculated from these three individual shots.

Jumping Ability

Individual maximum jumping power and maximum jump height in the CMJ were measured using the Leonardo Mechanograph GRFP (Novotec Medical GmbH, Pforzheim, Germany) with a sampling rate of 800 Hz. Ground reaction forces were recorded using a measuring pressure plate via the springboard and then evaluated using the accompanying LabVIEW software. For testing, the players stood with both legs in the predetermined areas of the plate and performed three valid consecutive CMJs. Sufficient time was provided between each CMJ. In terms of implementation, we decided to include arm swinging.

Sprint

The maximum sprint time in seconds for a 10 m track was recorded using Model RL S1c photocell (ALGE-Timing GmbH, Lustenau, Germany). The second sensor-reflector pair of the photocell was mounted centrally above the blue line. From there, the 10 m sprint distance was measured toward the short side of the boards, where then the first sensor-reflector pair was placed. The run-up took place from the red baseline. All participants lined up in turn. After this predetermined start-up distance each player passed the photocell construction of a distance of 10 m

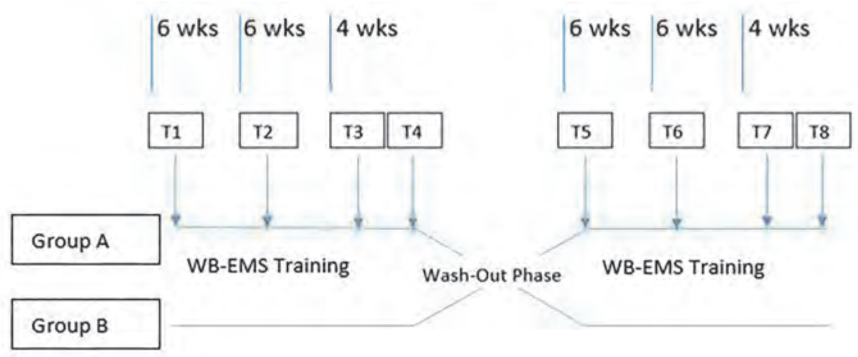

FIGURE 1 | Scheme of cross-over study course with consecutive wash-out phase between period 1 and period 2.

a total of three times. Sufficient recovery time was provided in between the rounds. Sprint times were determined at hip level.

Isokinetic Test

The maximum isokinetic force at 60 and 300°/s measurement of the knee extensors in Nm was determined by IsoMed 2000 (D. & R. Ferstl GmbH, Hemau, Germany). After a 5–10 min warm-up on the bicycle or treadmill ergometer, which was set as standardized choice for each player, a test round with approximately 75% of subjective sub maximum power took place at each angular velocity, followed by the actual test run. Five repetitions were required for the maximum force test at 300°/s and four passes were required for the subsequent maximum force measurement at 60°/s, as set by default of IsoMed 2000. Range of motion for the knee joint was set to 90° with start position at 90° and end position at 0. The best performance out of all passes was counted. Between each pass the athletes were given 45 s to rest. The subjects were equipped with straps on hip, chest, leg, and thighs, to minimize influencing movements.

Subjective Questionnaire

The survey was conducted before each WB-EMS series and at the end of both periods. Each participant completed the questionnaire including weight development, limb circumferences, injuries and self-assessment of sprint ability, shoot speed, jump performance, leg strength, body shape, fitness level, mood, safety on ice, stability, and overall satisfaction.

Statistical Analysis

Estimates and caseload calculations were made within statistical planning based on the work of other research groups and issues, as there had been no experience and data on the variability of values and possible intervention effects.

To reach a power of at least 90%, a caseload of a minimum of 25 participants was needed. All values were calculated using mean value and standard deviation. Each variable that underwent three passes during testing was standardized as an average value. Unrealistic values >2 SD or errors were removed from the calculation. The comparisons for verified differences were used as unilateral paired t-tests for unconnected samples. A normal distribution of the values was assumed. For data evaluation and interpretation, a power of 90% was estimated with significance accepted for p-values ≤ 0.05. The statistical support was provided by a statistician of the Institute for Medical Information Processing, Biometry and Epidemiology of the LMU Munich. All statistical methods were performed with the SPSS software (IBM Corp., Armonk, NY, United States).

RESULTS

Vertical Jump Power

Results for vertical jump power, obtained during 16 weeks of testing, are shown in **Figure 2** for both groups. In all following figures MV denotes mean value, the lightning bolt illustrates the respective intervention period. After WB-EMS training jump power increased significantly in Group A to 5.9% (251.5 ± 226.6 W) and 4.4% (168.5 ± 314.9 W) in Group B, respectively ($p < 0.05$). In corresponding phases of exclusive ice hockey training, jump power values decreased in both groups.

Vertical Jump Height

Results for vertical jump height obtained during the 16 weeks testing period are shown in **Figure 3** for both groups. Jump height increased in Group A to 4.6% (2.16 ± 3.34 cm) and 6.3% (3.18 ± 4.54 cm) in Group B, respectively. In corresponding phases of exclusive ice hockey training jump height values decreased in both groups.

Sprint Time

The 10 m skating time decreased significantly for Group A to 6.3% (0.1 ± 0.06 s) and Group B to 3.7% (0.05 ± 0.06 s) shown in **Figure 4**. Without WB-EMS training the sprint time results showed an increase in Group A and no significant changes in Group B.

Maximum Force at 60°/s

After 12 weeks of WB-EMS training the isokinetic torque at 60°/s increased to 24.6% (54.86 ± 69.07 Nm) for Group A and to 5.7% (11.33 ± 21.88 Nm) for Group B as shown in **Figure 5**.

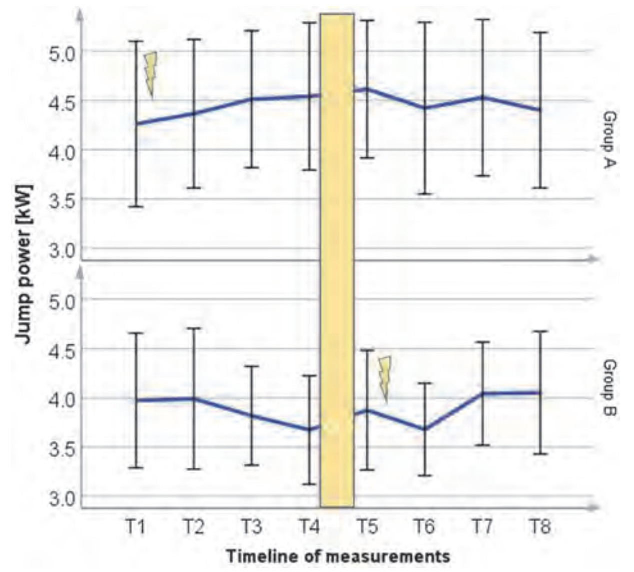

FIGURE 2 | Mean (±SD) change in jump power for Group A period 1 and Group B period 2, compared to each control group ($p = 0.04$). Lightning bolt represents each respective WB-EMS period; yellow area = wash-out phase.

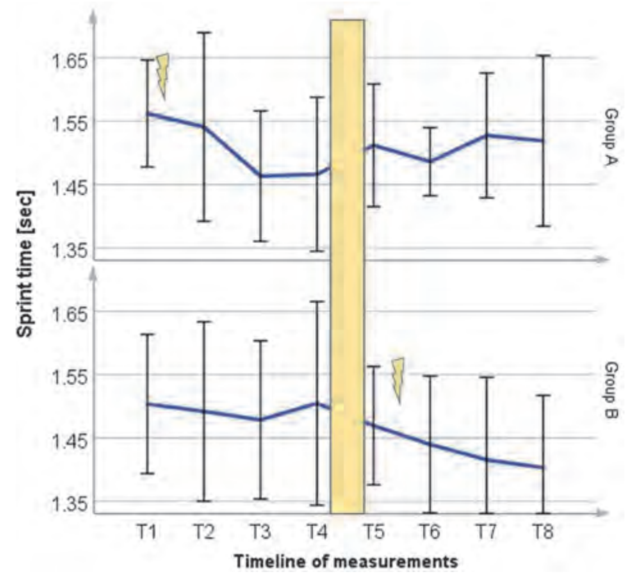

FIGURE 4 | Mean (±SD) change in sprint time for Group A period 1 and Group B period 2, compared to each control group ($p = 0.02$). Lightning bolt represents each respective WB-EMS period; yellow area = wash-out phase.

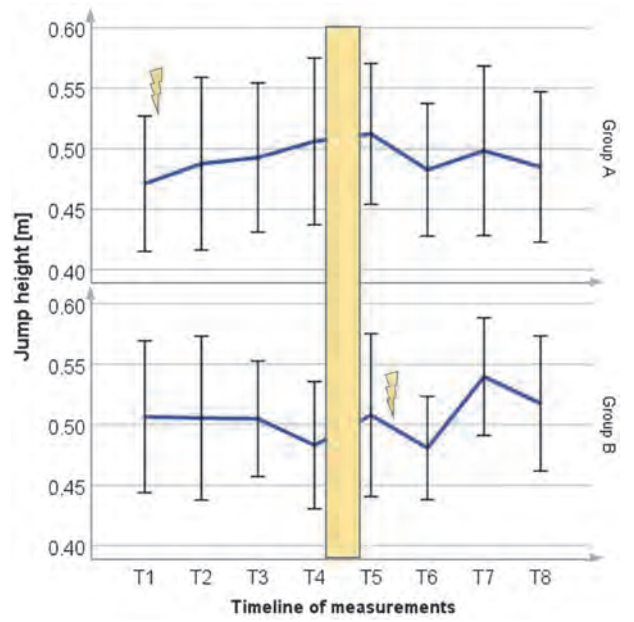

FIGURE 3 | Mean (±SD) change in jump height for Group A period 1 and Group B period 2. Lightning bolt represents each respective WB-EMS period; yellow area = wash-out phase.

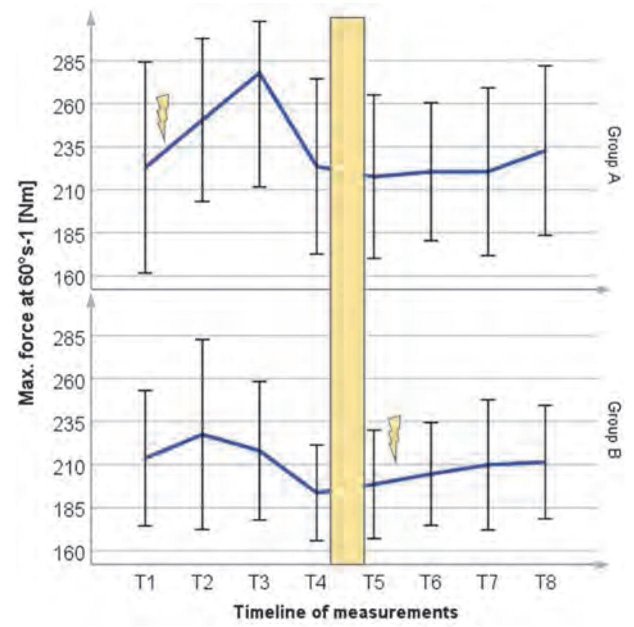

FIGURE 5 | Mean (±SD) change in maximum voluntary force at 60°/s for Group A period 1 and Group B period 2. Lightning bolt represents each respective WB-EMS period; yellow area = wash-out phase.

Without WB-EMS training the results of each group showed no significant changes.

Maximum Force at 300°/s

After 12 weeks of EMS training, the isokinetic torque at 300°/s increased significantly ($p < 0.05$) (**Figure 6**) for Group A to 6.1% (7.94 ± 20.73 Nm) and Group B to 7.9% (9.61 ± 13.57 Nm). When comparing torque changes after the 12-week period, WB-EMS groups had significantly higher torque increases than the control groups. Without WB-EMS training the results of each group showed no significant changes.

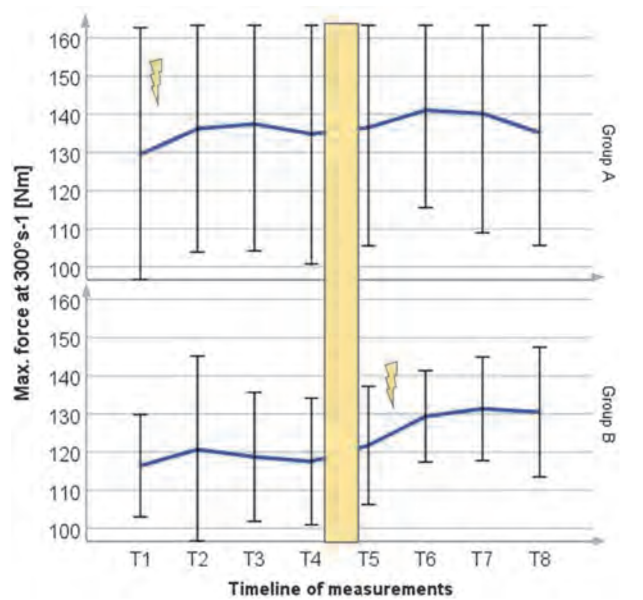

FIGURE 6 | Mean (±SD) change in maximum voluntary force at 300°/s for Group A period 1 and Group B period 2, compared to each control group ($p = 0.02$). Lightning bolt represents each respective WB-EMS period; yellow area = wash-out phase.

Shot Speed

After 12 weeks of WB-EMS training no changes were detected for both groups (±0; $p < 0.05$).

Subjective Questionnaire

The evaluation showed an increased self-assessment of all points after WB-EMS-training, except for the mood, which remained approximately constant in group A during the intervention. Regarding the injury rate, no new hockey-related injuries were detected during the study periods, although four injuries due to hobby or work were registered.

Comparison of Leagues

Comparing the two leagues, every parameter improved after WB-EMS training, except shot speed and maximum force at 300°/s considering hobby league players of Group A. Looking at the averaged scores, hobbyists achieved higher results when it came to jump power (6.35 vs. 3.25%), sprint time (7.4 vs. 4.6%), maximum force at 300°/s (7 vs. 5.85%), and jump height (11 vs. 2.3%) albeit hobby players represented a comparatively smaller proportion of our study population. District league players showed higher values for max force at 60°/s after WB-EMS training (16.1 vs. 11.75%).

DISCUSSION

In our study, a 12-week WB-EMS training in addition to normal ice hockey training of leisure players showed a comparable development of the sprint time (Filipovic et al., 2016), (e.g., by 4.8% in elite ice hockey players) (Brocherie et al., 2005), but less improvement in maximum force at 60 and 300°/s of the quadriceps (Maffiuletti et al., 2000; Brocherie et al., 2005; Billot et al., 2010; Filipovic et al., 2016), (e.g., 41.3 ± 37.6% at 60°/s and 49.2 ± 48.9% at 300°/s in elite ice hockey players) (Brocherie et al., 2005) and a contrary trend in terms of jump height (Brocherie et al., 2005). The different findings of our study in comparison to other authors regarding leg strength could be explained by our differing training concept. In contrast to other studies we used whole-body EMS training and did not only address the M. quadriceps physically. Therefore, overall less time was spent on stimulating the leg extensor. Furthermore, our training plan involved mainly static exercises for the first 6 weeks, followed by dynamic exercises only in the second 6 weeks, which could also be a cause for the lower improvement of the maximum force at 300°/s. All in all, the trend of the value development of sprint time, maximum force at 60 and 300°/s is consistent to the results of previous studies.

In addition to the variables described, we also tested jump power, which increased by 5.15% and shot speed. Regarding the evaluation of shot velocity no changes were observed in our study. At the present time, there are no studies evaluating the effect of EMS training on shot velocity. The slap shot is a very complex motion and highly depends on the level of technique and experience of the player. The lack of improvement could be partly explained by factors such as technique or motivation (Babault et al., 2007). Also, despite sport specific training exercises, improvements in complex motions are restricted (Micke et al., 2018).

Regarding the jump performance, many findings show no change or a decrease of jump performance after EMS training. At best little improvement was found after the end of the stimulation period. Ten days after the completion of the stimulation sessions and continued volleyball training jump performance improved by 5–6% (Malatesta et al., 2003). In line with this, elite basketball players did not experience any significant changes in CMJ height after local EMS training. A subsequent consecutive 4-week EMS break with basketball practice only also led to a significant gain in jump performance of 17% (Maffiuletti et al., 2000). Local EMS training on soccer players presented no significant changes in CMJ (Billot et al., 2010). In professional ice hockey players, local EMS training on the quadriceps resulted in a 6.1% decrease of vertical jump height (2.1 ± 2.0 cm) (Brocherie et al., 2005). Those results are contradictory to the findings of other researchers who found improvements after the end of an EMS period (Filipovic et al., 2016). For instance, a WB-EMS study with runners showed improved jumping skills (0.02 ± 0.02 m) after WB-EMS training, compared to a control group (Amaro-Gahete et al., 2018b), which is in accordance with our findings. Ameliorations in complex movements like jumping are limited (Micke et al., 2018). Authors state that performance in complex movements requires some time of specific training before the positive effects of local EMS can be observed (Maffiuletti et al., 2000). Therefore, longer EMS training sessions could be more efficient on jumping skills. Most authors used shorter EMS training periods. Our study involved 12 weeks of WB-EMS training. This could be one explanation why jumping performance increased at the end of our study. Micke et al. (2018) postulated that absence of improvement under WB-EMS training could be due to training without sport specific movements. It has been shown that specific exercises lead to higher gains in jump performance of runners compared to traditional WB-EMS training (Amaro-Gahete et al., 2018a). Therefore, we decided to use several specific exercises for ice hockey players.

Research has shown that there is a connection between weight training and a reduction in injury rate. Targeted strength training is useful as injury prevention (Tyler et al., 2002; Weisskopf, 2010). Moreover, studies show that training with local EMS and strength training have similar effects in terms of strength gains (Simpson and Willoughby, 1988; Colson et al., 2009). Our study questionnaire gave evidence to higher self-assessments in terms of safety and stability on the ice. Strength gains and increase of individual subjective performance could give an indirect effect on injury rate. Accordingly, in a large population, an effect on the injury rate could be expected.

Currently, the data on WB-EMS in leisure sports is limited. In our study, significant training effects were recorded after WB-EMS training. Regarding the influence of competitive status, our conclusion is that, by taking in account the above arguments, there is an even greater potential for improvement for hobby sportsmen. Because of the lower training potential of professional athletes, their training effect should be less pronounced than with leisure athletes.

