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REVIEW ARTICLE

Effectiveness of Focal Vibration on Muscle Tone, Kinematic Parameters, and Motor Function in Individuals with Stroke, Parkinson' Disease and Multiple Sclerosis: A Systematic Review, Meta-Analysis and Meta-Regression

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ABSTRAK

Kajian sistematik ini bertujuan untuk menyiasat kesan getaran fokus (FV) terhadap tonus otot, parameter kinematik dan fungsi motor pada individu yang menghidapi penyakit strok, Parkinson dan sklerosis berbilang. Kajian ini juga bertujuan untuk menentukan pengaruh parameter getaran seperti frekuensi dan amplitud, tempoh sesi stimuli, dan jumlah keseluruhan sesi intervensi pada hasil ukuran. Carian artikel yang relevan dengan kajian ini telah dilakukan melalui pangkalan data PubMed, Scopus, Cochrane, Web of Science dan EBSCO. Sebanyak 21 artikel telah memenuhi kriteria kemasukan yang ditetapkan. Dalam tempoh seminggu selepas rawatan, FV telah terbukti berkesan untuk mengurangkan spastisiti pada bahagian siku (P = 0.04), meningkatkan parameter kinematik anggota atas (SMD = -0.75, 95% CI: -1.50 hingga -0.01), dan meningkatkan kefungsian anggota atas (P = 0.05) dalam kalangan pesakit strok. Rawatan FV juga secara signifikan meningkatkan parameter kinematik anggota bawah pesakit Parkinson apabila dibandingkan dengan kumpulan kawalan (P = 0.03). Namun, kesan FV didapati tidak signifikan dalam mengurangkan spastisiti anggota atas pesakit strok (P = 0.25) serta dalam meningkatkan parameter kinematik anggota bawah pesakit Parkinson (SMD = 0.38, 95% CI: -0.58 hingga 1.35) apabila penilaian dilakukan selepas lebih dari seminggu dari sesi rawatan. Jumlah keseluruhan sesi terapi didapati berkait secara signifikan dengan saiz kesan (p = 0.042) terhadap hasil ukuran kefungsian

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anggota atas. Kesimpulannya, FV boleh digunakan dalam program pemulihan untuk memberi manfaat kepada pesakit yang mengalami gangguan neurologi seperti penyakit strok, Parkinson dan sklerosis berbilang.

Kata kunci: Getaran; kajian sistematik; penyakit sistem saraf

ABSTRACT

This systematic review aimed to investigate the effect of focal vibration (FV) on muscle tone, kinematic parameters and motor functions in individuals with stroke, Parkinson' disease and multiple sclerosis. It also determined the influence of vibration parameters such as frequency and amplitude, stimulation session duration, and the total number of intervention sessions on the outcome measures. PubMed, Scopus, Cochrane, Web of Science, and EBSCO were searched, yielding 21 qualifying articles. Within a week post-treatment, FV effectively reduced elbow spasticity (P = 0.04), improved upper limb kinematic parameters (SMD = -0.75, 95% CI: -1.50 to -0.01), and enhanced upper limb motor function (P = 0.05) in stroke patients. FV significantly improved lower limb kinematic parameters of Parkinson's disease patients (P = 0.03). Over a week post-treatment, the effect of FV was not significant in reducing spasticity for upper limb in stroke (P = 0.25) and improving kinematic parameters for lower limb in Parkinson's disease (SMD = 0.38, 95% CI: -0.58 to 1.35). The total therapy sessions significantly associated with the effect size (p = 0.042) for upper limb motor function outcome measure. Conclusion, integrating FV into rehabilitation may benefit patients with neurological disorders such as stroke, Parkinson's disease, and multiple sclerosis.

Keywords: Nervous system diseases; systematic review; vibration

INTRODUCTION

Neurological disorders are the leading cause of disability worldwide, accounting for 276 million disability-adjusted life years (DALYs). Over the years from 1990 to 2016, DALYs related to these disorders have escalated by 15%, prominently driven by the prevalence of stroke, constituting 42.2% of the burden (Feigin et al. 2020). Parkinson's disease and multiple sclerosis also contribute to DALYs in the amounts of 3.4% and 0.4%, respectively (Feigin et al. 2020). Individuals affected by stroke, Parkinson's disease and multiple sclerosis commonly suffer from somatosensory impairments that may affect their sensory perception, muscle tone and motor performance (Carlsson et al. 2018; Gorst et al. 2019; Jamali et al. 2017).

Presently, clinicians in the field of rehabilitation generally give greater consideration to traditional treatments

compared to sensory training (Carlsson et al. 2018). However, research has demonstrated that sensory training, namely through the use of vibration, can improve the motor function of individuals with neurological diseases (Aman et al. 2015). Integrating vibration as a supplementary approach within rehabilitation programs could be beneficial to the patients.

Focal vibration (FV) stimulates the somatosensory system via mechanical vibrations. FV can be applied to the localised muscle, tendon, or plantar region to stimulate the mechanoreceptors on the skin. Meissner's corpuscles and Pacinian corpuscles are sensitive to low (0-40Hz) and high (40-500Hz) frequency vibrations respectively (McGlone & Reilly 2010). Vibration can also activate the proprioceptive muscle spindle primary (Ia fibers) and secondary endings (II fibers) as well as the Golgi tendon organ (Ib fibers) (Roll et al. 1989) to produces the tonic vibration reflex (TVR). The potential benefits of FV have been explored in the existing systematic reviews.

Systematic reviews highlighted the positive effects of FV in reducing muscle spasticity in individuals with stroke (Alashram et al. 2019; Avvantaggiato et al. 2021). However, these studies revealed that FV did not yield a significant improvement in functional motor recovery for stroke survivors (Alashram et al. 2019; Alashram et al. 2022; Avvantaggiato et al. 2021; Mortaza et al. 2019). In the case of individuals with multiple sclerosis, a systematic review conducted by Etoom et al. (2018) suggested a significant enhancement in gait analysis due to FV, albeit without a notable reduction in spasticity. Another systematic review included whole-body vibration, reported a lack of clear evidence supporting the effectiveness of vibration treatment in reducing motor symptoms and enhancing balance, gait, and mobility for individuals with Parkinson's disease (Dincher et al. 2019).

Existing systematic reviews have primarily focused on the effects of FV within specific neurological disorders. Integrating research encompassing these disorders, including stroke, Parkinson's disease and multiple sclerosis offers an opportunity to enhance comprehension and overview regarding the efficacy of FV in enhancing muscle tone, kinematics parameters and motor function. Enhancements in these outcome measurements have the potential to improve the quality of daily life for the affected individuals. Moreover, this approach of aggregating data from multiple studies across diverse neurological conditions can reveal patterns or trends in the treatment's effectiveness. This insight can highlight commonalities or differences in how the treatment works across various conditions, aiding in the understanding of its mechanisms and potential variations in efficacy. In addition, the healthcare practitioners, policymakers, and researchers can use the observed trends to make more informed decisions regarding treatment choices, resource allocation, and further research directions across multiple diseases.

This systematic review aimed to investigate the effect of FV on muscle tone, kinematics parameters and motor function in individuals with stroke, Parkinson's disease and multiple sclerosis. In addition, a meta-regression analysis will be conducted to determine the influence of vibration parameters such as frequency and amplitude, as well as the stimulation duration and the total number of intervention sessions on the measured outcomes. The findings of this review may help healthcare professionals, researchers, and policymakers to plan clinical practice guidelines, especially for individuals with stroke, Parkinson's disease and multiple sclerosis.

MATERIALS AND METHODS

Study design

This review was conducted based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA 2009) statement (Moher et al. 2009).

Search Strategy

A systematic search was conducted on five electronic databases, namely PubMed, Scopus, Cochrane, Web of Science, and EBSCO. All articles published before 1st April 2022 were retrieved. The search was performed by four independent reviewers (TJY, ZMR, MIZR, and MFR). The keywords used for the search strategies were (focal muscle vibration OR focal vibration OR FMV OR vibration OR segmental muscle vibration OR localized muscle vibration OR localized vibration OR localized mechanical vibration) AND (neurological disease OR stroke OR neurological OR diseases OR disorders OR spinal cord OR Parkinson OR nervous system OR brain OR cerebral OR Alzheimer OR multiple sclerosis). The databases were imported into EndNote X8 and duplicates were removed.

