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Review

Functional Electrostimulation in Patients Affected by the Most Frequent Central Motor Neuron Disorders—A Scoping Review

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Abstract: Post-stroke sequelae, spinal cord injury and multiple sclerosis are the most common and disabling diseases of upper motor neurons. These diseases cause functional limitations and prevent patients from performing activities of daily living. This review aims to identify the potential of functional electrical stimulation (FES) for locomotor rehabilitation and daily use in upper motor neuron diseases. A systematic search was conducted. For the search strategy, MeSH terms such as "stroke", "functional electrical stimulus*" and "FES", "post-stroke", "multiple sclerosis", and "spinal cord injury*" were used. Of the 2228 papers from the raw search results, 14 articles were analyzed after inclusion and exclusion criteria were applied. Only four articles were randomized clinical trials, but with low numbers of participants. RehaMove, Microstim and STIWELL were reported in three independent studies, whereas Odstock was used in four articles. The results of the studies were very heterogeneous, although for lower extremity stimulation (11 out of 14 papers), walking speed was reported only in 6. Berg Balance Scale, Timed Up and Go, Functional Ambulation Category, 6-Minute Walk Test, 10-Meter Walk Test, Fugl-Meyer Assessment, Motricity Index and Action Research Arm Test were reported for functional assessment. For clinical assessment, the Modified Barthel Index, the Rivermead Mobility Index and the Stroke Impact Scale were used. Four studies were spread over 6 months, two investigated the effects of FES during one session, and the other eight were conducted for 3 to 8 weeks. Improvements were reported related to gait speed, functional ambulation, hand agility and range of motion. FES can be considered for large-scale use as a neuroprosthesis in upper neuron motor syndromes, especially in patients with impaired gait patterns. Further research should focus on the duration of the studies and the homogeneity of the reported results and assessment scales, but also on improvements to devices, accessibility and quality of life.

Keywords: functional electrical stimulation; assistive technology; post-stroke; multiple sclerosis; spinal cord injuries

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1. Introduction

The initiation and control of voluntary movements in the human body are possible through an extensive neural network in the cortex, cerebral trunk and spinal cord. Upper motor neuron (UMN) lesions cause a characteristic set of clinical symptoms known as UMN syndrome. The most common symptoms may include muscle weakness, spasticity, and clonus. UMN lesions may be caused by stroke, traumatic brain injuries, malignancies, infections, inflammatory disorders, neurodegenerative disorders and metabolic disorders [1,2]. This scoping review aims to identify the benefits and limitations of using functional electrical stimulation in patients with post-stroke, multiple sclerosis, and spinal cord injury, as these diseases are significant causes of disability worldwide [3,4] and require a review like the present one to gather together and present compact conclusions. Thus, medical practitioners and researchers shall be presented different perspectives so as to start new practice methods and trials.

Stroke and SCI have common motor loss manifestations on human body extremities, such as muscle weakness in distal segments. In addition, muscle overactivity can be encountered, altering activities of daily living (ADL) task performance and gait pattern [5]. Following a stroke or other UMN injury, the nervous system takes intrinsic repair actions, modifying neural circuits by suppressing some existing ones and forming new ones; it may also redesign cortical and spinal cord regions. In addition to the restoring blood flow, the neuroplasticity may cause a surprising level of spontaneous recovery in the UMN following post-traumatic events or brain injuries. Rehabilitation training and pharmacological interventions could modify and boost these neuronal processes, especially within the first three months after stroke onset, with significant improvements in neuromotor function [6,7]. The results of previous research suggest that neuroplasticity is more pronounced during the first 3–6 months after stroke. At the same time, in the chronic stage, its intensity decreases over time and with the formation of new patterns [8]. Moreover, individuals who have suffered incomplete spinal cord injuries (SCI) can regain some motor functionality in the 6 months following the incident, determined mainly by neuroplasticity. However, rehabilitation can take several years [9] and new research suggests that the rehabilitation window should be extended to at least one year after the onset of stroke or SCI event [10–12]. Although the symptoms of multiple sclerosis (MS) vary depending on its subtype, patients have neuromotor manifestations similar to those of post-stroke patients or SCI, related to the distal segment of the lower limbs. Therefore, patterns of muscle spasticity of the ankle and foot and dropped foot are usually encountered. Walking is also strained to a considerable extent; as a result, patients depend on walking assistive devices or wheelchairs. The impairment in the functioning of the upper extremities is not as pronounced as in the lower ones; the patient basically preserves motor function of the upper limbs [13–16]. Unlike post-stroke or SCI conditions, neuroplasticity in MS can manifest adaptively and improve motor motion performance, or manifest a maladaptive pattern, influenced by the localization of various injuries, inflammation, and the progressive nature of the disease. [17]. Therefore, the time-window of intervention from outside the central nervous system, through physiotherapy, is essential for the complete and complex rehabilitation [9]. Furthermore, rehabilitation techniques or devices are usually used in physical recovery to improve motor functions [18].

The beneficial role of physical exercise is well known regarding UMN disorders. However, besides performing physical training, the sensory-motor loss cannot always be fully restored, and recent research suggest that motor imagery of the movement seems to have a crucial role in brain plasticity. Therefore, any tool facilitating human body movement can play an essential role alongside motor imagery in increasing functional locomotor independence [19,20].