To summarize, we found additional WB-EMS training suitable as a supplement to normal training for lower league ice hockey athletes. It improved their physical performance in strength and speed parameters. In a larger study population, it might possibly serve as injury prophylaxis.

DATA AVAILABILITY

All datasets generated for this study are included in the manuscript and/or the supplementary files.

ETHICS STATEMENT

The study was approved by the Ethics Committee of the Ludwig Maximilian University of Munich. It was registered with the German clinical trials register (ID: DRKS00012249) and is therefore listed in the International Clinical Trials Registry of the World Health Organization.

AUTHOR CONTRIBUTIONS

ES trained the athletes, collected the data, analyzed the data, and prepared the manuscript. CB, HS-G, and VJ helped to prepare, translate, and review the manuscript. AP performed the isokinetic measurements. BW planned and supervised the study, prepared and wrote the manuscript.

FUNDING

For the project, miha-bodytec provided the WB-EMS devices free of charge.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

ORIGINAL RESEARCH
published: 23 September 2019
doi: 10.3389/fphys.2019.01187

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Superimposed Whole-Body Electrostimulation Augments Strength Adaptations and Type II Myofiber Growth in Soccer Players During a Competitive Season

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OPEN ACCESS

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Specialty section:
This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 31 March 2019
Accepted: 02 September 2019
Published: 23 September 2019

Citation:
Filipovic A, DeMarees M, Grau M,
Hollinger A, Seeger B, Schiffer T,
Bloch W and Gehlert S (2019)
Superimposed Whole-Body
Electrostimulation Augments Strength
Adaptations and Type II Myofiber
Growth in Soccer Players During
a Competitive Season.
Front. Physiol. 10:1187.
doi: 10.3389/fphys.2019.01187

Background: The improvement of strength and athletic performance during a competitive season in elite soccer players is a demanding task for the coach.

Aims: As whole-body electrostimulation (WB-EMS) training provides a time efficient stimulation potentially capable in exerting skeletal muscle adaptations we aimed to test this approach over 7 weeks in trained male soccer players during a competitive season.

Hypothesis: We hypothesized that a superimposed WB-EMS will increase maximal strength and type I and type II myofiber hypertrophy.

Methods: Twenty-eight male field soccer players were assigned in either a WB-EMS group (EG, $n = 10$), a training group (TG, $n = 10$), or a control group (CG, $n = 8$). The regular soccer training consists of two to four sessions and one match per week. In concurrent, the EG performed 3 × 10 squat jumps superimposed with WB-EMS twice per week, TG performed 3 × 10 squat jumps without EMS twice per week, and the CG only performed the regular soccer training. Muscle biopsies were collected and strength tests were performed under resting conditions before (Baseline) and after the intervention period (Posttest). Muscle biopsies were analyzed via western blotting and immunohistochemistry for skeletal muscle adaptive responses. To determine the effect of the training interventions a 2 × 3 (time * group) mixed ANOVA with repeated measures was conducted.

Results: Maximal strength in leg press ($p = 0.009$) and leg curl ($p = 0.026$) was significantly increased in EG along with a small but significant increase in type II myofiber diameter ($p = 0.023$). All of these adaptations were not observed in TG and CG.

Conclusion: WB-EMS can serve as a time efficient training method to augment strength capacities and type II fiber myofiber growth in soccer players when combined with specific resistance training. This combination may therefore be a promising training modification compared to traditional strength training for performance enhancement.

Keywords: electrostimulation, soccer, hypertrophy, mTOR, p70s6k, strength

INTRODUCTION

The improvement of physical performance of soccer players in short time courses is of crucial importance in high performance soccer. Here, running distances associated with high intensity have significantly increased in the last decade (Mohr et al., 2003; Di Salvo et al., 2009). Consequently physical requirements, especially the development of strength capacities, gained more importance. But with increasing number of games per season, a well-developed physical robustness and muscular performance also plays a crucial role in the context of injury prevention (Al Attar et al., 2017). However, assuring adequate recovery after a match and timelike integrating effective strength programs to systematically increase soccer-relevant strength parameters during the competitive season is a demanding task for the coach. Due to a lack of time, the implementation of alternative training methods that offer high efficient stimulation of muscle adaptation has increasing value. Among these, stimulation of muscle via electromyostimulation (EMS) to increase maximal strength and specific strength capacities such as jumping and sprinting of trained and elite team sport athletes seems promising (Delitto et al., 1989; Maffiuletti et al., 2000, 2002a; Malatesta et al., 2003; Gondin et al., 2005; Billot et al., 2010; Filipovic et al., 2016). The electrical stimulus leads to a mostly indirect involuntary contraction controlled by the central nervous system (Gregory and Bickel, 2005). Studies revealed that low frequency (approx. 50–120 Hz) EMS can produce a high muscle tension and thus a high metabolic and mechanical stress on the muscular structures (Gregory and Bickel, 2005; Jubeau et al., 2008; Nosaka et al., 2011) that trigger neuronal and hormonal adaptation processes (Paillard, 2008).

Studies showed that a single bout of intense whole-body electrostimulation (WB-EMS) can produce a high level of muscular damage or even rhabdomyolysis especially when it is performed with isometric contractions and with maximal intensity (Kemmler et al., 2015; Stollberger and Finsterer, 2019). Adusting the training intensity under EMS is difficult. Thus, when not applied with care, EMS exercises may induce health risks and bring this training mode under discussion. Thus, in the last years, studies were conducted to investigate the effects on health parameters and performance (Jee, 2018; Kemmler et al., 2018), and guidelines were developed for a safe and efficient implementation (Kemmler et al., 2016). But it is generally accepted, that when properly applied and supervised, WB-EMS represents a safe training method in healthy adults to develop physical performance and health.

Several authors conclude that the increases in maximal strength are mainly through a synchronous activation and higher frequency of motor units, as well as preferential recruitment of fast twitch fibers with relatively low muscle activity (Martin et al., 1994; Pichon et al., 1995; Colson et al., 2000; Maffiuletti et al., 2000, 2002b; Dudley and Stevenson, 2003). However, studies indicate that EMS can activate muscular adaptations and affect muscle characteristics such as a muscle fiber shift toward type IIa fibers (Cabric and Appell, 1987; Delitto et al., 1989; Bigard et al., 1993; Perez et al., 2002; Requena Sanchez et al., 2005) and can promote muscle hypertrophy (Gondin et al., 2005, 2011; Maffiuletti et al., 2006). Hortobagyi and Maffiuletti (2011) concluded in their review that an increase in maximum voluntary contraction in the early stage may not be due to muscle hypertrophy, but rather through changes within structures of the central nervous system. However, hypertrophic effects are possible with EMS, whereas these may only occur during longer stimulation periods of >6 weeks.

One of the major signaling pathways that regulates increased protein synthesis and muscle hypertrophy is the PI3kinase/Akt/mTOR pathway (Egerman and Glass, 2014). Even though limited data are available, some EMS studies have shown that EMS can stimulate the release of growth hormones or insulin-like-growth factor-1 (IGF-1) that can activate the mTOR-signaling pathway (Jubeau et al., 2008; Gondin et al., 2011; Wirtz et al., 2015). However, it has been shown that exercise-induced protein synthesis and muscle hypertrophy can be activated also in the absence of a release of growth hormones and IGF-1 (cf. Wilkinson et al., 2006; Schroeder et al., 2013; Egerman and Glass, 2014). Studies revealed that the mechanical strain of skeletal muscles can directly stimulate mTOR-related signaling (Jacobs et al., 2014) and p70s6k phosphorylation (Sandilands et al., 2015) via focal adhesion kinase. P70s6k has been shown to correlate with muscle growth and protein synthesis (Terzis et al., 2008, 2010). As EMS induces a significant mechanical stimulation of skeletal muscle fibers, assessment of p70s6k levels after EMS stimulation is promising.

In our previous study with professional soccer players (Filipovic et al., 2016) we achieved significant increases in maximal strength of the leg press (LP), jumping and sprinting performance with a dynamic WB-EMS training after 7 weeks (14 sessions). In this study we were not able to investigate skeletal muscle substructures; thus, it remains unclear whether muscle hypertrophy has occurred and an increase in muscle size has positively influenced maximal strength. Although the effects of EMS in various setups have been investigated, there is still a lack of knowledge concerning its application, e.g., in high performance soccer players, as a time-efficient training enhancement within a season and regular soccer training (cf. Billot et al., 2010; Filipovic et al., 2012, 2016).

Based on the capacity of EMS to significantly affect the neuromuscular level of skeletal muscle, we aimed to test in the present study whether EMS-induced strength gains are also associated with molecular and structural adaptations in skeletal muscle of high performance soccer players, when WB-EMS is applied with specific strength training during a continuous soccer training regimen. We hypothesized that WB-EMS in combination with a specific jumping training will increase strength capacities in skeletal muscle but not in non-WB-EMS stimulated athletes. We further hypothesized that this response was associated with increased diameter of myofibers reflected by increased protein levels of p70s6k and mTOR.

MATERIALS AND METHODS

Participants

Only healthy field soccer players were included which means no cardiovascular or metabolic diseases and no preinjury in the tested muscle groups. Participants needed to compete on a regional level for the last 3 years and train two to four sessions per week and play one soccer match per week. Experience in strength training was required. Twenty-eight soccer players were randomly assigned into three different groups. Control group (CG) was assigned based on preferences and availability, whereas both intervention arms have been assigned based on coin toss. The EMS group (EG, n = 10) performed 3 × 10 squats jumps superimposed by WB-EMS twice a week in addition to the regular soccer routine over a period of 7 weeks. To differentiate between the effects caused by EMS and by the squat jumps and soccer training, respectively, two CGs were included. A jump training group (TG, n = 10) performed the same number of squat jumps with identical intervals without EMS stimulus on the same days as the EG and a CG (n = 8) that only performed the regular soccer routine.

Basal anthropometric parameters of the subjects are shown in **Table 1**. All subjects abstained from alcohol consumption for 24 h prior to the Baseline diagnostics and during the training intervention and were non-smokers.

Twenty-seven players completed the two strength diagnostics. One player of the TG dropped out from the study because of an ankle joint injury before the Posttest and one sample could not be analyzed due to a missing Posttest of one subject. This subject was not willing to conduct a second biopsy. Muscle samples from 25 subjects were used for Western blotting and histology.

Definition of Daily Soccer Routine

The regular soccer training consists of 3.2 ± 1.0 sessions per week with a soccer match at the end of the week (90 min). The standard training sessions lasted 80.7 ± 10.1 min including general and specific warm-up (light to moderate intensity), athletic components with various intensities, technical skill activities (light to moderated intensity), offensive and defensive tactics (light to moderate intensity), small-sided game plays (e.g., 4 vs. 4 – 32 × 40 m; high intensity) and continuous play (e.g., 8 vs. 8 – 60 × 60 m; 10 vs. 10 – 100 × 60 m; moderate to high intensity). In a normal training week during season with a match on Sunday training was scheduled on Tuesdays, Wednesdays (optional), Thursdays, and Fridays. Number of training sessions and the training days varied according to the game schedule playing Sunday–Sunday or Sunday–Saturday. The number of training sessions and the total training minutes were documented. Training load included matches and was measured via Polar Team-2 Software (Polar Electro, Büttelborn, Germany) according to the training time spent in defined heart rate zones and related to the individual maximum heart rate during soccer training or match (**Table 1**). The training load provided by the Polar-Software determines the internal training load based on background variables [sex, training history, metabolic thresholds, and maximal oxygen consumption (VO_2max)] and parameters measured during training sessions (exercise mode, heart rate, and energy expenditure) (cf. Schumann et al., 2017). The individual maximum heart rate and maximum oxygen uptake VO_2peak of the players were measured in a maximal ramp test for calculation of training load via the Polar-software.

The players were asked to maintain their usual food intake and hydration and no nutrition supplementation was used. Additional strength training was not allowed during the study.

All players had a constant training volume during the first half of the season (July till December) and were in a well-trained condition. The intervention period started after the 3 week mid-season break from end of December till mid of January. During these 3 weeks the training load was relatively low (moderate endurance training twice per week) in order to maintain fitness level and not negatively affect baseline testing.

Exercise Protocol

Whole-body electrostimulation training was conducted on Tuesdays and Fridays in order to obtain a rest interval of 48 h between the two sessions and the championship game on Sunday. The EMS training was conducted using a WB-EMS-system by "*miha bodytec*" (Augsburg, Germany). WB-EMS was applied with an electrode vest to the upper body with integrated bilaterally two paired surface electrodes for the chest (10 × 4 cm), upper and lower back (14 × 11 cm), latissimus (10 × 4 cm), and the abdominals (23 × 10 cm) and with a belt system to the lower body including the muscles of the glutes (13 × 10 cm), thighs (44 × 4 cm), and calves (27 × 4 cm). Biphasic rectangular wave pulsed currents (80 Hz) were used with an impulse width of 350 μs (cf. Filipovic et al., 2016). The stimulation intensity (0–120 mA) was determined and set separately for each muscle group by using a Borg Rating of Perceived Exertion (cf. Tiggemann et al., 2010). The training intensity was defined for each players in a familiarization session 2 weeks before and set at a sub-maximal level that still assures a clean dynamic jump movement (RPE 16–19 "hard to very hard") and was saved on a personalized chip card. The EG performed 3 × 10 maximal squat jumps with a set pause of 60 s (no currents) per session. Every impulse for a single jump lasted for 4 s (range of motion: 2 s eccentric from standing position to an knee angle of 90° – 1 s isometric – 0.1 s explosive concentric – 1 s landing and stabilization) followed by a rest period of 10 s (duty cycle approx. 28%). The total duration time was 8.5 min per session with an effective stimulation time of 2 min per session. The players started with a 2–3 min standardized warm-up with movement preparations including squats, skipping, and

TABLE 1 | Anthropometric data (mean ± *SD*) and total training load (arbitrary units) during the 7-week intervention period calculated by Polar Team-2 Software according to training time spent in defined heart rates (see the section "Materials and Methods").

Group	Age (year)	Height (m)	Weight (kg)	Bodyfat (%)	VO_2peak	Sessions/week	Total training load (Polar Team-2)
EG	24.4 ± 4.2	1.82 ± 0.03	81.4 ± 5.3	12.9 ± 2.1	52.1 ± 3.4	3.4 ± 1.2	3430.6 ± 910.7
TG	21.1 ± 1.9	1.83 ± 0.06	79.7 ± 5.5	10.8 ± 2.8	56.3 ± 5.7	3.4 ± 1.3	3478.6 ± 1722.8
CG	23.6 ± 3.9	1.82 ± 0.05	79.7 ± 7.5	14.1 ± 3.6	54.3 ± 7.2	2.6 ± 0.7	2644.4 ± 1437.3

jumps in different variations (squat jumps, jumps out of skipping, or double jumps) at a light to moderate stimulation intensity. The players were told to slowly increase the intensity every few impulses. The training started when the players reached the defined training intensity that was saved on the chip card from the last session according to the RPE 16–19 ("hard to very hard"). The stimulation intensity was constantly increased individually every week (Tuesdays) in order to maintain a high stimulation intensity.

The TG performed the same amount of jumps with identical interval and conduction twice per week without EMS. The CG only performed the two to four soccer training session plus one match per week.

Experimental Protocol

Strength Diagnostics

Isometric strength and isoinertial power diagnostics were performed with the LP and leg curl (LC) machine (Edition-Line, gym80, Gelsenkirchen, Germany) equipped with digital measurement technique Digimax (mechaTronic, Hamm, Germany) and according to the protocol of the Institute of Training Science and Sport Informatics at the German Sport University Cologne (cf. Wirtz et al., 2016). The force-time and velocity-time variables were measured via strength sensors (5 kN strength sensor typ KM1506, distance sensor typ S501D, megaTron; Munich, Germany) and analyzed with the softwares IsoTest and DynamicTest 2.0. The sensors were installed in line with the steel band of the machines that lifts the selected weight plates. The maximum force in relation to body weight [Frel ($N \cdot kg^{-1}$)] was calculated and used for statistical analysis. After a 10 min standardized warmup including cycling on a ergometer and one set of 10 reps with moderate weight (approx. 40% 1RM) at the LP and the LC machine the players performed three isometric tests per test machine to measure maximal strength. Isometric attempts were conducted at an inner knee angle of 120°.

Muscle Biopsies and Tissue Treatment

Muscle biopsies were taken via Bergström needle biopsies (Bergstrom, 1975) from each player 2 weeks before (Baseline) and 48 h after the last training intervention (Posttest) (**Figure 1**). All biopsies were obtained under local anesthesia from the middle portion of the *m. vastus lateralis* between the lateral part of the patella and spina iliaca anterior superior 2.5 cm below the fascia. The muscle samples were freed from blood and non-muscular material and embedded in tissue freezing medium (TISSUE TEK, Sakura, Zoeterwoude/Netherlands). Samples were frozen in liquid nitrogen-cooled isopentane and stored at −80°C for further analysis. The distance between Baseline and Posttest incision was approx. 2.5 cm.

Immunohistochemistry

Seven micrometers of cross-sectional slices were obtained from the frozen muscle tissue using a cryo-microtome Leica CM 3050 S (Leica Microsystems, Nußbach, Germany) and placed on Polysine^{TM} microscope slides (VWR International, Leuven, Belgium). Sections were fixed for 8 min in −20°C pre-cooled acetone and air dried for 15 min at room temperature (RT), before blocking for 1 h at RT with Tris-buffered saline (TBS, 150 mM NaCl, 10 mM Tris–HCl, pH 7.6) containing 5% bovine serum albumin (BSA). After blocking, sections were incubated over night with rabbit polyclonal primary antibody which detects type I Myosin Heavy Chain (host: mouse; A4.951, DSHB Iowa, IA, United States), diluted 1:200 in 0.8% BSA. To confirm antibody specificity, control sections were incubated in TBS containing 0.8% BSA but without primary antibody. After incubation, sections were washed three times with TBS and incubated for 1 h with biotinylated goat anti-mouse secondary antibody (Dako, Glostrup, Denmark), diluted 1:400 in TBS, at RT. Thereafter, sections were washed three times before incubation for 1 h at RT with streptavidin biotinylated horseradish peroxidase complex (Amersham Biosciences, Uppsala, Sweden) 1:400 in TBS. Sections were washed once again and immunohistochemical staining was finalized using a 3,3′-diaminobenzidine (DAB) solution (0.09 M phosphate buffer, pH 7.4; 2.2 mM DAB; 7.03 mM ammonium chloride; 0.93 mM nickel sulfate; 10.44 mM β-D-glucose and 0.024 μM glucose oxidase). The procedures described are in accordance with the standard protocol for immunohistochemistry of the Institute of Molecular and Cellular Sport Medicine at the German Sport University Cologne (Germany) and have been described in detail before by Jacko et al. (2018).

