# Effects of Electrical Stimulation in Spastic Muscles After Stroke

## Systematic Review and Meta-Analysis of Randomized Controlled Trials

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***Background and Purpose***—Neuromuscular electric stimulation (NMES) has been used to reduce spasticity and improve range of motion in patients with stroke. However, contradictory results have been reported by clinical trials. A systematic review of randomized clinical trials was conducted to assess the effect of treatment with NMES with or without association to another therapy on spastic muscles after stroke compared with placebo or another intervention.

***Methods***—We searched the following electronic databases (from inception to February 2015): Medline (PubMed), EMBASE, Cochrane Central Register of Controlled Trials and Physiotherapy Evidence Database (PEDro). Two independent reviewers assessed the eligibility of studies based on predefined inclusion criteria (application of electric stimulation on the lower or upper extremities, regardless of NMES dosage, and comparison with a control group which was not exposed to electric stimulation), excluding studies with <3 days of intervention. The primary outcome extracted was spasticity, assessed by the Modified Ashworth Scale, and the secondary outcome extracted was range of motion, assessed by Goniometer.

***Results***—Of the total of 5066 titles, 29 randomized clinical trials were included with 940 subjects. NMES provided reductions in spasticity (−0.30 [95% confidence interval, −0.58 to −0.03], n=14 randomized clinical trials) and increase in range of motion when compared with control group (2.87 [95% confidence interval, 1.18–4.56], n=13 randomized clinical trials) after stroke.

***Conclusions***—NMES combined with other intervention modalities can be considered as a treatment option that provides improvements in spasticity and range of motion in patients after stroke.

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**Key Words:** electric stimulation ■ muscle spasticity ■ review ■ stroke

Stroke is a leading cause of serious long-term disability in the United States. The American Heart Association estimated an overall stroke prevalence of 6.8 million Americans over the age of 20 years, accounting for 2.8% of the population, based on The National Health and Nutrition Examination Survey data from 2007 to 2010.[1] The burden of stroke is a global problem that causes well-known long-term disabilities, and spasticity is one of them.[2]

Spasticity may be defined as a motor disorder characterized by velocity and acceleration-dependent increased resistance to passive muscle stretch and hyperactivity of stretch reflexes.[3] The exact prevalence of spasticity is unknown. Recent studies showed that spasticity occurs in 20% to 30% of all stroke victims,[4–6] and one recent study has reported contracture development in 50% of the cases 6 months after stroke.[7]

The pathophysiology of spasticity can occur as a result of abnormalities on different levels, including muscular and spinal properties, as well as supraspinal mechanisms.[8] Traditional treatment modalities include use of an ankle-foot orthosis, physical therapy, systemic medications, tendon surgeries, and focal alcohol neurolysis. More recent treatment options include neuromuscular electric stimulation (NMES).[9] It is one hypothesis that NMES induces specific plasticity of spinal chord pathways.[10]

However, although some randomized clinical trials (RCTs) showed the beneficial effects of NMES on the treatment of

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patients with spasticity after stroke,[11,12] others did not find an additional reduction of spasticity with its usage when compared with a control group.[13,14] A systematic review of the evidence would allow a more precise evaluation of its effectiveness and, if the benefits are proven, would aid in disseminating the use of NMES. Therefore, the aim of our study was to systematically review the effect of treatment with NMES on spastic muscles after stroke compared with placebo or another intervention.

## Methods

### Protocol and Registration

This systematic review was performed in accordance with the Cochrane Collaboration[15] and the Preferred Reporting Items for Systematic Review and Meta-Analyses: the PRISMA Statement.[16] The protocol of the study was registered at the International Prospective Register Of Systematic Reviews, PROSPERO, under the identification CRD42014008946 and can be integrally assessed online (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014008946#).

### Eligibility Criteria

To be included in the review, the studies had to be RCTs which determined the effects of NMES or NMES combined with other treatment techniques on spasticity in stroke patients and had to have at least one intervention group and one comparison group. Studies that applied NMES on the lower or upper extremities were included, regardless of NMES dosage. The comparison group should not have been exposed to NMES in the same regimen as the NMES group, and the intensity of stimulation should not lead to visible or palpable contractions.

The exclusion criteria were having stroke survivors without muscular spasticity as participants, implementation of the intervention in regions other than feet or hands, and interventions with <3 days.

### Search Strategy

Literature searches were conducted in the following electronic databases (from the inception to February 2015): MEDLINE (accessed by PubMed), EMBASE, Cochrane Central Register of Controlled Trials (Cochrane CENTRAL), and Physiotherapy Evidence Database (PEDro). The search terms used individually or combined included stroke, electric stimulation, and a string of words previously proposed, which yielded a high sensibility in the search for randomized controlled trials.[17] To enhance the sensitivity of the search, words related to the outcomes of interest were not included. There were no language restrictions in the strategy, but non-English studies were included in the review only when translation was available. The references included in the published articles identified in these searches were used as an additional source to identify other clinical trials. The complete search strategy used for the PubMed database is shown in Table 1. The terms were adjusted to fit the requirements of each electronic database.

### Study Selection and Data Extraction

Two reviewers (C. Stein, C.G. Fritsch) separately and independently screened the titles and abstracts of studies identified in the initial searches. A standard screening checklist based on the eligibility criteria was used for each study. Studies that did not meet the criteria according to the titles or abstracts were excluded. Full text versions of the remaining studies, including those potentially eligible and uncertain, were retrieved independently for a second review by the 2 reviewers to determine the eligibility. Disagreements regarding study eligibility were discussed between reviewers. When consensus was not reached, a third reviewer (C. Robinson) arbitrated. For studies without sufficient information to evaluate the eligibility, the authors were contacted via e-mail to obtain clarifications. The studies with insufficient information after this contact were excluded, or

**Table 1. Literature Search Strategy Used for the PubMed Database**

| | |
|---|---|
| No. 1, Patient | *"Stroke"[Mesh] OR "Stroke" OR "Strokes" OR "Apoplexy" OR "CVA (Cerebrovascular Accident)" OR "CVAs (Cerebrovascular Accident)" OR "Cerebrovascular Accident" OR "Cerebrovascular Accidents" OR "Cerebrovascular Apoplexy" OR "Apoplexy, Cerebrovascular" OR "Cerebrovascular Stroke" OR "Cerebrovascular Strokes" OR "Stroke, Cerebrovascular" OR "Strokes, Cerebrovascular" OR "Vascular Accident, Brain" OR "Brain Vascular Accident" OR "Brain Vascular Accidents" OR "Vascular Accidents, Brain" OR "Cerebral Stroke" OR "Cerebral Strokes" OR "Stroke, Cerebral" OR "Strokes, Cerebral" OR "Stroke, Acute" OR "Acute Stroke" OR "Acute Strokes" OR "Strokes, Acute" OR "Cerebrovascular Accident, Acute" OR "Acute Cerebrovascular Accident" OR "Acute Cerebrovascular Accidents" OR "Cerebrovascular Accidents, Acute"* |
| No. 2, Intervention | *"Electrical Stimulation"[Mesh] OR "Electrical Stimulation" OR "Electrical Stimulations" OR "Stimulation, Electrical" OR "Stimulations, Electrical" OR "Stimulation, Electric" OR "Electric Stimulations" OR "Stimulations, Electric" OR "Electric Stimulation Therapy" [Mesh] OR "Stimulation Therapy, Electric" OR "Therapy, Electric Stimulation" OR "Electrotherapy" OR "Therapeutic Electric Stimulation" OR "Electric Stimulation, Therapeutic" OR "Stimulation, Therapeutic Electric" OR "Electrical Stimulation Therapy" OR "Stimulation Therapy, Electrical" OR "Therapy, Electrical Stimulation" OR "Therapeutic Electrical Stimulation" OR "Electrical Stimulation, Therapeutic" OR "Stimulation, Therapeutic Electrical" OR "Neuromuscular Electrical Stimulation" OR "Functional Electrical Stimulation"* |
| No. 3, Type of study | *(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial"[tw]) OR ((singl*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR ("latin square"[tw]) OR placebos [mh] OR placebo*[tw] OR random*[tw] OR research design [mh: noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR crossover studies [mh] OR control*[tw] OR prospectiv*[tw] OR volunteer*[tw]) NOT (animal [mh] NOT human [mh]).* |
| Search | No. 1 and No. 2 and No. 3 |

the procedures for estimation of missing data[15] were performed when possible. Studies with >1 publication reporting the results from the same population were excluded, and the publication with the largest sample size was chosen. Abstracts published in academic conferences were evaluated by case, and the authors were contacted for details when necessary. The reviewers were not blinded to the authors and institutions of the studies undergoing review.

The following data were extracted from included studies: methodological design, number of subjects, comparison groups, intervention protocol, and results of the outcomes. The primary outcome extracted was spasticity, assessed by Modified Ashworth Scale, and the secondary outcome extracted was range of motion, assessed by Goniometer. Two review authors (C. Stein, C.G. Fritsch) separately and independently extracted the data, and disagreements regarding the data extraction were solved by discussion. When consensus was not reached, a third author (C. Robinson) arbitrated. When data were missing for synthesis or study quality assessment, we contacted the study authors via e-mail at least 2 times. The study was excluded if data were still insufficient after this process.

### Risk of Bias Assessment

Two review authors (C. Stein, C.G. Fritsch) independently assessed the risk of bias of the included studies by considering the items established in the Cochrane Collaboration's tool (27) for assessing risk of

bias within and across randomized trials: adequate sequence generation, allocation concealment, blinding of patients and investigators, blinding of outcome assessors, description of losses and exclusions, and intention-to-treat analysis. Studies without a clear description of these items were considered as unclear or not reporting the item. Given the small number of included studies, it was considered inappropriate to present publication bias through funnel plot.