Functional electrical stimulation (FES) is used as an adjunct therapy in stroke rehabilitation, but also for SCI patients, used either to assist in the voluntary rehabilitation of motor activity (early stages after stroke or incomplete SCI) or as a neuroprosthesis (when voluntary motor activity can no longer be restored) [21–24]; it is also an assistive technology with a beneficial effect for patients with MS with leg involvement (presence of leg drop syndrome) [25]. Functional electrostimulation is divided into two categories: assistance FES for the complete replacement of the motor function, and therapy FES. Therapy FES helps rehabilitate patients with central motor neuron damage (stroke, SCI, MS); it also plays a vital role in preventing muscle atrophy and maintaining the health of the muscular system. Assistive FES aims to restore motor function in patients with upper motor neuron syndrome by completely replacing motor signals. Evidence shows that FES uses brain plasticity to restore the ability to perform voluntary movements after spinal cord injury and stroke [26,27].

The parameters used to optimize FES effects are the duration, frequency and amplitude of electrical pulses. These parameters are precisely adjusted according to the patient's rehabilitation goals. The pulse duration of FES devices is typically between 300 and 600 microseconds, and these variations can have different effects on the targeted muscles. Electrical stimulation with a wide pulse width of 500–1000 microseconds associated with low frequency has been shown to cause additional muscle fatigue compared to a smaler pulse width. The frequency of the pulses varies between 20 and 50 Hz and is adjusted according to the goal pursued; the low frequency is used to achieve muscle contractions at a lower level of force, thus preventing the onset of early muscle fatigue. The intensity of the pulses varies between 0 and 100 mA; an amplitude value is selected according to the patient's needs and the targeted muscles. The selection of the amplitude interval is influenced by the pattern and the total simulation time [26]. When high-frequency ESF is applied, patients may experience a tingling sensation in addition to slow muscl contraction.

In this view, this scoping review shall underline the effectiveness of FES in the rehabilitation of neurological patients, either as a single therapy or in combination with other therapies. Different stimulation devices and parameter settings will be approached, according to tailored rehabilitation interventions. We also wanted to identify the latest research insights, therefore we conducted a scoping review of FES published over the last five years to provide valuable insight into the current state of research in this field.

2. Materials and Methods

2.1. Search Strategy

A systematic search of MEDLINE, PsychINFO, EMBASE, CENTRAL, ISRCTN, and ICTRP databases was carried out. For the search strategy, MeSH terms such as "stroke", "functional electrical stimul *" and "FES", "post-stroke", "multiple sclerosis", and "spinal cord injur *" were used. The database inquiry was performed in April 2022.

2.2. Selection of Studies

After using the aforementioned keywords, 2288 articles emerged. After applying the first set of inclusion and exclusion criteria (years of publication 2018–2022; article document type; excluding fields unrelated to rehabilitation such as chemistry, electrical engineering, veterinary medicine, dentistry, applied mathematics, psychology, pharmacology, etc.), 244 papers remained.

For secondary processing of the papers, additional inclusion criteria were used: (a) articles were original scientific reports of studies, (b) articles focused on post-stroke, multiple sclerosis or spinal cord injuries diagnosed by using paraclinical methods (e.g., magnetic resonance, functional magnetic resonance, computed tomography), (c) surface FES technology only, (d) articles were published in peer-reviewed journals in English, and (e) articles were available in full-text.

Secondary exclusion criteria included: (a) brain stimulation as a principal or adjunctive therapy, (b) other types of non-limb-dysfunction stimulation (e.g., dysphagia), (c) administration of drugs (e.g., botulinum toxin), (d) non-human subjects, (e) optogenetic stimulation, (f) other non-traditional adjunctive treatment (e.g., stem cells), (g) simple electrical stimulation (without functional training), and (h) new experimental technologies used on healthy subjects.

2.3. Charting Data

First, once the suitable papers were identified, Mendeley Reference Manager was used to gather the articles; it is also a tool which helped easily detect review research elements in every paper.

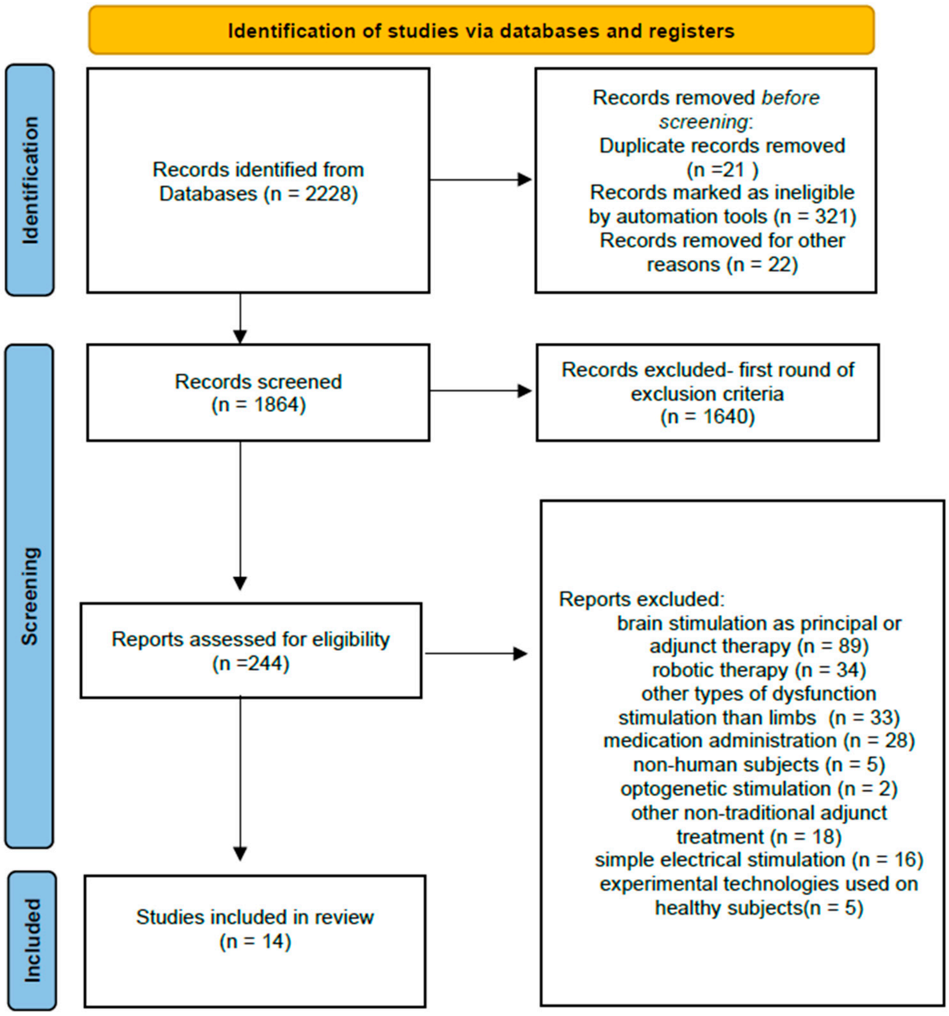
Therefore, the articles considered eligible for inclusion in the review were identified, and data related to FES application, type of population, and type of study (either randomized clinical trial (RCT) or clinical were extracted by the lead author (NAR) and reviewed by the second author (IVT). Subsequently, data related to the duration of the FES application, parameters used, types of evaluations and results were extracted. All the pieces of information were systematically synthesized by using the data table form in Microsoft Excel.