Westernblotting

Tissue was homogenized in ice-cold lysis buffer (Cell Signaling, Boston, MA, United States) using a micro-dismembrator (Braun, Melsungen, Germany). Homogenates were supplemented with a mixture of protease and phosphatase inhibitors (HaltTM, Thermo Scientific, Waltham, MA, United States). The protein concentration of each sample was quantified with a Lowry test kit (Bio Rad, Munich, Germany) on a multiplate reader (Multiscan FC, Thermo Scientific, Waltham, MA, United States). For gel electrophoresis, 3× Laemmli buffer was added to the samples and heated at 95°C for 5 min. Afterward samples were stored on ice but brought to RT before being loaded on a precast 6–12% *bis–tris* polyacrylamide gel system (Criterion^{TM} XT, Bio Rad, Munich,

FIGURE 1 | Timeline of strength testing and muscle biopsies during the study in the second half of the season.

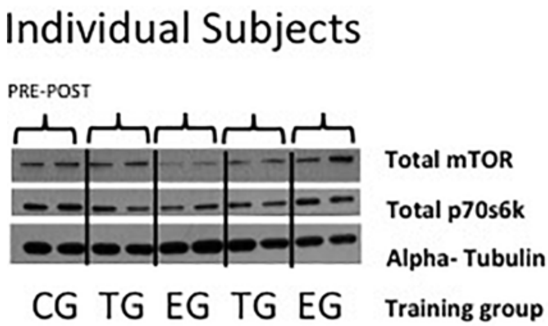

FIGURE 2 | Representative picture of Western blots of individual subjects of total mTor, total p70s6k, and alpha-tubulin in EMS-Group (EG), Training-Group (TG), and Control-Group (CG) measured 2 weeks before (Pre) and after the intervention period (Post).

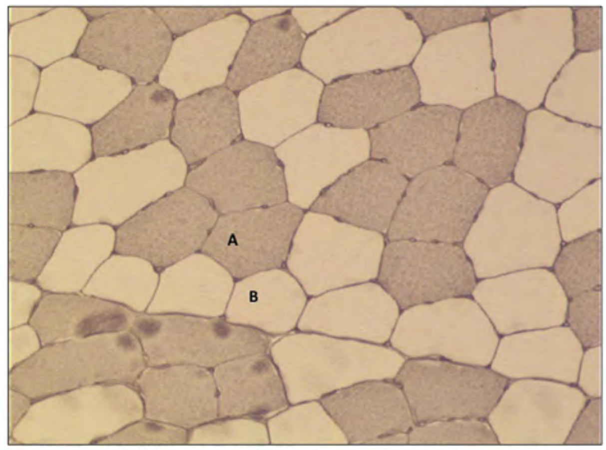

FIGURE 3 | Representative picture of immunohistochemical staining of myofiber cross-sections (10× fold magnification). **(A)** Type I fibers (stained) and **(B)** type II fibers (no stain).

Germany). After electrophoretic separation (100 volt, constant) in XT MOPS Running Buffer (Bio Rad, Munich, Germany), proteins were transferred (1.2 amp, 25 volt max, 34 min) to a polyvinylidene difluoride (PVDF) membrane (Bio Rad, Munich, Germany) using semi dry blotting systems (Criterion^{TM}, Bio-Rad, Munich, Germany). Membranes containing the separated proteins were blocked in 5% non-fat dry milk for 1 h at RT and incubated over night at 4°C with total mTOR (NEB 2983) and total p70s6k (NEB 2708) specific antibodies (Cell Signaling, Boston, MA, United States). Goat anti-rabbit antibodies diluted 1:1500 in 5% BSA, membranes were washed three times with TBST [TBS added with 1% Tween120 (Sigma–Aldrich, St. Louis, MO, United States)] and afterward incubated for 1 h at RT with the secondary antibody (goat anti-rabbit, diluted 1:10.000 in 5% non-fat dry milk, Thermo Scientific, Rockford, United States) and then washed in TBST. Proteins were detected by an enhanced chemo-luminescence assay (ECL-Kit, Amersham Life Science, Buckinghamshire, United Kingdom) exposed to an X-ray film (Kodak, X-OMAT Engineering, Eastman Kodak Co., Rochester, NY, United States) (**Figure 2**).

Determination of Myofiber Diameter

All slides were examined with a Zeiss Axiophot 200 light microscope coupled to a Sony 3CCD Color Video Camera. Up to 10 digital pictures were taken from each cross section with 10-fold magnification (10-fold objective) (**Figure 3**). A digital micrometer scale was applied to set the correct μm/pixel ratio for this magnification level. 1.2 pixel determined a length of 1 μm and this aspect ratio was used for all photos. Myofiber diameter was quantified by selection of the sarcoplasmic region within the borders of the sarcolemma of the myofiber and its subsequent measurement by the best fitting ellipse tool (Cluff et al., 2013) using the software ImageJ® (National Institutes of Health, United States). The minor axis was determined as the diameter of the myofiber. 55.4 ± 8.2 type I and type II myofibers per subject and time point analyses for changes in myofiber diameter.

Statistical Analysis

All descriptive and inferential statistical analyses were conducted using SPSS 25® (IBM®, Armonk, NY, United States). Kolmogorov–Smirnov test was applied to test for normal distribution. Data for muscle fiber size and mTOR were normally distributed. To determine the effect of the training interventions on maximal strength, muscle fiber size, and the signal protein, a separate 2 × 3 (time * group) mixed ANOVA with repeated measures was conducted. ANOVA assumption of homogenous variances was tested using Mauchly's test of Sphericity. Greenhouse–Geisser correction was used when a violation of Mauchly's test was observed. Partial eta-square (η_p^2) values are reported as effect size estimates. If 2 × 3 mixed ANOVA revealed a significant time-point * treatment or time * group interaction effect on any variable, this effect was further investigated carrying out Bonferroni corrected *post hoc* pairwise comparison. Group differences were determined by a one-way ANOVA. Bonferroni *post hoc* test was used to calculate significant differences between the tested groups. Effect size Cohen's *d*, defined as difference in means/standard deviation was calculated for groups between Baseline and Posttest (0.2–0.4 small; 0.5–0.7 medium; >0.8 large effects) (Cohen, 1988).

To detect correlations between the increase in Frel of LP and LC and muscle fiber size Pearson product-moment correlation (one-tailed) was used.

RESULTS

Changes of anthropometric data and the results of maximal strength testing of the players are shown in **Table 2**. The results in type I and type II myofiber diameter are presented in **Table 3**.

Anthropometric Data and Training Load

No changes were observed in bodyweight (kg) or bodyfat (%) from Baseline to Posttest. CG tends to have a higher percentage of bodyfat in general but no group differences could be observed between the groups at Baseline or Posttest.

Regarding training volume and load no differences were observed between the groups in the total number of soccer training sessions (EG 23.9 ± 7.8; TG 25.9 ± 6.6; CG 18.1 ± 5.6 sessions), soccer training minutes (EG 2103 ± 630; TG 1812 ± 919; CG 1437 ± 381 min), and the total recorded training load via Polar Team-2 software (**Table 1**).

Strength Parameters

The 2 × 3 mixed ANOVA revealed a significant main effect of within subjects factor time for LP ($F = 8.647$, $df = 1$, $p = 0.007$, $\eta_p^2 = 0.265$) and for LC ($F = 5.865$, $df = 1$, $p = 0.023$, $\eta_p^2 = 0.196$) but no group * time effect was observed. *Post hoc* analysis showed a significant increase in Frel from pre-to-post for the EG in LP ($p = 0.009$) and in LC ($p = 0.026$). Frel remained unchanged for TG and CG in the two test machines (**Table 2**).

Group comparison showed no differences between the groups at Baseline in LP and LC. At Posttest EG showed a significant higher Frel in LC ($p = 0.036$) compared to CG. No differences were observed between the groups at Posttest in the LP machine.

TABLE 2 | Results for anthropometric data and relative maximal strength (Frel) at leg press and leg curl for EMS-Group (EG), Training-Group (TG), and Control-Group (CG) 1 week before (Baseline) and 1 week after intervention period (Posttest).

	Group	*n*	Baseline (MW ± *SD*)	Posttest (MW ± *SD*)	Delta (baseline vs. Posttest) (%)	*Post hoc* Bonferroni correction (*p*-value)	Effect size (Cohen's *d*)
Bodyweight (kg)	EG	10	81.4 ± 5.3	81.7 ± 5.4	0.3 ± 2.8	0.741	0.11
	TG	10	79.2 ± 5.7	79.7 ± 5.5	0.6 ± 2.6	0.243	0.41
	CG	8	80.2 ± 7.3	80.9 ± 6.5	1.0 ± 2.7	0.519	0.25
Bodyfat (%)	EG	10	12.9 ± 2.2	12.5 ± 2.1	−2.3 ± 12.7	0.494	0.24
	TG	10	10.6 ± 2.7	10.3 ± 2.5	−3.0 ± 7.9	0.176	0.01
	CG	8	14.1 ± 3.4	14.0 ± 4.5	−0.9 ± 19.6	0.812	0.49
Leg press Rel. Fmax ($N \cdot kg^{-1}$)	EG	10	41.1 ± 9.3	47.0 ± 11.1**	15.1 ± 13.3	0.009	1.11
	TG	9	43.3 ± 11.5	46.7 ± 12.4	8.6 ± 15.6	0.203	0.49
	CG	8	41.9 ± 11.4	43.8 ± 16.9	4.3 ± 14.9	0.436	0.31
Leg curl Rel. Fmax ($N \cdot kg^{-1}$)	EG	10	17.9 ± 1.5	19.3 ± 2.2*	8.5 ± 9.3	0.026	0.89
	TG	9	17.4 ± 2.4	18.2 ± 1.7	4.7 ± 9.2	0.225	0.47
	CG	8	16.6 ± 2.2	16.4 ± 2.3	2.9 ± 4.7	0.796	0.10

Values are presented in means ± SD, significant differences at $^*P < 0.05$, $^{**}P < 0.01$.

TABLE 3 | Results for myofiber diameter (minor axis) in Type I and Type II fibers in EMS-Group (EG), Training-Group (TG), and Control-Group (CG) 2 weeks before (Baseline) and after intervention period (Posttest).

Muscle fiber type	Group	*n*	Baseline (minor axis) (MW ± *SD*) (μm)	Posttest (minor axis) (MW ± *SD*) (μm)	Delta (baseline vs. posttest) (%)	*Post hoc* Bonferroni correction (*p*-value)	Effect size (Cohen's *d*)
Type I	EG	8	69.39 ± 5.03	72.18 ± 5.63	4.1 ± 5.5	0.088	0.75
	TG	9	71.83 ± 5.10	72.90 ± 4.40	1.8 ± 7.9	0.599	0.19
	CG	8	72.80 ± 5.60	75.00 ± 5.96	3.3 ± 6.9	0.279	0.44
Type II	EG	8	74.10 ± 6.14	80.36 ± 5.53*	8.9 ± 8.5	0.023	1.10
	TG	9	76.56 ± 5.78	78.35 ± 7.38	2.6 ± 10.0	0.505	0.24
	CG	8	77.75 ± 7.67	79.23 ± 5.08	2.7 ± 10.5	0.629	0.19

Values are presented in means ± SD, significant differences at $^*P < 0.05$, $^{**}P < 0.01$.

Myofiber Diameter

For type I fibers no significant time or time * group effect was observed. The analysis of the type II fibers showed a significant effect over time (F = 4.369, df = 1, p = 0.048, η_p^2 = 0.166) but no group * time interaction effect. *Post hoc* analysis detected a significant increase in type II myofiber diameter (minor axis) for EG at pre-to-post (p = 0.023). Myofiber diameter remained unchanged in TG and CG. One-sided ANOVA for group comparison showed no differences between the groups at Baseline and Posttest for type I and type II (**Table 3** and **Figure 4**).

MTOR Signaling Proteins

A 2 × 3 ANOVA of repeated measures revealed no effects over time and no interaction effect for total mTOR and total p70s6k. No group differences were observed between the groups at Baseline or Posttest (**Figure 5**).

Correlations

A significant positive correlation (r = 0.355; n = 23; p = 0.048) was shown between changes (%delta = Posttest—Baseline) in Frel and changes in muscle fiber size of type II fibers. Significant increases in LP Frel are associated with increases in LC Frel (r = 0.349; n = 26; p = 0.040).

DISCUSSION

The study was designed to investigate the effects of superimposed WB-EMS on muscular adaptations during a competitive season in trained soccer players. After 7 weeks we observed significant increases in myofiber size of 8.9 ± 8.5% in type II fibers only in the EG but not in TG and CG. Although insignificant, EG showed also the highest increase in type I muscle fiber size of 4.1 ± 5.5% compared to TG and CG. Regarding strength capacity we also observed significant increases in Frel at LP (15.1 ± 13.3%) and at LC machine (8.5 ± 9.3%) only in the EG. The results in maximal strength are in line with the result of our previous investigation with professional soccer players (Filipovic et al., 2016) and comparable to the increases shown in local EMS studies with trained and elite athletes after 12–28 sessions (cf. Willoughby and Simpson, 1998; Maffiuletti et al., 2000, 2002a; Babault et al., 2007; Billot et al., 2010; Filipovic et al., 2012). It seems that 3 × 10 squat jumps twice per week in addition to two to four soccer training sessions or soccer training alone have no significant effects on muscular adaptation and strength capacity of the leg muscles. Accordingly, we could isolate the effect of the EMS stimulus and address the observed effects to the combination of WB-EMS and soccer training.

We assume that the increase of the myofiber diameter was small because all of the subjects had previous strength training experience and were trained soccer players. It has also to be accounted for that the entire net time under tension in the TG and EG were 28 min (2 × 2 min per week). A regular strength training unit with moderate movement and speed, consisting of three exercises with 5 sets and 10 repetitions for the leg muscles will result in a time under tension of approximately 25 s per set, 6 min for the entire session and around 90 min in 7 weeks. This would represent a more than threefold loading time of muscle. The EG and TG conducted in total only 14 training sessions (approx. 12–15 min) over a 7-week time period. In a comparable EMS study by Gondin et al. (2011) increases of 12% in type I and 23% type II fibers were observed after 8 weeks (three sessions/week) in trained athletes in combination with usual sport-specific training (4–6 h per week). We applied a significant lower number of sessions in total (14 vs. 24 session) and also a significant lower time under tension per week (4 vs. 12.5 min). Compared to regular hypertrophic strength training, WB-EMS provided a minimalistic time pattern of stimulation on muscle fibers. In comparable studies applying resistance exercise on subjects, two to three training sessions a week (approx. 70%; 3–5 sets; 8–12 reps) are associated with increased strength capacities and muscular hypertrophy (Izquierdo et al., 2009; Andersen and Aagaard, 2010).

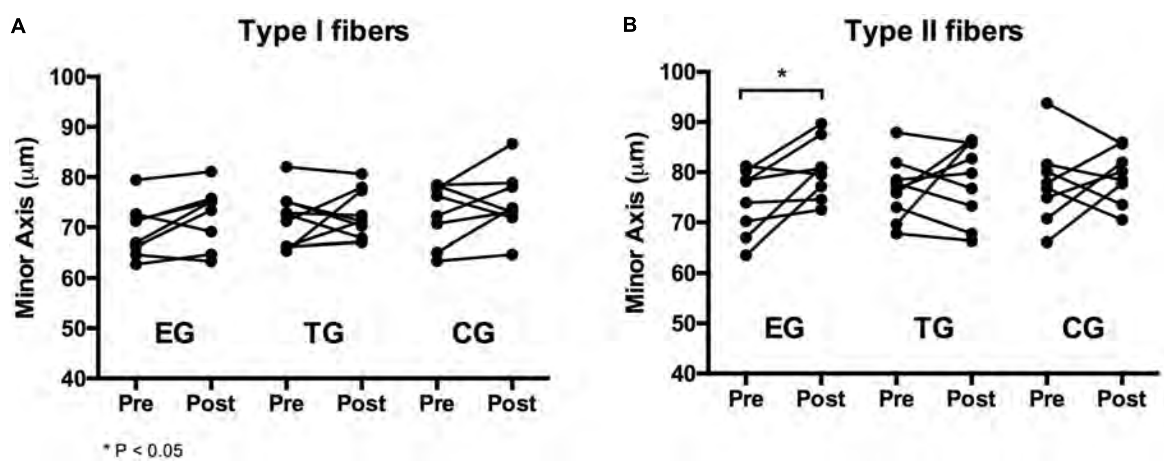

FIGURE 4 | Individual changes in myofiber diameter of **(A)** type I and **(B)** type II fibers in the EMS-Group (EG), Training-Group (TG), and Control-Group (CG) measured 2 weeks before (Pre) and after the intervention period (Post).

