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The Effectiveness of Neuro Muscular Electrical Stimulation on Hand Function in Sub Acute Stroke Survivors: A Systematic Review of Randomized Controlled Trials

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Abstract

Background: Role of Neuro Muscular Electrical Stimulation on hand function in patients with stroke has not being well established. **Objective:** To estimate the effectiveness of Neuromuscular Electrical Stimulation in improving hand function of patients with sub acute stroke**. Data Source**: Systemic search was carried out in Medline, Cochrane and Pubmed Databases from August 2018 to June 2019. **Study Selection**: Randomized controlled trials. Eligibility criteria: subjects >18 yrs suffering from haemorrhagic /ischaemic stroke within 6 months, NMES as intervention applied on affected hand using surface electrodes, outcome measures related to skeletal, muscular and functional characteristics of arm and statistical analysis of results. **Data Extraction:** Participant's characteristics, NMES parameters, and other relevant data was extracted from the articles and then tabulated. Cochrane collaboration's tool for assessing risk of bias was applied to all articles and methodological quality was assessed by PEDro scale. **Data Synthesis**: Eighty-one articles were selected through database and citation by title content, 48 articles were screened after reading the abstract. 31 full text articles were found and 15 comply with inclusion criteria. The methodological quality of the articles was assessed through PEDro scale which was between 5/10 and 8/10. Beneficial impact of NMES on muscle tone, motor function, manual dexterity and upper limb ADL's was established in level of evidence synthesis. **Limitation**: It was difficult to group studies and quantitatively evaluate outcomes due to the variance in protocol s, participant features, outcome measures and NMES parameters.**Conclusion**:Randomized trials ha ve shown beneficial impacts of electrical stimulation on the wrist and hand despite methodological constraints, implying that NMES is efficient in encouraging the impacted hand in stroke.

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Introduction

Stroke is a major health care problem and an important cause of morbidity and mortality (Gourie 2008). Among neurological disorders in adults, it is a major cause of disability which can result in highly complex clinical conditions (Wilson et al., 2016). It is third major cause of death worldwide and nine out of ten strokes occur in people over the age of 55. In India, the prevalence of stroke is

44-843/100,000, and according to the Indian Council of Medical Research 2015 India reports 1.6 million cases of stroke per year. In India stroke population is relatively young (Indian population>=60 yr: 7.5%) as compared to the western countries (British population >=65 yr) (Mishra and Khadilkar 2010).Hand dysfunction such as difficulties in grasping, reaching, manipulating objects is most common consequences of stroke (Lai et al., 2002). These chronic problems lead to difficulty in performing functional movement such as picking up a glass, buttoning a shirt in post stroke patient and leads to difficulty in performing tasks of daily living and limit their community participation (Gowland et al., 1992). Even in stroke survivors, whose neuro-cognitive function are upgraded, 55-85% of the sufferers continue with upper limb dysfunction (Nakayama et al., 1994). In upper limb recovery, the regaining wrist and fingers control is challenging and the impaired hand function is one of the remaining consequences of stroke (Lee et al., 2012). As per the literature, it is assumed that only 5 to 20% of the stroke sufferers gain complete functional recovery of their affected upper limb and remaining 70-80% continue with upper limb impairment and do not regain functional use of paretic upper extremity (Kwakkel et al., 2003). Thus the post stroke rehabilitation techniques are growing interest in neurophysiological therapy, since it can improve the functional outcome and quality of life to many stroke survivors. Neuro muscular electrical stimulation (NMES) is a neuroprosthetic technique which applies programmed short electrical pulses to the muscles affected by stroke for restoring lost motor function. It can be either applied to the hemi paretic muscles or to the peripheral nerve system associated to the hemiplegia. Neuro muscular electrical stimulation is used for correction of contractures, muscle strengthening, and facilitation of voluntary motor control and increased passive range of motion. The NMES is also used for improvement muscle spindle reflex activity (Glanz et al., 1996).Recent clinical studies promote the use of NMES for the recovery of muscle strength after stroke. NMES specific for the upper limb rehabilitation is receiving increasing attention as a therapeutic modality due to clinically significant results (Weingarden et al., 1998).
Nowadays NMES is used to improve gait and upper limb function in patients suffering from stroke. Its use in regaining wrist and finger control is yet to be established. Hand is driving force for upper limb recovery after stroke. Recovery of hand function spans from regaining power grip to single digit individuation. Despite the promising advantages of NMES in stroke, there is lack of understanding of the appropriate stimulation parameters for NMES for wrist extensors (Warlow et al., 2008). Many clinical trials had shown the impact of NMES on the wrist and fingers of hemiparetic patients (Gondkar et al., 2019; Jonsdottir, et al., 2017; Etoh, et al., 2015 ; Francisco et al., 1998). Therefore , a systematic literature review would assist in the planning of intervention by providing a synthesis of the evidence on the impacts of this useful resource. The study aims to perform a systematic literature review using sound selection and analysis of scientific papers that investigate the impact of this stimulation.

Materials and Method

Data source and search:

A systemic search for randomized control trials in the digital databases Medline, Cochrane and Pub med was conducted between August 2018 and June 2019.The keywords used were: "electrical stimulation" or "neuromuscular electricalstimulation" and "wrist" or "hand" or "paresis with "stroke", "hemiplegia", "dexterity" and "CVA".