2.4. Gathering, Outlining and Reporting Results

The data graph organized the information on the research topic by splitting FES use into the three major UMN disorders with locomotor sequelae. The typology of the essential data on the type of population, duration of treatment, devices used, stimulation parameters and outcomes were extracted and structured.

After screening all 244 papers and applying the inclusion and exclusion criteria, 14 articles were included in the research. After analyzing them, a critical investigation regarding research methodology, statistical analysis, outcomes and limitations was performed, for a transparent framework on the use of FES. No further statistical analysis could be performed due to the heterogeneity of assessments and outcomes across the studies reviewed.

Accordingly, after reviewing the abstract or the integral texts of the selected papers and applying the exclusion criteria also by using PRISMA flowchart, fourteen studies were considered for review (Figure 1).



Other reasons for initial exclusion of papers: dysphagia stimulation, description of functional stimulation devices, aphasia cortical stimulation, and botulinum toxin therapy as first-line therapy.

Figure 1. The PRISMA Flow Diagram.

3. Results

3.1. FES Results on Patients with Post-Stroke Sequelae

The studies carried out on patients who had suffered a stroke included groups of 6 to 48 subjects, as presented in Table 1. The duration of these studies was between 3 and 8 weeks, or even 6 months, depending on the objectives pursued.

In the included studies, 133 participants were reported in the post-stroke category, from which 30 were assigned to the control (post-stroke patients) groups. The left side was affected in 67 patients, and the right side in 66. In the analyzed studies, the time since stroke was very heterogeneous, some considering an onset of 14 days [28] up to an average of 5.8 years [29]. The mean age of the participants was 61.58 years, with a standard deviation of 11.91 (weighted to their count) for six of the seven studies; unfortunately, one study [30] did not report the age or gender of the subjects; the other six studies included 68 men and 45 women.

Table 1. FES in post-stroke patients.

Authors	Body Part	Description	Subjects	Intervention	Findings
Ha et al. [30]	Lower Extremity/RCT	– FES and ankle exercise in post-stroke chronic stage.	– 25 chronic (>6 months) post-stroke patients with ankle spasticity. – one minute standing position without assistance. – one control group I (n = 8), one placebo group FES I (n = 8), and an experimental group FES II (n = 9).	– FES device: Microstim Model GmbH, Stanberg, Germany. – FES was simultaneously applied on the agonists and antagonists (tibialis anteriorus and gastrocnemius) combined with ankle exercises for 30 min in daily sessions, five times a week, for 8 weeks. – FES parameters: pulse duration = 250 µs, frequency 40 Hz, and intensity 20–40 mA.	– FRT improved in experimental group II and the control group ($p = 0.024$). – TUG results improved between experimental group I and experimental group II ($p = 0.023$) compared to the control group. – For TUG, no significant difference between experimental groups I and II.
Zheng et al. [31]	Lower Extremity/RCT	– RCT patterned FES gait stimulation for subacute (< 3 months) post-stroke patients.	– 48 patients. – able to perform cyclic movements of the lower limbs in the Brunnstrom I, II or IV rehabilitation stages. – two (n = 15) and four (n = 18) FES channels were applied in the two experimental groups, while in the placebo group 15 participants were reported.	– FES device designed at SunYat-sen Memorial Hospital of Sun Yat-sen University. – 5 days per week during 3 weeks of experiments. – FES parameters: 40 Hz frequency, pulse duration 0.2 ms. – intensity increased until a gross muscle contraction was observed. – no detailed description of therapy was provided.	– PASS, BBA, BBS, FMA and MBI scores significantly improved weekly in all three groups. – MBI score showed greater improvement in the four-channel group than in the placebo and two-channel groups one week after starting treatment. – Three weeks post therapy, PASS, BBS, FMA and MBI scores were significantly improved in the four-channel FES group.
Smith et al. [32]	Upper extremity	– FES on UE impairment in the acute, subacute or chronic post-stroke stages.	– 21 subjects with stroke affecting one or both upper limbs. – FMA median of initial assessment with severe UE impairment. – no control group was used.	– FES-UP system – up to eight sessions of one-hour therapy for up to 6 weeks. Functional training was encourgaed during FES use. – personalised parameters were set for the patients, with 40 Hz frequency.	– mean WMF–FAS scores of 2.6 and 2.2 (with FES) improved vs. the average scores of 1.5 and 1.3 (without FES).