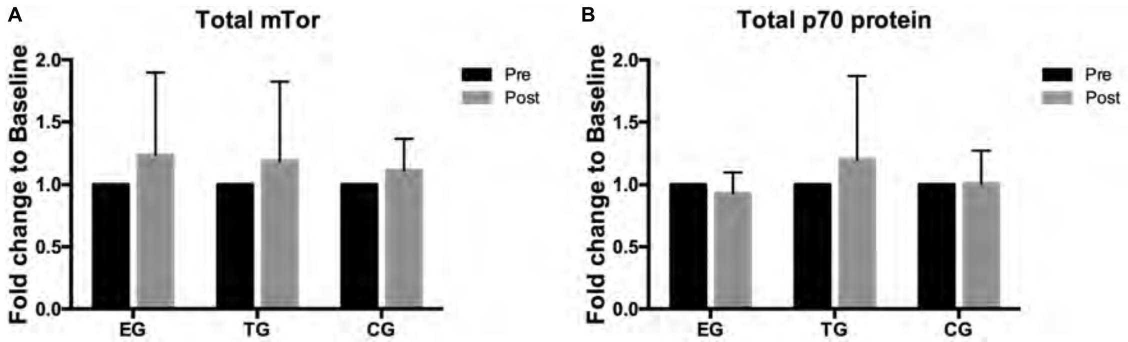

FIGURE 5 | Total levels of **(A)** mTOR, **(B)** p70s6k in EMS-Group (EG), Training-Group (TG), and Control-Group (CG) measured 2 weeks before (Pre) and after the intervention period (Post). Values are presented in means ± *SD*.

Electromyostimulation provides a stimulus where during a voluntary recruitment of myofibers; artificially, high supramaximal recruitment of myofibers is generated (Gregory and Bickel, 2005). Fast type II muscle fibers are recruited from the beginning; in addition to, the small type I fibers even at relative low intensities and moderate movement velocities suggest a preferential activation of the type II fibers (Gregory and Bickel, 2005). This offers a high, but short mechanical strain on myofibers implying also a high neuronal activation of motor units at the motoric endplate (cf. Hortobagyi and Maffiuletti, 2011). This probably does not include involvement of supraspinal neuronal centers to a higher extent than voluntary contractions with high force output, therefore explaining only moderate changes in general strength abilities; however, EMS may exert mechanical stimulation of myofibers to a high extent. Although this can be assumed, it will probably not mimic the myofibrillar loading that occurs during regular resistance training. Differences in the activation of signaling proteins between EMS and regular resistance exercise modes are to date not well investigated. High mechanical strain of myofibers is associated with increased signaling via mTOR pathway reflected by increased protein synthesis (Egerman and Glass, 2014; Gehlert et al., 2015b). Due to the time point of biopsy sampling in the rested state, we were unable to detect acute changes in the activation of mTOR-related signaling via phosphorylation of mTORC1 and p70s6k between and within groups and instead determined total levels of p70s6k and mTOR. We did not determine direct changes of these proteins in any of our groups. First, the time course of stimulation might has been be too short and second the accumulation of total protein levels will probably not limit the system in generating substantial hypertrophy; however, the cellular communication via p70s6k will not strictly reflect protein synthesis rates exceeding the acute phase after resistance exercise (Bamman et al., 2018). After 7 weeks we detected significant increased Type II diameter in the EG pointing to a substantial recruitment and stimulation of this fiber type during EMS (cf. Gregory and Bickel, 2005). Only small increases were observed in type I fibers. Type I fibers need a higher time under tension and also have a significantly lower capacity for hypertrophy (Bagley, 2014). We further have to assume that regular soccer training, associated with high energy turnover in muscle, will at least partly inhibit mTOR-related signaling (Coffey and Hawley, 2017) and prevent substantial increases in mTOR and p70s6k protein. The inhibition of growth via concurrent pathway interaction can also explain the lower degree in hypertrophy in the EG due to endurance-based soccer training (Fyfe et al., 2014) especially in type I fibers.

Regarding increase in muscle size of the *m. quadriceps femoris* and its influence on strength capacity of the leg extensor it is likely that the increases in Frel of the LC machine are also associated to an increase in muscle mass of the hamstrings. Regarding injury prevention, this could reduce the risk of hamstring injuries that represent one of the most common injuries in sprint demanding sports like soccer (Ekstrand et al., 2011). Thus, WB-EMS can be of great interest in team sports and soccer especially (Goode et al., 2015).

In general, the determined improvements in myofiber diameter and strength show a substantial interindividual variability reflecting a high individual pattern in the adaptation (high/low/none-responder) to the EMS stimulus. This was observed in previous EMS studies (Kreuzer et al., 2006; Wirtz et al., 2015, 2016; Filipovic et al., 2016; Micke et al., 2018) but also after strength training concerning hypertrophy (Petrella et al., 2008). Furthermore, the differences in playing time, high intensity running, and/or sprint distances during soccer match and training produce great deviations in training/work load within the players (Mohr et al., 2003; Suarez-Arrones et al., 2015; Pettersen et al., 2018) that can influence adaptative processes.

The results reveal that the increase in type II muscle fiber size may have positively influenced the force–velocity characteristic of the whole muscle (cf. Suchomel et al., 2018). However, increases in strength capacity are not only associated with hypertrophy. A variety of structural adaptation mechanism, e.g., muscle fiber shift toward type IIa fibers (Perez et al., 2002; cf. Requena Sanchez et al., 2005) or an increase in muscle stiffness via Ca^{2+}-induced modification of titin-isoforms (Rassier, 2017) as well as adaptation in the electromechanical coupling or energetic supply of the muscle (cf. Gehlert et al., 2011; Baird et al., 2012; Gehlert et al., 2015a; Ulbricht et al., 2015) could have been involved to promote increases in strength capacity.

A limitation of the present study was that the weekly training load could not be entirely standardized. This was due to the fact that players, depending on their position, received different tasks during training units and players had also distinct playing time during matches. On the other hand, this was distributed over the entire group of subjects and not only in EG, TG, or CG. Due to extreme difficulties in managing training and the intervention during the training day, it was not possible to collect biopsies acutely after exercise. This would have enabled us to determine acute changes in phosphorylation of mTOR targets and chaperones which might indicate the impact of WB-EMS on fiber recruitment, protein synthesis, and also muscle damage (Jacko et al., 2019). However, the current approach, using well-trained soccer players, created a realistic training situation, which was not scientifically overadapted. Further, we determined that WB-EMS is a safe training method and does not negatively influence players' performance.

Based on our results we conclude that implemented WB-EMS indeed will not dramatically change muscle adaptive responses when maintaining soccer training during a competitive season. However, it can emphasize the adaptability of fast type II fibers and may therefore result in a fine tuning of strength capacities while maintaining other performance parameters. The results reveal that WB-EMS training can be implemented as a time efficient alternative to traditional strength training in order to increase strength capacity during competitive season in soccer players. It could also be a promising training alternative for other team sports, e.g., track and field, handball, or basketball. More studies should investigate the effects of WB-EMS in other competitive sports in various intensities, training frequencies, and over extended time courses to elucidate chronic and long-term effects of this training tool.

DATA AVAILABILITY

The datasets for this manuscript will be made available by the authors. Requests to access the datasets should be directed to the corresponding author AF.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the "Ethics Committee of the German Sports University Cologne". All subjects gave written informed consent in accordance with the latest version of the Declaration of Helsinki. The protocol was approved by the "Ethics Committee of the German Sports University Cologne" [06-02-2014].

AUTHOR CONTRIBUTIONS

AF, SG, MG, and WB conceived and designed the research. AF conducted the experiments. MD conducted the muscle biopsies. BS assisted the biopsies and supervised the WB-EMS training. AH prepared, processed muscle tissue, and measured the parameters. AF and SG analyzed the data and wrote the manuscript. TS, MD, and WB revised the manuscript. All authors read and approved the manuscript.

FUNDING

This study was funded by the Bundesinstitut für Sportwissenschaft (Grant number BISP: ZMVI4-070101/16-17) and the Department of Molecular and Cellular Sports Medicine, Institute of Cardiology and Sports Medicine, German Sport University Cologne, Cologne, Germany.

ACKNOWLEDGMENTS

The authors would like to thank Bianca Collins, Anika Voß, and Thomas Dietz for their excellent technical assistance.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The handling Editor declared a shared affiliation, though no other collaboration, with several of the authors AF, MG, AH, BS, TS, WB, and SG at the time of the review.

frontiers in Physiology

SYSTEMATIC REVIEW
published: 08 November 2019
doi: 10.3389/fphys.2019.01336

Effects of Whole-Body Electromyostimulation on Strength-, Sprint-, and Jump Performance in Moderately Trained Young Adults: A Mini-Meta-Analysis of Five Homogenous RCTs of Our Work Group

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Background: Whole-body electromyostimulation (WB-EMS) gained increasing interest in sports within recent years. However, few intervention studies have examined the effects of WB-EMS on trained subjects in comparison to conventional strength training.

Objective: The aim of the present mini-meta-analysis of 5 recently conducted and published randomized controlled WB-EMS trails of our work group was to evaluate potentially favorable effects of WB-EMS in comparison to conventional strength training.

Methods: We included parameter of selected leg muscle's strength and power as well as sprint and jump performance. All subjects were moderately trained athletes [>2 training sessions/week, >2 years of experience in strength training; experimental group (n = 58): 21.5 ± 3.3 y; 178 ± 8 cm; 74.0 ± 11 kg; control group (n = 54): 21.0 ± 2.3 y; 179.0 ± 9 cm; 72.6 ± 10 kg]. The following WB-EMS protocols were applied to the experimental group (EG): 2 WB-EMS sessions/week, bipolar current superimposed to dynamic exercises, 85 Hz, 350 μs, 70% of the individual pain threshold amperage. The control groups (CG) underwent the same training protocols without WB-EMS, but with external resistance.

Results: Five extremely homogenous studies (all studies revealed an $I^2 = 0\%$) with 112 subjects in total were analyzed with respect to lower limb strength and power in leg curl, leg extension and leg press machines, sprint—and jump performance. Negligible effects in favor of WB-EMS were found for F_{max} of leg muscle groups [SMD: 0.11 (90% CI: −0.08, 0.33), $p = 0.73$, $I^2 = 0\%$] and for CMJ [SMD: 0.01 (90% CI: −0.34, 0.33), $p = 0.81$, $I^2 = 0\%$]. Small effects, were found for linear sprint [SMD: 0.22 (90% CI: −0.15, 0.60), $p = 0.77$, $I^2 = 0\%$] in favor of the EMS-group compared to CON.

OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to
Exercise Physiology,
a section of the journal
Frontiers in Physiology

Received: 10 April 2019
Accepted: 07 October 2019
Published: 08 November 2019

Citation:
Wirtz N, Dörmann U, Micke F, Filipovic A, Kleinöder H and Donath L (2019) Effects of Whole-Body Electromyostimulation on Strength-, Sprint-, and Jump Performance in Moderately Trained Young Adults: A Mini-Meta-Analysis of Five Homogenous RCTs of Our Work Group. Front. Physiol. 10:1336. doi: 10.3389/fphys.2019.01336

Conclusion: We conclude that WB-EMS is a feasible complementary training stimulus for performance enhancement. However, additional effects on strength and power indices seem to be limited and sprint and jump-performance appear to be benefiting only slightly. Longer training periods and more frequent application times and a slightly larger stimulus could be investigated in larger samples to further elucidate beneficial effects of WB-EMS on performance parameters in athletes.

Keywords: WB-EMS, electrical stimulation, strength training, MVC, peak power output

INTRODUCTION

Electromyostimulation (EMS) is a common and established method to enhance muscular strength and performance. Systematic reviews have well documented beneficial influence of locally applied EMS on strength (Delitto et al., 1989; Bax et al., 2005; Requena Sánchez et al., 2005; Paillard, 2008; Filipovic et al., 2012) and the neuromuscular parameters (Vanderthommen and Duchateau, 2007). Further studies revealed positive effects on jump and sprint capacity (Wolf et al., 1986; Brocherie et al., 2005; Herrero et al., 2006, 2010a,b; Babault et al., 2007; Maffiuletti et al., 2009; Billot et al., 2010; Voelzke et al., 2012; Filipovic et al., 2016; Wirtz et al., 2016). The reasons for the improvements using EMS are a higher number of motor units recruited during exercise with EMS compared to voluntary dynamic contractions only (Kots and Chwilon, 1971). Additionally, the activation of fast-twitch fibers at relatively low force levels plays also a relevant role (Gregory and Bickel, 2005). Most studies used the maximum pain threshold (maximum tolerated amperage) to regulate the impulse intensity (amperage) (Brocherie et al., 2005; Maffiuletti et al., 2009). However, a high level of muscle tension due to EMS limits the range of dynamic movements. Therefore, in dynamic exercise modes with superimposed EMS, the impulse intensity need to be adjusted to ensure sufficient movement. 70% of maximum pain threshold is considered practicable and might be more promising, as the subjective feeling of increased remains comfortable (Wirtz et al., 2016; Micke et al., 2018). Dynamic movements with additional EMS can also increase activation levels at different muscle length and during different contraction modes, e.g., during eccentric work phases (Westing et al., 1990). Authors hypothesized that type II muscle fibers remain active during EMS in contrast to the normal continuing de-recruitment of motor units during the eccentric phase. Therefore, the intensification of exercise by superimposed EMS can potentially induce an increase in recruitment of high-threshold motor units.

Technical innovations made EMS progress from a local stimulation to a whole-body training method where several muscle groups can be trained simultaneously through an electrode belt- and vest system (e.g., miha bodytec, Augsburg, Germany). Improved handling and simplified use led to increased recognition of whole-body-EMS (WB-EMS) training for coaches and athletes. Today WB-EMS is used in leisure sports and showed effects in both individual sports (Amaro-Gahete et al., 2018) and field sports on a high-performance level (Filipovic et al., 2016). WB-EMS enables the activation of several muscle groups simultaneously, e.g., muscle chains or agonist/antagonist during multi joint movements. This allows to train strength exercise like squats or sport specific skill exercises like jumps with superimposed WB-EMS that may support a strength transfer to more complex movements.

Strength and performance adaptations are evident for trained subjects by the use of local EMS (Filipovic et al., 2012) and for untrained subjects using WB-EMS (Kemmler et al., 2018). There is however a lack of studies including performance parameters of trained subjects. Therefore, the aim of this study is to provide evidence for the effect of training with superimposed WB-EMS on lower leg strength and power as well as sprint and jump performance in trained subjects. In this regard we conducted a mini-meta-analysis focusing on individual data of 5 recent in-house WB-EMS studies (Dörmann, 2011; Wirtz et al., 2016; Micke et al., 2018; Dörmann et al., 2019; Filipovic et al., 2019). All studies were designed to characterize the impact of superimposed WB-EMS during different exercise conditions. Exercises were designed to improve strength and power of leg muscle chain and to improve jump and sprint performance. All studies included the outcome parameter strength and power of certain leg muscle groups. Furthermore, a high standardization of EMS-adjustments characterizes all studies. Our primary hypothesis was that superimposed WB-EMS favors strength and power of lower limb muscles significantly. Our secondary hypothesis was that WB-EMS favors jumping and sprinting performance significantly.

MATERIALS AND METHODS

Participants

One hundred and twelve male (68%) and female (32%) subjects were included into this mini-meta-analysis ($n = 112$; participants characteristics are presented in **Table 1**). All subjects were moderately trained doing > 2 training sessions/week on a regional to national level in sports that require sprint and/or jump performances (e.g., soccer, handball, basketball, track, and field, tennis). They were examined medically and signed a written consent about the possible risks and benefits of the study. Exclusion criteria were (a) planned absences during the whole study period, (b) any training experience in WB-EMS, (c) current training programs focusing on sprinting and jumping as well as, (d) inadequate technique in the strength exercises. In order to minimize influences of unspecific training loads, all participants were asked to refrain from any changes of their habitual physical activity behavior. Furthermore, all participants were instructed to maintain their normal dietary intake before and during the study.

TABLE 1 | Anthropometric data (mean ± SD).

	N (male/female)	Age [years]	Height [cm]	Weight [kg]	BMI [kg/m²]	Strength training experience [years]
EG	58 (39/19)[a]	21.5 ± 3.3	178.2 ± 7.5	74.0 ± 11.2	23.2 ± 2.5	5.4 ± 3.7
CG	54 (37/17)[b]	21.0 ± 2.3	179.0 ± 8.5	72.6 ± 9.8	22.6 ± 2.1	4.4 ± 2.9

[a] *Dörmann et al. (2011) (5/2); Dörmann et al. (2019) (0/10); Micke et al. (2018) (14/7); Filipovic et al. (2019) (10/0); Wirtz et al. (2016) (10/0).*
[b] *Dörmann et al. (2011) (5/2); Dörmann et al. (2019) (0/11); Micke et al. (2018) (12/4); Filipovic et al. (2019) (10/0); Wirtz et al. (2016) (10/0).*

The study protocols were approved by the "Ethics Committee of the German Sport University Cologne" and complied with the Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects."

Study Design

The aim of the current mini-meta-analytical review was to compare the pooled favorable effects of submaximal, superimposed dynamic WB-EMS (EG) with the effects of dynamic athletic training without WB-EMS (CG) on (1) strength and power performance as well as on (2) sprinting and jumping performance. To adequately address our hypothesis we conducted individual data analysis derived from 5 randomized controlled trials (RCT) with parallel group designs (WB-EMS vs. active control) carried out between 2010 and 2017 by the Institute of Training Science and Sport Informatics, German Sport University Cologne, Germany. For the present meta-analysis, we initially selected in-house studies that (1) included trained subjects aged 18–30 years training on regional to national level and had at least 2 years of strength training experience but NO previous WB-EMS experience; (2) applied a randomized controlled trial (RCT) approach with parallel group designs (WB-EMS vs. active control); randomization by minimization method (strata: age, gender, strength training experience); (3) applied a WB-EMS protocol for 4–8 weeks with 2 training sessions per week; (4) conducted the same test settings for sprint, jump, power and strength diagnostics. Eligibility and study quality [Physiotherapy Evidence Database (PEDro) scale] were assessed (**Table 2**).

Training Procedure

For detailed training procedures of the single trials, the reader is kindly referred to the corresponding studies. Studies conducted squats (Wirtz et al., 2016), squats and lunges (Dörmann et al., 2011), squat jumps (Filipovic et al., 2019) or different strength and conditioning exercises such as squats, lunges, nordic curl, skippings, heelings, lateral, horizontal, and vertical jumps (Micke et al., 2018; Dörmann et al., 2019) (**Table 3**). These exercises followed the recommendations to increase sprinting and jumping performance (Young, 2006; Stojanovic et al., 2017).

All studies implemented an active control group that completed the same exercise protocol without superimposed WB-EMS. All studies had a standardization procedure using the same parameters for both tested groups (EG and CG) like exercises, number of repetitions, number of sets, range of motion, movement velocity, and rate of perceived exertion. In general, all participants completed 8–16 training sessions during a 4–8 week period conducting 2 training sessions per week with a total intervention time under tension between 32 and 113 min.