Study Selection: The studies which fulfilled the following inclusion criteria: subjects >18 yrs suffering from haemorrhagic /ischaemic stroke within 0-6 months, NMES as intervention applied on affected hand using surface electrodes, presence of control group with randomization, outcome measures related to skeletal, muscular and functional characteristics of arm and statistical analysis of results was selected.

Data Extraction, Risk of Bias and Quality Assessment: Full text of selected article was recovered and assessed according to the selection criteria. The information in the studies was condensed in a tabular manner according to: author(s) name, characteristics of the participants, methodological design, characteristics of intervention (session frequency and duration, total treatment time and stimulation characteristics), outcome measured, statistical analysis used and results. Cochrane collaboration's tool for assessing risk of bias was applied to all articles. The studies were also evaluated using the PEDro scale for their methodological quality (PEDro). This scale is made up of 11 items, each item adding 1 point (except for item 1). The total score varies from 0 to 10. Risk of bias and quality assessment information was considered in interpretation of finding.

Data Synthesis and Analysis: Eighty-one articles were selected through database and citation by title content. Sixty nine studies were left after duplicates were removed .Twenty one records were excluded of non RCT, old records (before 2015), non stroke records. Thereafter 48 articles were screened for abstract out of which only thirty one full text articles were found and just 15 articles complied with the inclusion criteria. The methodological quality of the articles was assessed through PEDro scale which was **between 5/10 and 8/10**. Table 1 shows the summarized data extracted from each article. Article scores in each item of the PEDro scale is shown in Table 2.

Two writers separately evaluated each article in relation to the existence or lack of indexes of the quality scale. The PEDro scale showed moderate rates of reliability among assessors (ICC=0.68; IC 95 percent= 0.57-0.76). Differences of view were discussed for the final classification of the article until a consensus was reached between writers. It was not possible to carry out a meta-analysis because there was differences in characteristics of patients, intervention protocols and measured outcomes or insufficient quantitative data (standard deviation means) in the examined studies, therefore a result summary was used by means of an evidence level classification system shown in Table 3. The classification, included five scientific evidence categories according to the PEDro score and the results are available in the studies (Van et al., 2004).

Results

Eighty one studies were pre-selected by title content. After the abstracts were read, 48 articles were selected, of which 32 were excluded for failing to comply with the inclusion criteria. Therefore, 15 studies, all of them controlled and randomized, were included in the critical evaluation phase.

The information in the studies was condensed in a tabular manner, according to: author(s) name, characteristics of participants, evaluated results, methodological design, characteristics of intervention (session frequency and duration, total treatment time and stimulation characteristics), used statistical analysis and effects of outcome. The included studies contained total of 811 participants out if which 467 participated in intervention group and 344 in control group. The mean age of participant was 57.32 yrs and mean duration of stroke was 4.46 months.

Participants' characteristics

Five of the assessed studies included subjects diagnosed with acute stroke, with duration period of one to 2 month (Qian, et al., 2018 ; Marquez et al., 2017 ; Park et al., 2017 ; Schick et al., 2017; Kwakkel et al., 2016). Rest all assessed studies had a sample with sub acute stroke diagnosis, with duration periods varying from 3 month to 8 months.The sample size ranged from 17 to 159 subjects which were divided into treatment and control group. The participant's average age was between 40 to 75 yr. Both right and left hemiparesis subjects were included in the study. The severity of the damage was defined in various ways. Participants, however, had to show at least 10º to 20º of active wrist and fingers extension in all research.

Risk of Bias and Quality Assessment

Table 4 details the full critical appraisal information of all articles. Included studies span a arrange of methodological quality, eight studies had low risk of bias (Carrico et al., 2018 ; Schick et al., 2017; Marquez et al., 2017; Al Dajah & Salameh. 2016; Kwakkel et al., 2016; Wilson et al., 2016; Kim et al., 2015; Kim et al., 2014), four studies had unclear risk of bias (Demir et al., 2018 ; Guo et al., 2018 ; Qian et al., 2018 ; Cui et al., 2015) and three studies had high risk of bias (Nakipoğlu et al., 2017 ; Park et al., 2017; Nagapattinam et al., 2015).

Quality assessment using PEDro criteria found medium quality evidence in all analysis performed as a result of the heterogeneity and lack of blinding in most of the studies.

Intervention program characteristics

Intervention duration varied from 12 (Guo et al., 2018 ; Nagapattinam et al., 2015) to 80 sessions (Demir et al., 2018 ; Marquez et al., 2017 ; Wilson et al., 2016) with seven of the articles having an intervention period of 20 (Kwakkel et al., 2016) to 30 sessions (Qian et al., 2018 ; Nakipoğlu et al.,2017 ; Park, et al., 2017 ; Cui et al., 2015 ; Kim et al., 2015 ; Kim et al., 2014). Application of NMES varied from 1 to 2 (Qian et al., 2018 ; Kwakkel et al., 2016 ; Wilson et al., 2016) times a day, from 3 (Guo et al., 2018) to 6 (Carrico et al., 2018 ; Qian et al., 2018 ; Al Dajah et al., 2016 ; Nagapattinam et al., 2015) times a week. Session duration varied from 20 minutes (Al Dajah et al., 2016) to 120 minutes (Carrico et al., 2018). Current parameters varied, with frequency ranging from 20Hz (Wilson et al., 2016) to 60Hz (Kim et al., 2015), amplitude from 20mA (Kim et al., 2015) to 90mA (Nagapattinam et al., 2015) and pulse width from 100µs (Qian et al., 2018) to 300µs (Guo et al., 2018; Nakipoğlu et al., 2017 ; Marquez et al., 2017 ; Schick et al., 2017 ; Wilson et al., 2016; Cui et al., 2015). In all studies, NMES was applied to extensor muscles of wrist and finger.