Table 1. *Cont.*

Authors	Body Part	Description	Subjects	Intervention	Findings
Ambrosini et al. [28]	Lower Extremity	– FES cycling effects.	– nine patients with a mean age of 75 years, with first-ever stroke within 6 months. – low spasticity, good cognitive capacity (MMSE > 20) and patient ability to tolerate FES – no control group was used.	– 3 weeks, five sessions per week. – 60 min of standard physiotherapy and 25 min of FES cycling on a cycle ergometer. – an 8-channel current-controlled stimulator which coordinated bilateral neuromuscular stimulation of the quadriceps, hamstrings, anterior tibialis and lateral gastrocnemius muscles according to a muscle stimulation strategy. – rectangular biphasic pulses with a pulse duration of 400 microseconds and a frequency of 20 Hz were used.	– positive changes ($p < 0.05$) in subjects' status for MI Trunk Control Test, BBS, FIM motor subscale, and gait speed. – no statistical differences were found in cadence, exceping the work produced by the affected leg ($p = 0.044$) and the Area Symmetry Index between the affected and unaffected legs. – post training, the muscle synergies did not change significantly in the affected limb ($p = 0.405$); instead, the healthy extremity showed a significant decrease in the number of synergies ($p = 0.046$).
Hakakzade et al. [33]	Lower Extremity	– bilateral FES use on post-stroke patients during treadmill walking.	– six chronic stroke survivors (>6 months and <5 years). – communication and ambulation capacities. – no control group was used.	– 10 FES therapy sessions on a treadmill over 3 weeks (ten minutes/session), with a follow-up assessment after one month. – a controlled 8-channel stimulator (FES, Hasomed, Germany), with surface electrodes, in a bipolar configuration situated on the quadriceps, hamstrings, peroneals, and plantar flexors muscle groups. – pulse duration of 350 µs, frequency of 35 Hz, and amplitude were set to obtain muscle contractions under the electrode. Intensity variation in the first session from 20 mA to and 34 mA, and reached between 40 mA and 45 mA during the next session.	– MAS showed no improvement. – walking speed ($p < 0.001$), functional mobility (FAC) improved only after the intervention ($p = 0.039$), while no significant difference was found in the follow-up ($p = 3.17$). – TUG improved after therapy ($p = 0.011$), with 2.89 s decrease time, but no difference was registered after one month. – the 10 m walk test ($p = 0.031$) showed improvement, which was maintained after one month follow-up.

Table 1. *Cont.*

Authors	Body Part	Description	Subjects	Intervention	Findings
Tenniglo. J ett al. [29]	Lower Extremity	– influence of FES on hamstrings, knee kinematics and walking, in a stiff knee gait pattern.	– 16 chronic post-stroke patients, knee flexion reduction during the swing phase. – capacity to walk without help (physical support such as cane, frame). – eight participants used an AFO, five patients walked with a cane, and one used a quad cane. – no control group was used.	– three sessions of 1 h per week, 5 weeks. – Odstock 2-channel footswitch controlled stimulator system (Odstock Medical Limited, Salisbury, UK) was used for stimulation. – The stimulation frequency was 40 Hz, and the pulse duration varied between 0.125 and 0.475 s. – walking with electrodes placed at the level of the hamstring muscles on the paretic lower limb.	– an increase in knee mobility was observed during the swing phase of gait; also, the rise during flexion was considerable (flexion increased from 32.2 degrees to 37.9 degrees, $p < 0.001$). – walking speed grew from 0.91 m/s to 0.97 m/s ($p < 0.001$).
Schick et al. [34]	Upper extremity/RCT	– FES usability to perform ADLs in subacute post-stroke with moderate UE paresis.	– 12 subjects in the late post-acute ischemic post-stroke (1–6 months) – six subjects were in the experimental group and six in the control group. – two particpants from the interventin group and four from the control group had severe to moderate arm paresis.	– 3 weeks with 15 FES sessions, with 30 min of therapy. – FES was performed with the STIWELL® med4 device. – conventional rehabilitation program for the upper limb. – five FES interventions of 30 min per week. – four channels for muscle stimulation and up to two tracks for EMG signal acquisition was used. – biphasic rectangular pulses with a duration of 300 μs were used, with a frequency of 30 Hz. – intensity was set to visible contraction.	– the FMA for the upper extremity scale scores improved by +7.17 ($p < 0.05$) for the intervention group. – For BBT, both groups had an improved score on the affected side ($p < 0.05$). – SIS score improved significantly for the intervention group in all subdomains – no significant statistical differences were identified between groups in FMA, SIS or BBT.

FMA = Fugl-Meyer Assessment, PASS = Postural Assessment Scale for Stroke Patients, BBS = Berg Balance Score, BBA = Brunel Balance Assessment, MBI = Modified Barthel Index, TUG = Timed Up and Go, 6MWT = 6-Minute Walk Test, 10 mWT = 10 m Walk Test, FRT = Functional Reach Test, MI = Motricity Index MI, FIM = Functional Independence Measure, FAC = Functional Ambulation Category, BBT = Block and Box Test, WMF–FAS = Wolf Motor Function Test Functional Ability Scale, MAS = Modified Ashworth Scale, RMI = Rivermead Mobility Index RMI, DET = Duncan-Ely Test, AFO = Ankle Foot Orthosis, SIS = Stroke Impact Scale.