All WB-EMS interventions complied with the guidelines for a safe and effective WB-EMS training (Kemmler et al., 2016). The miha bodytec system (Augsburg, Germany) was employed as EMS device (cf. Kemmler et al., 2012). The application unit was connected via electrical cords to a stimulation vest and belts. Thereby, bilaterally paired surface electrodes were integrated. 8 muscle areas could be stimulated synchronously with freely selectable impulse intensities (0–120 mA) for each pair of electrodes. In our studies, 3 paired electrodes were applied around the muscle belly of the lower legs (27 cm length × 4 cm width), the thighs (44 × 4 cm) and at the buttocks (13 × 10 cm). Additionally, the upper body was stimulated with 2 bilaterally paired electrodes integrated in the stimulation vest at the lower back (14 × 11 cm) and abdominals (23 × 10 cm).

The WB-EMS adjustments as well as the progression for the conventional strength and conditioning programs were equal for all interventions. The intensity of each exercise set was controlled by Borg Rating of Perceived Exertion (RPE) (Tiggemann et al., 2010). If a set was no longer exhaustive (RPE <16 "hard") the intensity was raised and by increasing additional loads or the use of stiffer rubber bands and by higher amperage for EG. The WB-EMS impulse frequency was set at 85 Hz, the impulse width at 350–400 μs, the impulse type as bipolar and rectangle. The intensity of WB-EMS was adjusted to 70% of the individual pain threshold (iPT = maximum tolerated amperage, 0–120 mA). The iPT was verified separately for each pair of electrodes before each session. The participants stood with an inner knee angle of 170° while tensing their muscles voluntary. The verification of iPT began increasing current to iPT at the buttock, followed by the thigh, the lower leg, the abdominal, and the lower back. Then, the intensity was subsequently downregulated using the main controller at the WB-EMS device to an intensity of 70% to enable dynamic movements.

Testing Procedure

Strength and Power Testing

Strength and power diagnostics took place on the Leg Curl (LC), the Leg Extension (LE), and the Leg Press (LP) machine (Edition-Line, gym80; Gelsenkirchen, Germany). Those were equipped with the digital measurement equipment Digimax (mechaTronic; Hamm, Germany). The software IsoTest and DynamicTest 2.0

TABLE 2 | PEDro scores and sum of the included study scores.

References	Eligibility specified	Subjects randomly allocated	Concealed allocation	Similar baseline values	Blinding of subjects	Blinding of therapist	Blinding of assessor	Dropout <15%	Received treatment as allocated	Statistical between-group comparison	Point measures and variability provided	Sum
Dörmann et al. (2011)	✓	✓	–	✓	–	–	–	✓	✓	✓	✓	7
Dörmann et al. (2019)	✓	✓	–	✓	–	–	–	✓	✓	✓	✓	7
Filipovic et al. (2019)	✓	✓	–	✓	–	–	–	✓	✓	✓	✓	7
Micke et al. (2018)	✓	✓	–	✓	–	–	–	✓	✓	✓	✓	7
Wirtz et al. (2016)	✓	✓	–	✓	–	–	–	✓	✓	✓	✓	7

enabled the measurement of the peak force F_{max} and the peak power P_{max} (5 kN strength sensor typ KM1506, distance sensor typ S501D, megaTron; Munich, Germany). The sensors were installed in line with the steel belt of the machines that lifts the selected weight plates.

Diagnostic procedures consisted of 3 isometric trials as well as 3 isoinertial trials on LE, LC, and LP. Isometric attempts were conducted at an inner knee angle of 120° on LE and LP as well as of 150° on LC. The instruction was to press as forcefully and as fast as possible against the fixed lever arm. This enabled the determination of knee joint angle-dependent force-time curve during explosive maximum voluntary contraction. Concerning isoinertial tests, the participants were requested to move the lever arm as forcefully and as fast as possible over the complete concentric range of motion (ROM). This enabled the examination of knee joint angle-dependent power-load curve during explosive maximum voluntary leg extension on LP, knee extension on LE or knee flexion on LC. The concentric ROM corresponded to 90–180° inner knee angles on LP and LE as well as to 170–80° inner knee angles on LC. Additional load (AL) was calculated individually as a percentage of an isometric attempt at starting position of isoinertial tests. These were 90° on LP and LE as well as 170° on LC. Three attempts were conducted with 40% AL on LE and LC as well as 3 attempts with 60% AL on LP. The rest was defined as 60s between every single trial and 3 min between the different test types. The parameters F_{max} [N] and P_{max} [W] were calculated for statistical analysis and data presentation as best performance data. Reliability was determined by the coefficient of variation (CV) and the intraclass correlation coefficient (ICC) for parameters force (F) (CV < 8%; ICC 0.95–0.97), as well as for power (P) and power factors (F·V) (CV < 9%; ICC 0.84–0.97) for all used machines (Dörmann, 2011).

Sprint Testing

Sprint testing involved a 20 m sprint. The test was performed with a self-initiated standing start with no hopping or backward movement prior the start. Double infrared photoelectric barriers (DLS/F03, Sportronic; Leutenbach-Nellmersbach, Germany) were used to measure the time. The best sprinting time out of 2 attempts was used for subsequent analysis. The participants had 2 min rest between the trials. Sprint running performance tests (linear and change of direction) were shown as highly relative reliable (CV 1–6%; ICC 0.80–0.96) (Green et al., 2011).

Jump Testing

Following one familiarization jump trial, the participants performed 3 counter movement jumps (CMJ). The participants were instructed to start jumping from an upright standing position, squatting down to a knee angle of approximately 90° in order to jump as high as possible. Hands had to remain in the akimbo position for the entire movement of each jump to minimize the influence of arm swing. The highest jump was used for subsequent analysis. The Optojump system (Microgate; Bolzano, Italy) was used to verify jump height by the flight time method. It is based on measurements of optical light emitting diodes. Optojump based jump height was

TABLE 3 | Overview of the included studies.

References	Study design	Sample: population; sample size (n); age, y (mean ± SD)	Groups	Intervention	Training characteristics	Outcome measures	Study quality (PEDro score)
Dörmann et al. (2011)	Randomized controlled trial, two arms	Healthy sport students, $n = 14$; 21.3 ± 1.7 y	EG ($n = 7$) CG ($n = 7$)	Supervised training: (a) WB-EMS superimposed to squat exercises (b) Squat exercise with additional loads (10RM)	4 weeks, 2 sessions/week; 3 exercises/session, 3 sets, total net exercise time: 72 min	F_{max} and P_{max} at Leg Curl and Leg Press Machine; Linear Sprint time; counter movement jump height	7
Dörmann et al. (2019)	Randomized controlled trial, two arms	Healthy sport students, $n = 21$; 19.7 ± 1.7 y	EG ($n = 10$) CG ($n = 11$)	Supervised training: (a) WB-EMS superimposed to squat exercises, nordic curl, sprint and jump training (b) Squat exercise (10 RM), sprint and jump training	4 weeks, 2 sessions/week; 4–5 exercises/session, 3 sets, total net exercise time: 91 min	F_{max} and P_{max} at Leg Curl, Leg Extension and Leg Press Machine; Linear Sprint time; counter movement jump height	7
Filipovic et al. (2019)	Randomized controlled trial, two arms	Healthy sport students, $n = 20$; 24.4 ± 4.0 y	EG ($n = 10$) CG ($n = 10$)	Supervised training: (a) WB-EMS superimposed to jump training (b) Jump training	8 weeks, 2 sessions/week; 1 exercise/session, 3 sets, total net exercise time: 32 min	F_{max} and P_{max} at Leg Curl, Leg Extension, and Leg Press Machine; counter movement jump height	7
Micke et al. (2018)	Randomized controlled trial, two arms	Healthy sport students, $n = 37$; 20.8 ± 2.1 y	EG ($n = 21$) CG ($n = 16$)	Supervised training: (a) WB-EMS superimposed to squat exercises, Nordic curl, sprint and jump training (b) Squat exercises, Nordic curls, sprint and jump training	8 weeks, 2 sessions/week; 4–5 exercises/session, 3 sets, total net exercise time: 113 min	F_{max} and P_{max} at Leg Curl, Leg Extension, and Leg Press Machine; Linear Sprint time; counter movement jump height	7
Wirtz et al. (2016)	Randomized controlled trial, two arms	Healthy sport students, $n = 20$; 22.1 ± 1.9 y	EG ($n = 10$) CG ($n = 10$)	Supervised training: (a) WB-EMS superimposed to squat exercises with additional loads (10 RM) (b) Squat exercise with additional loads (10 RM)	6 weeks, 2 sessions/week; 1 exercise/session, 4 sets, total net exercise time: 48 min	F_{max} and P_{max} at Leg Curl, Leg Extension, and Leg Press Machine; Linear Sprint time; counter movement jump height	7

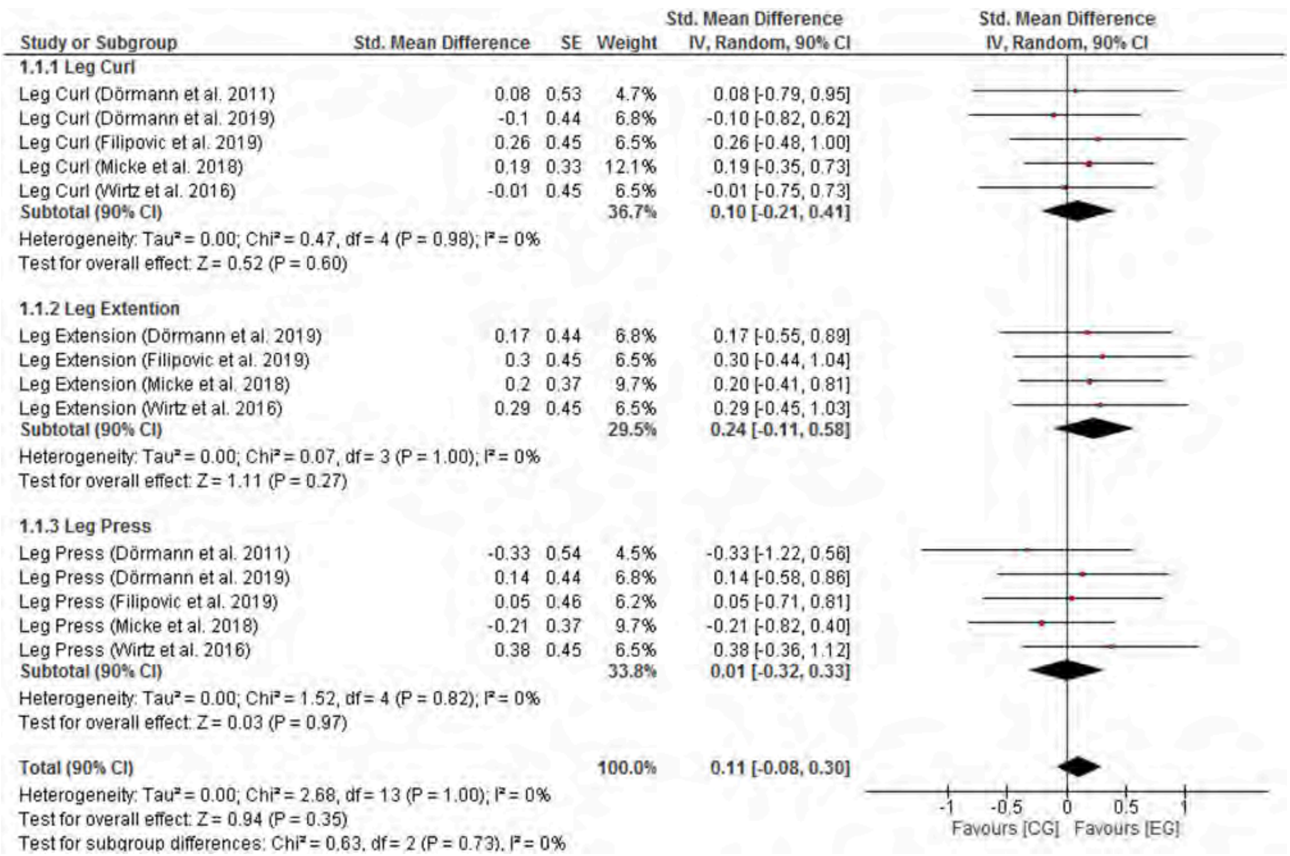

FIGURE 1 | Fmax for CG vs. EG. SE, standard error; CI, confidence interval; Std., standardized; IV, independent variable.

shown as highly relative reliable (CV < 3% and ICC > 0.9) (Glatthorn et al., 2011).

Statistical Analysis

Standardized mean differences (SMD, with 90% confidence intervals) were computed for each study using the adjusted Hedges' g (Equation 1). This adjustment takes small sample biases into account. The Cochrane Review Manager Software (RevMan 5.3.5, Cochrane Collaboration, Oxford, UK) was used to compute the inverse-variance method according to Deeks and Higgins (2010). Analyses were conducted with a random effects model (Borenstein et al., 2010). Forest plots were generated for each outcome category (performance, physical performance surrogates and psychological variables). The magnitude of effect sizes was classified according to the following scale: 0–0.19 = negligible effect, 0.20–0.49 = small effect, 0.50–0.79 = moderate effect and 0.80 = large effect (Cohen, 1988).

Equation 1: Equation to calculate standardized mean differences (SMD) adjusting for small sample sizes.

$$SMD_i = \frac{m_{1i} - m_{2i}}{s_i}\left(1 - \frac{3}{4N_i - 9}\right) \quad (1)$$

RESULTS

Strength and Power

Negligible effects with low heterogeneity were found for F_{max} leg muscle groups [SMD: 0.11 (90% CI: −0.08, 0.33), $p = 0.73$, $I^2 = 0\%$; **Figure 1**)]. Negligible effects with low heterogeneity were also found for P_{max} leg muscle groups [SMD: 0.12 (90% CI: −0.07, 0.30), $p = 0.90$, $I^2 = 0\%$; **Figure 2**].

Linear Sprint

Small effects with low heterogeneity were found for linear sprint [SMD: 0.22 (90% CI: −0.15, 0.60), $p = 0.77$, $I^2 = 0\%$; **Figure 3**] in favor of EG to CG.

Counter Movement Jump

Neglibible effects with low heterogeneity were found for CMJ height [SMD: 0.01 (90% CI: −0.34, 0.33), $p = 0.81$, $I^2 = 0\%$; **Figure 4**]. Data of all analyzed parameter are summarized in supplementary material (**Data Sheet 1–4**).

DISCUSSION

This meta-analysis investigated the pooled effect sizes of superimposed WB-EMS in comparison to conventional strength and conditioning training on (1) strength and power of

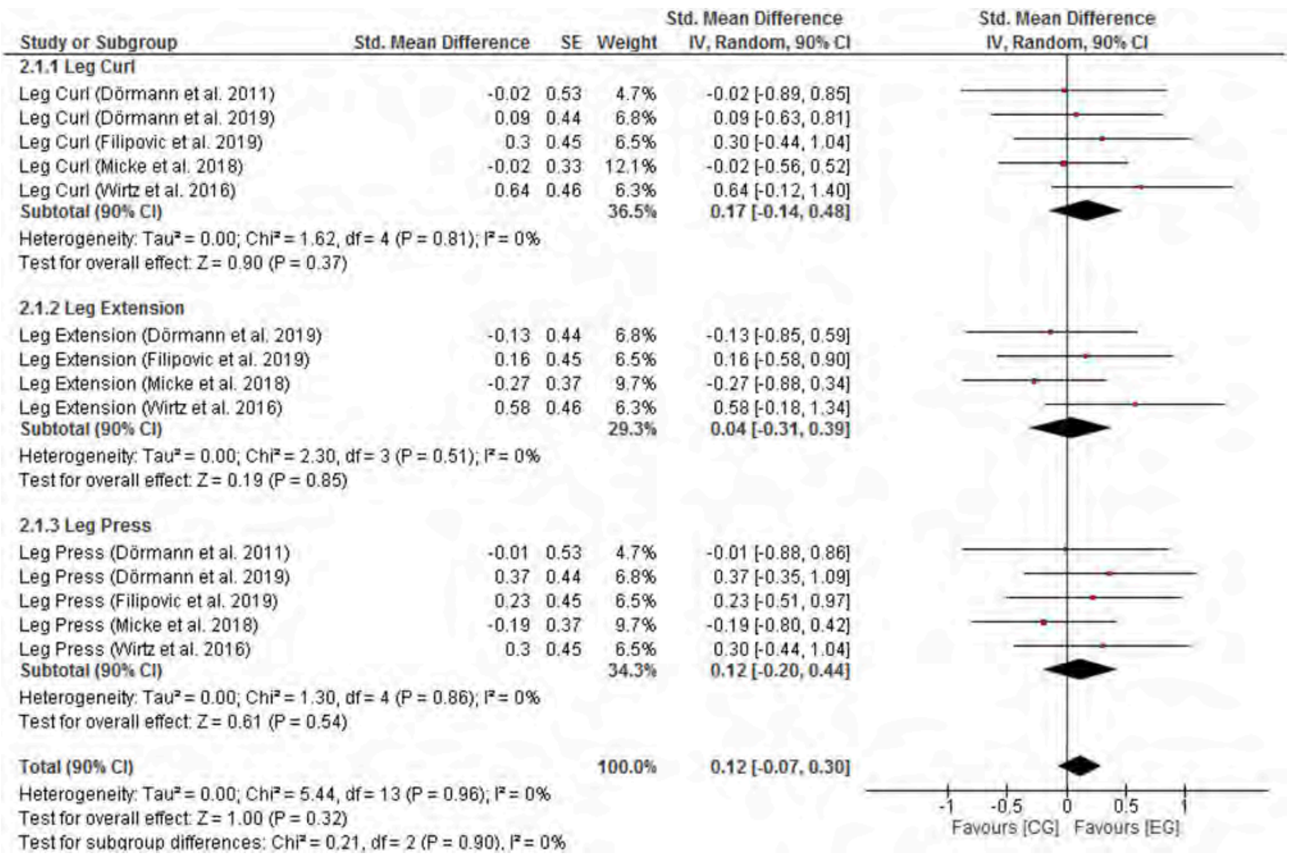

FIGURE 2 | Pmax for CG vs. EG. SE, standard error; CI, confidence interval; Std., standardized; IV, independent variable.