Effects of FES on neuromuscular and musculoskeletal characteristics

Hand strength

With the help of the hand grip dynamometer, two randomized controlled trials (RCTs) (Demir et al., 2018 ; Kim et al., 2014) measured the hand grip isometric force and found significant gains in the NMES treated group. Though these gains were higher than the control group in both studies but there is low evidence of the increase in isometric strength after NMES for power grip.

Wrist tonus

Tonus was evaluated using Modified Ashworth scale and Brunnstorm hand grading in four RCTs (Demir et al., 2018; Nakipoğlu et al., 2017; Cui et al., 2015 ; Kim et al., 2014). All the four trials showed a substantial decrease in tone compared to the control group only in the high-functioning group (at least 20º of active wrist extension). and no important decrease was observed in the low-functioning group (active extension between 10º and 20º) (Nakipoğlu et al., 2017). Qian et al (2017) showed significant reduction in MAS of wrist in NMES group after training ($p<0.05$,EF=0.145) and the effects were maintained for 3 months. The finding show medium proof of tonus reduction after NMES, emphasizing that this impact can be restricted to patients with more than 20º active wrist extension prior to intervention.

Wrist Range of motion (ROM)

The range of active wrist extension was assessed in five RCT (Nakipoğlu et al., 2017 ; Al Dajah & Salameh 2016 ; Kwakkel et al., 2016; Kim et al., 2015; Kim et al., 2014). The recent studies showed significant improvement of FES on wrist ROM outcome as compared to control group.. Thus, there is moderate evidence of NMES as an effective method to increase wrist ROM in patient suffering with stroke.

Effects of FES on functional characteristics

Hand Motor function

Total fourteen RCTs assessed effect of NMES on motor function.In the included studies hand function was assessed with FMA, ARAT,WMFT. Elevan studies measured hand motor function with FMA scale (Carrico et al., 2018 ; Demir et al., 2018 ; Qian et al., 2018 ; Park et al., 2017 ; Marquez et al., 2017 ; Nakipoğlu et al., 2017 ; Schick et al., 2017 ; Kwakke et al., 2016 ; Wilson et al., 2016 ; Cui et al., 2015; Kim et al., 2015). Five studies included ARAT scale to check hand motor function (Carrico et al., 2018; Qian et al., 2018; Kwakkel et al., 2016 ; Cui et al., 2015; Nagapattinam et al., 2015) and three studies assessed motor function with WMFT (Carrico et al., 2018; Al Dajah & Salameh 2016; Kwakkel et al., 2016). Qian etal (2017) showed significant improvement in FMA wrist and hand in NMES group ($p<0.001$) EFs=0.435 and ARAT ($P<0.001$) , EF>0.279 after the treatment. Carrico et al., (2018) found significant gains in the grip and grasp subscores of the Action Research Arm Test when compared to a control group. Statistically significant between group differences favoured the active condition on WMFT at post ($p=0.04$) and ARAT at post ($p=0.02$), 1 month ($p=0.01$) and 4 month ($p=0.01$) There is strong evidence of improved motor function after NMES. But Guo et al., (2018) and Wilson et al., (2016) showed no significant improvement in FMA score of UE and hand as compared to control group.

Manual dexterity of hand

Six RCTs evaluated manual dexterity after application of NMES (Demir et al., 2018; Nakipoğlu et al., 2017; Schick et al., 2017; Kwakkel et al., 2016; Wilson et al., 2016; Kim et al., 2014) with the help of Block and Box test, J ebsen Taylor Hand function,UEFT (Nakipoğlu et al., 2017) AMAT (Wilson et al., 2016) NPHT (Kwakkel et al., 2016). Kim *et al.*, (2015) and Schick (2016) evaluated this result after 3 Weeks of NMES using the Box and Block Test , achieving important gains compared to the control group($P<.05$). Kim *et al.*, (2015) and Demir et al., (2018) found a significant gain in the performance of subtests of the Jebsen Taylor Hand Function Test only for the NMES group. There is moderate evidence of the effects of NMES on manual dexterity depending on the quality of the results of the papers reviewed.

Use of upper limbs in daily routine

FIVE RCTs (Demir et al., 2018; Park et al., 2017; Kwakkel et al., 2016; Kim et al., 2015 ; Kim et al., 2014) found favourable results for NMES that measured this outcome. MAL (Demir et al., 2018; Park et al., 2017; Kwakkel et al., 2016; Kim et al., 2015), SSQOL (Kim et al., 2014) was used to assess ul function in daily activities. Park et al., (2017) showed significant improvement in in experimental group from 0.95+/-0.33 to 2.43+/-0.51,0.99+/-0.38 to 2.67+/-0.46 for MAL (AOU and QOM) after 4 weeks of NMES. Demir *et al.*, (2018) and Kwakkel et al., (2016) used the Reduced Upper Extremity Motor Activity Log test and found significant gains in the high-functioning group compared to the control group. Nakipoglu *et al* (2017), also used the Upper Extremity Function Test and found a significant difference between subjects from the high and low-functioning groups that received NMES treatment and their respective control groups. There is strong evidence of functional gains in daily routine after NMES, with intervention appearing to having higher potential for patients with at least 20º of active wrist extension before intervention.