3.2. FES in Multiple Sclerosis

In the MS category, 215 subjects were investigated in three studies, as presented in Table 2; with 86 patients in the control groups, including 5 [35] with passive cycling and 81 using ankle foot orthosis [36,37]. In the studies carried out by Jukes et al. [36] and Renfrew et al. [37] there were 78 men and 126 women; the mean age of the participants was 51.68 years with a standard deviation of 11.50 (weighted to their count). Among all the 215 subjects, mean MS diagnosis age was 14.23 years, and the Expanded Disability Status Scale mean score was 5.82. Jukes et al. [36] and Renfrew et al. [37] reported 95 subjects with secondary progressive multiple sclerosis, 48 subjects with SPMS, and 39 subjects with primary progressive multiple sclerosis, whereas 21 subjects had an undefined MS subtype.

Table 2. FES in Multiple Sclerosis.

Authors	Body Part	Description	Subjects	Intervention	Findings
Jukes et al. [36]	Lower Extremity	– retrospective research on the daily use of ankle FES versus ankle foot orthosis, for 6 months, for patients with RRMS, SPMS and PPMS.	– 82 patients were assessed at baseline and after using FES for six months. – a group of 44 simple AFO users with MS was considered the control group.	– daily use for six months. – Odstock Dropped Foot Stimulator was used. – assessment before FES use, at six weeks, three months and six months. – subjects received indications and support regarding the use of FES.	– increase in walking speed of 0.1 m/s (15% improvement) and $p < 0.001$ was registered when stimulation was used. – QoL improved for FES users; the impact on the Psychosocial Impact of the Assistive Device Scale was also significant.
Renfrew et.al [37]	Lower Extremity	– RCT to compare the effects of AFO and FES in MS patients.	– 78 participants with MS lower limb impairment and leg drop. – persistent foot drop observed in the 5 min walk test; – no change in medication taken during the previous 3 months. – one group received FES (n = 41) and one group received only AFO use (n = 37).	– September 2014–January 2017. – one session of assessment – Odstock Dropped Foot Stimulator was used. – FES frequency was of 40 Hz; the pulse duration was adjusted according to the patient, and the intensity varied between 17 mA and 72 mA. – in the 5 min self-selected walk test, patients walked for 5 min for a distance of 10 m forward and backward.	– in the 5 min self-selected walk test, the group with orthosis walked more slowly than the group with FES. – subjects who had a slower gait were able to increase their gait speed with FES compared to those who used ankle foot orthosis. – the slow-walking group walked significantly faster with FES in comparison to those without FES, for both 25 ft WT ($p = 0.029$) and 5 min SSWT ($p = 0.037$) tests.
Edwards et.al [35]	Lower extremity	– cardiorespiratory response in cycling combined with FES in people with MS with severe mobility impairment.	– 11 subjects aged between 18 and 64 years who needed assistance to walk. – MS diagnosis and use of a walking aid. – patients should not have participated in the exercise session more than 2 times a week. – no control group was used, but patients were assigned to FES cycling or passive cycling.	– six months of FES daily use. – cyclic movements with FES, self-adhesive electrodes were placed on the quadriceps, hamstrings, and glutes; no specific FES device was used. – Training consisted of a 5 min rest period where they were monitored, a 1 min warm-up, 15 min of active cycling, and a 5 min cool-down (rehabilitation) period. – symmetrical and biphasic waveform, with a duration of 250 ms and a frequency of 50 Hz. The intensity was adjusted for every muscle group according to every patient's tolerance, and they had to maintain a cadence of 50 rotations per minute.	– a considerable difference in mean oxygen volume, with mean values higher during FES training than during passive training. – average heart rate was higher during FES cycling. Cycling combined with FES is more intense than passive cycling movements, so it can improve the physical condition of people with MS.

QoL = Quality of life, 5 min SSWT = 5-min self-selected walk test, 25 ftWT = 25-foot walk test.

3.3. FES in Spinal Cord Injuries

The SCI subsection of the analysis included 48 subjects in four studies, plus four subjects with post-stroke sequelae [38], as depicted Table 3. With the exception of Street et al. [39], the acquired data suggest that the spinal lesion was diagnosed with a mean of 7.04 years and the average age of the participants was 36.54 years, with a standard deviation of 11.78 (weighted to their count). Street et al. [39] did not report the genders of the participants nor the cause of SCI. Additionally, the participants' scores on the American Spinal Injury Association (ASIA) Impairment Scale were not specified; the authors only reported that the analyzed group matched the C and D scores. Furthermore, the study had gaps and missing data regarding the average age of the investigated participants after dropout. In the other three papers, 18 subjects had spinal injuries due to trauma (n = 18), and 6 caused by infection (n = 2), degeneration (n = 2) and tumor (n = 2); 9 participants scored A on the ASIA scale whereas 2 of the participants were evaluated with B, 11 with C, 1 with D and 1 with E [38,40,41].

Table 3. FES in spinal injury.

