



Functional Electrical Stimulation Cycling Exercise for People with Multiple Sclerosis

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Abstract

Purpose of review There has been substantial interest in the role of exercise for managing impairments, limitations, and disability progression among persons with multiple sclerosis (MS). Despite established benefits of exercise training for persons who have mild-to-moderate MS, the ability to deliver exercise to persons who experience higher disability remains challenging. One promising approach for exercise in this population is functional electrical stimulation (FES) cycling. This review provides a summary of the current evidence for FES cycling as an exercise training modality in persons with MS with respect to prescription, safety, tolerability, and acute and chronic effects.

Recent findings We searched the literature for studies involving FES cycling exercise in persons with MS published in English up until July 2019. Eight studies were retrieved: two studies examined acute effects, two studies examined chronic effects, and four studies reported on both acute and chronic effects of FES cycling exercise. The overall quality of the studies was low, with only one, small, randomized controlled trial (RCT).

Summary There is limited but promising evidence for the application of FES cycling exercise among persons with MS who have moderate-to-severe disability. Participants were capable of engaging in regular FES cycling exercise (~30 min, 2–3×/week), with few, mild adverse events experienced. Preliminary evidence from small, mostly uncontrolled trials supports the potential benefits of FES cycling on

physiological fitness, walking mobility, and symptoms of fatigue and pain. High-quality RCTs of FES cycling exercise are necessary for providing recommendations for integrating exercise training in the management of advanced MS.

Introduction

Multiple sclerosis (MS) is an immune-mediated, progressive neurodegenerative disorder that results in demyelination and transection of axons and loss of neurons within the central nervous system [1]. The clinical manifestations of the disorder include impairments in motor, sensory, and cognitive functions that limit participation in everyday activities and overall quality of life (QOL) [2]. The progression of disability in MS has been associated with greater functional impairments and increased symptom severity [3–8], as well as direct and indirect socioeconomic costs [9, 10]. Disease-modifying agents that target populations of lymphocytes and/or cytokines represent the first line of treatment for altering disease progression, but these have limited efficacy in preventing the progression of disability over long periods of time [11]. The disease-modifying agents further do not target improvements in other clinical, functional, or symptomatic manifestations of MS.

There has been substantial interest in the role of non-pharmacological approaches, including exercise training, for managing impairments, limitations, and disability progression in MS. The benefits of exercise training for persons with MS have been well-documented in systematic reviews and meta-analyses of clinical trials [12•, 13•], and include improvements in physiological fitness, walking mobility, balance, fatigue, and depressive symptoms. The clinical trials of exercise training have primarily been conducted among persons with MS who have mild-to-moderate disability levels (i.e., Expanded Disability Status Scale score < 6.0), rather than those with advanced disease characterized by severe disability (i.e., EDSS of 6.0 or above) that may require specialized or adapted exercise strategies. The application of specialized or adapted exercise modalities is necessary as these could enhance the capacity of this population for achieving higher intensities and durations of exercise necessary for

yielding training adaptations. The low levels of physiological fitness observed among persons with MS who have moderate-to-severe disability [4, 14] further suggest that specialized or adapted modalities might be particularly beneficial for the delivery of exercise training.

One specialized approach involves the application of functional electrical stimulation (FES) exercise. FES exercise involves neuromuscular stimulation delivered in a specific recruitment pattern for performing a muscular movement necessary for exercise. FES cycling, in particular, involves systematic, transcutaneous electrical stimulation of the lower extremity muscle groups for production of leg movement on a cycle ergometer. FES cycling can be delivered with participants seated in a chair or personal wheelchair, thereby minimizing the need for transfers among persons with severe mobility limitations that restrict ambulation. There are reported benefits of FES cycling on physiological fitness, body composition, motor function, and spasticity in persons with spinal cord injury and stroke [15–20]. The increased interest in applying exercise among people with MS who have moderate or severe disability combined with the benefits of FES cycling reported in other populations with neurological conditions, indicates that FES cycling may be a viable approach for exercise delivery and disability management in persons with MS who have advanced disease.