Independence in self-care activities

Nine RCTs used self-care items of the Functional Independence Measure (Marquez et al., 2017 ; Kim et al., 2014), Barthel Index (Guo et al.,2018; Nakipoğlu et al., 2017; Schick et al., 2017) SF-36 (Demir et al., 2018) Stroke impact Scale (Carrico et al., 2018; Kwakkel et al., 2016) MBI (Kim et al., 2015) to assess the outcome. Chin et al., (2017) showed FIM self care subscores increased 22.8(+6.7) points in the intervention group. Except for Guo et al.,(2018) all studies showed

significant improvement in self care activities. There is therefore, sufficient evidence of the impact of NMES on independence.

Discussion

FES is an upcoming neuroprosthetic technique of 21 century. Researchers are still establishing the intervention parameters of FES to regain muscle strength after stroke. In the period 2008-2014 FES was used for gait rehabilitation and upper limb recovery especially deltoid, biceps and triceps strengthening. Jing et al., (2016) shifted the focus of stroke upper limb rehabilitation on hand. He concluded that hand is the driving force for upper limb recovery. Now the thrust of current studies are focussing on hand stimulation rather than arm stimulation in stroke rehabilitation. He also focused that hand recovery includes power grip and finger individuation. Therefore current study included latest RCT (2015-2018) which aims to analyse the effectiveness of surface FES stimulation of wrist extensors on neuromuscular and functional characteristics of hand in acute and subacute stroke. Earlier systematic review conducted by Yang et al., (2019) and Eraifej et al., (2017) established the effectiveness of FES on upper limb function (as a whole) in patients suffering from stroke. The type of current, electrode used (surface, robotic, insertional), application of electrode, site of application, muscle stimulated, were not taken in to consideration while selecting RCT. The outcome measures lack the assessment of the effect of FES on wrist ROM, wrist tone, hand power grip. The finding of the present study were supported by systematic review of Montesilva et al., (2019) which included 26 studies and revealed the effectiveness of EMG related NMES effect in restoring hand function in chronic stroke patients. It also concluded robust short term effect on body structure and function according to ICF framework, but no evidence favoured for activity and participation domains.

In the Present study all the trials used experimental methodology, comparing two or more treatments, with one control or reference group. Therefore it assesses the cause and effect relationship in the group of variables and thereby shows the causality of possible changes seen in the participants. There was random allocation of subjects in all the studies and they were classified as randomized controlled trials. Carrico et al., (2017) used simple randomization and Cui et al., (2017) used block randomization for distribution of subject in groups. Randomization does not allow selection bias influence the outcome that may predispose a group to be more susceptible to intervention impacts. Although blinding of assessors was found in SEVEN studies (Carrico et al., 2018 ; Qian et al., 2018 ; Marquez et al., 2017 ; Schick et al., 2017 ; Kwakkel et al., 2016; Kim et al.,2015; Kim et al.,2014) Blinding is a important element because the expectation of researcher about the evaluated result and the understanding of respondent about their therapy can affect the results of the measurement. Demir et al., (2018) did a prospective trial. Out of all assessed trials, one by Wilson et al., (2016) and Kwakkel et al., (2016) were experimental, randomized and double-blinded studies, for evaluating the effectiveness and consistency of intervention. Kwakkel et al., (2018) found significant gains in motor function (Fulg-meyer and Action Research Arm Test), manual dexterity(WMFT,NHPT)and use of hand in daily function (MAL) in the following 3 week post-treatment phase. Gains in manual dexterity and functionality in daily life in the NMES group compared to the control group were reported by Kim et al (2015). According to the results of this systematic review electrical stimulation is safe and effective in improving wrist and hand function in sub acute stroke. Earlier application of currents in acute stage can result in better hand function as compared to application of NMES on hand in chronic stage (Jheng et al., 2019). Consolidation with more cognitive effort to initiate electrical stimulation and training in combination with functional tasks can further improve the efficacy of the treatment. It should be regarded in further research and with practitioners working with clientele.

Conclusion

Randomized trials have shown beneficial impacts of NMES on affected wrist and hand despite methodological constraints, implying that NMES is efficient in encouraging the impacted hand in stroke. The finding of this systematic review research synthesizes evidence of the impact of NMES that can add to clinical behaviour of practitioner working with clientele and using NMES, favouring evidence-based practice.