### Data Analysis

After data extraction, if the outcome measurements could not be transformed in a common numeric scale for quantitative synthesis, a descriptive synthesis was performed. For quantitative synthesis, pooled-effect estimates were obtained by comparing the change from baseline to study end for each group. Regarding the continuous outcomes, if the unit of measurement was consistent across trials, the results were presented as the weighted mean difference with 95% confidence intervals (95% CIs), and if the unit of measurement was inconsistent, the results were expressed as the standard mean difference with 95% CI. Calculations were performed using the random effects method, given the heterogeneity of outcome measurements ($I^2$>0). A $P$ value ≤0.05 was considered statistically significant. The statistical heterogeneity of the treatment effects among studies was assessed using Cochran's Q test and the inconsistency $I^2$ test, in which values above 25% and 50% were considered as indicatives of moderate and high heterogeneity, respectively. To reduce the statistical heterogeneity, a sensitivity analysis was performed considering the type of comparison (control or placebo) group. All analyses were conducted using Review Manager, version 5.2.

## Results

### Description of Studies

From 5066 potentially relevant citations retrieved from electronic databases and reference lists searches, 29 RCTs[11–14,18–42] met the inclusion criteria and were included in the systematic review, providing data on 940 subjects. Six additional studies were found from the reference list of published articles. The 29 included studies reported data on spasticity, but only 14 where included in the meta-analysis. Fifteen studies were not included in the meta-analysis for spasticity because it was not possible to obtain clarifications about the missing data on the publication[18,26,30–33,40,41] and because other scales were used to assess spasticity.[19,34–39] The 13 studies which assessed range of motion were included in our second meta-analysis. Figure 1 shows the flow diagram of the included studies, and Table I in the online-only Data Supplement summarizes the characteristics of these studies (online-only Data Supplement).

In 22 studies,[11,13,14,18–36] the stimulation frequencies with NMES ranged from 18 to 50 Hz and pulse duration from 0.1 to 0.4 ms. In 3 studies[12,37,38] the stimulation frequencies with NMES ranged from 80 to 100 Hz and pulse duration from 0.1 to 0.3 ms. Four studies[39–42] did not describe the stimulation characteristics. The time of intervention the studies was averaged 3038.75 minutes. The intervention occurred in an outpatient environment, except for one study that performed a domiciliary approach.[31]

### Risk of Bias

93% of the studies presented adequate sequence generation and 86% described losses to follow-up and exclusions, showing a low risk of bias for these analyses. When considering the assessment of the outcomes, 62% reported blinding of the investigators, with a moderate risk of bias. Therefore, 28% reported adequate allocation concealment, 14% reported blinding, and 24% performed intention-to-treat analyses, showing high risk of bias for these characteristics (Table 2).

### Effects of Interventions

#### *Spasticity*

Fourteen studies[11–14,20–25,27–29,41] (n=383) evaluated spasticity using the Modified Ashworth Scale and were included in the meta-analysis. NMES or NMES combined with other treatment techniques was associated with reductions in spasticity

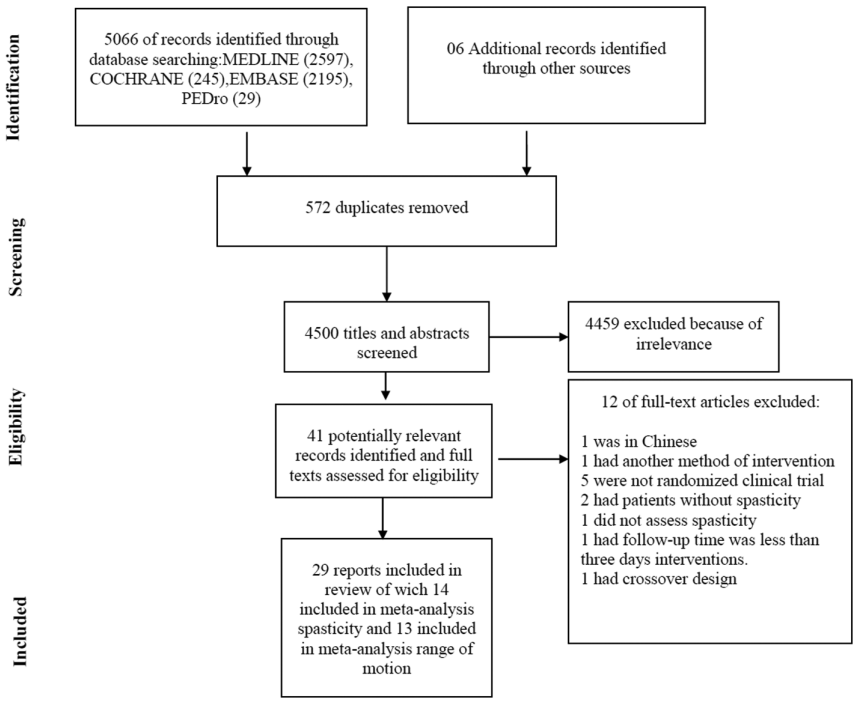


**Figure 1.** The flow diagram of studies included in the review.

**Table 2. Risk of Bias of the Included Studies**

| Author, Year | Adequate Sequence Generation | Allocation Concealment | Blinding of Patients and Investigators | Blinding of Outcome Assessors | Description of Losses and Exclusions | Intention-to-Treat Analysis |
|---|---|---|---|---|---|---|
| Bakhtiary and Fatemy, 2008[12] | Yes | Yes | No | Yes | Yes | Yes |
| Barker et al, 2008[20] | Yes | Yes | No | Yes | Yes | Yes |
| Bauer P et al, 2015[18] | Yes | Yes | No | Yes | Yes | Yes |
| Boyaci et al, 2013[21] | Yes | No | No | Yes | Yes | Not report |
| Chan et al, 2009[22] | Yes | No | No | Yes | Yes | Not report |
| Cheng et al, 2010[34] | Yes | Yes | No | Yes | Yes | Not report |
| de Kroon et al, 2004[23] | Yes | No | Yes | Yes | Yes | No |
| Duarte et al, 2011[24] | Yes | No | Yes | Yes | Yes | Yes |
| Embrey et al, 2010[30] | Yes | No | No | No | Yes | Not report |
| Hara et al, 2008[40] | Yes | No | No | No | Yes | Not report |
| Hara et al, 2006[41] | Yes | No | No | No | No | Not report |
| Heckmann et al, 1997[38] | No | No | No | No | No | Not report |
| Hesse et al, 1995[26] | Yes | No | No | No | No | Not report |
| Hesse et al, 1998[25] | Yes | No | No | Yes | Yes | Not report |
| Johnson et al, 2004[14] | Yes | Yes | No | No | Yes | Not report |
| Jong et al, 2013[39] | Yes | Yes | Yes | Yes | Yes | Yes |
| Karakus et al, 2012[31] | Yes | No | Yes | Yes | Yes | Not report |
| Kim and Lee, 2014[42] | Yes | No | No | No | Yes | No |
| Lin and Yan, 2011[27] | Yes | No | No | Yes | Yes | Not report |
| Malhotra et al, 2012[36] | Yes | Yes | No | Yes | Yes | Yes |
| Mangold et al, 2009[13] | Yes | No | No | No | Yes | Yes |
| Mesci et al, 2007[28] | Yes | No | No | No | Yes | Not report |
| Mesci et al, 2009[11] | Yes | No | No | Yes | Yes | Not report |
| Mokrusch, 1997[32] | Yes | No | No | No | No | Not report |
| Ring and Rosenthal, 2005[33] | No | No | No | Yes | Yes | Not report |
| Sabut et al, 2011[29] | Yes | No | No | No | Yes | Not report |
| Sahin et al, 2012[37] | Yes | Yes | No | Yes | Yes | Not report |
| Yan et al, 2005[35] | Yes | No | No | Yes | Yes | Not report |
| You et al, 2014[19] | Yes | No | No | Yes | Yes | No |

when compared with control group (−0.30 [95% CI, −0.58 to −0.03; $I^2$ 81%]; Figure 2A). Fifteen studies were not included in the meta-analysis for spasticity because it was not possible to obtain clarifications about the missing data on the publication[18,26,30–33,40,41] and because other scales were used to assess spasticity.[19,34–39]

To investigate possible differences between studies, a sensitivity analysis related to type of intervention and the site of application of NMES was performed. Twelve studies[11–14,20,22,24,25,27–29,41] that applied NMES combined with other treatment technique interventions showed significant reductions in spasticity compared with control (−0.35 [95% CI, −0.63 to −0.07; $I^2$ 80%]; Figure 2B). The other 2 studies[21,23] applied only NMES and showed no significant reductions in spasticity (0.13 [95% CI, −1.53 to 1.78; $I^2$ 92%]; Figure 2B). Five studies that used NMES on the leg[11,12,14,28,29] showed significant reduction in spasticity compared with control (−0.78 [95% CI, −1.02 to −0.54; $I^2$ 48%]; Figure 2C), whereas six studies which used NMES on the wrist[13,21–23,25,41] showed no significant reduction in spasticity (0.12 [95% CI, −0.41 to 0.64; $I^2$ 81%]; Figure 2C). Four other trials applied NMES on the elbow[20,22,25,42] and reported no significant reduction in spasticity (−0.39 [95% CI, −0.89 to 0.11; $I^2$ 54%]; Figure 2C).

We performed a sensitivity analysis to evaluate possible differences in RCTs that comprised botulinum toxin combined with NMES compared with control group. Three studies had this characteristic and in 2 of them the control group intervention was botulinum toxin,[24,25] whereas the other was physiotherapy. The 3 studies[14,24,25] showed no significant improvements on spasticity (−0.39 [95% CI, −0.97 to 0.19; $I^2$ 47%)]; Figure 2D) with the addition of NMES in comparison with the control groups.