This review provides a summary of the current evidence for FES cycling as an exercise training modality in persons with MS. We searched four electronic databases (PubMed, Web of Science, EMBASE, and Ovid MEDLINE) and our personal libraries for relevant literature. The studies summarized in this review included clinical trials of acute and chronic FES cycling as an exercise modality in persons with MS that were published in English through July, 2019.

Summary of the research

To date, eight studies of FES cycling exercise have been conducted in persons with MS (Table 1). Two studies examined the effects of acute bouts (i.e., single sessions) of FES cycling exercise [21•, 22], whereas two studies examined both acute and chronic (i.e., training) effects [23, 24]. There were four studies that examined chronic effects of FES cycling exercise [25•, 26, 27•, 28••, 29•]. Five [23, 24, 25•, 26, 27•] of the six training interventions applied pre-post designs, and one study [28••, 29•] involved a randomized controlled trial (RCT) design. Overall, the study samples were small ($n = 1-14$), and most participants had moderate-to-severe disability (EDSS range reported = 4.0–7.5). The intervention durations ranged between 2 and 24 weeks, with sessions delivered 2–3×/week for between 10 and 60 min/session. The stimulation parameters for most trials involved a pulse width of 200–300 μsec at a frequency of 20–50 Hz and a cycling cadence of 10–50 rpm. All interventions stimulated the quadriceps, hamstrings, and gluteal muscle groups, with the exception of one trial [23] that stimulated the quadriceps and hamstrings only. Based on the corpus of literature, we provide a summary of the safety, tolerability, and acute and chronic effects of FES cycling exercise in persons with MS (Table 2). The study results were interpreted based on statistical significance, clinical relevance, percent changes, and effect sizes, when presented, or when data were available for calculation.

Safety and tolerability of FES cycling exercise in persons with MS

Six studies [21, 24, 25•, 26, 27•, 28••] reported, with varying degrees, on participant safety and tolerability with FES cycling exercise. One case study reported that the participant tolerated an acute bout of FES cycling very well and received stimulation intensities of up to 90 mA [21]. Two studies reported that participants experienced no related adverse events (AEs) or any observed increases in MS-related symptoms with 4-weeks of FES cycling [25•, 26]. Studies of longer FES cycling interventions (10–24 weeks) [24, 27•, 28••] reported few AEs that were directly related with the intervention and that were mostly mild in severity. The AEs included leg stiffness, fatigue, increased spasticity, bowel incontinence, mild heat sensitivity, and skin irritation/redness. In most cases, these events resolved quickly and did not interfere with daily living. AEs that were reported as not related to the intervention (i.e., shoulder dislocation, fall) were rare, occurring in 2 out of 43 participants. No serious AEs were reported in the published studies.

Collectively, this preliminary evidence supports the safety and tolerability of FES cycling exercise for persons with MS who have moderate-to-severe disability. Therapists and clinicians can expect some mild AEs associated with the electrical stimulation and/or the increase in activity levels among persons with MS who are not currently active and who begin FES cycling. Such a response to an unfamiliar exercise stimulus is common when becoming more active, and musculoskeletal injuries and illnesses were commonly reported AEs in other exercise interventions in persons with mild-to-moderate MS [30]. Of note, two studies did not report on safety or tolerability, and there was a lack of

Table 1. Study, participant and protocol characteristics of FES cycling exercise in persons with MS