Eligible Criteria

The inclusion criteria for studies in this systematic review were: (i) clinical trials conducted on patients with neurological disorders; (ii) the intervention was FV; (iii) it was a randomised controlled trial (RCT); (iv) measurement outcomes such as Modified Ashworth Scale (MAS), rigidity, kinematic parameters, and motor functional tests were available; (v) amplitude, frequency, and duration were described in the paper and (vi) written in English. The excluded criteria were: (i) the intervention involved whole-body vibration; (ii) patients treated for low back pain; (iii) not an RCT; (iv) patients without a neurological disorder; (v) other sensory stimulation such as thermal stimulation applied and (vi) animal studies. The purpose of this review was to evaluate the effectiveness of FV in improving muscle tone, kinematic parameters, and motor functions in individuals with neurological diseases. Consequently, studies that examined different types of vibrations, such as whole-body vibration, had been disregarded since the vibrations were not specifically targeted towards certain muscles.

Data Extraction

The data extracted from each study included: (i) author, publication year, and publication country; (ii) trial design; (iii) participant characteristics (type of disease, affected limb, time since disease incidence, and age); (iv) intervention parameters (apparatus, region treated, frequency and amplitude of the vibration, and duration of the stimulus sessions); (v) intervention and control group design; (vi) assessment time and (vii) measured outcomes. Any discrepancies encountered during the data extraction were resolved via group discussion.

Assessment of Risk of Bias

The risk of bias was assessed by four independent reviewers (TJY, ZMR, MIZR, and MFR) using the Cochrane Collaboration tool (Higgins et al. 2011). The domains for this tool included: (i) selection bias of sequence generation and allocation concealment; (ii) performance bias in the blinding of participants and personnel; (iii) detection bias; (iv) attrition bias; (v) reporting bias and (vi) others. Each domain can be rated as low, unclear, or high risk. The fifth reviewer (MHH) was consulted to resolve any disagreement through comprehensive discussions.

Statistical Analysis

The meta-analysis and meta-regression were conducted using the R programming language (Schwarzer & Schwarzer 2012). A random effect model with continuous outcome data and a 95% confidence interval (CI) was used. Mean and standard deviation (SD) of post-treatment outcome measures, along with the number of samples in both the intervention and control groups, were collected from each study. In cases where post-study values were not reported, the final value was imputed based on the baseline and change readings. Due to the lack of available data on the correlation coefficient between the baseline and final values, as well as the absence of any similar trials reporting summaries for changes from baseline values and final values, it was not possible to determine the correlation coefficient using a formula. Based on the articles (Dias et al. 2014; Higgins et al. 2019), 0.5 is often used for the correlation coefficient between the baseline and final values. Mean difference (MD) was used when the outcome units were the same. Otherwise, a standard mean difference (SMD) was employed (Higgins et al. 2019), calculated using Hedges' g. The estimator of the between-study heterogeneity was determined using Restricted Maximum Likelihood (REML) (Veroniki et al. 2016). Besides, Knapp-Hartung adjustment was used in the meta-analysis. Heterogeneity was assessed using I^2, categorised as low (0-40%), moderate (30-60%), substantial (50-90%), or considerable (75-100%) (Higgins et al. 2019). Sensitivity analysis was conducted in the presence of moderate or large heterogeneity. The impact of covariates (frequency, amplitude, duration of the stimulus sessions, and total therapy sessions) on the effect size of the outcome measures

was examined using a random effect meta-regression model. The meta-regression analysis was conducted only if the number of included studies for each assessed outcome exceeded five. According to the Cochrane Handbook, it is recommended to have at least 10 studies for each covariate that is being studied (Higgins et al. 2019). However, the number of studies currently included for each covariate was less than 10. Therefore, a threshold of more than five studies was selected for the execution of meta-regression. In addition, research additionally selected a cut-off number of less than 5 studies per covariate to identify meta-regression analyses that may be at risk of overfitting (Geissbühler et al. 2021).

RESULTS

Study Selection and Risk of Bias

A total of 697 research studies were initially identified during database search. However, 134 studies were removed due to duplication. Following the screening process, studies with irrelevant titles and abstracts were excluded. Ultimately, 21 articles (Annino et al. 2019; Ayvat et al. 2021; Calabrò et al. 2017; Caliandro et al. 2012; Camerota et al. 2016; Casale et al. 2014; Celletti et al. 2017; Choi 2017; Cordo et al. 2022; Costantino et al. 2017; Lee et al. 2013; Marconi et al. 2011; Noma et al. 2012; Önal et al. 2022; Paoloni et al. 2010; Peppe et al. 2019; Seo et al. 2020; Seo et al. 2019; Spina et al. 2016; Spolaor et al. 2020; Tavernese et al. 2013) were included in the systematic review as illustrated in Figure 1. Among these, 16 were focused on stroke (Annino et al. 2019; Calabrò et al. 2017; Caliandro et al. 2012; Casale et al. 2014; Celletti et al. 2017; Choi 2017; Cordo et al. 2022; Costantino et al. 2017; Lee et al. 2013; Marconi et al. 2011; Noma et al. 2012; Önal et al. 2022; Paoloni et al. 2010; Seo et al. 2020; Seo et al. 2019; Tavernese et al. 2013), two pertained to multiple sclerosis (Ayvat et al. 2021; Spina et al. 2016) and three were relevant to Parkinson's disease (Camerota et al. 2016; Peppe et al. 2019; Spolaor et al. 2020).

Figure 2 illustrated the risk of bias evaluation. Out of the total, 11 studies were categorised as high risk (Annino et al. 2019; Ayvat et al. 2021; Caliandro et al. 2012; Celletti et al. 2017; Choi 2017; Marconi et al. 2011; Noma et al. 2012; Önal et al. 2022; Paoloni et al. 2010; Seo et al. 2020; Tavernese et al. 2013). Additionally, five studies were determined as unclear risk (Camerota et al. 2016; Cordo et al. 2022; Costantino et al. 2017; Lee et al. 2013; Spina et al. 2016) while another five studies were assessed as low risk (Calabrò et al. 2017; Casale et al. 2014; Peppe et al. 2019; Seo et al. 2019; Spolaor et al. 2020). The RCTs with a lack of participant and personnel blinding (D3) were identified as having a high risk of bias.

Study Characteristics

Table 1 showed a summary of the characteristics of the studies included in this systematic review. The majority of the studies (n=13) originated from Italy (Annino et al. 2019; Calabrò et al.

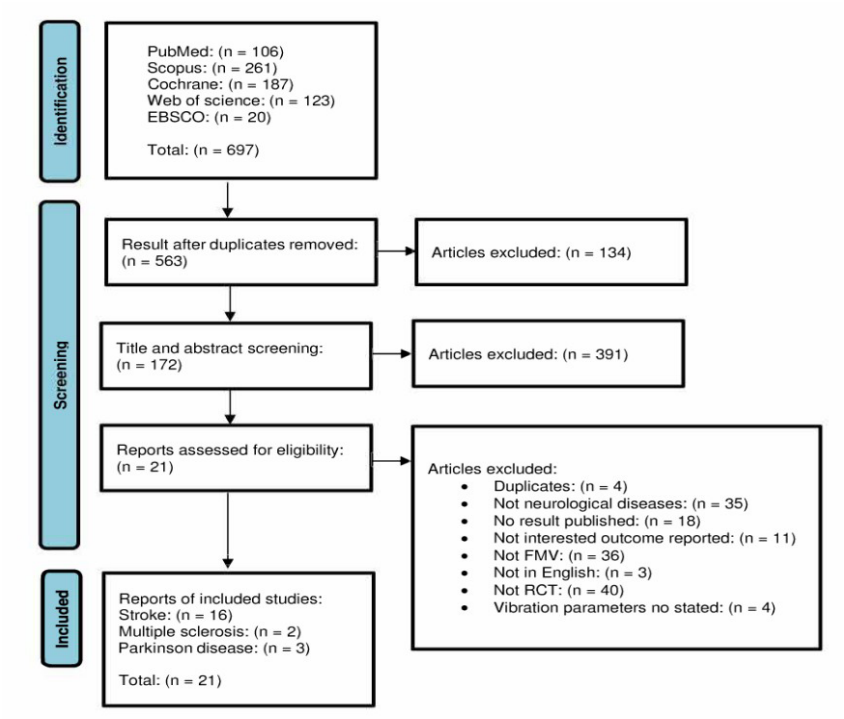

FIGURE 1: PRISMA flow diagram

2017; Caliandro et al. 2012; Camerota et al. 2016; Casale et al. 2014; Celletti et al. 2017; Costantino et al. 2017; Marconi et al. 2011; Paoloni et al. 2010; Peppe et al. 2019; Spina et al. 2016; Spolaor et al. 2020; Tavernese et al. 2013), followed by three from the United States (US) (Cordo et al. 2022; Seo et al. 2020; Seo et al. 2019), two each from Korea (Choi 2017; Lee et al. 2013) and Turkey (Ayvat et al. 2021; Önal et al. 2022), and one from Japan (Noma et al. 2012).