The studies that were not included in the spasticity meta-analysis reported different results. In 8 studies,[19,26,32–35,37,38] there was an improvement in the spasticity on the intervention group when compared with control group ($P$<0,05). In 2 RCTs,[40,41] there was a tendency of reduction in spasticity on the intervention group when compared with control group. In 5 studies,[18,30,31,36,39] there was no differences between intervention and control groups ($P$>0,05).

### Range of Motion

Range of motion was evaluated with the use of goniometer in 13 trials[11,12,21–23,28,29,34,36–39,42] (n=447), and they were all included in meta-analysis. NMES or NMES combined with other treatment technique interventions was associated with an increase in range of motion when compared with the control group (2.87 [95% CI, 1.18–4.56; $I^2$ 60%]; Figure 3A).

Sensitivity analysis was performed to investigate possible differences between studies toward type of intervention and site of application of NMES. Eleven studies[11,12,22,28,29,34,36–39,42] that applied NMES combined with other treatment techniques showed significant increase in range of motion when compared with control (2.73 [95% CI 1.07–4.39; $I^2$ 62%]; Figure 3B). The other 2 studies[21,23] that used only NMES showed no significant improvement in range of motion (6.93 [95% CI, –9.31 to 23.16; $I^2$ 62%]; Figure 3B). Five RCTs applied NMES on the leg combined with other treatment techniques interventions[11,12,28,34,38] and reported a significant increase in range of motion when compared with control (3.13 [95% CI 0.61–5.64; $I^2$ 77%]; Figure 3C). Seven trials applied NMES or NMES combined with other interventions on the wrist[21,23,36,38,39,42] and showed no significant improvement in range of motion (0.46 [95% CI –2.28 to 3.21; $I^2$ 60%]; Figure 3C). Three other trials applied NMES combined with other interventions on the elbow[22,39,42] and showed significant effects on range of motion (4.57 [95% CI 0.57–8.57; $I^2$ 0%]; Figure 3C).

## Discussion

This systematic review with meta-analysis showed that NMES combined with other treatment techniques is an additional

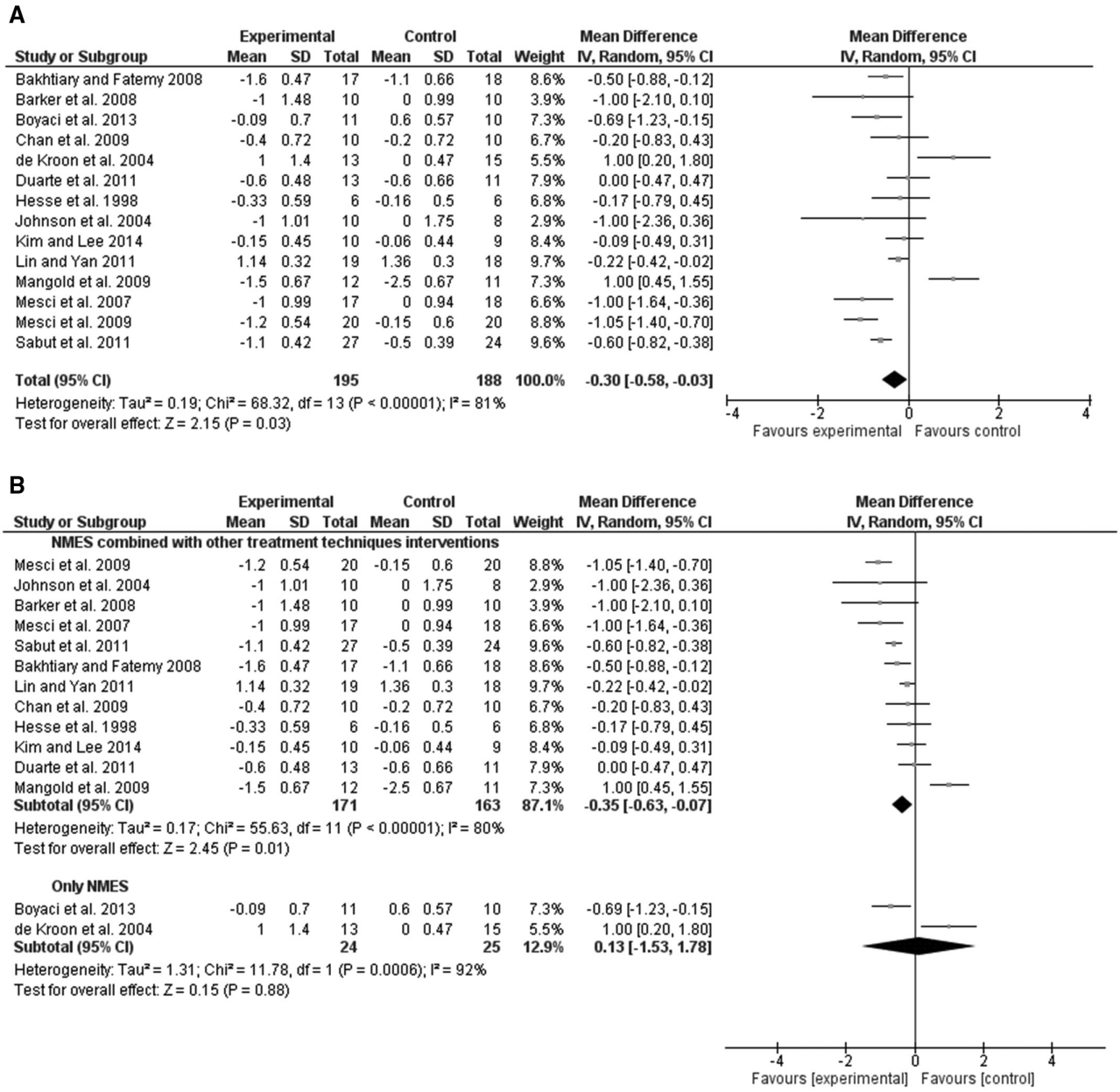


**Figure 2.** The standard mean difference and 95% confidence interval (CI) in spasticity for interventions (**A**), and for interventions type (**B**).

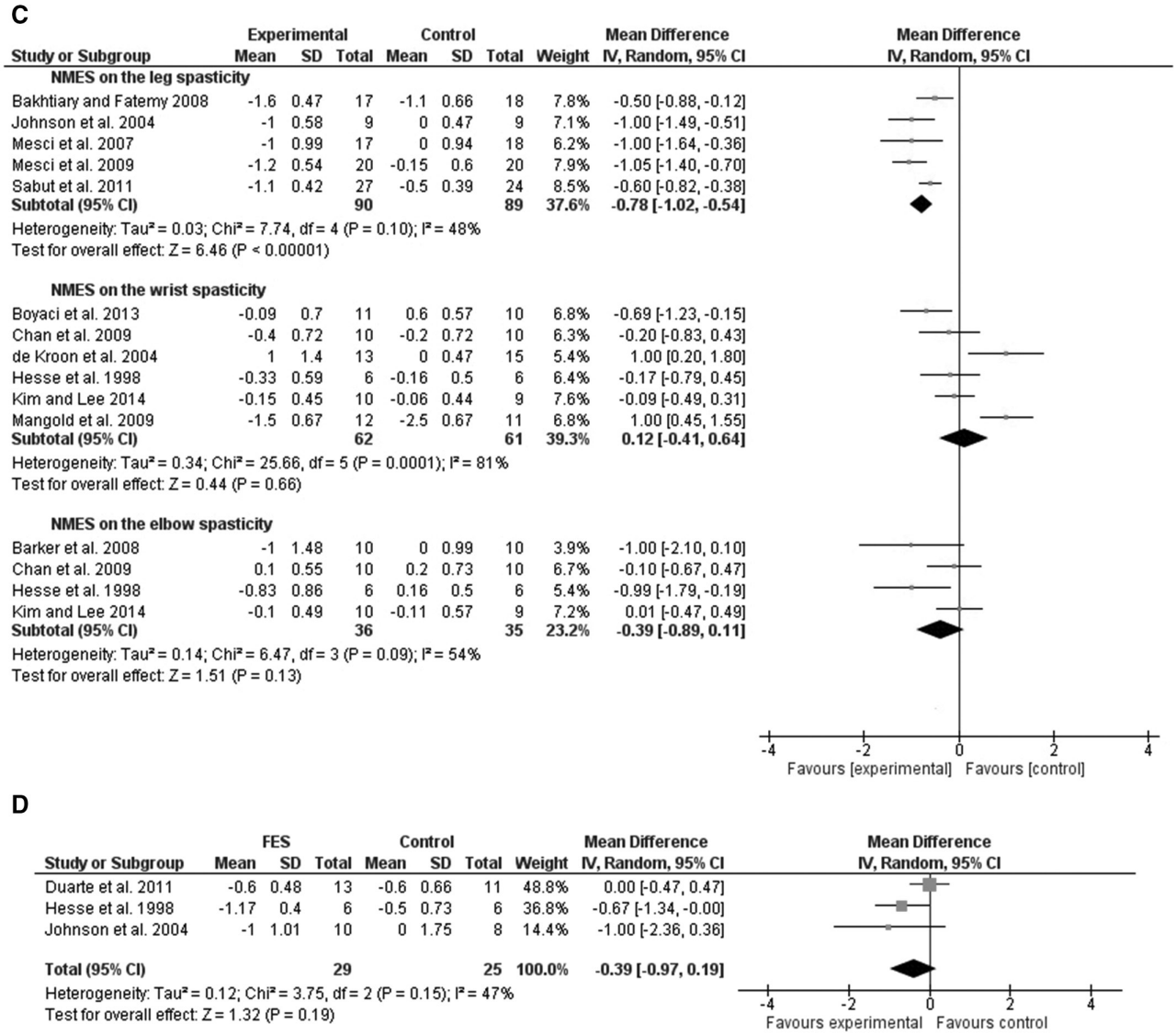


**Figure 2 (Continued).** The standard mean difference and 95% confidence interval (CI) in spasticity for site of application of the neuromuscular electric stimulation (NMES; **C**), and for treatment with NMES combined with botulinum toxin (**D**).

treatment option that provides improvements in spasticity and increase in range of motion in stroke patients. To the best of our knowledge, this is the first systematic review with meta-analysis evaluating the effectiveness of treatments with NMES on spastic muscle after stroke compared with placebo or another intervention.