Search strategy: Pubmed

01.	Stroke
02.	Cerebro vascular accidents
03.	Controlled trials
04.	Randomized controlled trials
05.	Hemiplegia
06.	Neuromuscular stimulation
07.	Functional electrical stimulation
08.	Electrical stimulation
09.	Hand
10.	Wrist and hand
11.	Upper limb
12.	Dexterity
13.	Hand function
14.	Finger individualization
15.	Sub acute stroke

Table 1. Data Items

Author's Name	No. of Patients	Documented Outcomes	Study Design	Intervention	Statistical Analysis	Observed Effect
1.Guo et al., 2018	N=82 pts Mean age 64.3+/-11.8 Onset 8.8+/-3.7(Months)	1.ARAT PRE AND POST 4 WK 2.BI 3.NRS	Retrospective Study	N=41(Physical Training) Control Group N=41(Experimental Group)30 MIN /DAY,3 DAYS /WK 3 Sessions/wk for 4wks	SPSS Version 17.0 Fisher's Exact Test Mann Whitney Test	No effect of NMES Was Seen Due To As Only 12 Sessions Of NMES Was Given For 30 Minutes For 4 Weeks. It Was recommended than for the effectiveness of

						NMES 30 min. session for 5 days over 6 wks should be given.
2.Demir *et al.*, 2018	N=17pts Mean Age 52.6+/-16.5, Onset 306.2+/-219.5 Days	Primary Outcomes 1.FMA 2.MAS Secondary Outcomes 1.MAL-28 2.Jebson Taylor Test 3. Hand Grip Strength Test 4. Short Form 36	Randomized Controlled Prospective Trial	N=8 (Standard Rehabilitation) N=9 (FES + Standard Rehabilitation) FES for 45 min, twice a day for Wrist & Finger Extensors MS 5 days a Week over 8 Weeks	SPSS Version 15.0 Chi-Square Test($P<0.05$) Mann Whitney U Test($P<0.017$)	FES + Standard Rehabilitation Patients Showed Improvement In Motor Function, Hand Grip Strength And Independence In ADL'S.
3. Carrico *et al.*, 2018	N=55 Acute pts Mean age 58+/-12.1 Onset 7.48+/-2.48 mths	1. WMFT 2. ARAT 3. FMA 4. SIS Pre and post 1 mth Follow up 4 mths	Simple Random Allocation Computer Generated RCT	18 intervention sessions pairing 2 hours of active (n=33) or sham (n=22) somatosensory stimulation with 4 hours of intensive task-oriented motor training. 3 times/wkfor 6 wk	SPSS version 9.4 MANOVA	1. Statistically significant between-groups differences favoured the active condition on Wolf Motor Function Test at post ($p=0.04$) and Action Research Arm Test at post ($p=0.02$), 1-month ($p=0.01$), and 4-month ($p=0.01$) but favored the sham

						condition on Stroke Impact Scale at 1-month (p=0.03). 2. There were no significant between-groups differences on Fugl-Meyer Assessment.
4.Qian et al., 2017	N=24 Mean Age 54.6+/-11.3 Onset 0.5-4.7 Mths	1.FMA 2.MAS 3.ARAT 4.FIM Follow Up 12 Wk	RCT-Pilot	N=14 (Experimental Group NMES Robot) N=10 (Control Group Traditional Therapy) FES 20 min /day for 5 Session/week. Total 20 Sessions follow up 3 months	ANOVA-2 Way	1.Significant improvements were obtained in FMA (full score and shoulder/ elbow), ARAT, and FIM [$P < 0.001$, effect sizes (EFs) > 0.279] for both groups. 2.Significant improvement in FMA wrist/hand was only observed in the NMES-robot group ($P < 0.001$, EFs = 0.435) after the treatments. 3.Significant reduction in MAS

						wrist was observed in the NMES-robot group after the training ($P < 0.05$, EFs = 0.145) and the effects were maintained for 3 months.
5.Nakipoglu, 2017	30 Stroke Pts Mean Age 60.20, Range 48-72.5, Onset 4.60, Range 3.3-5.9 months	1.FMA 2.MAS, Brunnstron Hand Grading 3.Barthel Index, UEFT	RCT With Simple Randomization	FES GP(15) CTRL GP(15) FES to Wrist & Finger Extensors for 30 min a day for 5 days a week Total 20 Sessions	SPSS Version 11.0 Mann Whitney U Test (P<0.017) Wilcoxon Rank Test for between group	FES group shows decrease in spasticity and improved ROM and functional measure No significant difference in ROM, BI value on admission but sig diff on discharge No significant difference in RMA,BS, UEFT in ctrl group Both groups show improvement in MAS
6.Park,2017	N=40 Pts (Acute Stroke) Mean Age 58.8+/-11.93 Onset 31.89+/-	1. FMA-UE 2. MAL-AOU - QOM	Experimental Study	EXP GP N=20(EMG – ES MP) +CRT CTRL GP N=20(Mental	SPSS 15.0 Paired t test, Independent	1. The experimental group showed significant

	55.59			Practice) +CRT total treatment duration 60 min FES for 30 minutes/day, 5 days/week, for 4 weeks.	t test	improvements from 21.69 ± 5.80 to 34.19 ± 7.82 for the FMA, and from 0.95 ± 0.33 to 2.43 ± 0.51, 0.99 ± 0.38 to 2.67 ± 0.46 for the MAL (AOU and QOM). 2.MP – EMG ES improve arm and hand function in sub acute stroke
7.Salameh , 2017	N=60 (Sub Acute Stroke) Mean Age:66.4 Duration :2-6 mths	1. WMFT pre and post 12 week	RCT	EXP GP N=30 (NMES and Functional Activity) CTRL GP N=30 (Functional Activity) Dorsum splint was applied to both gps for 2x3/day hours for 12 weeks.	SPSS Version 20.0 ANCOVA test	1. There was significant difference $p<0.05$ in t test for the pre and posttest in both groups. 2.Comparison between the means of the posttest in the experimental and control group, using ANCOVA test showed significant