Study Ref.	Design	n	Participants		FES protocol									
			Age (years) mean ± SD	Disease duration (years) mean ± SD	EDSS (mdn, IQR)	Weeks	Sessions/week	Minutes/session	Pulse width (µsec)	Frequency (Hz)	Cadence (rpm)			
[21]	Acute	1	46	> 20	7.5	NA	2 total	30	0.1–500	0.1–50	NR			
[22]	Acute	E, 6 C, 5	E, 58.0 ± 6.0 C, 47.8 ± 7.4	E, 20.8 ± 7.8 C, 21.0 ± 7.3	E, 6.25, 0.63 C, 6.0, 0.75	NA NA	1 total	15	250	50	40–50			
[23]	Acute and Pre-post	8	52.1 ± 7.5	13.3 ± 8.0	4.0–7.5 (range)	2	3	20–30	300	20	NR			
[23]	Acute and Pre-post	7	48.0 ± 9.0	NR	7.4 ± 0.7 (mean ± SD)	10	18 total	40	300	35	10			
[25•]	Pre-post	14	55.4 ± 11.0	15. ± 7.4	NR	4	2–3	30	200	50	35–50			
[26]	Pre-post	8	54.5 ± 13.9	16.8 ± 6.9	> 6.0	4	3	30	NR	NR	40–50			
[27•]	Pre-post	5	50 (mdn)	13	6.5	24	3	60	250	33–45	NR			
[28••, 29•]	RCT	E, 4 C, 4	E, 57.3 ± 6.0 C, 48.5 ± 7.7	E, 22.3 ± 5.3 C, 20.8 ± 8.5	E, 6.3, 0.5 C, 6.3, 0.9	24	3	10–30	250	50	40–50			

E exercise; C control; FES functional electrical stimulation; mdn median; NR not reported; RCT randomized controlled trial

Table 2. Safety, tolerability, acute, and chronic effects of FES cycling exercise in persons with MS

Study	Safety and tolerability	Acute effects	Chronic effects
[21]	Protocol reported as well-tolerated by the participant.	↓ Spasticity	NA
[22]	NR	↑ VO ₂ *, PO*, HR*, RPE* (comparison FES cycling exercise vs. passive cycling)	Reported in [29, 30]
[23]	NR	↑ PO* ↓ RI* ↓ spasticity* (comparison with vs. without stimulation)	↔ Cycling PO, RI ↔ strength (KE, KF) ↔ walking speed ↔ spasticity Participant feedback: improved ADLs, gait; sensory changes
[24]	Negative effects reported by 2 participants: tiring; leg stiffness Mild heat sensitivity during last 10 min of the sessions—resolved with cooling fan.	↑ VO ₂ , PO, VE, HR (<i>n</i> = 5; tested at session 18)	↑ Thigh circumference* Participant feedback: improved strength, leg circulation, transfer ability; decreased spasticity
[25•]	No AEs; no increase in MS-related symptoms. (only training-related events reported)	NR	↑ Active cycling time*, PO (unable to cycle ≥ 30 min) ↑ cycling PO, resistance* (able to cycle ≥ 30 min) ↔ strength (combined score hip flexors, KF, KE, and dorsiflexors) ↔ spasticity ↓ fatigue impact* (physical and psychosocial) ↓ fatigue impact (total and cognitive) ↓ pain ↔ QOL
[26]	No AEs; no increase in MS-related symptoms.	NR	↑ mVO ₂ *
[27•]	No serious AEs. 3 AEs: shoulder dislocation (not related); increased spasticity; bowel incontinence.	NR	↑ Cycling distance, PO ↑ strength (hip extensors, KE, KF) ↓ strength (hip flexors, dorsiflexors) ↑ walking speed, endurance, agility ↑ cognitive performance ↔ spasticity ↑ QOL
[28••, 29•]	1 moderate AE: fall (not related) 6 mild AEs: skin irritation/redness (<i>n</i> = 3); non-debilitating fatigue (<i>n</i> = 2); increased spasticity (<i>n</i> = 1).	Reported in [23]	↑ Cycling distance, PO, resistance ↑ VO _{2peak} , PO _{peak} ↑ strength (KE) ↔ strength (KF) ↔ FFM, FM, %BF ↑ BMD

Table 2. (Continued)