The use of NMES in the rehabilitation of patients with neurological diseases has increased in recent years.[43] Its effects on the reduction of spasticity may be explained by its actions on increasing Ib fiber activation via mechanisms that facilitate the Renshaw cell recurrent inhibition, on antagonist reciprocal inhibition, and on increasing cutaneous sensory stimuli.[44,45]

The application of NMES combined with other interventions was associated with reductions on spasticity and improvements in range of motion when compared with a control group. As spasticity may impair functional activities in stroke patients, it is necessary to control it before applying any motor control therapeutic protocol.[12] From our findings, the application of NMES to reduce spasticity in these patients can be recommended. It would lead to a bigger benefit from motor control programmes and a better improvement in the functional activity. The usage of NMES could not inhibit the use of the unaffected hand, but it could enhance and facilitate the patient to use the affected hand for day-to-day tasks, resulting in improvements in range of motion.[22]

Additionally, when we performed sensitivity analysis related to the site of application of NMES, applications on wrists showed no effects on both spasticity and range of motion and on elbows showed no effects only on spasticity. These results may be because of differences between trials. For example, participant groups varied between studies in time after stroke (ranged from 1.5 months to >12 months), time of treatment, degree of spasticity, and degree of functional deficit. It is possible that time after stroke, time of treatment, degree of spasticity, and degree of ability to voluntarily contract a muscle might affect response to electric stimulation. Another source of variation was the different conventional therapies

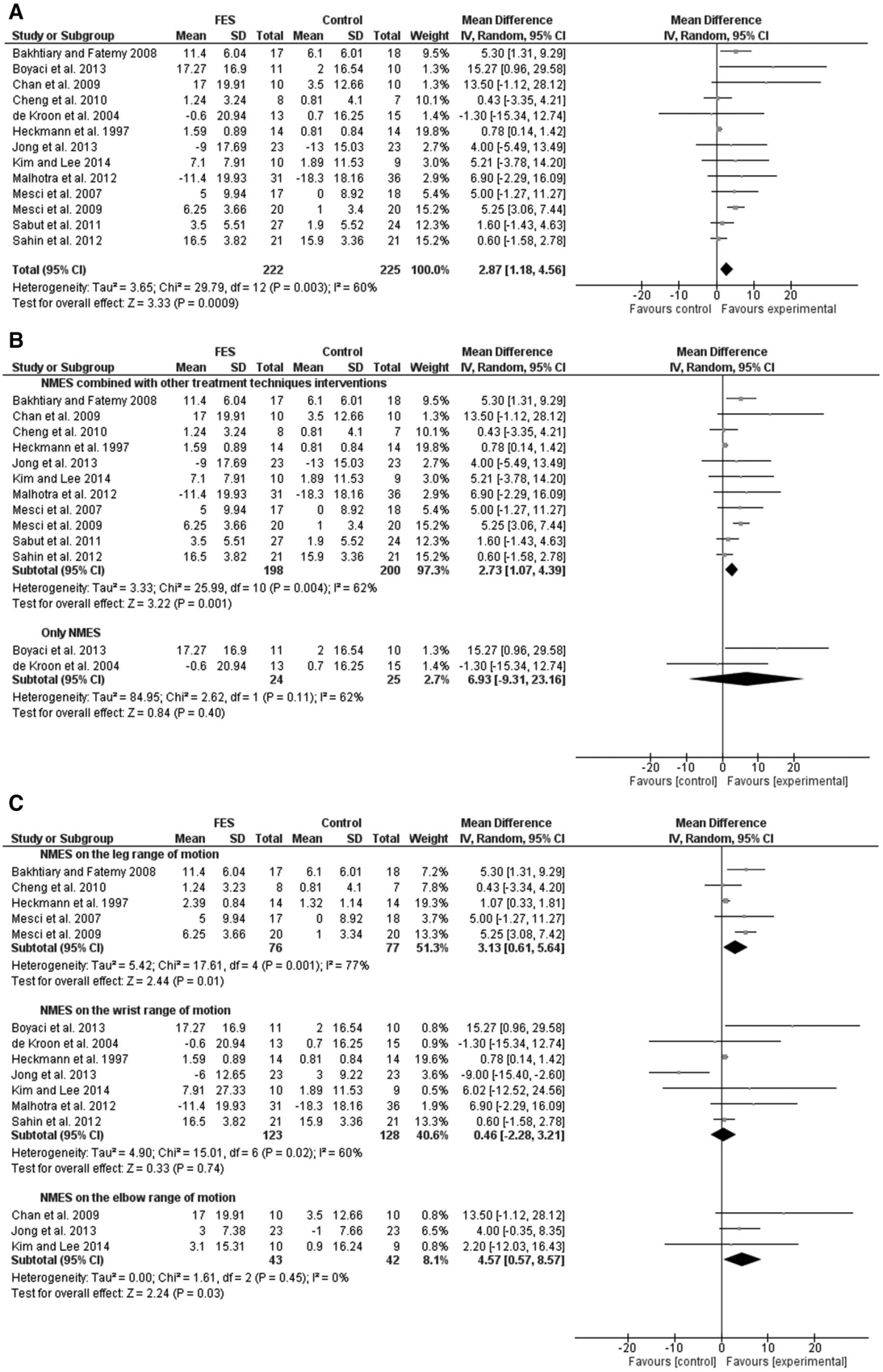


**Figure 3.** The standard mean difference and 95% confidence interval (CI) in range of motion for interventions (**A**), for interventions type (**B**), and for site of application the NMES (**C**).

used as comparator treatments in included trials, which were Bobath,[12] Active leg cycling,[19] SMART Arm,[20] Conventional Occupational Therapy,[22] Botulinium Toxin A,[24] and Stretching with proprioceptive neuromuscular facilitation technique.[37] Furthermore, the different outcome measures, which were not always possible to combine, resulted in some units of analysis containing data from only one study.

Moreover, chronic tissue changes because of immobilization, such as atrophy, loss of sarcomeres, muscle conversion to connective tissue, and decreased resting length of the muscle, may compromise the success of NMES.[46] In addition, loss of motor units in the paretic arm, which might be caused by secondary trans-synaptic degeneration, could compromise effective NMES performance.[47]

When we analyze Figure 2A, we observe that the studies[11,12,21,28,29] that are favorable to the usage of NMES or NMES combined with other treatment techniques have a greater weight in determining the final result. In relation to range of motion (Figure 3A), 3 studies[11,12,21] that have a greater weight have a favorable result for the intervention, whereas the remaining studies did not favor any group.

In the subanalysis with the 3 studies concerning botulinum toxin combined NMES showed no significant reduction in spasticity.[14,24,25] This can be explained by the small number of studies included in the subanalysis and the insufficiency of the sample size to demonstrate efficacy.

Concerning the stimulation parameters to be used, there are still discussions in the literature. There is scope of variation not only across studies but also across interindividuals to evoke optimal muscle contraction and to avoid discomfort, pain, and skin irritations.[48] In this review, the usage of NMES with a frequency between 30 and 50 Hz and a pulse width between 0.1 and 0.5 ms for 30 minutes 5 times per week for 3 to 4 weeks were associated with successful results.

A limitation of this systematic review and meta-analysis is that most of the studies retrieved showed some biases. Two studies no properly described the generation of a random sequence[33,38] and only 8 studies[12,14,18,20,34,36,37,39] clearly described allocation concealment. Moreover, only 4 studies[23,24,31,39] reported the patient blinding. Nonpharmacological studies that involve physical activity interventions have several limitations compared with drug RCTs. These limitations can involve learning curves, standardization of interventions, lack of blinding, and cointervention. The lack of blinding could be considered a major limitation of RCTs included in this review, but, as discussed earlier, this is an inherent limitation of nonpharmacological studies.

In addition to that, 11 studies[13,14,26,28–30,32,38,40–42] did not describe the blinding of the assessors, 4 studies[26,32,38,41] did not report drop-outs and exclusions that occurred during the treatment period, and only 7 studies[12,13,18,20,24,36,39] used the intention to treat analysis. Therefore, sensitivity analyses were limited because of lack of methodological quality of the included studies and the small number of studies and participants.

In the meta-analysis of studies involving NMES or NMES combined with other treatment techniques versus control group, the criteria for spasticity assessment were different. Some studies used the 6-level Modified Ashworth Scale instead of the regularly used 5-level Ashworth Scale. Although the Ashworth Scale is a widely used measure of spasticity, it may not be sensitive enough to detect minimum changes. A modification of the scale has been created and adds an additional intermediate grade (1+).[49]

## Conclusions

NMES combined with other intervention modalities is a treatment option that provides improvements in spasticity and range of motion in stroke patients. This data provides support for further NMES use as an additional therapy technique, but the conduction of large scale and high-quality RCTs is needed to establish its true efficacy.

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C. Stein elaborated the systematic review protocol and the search strategy, performed the search strategy, the analysis process, and the redaction of the article, as well as its final revision. C.G. Fritsch performed the search strategy, the studies selection, the data extraction, gave intellectual support for the analysis process, the redaction of the article, and its final revision. C.C. Robinson gave intellectual support for the search strategy construction, arbitrated in the final consensus of included articles and risk of bias assessment, gave intellectual support for the analysis process, the redaction of the article, and its final revision. G. Sbruzzi gave intellectual support for the systematic review protocol elaboration, the search strategy construction, the analysis process, the redaction of the article, and performed its final revision. R.D.M. Plentz gave intellectual support for the systematic review protocol, the search strategy construction, the analysis process, the redaction of the article, and performed its final revision.