A total of 13 studies specifically addressed upper limb impairments in stroke patients (Annino et al. 2019; Calabrò et al. 2017; Caliandro et al. 2012; Casale et al. 2014; Celletti et al. 2017; Choi 2017; Cordo et al. 2022; Costantino et al. 2017; Marconi et al. 2011; Noma et al. 2012; Seo et al. 2020; Seo et al. 2019; Tavernese et al. 2013), while three studies were dedicated to the study of lower limb impairment in stroke patients (Lee et al. 2013; Önal et al. 2022; Paoloni et al. 2010). Moreover, two studies addressed lower limb impairment in multiple sclerosis populations (Ayvat et al. 2021; Spina et al. 2016) and three studies assessed Parkinson's disease with lower limb impairments (Camerota et al. 2016; Peppe et al. 2019; Spolaor et al. 2020). Regarding study design, 15 studies employed a parallel trial design (Annino et al. 2019; Calabrò et al. 2017; Caliandro et al. 2012; Camerota et al. 2016; Casale et al. 2014; Celletti et al. 2017; Choi 2017; Costantino et al. 2017; Lee et al. 2013; Marconi et al.

FIGURE 2: Risk of bias

2011; Önal et al. 2022; Paoloni et al. 2010; Seo et al. 2019; Spina et al. 2016; Tavernese et al. 2013), three employed crossover trials (Peppe et al. 2019; Seo et al. 2020; Spolaor et al. 2020), two employed a factorial design (Ayvat et al. 2021; Noma et al. 2012), and one employed a semi-crossover trial design (Cordo et al. 2022). The time since disease incidence was more than four weeks. Furthermore, the age range of populations in the intervention and control groups were 28-78 years old and 27- 80 years old respectively.

Intervention Design

Table 2 depicted the methodology employed for both intervention and control groups. The frequency of FV applied to the upper limb of stroke patients ranged from 30 Hz to 500 Hz, with an amplitude ranging from 0.01 mm to 3 mm. Likewise, for the lower

TABLE 1: General characteristics of the included studies

No	Study	Ctry	RCT	Participant characteristics		
				Disease	Time since disease incidence	Age, Mean (SD)
			Upper limb			
1	Annino et al. (2019)	Italy	P	Stroke	> 6 months	Intervention: 67.8 (8.3) Control: 69.4 (10.4)
2	Calabro et al. (2017)	Italy	P	Stroke	> 3 months	Intervention: 66 (5) Control: 67 (4)
3	Caliandro et al. (2012)	Italy	P	Stroke	> 12 months	Intervention: 57.42 (12.79) Control: 61.85 (15.74)
4	Casale et al. (2014)	Italy	P	Stroke	> 12 months	Intervention: 64.7 (5.4) Control: 65.1 (5.8)
5	Celletti et al. (2017)	Italy	P	Stroke	> 12 months	Intervention: 43.25 (7.8) Control: 60 (6.62)
6	Choi (2017)	Korea	P S	Stroke	> 6 months	Intervention: 62 (9) Control: 59 (10.1)
7	Cordo et al. (2022)	US	C	Stroke	> 5 weeks	Intervention: 56.3 (12.7) Control: 57.7 (12.9)
8	Costantino et al. (2017)	Italy	P	Stroke	> 12 months	Intervention: 62.59 (15.39) Control: 60.47 (16.09)
9	Marconi et al. (2012)	Italy	P	Stroke	> 12 months	Intervention: 63.6 (7.6) Control: 66.3 (11)
10	Noma et al. (2012)	Japan	F	Stroke	> 4 weeks	Intervention: 59 (12.99) Control 1: 58 (16.16) Control 2: 61.75 (12.13)
11	Seo et al. (2019)	US	P	Stroke	> 3 months	Intervention: 61 (10) Control: 64 (8)
12	Seo et al. (2020)	US	C	Stroke	> 3 months	Intervention: 61 (10) Control: 64 (8)
13	Tavernese et al. (2013)	Italy	P	Stroke	> 6 months	Intervention: 58.9 (14.7) Control: 58.3 (12.4)
			Lower limb			
14	Ayvat et al. (2021)	Turkey	F	MS	> 12 months	Intervention 1: 37.7 (9.7) Intervention 2: 38.4 (11.07) Control: 33.86 (6.74)
15	Spina et al. (2016)	Italy	P	MS	> 6 months	Intervention: 47 (12.17) Control: 48 (12.34)
16	Camerota et al. (2016)	Italy	P	PD	> 6 months	Overall: 64.85 (8.74)
17	Peppe et al. (2019)	Italy	C	PD	> 5 years	Overall: 60.27 (9.9)
18	Spolaor et al. (2020)	Italy	C	PD	> 5 years	Overall: 67.46 (10.27)
19	Lee et al. (2013)	Korea	P	Stroke	> 6 months	Intervention: 53.31 (8.37) Control: 55.73 (8.27)
20	Önal et al. (2022)	Turkey	P	Stroke	> 8 weeks	Intervention: 60 (9) Control: 59 (9)
21	Paoloni et al. (2010)	Italy	P	Stroke	> 6 months	Intervention: 59.5 (13.3) Control: 62.6 (9.5)

C: Crossover study; Ctry: Country; F: Factorial study; MS: Multiple sclerosis; P: Parallel study; PD: Parkinson' disease; RCT: Randomized controlled trial; SC: Semi-crossover study; US: United States

TABLE 2: Intervention and control design for the included studies

No	Study	Vibration parameters	Intervention	Control	Assessment time	Outcome measures
			Upper limb			
1	Annino et al. (2019)	Freq: 30 Hz Amp: 2mm DSS: 5 min TTS: 24 sessions	PT (30 min X 3/wk X 8 wk) + FV N: 17 APP: - RT: Triceps	PT (30 min X 3/wk X 8 wk) N: 17	T0: Baseline T1: End of Week 8 treatment	BI, MAS for elbow, AROM for elbow, MMT for elbow
2	Calabro et al. (2017)	Freq: 80 Hz Amp: 0.2–0.4 mm DSS: 60 min TTS: 40 sessions	Armeo-Power with FV (60 min X 5/wk X 8 consecutive wk) N: 10 APP: Pneumatic vibrator RT: Triceps brachialis, supraspinatus, and deltoid	Armeo-Power with sham FV (60 min X 5/ wk X 8 consecutive wk) N: 10	T0: Baseline T1: Directly after the training T2: After 1 month of rest from the training	MAS for shoulder and elbow, SICI, HMR, FMA-UE, FIM, HRS-D, HRS-A, PROM, force, MEP amplitude, ICF
3	Caliandro et al. (2012)	Freq: 100Hz Amp: 0.2–0.5 mm DSS: 30 min (3 sessionsX10 min) TTS: 3 sessions	FV + PT (60 min X 3 days/ wk) N: 21 APP: Crosystem RT: Pectoralis minor, biceps brachii, flexor carpi muscle	Placebo FV + PT (60 min X 3 days/ wk) N: 15	T0: Baseline T1: 1 wk after treatment T2: 1 month after treatment	WMFT, MAS for shoulder, elbow, and wrist, VAS for shoulder, elbow, and wrist
4	Casale et al. (2014)	Freq: 100 Hz Amp: 2 m DSS: 30 min TTS: 10 sessions	FV + PT (60 min X 5 consecutive days X2 wk) N: 15 APP: Vibra @circle RT: Triceps brachii	Sham + PT (60 min X 5 consecutive days X2 wk) N: 15	T0: Baseline T1: 48 hours after the fifth session T2: 48 hours after the last session	MAS for elbow, Robot- aided evaluation
5	Celletti et al. (2017)	Freq:100 Hz Amp: 0.2–0.5 mm DSS: 30 min (3 sessionsX10 min) TTS: 12 sessions	FV + PT (60 min X 2/ wk X 6 wk) N: 6 APP: -	PT (60 min X 2/ wk X 6 wk) N: 6	T0: Baseline T1: After treatment	WMFT, MAS for elbow, VAS for shoulder, elbow, and wrist, MI
6	Choi (2017)	Freq: 91 Hz Amp: 1 mm DSS: 20 min TTS: 12 sessions	FV (30 min X 3/ wk X 4 wk) N: 5 APP: Thrive MD-01 RT: Biceps brachii, flexor carpi radialis	PT (30 min X 3/ wk X 4 wk) N: 5	T0: Baseline T1: After treatment	BBT, GS, Weinstein monofilament
7	Cordo et al. (2022)	Freq: 60 Hz Amp: 2-3mm DSS: 30 min TTS: 18 sessions	FV (2-3/ wk X 6-10 wk) N: 38 APP: AMES RT: Tendons to the finger and thumb	Placebo (2/ 3/ wk X 6-10 wk) N: 35	T0: Baseline T1: 1 wk after treatment T2: Crossover result	FMA-UE, SIS, MAS for fingers and wrist, RLA