Study	Safety and tolerability	Acute effects	Chronic effects
			↑ walking speed, endurance, agility, MSWS-12 ↑ cognitive performance ↑ fatigue severity & impact ↓ pain ↔ QOL
*Indicates statistically significant change ($p \leq 0.05$) ADL activities of daily living; FES functional electrical stimulation; KE knee extensors; KF knee flexors; HR heart rate; MS multiple sclerosis; MSQOL Multiple Sclerosis Quality of Life Index; MSWS-12 12-item Multiple Sclerosis Walking Scale; mVO_2 muscle oxygen consumption; PO power output; RI roughness index; RPE rating of perceived exertion; VAS visual analog scale; VO_2 oxygen consumption			

consistency in the recording and reporting of these outcomes (e.g., definition of AEs, related vs. not related AEs). These factors should be addressed in future trials to fully establish the safety and tolerability of FES cycling for persons with MS.

Acute effects of FES cycling exercise in persons with MS

Four studies [21–24] have reported on the acute effects of FES cycling among persons with MS. These studies have primarily reported on cardiorespiratory and cycling performance, as well as acute changes in muscle spasticity. One of the earliest studies of FES cycling in persons with MS examined cycling parameters with and without the use of electrical stimulation [23]. This study reported that the addition of stimulation resulted in significantly greater power output (PO; + 2.75 W; $p = 0.02$) and improved cycling smoothness (– 7.35 on roughness index; $p = 0.02$), and acutely decreased spasticity assessed with the Modified Ashworth Scale (MAS; $p = 0.05$) [23]. Similarly, single sessions of FES cycling reduced spasticity assessed with the MAS and semi-automated pendulum testing in one non-ambulatory individual with progressive MS [21].

Two studies [22, 24] characterized the cardiorespiratory response associated with a single FES cycling session using an open-circuit spirometry metabolic measurement system. One of these studies involved 18 sessions of neuromuscular electrical stimulation (NMES) cycling in which pedaling cadence was independent of stimulation intensity. The study reported peak oxygen consumption (VO_2), ventilation, and heart rate (HR) values of 407 ml/min, 17.0 L/min, and 85 bpm, respectively, during the last training session [24]. The mean power output for the session was 5.2 W, and the mean rating of perceived exertion (RPE) was 12, and this corresponded with an exercise intensity of between “light” and “somewhat hard” [24]. Another study comparing FES cycling exercise with passive leg cycling reported that participants exercised at a mean VO_2 , PO, and HR of 8.7 ml/kg/min (63.5% VO_{2peak}), 27.0 W (57.3% of PO_{peak}), and 102 bpm (76.4% HR_{peak}) during a single training session at mid-point of an intervention (~ 12 weeks) [22]. The mean RPE for the session was 13.5 (i.e., “somewhat hard”) [22]. The difference in exercise intensity observed between these trials is likely attributed to the different cycling protocols. Participants in the FES cycling trial pedaled volitionally while receiving stimulation, whereas participants in the NMES cycling trial only

received stimulation and were instructed not to pedal the cycle ergometer, likely resulting in lower intensities.

Although limited, these studies support the potential for modification of muscle spasticity, cycling kinematics, and cardiorespiratory metabolism with single sessions of FES cycling in persons with MS. We further note the potential for greater cardiorespiratory responses (e.g., higher intensities) with combined electrical stimulation and volitional cycling. Importantly, such acute benefits may, with chronic exposure to FES cycling, result in long-term adaptations. Of particular importance is the potential for cardiorespiratory adaptations with cumulative bouts of FES cycling for persons with MS who have moderate-to-severe disability and low fitness levels [4, 14], and who may have increased risk for inactivity-related comorbid health conditions [31–33]. Indeed, the RCT of FES cycling exercise [22] reported that the intensity of this exercise session fell within the range of moderate-to-vigorous physical activity using standard corresponding cut-points for exercise intensities [34]. This specific intensity of exercise is necessary for generating improvements in physiological fitness long-term and has been associated with health-related benefits in the general population [34]. Future trials are needed to establish optimal parameters for prescriptions of FES cycling exercise among persons with MS and the dose-response relationship of FES cycling exercise with health benefits and disease-related outcomes in this population. Further examination of training protocols with and without volitional cycling will be important for establishing the contributions of exercise and/or stimulation for generating outcomes, and for understanding the potential of FES cycling exercise among individuals with higher disability where volitional cycling is limited or not possible.