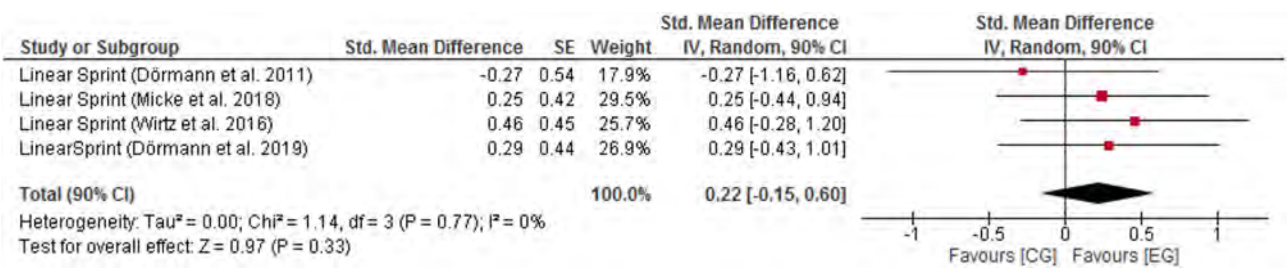

FIGURE 3 | Linear sprint for CG vs. EG. SE, standard error; CI, confidence interval; Std., standardized; IV, independent variable.

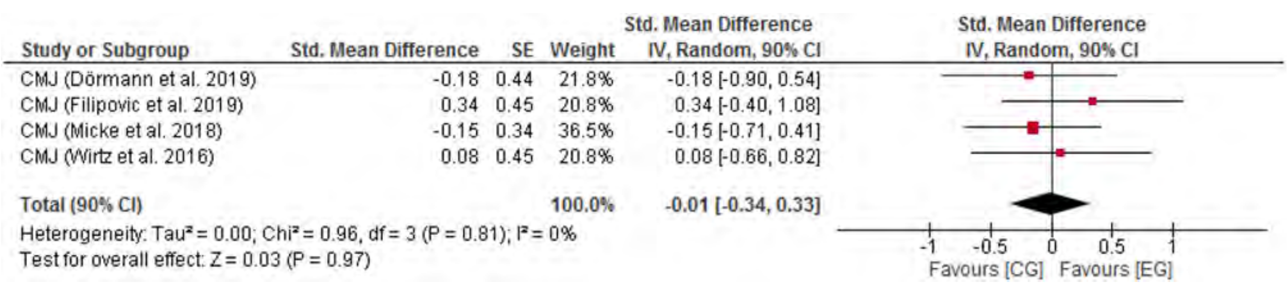

FIGURE 4 | Counter Movement Jump for CG vs. EG; SE, standard error; CI, confidence interval; Std., standardized; IV, independent variable.

lower limb muscles as well as on (2) jumping and sprinting performance. Our analyses rely on findings of five homogenous studies of overall high study quality of our work group. It was hypothesized that additional superimposed WB-EMS may lead to favorable strength and power improvements of lower limb muscles as well as increases in jumping and sprinting performance compared to training without WB-EMS.

The main findings indicate that superimposed WB-EMS did not lead to superior effects of strength and power of lower limb muscle groups and jumping performance. Interestingly, sprint performance benefited with small but meaningful effects when applying WB-EMS. Generally, PEDro score analyses of the included studies revealed a "low risk of bias." Blinding of participants and personnel is difficult in exercise studies in general and WB-EMS investigation in particular. Promoting evidence-based WB-EMS training programs requires studies that consider intention to treat analysis, blinding assessors, and reporting the risk of co-interventions. Future studies should account for these quality criteria.

Our pooled data analyses do not corroborate superior effects of WB-EMS on certain muscle groups. A small effect was merely observed for F_{max} for leg extension, but not for leg curl and leg press or LP. These results are surprising as leg extension exercise, such as squats were included in each intervention in both groups (EG and CG). The application of superimposed WB-EMS might beneficially affect maximal strength of the quadriceps muscles when additional motor unit recruitment with (a) a continuous and exhausting contractile activity in the same pool of motor units during the entire exercise period, (b) a supramaximal temporal recruitment imposed by the high stimulation frequency chosen, and (c) a synchronous recruitment of neighboring muscle fibers might account for these strength gains (Requena Sánchez et al., 2005) is guaranteed. Nevertheless, the overall effects are close to the zero-line of the forest plot and it would be speculative to assume that a higher sample sizes or longer application time lead to differential results. However, one study showed muscle group-specific adaptations of hamstring power after squats with superimposed WB-EMS (Wirtz et al., 2016). Despite notable co-activation (Zink et al., 2001), it has been reported that the activation of hamstring muscles is not affected by additional loading during squat exercise (Nuzzo and McBride, 2013). EMS can lead to higher hamstring muscle activation during lengthening and shortening, which would then results in higher hamstring maximum force in the WB-EMS training group. One potential explanation for these inconsistent results could be that the different underlying exercises and populations of the included studies, such as squats (Wirtz et al., 2016), jumps (Filipovic et al., 2019) or different strength and conditioning hamstring exercises (Micke et al., 2018) increase variability of the occurrence and magnitude of potential effects. Available evidence on the adaptability of the hamstrings employing WB-EMS independent from the type of exercise is needed and would provide specific insights into WB-EMS use to strengthen the hamstrings and to possibly prevent injuries. Particularly hamstring strains are reported to be the most prevalent muscle injury in various team and sprint related sports (Goode et al., 2015).

The simultaneous activation of (1) multiple muscle groups and (2) agonistically and antagonistically working muscles through WB-EMS combined with strength and training exercises was repeatedly reported to have the potential to improve sport-specific skills such as sprinting and jumping. Although WB-EMS triggers a seemingly counterproductive firing of the agonist and antagonist, a voluntary contraction reduces relative co-activation of antagonistic muscles, in order to continue the required dynamic exercise. Indeed, available data do not suggest such effects during superimposed WB-EMS for jumping performance. Thus, it might be beneficial to focus on specific jump exercise with superimposed EMS (Filipovic et al., 2019). In line with this reasoning, one study with professional soccer players revealed that jumps with superimposed WB-EMS in addition to soccer training sessions can be effective for jump improvements (Filipovic et al., 2016). Overall, it appears to be plausible to assume that exercise specificity and the training status of the participants affect the effects of superimposed WB-EMS. Potential improvements by the use of maximal and locally applied EMS also rely on training specificity, such as combined plyometric training (Herrero et al., 2006) and sport specificity on a higher level in sports with numerous jumps like volleyball (Malatesta et al., 2003; Voelzke et al., 2012) or basketball (Maffiuletti et al., 2000). For sprinting performance, however, minor effects could be found. The results of linear sprint are in accordance with studies that applied isometric local EMS with additional separately performed strength and sprint training sessions: One study reported improvements of 10 m skating time for 2nd league ice hockey players, who trained on ice parallel to training intervention, what could elicited utilization effects (Brocherie et al., 2005). It is however reasonable that effects of WB-EMS on sprinting performance as well as jumping performance could depend on athletes' training status.

However, some limitations of the present study need to be addressed that should be considered for further research on WB-EMS. One is seen in the small sample sizes of each included studies. However, outcomes and assessment over all studies are very homogenous. Although we intended to increase the cumulative power by pooling the data, a compiled and robust effect cannot be found. Although minor improvement in top level athletes can be considered relevant, negligible additional benefits from WB-EMS in comparison to conventional training can be summarized. Ultimately, WB-EMS provides a variety of different training stimuli but a notable transfer of the results to top level athletes is speculative. Furthermore, the lack of data after a detraining phase hamper an identification of delayed effects that could potentially occur. The adaptations of WB-EMS over time need to be further investigated and concepts for periodization in high performance sports also including WB-EMS need to be developed. A further limitation is seen in the inclusion of both genders. Although Maffiuletti et al. (2008) demonstrated that supra-motor thresholds were significantly lower in women than in men, contrary to the expected constitutional differences like subcutaneous fat thickness, women showed no significant differences at motor threshold. However, the subjective tolerance to current intensity remains a key limiting factor of WB-EMS, regardless of sexes (Gregory and Bickel, 2005). Nevertheless, we did not focus on sex differences in trainability. Further limitations are seen in the different designs for lower limb exercises in the studies and the different intervention duration (4–8 weeks) that result in 8–16 total training sessions. However, 4–8 weeks can be regarded as a common and reasonable meso-cycle within periodization considerations.

Only few drop-outs occurred independent of the WB-EMS intervention and an attendance rate of 100% for all of the 112 included participants was observed and no adverse event was reported. Current intensities around 70% of maximum pain threshold that enables movement complied with the safety recommendations published by Kemmler et al. (2016). This is particularly important with regard to cases of rhabdomyolysis after WB-EMS training at maximum intensity with professional soccer players (Kastner et al., 2015).

Finally, we can conclude that WB-EMS is a feasible complementary training stimulus for performance enhancement. Additional effects of WB-EMS on relevant strength, power and performance indices seem limited. Longer training periods and more frequent application times and a slightly larger stimulus could be investigated in larger studies in order to further elucidate beneficial effects of WB-EMS on crucial performance parameters in athletes.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

AUTHOR CONTRIBUTIONS

UD, NW, FM, AF, and HK conceived and designed research. UD, NW, FM, and AF conducted experiments. UD, LD, and NW analyzed data. NW, LD, and UD wrote the manuscript. HK, UD, NW, FM, AF, and LD revised the manuscript. All authors read and approved the manuscript.

FUNDING

Three of the studies under consideration were funded by the German Federal Institute of Sport Science on behalf of the Federal Ministry of the Interior of Germany as the major funding bodies (Wirtz et al., 2016: BISp AZ 070509/13; Micke et al., 2018: ZMV I 1-070506/14-16; Filipovic et al., 2019: ZMV I 4-070101/16/17). All studies were funded by the Department of Intervention Research in Exercise Training, Institute of Exercise Training and Sport Informatics, German Sport University Cologne, Cologne, Germany.

ACKNOWLEDGMENTS

The authors would like to acknowledge the time and effort of all participants involved in this investigation.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphys.2019.01336/full#supplementary-material

Data Sheet 1 | Fmax pre-post in Leg Curl (LC), Leg Extension (LE), and Leg Press (LP) for CG and EG (mean, standard deviation, difference pre-post in %, effect sizes pre-post and standard error).

Data Sheet 2 | Pmax pre-post in Leg Curl (LC), Leg Extension (LE), and Leg Press (LP) for CG and EG (mean, standard deviation, difference pre-post in %, effect sizes pre-post and standard error).

Data Sheet 3 | Sprint time 20 m pre-post for CG and EG (mean, standard deviation, difference pre-post in %, effect sizes pre-post and standard error).

Data Sheet 4 | Jump high pre-post for CG and EG (mean, standard deviation, difference pre-post in %, effect sizes pre-post and standard error).

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

MINI REVIEW
published: 29 November 2019
doi: 10.3389/fphys.2019.01461

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(Whole-Body) Electromyostimulation, Muscle Damage, and Immune System: A Mini Review

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Exercise-induced muscular damage (EIMD) is a well-known phenomenon in exercise medicine that is closely related to the type and intensity of training, with especially eccentric training content providing various physiological irritations, including mechanical as well as metabolic. Besides the increase in markers of muscular damage, such as creatine kinase (CK) and myoglobin (Mb), several physiological shifts trigger a kind of stepwise repair chain reactions lasting over a time course from several hours to days. Subsequent inflammatory processes are closely related to muscular damage with decisive influence on physiological repair mechanisms, as indicated by an increased invasion of immune cells and typical patterns of pro- and anti-inflammatory cytokines. Previously, whole-body electromyostimulation (WB-EMS) showed significant, partly extreme distractions in markers of muscular damage lasting over several days. Because of the large area of stimulated muscle mass and a relatively high proportion of eccentric movements, initially too intense WB-EMS is predisposed to produce serious changes on several physiological levels due to its unfamiliar muscular strain. Therefore, it is the aim of this short review to focus on the possible immunological side effects of this aspiring training technology. As the number of original investigations in this field is rather small, we will include data from other studies about the relation of exercise-induced muscle damage and immune regulation.

Keywords: whole-body electromyostimulation, eccentric, cytokine, training, exercise-induced muscle damage

Edited by:
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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *10 May 2019*
Accepted: *12 November 2019*
Published: *29 November 2019*

Citation:
Teschler M and Mooren FC (2019) (Whole-Body) Electromyostimulation, Muscle Damage, and Immune System: A Mini Review. Front. Physiol. 10:1461. doi: 10.3389/fphys.2019.01461

INTRODUCTION

Recently, whole-body electromyostimulation (WB-EMS) has shown to be an effective tool in order to improve muscle strength outcome measurements in deconditioned subjects (Kemmler et al., 2016b, 2017). However, a too intense initial application has been accompanied by some severe side effects. A few case reports have characterized substantial muscle damage and rhabdomyolysis following just one single training session of WB-EMS (Kastner et al., 2014; Finsterer and Stollberger, 2015; Hong et al., 2016; Herzog et al., 2017). In fact, recent studies showed an extreme increase of markers of muscle damage, such as creatine kinase (CK) and myoglobin (Mb) (Teschler et al., 2016; Kemmler et al., 2016a). Symptoms and loss of function during the next hours respectively days following these peak values involved the usual conditions of exercise-induced muscle damage: loss of muscle strength and power, delayed onset of muscle soreness, swelling, reduced range of motion and systemic increases of myocellular enzymes and proteins, or a combination of these (Hyldahl and Hubal, 2014). Frequently, these symptoms last for at least up to 72 h, depending on the volume of muscle-damaging exercise and the extent of disruption of subcellular structures (Fatouros and Jamurtas, 2016).

Such a destruction of tissue and cellular structure is answered by an inflammatory process. This involves a cascade of physiological processes presenting inflammation as a complex interaction of cellular signals and responses (Scott et al., 2004) which initiate subsequent tissue repair and remodeling. The recovering process is dependent on a fine tenement and communication of different cell types such as inflammatory cells (e.g., neutrophils, macrophages); satellite cells (muscle stem cells); vascular cells (e.g., pericytes); and stromal cells (e.g., fibroblasts) (Peake et al., 2017).

The aim of this mini review is (1) to characterize and summarize the basics and key elements of (WB-)EMS, (2) to explore exercise-induced muscle damage and its impact on parameters of the immune system (3) in order to derive conclusions for a reasonable WB-EMS application to avoid negative physiological effects with a special view on immunological effects.

In order to adequately get to the bottom of these questions, we use articles published on Pubmed with relevance to keywords, muscle damage, eccentric, training, exercise, whole-body, electromyostimulation, WB-EMS, cytokine, immunology.

BASICS OF ELECTROMYOSTIMULATION

The terms electromyostimulation or electrical muscular stimulation (EMS) describe a non-invasive option to stimulate and amplify voluntary muscular contractions. For decades, the use of artificial muscle contractions has been used by physical therapist during rehabilitation processes to postoperatively preserve individual, mostly isolated local muscle groups. Furthermore, EMS is used in the treatment of sports injuries (Lake, 1992), post exercise recovery (Babault et al., 2011; Nedelec et al., 2013) as well as improving athletic performance (Maffiuletti et al., 2000, 2007; Malatesta et al., 2003; Brocherie et al., 2005; Herrero et al., 2005; Babault et al., 2007; Billot et al., 2010).

For more detailed information on local EMS, see Dehail et al. (2008) and Filipovic et al. (2011, 2012).

Whole-Body Electromyostimulation

Basically, WB-EMS uses the same physical principle as local electromyostimulation. However, it addresses large muscle groups across the whole body. Instead of reaching just one muscle group, WB-EMS stimulates a muscle area up to 2,800 cm^2 (Kemmler and von Stengel, 2013) and allows the optional simultaneous stimulation of different muscle groups usually involving the chest, the abs, and back muscles as well as arms, buttocks, and thighs (see **Figure 1**).

Via control module, each single muscle group can separately be controlled, a necessity, as each muscle group has a different impulse sensitivity toward impulse intensity, but also to pain. This depends on the muscular surface and insulation of the muscle by body fat, but also on different pre-activated "starting" positions during various movement patterns performed.

A common training protocol of WB-EMS consists of ~1.5 training sessions per week, each lasting just ~20 min. Despite the low expenditure of net-training time, several studies show significant positive effects on parameters of body composition, especially body fat reduction, strength and power abilities (Kemmler et al., 2010, 2015b,c, 2018; Filipovic et al., 2012). Based on these investigations, the use of a bipolar low-frequency protocol (frequency: 85 Hz, pulse width: 350 μs) is considered as effective for optimal health and training purposes.

Almost all WB-EMS studies use an electrical load ratio of 4–6 s of current vs. 4 s of rest interval (Filipovic et al., 2012; Kemmler et al., 2015b), meaning 10–12 min under load with 8–10 min of rest. The current phase usually characterizes the start of one single repetition, seen in a slow eccentric but joint-friendly and functional full-body movement pattern in manageable range of motion, which makes the training also accessible for people with orthopedic limitations. The rest interval (without current) usually represents the concentric part of the movement to complete the repetition, meaning the (quick) return to the original starting position to recover. An exemplary selection of exercises is shown in **Table 1**. One training session is therefore defined by the load ratio, while the participants usually go through 1–2 sets with 8–10 exercises and 8–10 repetitions each (Kemmler et al., 2015b,c).

Treatment With Whole-Body Electromyostimulation

Besides the evaluated positive effects of WB-EMS, some articles report of negative side effects and simultaneously show that EMS is independent of training status (Kastner et al., 2014; Finsterer and Stollberger, 2015; Hong et al., 2016; Herzog et al., 2017). In fact, conducted studies confirmed the symptoms of WB-EMS-induced muscle damage reflected by increases in serum creatine kinase (CK) (Kemmler et al., 2015a; Teschler et al., 2016). Depending on subject groups and their individual training regime, different levels of intensity have been applied. Thus, CK levels after WB-EMS training can range from 1,000 up to 240,000 U/L (Fritzsche et al., 2010; Wahl et al., 2012, 2015; Kastner et al., 2014; Finsterer and Stollberger, 2015; Wirtz et al., 2015; Kemmler et al., 2015a; Filipovic et al., 2016; Hong et al., 2016; Teschler et al., 2016; Herzog et al., 2017) peaking from 72 to 96 h post-exercise (Kemmler et al., 2015a; Teschler et al., 2016). Especially the top levels of this CK range may indicate muscle cell necrosis or severe tissue damage respectively rhabdomyolysis (Baird et al., 2012), which usually cannot be achieved by voluntary training (Yu et al., 2013).