8	Costantino et al. (2017)	Freq: 300 Hz Amp: 2 mm DSS: 30 min TTS: 12 sessions	FV (3/ wk X 4 wk) N: 17 APP: ViSS device RT: Triceps brachii, extensor carpi radialis longus, brevis muscle	Sham N: 15	T0: Baseline T1: After treatment	GS, MAS for shoulder, elbow, and wrist, FIM, FMA-UE, QuickDash score, JTT, VNRS
9	Marconi et al. (2012)	Freq: 100 Hz Amp: 0.2–0.5 mm DSS: 30 min (3 sessionsX10 min) TTS: 3 sessions	FV + PT (60 X 3 consecutive days) N: 15 APP: Crosystem RT: Flexor carpi radialis, biceps brachii	PT (60 min X 3 consecutive days) N: 15	T0: Baseline T1: 1 h after treatment T2: 1 wk after treatment T3: 2 wk after treatment	MAS for elbow and wrist, MI, WMFT, MEP amplitude, RMT, SICI, area map, volume map
10	Noma et al. (2012)	Freq: 91 Hz Amp: 1 mm DSS: 5 min TTS: 1 session	Relax (30 min) + FV N: 12 APP: Thrive MD-01 RT: Abdominal side of all fingers, palm, and wrist flexor tendon	Relax (30 min) + rest (5 min) N: 12 Control 2: Relax (30 min) + stretch (5 min)	T0: Baseline T1: After treatment T2: 30 min after treatment	F wave, MAS for elbow and wrist
11	Seo et al. (2019)	Freq: 500 Hz (random frequency) Amp: 0.063 mm DSS: 120 min TTS: 6 sessions	FV + PT (2 hours X 3/ wk X 2 wk) N: 6 APP: TheraBracelet RT: Wrist	Sham + PT (2 hours X 3/ wk X 2 wk) N: 6	T0: Baseline T1: 6 days after treatment T2: 19 days after treatment	BBT, WMFT
12	Seo et al. (2020)	Freq: 500 Hz (random frequency) Amp: 0.063 mm DSS: 480 min TTS: 30 sessions	FV (8 hours/day X 4 wk) N: 13 APP: TheraBracelet RT: Wrist	Sham (8 hours/day X 4 wk) N: 12	T0: Baseline T1: After treatment	2-point discrimination, NHPT, GS
13	Tavernese et al. (2013)	Freq: 120 Hz Amp: 0.01 mm DSS: 30 min TTS: 10 sessions	FV + PT (60 min X 5/ wk X 2 wk) N: 24 APP: Horus RT: Biceps brachii, flexor carpii ulnaris	PT (60 min X 5/ wk X 2 wk) N: 20	T0: Baseline T1: 2 wk after treatment	Kinematic, ROM
			Lower limb			
14	Ayvat et al. (2021)	Freq: 50 Hz (intervention1); 100 Hz (intervention 2) Amp: 1 mm DSS: 10 min (5 min for each muscle) TTS: 24 sessions	FV + PT (60 min X 3/ wk X 8 wk) N: 10 APP: Vibrasens RT: Gastrocnemius muscle	PT (60 min X 3/ wk X 8 wk) N: 7	T0: Baseline T1: After treatment	MAS, Gait parameters, Single Leg Stance Test, ROM

15	Spina et al. (2016)	Freq: 9000 Hz Amp: 0.002 mm DSS: 60 min TTS: 15 sessions	FV (1h/day, 5days/ wk X 3 wk) + PT N: 9 APP: Equistasi RT: 7th cervical vertebra and the triceps surae tendon bilaterally (without pyramidal system impairment); triceps surae, patellar tendon, medius gluteus (with pyramidal system impairment)	Placebo + PT N: 10	T0: Baseline T1: After treatment T2: 3 weeks after treatment	Gait analysis, BBS, DGI, FRT, 25FWT, MSWS-12, MAS, FSS
16	Camerota et al. (2016)	Freq: 100 Hz Amp: 0.2-0.5 mm DSS: 60 min (3 sessionsX10 min for each muscle) TTS: 3 sessions	FV (3 consecutive days) N: 9 APP: Crosystem RT: Lumbar paraspinal muscles, quadriceps tendon	Sham N: 8	T0: Baseline T1: 24 h after treatment T2: 1 wk after treatment T3: 3 wk after treatment	Gait analysis
17	Peppe et al. (2019)	Freq: 9000 Hz Amp: 0.002 mm DSS: 60-240min TTS: 44 sessions	FV (8 wk - 6 days/ wk for 1 h during the first week, increased by 1 h/ wk until the 4th wk, the wearing time was stable for the subsequent 4 wk during which the device was worn 5 days/ wk) N: 40 APP: Equistasi RT: 7th cervical vertebra, soleus muscle tendons	Placebo N: 40	T0/T2: Baseline T1/T3: After treatment	Gait analysis
18	Spolaor et al. (2020)	Freq: 9000 Hz Amp: 0.002 mm DSS: 60-240min TTS: 44 sessions	FV (6 days/ wk for 1 h during the first week, increased by 1 h/ wk until the 4th wk, the wearing time was stable for the subsequent 4 wk during which the device was worn 5 days/ wk) N: 20 APP: Equistasi RT: 7th cervical vertebra, soleus muscles	Placebo N: 20	T0/T2: Baseline T1/T3: After treatment	Gait analysis, Romberg test, sEMG

19	Lee et al. (2013)	Freq: 90 Hz Amp: 0.015 mm DSS: 30 min TTS: 18 sessions	FV (3/ wk X 6 wk) N: 16 APP: - RT: heel, Achilles, and tibialis anterior tendon	Sham N: 15	T0: Baseline T1: 1 day after treatment	Postural sway, gait analysis
20	Önal et al. (2022)	Freq: 80 Hz Amp: 1 mm DSS: 15 min TTS: 20 sessions	FV (4 wk: Monday, Wednesday, and Friday = 15 min of LVT + 45 min of PT; Tuesday and Thursday = 60 minutes of PT) N: 15 APP: Vibrasens RT: Metatarsal heads, lateral arch, and heel	PT (60 min X 5 days/ wk X 4 wk) N: 15	T0: Baseline T1: After treatment	OSI, Postural Stability Test, fall risk, BBS, FRT, TUG, 10MWT, TIS
21	Paoloni et al. (2010)	Freq: 120 Hz Amp: 0.01 mm DSS: 30 min TTS: 12 sessions	FV + CPT (50 min X 3/ wk X 4 wk) N: 22 APP: Horus RT: Tibialis anterior, peroneus longus	PT (50 min X 3/ wk X 4 wk) N: 22	T0: Baseline T1: 1 month after treatment	Gait analysis

Amp: Amplitude; AMES: Assisted Movement with Enhanced Sensation; APP: Apparatus; AROM: Active range of motion; BBT: Box and block test; BI: Barthel Index; DDS: Duration of stimulation sessions; DGI: Dynamic Gait Index; EMG: Electromyography; FIM: Functional Independence Measure; FMA-UE: Fugl Meyer Assessment – Upper Extremity; Freq: Frequency; FRT: Functional Reach Test; FSS: Fatigue Severity Scale; FV: Focal vibration; 25FWT: Timed 25-foot Walk; GS: Grip strength; HMR: Hmax/Mmax ratio; HRS-A: Hamilton Rating Scale for anxiety; HRS-D: Hamilton Rating Scale for depression; ICF: Intracortical facilitation; JTT: Jebsen-Taylor Hand Function Test; MAS: Modified Ashworth Scale; MEP: Motor evoked potential; MI: Motricity Index; MMT: Manual muscle testing; MSWS-12: Multiple Sclerosis walking scale; 10MWT: 10 Metre Walk Test; N: Number of participants; NHPT: Nine-Hole Peg Test; OSI: Overall Stability Index; PROM: Passive range of motion; PT: Physical therapy; RLA: Rancho Los Amigos; RMT: Resting motor threshold; ROM: range of motion; RT: Regions treated; SICI: Short intracortical inhibition; SIS: Stroke Impact Scale; TIS: Trunk Impairment Scale; TTS: Total therapy sessions; TUG: Timed Up and Go Test; VAS: Visual analog scale; VNRS: Verbal Numerical Rating Scale; wk: weeks; WMFT: Wolf Motor Function Test

limbs of stroke survivors, the applied FV frequency ranged between 80 Hz and 120 Hz, with an amplitude between 0.01 mm and 1 mm. In the case of multiple sclerosis patients, the applied frequency and amplitude ranged from 50 Hz to 9000 Hz and 0.002 mm to 1 mm, respectively. Lastly, individuals with Parkinson's disease received FV within a frequency range of 100 Hz to 9000 Hz and an amplitude range of 0.002 mm to 0.5 mm.