Chronic effects of FES cycling exercise in persons with MS

Six trials [23, 24, 25•, 26, 27•, 28••, 29•] have delivered chronic FES cycling exercise interventions involving varying training prescriptions among persons with MS. These studies have reported on changes in cycling performance, physiological fitness, motor and cognitive performance, symptoms, and participatory outcomes. Regarding cycling performance, four trials [23, 25•, 27•, 28••] reported on changes in cycling time, distance, PO, resistance, or smoothness over the course of the intervention. One trial of NMES cycling did not observe significant changes in PO or cycling smoothness after 2 weeks [23]. The other three trials [25•, 27•, 28••] of FES cycling exercise reported an increase in active cycling time (~4 min), distance (1.1–8.7 km), PO (0.55–5.3 W), and/or resistance (0.3–1.1 Nm) after 4–24 weeks of training, although statistical significance testing was not performed on most outcomes. There were larger volumes of exercise with protocols involving voluntary cycling, specifically prescribed training intensities and progressions, and longer training interventions. Therapists who prescribe FES cycling exercise should consider these factors when designing and implementing such interventions. For instance, tools for recording and monitoring training parameters (e.g., heart rate monitor, RPE scale, web-based monitoring) might be particularly helpful for monitoring and ensuring compliance and progression with prescribed training protocols.

Several studies examined the efficacy of FES cycling exercise for improving physiological fitness, primarily muscular strength. Two trials [23, 25•] reported no changes in hip flexor, knee extensor (KE), knee flexor (KF), or dorsiflexor

strength (all $p > 0.05$; $d = 0.04$ – 0.11) assessed by manual muscle testing after 2–4 weeks of training. However, two longer FES cycling interventions [27•, 28••] did report strength improvements in some muscle groups assessed using a hand-held or computerized dynamometer after 24-weeks of training. One of these studies involved home-based FES cycling exercise and reported small strength improvements in the hip extensors ($d = 0.17$; 34%), KE ($d = 0.33$; 15%), and KF ($d = 0.29$; 19%), but not other leg muscle groups (hip flexors $d = -0.34$; -30%; dorsiflexors $d = -0.17$; -19%) [27•]. There was a moderate increase in peak torque of the KE ($d = 0.56$; 22.7%), but not the KF ($d = -0.07$; 3.6%), among participants who completed FES cycling exercise compared with a passive cycling condition [28••]. The potential for strength adaptations with FES cycling likely depends on the specific muscle groups that are peripherally stimulated, as well as those engaged biomechanically during leg cycling movement.

Other fitness outcomes examined with FES cycling have included measures of cardiorespiratory fitness and body composition. One RCT [28••] reported clinically relevant [35] improvements in $VO_{2\text{peak}}$ ($d = 0.34$; 13.8%) and PO_{peak} ($d = 0.65$; 15.3%), whereas one uncontrolled trial [26] reported a significant increase in muscle oxygen consumption ($p = 0.047$; 47%) assessed by near-infrared spectroscopy. Using dual-energy X-ray absorptiometry, no changes in soft tissue compositions (%body fat, lean mass, fat-free mass; $d = 0$ – 0.16 – 0.18 ; 0.7–5.2%) were reported in one RCT of FES cycling exercise, although there was a moderate increase in bone mineral density ($d = 0.57$; 5.7%) [28••]. Another trial of NMES cycling, however, reported a significant increase in thigh circumference (left $p = 0.005$; +10.7%; right: $p > 0.001$; +11.6%) [24]. Collectively, the current evidence supports potential improvements in muscular and cardiorespiratory fitness domains after chronic FES cycling in persons with MS who have moderate-to-severe disability, and longer interventions may be necessary for fitness adaptations in this population. The potential for changes in body composition in response to FES cycling exercise in persons with MS are unclear at this time.