Besides the large volume of muscle mentioned above, and the repetitive activation pattern of the same muscle fibers

FIGURE 1 | miha bodytec© WB-EMS equipment; from left to right: vest; cuffs for glute, arm, and legs; control device (Permissions were obtained from the copyright holders of the miha bodytec© product for the use for research purposes).

TABLE 1 | Exemplary selection of exercises (1–5) performed during WB-EMS with a detailed description of the individual phases of one single repetition (eccentric and concentric).

	Current interval (eccentric)	Non-current interval (concentric)
1.	Squat (4–6 s) and vertical chest press	Squat (4 s up) and vertical rowing
2.	Squat (4–6 s) and latissimus pulldown	Squat (4 s up) with military press
3.	Lunge (4–6 s) with arm-rowing	Lunge (4 s up) with chest press
4.	Squat (4–6 s), crunch with butterfly	Squat (4 s up) and reverse fly
5.	Squat (4–6 s) and trunk flexion (crunch)	Squat (4 s up) and trunk extension

(Gregory and Bickel, 2005), the underlying decisive but avoidable error in dealing with WB-EMS is the combination of two aspects: (1) type of contraction: WB-EMS uses an increased ratio of eccentric muscular load during each single repetition; and (2) intensity of stimulus: the WB-EMS application may be too intense for the often unaccustomed user. Regarding the practical application of WB-EMS, the focus is usually on the current phase, in which the eccentric part of one single repetition is carried out. Since eccentric workouts are known for higher muscle damage (see section "Exercise-Induced Muscle Damage"), the combination with very intense additional stimulation can especially harm novices more severely.

This misuse of initially intense WB-EMS exposure with corresponding possible severe medical/health-related side effects is meanwhile well examined (Kemmler et al., 2015a; Teschler et al., 2016) and has led to the development of safety guidelines for training with WB-EMS (Kemmler et al., 2016a). Comparable to conventional strength training programs, the guidelines recommend a reduced initial WB-EMS load and the necessity to carefully increase intensity over time. WB-EMS follows the same muscular adaptation principles as seen after conventional strength training protocols. Aldayel et al. (2010) showed a significant reduction of markers of muscle damage already after a second bout of stimulation, as a recent 10-week intervention (1 intense WB-EMS session/week) ultimately showed only moderate enhanced CK levels even after one final WB-EMS session to exhaustion (Kemmler et al., 2015a; Teschler et al., 2016).

EXERCISE-INDUCED MUSCLE DAMAGE AND ITS PHYSIOLOGICAL CONSEQUENCES

Exercise-Induced Muscle Damage

The phenomenon of exercise-induced muscle damage (EIMD) is based on an unaccustomed exercise load in relation to the individual's training status. Thereby, the exercise load may be too intense and/or too frequent and can be followed by a set of symptoms (Paulsen et al., 2012) such as force loss, pain, and stiffness. Those are summarized as the delayed onset of muscle soreness (DOMS), which is biochemically characterized by the release of muscle proteins such as CK and Mb into the circulation (Hyldahl and Hubal, 2014). Tissue histology shows microtrauma to the muscle fiber with the characteristic loss of sarcomere structure such as z-line streaming. Their time courses vary due to the expression of EIMD. The severity of injured tissue may vary from the release of affected macromolecules to large tears in z-disks, sarcolemma, and supportive connective tissue, and induce injury to contractile elements and the cytoskeleton (Paulsen et al., 2012; Koch et al., 2014). Often there is no clear relation between clinical symptoms and the degree of tissue injury.

There is still a discussion whether any kind of muscle action (concentric, eccentric, static) can cause muscular damage (Clarkson et al., 1986; Lavender and Nosaka, 2006; Koch et al., 2014). According to literature, lengthening contractions during slow eccentric movements cause the greatest mechanical strain and consecutive myofibrillar disruption (Newham et al., 1983; Gibala et al., 2000; Lee and Clarkson, 2003; Lavender and Nosaka, 2006; Paulsen et al., 2012; Peake et al., 2017). Different approaches define muscle damage by assessing the change in force development and histological observations. However, the correlation between these parameters often is not very high. The transient ultrastructural myofibrillar disorders are followed by an efflux of myocellular enzymes and proteins, like CK and Mb into the circulation (Peake et al., 2017). This happens in close relation to duration, intensity, and type of muscular activity (Stein, 1998; Howatson et al., 2005). Although CK levels show a high interindividual variability, their high sensitivity makes CK a considerable marker of severe muscle cell damage, muscle cell disruption, or disease (Brancaccio et al., 2008; Baird et al., 2012).

Mild to moderate EIMD is defined by a force reduction by 20–50% of the one-repetition-maximum (1RM) with total recovery in between 2 and 5 days and CK levels below 10,000 U/L. Pronounced manifestations are characterized by reduced force-capacity above 50% 1RM with serum CK levels rising above 10,000 U/L (Paulsen et al., 2012) including a total recovery phase of longer than 7 days. This range of severe EIMD includes the criteria for a clinically relevant rhabdomyolysis, which is defined as a 50-fold rise in serum CK and muscle necrotic symptoms like pain/tenderness, swelling, weakness, and myoglobinuria (Visweswaran and Guntupalli, 1999; Paulsen et al., 2012; Zutt et al., 2014). Finally, muscle damage is followed by an inflammatory response including cellular infiltration, phagocytosis, and cytokine release (Newham and Jones, 2016).

Exercise-Induced Muscle Damage, Inflammation, and Regeneration

The link between exercise, muscle damage, and inflammatory processes after (eccentric) exercise has been extensively investigated (Paulsen et al., 2012; Hyldahl and Hubal, 2014; Chazaud, 2016). Exercise is a well-accepted modulator of immune cell count and function (Simpson et al., 2015), seen in its capability to mobilize leucocytes, especially neutrophils, into the circulation and prolongate their lifespan *via* different hormonal pathways (Mooren et al., 2012). Meanwhile there is an increased acceptance that the initiated inflammatory process is a mandatory key for muscle repair and regeneration (Chazaud, 2016). Exercise-associated alterations of the hormonal environment such as the catecholamines, adrenaline and noradrenalin, and/or cortisol are important in activating and modulating several types of immune cells (Koch, 2010). Several physiological processes lead to an adaptive remodeling and a renewed homeostasis (Chazaud, 2016) of muscle and connective tissue including the extracellular matrix (ECM) (Mackey and Kjaer, 2017).

The initial physiological stress causes mechanical damage seen in microtrauma in myofibers followed by an invasion of pro-inflammatory macrophages. An early release of further inflammatory mediators leads to vasodilation including subsequent increase in vascular permeability (Sass et al., 2018). This affects injured muscle cells and the adjacent connective tissue leading to tissue swelling and muscle stiffness. Additionally, the training stimulus causes metabolic irritations (e.g., temperature, reduced mitochondrial respiration, lowered pH value, reactive oxygen production). The progressive loss of Ca^{2+} homeostasis happens due to the release from either leaky intracellular stores or the influx across leaky plasma membrane. Such increases of intracellular Ca^{2+} activate Ca^{2+}-dependent proteases such as calpain that is known to degrade contractile proteins and/or excitation-contraction coupling proteins, which is supposed to be one explanation for prolonged force reduction (Kendall and Eston, 2002; Hyldahl and Hubal, 2014; Sass et al., 2018).

Increased intracellular Ca^{2+} causes damage on myofilaments of skeletal muscle (Bingham et al., 1997) also through activation of phospholipase A_2. The induced injury to the sarcolemma is supported by the production of leukotrienes and prostaglandins through free reactive oxygen species (ROS) and/or release of detergent-like lysophospholipids (Armstrong, 1990; Kendall and Eston, 2002). Permeable membrane conditions favor a further efflux of intracellular lysosomal enzymes (Armstrong, 1990; Byrd, 1992; Clarkson and Sayers, 1999).

The post-exercise-initiated regeneration process of muscle tissue is characterized by a stepwise invasion and activation of different types of immune cells. Initially, the muscular cell composition is altered by an evenly doubled number of neutrophils and lymphocytes, a small contribution of monocytes (Koch, 2010), and a 10-fold increase of natural killer cells (Campbell and Turner, 2018). Thereby, the acute and persistent sympathetic nervous activity with increased number of catecholamines plays an important role in recruiting neutrophils and lymphocytes, especially T- and B-cells (β2) *via* expressed α- and β-adrenergic receptors (Peake et al., 2017). In contrast, the post-exercise period is characterized by alternations of an exercise volume-dependent lymphopenia (Kruger and Mooren, 2007).

Neutrophils directly migrate into the inflamed area and start to remove cell debris (phagocytosis). After leaving the circulation, monocytes enter the injured tissue and transform into macrophages (Koch, 2010). These interactions define the first line of defense though increased numbers of neutrophils and pro-inflammatory macrophages (M1) contribute to further muscle injury and further impairment of muscle remodeling and functional recovery due to high cytotoxicity and capacity to lyse muscle cells (Peake et al., 2017).

The high potential of phagocytic cells releases additional ROS with a high oxidizing effect on fats, proteins, nucleic acid, and ECM. These metabolic processes support the inflammatory response and progressive cell damage by promoting the expression of pro-inflammatory cytokines (Pyne, 1994; Best et al., 1999). The alternations in muscle tissue integrity are accompanied by impairments of oxygen supply. This results in a hypoxic atmosphere with decreasing pH value. Here, just certain immune cells are capable to switch to anaerobic metabolism, to survive and to consequently trigger the necessary inflammatory response by cytokines and chemokines (Sass et al., 2018). Lymphocytic B-cells interact with T-helper cells, whereas lymphocytic T-cells accelerate the immune response through cytokine secretion (Koch, 2010). Mediating the communication between different types of cells such as immune, muscle, and ECM cells, the production of cytokines is one of the most important responses to exercise.

Early post-exercise hours (4–24 h) of muscle damage are typified by pro-inflammatory macrophages (M1); extended release of pro-inflammatory cytokines like interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and IL-6; and initiation of myoblast proliferation. Depending on tissue environment, the dynamic phenotype plasticity of macrophages allows a shift from pro-inflammatory (M1) to anti-inflammatory (M2) status – this presents a central part of resolution of an inflammation, influenced by phagocytosis, IL-10 and AMP-activated protein kinase-alpha (AMPK-α). This first step of regeneration attenuates inflammation through production of anti-inflammatory cytokines like IL-10, tumor growth factor-β1 (TGF-β1), and insulin-like growth factor (IFG-1) (Peake et al., 2017).

Twenty-four hours post EIMD, the rise in anti-inflammatory macrophages (M2), CD8- and T-regulating lymphocytes promotes further anti-inflammatory cytokines and macrophages, increasing myoblast and satellite cell (SC) proliferation. The activation of stromal cells (fibro-adipogenic progenitors, pericytes) supports the myoblast differentiation. Muscle regeneration as a process of increased muscle protein synthesis is characterized by increased numbers of SC that subsequently proliferate, differentiate, and enter damaged myofibers either to heal fibers or to synthesize new fibers (Fatouros and Jamurtas, 2016). In this regard, Crameri et al. (2007) found histological evidence for significant increased numbers of myofiber proteins and SC markers in electrically stimulated leg muscles compared to voluntarily trained ones. The invasion of macrophages, which contribute to SC proliferation, their differentiation into myoblasts, and forming of new myotubes, thus presents the necessary prerequisite for muscle regeneration (Kendall and Eston, 2002).

As seen, exercise is a potent effector of several leucocyte functions such as oxidative burst, phagocytosis and, with increasing importance, the expression of cytokines. The role of cytokines in intercellular signaling processes has been rewritten by findings that show that tissues besides the classical immunological tissues are able to release cytokines (Munoz-Canoves et al., 2013). As muscle tissue has been shown to be a major source of interleukin-6 (IL-6) during exercise, these most prominent alternations led to the acceptance of IL-6 as myokine.

The effect of EMS on exercise-induced alternations of the immune phenotype, immune cell count, or immune function has rarely been investigated. Two studies investigated the effect of superimposed EMS during cycling on IL-6 and brain-derived neurotrophic factor (BDNF) (Wahl et al., 2015) respectively on IL-6 and human growth hormone (GH) (Omoto et al., 2015). While EMS application was followed by a substantial release of muscle damage markers such as CK and Mb, the effect on the myokines was only marginal (Omoto et al., 2015; Wahl et al., 2015). Likewise, no effects of EMS on strength training-induced mobilization of testosterone, cortisol, and human growth hormone could be observed (Wirtz et al., 2015). On the other hand, one single bout of isometric electrical stimulation found significantly greater muscle damage and GH (Jubeau et al., 2008) compared to voluntary exercise.

CONCLUSION, RECOMMENDATIONS, AND PRACTICAL CONSIDERATIONS FOR (WHOLE-BODY) ELECTROMYOSTIMULATION

As the literature concerning (WB-)EMS is rather manageable, the few presented studies additionally provide a high inconsistency in the application (dynamic vs. isometric, frequency, load ratio, different electrodes). Thus, in addition to pronounced ranges of muscle damage, there is currently insufficient knowledge about the effect of (WB-)EMS on immunological parameters to report.

The abovementioned evidence of EIMD, seen in, e.g., CK, after a very intense application of (WB-)EMS shows that the technique must be handled with a certain responsibility and special care. As seen, a misapplication may also be followed by immunological deflections; however, in this regard detailed investigations are still lacking.

By now, there is no evidence for severe immunological alternations after WB-EMS. But the meanwhile widespread use of WB-EMS in general and especially the growing interest for implementation of (WB-)EMS training in clinical and rehabilitation settings require even more detailed evidence about further underlying mechanisms and physiological side effects. To ailing patients, knowledge about acute and prolonged immunological effects would be useful and essential. Closing this gap should be one objective of further research to guarantee an even safer application of WB-EMS in the future.

Nevertheless, the influence of EMS on muscle damage and immunological findings or deflections is quite manageable if the technology is used correctly.

AUTHOR CONTRIBUTIONS

MT and FM revised the literature and wrote, revised, and approved the manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Physiology

BRIEF RESEARCH REPORT
published: 28 February 2020
doi: 10.3389/fphys.2020.00150

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Frequency-Dependent Reaction of the Triceps Surae Muscle of the Mouse During Electromyostimulation

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The difference in the efficacy of altered stimulation parameters in whole-body-electromyostimulation training (WB-EMS) has hardly been examined. Higher impulse frequencies (>50 Hz) might be most adequate for strength gains because of the force frequency relationship (FFR), which describes a greater force production by increasing the applied frequency. Frequencies below this value, however, also seem to have positive influences on muscle strength increases. Therefore, the aim of this study was to analyze possible muscle length changes to different stimulation frequencies of the dissected mouse triceps surae muscle. A bending rod transducer was used to measure and compare changes in muscle lengths at different frequencies in relation to the initial length in the prepared muscle. We found significant differences between the muscle shortening at different frequencies ($p < 0.001$). At 20 Hz the largest muscle shortening was observed (20 Hz = 3.32 ± 2.06, 60 Hz = 0.77 ± 0.58, 85 Hz = 0.32 ± 0.29, 100 Hz = 0.31 ± 0.29). From a frequency of 60 Hz, the muscle shortening decreased progressively, at stimulation frequencies above 60 Hz the lowest shortenings were recorded. The results demonstrate a different behavior of the isolated triceps surae muscle of the mouse in an *ex vivo* environment. Even if there is no FFR in this investigation, the results indicate a higher metabolic demand using higher frequencies in electromyostimulation, despite the experimental execution in *ex vivo* design. Therefore, future studies should take this faster fatigue into account when drawing up training protocols in order to counteract possible frequency modulations.

Keywords: electrostimulation, mice, muscle activation, whole-body EMS, frequency

OPEN ACCESS

Edited by:
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Reviewed by:
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Specialty section:
This article was submitted to Exercise Physiology, a section of the journal Frontiers in Physiology

Received: *12 February 2019*
Accepted: *11 February 2020*
Published: *28 February 2020*

Citation:
Zart S, Berger J, Ludwig O, Knauth J and Fröhlich M (2020) Frequency-Dependent Reaction of the Triceps Surae Muscle of the Mouse During Electromyostimulation. Front. Physiol. 11:150. doi: 10.3389/fphys.2020.00150

INTRODUCTION

Electromyostimulation (EMS) training has been an effective form of strength training for many years now, both in rehabilitation and in competitive and popular sports. However, there has been no clear consensus on the selection of stimulation parameters in training planning and execution over the last decades. A stimulation parameter whose influence on the effectiveness of EMS training has not yet been sufficiently clarified is the stimulation frequency. In conventional EMS training, a frequency in the range around 85 Hz is usually used, but there is no evidence for this. Various studies differentiate the frequency range used according to age or state of fatigue. Optimal force increases seem to take place at a frequency in the range of 76.4 ± 20.9 Hz (Filipovic et al., 2011). In general, more than 50 Hz seem to be necessary to generate optimal force increases, since at a frequency below 50 Hz mainly slower Type I fibers and from 50-120 Hz mainly faster Type II fibers are supposed to be stimulated (Frenkel et al., 2004). According to Kramme (2007), optimal faradic stimulation of the striated musculature occurs from 50 Hz, while Moreno-Aranda and Seireg (1981) were able to generate maximum electrical muscle activity at a frequency in the range between 50 and 110 Hz. However, frequency ranges below 50 Hz are also considered to have a positive influence on force increases. Dreibati et al. (2010) recommend a stimulation frequency below 60 Hz in order to prevent a loss of strength during training.