The duration of the stimulus sessions varied between studies with a range of 5 minutes to 480 minutes. Lower limb stimulation sessions lasted between 15 minutes to 30 minutes for those recovering from a stroke, 10 minutes to 60 minutes for multiple sclerosis, and 60 minutes to 240 minutes for Parkinson's disease. In addition, the total therapy sessions ranged between 1 and 44 in all the RCTs.

Outcome Measure

The outcome measures assessing muscle tone included the MAS for evaluating spasticity. Kinematic evaluation involved measuring velocity, time or employing the 10-meter walk test. The outcome measure for motor functional test, i.e. Wolf Motor Function Test (WMFT), Jebsen-Taylor Hand Function Test (JTT), Box and block test (BBT), and Nine Hole Peg Test (NHPT) (Salter et al. 2013; Santisteban et al. 2016).

In order to enhance comparability among the included studies, the results presented in the forest plot were categorised into two distinct groups based on the timing of assessment. One forest plot displayed the results of studies assessed within a week after the treatment, while the other forest plot showcased the results of studies assessed over a week after the treatment.

Effectiveness of FV Treatments on Upper Limb - Muscle tone

Figure 3(a) compared the results of upper limb spasticity between the intervention and control groups in stroke patients, focusing on elbow (n=7) (Annino et al. 2019; Calabrò et al. 2017; Casale et al. 2014; Celletti et al. 2017; Costantino et al. 2017; Marconi et al. 2011; Noma et al. 2012), shoulder (n=2) (Calabrò et al. 2017; Costantino et al. 2017), and wrist (n=4) (Cordo et al. 2022; Costantino et al. 2017; Marconi et al. 2011; Noma et

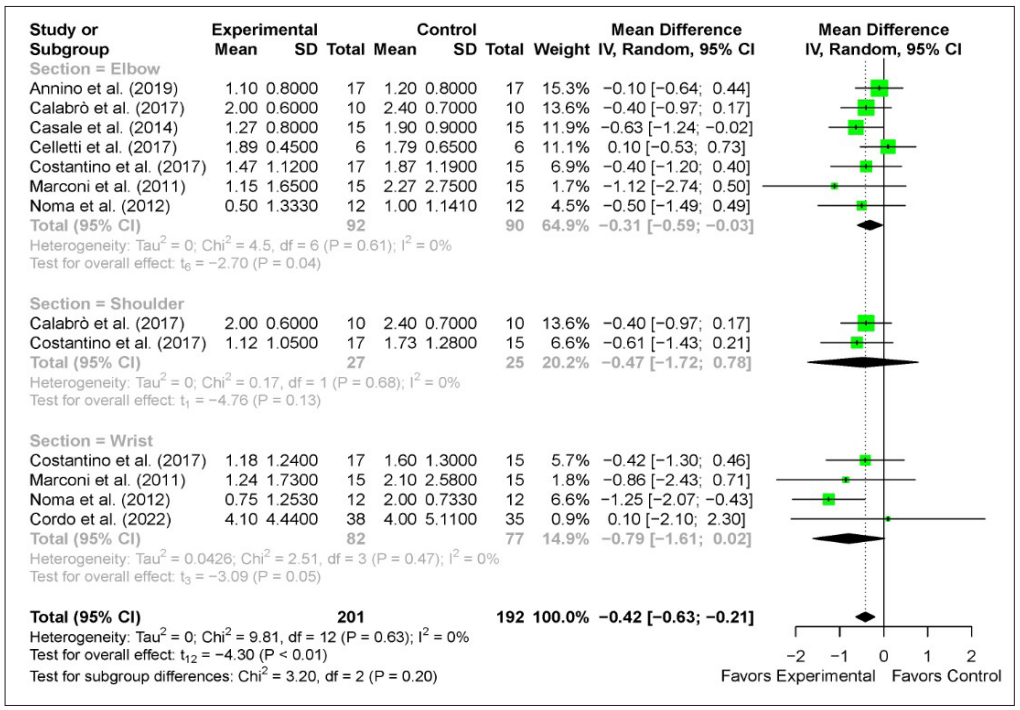

FIGURE 3(a): Forest plots of the assessment of upper limbs muscle tone (spasticity) in stroke populations using MAS. The assessments were conducted within a week after treatment

al. 2012) MAS scores within a week after the treatment. The FV treatment significantly reduced elbow spasticity when compared to the control group (MD = -0.31, 95% CI -0.59 to -0.03, I^2 = 0%). However, no significant differences were observed in shoulder (MD = -0.47, 95% CI -1.72 to 0.78, I^2 = 0%) and wrist (MD = -0.79, 95% CI -1.61 to 0.02, I^2 = 0%) spasticity reduction. Overall, FV treatment significantly decreased spasticity in stroke patients when assessed within a week after the treatment in comparison to the control group (MD = -0.42, 95% CI -0.63 to -0.21, I^2 = 0%).

Figure 3(b) depicted MAS scores for shoulder, elbow, and wrist spasticity in stroke patients were assessed over a week after FV application. No significant difference was found between FV therapy and control groups in terms of spasticity reduction, with MD values of -0.14 (95% CI -1.32 to 1.05, I^2 = 0%),

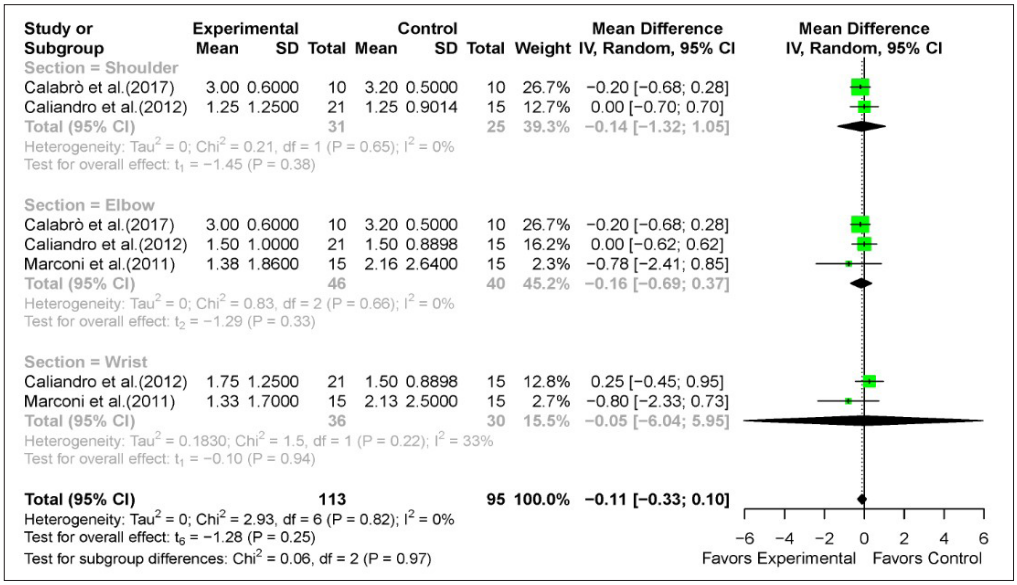

FIGURE 3(b): Forest plots of the assessment of upper limbs muscle tone (spasticity) in stroke populations using MAS. The assessments were conducted over a week after treatment

-0.16 (95% CI -0.69 to 0.37, I^2 = 0%), and -0.05 (95% CI -6.04 to 5.95, I^2 = 33%) for shoulder, elbow, and wrist, respectively. Figure 3(c) displayed the results of the sensitivity analysis, addressing the moderate heterogeneity observed in MAS wrist scores (I^2 = 33%). Upon excluding Marconi et al. (2011), whose assessments were conducted after two weeks instead of one month, no significant difference was found between FV treatment and control groups in upper limb spasticity reduction for stroke patients after one month of follow-up (MD = -0.08, 95% CI -0.30 to 0.14, I^2 = 0%).