Authors	Body Part	Description	Subjects	Intervention	Findings
Hodkin et al. [38]	Upper Extremity	– muscle stimulation in neurological pathology of central origin for the rehabilitation of movements both after stroke and SCI.	– four chronic post-stroke participants and seven with SCI. – moderate or severe SCI in the cervical region (five ASIA C and two ASIA A scores), with upper limb involvement and an ARAT score less than 57 on the affected side. – no control group was used.	– SCI participants attended 5 sessions whereas stroke participants attended 9 to 10 sessions. – sessions were planned for 1 h, with the aim of 200 repetitions per session. – low-cost device which automatically delivers assistive FES concurrent with the users' volitionally activated movements. – FES 2-channel stimulator (Odstock Medical Ltd.) was applied to open the hand and achieve elbow extension. – for the grasping movement, the participant receives visual and auditory stimuli to perform this movement. Current values ranged from 20 to 35 mA, and stimulation pulses with a duration between 130 and 350 µs were used. The stimulation frequency was fixed at 40 Hz.	– for stroke survivors, ARAT scores improved by an average of 8 (±3.1) and were maintained for one week and one month follow-up. – for the SCI group, the improvement in the ARAT score was 3.4 (±1.1) on the trained side.
Street et al. [39]	Lower Extremity	– daily use of FES for the peroneal nerve, glutes and hamstrings for incomplete SCI with drop foot.	– 24 patients (ASIA C and D scores) who could walk at least 10 m with assistive devices were studied. – interval from diagnosis between 5 months and 39 years. – no control group was used.	– daily use for six months. – the Odstock Dropped Foot Stimulator was used. Participants were instructed how to use the FES device. – biphasic symmetrical or asymmetrical pulse stimulus at a frequency of 40 Hz with current intensity up to 100 mA and pulse width up to 360 µs was used. – the following muscles and nerves were stimulated: dorsiflexors of the foot, hamstrings to help knee flexion during the swing phase of gait, peroneal nerve stimulation combined with gluteal muscle stimulation to help hip extension in walking and to provide support with weight bearing and correct upright posture.	– after using FES for six months, an improvement in walking speed was observed ($p < 0.05$).

Table 3. *Cont.*

Authors	Body Part	Description	Subjects	Intervention	Findings
Sivaramakrishnan et al. [40]	Lower extremity/RCT	– double-blinded RCT for spastic SCI survivors, with one session of FES followed by TENS on the lower extremity.	– 10 subjects with spinal cord injuries with lower limb spasticity. – six subjects with ASIA C, two with ASIA A, one with D and one with E score	– one session of 30 min of FES, followed by TENS at an interval of 24 h. – for the TENS group, an ACU-TENS (TechnoMed) device with four bipolar channels was used whereas for the FES group, a Functional Electrical Stimulator (MEGA XP) Cybermedic device with eight channels was used. – FES was used with biphasic rectangular pulses with a frequency of 35 Hz and a duration of 300 µs, applied to the quadriceps, adductors and plantar flexors, fixed with straps. – the intensity was increased until a visible muscle contraction was observed, afterward the intensity was increased up to 300%, depending on tolerance.	– no significant differences were reported for hip adductors, knee extensors, and plantar flexors spasticity between groups – within-group analysis revealed a statistically significant difference in hip adductors ($p < 0.001$) and knee extensors ($p < 0.001$) both after TENS and FES application. – for SCATS assessment, no significant differences between groups were recorded.
Casabona et al. [41]	Lower Extremity	– FES during cycling on chronic paraplegic patients.	– six men and one woman aged 27–40 years. – more than 3 years following the injury, with complete lack of motor function below the level of the lesion. 5 participants with score ASIA A and two with B.	– one 20 min session was followed by a week off, then another 40 min session. – a motorized leg pedal exerciser (RECK MOTOmed viva 2) and FES technology (CHINESPORT, RehaStim) were used. – the patients sat in the wheelchair, and the electrodes were placed on the rectus femoris, biceps femoris and gluteus maximus on both lower limbs. – the muscles were stimulated to produce the cyclic movement, while the motorized system of the bike assisted participants during all the stages of the protocol. – intensity up to 130 mA, biphasic electric current with a duration between 50 and 400 µs was applied. – exercise session included an initial warm-up phase lasting for 2 min at a speed of 20 rotations per minute; an active stage, with electrical stimulation for 20 or 40 min, with speed set at 40 cycles per minute; and a comeback phase of 1 min at a rate of 20 revolutions per minute	– the functional angles of the knee decreased, and the degree of stiffness increased. – in the 20 min protocol for both flexion and extension, the muscle activity increased. – the phasic activity of rectus femoris decreased in the 40 min protocol, compared to 20 min protocol.

TENS = Transcutaneous electrical nerve stimulation, ARAT = Action Research Arm Test, SCATS = Spinal Cord Assessment Tool for Spastic Reflexes.

4. Discussion

4.1. Current State of the Use of FES in UMN Diseases

The studies in this scoping review report the main findings on the practice and use of FES for the functional rehabilitation of the upper or lower extremities in patients with post-stroke disorders, SCI or MS. Although the analyzed studies were carried out with different devices, on different pathologies, and using various durations of therapy, the review describes the current state of the use of FES in upper motor neuron disease.

Regarding the quality of the analyzed papers (Table 4), two of them do not provide detailed information on the statistical analysis, in particular on the baseline comparison to control groups, sample sizes and effect. If such an in-depth analysis is not carried out, the final results may not be statistically significant. Only six out of the fourteen papers reported the verification of the normality of the data distribution. On the other hand, the other eight articles, even if they used non-parametric tests (Wilcoxon, Mann–Whitney, Friedman), did not specify anything about the normality of the distribution of data. In one study, the power of the sample size and effect size was reported, both a priori and a posteriori [34]. Although in five pieces of research ANOVA was used to identify pre- and post-therapy modifications, none of the authors reported the effect size for every measured parameter. However, partial eta squared can be obtained within ANOVA and provide an effect size of the data.

Table 4. Quality of reviewed papers.