						difference between groups with $p<0.05$ in all factors except for index finger ROM and reach to table . **3.** Dorsum hand splint and NMES could be helpful to reduce flexion synergistic spasticity of the stroke hand and improve hand functional activities.
8.Schick T et al 2017	N=33 (Acute Stroke) Mean Age 62+/-19.6 Onset 51+/-32.4 Days	1.FMA 2.RASP-DT 3.GAS 4.Barthel Index 5.BBT	Randomized, controlled, mulicenter, and single (assessor) blinded study	CTRL GP-EMG-ES n=16 INT GP-EMG-MES and MT n=17 5days/wk for 30 min over 3 wks	IBM SPSS-Statistics for Windows Version 22 Mann-Whitney Test	The Interventio n Group with very severe paresis had significantl y better motor recovery in total Fugl-Meyer Assessmen t ($p = 0.017$) at a medium effect size (Cohen) of $d = 0.7$, due to a significant recovery of

						shoulder and elbow function (p = 0.003) in the Fugl-Meyer Assessment Part A subtest. For subjects with severe paresis, additional mirror therapy did not significantly influence outcome.
9. Chin ,2017	N=21 Stroke Patients Mean Age 58+/-18.8 Onset 15-57 Days	1.FMA-UE 2.FIM	Assessor Blind RCT	N=10 (FES Group) N=11 (Ctrl Group) 45 min /day 5 days /wk 12-16 wks	R Version 3.0.2 Non parameteric test	1.Functional Independence Measure Self-Care subscores increased 22.8 (+6.7) points in the intervention group and 9 (+6.5) in the control group. 2. FMA-UE score changes were 27.2 (+13.5) and 5.3 (+11.0) for the intervention and control groups, respectively.

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10.Wilson et al., 2016	N=122 Acute Stroke PTS Mean Age 55, Range 47.4-65.9, Onset 0.7-1.3	1. FMA-UE pre and post 4 weeks 2.Voluntay Movement of Upper Limb Secondary Outcomes 1. Modified AMAT follow up 24 wk	Multicentred, Multi Arm Parallel Group Assessor Blinded RCT	Allocation of Subjects N=39(Cyclic NMES) N=41(EMG Triggered NMES) N=42 (Cyclic Sensory Stimulation) 40 min Session 2 Days in a week over 8 week Period .Follow up 6 mths	SAS Software (93 Version) Kruskal Wallis Test	1.There were significant increases in the Fugl-Meyer Assessment [$F(1, 111) = 92.6$, $P < .001$], FMA Wrist and Hand [$F(1, 111) = 66.7$, $P < .001$], and modified Arm Motor Ability Test [mAMAT; time effect: $F(1, 111) = 91.0$, $P < .001$] for all 3 groups. 2.There was no significant difference in the improvement among groups in the FMA [$F(2, 384) = 0.2$, $P = .83$], FMA Wrist and Hand [$F(2, 384) = 0.4$, $P = .70$], or the mAMAT [$F(2, 379) = 1.2$, $P = .31$].

						3.EMG Triggered NMES subjects Showed significant improvement in arm function as compared to cyclic NMES and Cyclic sensory stimulation.
11.Kwakkel *et al.*, 2016	159 Ischemic Stroke Patients ,Mean Age 58.97(+/-14.05), Onset 8.17(+/-4.28)Days	1. ARAT 8,12,26 WK 2. FMA-UE 3. WMFT 4. NHPT 5. MAL-QOM	Multicentred observer blinded stratified RCT	EXP GP-(EMG-NMS) C GP-(CIMT) 30 Min session /day for 5 days/wk-3 weeks	SPSS 2.0 Non Parametric Test	1.Significant improvement in both group on ARAT and FMA-UE 2. Large significant improvement in EMG-NMS than Control Group
12.Nagapattinam et al., 2015	N=60 sub acute stroke Subjects Mean Age 44.65 Onset 4.17(+/-1.15) mths	ARAT pre and post 2 week	Experimental Study	1.Experimental Group=Conventional Physiotherapy+ NMES 20 minutes 2. Conventional Physiotherapy +Task Specific Mirror Therapy 20 Min 3 Ctrl Gp consist of combination of NMES and TSMT 40 min sessions 12 Sessions /Wk for 2 Wk	SPSS version 16.0 Non Parameteric Test Krushal Wallis Test	It is concluded that a combination therapy of task specific mirror therapy with functional electrical stimulation for two weeks duration, is shown to be effective for recovery