- **Kinematic parameters**

Figure 4(a) illustrated three studies were

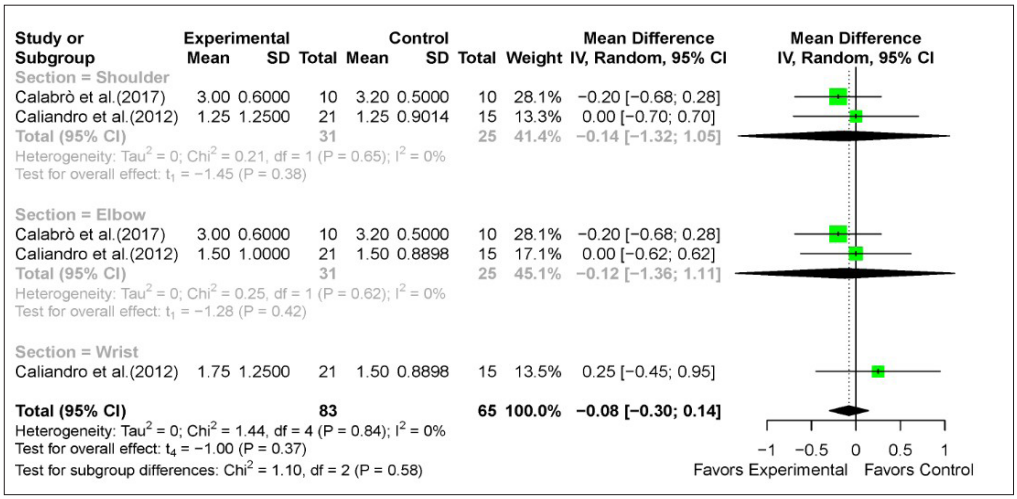

FIGURE 3(c): Sensitivity analysis of the forest plot for MAS on the upper limbs in stroke populations with assessment time over a week after treatment (Marconi et al. (2011) was removed)

included to examine the effectiveness of FV on upper limb kinematic parameters in stroke patients (Casale et al. 2014; Cordo et al. 2022; Tavernese et al. 2013). Within a week after treatment, no significant difference was observed in kinematic parameters improvement for stroke patients with upper limb deficits between the FV therapy and the control groups (SMD = -0.32, 95% CI –4.95 to 4.31, I^2 = 64%). Interestingly, FV treatment exhibited a more effective impact on kinematic parameters compared to the control group when assessed over a week after the treatment (SMD = -0.65, 95% CI: -1.27 to -0.04).

In Figure 4(b), a sensitivity analysis was conducted by excluding Cordo et al. (2022) due to high level of heterogeneity (I^2 = 64%) in upper limb kinematic parameters measured within a week after the treatment (Figure 4(a)). Given that the I^2 value is

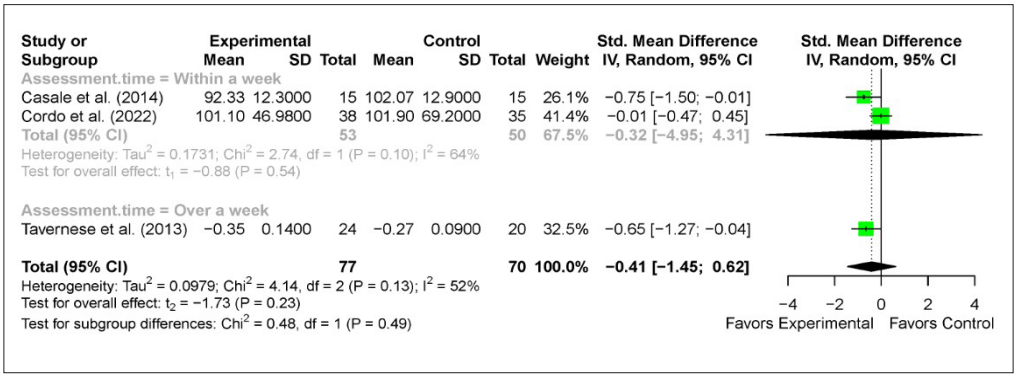

FIGURE 4(a): Forests plot of upper limb kinematic parameters in stroke populations, comparing assessments within a week and those conducted over a week after treatment

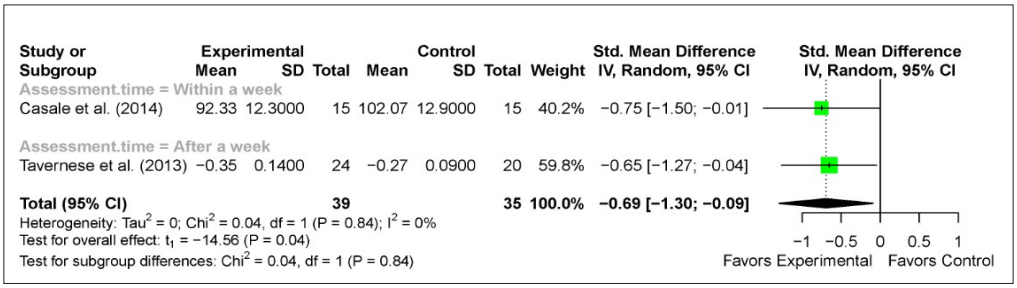

FIGURE 4(b): Sensitivity analysis of the forest plot for upper limb kinematics in stroke populations (Cordo et al. (2022) was excluded)

64% for the subgroup of assessments conducted within a week, it is likely that either Casale et al. (2014) or Cordo et al. (2022) work is responsible for the observed heterogeneity. When Casale et al. (2014) result was not considered, the overall heterogeneity rose from 52% to 63%. Excluding Cordo et al. (2022) study resulted in a decrease in overall heterogeneity from 52% to 0%. This result suggested that variations in stroke stages, such as acute and chronic, may lead to disparities in responsiveness to the treatments. Excluding the acute stroke studies had a significant influence on the overall interpretation, which limited the representativeness of the whole stroke populations. The subsequent results showed that FV treatment significantly enhanced upper limb kinematic parameters compared to the control group during the one-week assessment time (SMD -0.75, 95% CI -1.50 to -0.01) after the omission of Cordo et al. (2022).

- Motor function

In Figure 5, seven studies were examined for the effectiveness of FV application in enhancing the upper

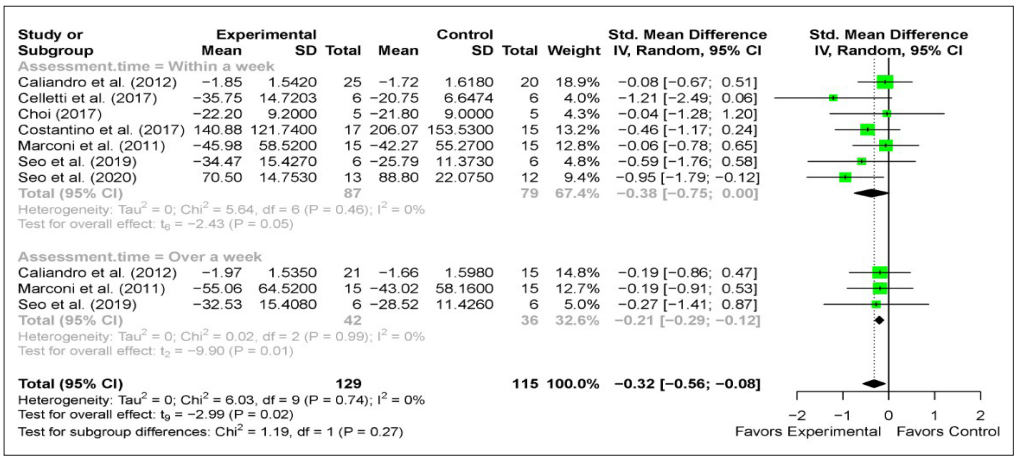

FIGURE 5: Forest plot of motor function for the upper limbs in stroke, comparing assessments within a week and those conducted over a week after treatment

limb motor function of stroke patients within a week after the treatment (Caliandro et al. 2012; Celletti et al. 2017; Choi 2017; Costantino et al. 2017; Marconi et al. 2011; Seo et al. 2020; Seo et al. 2019). The subgroup result indicated that FV treatment effectively enhance upper limb motor function in stroke patients (SMD = -0.38, 95% CI -0.75 to 0.00, I^2 = 0%). On the other hand, three studies demonstrated a significant improvement in upper limb motor function for stroke patients with FV therapy when assessed over a week after treatment (SMD -0.21, 95% CI -0.29 to -0.12, I^2 = 0%).

Effectiveness of FV on Lower Limb - Muscle tone

As shown in Figure 6, only two studies assessed the effectiveness of FV therapy in reducing spasticity in lower limb muscles of multiple sclerosis patients