	Authors	RCT/ RCT No. Provided	CG	EG (n)	Blinding	Inclusion and Exclusion Criteria	Intervention Repro-ductibility	Statistycal Analysis	Baseline Comparison	Power, Sample and Effect Size	Data Normal Distribution	Outcomes/ Assessments	Limitations
Post-stroke FES (n = 7)	Ha e et al. [36]	yes/no	yes	22	no	yes	yes	ANOVA	no	no	Shapiro–Wilk	FRT, TUG, H-Reflex	yes
	Zheng et al. [31]	yes/no	x	33	single-assessor blinded	yes	partial	ANOVA, Chi-Squared	yes	no	no	FMA, BBS, PASS, BBA, MBI, Functional MRI	no
	Smith et al. [32]	no/no	no	21	no	yes	yes	Agreement correlation	NA	no	no	Adapted Wolf Motor Test	yes
	Ambrosini et al. [28]	yes/yes	no	9	no	yes	yes	Wilcoxon, Mann–Whitney, Friedman, Spearman Corrrelation	NA	no	no	MI, Trunk Control Test, FIM, BBS, Gait Speed	yes
	Hakakzade et al. [33]	no/no	no	6	no	yes	yes	One-Way ANOVA, Friedman, Wilcoxon	NA	no	Shapiro–Wilk	MAS, SLT (Step Length Test), ROM, TUG, FAC, 10-m WT	yes
	Tenniglo et al. [29]	no/no	no	16	no	yes	yes	Paired *t*-Test, Pearson Correlation	NA	no	Visual distribution	Rivermead, FAC, Motricity Index, Duncan-Ely Test,	yes
	Schick et al. [34]	yes	yes	yes	single-assessor blinded	yes	yes	Wilcoxon, Mann–Whitney, Kolmogorov–Smirnov	no	yes	Shapiro–Wilk	FMA, BBT, SIS	yes
MS FES (n = 3)	Jukes et al. [36]	no	no	yes	82	no	no	Paired *t*-Test, Pearson Correlation	NA	no	no	Walking speed, EDSS	yes
	Renfrew (Miller) et.al [37]	yes	no	yes	41	no	yes	Chi-Squared, *t*-Test, Mann–Whitney	yes	no	yes	5 min self-selected walk test, Oxygen cost of walking, 25 foot walk test., EDSS,	yes
	Edwards et.al [35]	yes	no	no	6	no	yes	*t*-Tests, Chi-Squared, ANOVA	yes	no	no	EDSS, Peak CRF	yes
SCI FES (n = 4)	Hodkin et al. [38]	no	no	no	11	no	yes	Two-sided Wilcoxon	NA	no	no	ASIA, ARAT	no
	Street et al. [39]	no	no	no	24	no	yes	Not specified	NA	no	no	ASIA, minimal clinically impor-tant difference (MCID), 10 m walking speed.	yes
	Sivaramakrishnan et al. [40]	yes	yes	yes	5	double-blinded	yes	Wilcoxon, Friedman	no	no	no	ASIA, MAS, Spinal Cord Assessment Tool for Spastic Reflexes (SCATS)	yes
	Casabona et al. [41]	no	no	no	6	no	yes	ANOVA, Pearson Correlation	NA	no	Shapiro–Wilk, Levene	ASIA, MAS, knee joint biomechanics, EMG	yes

With regard to the process of blinding in physiotherapy or rehabilitation, it is often challenging to use since many participants may be used to the techniques or procedures of applying electrophysical agents. However, most of the analyzed papers provided sufficient information for the reproducibility of the intervention and the use of inclusion and exclusion criteria. Additionally, the therapists can identify the groups by carefully analyzing the patients' exercise protocols.

A significant obstacle in post-stroke rehabilitation reviews and meta-analysis is linked to the research outcomes. As can be seen in Table 4, for SCI and MS, ASIA and EDSS are used. However, for post-stroke rehabilitation, numerous statistically validated scales with good psychometric properties are available, making the extraction of specific data into a more robust framework or statistical analysis challenging. A higher-qualitative and specific design for more types of post-stroke rehabilitation assessment is needed.

The reliance on FES as a potential tool for lower extremity impairment in UMN injuries was related to gait, primarily to improve gait parameters, as recent research also suggests [36,37]. The recorded results showed improvement in gait parameters, especially in the study where the patients were trained on an FES-assisted cycle ergometer. Additionally, improved balance and decreased spasticity were identified in the FES-assisted training progress in gait parameters [37].

The connection point in the studies carried out on post-stroke patients is represented by the research of gait parameters after the application of FES. The results are promising, with a significant increase in gait speed, but not all the studies use the same types of tests and measurements, and the results cannot be generalized. Another obstacle in data collection and interpretation is the small number of participants.

For the patients with MS and SCI, the duration of FES therapy was longer than for post-stroke patients. Although the sample sizes of patients and the primary disease are different, after six months of use in MS [30] and incomplete SCI [33] for lower extremity dysfunctions, the results of these two studies suggest that FES could be used to improve gait speed by daily use in both MS or incomplete SCI patients.

Recent research on SCI suggests that lumbar and incomplete SCIs have better rehabilitation outcomes than cervical or thoracic injuries, either complete or incomplete [42]. The analyzed papers, although FES was used on A to E grade ASIA impairments, showed that even for a complete SCI, a motor response can be obtained during FES. The therapy parameters used a frequency of 35 to 40 Hz, and a pulse width between 300 and 400 microseconds for the lower extremity was used. The intensity of the FES device was adjusted from 20 mA to 130 mA and to visible contraction [25].

An essential feature of FES in SCI is described in the research carried out by Casabona et al. [41]. Their results show that a 20 min FES therapy session can determine the increase of muscle stiffness, but in 40 min sessions, fatigue appears and negatively influences motor response; therefore, maladaptive feedback seems to manifest in complete SCI patients when FES is overused, somehow depicting a similar response of the upper motor neuron response as in MS [17], with hyperstimulation of the central nervous system or motor deficit units recruiting in a long repetitive task. Moreover, recent research also suggests the need to adjust FES parameters according to muscle fatigue and type of UMN injury, by lowering the frequency of stimuli [35]. Therefore, the duration of an FES session, either as therapy for rehabilitation of normal movement pattern or as neuroprosthesis for UMN locomotor impairments, should be carefully considered in future research, especially in clinical practice. Otherwise, results suggest that clinicians should identify the optimal duration of the FES training session in SCI patients. A limitation of the studies carried out on patients with incomplete SCI is that every study pursues a specific objective (walking speed, grasping ability of the upper extremity, reduction of spasticity); furthermore, there is heterogeneity regarding ASIA scoring in subjects which used FES. Consequently, the evaluation scales and tests are different, the severity of the spine injuries are mixed, and comparison of the results is difficult.