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## Disclosures

None.

## References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6–e245. doi: 10.1161/CIR.0b013e31828124ad.
2. Sommerfeld DK, Gripenstedt U, Welmer AK. Spasticity after stroke: an overview of prevalence, test instruments, and treatments. *Am J Phys Med Rehabil*. 2012;91:814–820. doi: 10.1097/PHM.0b013e31825f13a3.
3. Lance JW. The control of muscle tone, reflexes, and movement: Robert Wartenberg Lecture. *Neurology*. 1980;30:1303–1313.
4. Wissel J, Schelosky LD, Scott J, Christe W, Faiss JH, Mueller J. Early development of spasticity following stroke: a prospective, observational trial. *J Neurol*. 2010;257:1067–1072. doi: 10.1007/s00415-010-5463-1.
5. Lundström E, Terént A, Borg J. Prevalence of disabling spasticity 1 year after first-ever stroke. *Eur J Neurol*. 2008;15:533–539. doi: 10.1111/j.1468-1331.2008.02114.x.
6. Lundström E, Smits A, Terént A, Borg J. Time-course and determinants of spasticity during the first six months following first-ever stroke. *J Rehabil Med*. 2010;42:296–301. doi: 10.2340/16501977-0509.
7. Kwah LK, Harvey LA, Diong JH, Herbert RD. Half of the adults who present to hospital with stroke develop at least one contracture within six months: an observational study. *J Physiother*. 2012;58:41–47. doi: 10.1016/S1836-9553(12)70071-1.

8. Burke D, Wissel J, Donnan GA. Pathophysiology of spasticity in stroke. *Neurology*. 2013;80(3 suppl 2):S20–S26. doi: 10.1212/WNL.0b013e31827624a7.
9. Wilkenfeld AJ. Review of electrical stimulation, botulinum toxin, and their combination for spastic drop foot. *J Rehabil Res Dev*. 2013;50:315–326.
10. Motta-Oishi AA, Magalhães FH, Mícolis de Azevedo F. Neuromuscular electrical stimulation for stroke rehabilitation: is spinal plasticity a possible mechanism associated with diminished spasticity? *Med Hypotheses*. 2013;81:784–788. doi: 10.1016/j.mehy.2013.08.013.
11. Mesci N, Ozdemir F, Kabayel DD, Tokuc B. The effects of neuromuscular electrical stimulation on clinical improvement in hemiplegic lower extremity rehabilitation in chronic stroke: a single-blind, randomised, controlled trial. *Disabil Rehabil*. 2009;31:2047–2054. doi: 10.3109/09638280902893626.
12. Bakhtiary AH, Fatemy E. Does electrical stimulation reduce spasticity after stroke? A randomized controlled study. *Clin Rehabil*. 2008;22:418–425. doi: 10.1177/0269215507084008.
13. Mangold S, Schuster C, Keller T, Zimmermann-Schlatter A, Ettlin T. Motor training of upper extremity with functional electrical stimulation in early stroke rehabilitation. *Neurorehabil Neural Repair*. 2009;23:184–190. doi: 10.1177/1545968308324548.
14. Johnson CA, Burridge JH, Strike PW, Wood DE, Swain ID. The effect of combined use of botulinum toxin type A and functional electric stimulation in the treatment of spastic drop foot after stroke: a preliminary investigation. *Arch Phys Med Rehabil*. 2004;85:902–909.
15. Higgins JPT, Sally G. *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 March 2011[e-book online]*. http://www.cochrane-handbook.org. Accessed December 2013.
16. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097. doi: 10.1371/journal.pmed.1000097.
17. Robinson KA, Dickersin K. Development of a highly sensitive search strategy for the retrieval of reports of controlled trials using PubMed. *Int J Epidemiol*. 2002;31:150–153.
18. Bauer P, Krewer C, Golaszewski S, Koenig E, Müller F. Functional electrical stimulation-assisted active cycling–therapeutic effects in patients with hemiparesis from 7 days to 6 months after stroke: a randomized controlled pilot study. *Arch Phys Med Rehabil*. 2015;96:188–196. doi: 10.1016/j.apmr.2014.09.033.
19. You G, Liang H, Yan T. Functional electrical stimulation early after stroke improves lower limb motor function and ability in activities of daily living. *NeuroRehabilitation*. 2014;35:381–389. doi: 10.3233/NRE-141129.
20. Barker RN, Brauer SG, Carson RG. Training of reaching in stroke survivors with severe and chronic upper limb paresis using a novel nonrobotic device: a randomized clinical trial. *Stroke*. 2008;39:1800–1807. doi: 10.1161/STROKEAHA.107.498485.
21. Boyaci A, Topuz O, Alkan H, Ozgen M, Sarsan A, Yildiz N, et al. Comparison of the effectiveness of active and passive neuromuscular electrical stimulation of hemiplegic upper extremities: a randomized, controlled trial. *Int J Rehabil Res*. 2013;36:315–322. doi: 10.1097/MRR.0b013e328360e541.
22. Chan MK, Tong RK, Chung KY. Bilateral upper limb training with functional electric stimulation in patients with chronic stroke. *Neurorehabil Neural Repair*. 2009;23:357–365. doi: 10.1177/1545968308326428.
23. de Kroon JR, IJzerman MJ, Lankhorst GJ, Zilvold G. Electrical stimulation of the upper limb in stroke: stimulation of the extensors of the hand vs. alternate stimulation of flexors and extensors. *Am J Phys Med Rehabil*. 2004;83:592–600.
24. Duarte E, Marco E, Cervantes C, Díaz D, Chiarella SC, Escalada F. Efectos de la toxina botulínica tipo A y electroestimulación en la espasticidad flexora distal de la extremidad superior en el ictus. Ensayo clínico aleatorizado. *Rehabilitación (Madr)*. 2011;45:194–201.
25. Hesse S, Reiter F, Konrad M, Jahnke MT. Botulinum toxin type A and short-term electrical stimulation in the treatment of upper limb flexor spasticity after stroke: a randomized, double-blind, placebo-controlled trial. *Clin Rehabil*. 1998;12:381–388.
26. Hesse S, Jahnke MT, Luecke D, Mauritz KH. Short-term electrical stimulation enhances the effectiveness of Botulinum toxin in the treatment of lower limb spasticity in hemiparetic patients. *Neurosci Lett*. 1995;201:37–40.
27. Lin Z, Yan T. Long-term effectiveness of neuromuscular electrical stimulation for promoting motor recovery of the upper extremity after stroke. *J Rehabil Med*. 2011;43:506–510. doi: 10.2340/16501977-0807.
28. Mesci N, Özdemir F, Kabayel DD, Tokuç B. The Effect of Neuromuscular Electrical Stimulation on Gait Speed and Distance in Patients with Stroke. *Turk J Phys Med Rehab*. 2007;53:144–149.
29. Sabut SK, Sikdar C, Kumar R, Mahadevappa M. Functional electrical stimulation of dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity, and motor recovery in stroke patients. *NeuroRehabilitation*. 2011;29:393–400. doi: 10.3233/NRE-2011-0717.
30. Embrey DG, Holtz SL, Alon G, Brandsma BA, McCoy SW. Functional electrical stimulation to dorsiflexors and plantar flexors during gait to improve walking in adults with chronic hemiplegia. *Arch Phys Med Rehabil*. 2010;91:687–696. doi: 10.1016/j.apmr.2009.12.024.
31. Karakus D, Ersoz M, Koyuncu G, Türk D, Münevver sasmaz F, Akyüz N. Effects of functional electrical stimulation on wrist function and spasticity in stroke: a randomized controlled study. *Turk J Phys Med Rehab*. 2013;59:97–102.
32. Mokrusch T. Behandlung der hirninfarktbedingten spastis- chen Hemiparese mit EMG-getriggerter Elektrostimulation. *Neuro Rehabil*. 1997;2:82–86.
33. Ring H, Rosenthal N. Controlled study of neuroprosthetic functional electrical stimulation in sub-acute post-stroke rehabilitation. *J Rehabil Med*. 2005;37:32–36. doi: 10.1080/16501970410035387.
34. Cheng JS, Yang YR, Cheng SJ, Lin PY, Wang RY. Effects of combining electric stimulation with active ankle dorsiflexion while standing on a rocker board: a pilot study for subjects with spastic foot after stroke. *Arch Phys Med Rehabil*. 2010;91:505–512. doi: 10.1016/j.apmr.2009.11.022.
35. Yan T, Hui-Chan CW, Li LS. Functional electrical stimulation improves motor recovery of the lower extremity and walking ability of subjects with first acute stroke: a randomized placebo-controlled trial. *Stroke*. 2005;36:80–85. doi: 10.1161/01.STR.0000149623.24906.63.
36. Malhotra S, Rosewilliam S, Hermens H, Roffe C, Jones P, Pandyan AD. A randomized controlled trial of surface neuromuscular electrical stimulation applied early after acute stroke: effects on wrist pain, spasticity and contractures. *Clin Rehabil*. 2013;27:579–590. doi: 10.1177/0269215512464502.
37. Sahin N, Ugurlu H, Albayrak I. The efficacy of electrical stimulation in reducing the post-stroke spasticity: a randomized controlled study. *Disabil Rehabil*. 2012;34:151–156. doi: 10.3109/09638288.2011.593679.
38. Heckmann J, Mokrusch T, Krockel A, Warnke S, von Stockert T, Neundorfer B. EMG-triggered electrical stimulation in the treatment of central hemiparesis after a stroke. *Eur J Phys Med Rehab*. 1997;7:138–141.
39. de Jong LD, Dijkstra PU, Gerritsen J, Geurts AC, Postema K. Combined arm stretch positioning and neuromuscular electrical stimulation during rehabilitation does not improve range of motion, shoulder pain or function in patients after stroke: a randomised trial. *J Physiother*. 2013;59:245–254. doi: 10.1016/S1836-9553(13)70201-7.
40. Hara Y, Ogawa S, Tsujiuchi K, Muraoka Y. A home-based rehabilitation program for the hemiplegic upper extremity by power-assisted functional electrical stimulation. *Disabil Rehabil*. 2008;30:296–304. doi: 10.1080/09638280701265539.
41. Hara Y, Ogawa S, Muraoka Y. Hybrid power-assisted functional electrical stimulation to improve hemiparetic upper-extremity function. *Am J Phys Med Rehabil*. 2006;85:977–985. doi: 10.1097/01.phm.0000247853.61055.f8.
42. Kim JH, Lee BH. Mirror therapy combined with biofeedback functional electrical stimulation for motor recovery of upper extremities after stroke: a pilot randomized controlled trial. *Occup Ther Int*. 2015;22:51–60. doi: 10.1002/oti.1384.
43. Popović DB, Sinkaer T, Popović MB. Electrical stimulation as a means for achieving recovery of function in stroke patients. *NeuroRehabilitation*. 2009;25:45–58. doi: 10.3233/NRE-2009-0498.
44. Alfieri V. Electrical treatment of spasticity. Reflex tonic activity in hemiplegic patients and selected specific electrostimulation. *Scand J Rehabil Med*. 1982;14:177–182.
45. King TI II. The effect of neuromuscular electrical stimulation in reducing tone. *Am J Occup Ther*. 1996;50:62–64.
46. Gracies JM. Pathophysiology of spastic paresis. I: Paresis and soft tissue changes. *Muscle Nerve*. 2005;31:535–551. doi: 10.1002/mus.20284.
47. Chang CW. Evident trans-synaptic degeneration of motor neurons after stroke: a study of neuromuscular jitter by axonal microstimulation. *Electroencephalogr Clin Neurophysiol*. 1998;109:199–202.
48. Quandt F, Hummel FC. The influence of functional electrical stimulation on hand motor recovery in stroke patients: a review. *Exp Transl Stroke Med*. 2014;9:1–7. doi: 10.1186/2040-7378-6-9.
49. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther*. 1987;67:206–207.