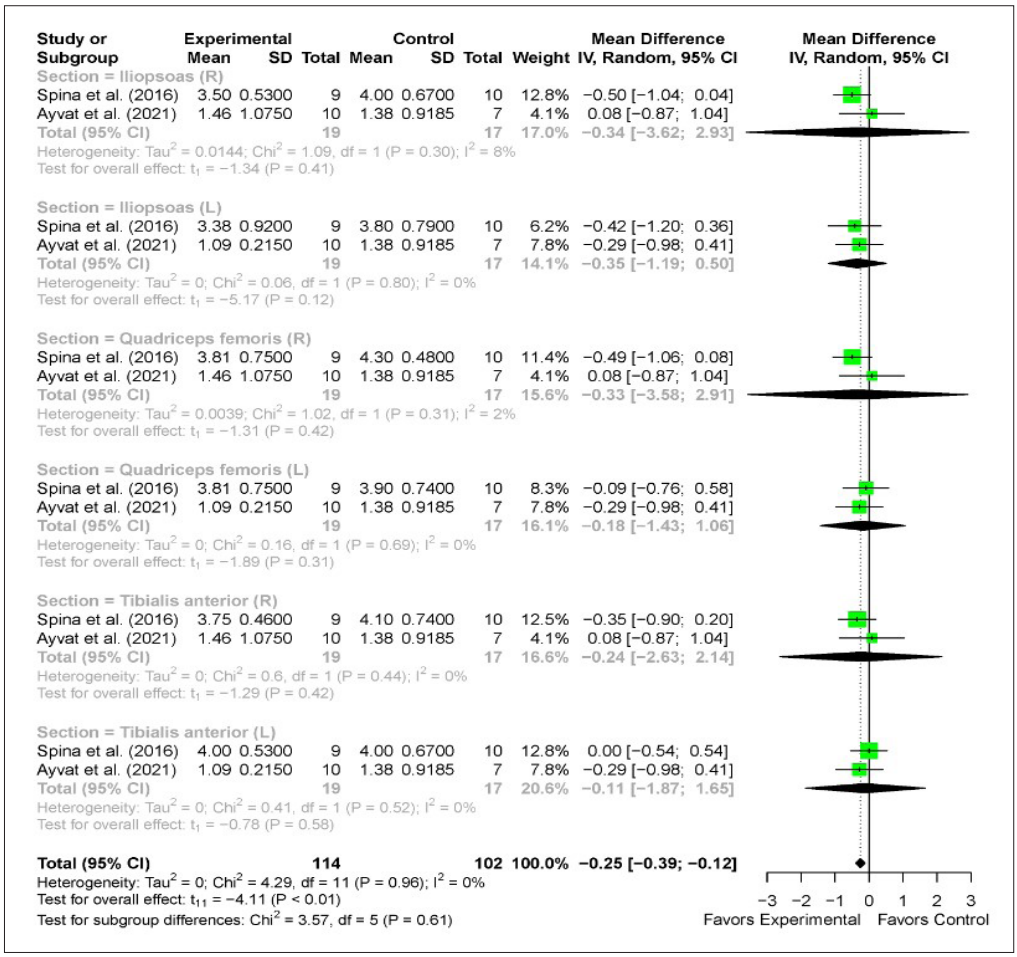

FIGURE 6: Forest plot of muscle tone (spasticity) in the lower limbs of individuals with multiple sclerosis, assessed using the MAS within a week after treatment

(Ayvat et al. 2021; Spina et al. 2016). No significant difference was observed in MAS scores for the iliopsoas, quadriceps femoris, or tibialis anterior muscles between the FV treatment and control group. The SMD values for the right limb were -0.34 (95% CI -3.62 to 2.93, I^2 = 8%) for iliopsoas, -0.33 (95% CI -3.58 to 2.91, I^2 = 2%) for quadriceps femoris and -0.24 (95% CI –2.63 to 2.14, I^2 = 0%) for tibialis anterior. On the left limb, the SMD values for iliopsoas, quadriceps femoris, and tibialis anterior were -0.35 (95% CI -1.19 to 0.50, I^2 = 0%), -0.18 (95% CI -1.43 to 1.06, I^2 = 0%) and -0.11 (95% CI -1.87 to 1.65, I^2 = 0%), respectively.

- **Kinematic parameters**

In Figure 7(a), the effectiveness of FV therapy in enhancing lower limb kinematic parameters within a week after treatment was highlighted for

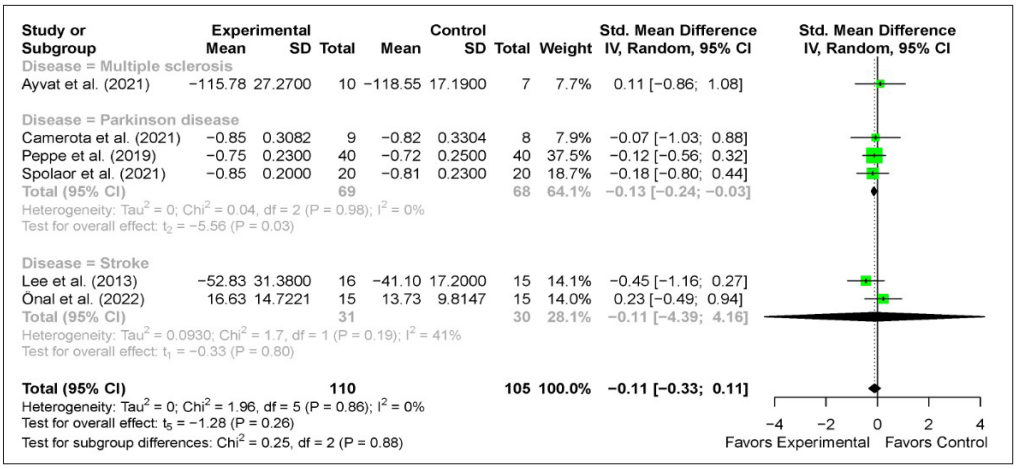

FIGURE 7(a): Forest plot of lower limbs kinematic parameters in individuals with stroke, Parkinson's disease and multiple sclerosis. The assessment was conducted within a week after treatment

individuals with stroke, multiple sclerosis, and Parkinson's disease. For multiple sclerosis populations, only a single study was available (Ayvat et al. 2021), showing no significant difference in kinematic parameters between the FV treatment and control groups (SMD = 0.11, 95 % CI -0.86 to 1.08). Furthermore, three studies assessed lower limb kinematic parameters in individuals with Parkinson's disease (Camerota et al. 2016; Peppe et al. 2019; Spolaor et al. 2020). The FV treatment significantly improved kinematic parameters compared to the control group (SMD = -0.13, 95% CI = -0.24 to -0.03, I^2 = 0%). Conversely, two studies examining lower limb kinematic parameters in stroke populations found no significant improvement with FV therapy (Lee et al. 2013; Önal et al. 2022) (SMD = -0.11, 95% CI -4.39 to 4.16, I^2 = 41%).

Figure 7(b) demonstrated the sensitivity analysis conducted by excluding Önal et al. (Önal et al. 2022) due to the moderate heterogeneity observed in the stroke subgroup (I^2 =

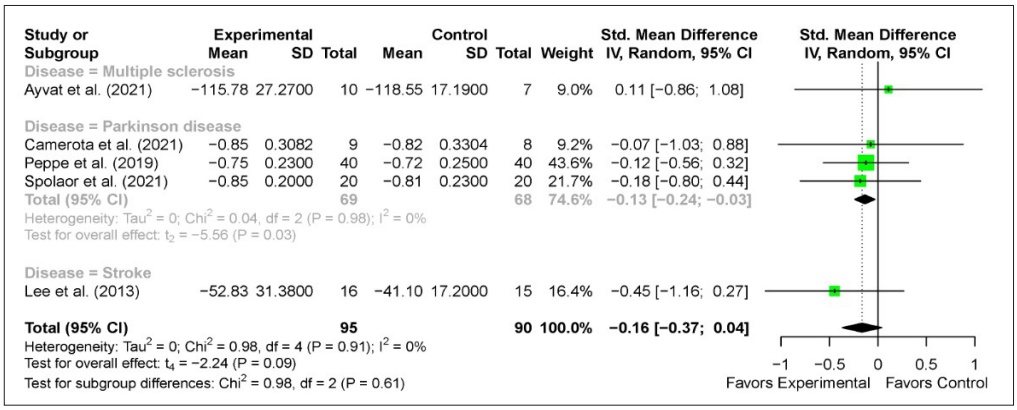

FIGURE 7(b): Sensitivity analysis of the forest plot for lower limb kinematic parameters in stroke, Parkinson's disease andmultiple sclerosis with an assessment time within a week after treatment (Önal et al. (2022) excluded)

41%) from Figure 7(a). It was believed that the heterogeneity originated from the non-homogenous baseline population. The revised SMD value for stroke patients changed from SMD = -0.11 (95% CI -4.39 to 4.16, I^2 = 41%) to -0.45 (95% CI -1.16 to 0.27), indicating no significant difference in the improvement of lower limb kinematics parameters between the treatment group and control group within a week after treatment for stroke populations.

Figure 7(c) compared lower limb kinematic parameters between the FV treatment and control groups for individuals with stroke and Parkinson's disease evaluated over a week after treatment. Only one study reported the lower limb kinematic parameters for stroke (Paoloni et al. 2010) and Parkinson's disease populations (Camerota et al. 2016). Over a week after treatment, no significant difference was observed between the FV group and the control group in term of kinematics parameters improvement. The SMD value for stroke was -0.39 (95% CI -0.99 to 0.20) and for Parkinson's disease was 0.38 (95% CI -0.58 to 1.35).