Three studies [23, 27•, 28••] have examined the efficacy of FES cycling exercise on cognitive and motor performance, primarily mobility outcomes. One study examined 2-weeks of FES cycling exercise and did not report any changes in 10-m walk test performance [23]; this was likely associated with the short training duration. Two 24-week interventions [27•, 28••] reported small-to-moderate, positive effects of FES cycling exercise on the timed 25-ft walk test (T25FW; $d = 0.40$ – 0.72 ; 22.9–36%), 2-min walk test ($d = 0.20$ – 0.22 ; 11.9–13%), Timed Up-and-Go ($d = -0.30$ – 0.40 ; 27.6–36%), and 12-item Multiple Sclerosis Walking Scale ($d = -.68$; -15.8%). Importantly, the improvement in T25FW performance in both trials met common criteria for a minimal clinically important difference (i.e., 20% change) [36]. Of note, one of the trials further reported large correlations ($\rho = 0.62$ – 0.69) between the change in T25FW performance and change in cardiorespiratory fitness outcomes ($VO_{2\text{peak}}$ and PO_{peak}), and this suggests that improvements in physiological fitness might, in part, contribute to improved walking mobility with FES cycling exercise. The same 24-week interventions [27•, 28••] further reported small-to-moderate improvements in cognitive performance assessed with the Symbol Digit Modalities Test (SDMT; $d = 0.53$; 14.5%) and the Paced Auditory Serial Addition

Test ($d = 0.37$; 8.7%), and the change in SDMT score was considered clinically important [37, 38].

Researchers have further examined symptomatic and participatory outcomes with FES cycling exercise, and the most common included spasticity, fatigue, pain, and QOL. Three studies [23, 25•, 27•] examined changes in spasticity with FES cycling exercise. These studies reported no effect of FES cycling delivered between 2 and 24 weeks on spasticity assessed with the MAS ($d = 0.04$ – 0.11 ; 3–8%; $p = 0.30$ – 0.92) [23, 25•] or the Lower Limb Spasticity Measurement System ($d = 0.15$; 17%) [27•]. Two studies [25•, 29•] reported small-to-large decreases in symptoms of fatigue, including the severity ($d = -0.92$) and impact of fatigue ($d = -0.31$ – 0.74), with short- (4 weeks) [25•] and long-term (24 weeks) [29•] FES cycling exercise. Both of these trials reported the largest effect on physical ($d = -0.43$ and -0.68) and psychosocial ($d = -0.67$ and -0.74) fatigue impact subscales. There were moderate ($d = -0.55$ and -0.67) decreases in pain symptoms, assessed using the Medical Outcomes Study Pain Effects Scale and the McGill Pain Questionnaire, reported in the same studies [25•, 29•]. Three studies [25•, 27•, 29•] reported on QOL with FES cycling exercise using a variety of measures. Two studies examined the effects of FES cycling exercise on the 36-item Short Form Health Status Survey (SF-36); one home-based trial reported a small improvement ($d = 0.37$; 13%) [27•], whereas the other supervised trial reported no change ($d = 0.19$; 2.3%; $p = 0.79$) [25•]. There were no improvements reported on the 29-item MS Impact Scale [29•] or other scales within the MS Quality of Life Index [25•] after 4–24 weeks of FES cycling exercise. Overall, the research suggests that FES cycling exercise may be most effective for reducing symptoms of fatigue and pain and is inconclusive with QOL. These symptoms are prevalent and impactful in persons with MS, particularly among those with higher disability [6, 39–41], and FES cycling exercise might be an effective alternative or complementary strategy for managing symptoms within this population.