# Effects of Electrical Stimulation in Spastic Muscles After Stroke: Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Supplemental Material

Supplemental table I. Characteristics of Studies Included in Systematic Review

| Author, Year | Intervention | Participants | Comparator | N (IG/CG) | Age ± SD (IG/CG) | Masculine gender (IG/CG) | Protocol |
|---|---|---|---|---|---|---|---|
| 1. Bakhtiary and Fatemy, 2008 | Bobath + NMES | Stroke patients with ankle spasticity | Bobath | 17/18 | Not reported | Not reported | IG: 20 daily sessions: infrared for 10min, Bobath inhibitory techniques for 15 min, NMES on tibialis anterior (100 Hz pulse stimulation, 0.1ms pulse duration, 0.9ms pulse interval) for 9min of submaximal muscular contraction (4sec contraction, 6sec rest)<br><br>CG: 20 daily sessions: infrared for 10 min and Bobath inhibitory techniques for 15 min<br><br>Outcomes: Spasticity and Range of Motion |
| 2. Barker et al., 2008 | SMART Arm + NMES | Stroke patients with upper limb spasticity | SMART Arm and Control Group | 10/13/10 | 61±16/ 67±8 /69±11 | 6/11/5 | IG: 12 sessions over 4 weeks (60min/day): 60-80 reps/session reaching task with load + NMES on triceps brachii (50 Hz pulse stimulation, 0.2ms pulse duration, 7-12 sec of contraction and 10-20 sec of rest)<br><br>SMART Arm: 12 sessions over 4 weeks (60min/day): 60-80 reps/session reaching task with load<br><br>CG: no intervention<br>Outcome: Spasticity |
| 3. Bauer et al., 2015 | Active leg cycling + NMES | Stroke patients with upper or lower limb spasticity | Active leg cycling | 19/18 | 59±14/64±11 | 12/9 | IG: 12 sessions: cycled at a self-selected speed for 20 minutes, 3 times/wk for 4 weeks, NMES on paretic lower limb (25 Hz pulse stimulation, 0.25 ms pulse duration).<br><br>CG: 12 sessions: cycled at a self-selected speed for 20 minutes, 3 |

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| | | | | | | | times/wk for 4 weeks<br><br>Outcomes: Spasticity and Range of Motion<br><br>Outcome: Spasticity |
| 4. Boyaci et al., 2013 | Active NMES | Stroke patients with upper limb spasticity | Passive NMES and Control Group | 11/10/10 | 56.1±6.8/64.4±9.5/57.6±16.4 | 7/7/4 | IG: 5 sessions/week with 45min of duration over 3 weeks; patients initiate wrist/finger extension until a target threshold level of EMG activity was voluntarily achieved, which triggered the NMES to assist the muscle to reach full ROM (50 Hz pulse stimulation, 0.2ms pulse duration, 14 sec of contraction)<br><br>Passive NMES: 5 sessions/week with 45min of duration over 3 weeks; stimulation produces full wrist and finger extension with duty cycle of 10sec on and 15sec off (50Hz pulse stimulation, 0.2ms pulse duration)<br><br>CG: 5 sessions/week with 45min of duration over 3 weeks; stimulation just above sensory threshold without motor activation<br>Outcomes: Spasticity and Range of Motion |
| 5. Chan et al., 2009 | OT + NMES | Stroke patients with upper limb spasticity | COT+ Placebo NMES | 10/10 | 46±17/45±16 | 5/6 | IG: 15 sessions of 1.5 hours: 10 min stretching/mobilization, 20 min NMES (40 Hz pulse stimulation, 0.2ms pulse duration, 8sec of contraction) on extensor digitorium superficialis with bilateral upper limb training tasks; 60 min of OT<br><br>CG: 15 sessions of 1.5 hours: 10 min |

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| | | | | | | | stretching/mobilization; 20 min placebo NMES on extensor digitoriumsuperficialis with bilateral upper limb training tasks; 60 min of OT<br><br>Outcomes: Spasticity and Range of Motion |
| 6. Cheng et al., 2010 | Motor Training Paradigm + NMES | Stroke patients with ankle spasticity | General range of motion and strength exercises | 8/7 | 52.87±8.74/58.53±5.06 | 5/7 | IG: 3 sessions/week over 4 weeks: 30 min of NMES on tibilais anterior and common peroneal nerve (40Hz pulse stimulation, 0.2 pulse duration, 10sec of contraction and 10sec of rest) combined with active dorsiflexion movement on the rocker board while standing and 15 min of ambulation training<br><br>CG: 3 sessions/week over 4 weeks: 30 min of general exercise training, 15 min of ambulation training<br><br>Outcomes: Spasticity and Range of Motion |
| 7. de Kroon et al., 2004 | NMES on flexors and extensors muscles of the wrist | Stroke patients with upper limb spasticity | NMES on wristextensors only | 13/15 | 58±17.3/61.7±9.7 | 9/11 | IG: 3daily sessions for 20min for the first 10 days and then individually increased duration until a maximum of 1hr/session during 6 weeks. Handmaster ES alterning on hand extensors and flexors(36Hz pulse stimulation and duty cycle of 40%; pulse duration and amplitude were adjusted individually)<br><br>CG: 3 daily sessions for 20min for the first 10 days and then individually increased duration until a maximum of 1hr/session during 6 weeks. Handmaster ES on hand extensors (36 Hz pulse stimulation and duty cycle of |

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| | | | | | | | 40%; pulse duration and amplitude were adjusted individually)<br><br>Outcomes: Spasticity and Range of Motion |
| 8. Duarte et al., 2011 | BT-A + NMES | Stroke patients with upper limb spasticity | BT-A + Placebo NMES | 13/11 | 57.7±13.4/55.2±16.3 | 8/8 | All groups: received injections of BT-A on wrist and finger flexors and 3 sessions of 30 min of NMES (20 Hz, 0.2ms of pulse duration).<br><br>IG: 3 sessions/week over 4 weeks: 30 min of NMESto produce active extension of the wrist and fingers (50 Hz pulse stimulation, 0.3 pulse duration, 6sec of contraction)<br><br>CG: 3 sessions/week over 4 weeks: placebo NMES<br><br>Outcome: Spasticity |
| 9. Embrey et al., 2010 | Walking Program + NMES | Stroke patients with ankle spasticity | Walking Program | 16/13 | 62.1±11.6/57.7±10 | Not reported | IG: patients walked 1hr/day, 6 days/week wearing NMES device on dorsiflexor muscles and worn NMES, activated automatically during walking,for 6-8 hours every day, for 3 months ( 35 or 50Hz depending on patient) preference. Then patients performed the same walking program for more 3 months but without wearing FES device<br><br>CG: did the same interventions as IG, but in the opposite order<br><br>Outcome: Spasticity |
| 10. Hara Y; Ogawa S and Muraoka Y, | Standard Therapy + NMES | Stroke patients with upper limb spasticity | Standard Therapy | 8/6 | 57.6/61.5 | 7/4 | IG: 1 or 2 sessions/week with 40 min of duration for 4 months: stretching of wrist and finger flexors, extension of wrist and finger and cup grasping |