						of upper limb function in subjects with sub-acute hemiplegia.
13. Kim JH, 2015	33 Subjects(Stroke> 6Months) Age 58.10+/-8.32, Onset 4.6-10 months	Dynameter, Goniometer, Box+Block FIM, Jebsen Taylor MAS, SSQOL	RCT pre and post 4 wk	INT GP1-FES+Mirror Therapy+BF INT GP 2-FES+Mirror Therapy CTRL GP Mirror 30 min session 5 times /wk for 4 wk	SPSS version 17.0 ANOVA Post hoc Analysis	1. Sig UE improvement in INT and CTRL GP for FIM, BMRS, BBT, MFT (P<.05) 2. Infact FM subscore for wrist and hand were more sig than INT GP(p<.05)
14. Tae Hoon Kim et al., 2015	N=30 MEAN AGE 59.07+/-8.07 ONSET 8.27+/-1.98 mths	1.FMA-UE 2.MAL 3.MBI 4.ROM of Wrist Flexion	Blinded Assessor ,computer generated RCT	Control Group (N=15) Conventional Physiotherapy Experimental Group(N= 15) BCI-FES Conventional Physiotherapy 30 min/day 5 times/wk for 4 weeks	SPSS Version 18.0 Shapiro Wilk Test Paired T-Test	BCI-FES patients showed significant improvement as compared to conventional physiotherapy alone.
15. Cui *etal*.,2015	N=45 mean age 61.5+/-14.8 onset 12.6+/-6.1 weeks	1.FMA 2. MAS 3. ARAT Assessment before and after intervention, and 4 weeks later.	Block Randomized Controlled Trial	1. 12 H NMES GP (N=15) 2.NMES GP (N=15) 3. CTRL GP (N=15) 30 min session /day 6days/week for 4 weeks.	SPSS version 15.0 ANOVA	The 12-hour neuromuscular electrical stimulation group achieved better improvement in upper extremity

						motor function, especially in the wrist-hand function

Table 2. PEDro Scale Scores

	Guo et al., 2018	Demir et al., 2018	Carrico et al .,2018	Qian et al., 2017	Nakipoglu et al., 2017	Park et al., 2017	Salameh et al., 2017	Schick T. et al., 2017	Chin et al., 2017	Wilson et al., 2016	Kwakkel et al., 2016	Nagapatinum et al., 2015	Kim JH et al., 2015	Taehu Kim et al., 2015	Cui et al., 2015
Eligibility criteria specified	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Random allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concealed allocation	No	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Similar group at baseline	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blinding of subjects	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
Blinding of therapies	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No
Blinding of assessors	No	No	Yes	Yes	No	No	No	Yes	Yes	No	Yes	No	Yes	Yes	No
Measure of one key outcome obtained for 85%of subjects	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention to treat analysis	No	No	No	No	No	No	Yes	No	No	No	Yes	Yes	No	No	No
Between group comparison of at least one key	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

outcome															
Point and variability measures for at least one key outcome	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Score	5	5	6	6	5	5	6	7	7	8	8	5	7	7	6

Table 3. Data Synthesis Criteria

Level of Evidence Synthesis Criteria	
Strong Evidence	Provided by statistically significant finding in outcome measures in • Atleast 2 high quality RCT with PEDro scores of atleast 4 points*
Moderate Evidence	Provided by statistically significant finding in outcome measures in • Atleast 1 high quality RCT and • Atleast 1 low quality RCT(5/3 points in PEDro) or 1 high quality clinical controlled trial(CCT)*
Limited Evidence	Provided by statistically significant finding in outcome measures in • Atleast 1 high quality RCT or • Atleast 2 high quality clinical controlled trial(CCTs)* in the absence of high quality RCTs
Indicative Findings	Provided by statistically significant finding in outcome measures in • 1 high quality CCT or low quality RCTs* (in absence of high quality RCTs) • Two studies of non experiment nature with sufficient quality(in absence of RCTs and CCTs)
Insufficient or no Evidence	• In the event that results of eligible studies do not meet the criteria for one of the above stated levels of evidence or • In the event of conflicting(statistically significant positive or statistically significant negative)result among RCTs and CCTs or • In the event of no significant studies
**if the number of the studies that show evidence is 50% of the total number of the studies found within same category of methodological quality and study design(RCT,CCT ,non experimental studies) no evidence will be classified.*	

Table 4. Critical Appraisal Table

Study	Random sequence generator	Allocation concealment	Blinding of participant & personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other source of bias
Guo et al (2018)	Low	Low	Low	Low	Low	Low	Unclear
Demir et al (2018)	Unclear	Unclear	High	High	Low	High	Unclear
Carrico et al (2018)	Low	Low	High	High	Low	Low	Unclear
Qian et al (2017)	Low	Unclear	High	Low	Low	High	Unclear
Nakipoglu et al (2017)	Low	High	High	High	Low	Low	Unclear
Park et al(2017)	Low	Low	High	High	Low	High	Unclear
Salameh et al (2017)	Low	Low	High	High	Low	Low	Unclear
Schick T et al (2017)	Low	Low	High	Low	Low	Low	Unclear
Chin et al (2017)	Low	Low	High	Low	Low	Low	Unclear
Wilson et al (2016)	Low	Low	Low	High	Low	Low	Unclear
Kwakkel et al (2016)	Low	Low	Unclear	Low	Low	Low	Unclear
Nagapattinum et al(2015)	Unclear	Unclear	Unclear	High	Low	Unclear	Unclear
Kim JH et al (2015)	Low	Low	High	Low	Low	Low	Unclear
Tae Hoon Kim et al (2015)	Low	Low	High	Low	Unclear	Unclear	Low
Cui et al (2015)	Low	Low	Unclear	Unclear	Low	Unclear	unclear