Of note, three studies [23, 24, 28••] reported on feedback received from participants regarding perceived benefits and satisfaction with the FES cycling interventions. Participants reported perceived improvements in strength, gait, leg circulation, ability to perform everyday activities, including transfers, standing, stair climbing, as well as sensory changes, and reduced spasticity [23, 24]. These findings highlight the potential of FES cycling exercise for improving function and participation in everyday life, and this should be systematically evaluated with objective tools in future trials. Participants in one RCT of FES cycling exercise [28••] reported high levels of satisfaction with the leg cycling equipment and exercise program overall. The FES cycling intervention was rated favorably compared with other exercise programs, and participants were highly likely to recommend FES cycling exercise to others with MS [28••]. This feedback is important to support the long-term adoption of FES cycling as viable and enjoyable exercise modality for persons with MS.

Conceptual framework for application of FES uptake

The accumulating evidence for FES cycling exercise in MS requires careful consideration of factors that might influence its uptake. We located one examination of key factors that influence FES uptake and compliance in populations

with muscle weakness or paralysis (i.e., not MS specific) based on a series of semi-structured qualitative interviews [42, 43•] that were conducted with participants of the 12th triennial Vienna International Workshop on Functional Electrical Stimulation. Perspectives on FES technology and use were sought from a variety of stakeholders, including clinicians, researchers, engineers, and retailers [43•]. Key themes were identified surrounding daily use of FES exercise with paralyzed populations including issues with technology (e.g., stimulation parameters), education and knowledge base (e.g., requiring education and understanding of FES), motivation and support networks (e.g., requiring expert assistance), and environmental factors (e.g., commuting required to get to clinic) [43•]. Participants in this study expressed views about the home vs. laboratory or clinic environment for FES delivery, and some suggested that the home environment was seen as requiring supervision, greater motivation, and simplicity in device design and implementation [43•]. Several participants further noted that patients often had unrealistic, high expectations for benefits from participation in FES. Based on these findings, the authors proposed a conceptual framework that describes the importance of initial education of patients, providers, and engineers, as well as expectations for health benefits as key factors that influence the adoption of and compliance with FES exercise [43•].

Although this framework is not specific to persons with MS, the proposed approach has relevance for the update and delivery of FES cycling exercise in this population. This qualitative research highlights the importance of education and training on FES cycling exercise for various stakeholder groups. These efforts can be supported by conducting high-quality studies that establish the efficacy and optimal prescription of this modality for persons with MS. Therapists and clinicians can then promote realistic outcome expectations for health benefits related to FES cycling exercise for persons with MS to support long-term compliance in supervised and home environments.

Limitations and future directions

The current evidence for benefits of FES cycling exercise in persons with MS is generally of low quality, as there is only one, small RCT. The key limitations in study design include small samples, lack of control conditions, and lack of blinding of outcome assessors. The FES cycling protocols were generally consistent in stimulation parameters (i.e., pulse width, frequency, session duration); however, few studies have examined longer training durations (i.e., 24 weeks or longer) necessary for larger adaptations and benefits in this population. There is no further research on the long-term and lasting effects of FES cycling exercise, and this should be examined in future trials. There was considerable variability in primary outcomes of the studies reviewed, and future research might identify the outcomes that are most responsive to FES cycling exercise and if these responses differ based on participant clinical characteristics (e.g., moderate or severe disability status or relapsing-remitting or progressive courses of MS). The recording and reporting of AEs using standard and consistent approaches, such as the Common Terminology Criteria for Adverse Events (CTCAE) [44], should be incorporated in future trials.

Conclusions

There is limited but promising evidence for the application of FES cycling exercise among persons with MS who have moderate-to-severe disability. The application of FES cycling exercise appears to be well-tolerated, based on the few, mild adverse events reported in the literature. The existing research supports the capacity of persons with MS who have moderate-to-severe disability to comply with regular FES cycling exercise (~30 min, 2–3×/week) and progress in training volume over time. Preliminary evidence from small, mostly uncontrolled trials, supports potential benefits of FES cycling on physiological fitness, walking mobility, and symptoms of fatigue and pain. High-quality RCTs of FES cycling exercise are now needed to establish the safety and efficacy of this promising modality for people living with MS who cannot undertake exercise training using unassisted equipment and modalities. This will be necessary for improving the knowledge base required for the integration of exercise in the clinical management of advanced MS [12•].

Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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