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| 2006 | | | | | | | exercises assisted by NMES<br><br>CG: 1 or 2 sessions/week with 40 min of duration for 4 months: same as NMES group, but with motor point blockage and without NMES assistance<br><br>Outcome: Spasticity |
| 11. Hara et al., 2008 | Standard Therapy + NMES | Stroke patients with upper limb spasticity | Standard Therapy | 10/10 | 56/60.5 | 8/6 | IG:5 sessions/week beginning with 30 min of duration for the first 2 weeks and then increasing to a maximum duration of 1h for 5 months of training protocol to daily exercise at home.Patients were subdivided into A and B groups, which performed exercises for wrist and shoulder respectively. Both performed instrumental and daily tasks assisted by NMES.<br><br>CG: 1 session/week for 40 min over 5 months. Patients were subdivided into A and B groups, which received stretching and specific active exercises and daily living tasks according to their impairment.<br><br>Outcome: Spasticity |
| 12. Heckmann et al., 1997 | PT + EMG triggered NMES | Stroke patients with upper or lower limb spasticity | Standard Therapy | 14/14 | 50.1±14/54±11 | 9/8 | IG: 5 sessions/week over 4 weeks of EMG triggered NMES (80Hz of frequency, 0.3ms pulse width) on upper arm extensors, forearm hand extensors, knee flexors and ankle extensors and PT. Each group of muscles was stimulated 15 times per session.<br><br>CG: 5 sessions/week over 4 weeks of PT(45 min) and OT |

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| | | | | | | | Outcomes: Spasticity and Range of Motion |
| 13. Hesse et al., 1995 | BT-A + NMES | Stroke patients with ankle spasticity | BT-A | 5/5 | Not reported | Not reported | IG: received BT-A on gastrocnemius, soleus and tibialis anterior muscles and alternating ES (20 Hz, 0.2ms of pulse duration) on tibialis anterior and plantar flexor muscles for 30 min 6x/day during 3 days following the injection<br><br>CG: received just BT-A injections<br><br>Outcome: Spasticity |
| 14. Hesse et al.,1998 | BT-A + NMES | Stroke patients with upper limb spasticity | BT-A Group (BTAG); Placebo BT-AGroup (PBTAG); Placebo BT-A + NMES (PBTA + NMES G) | 6/6/6/6 | 50.8/54.3/42.7/53.6 | Not reported | IG: received injections of BT-A on elbow, wrist and finger flexors, PT 2x/week during 30 min and NMES on arm and forearm muscles for 30 min 3x/day during the 3 following days after injection (20 Hz pulse stimulation, 0.2 ms of pulse duration)<br><br>BTAG: Same as IG without NMES application<br><br>PBTAG: Same as BTAG, but received placebo BT-A<br><br>PBTA + NMES G: same as IG, but received placebo BT-A<br><br>Outcome: Spasticity |
| 15. Johnson et al., 2004 | BT-A + PT + NMES | Stroke patients with ankle spasticity | PT | 10/8 | 58.2±12.7/59.3±12.5 | 8/4 | IG: individualized PT 2-3 times/week for 45 min over 12 weeks, 1 BT-A injection on gastrocnemius on week 4 and NMES (40 Hz pulse stimulation, 0.35 ms pulse duration - portable stimulator used on peroneal nerve during walking activities and PT)<br><br>CG: individualized PT 2-3 times/week |

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| | | | | | | | for 45 min over 12 weeks<br><br>Outcome: Spasticity |
| 16. Jong et al, 2013 | Arm stretch positioning+ NMES | Stroke patient with upper limb spasticity | Sham arm positioning + Sham NMES | 23/23 | 56.6±14.2/58.4±9.6 | 15/12 | IG: multidisciplinary stroke rehabilitation and 2 sessions/day for 45 min over 8 weeks of arm stretch positioning with simultaneous NMES<br><br>CG: multidisciplinary stroke rehabilitation and 2 sessions/day for 45 min over 8 weeks of arm stretch positioning with simultaneous sham NMES<br><br>Outcomes: Spasticity and Range of Motion |
| 17. Karakus et al., 2012 | Standard rehabilitation program + NMES | Stroke patients with upper limb spasticity | Standard rehabilitation program | 14/14 | 55.6±14.1/62.3±9.6 | 7/8 | IG: 5 days/week over 2 weeks of standard rehabilitation program + NMES on wrist extensors 30 min (36 Hz pulse stimulation, 0.25 ms pulse duration, 12sec of contraction and 10 sec of rest)<br><br>CG: 5 days/week for 30 min over 2 weeks of standard rehabilitation program<br><br>Outcome: Spasticity |
| 18. Kim and Lee, 2014 | BF-NMES + mirror group | Stroke patients with upper limb spasticity | NMES + mirror group and control group | 10/10/9 | 58.1±8.32/ 53.2±7.91/ 62.1±1.3 | 8/7/5 | IG: 30 min training sessions five times per week, for a period of four weeks of electromyography sensor sampled at 256 Hz by an electromyography and FES device connected to the wrist extensor of the affected side was turned on for 5 s to induce wrist extension and mirror therapy program, which consisted of physiological |

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| | | | | | | | and object-related movements<br><br>NMES + mirror group: 30 min training sessions five times per week, for a period of four weeks of NMES adjusted to induce muscle contractions every 5 s through attachments to the distal and proximal portions of the wrist extensor digitorum and and mirror therapy program, which consisted of physiological and object-related movements<br><br>.<br>CG: 30 min training sessions five times per week for a period of four weeks of conventional physical therapy program<br><br>Outcomes: Spasticity and Range of Motion |
| 19. Lin and Yan, 2011 | Standard treatment+ NMES | Stroke patients with upper limb spasticity | Standard treatment | 19/18 | 62.2±8.7/66.0±9.6 | 11/11 | IG: 5 sessions/week over 3 weeks of PT and OT (30 min) and NMES on shoulder abductors and on wrist extensors (30 min, 30 Hz frequency, 0.3 ms pulse width)<br><br>CG: 5 sessions/week over 3 weeks of PT and OT (30 min)<br><br>Outcomes: Spasticity |
| 20. Malhotra et al., 2012 | PT+NMES | Stroke patients with upper limb spasticity | PT | 45/45 | 74(32-98)/ 74(52-90)* | 23/21 | IG: 30 min at least 2x/day for 5 days/week of NMES on wrist and finger extensors (40Hz frequency, 0.3ms pulse width, 15sec of contraction and 15sec of rest) and PT (passive, active assisted, active-strengthening and functional exercises) over 6 weeks. |

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| | | | | | | | CG: 6 weeks of PT (passive, active assisted, active-strengthening and functional exercises)<br><br>Outcomes: Spasticity and Range of Motion |
| 21. Mangold et al., 2009 | Conventional Training +NMES | Stroke patients with upper limb spasticity | Conventional Training | 12/11 | 57.5±16.7/62.0±16.2 | 10/7 | IG: 3-5 sessions/week of 45 min over 4 weeks of conventional therapy for the upper limb (mobilization, exercise and sensory retraining). NMES on proximal and distal muscles for reach, grasp and release tasks on 3 sessions (25 Hz of frequency, pulse width 0-0.25 ms) for 45 min.<br><br>CG: 3-5 sessions/week of 45 min over 4 weeks of conventional therapy for the upper limb<br><br>Outcomes: Spasticity |
| 22. Mesci et al., 2007 | Conventional Exercise Program + NMES | Stroke patients with ankle spasticity | Conventional Exercise Program | 17/18 | 61.3±7.3/58.6±8.5 | 10/10 | IG: 5 sessions/week over 4 weeks ofConventional Exercise Program for 45 min (passive and active exercises and balance training) + NMES (50 Hz of frequency, 0.4 ms of pulse width) on dorsiflexors for 45 min<br><br>CG: 5 sessions/week over 4 weeks of Conventional Exercise Program for 45 min<br><br>Outcomes: Spasticity and Range of Motion |
| 13. Mesci et al., 2009 | Conventional Exercise Program + NMES | Stroke patients with ankle spasticity | Conventional Exercise Program | 20/20 | 62.6±7.5/59.1±8.6 | 12/11 | IG: 5 sessions/week over 4 weeks of Conventional Exercise Program + 5 sessions/week of NMES over 4 weeks on dorsiflexor muscles (50Hz of |

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| | | | | | | | frequency, 0.4 ms of pulse width) for 20 min<br><br>CG: 5 sessions/week over 4 weeks of Conventional Exercise Program<br><br>Outcomes: Spasticity and Range of Motion |
| 24. Mokrush 1997 | EMG triggered NMES Group | Stroke patients with upper or lower limb spasticity | NMES Group and Control Group | 22/12/10 | Not reported | Not reported | IG: 1-2 daily sessions of EMG triggered NMES (30-50Hz of frequency, 0.3ms pulse width) on antagonist muscles of spasticity during 30 min + OT + PT<br><br>NMES Group: 1-2 daily sessions of NMES (30-50Hz of frequency, 0.3ms pulse width) on antagonist muscles of spasticity during 30 min + COT + Physiotherapy<br><br>CG: OT + PT<br><br>Outcome: Spasticity |
| 25. Ring and Rosenthal 2005 | Standard Treatment + NMES | Stroke patients with upper limb spasticity | Standard Treatment | 11/11 | 54.1±11.2/ 57.3±10.3 | 9/7 | IG: 3 sessions/week of 3 hours over 6 weeks of PT and OT (functional treatment and Bobath techniques) + NMES protocol started with 10 min 2x/day and progressed up to 50 min 3x/day with parameters individually adjusted to obtain full arc of finger motion (18-36 Hz of frequency, 0.1-0.5 ms pulse width)<br><br>CG: 3 sessions/week of 3 hours over 6 weeks of PT and OT (functional treatment and Bobath techniques)<br><br>Outcome: Spasticity |
| 26. Sabut et | Conventional Rehabilitation | Stroke patients with ankle | Conventional | 27/24 | 49.1±8.8/50.1±10.4 | 4/2 | IG:5 sessions/week of 1 hour over 12 |