In chronic post-stroke patients, no modification of muscle spasticity was observed during ten therapy sessions of 10 min done over 6 weeks [27]. However, in the research performed on incomplete SCI [29] (eight of ten participants had a C score or higher on ASIA), where 30 min of FES were applied, the results suggested a significant change in hip abductors and knee extensors within four hours after therapy. Recent research on the effects of FES on SCI spasticity suggests that twenty sessions of FES combined with cycling decrease spasticity [38]; therefore, the results of the two studies in our review may be influenced by the FES research and therapy protocol and not by efficacy.

4.2. New Approaches to the Use of FES in UMN Diseases

For the upper extremities, a new system was investigated for the use of FES with biofeedback [43] for 21 post-stroke patients with severe upper extremity impairment, over five weeks, with movement improved with a FES device. However, in a group comparison for moderate upper extremity impairment, no significant difference was found during three weeks of FES and conventional therapy, respectively [27]. Whereas in the research carried out by Hodkin et al. [38] regarding the use of FES for chronic post-stroke and moderate or severe SCI, while the ARAT score improved for both groups, there was a better outcome in the ARAT score for post-stroke patients than for SCI survivors.

The Berg Balance Scale, Time Up and Go, Functional Ambulation Category, 6-Minute Walk Test, 10-Meter Walk Test, Fugl-Meyer Assessment, Motricity Index and Action Research Arm Test were reported for functional assessment. For clinical assessment, the Modified Barthel Index, Rivermead Mobility Index and Stroke Impact Scale were used. Four studies spread over six months, two investigated the effects of FES for one session, and the other eight were carried out for three to eight weeks. The outcomes of the analyzed papers were very heterogeneous, although gait speed was reported in 6 for the lower extremity stimulation (11 out of 14 papers). Further research should focus on the length of the research in time and the homogeneity of the reported outcomes and assessment scales [44].

For post-stroke FES users, the pulse duration was from 250 µs to 475 µs. Four studies used 40 Hz as the primary frequency, whereas one reported 20 Hz, and another, frequencies of 30 Hz and 35 Hz. The intensity used varied from 20 mA to visible contraction. Although FES orthotic devices should not allow skin irritations or injuries, skin erythema was reported in some cases. Nevertheless, we must emphasize that FES should not produce skin injuries if the electrodes are applied without error following the manufacturers' indications and if FES is performed by medical personnel trained and experienced in electrical stimulation.

Previous systematic reviews and meta-analyses were performed on post-stroke, spinal cord injury or MS patients and suggested that FES was better than other methods of electrical stimulation (for instance, neuromuscular electrical stimulation and transcranial direct current stimulation) for improving motor function of the upper extremities and the abilities to perform ADL in post-stroke patients and spinal cord injuries [26,45]. However, with post-stroke patients, FES combined with cycling needs further research [46].

Although much information regarding the use of FES in UMN disorders suggests patient improvements in ADL and walking, new technologies or strategies of combined therapies are needed. Recent product development research depicts that FES uses necessary adjustments, such as closed-loop operation and real-time feedback, but also emphasizes the ease of access to these devices for UMN-disabled subjects [47].

Among the papers analyzed, only Jukes et al. [36] approaches FES from the point of view of quality of life improvement and cost–benefit analysis for MS patients in a retrospective study; results suggests that although the cost is increased, efficiency and quality of life of MS patients improve compared to standard care. However, information on the costs of FES therapy is not presented in the other reviewed papers, and it represents a major gap in the existing literature and research. Therefore, future studies should also consider cost–benefit analysis in their research.

Although specific studies have investigated the effect of FES together with other rehabilitation methods such as super inductive system therapy, robotic therapy, or direct current transcranial stimulation, which have proven to be effective therapies in motor neuron pathologies [48–50], the purpose of this scoping review was to identify the efficiency of FES in addition to physical therapy or functional task training for UMN rehabilitation. Although the analyzed studies are heterogeneous and the evaluation methods are mixed, FES requires improvement in the methodology of clinical trials and guidelines of therapy protocols to prove its significant benefits on the quality of life and the functional independence of patients with central motor neuron diseases. Regarding future perspectives, besides the identification of therapy parameters and protocols, the potential use of FES as a neuroprosthesis, or the potential of a combination of action observation therapy alongside FES to enhance neuroplasticity, should be investigated [51]. The results of this scoping review may be heterogeneous due to the comprehensive nature of the review question, highlighting one of its limitations. In such circumstances, further actions to identify the potential use of FES in CNS disorders may be required as well; and consequently, further studies could be designed from the data based on the present findings.

5. Conclusions

After a stroke, patients with upper central motor neuron injuries, spinal cord injuries or MS can benefit from FES therapy. However, it is necessary to establish a protocol for daily training by identifying therapy parameters and session length, but also identify costs and benefits for the use of this technology as a neuroprosthesis in progressive UMN disorders primarily through the possibility of customization. Future directions should also be considered by identifying the impact on quality of life for UMN disorders and the use of FES, but also investigate the possibility of combining FES with virtual reality training or action observation therapy to enhance brain plasticity and strengthen real-time feedback.

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