In animal experiments the muscle behavior was also investigated with different frequencies. 20 Hz seem to have a positive influence on strength increases in the m. soleus of the mouse during a 14-day stimulation period (two times daily per 3 h of stimulation), furthermore positive influences on the development of the satellite cells can be determined (Guo et al., 2012). Exemplary studies showed an increased force production and tension with increasing frequency (Guo et al., 2012; Hering et al., 2016). However, an increased frequency cannot be maintained indefinitely. A constant stimulation with a higher frequency (e.g. 80 Hz or 100 Hz) results in a drop in force, which can be reduced by adjusting the frequency to 20 Hz for example. This fatigue during high frequency stimulation may be due to the failure of electrical propagation at the muscle fiber membrane, a reduction in the activity of the motor unit activity seems to minimize fatigue. A constant stimulation of 20 Hz generates a constant force diagram with a force increase after continuous stimulation. In comparison, in voluntary contraction the force generation is optimized by a reduction in motor neuron firing frequency to avoid this type of fatigue (Bigland-Ritchie et al., 1979; Jones et al., 1979).

On this basis, the aim of the present study was to observe the frequency-dependent response behavior of the triceps surae muscle of the mouse in EMS.

METHODS

The experiments were performed on triceps surae muscle (m. soleus and m. gastrocnemius) of 19 wild type laboratory mice (C57BL/6N; age: 34.7 ± 2.2 days; weight: 17.2 ± 1.7 g). Animals were raised in the animal facilities of the University of Kaiserslautern under normal nutritional conditions. Lights were set to a 12 h day-12 h night cycle. Animal breeding and experiments were approved by the regional council according to the German animal protection act (TSchG §4, Absatz 3) and in accordance with EU Directive 2010/63/EU. To carry out the experiment, the neck of 19 mice was broken with the preparation scissors and then the head was severed. The lower leg was separated from the thigh 5 mm above the knee joint and the coat, skin and connective tissue were removed. The exact muscle fiber composition of the examined musculature is shown in **Table 1**, the myosin isoform percentage (MHC) in **Table 2**. The preparation was clamped vertically in the area of the tarsus as well as below the knee joint by two threads with the same pre-tension in a tripod apparatus (**Figure 1**).

TABLE 1 | Percentage of muscle fiber types in the soleus and gastrocnemius muscle, modified according to Augusto et al. (2004).

Muscle fiber type	m. soleus [%]	m. gastrocnemius [%]
Type I	37.42	5.74
Type IIA	38.62	5.73
Type IID	5.69	2.26
Other type II (AD, DB and B)	18.74	86.19

TABLE 2 | Myosin isoform percentages (MHC) in the soleus and gastrocnemius muscle, modified according to Augusto et al. (2004).

MHC	m. soleus [%]	m. gastrocnemius [%]
I	41.5	0.81
IIa	57.56	17.01
IId	0.15	0.00
IIb	0.00	84.50

After the preparation of the muscle, it was immediately clamped into the apparatus to avoid a long period of time between preparation and analysis. At the lower end a bending rod transducer with amplifier was fixed, the signal was amplified tenfold. The amplified signal was output and stored optically and digitally via an oscilloscope (Tektronix TDS1001B, Tektronix, Schwalbach am Taunus, Germany) at 250 Hz. For the stimulation a clamp electrode was fixed to the paw and a needle electrode was inserted through the muscle belly of the muscle. The sequence of the selected frequencies was randomized from muscle to muscle so each frequency was used at each measurement time point. The monopolar stimulation of the triceps surae muscle was performed by a self-developed stimulation generator which modulated the pulse duration (4 s), frequency (20, 60, 85, 100 Hz) and width (350 μs) for a rectangular signal. The resulting stimulation scheme largely corresponded to the electrical stimulation used in a whole-body-EMS (WB-EMS) application. In order to realize a stimulation at a desired current strength of 30 mA, a voltage of 8.7 V with a resistance of 270 Ohm was determined on the oscilloscope.

During the stimulations, the shortening of the triceps surae muscle was measured via the bending rod transducer as relative units (here designated by a.u. = arbitrary units). The present equilibrium length of the muscles before stimulation corresponded to the initial value of zero. Positive values during stimulation showed muscle shortening. Thus, a comparison between the frequencies was performed on the basis of the relative unit. We determined maximum and mean shortening and the integral over the time-length diagram in relation to frequency. The results are expressed as mean values and standard deviations.

We included only measurements of 15 mice or mouse muscles in the analysis because measurement errors occurred in four cases. The statistical analysis was performed with IBM SPSS (SPSS Version 25.0, Chicago, IL, United States). Because of missing normal distributions Kruskal-Wallis-Tests were performed to evaluate differences of mean value changes in relative muscle

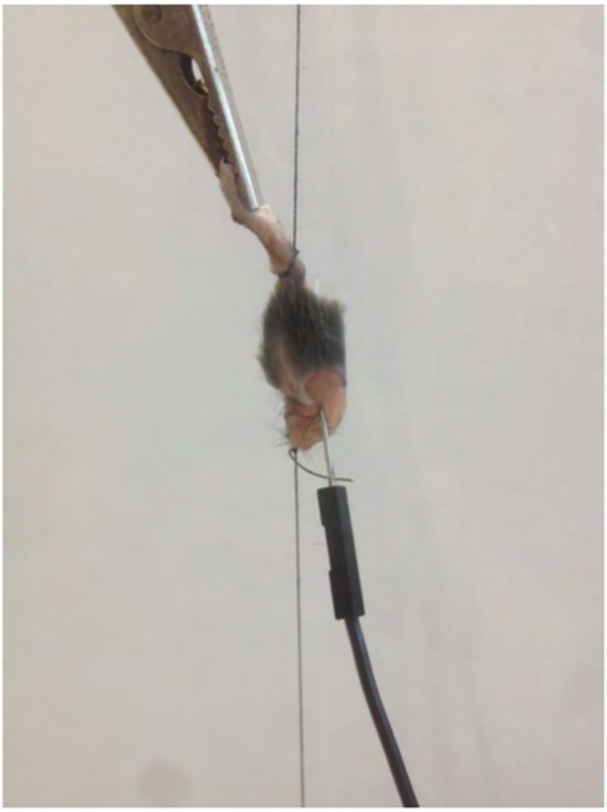

FIGURE 1 | Fixed mouse muscle with needle and clamp electrode.

lengths between the frequencies. Follow up Mann-Whitney-U-tests were conducted to evaluate pairwise differences, controlling for Type I error across tests by using Bonferroni approach.

RESULTS

With regard to the frequency-dependent, averaged integrals, no significant differences in triceps surae muscle shortening could be observed depending on the selected frequency sequence. Therefore, we could exclude a sequence-related fatigue effect. In spite of different preloads due to randomized stimulation, we found the largest muscle shortenings at 20 Hz (**Table 3**).

In addition, we found continuous muscle shortening (tetanus) during stimulation at 20 Hz. For frequencies above 50 Hz there was no permanent and constant muscle shortening, the muscle length increased again in the course of the stimulation. At 85 and 100 Hz this course was even more obvious in the graph (**Figure 2**). Already after 0.5 s, the muscle almost regained its equilibrium length.

The Kruskal-Wallis-Test revealed significant differences between the frequencies used ($p < 0.050$). The results of the Mann-Whitney-U-tests indicated a significant difference between 20 Hz and all other frequencies (all $p < 0.050$), but none in any other pairwise comparison.

DISCUSSION

In this study, the dissected triceps surae muscle of the mouse was subjected to muscle stimulation corresponding to WB-EMS training. Four frequencies were randomly applied and the respective stimulus response was determined by means of relative muscle length changes. On basis of this experimental setup with the same external weight load and pre-tension of the triceps surae muscle we found different muscle activation levels.

At 20 Hz, the largest change in muscle length was induced approximately over the full stimulation time. Only for this frequency a permanent and constant muscle shortening had occurred and thus a tetanic contraction could be assumed. The time-length-diagrams for the frequencies of 60, 85, and 100 Hz, on the other hand, showed less muscle shortening. The question now arises why we could not find an increased shortening at higher frequencies, what the force frequency relationship (FFR) suggests. Studies found an increase in muscle tension (Guo et al., 2012) or strength production (Hering et al., 2016) due to an increase in the frequency in animal experiments. First of all, it has to be taken into account that our experiments are carried out *ex vivo*, using a needle electrode, which complicates the comparability to *in vivo* or *in vitro* studies.

According to Augusto et al. (2004), 2–3 months old mice have a fiber composition with over 80% type II fibers in triceps surae muscle. Due to the young age of the mice used, the differentiation of the muscle fiber types are not complete, which could result in an insufficient number of motor units responding to high frequencies. It is known that muscle activity induced by EMS causes altered recruitment behavior in muscle fibers compared to voluntary contractions. Contrary to the activation sequence of Henneman's size principle, studies with EMS show either a selective activation of fast motor units (Cabric et al., 1988; Trimble and Enoka, 1991) or a non-selective, spatially fixed and temporally synchronous recruitment pattern of muscle fibers (Bickel et al., 2011). In the first case, there might be no increase in muscle activity, since the muscle fibers of the growing mouse are not yet sufficiently differentiated and thus less fast-twitching fibers can be activated. In addition, one could assume that most muscle fibers had already reached their stimulation threshold at low frequencies and therefore no increase in muscle activity and further shortening of muscle length could be achieved at higher frequencies. In the second case, slow and fast muscle fibers are activated at both low and high strength levels (Gregory and Bickel, 2005). Thus, according to Bickel et al. (2011), stimulation with low (20 Hz) and high frequency (>50 Hz) should have activated all types of muscle fibers.

However, it is assumed that higher frequencies may lead to faster muscle fatigue, as during EMS it is not possible to reduce the innervation frequency or modulate the recruitment pattern through physiological control processes (Gregory and Bickel, 2005; Dreibati et al., 2010). Experimental investigations on the soleus muscle of the mouse show exactly this behavior by means of the force progression. At 100 Hz stimulation frequency, the force drops to 10% of the initial value after 40 s. In contrast, force remains at the same level for at least 60 s when stimulated at 20 Hz (Jones et al., 1979). Compared to the results presented

TABLE 3 | Averaged results across all mice for the frequencies 20, 60, 85, and 100 Hz.

Stimulation Frequency (Hz)	Integral (a.u.)	Mean (a.u.)	Maximum (a.u.)
20	13.27 ± 8.25	3.32 ± 2.06	3.71 ± 2.27
60	3.09 ± 2.32	0.77 ± 0.58	2.49 ± 1.64
85	1.27 ± 1.03	0.32 ± 0.29	1.68 ± 0.85
100	1.24 ± 1.14	0.31 ± 0.29	1.36 ± 1.00

Values are reported as means ± standard deviations. a.u. = arbitrary unit.

in this study, only the time of fatigue differs significantly. The much earlier decrease in muscle activity could be explained by the experimental setup. In the study by Jones et al. (1979), the mouse muscle is placed in a sodium solution so that an ion exchange between muscle tissue and fluid is possible. In the present study, the muscle was isolated and separated from any circulation, which would allow the fatigue processes to progress more rapidly. Nevertheless, the graphs of force development at different frequencies from Bigland-Ritchie et al. (1979) show very strong similarities to the *ex vivo* results presented here. A continuous force development at 20 Hz can be seen, whereas higher frequencies (50 Hz and 80 Hz) already after a short stimulation time of about 5 s lead to a continuous decrease in force production, which remains constant until the end of the stimulation (Bigland-Ritchie et al., 1979). Furthermore, frequency modulation from 100 Hz to 20 Hz after continuous stimulation can in turn bring about a clear increase in force (Jones et al., 1979).

With regard to the behavior of human muscles in comparison to mouse muscles during EMS, studies show the same fatigue behavior (Jones et al., 1979; Moritani et al., 1985). As a reason for the decrease in strength during stimulation with high frequencies, it is assumed that the transmission of the action potentials via the T-tubules is no longer possible and therefore the strength production collapse. A changed ion concentration leads to a reduction of the membrane excitability and thus to a lower power development (Bigland-Ritchie et al., 1979). Binder-Macleod and McDermond (1992) show that the contraction rate of skeletal muscles slows down when tired muscles are excited voluntarily or by EMS. This means that although muscle twitching is faster when stimulated electrically, the half relaxation time is significantly longer. Thus, at high frequency, a new electrical stimulus occurs during the repolarization phase and therefore remains ineffective. This could signify for WB-EMS that lower frequencies guarantee an adequate repolarization time of the muscle fiber membrane especially in a fatigued state, which could be important for the periodization of the WB-EMS training in competitive sports. At a higher frequency, an increased metabolic demand leads to a faster fatigue of the muscles. However, in WB-EMS this could be an important factor for modulating the applied frequency during the training from a higher to a lower frequency (Dreibati et al., 2010).

The study carried out here showed the highest force development at a frequency of 20 Hz. This could be a further indication of an increased metabolic need of the muscle at higher frequencies, since the musculature could only cause a continuous contraction at 20 Hz. Only at higher frequencies a lower force impulse could be generated. A decisive factor here, however, is the conduct of the study in an *ex vivo* experimental design. Nevertheless, other authors such as Glaviano and Saliba (2016) or Dreibati et al. (2010) also describe an improved force production at lower frequencies and stated an increased metabolic demand in higher frequencies (ph level, inorganic phosphocreatine values, energy costs), which would confirm our results due to the lack of new energy production in the *ex vivo* muscle. A further reason for the strength loss with increased frequencies could be the reduction in the extracellular Na^+ due to the shorter action time for the sodium-potassium pump. The depletion of the Na^+ (or the accumulation of K^+) could reduce the muscle membrane excitability sufficiently to explain the force loss during a higher frequency (Moritani et al., 1985).

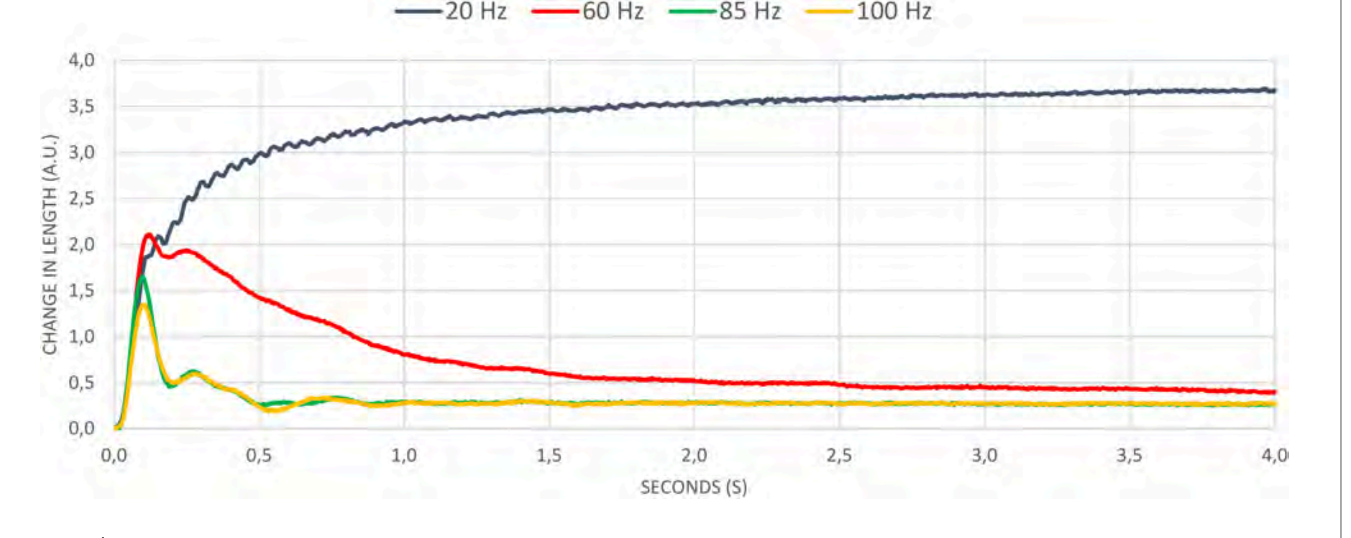

FIGURE 2 | Mean values of all frequencies.

Due to different stimulation protocols and other environmental conditions, the comparison of the results presented here to other animal studies remains complicated (Guo et al., 2012; Kobayashi et al., 2012; Tsutaki et al., 2013; Hering et al., 2016; Li et al., 2016; Valenzuela et al., 2017). Nevertheless, similar results could be observed in the behavior of the muscle during stimulation with different frequencies, even if the environmental influences and the way of stimulation of the muscle (*ex vivo*, needle electrode) were different. In future experiments, the influence of surface electrodes and needle electrodes on stimulation behavior of the muscle should be investigated. Since comparative studies in animals use surface electrodes in the experiments, this could be a source of interference in the experimental setup. It should also be examined to what extent an examination with intact blood circulation would generate similar muscle behavior. In addition, the relationship between stimulation frequency and intensity should be further examined in a combined study protocol. Nevertheless, the available results provide an insight into the behavior of the *ex vivo* mice muscles at different applied frequencies.

In addition to the limitations described such as the use of a needle electrode instead of surface electrodes and the *ex vivo* implementation of the study without nutrient supply for the muscle, the lack of knowledge about the MHC isoform of the muscles used is a further limitation. Although comparisons can be made with the studies carried out by Augusto et al. (2004), future studies should carry out a detailed MHC isoform analysis of the examined muscles in each case in order to be able to interpret possible fluctuations of the muscle fiber composition (Zhang et al., 2010) and corresponding divergent reactions to an electrical stimulus more accurately.

The frequency used seems to have a significant influence on fatigue, which must also be considered in the context of training planning for WB-EMS. Since active movements of the athlete (e.g. light strengthening exercises) lead to greater muscle strength compared to passive WB-EMS, the frequency should be chosen accordingly in order to be able to perform the movements in a controlled manner throughout the training (Kemmler et al., 2018).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of the regional council according to the German animal protection act (TSchG §4, Absatz 3) and in accordance with EU Directive 2010/63/EU. The protocol was approved by the regional council.

AUTHOR CONTRIBUTIONS

SZ, JB, JK, and MF conceived and designed the experiments. JK performed the experiments. JK, SZ, and JB analyzed the data. SZ and MF contributed materials and analysis tools. SZ, JB, and OL wrote the manuscript.

ACKNOWLEDGMENTS

Many thanks to Prof. Eckhard Friauf (Department of Animal Physiology, Technische Universität Kaiserslautern) without his help the implementation of this study would not have been possible.

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