Table 5. Outcome Measure Definitions with References

Outcome measures	**Description**
Action Research Arm Test (ARAT)	ARAT qualitatively measures the ability to manipulate objects. It is split into 4 subsections: grasp, grip, pinch and gross movement.
Fugl-Meyer Assessment (FMA)	FMA is a 33 item score that assesses movement, reflexes and coordination of the upper limb on a 3 point scale
Modified Ashworth Score (MAS)	MAS is a measure of resistance to passive movement (spasticity) of the upper limb, which is rated on a 5 point scale.
Motor Assessment Scale: Hand Movement (MAS HM)	MAS examines 9 areas of motor function and scores them on a 7-point qualitative scale based on participant ability to perform the relevant tasks. The hand movement (HM) subscale assesses ability to perform various functional movements of the hand, scoring the patient's overall performance on a scale from 0-6.
Motor Assessment Scale: Upper Arm Function (MAS UAF)	MAS examines 9 areas of motor function and scores them on a 7-point qualitative scale based on participant ability to perform the relevant tasks. The Upper Arm Function (UAF) subscale assesses ability to perform various movements of the upper arm at the shoulder joint in supine and standing positions. Performance is overall scored on a scale from 0-6.
Motor Activity Log-14: Amount of Use (MAL AOU)	MAL is an interview technique that assesses subjective reporting of participants on 14 common daily activities involving the upper limb. The Amount of Use (AOU) subscale assigns each patient a score on an 11-point scale according to the amount of use they retain of their more affected arm, as compared to their motor function prior to stroke.
Motor Activity Log-14: Quality of Movement (MAL QOM)	MAL is an interview technique that assesses subjective reporting of participants on 14 common daily activities involving the upper limb. The Quality of Movement (QOM) subscale assigns each patient a score on an 11-point scale. Their responses are scored according to how well they are now able to use their more affected arm to perform specific functional activities, as compared to their motor function prior to stroke.
Box & Block Test (BBT)	This test requires participants to grasp and move a small wooden cube over a central barrier in a box and drop it on the other side. The number of boxes moved in 1 minute is then counted.
Barthel Index Score (BIS)	Barthel Index is a score based on 16 items which include act ivies of daily living, mobility, cognitive and social functioning. A 4 item subset of the score focuses on items specifically related to activities of daily living that require the upper limb.
Functional independence Measure (FIM)	FIM is a score, originally derived from the Barthel Index, which considers 18 items related to upper limb requiring activities of daily living. Participant ability to perform each item independently is measured on a 7 point qualitative scale.
Upper Extremity Function Test (UEFT)	UEFT is a measure of ability to perform common activities of daily living. Participants have to complete as many repetitions of each task as they can in 2 minutes.
Arm Mobility Arm Test (AMAT)	AMAT assess functional ability to carry out 28 upper limb specific activities involving everyday objects.
Chedoke Arm & Hand Activity Inventory (CAHAI)	CAHAI is a 7-point quantitative scale that assesses functional recovery of the arm and hand post-stroke across a range of activities of daily living. Activities are scored according to the patient's ability to complete them, from entirely assisted to totally independent.

Table 6. NMES Intervention characteristics

Author ,Yr	**Ms Stimulated**	**Session Duration**	**# of session**	**Total# hrs**	**Pulse width(micro sec)**	**Frequency (Hz)**	**Duty cycle**	**Intensity** (mA)
Guo et al (2018)	Wrist and finger extensors(dorsum of fore arm)	30 min, 3 times /wk	12 sessions in 4 wk	6	300	40	15sec on/ off	pt tolerance
Demir et al (2018)	ED,EPL,FDS,FPL	45min,twice/day, 5 times/wk	80 sessions in 8 wk	60	-	-	-	-
Carrico et al (2018)	Opponence pollicis brewis	120 min,10 wk days,3 times/wk	18 sessions in 6 wks	36	100	10	-	50-100 micro volt
Qian et al (2017)	ECU,EDC	40 min /day,5 times /wk	20 sessions in 4 wks	13	100	-	-	80v
Nakipoglu et al (2017)	ECRL,ECRB,ECU, EDC	30 min /day,5 days/wk	20 sessions	10	300	30	10sec on/ off	-
Park et al(2017)	wrist ext	30 min/day,5 times/wk	20 sessions in 4 wks	10	-	-	6/12	-
Salameh et al (2017)	ED,Supinator	20 min/day,6 times/wk	72 sessions in 12 wks	24	-	150-200MH	-	pt tolerance
Schick T et al (2017)	ECRL,ECRB,FDS	30 min, 5 times /wk	15 sessions in 3 wks	7.5	300	30-35	-	5-60
Chin et al (2017)	FCR,FCU,FDS,ED, FDP,Thenar Ms,Lumbricals	45 min/day,5 days /wk	80 sessions in 16 wks	60	300	40	-	50
Wilson et al (2016)	ECR,EDC	40 min, twice /day,5 times /wk	80 sessions in 8	53	300	20-40	5/5	-

			wks					
Kwakkel et al (2016)	Finger extensors	30 min,2 times /day, 5 times /wk	30 sessions in 3 wks	15	-	-	5/25	-
Nagapattinum et al(2015)	EDC,ECRB,ECRL	30 min, 6 times /wk	12 session in 2 weeks	6	250	35	5sec on/off	90
Kim JH et al (2015)	Wrist extensors-extensor digitorum	30 min, 5 times /wk	20 sessions in 4 wks	10	-	256	-	pt tolerance
Tae Hoon Kim et al (2015)	Finger extensors	30 min, 5 times /wk	20 sessions in 4 wks	10	150	60	0.5 sec on /off	20-27
Cui et al (2015)	Wrist And Finger Extensors	30 min, 5 times /wk	20 sessions in 4 wks	10	300	40	1 sec on/off	pt tolerance

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