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| al., 2011 | Program + NMES | spasticity | Rehabilitation Program | | | | weeks ofconventional rehabilitation techniques (neurodevelopmental facilitation techniques, PT, OT) + NMES on tibialis anterior for 20-30 min (35Hz of frequency, 0.28 ms of pulse width)<br><br>CG: 5 sessions/week of 1 hour over 12 weeks of conventional rehabilitation techniques<br><br>Outcomes: Spasticity and Range of Motion |
| 27. Sahin et al., 2012 | Stretching with PNF techniques+ NMES | Stroke patients with upper limb spasticity | Stretching with PNF techniques | 21/21 | 60.2±6.2/59.3±9.3 | 11/12 | IG: 5 sessions/week over 4 weeks of 15 min of infrared hot treatment on extensor muscles, stretching with PNF techniques to upper extremity and NMES(100 Hz of frequency, 0.1ms of pulse width) on wrist extensors for 15 min<br><br>CG: 5 sessions/week over 4 weeks of 15 min of infrared hot treatment on extensor muscles, stretching with PNF techniques to upper extremity<br><br>Outcomes: Spasticity and Range of Motion |
| 28. Yan et al., 2005 | NMES + Standard Rehabilitation | Acute stroke patients | Placebo NMES + Standard RehabilitationGroup and Control Group | 13/15/13 | 68.2±7.7/ 73.3±8.1/ 70.4±7.6 | 7/7/6 | IG: 5 sessions/week of 60 min over 3 weeks of PT and OT and 5 sessions/week of 30 min over 3 weeks of NMES on quadriceps, hamstrings, tibialis anterior and gastrocnemius (30 Hz of frequency, 0.3ms of pulse width) mimicking normal gait<br><br>Placebo NMES + Standard Rehabilitation Group: 5 sessions/week |

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|---|---|---|---|---|---|---|---|
| | | | | | | | of 60 min over 3 weeks of PT and OT and 5 sessions/week of 60 min over 3 weeks of placebo NMES<br><br>CG: 5 sessions/week of 60 min over 3 weeks of PT and OT<br><br>Outcome: Spasticity |
| 29. You, Liang and Yan, 2014 | NMES + Standard Rehabilitation | Acute stroke patients | Placebo NMES + Standard RehabilitationGroup and Control Group | 19/18 | 60.8±10.8/64.1±9.7 | 11/10 | IG: 5 sessions/week of 60 min over 3 weeks of PT and OT and 5 sessions/week of 30 min over 3 weeks of NMES on tibialis anterior (30 Hz of frequency, 0.2 ms of pulse width)<br><br>CG: 5 sessions/week of 60 min over 3 weeks of PT and OT<br><br>Outcome: Spasticity |

IG Intervention group; CG Control Group; NMES Neuromuscular electrical stimulation; SA Smart Arm; EMG Electromyography; OT Occupational Therapy; BT-A Botulinum Toxin A; PT Physiotherapy; ES Electrical Stimulation;
* Median and range

References

1. Bakhtiary AH, Fatemy E; Does electrical stimulation reduce spasticity after stroke? A randomized controlled study. Clin Rehabil. 2008; 22:418-25.

2. Barker RN, Brauer SG, Carson RG; Training of reaching in stroke survivors with severe and chronic upper limb paresis using a novel nonrobotic device: a randomized clinical trial. Stroke. 2008; 39:1800-7.

3. Bauer P, Krewer C, Golaszewski S, Koenig E, Muller F; Functional electrical stimulation-assisted active cycling-therapeutic effects in patients with hemiparesis from 7 days to 6 months after stroke: a randomized controlled pilot study. Arch Phys Med Rehabil. 2014; 96: 188-96.

4. Boyaci A, Topuz O, Alkan H, Ozgen M, Sarsan A, Yildiz N, et al; Comparison of the effectiveness of active and passive neuromuscular electrical stimulation of hemiplegic upperextremities: a randomized, controlled trial. Int J Rehabil Res. 2013; 36:315-22.

5. Chan MK, Tong RK, Chung KY; Bilateral upper limb training with functional electric stimulation in patients with chronic stroke. Neurorehabil Neural Repair. 2009; 23:357-65.

6. Cheng JS, Yang YR, Cheng SJ, Lin PY, Wang RY; Effects of Combining Electric Stimulation With Active Ankle Dorsiflexion While Standing on a Rocker Board: A Pilot Study for Subjects With Spastic Foot After Stroke. Arch Phys Med Rehabil. 2010; 91: 505-512.

7. de Kroon JR, IJzerman MJ, Lankhorst GJ, Zilvold G; Electrical stimulation of the upper limb in stroke: stimulation of the extensors of the hand vs. alternate stimulation of flexors and extensors. Am J Phys Med Rehabil. 2004; 83:592-600.

8. Duarte E, Marco E, Cervantes C, Díaz D, Chiarella SC, Escalada F; Efectos de la toxina botulínica tipo A y electroestimulación en la espasticidad flexora distal de la extremidad superior en el ictus. Ensayo clínico aleatorizado. Rehabilitación (Madr). 2011;45:194—201.

9. Embrey DG, Holtz SL, Alon G, Brandsma BA, McCoy SW; Functional electrical stimulation to dorsiflexors and plantar flexors during gait to improve walking in adults with chronic hemiplegia. Arch Phys Med Rehabil. 2010; 91:687-96.

10. Hara Y, Ogawa S, Muraoka Y; Hybrid power-assisted functional electrical stimulation to improve hemiparetic upper-extremity function. Am J Phys Med Rehabil. 2006; 85:977-85.

11. Hara Y, Ogawa S, Tsujiuchi K, Muraoka Y; A home-based rehabilitation program for te hemiplegic upper extremity by power-assisted functional electricalstimulation. Disabil Rehabil. 2008; 30:296-304.

12. Heckmann J, Mokrusch T, Krockel A, Warnke S, von Stockert T, Neundorfer B; EMG-triggered electrical stimulation in the treatment of central hemiparesis after a stroke. European Journal of Physical Medicine and Rehabilitation. 1997; 7: 138–141.

13. Hesse S, Jahnke MT, Luecke D, Mauritz KH; Short-term electrical stimulation enhances the effectiveness of Botulinum toxin in the treatment of lower limbspasticity in hemiparetic patients. Neurosci Lett. 1995; 201:37- 40.

14. Hesse S, Reiter F, Konrad M, Jahnke MT; Botulinum toxin type A and short - term electrical stimulation in the treatment of upper limb flexor spasticity after stroke: a randomized, double-blind, placebo-controlled Trial. Clinical Rehabilitation 1998; 12: 381–388.

15. Johnson CA, Burridge JH, Strike PW, Wood DE, Swain ID; The effect of combined use of botulinum toxin type A and functional electric stimulation in the treatment of spastic drop foot after stroke: a preliminary investigation. Arch Phys Med Rehabil. 2004; 85:902-9.

16. Jong LD, Dijkstra PU, Gerritsen J, Geurts AC, Postema K; Combined arm stretch positioning and neuromuscular electrical stimulation during rehabilitation does not improve range of motion, shoulder pain or function in patients after stroke: a randomised trial. J Physiother. 2013; 59:245-54.

17. Karakus D, Ersoz M, Koyuncu G, Türk D, Münevver sasmaz F, Akyüz N; Effects of Functional Electrical Stimulation on Wrist Function and Spasticity in Stroke: A Randomized Controlled Study. Turk J Phys Med Rehab. 2013; 59:97-102

18. Kim JH and Lee BH; Mirror Therapy Combined with biofeedback functional electrical stimulation for motor recovery of upper extremities after stroke: a pilot randomized controlled trial. Occup Ther Int. 2015; 22:51-60

19. Lin Z, Yan T; Long-term effectiveness of neuromuscular electrical stimulation for promoting motor recovery of the upperextremity after stroke. J Rehabil Med. 2011; 43:506-10.

20. Malhotra S, Rosewilliam S, Hermens H, Roffe C, Jones P, Pandyan AD; A randomized controlled trial of surface neuromuscular electrical stimulation applied erly after acute stroke:effects on wrist pain, spasticity and contractures. Clin Rehabil. 2013; 27:579-90.

21. Mangold S, Schuster C, Keller T, Zimmermann-Schlatter A, Ettlin T; Motor training of upper extremity with functional electrical stimulation in early stroke rehabilitation. Neurorehabil Neural Repair. 2009; 23:184-90.

22. Mesci N, Özdemir F, Kabayel DD, Tokuç B; The Effect of Neuromuscular Electrical Stimulation on Gait Speed and Distance in Patients with Stroke. Turk J Phys Med Rehab. 2007; 53:144-9.

23. Mesci N, Ozdemir F, Kabayel DD, Tokuc B; The effects of neuromuscular electrical stimulation on clinical improvement in hemiplegic lower extremityrehabilitation in chronic stroke: a single-blind, randomised, controlled trial. Disabil Rehabil. 2009; 31:2047-54.

24. Mokrusch, T; Behandlung der hirninfarktbedingten spastis- chen Hemiparese mit EMG-getriggerter Elektrostimulation. Neuro Rehabil. 1997; 2:82-86.

25. Ring H, Rosenthal N; Controlled study of neuroprosthetic functional electrical stimulation in sub-acute post-stroke rehabilitation. J Rehabil Med. 2005; 37:32-6.

26. Sabut SK, Sikdar C, Kumar R, Mahadevappa M; Functional electrical stimulation of dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity, and motor recovery in stroke patients. NeuroRehabilitation. 2011; 29:393-400.

27. Sahin N, Ugurlu H, Albayrak I; The efficacy of electrical stimulation in reducing the post-stroke spasticity: a randomized controlled study. Disabil Rehabil. 2012; 34:151-6.

28. Yan T, Hui-Chan CW, Li LS; Functional electrical stimulation improves motor recovery of the lower extremity and walking ability of subjects with first acute stroke: a randomized placebo-controlled trial; Stroke. 2005; 36:80-5.

29. You G, Liang H, Yan T; Functional electrical stimulation early after stroke improves lower limb motor function and ability in activities of daily living. NeuroRehabilitation. 2014; 35: 381-9