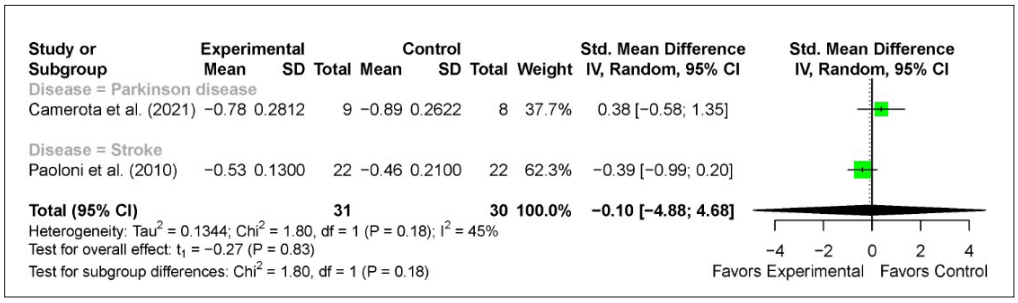

FIGURE 7(c): Forest plot of lower limbs kinematic parameters in individuals with stroke, Parkinson's disease and multiple sclerosis. The assessment was conducted over a week after treatment

Meta Regression

In Table 3, meta-regression analysis was conducted for MAS values related to elbow spasticity and upper limb motor function outcomes assessed within a week after treatment among stroke patients. Only outcomes reported in more than five studies were included. The results showed that covariant frequency, amplitude, and duration of stimulus sessions, as well as total therapy sessions did not significant impact the effect size of elbow spasticity. However, the covariance of total therapy sessions had a significant effect on the effect size of motor function in stroke patients with upper limb impairment (p= 0.0423). Furthermore, a negative correlation was observed between the total number of therapy sessions and the motor function of upper limbs. With an increase in the total number of therapy sessions, FV treatment exhibited greater benefits in terms of motor function improvement compared to the control group.

DISCUSSION

This systematic review analysed a total of 21 RCTs involving 660 patients. A total of 13 articles were dedicated to investigating the effects of FV on upper limb function, while eight articles focused on lower limb function. This study investigated the effects of FV treatment on individuals with upper limb impairment resulting from neurological disorders. It assessed muscle tone, kinematic parameters, and motor functions within and over a week after the treatment. Notably, all the studies examining the effects of FV on upper limbs were exclusively conducted in stroke populations. Surprisingly, no studies were found that explored the effects of FV on upper limb impairment among individuals with Parkinson's disease and multiple sclerosis.

In the evaluation of muscle tone, Figure 3(a) showed a statistically significant overall effect of FV treatment in reducing upper limb spasticity within a week after the

TABLE 3: Univariant meta-regression

Outcome measures	Var	Coef	SE	95% Lower	95% Upper	t	p
MAS (elbow) Assessment time within 1 week	Freq	-0.0009	0.0017	-0.0052	0.0034	-0.5361	0.6149
	Amp	-0.0571	0.1554	-0.4565	0.3422	-0.3678	0.7281
	DSS	-0.0039	0.0063	-0.0200	0.0122	-0.6245	0.5597
	TTS	0.0035	0.0100	-0.0223	0.0294	0.3515	0.7396
Motor function Assessment time within 1 week	Freq	-0.0016	0.0008	-0.0035	0.0004	-2.0798	0.0921
	Amp	0.0520	0.2493	-0.5889	0.6929	0.2086	0.8430
	DSS	-0.0016	0.0008	-0.0037	0.0006	-1.8746	0.1197
	TTS	-0.0323	0.0119	-0.0630	-0.0017	-2.7101	0.0423*

Amp: Amplitude; Coef: Coefficient; DDS: Duration of stimulation sessions; Freq: Frequency; SE: Standard error; TTS: Total therapy sessions; Var: Variables
*p ≤ 0.05.

treatment in stroke populations. This effect showed a small effect size (MD = -0.42, P<0.01) compared to the control group. The results from this study were consistent with studies by Alashram et al. (2019) and Avvantaggiato et al. (2021), suggesting that FV treatment might relieve spasticity in stroke populations. Figures 3(b) and (c) did not reveal statistically significant results (P>0.05) for the impact of FV treatment on reducing upper limb spasticity over a week after the treatment when compared to the control group. This finding aligned with Marconi et al.'s (2011) observations, where the benefits of FV persisted for at least two weeks but became undetectable with a longer follow-up period of one month (Calabrò et al. 2017; Caliandro et al. 2012).

Regarding kinematic parameters, Figure 4(b) depicted a statistical improvement in the kinematic parameters for stroke populations, showing an SMD value of -0.75 with a 95% CI ranging from -1.50 to -0.01 for assessments conducted within a week after treatment. Additionally, it showed an SMD value of -0.65 with a 95% CI ranging from -1.27 to -0.04 for assessments conducted over a week after the treatment. Regarding motor functions, Figure 5 revealed a statistically significant effect of FV treatment in enhancing motor function within the stroke population, displaying a small effect size for assessments conducted within (SMD = -0.38, P = 0.05) and over a week (SMD = -0.21, P = 0.01) after the treatment. The results also confirmed the finding of Mortaza et al. (2019), demonstrating that FV administered to the upper limb of stroke populations has a moderate effect size on kinematic parameters and a small effect size on improving upper limb motor function.

From the reported results, FV treatment has the potential to enhance muscle tone, kinematic parameters, and motor function in the upper limbs of stroke populations. The results of this study aligned with the research conducted by Hagbarth & Eklund (1968) suggesting that vibration has the potential to facilitate muscle contraction in individuals with weakened muscles, counteract spastic resistance in antagonistic muscles, and contribute to motor recovery. Furthermore, this study observed that the effect of FV treatment on reducing spasticity was insignificant when assessments were conducted over a week following treatment. At the same time, it had a notable impact on kinematic parameters and motor function. As highlighted in previous studies, the implementation of FV treatment is recommended for stroke rehabilitation. This is because the FV treatment has been observed to improve blood flow in the affected hemisphere, attributed to sensory input reaching the primary sensory cortex and primary motor cortex through Ia fiber afferents, thus promoting motor and functional recovery through intrinsic plasticity-related mechanisms (Toscano et al. 2020). According to Marconi et al. (2011) FV treatment can reduce abnormalities in corticospinal excitability and intracortical inhibitory systems among chronic post-stroke patients. Rocchi et al. (2018) discovered

that FV could induce long-term depression-like plasticity in specific spinal cord circuits depending on the vibrated muscle.

This study also examined the effect of FV treatment on lower limb muscle tone and kinematic parameters in individuals with neurological disorders. The examination related to lower limbs encompassed individuals afflicted with stroke, Parkinson's disease and multiple sclerosis. However, the assessment of muscle tone in lower limbs was confined to individuals specifically diagnosed with multiple sclerosis.

Regarding muscle tone, Figure 6 indicated that FV treatment did not exhibit a significant difference from the control group in reducing lower limb spasticity across each muscle group within the multiple sclerosis population. No reported data was available for follow-up assessments, such as lower limb spasticity evaluation conducted over a week after the treatment. The findings of this study were consistent with Etoom et al. (2018), who similarly reported no effect of FV therapy on reducing spasticity in multiple sclerosis populations. However, this contrasts with the study conducted by Paoloni et al. (2013), which suggested that FV treatment might indeed decrease muscle tone in the multiple sclerosis population.

In terms of kinematic parameters, Figure 7(a) presented the effect of FV treatment within a week after treatment on individuals with multiple sclerosis (SMD = 0.11; 95% CI -0.86 to 1.08) and stroke (SMD = -0.45, 95% CI -1.16 to 0.27) displayed no statistical difference from the control group. This study's outcomes differed from the evidence presented by Spina et al. (2016), who demonstrated a significant improvement in step length and a reduction in double support time in multiple sclerosis populations. Their findings suggested that multiple sclerosis patients exhibited a faster walking velocity and cadence, taking longer steps within a shorter time interval (Spina et al. 2016). The limited number of studies evaluating the effects of FV on multiple sclerosis populations might contribute to the lack of significant findings in this group. Recent research by Yin et al. (2022) investigated the effects of FV treatment on rats and discovered its potential for stimulating axonal regeneration and remyelination. It is reported that myelin repair can impact motor performance by improving the efficacy of communication between the brain and the body.

The impact of FV treatment on improving kinematic parameters in individuals with Parkinson's disease exhibited a significant difference (SMD = -0.13, P = 0.03) compared to the control group within a week after the treatment. The use of FV is anticipated to enhance the quantity of dopaminergic neurons in the substantia nigra, as well as boost dopamine levels and the content of brain-derived neurotrophic factor in the striatum. The afore-mentioned effects were seen in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of Parkinson's disease (Zhao et al. 2014). Additionally, it has been found that the levels of dopamine in the striatum have an

important role in motivating and enhancing movement (Gepshtein et al. 2014). However, this effect was not significantly different (SMD = 0.38; 95% CI -0.58 to 1.35) when the assessment was conducted over a week after the treatment (Figure 7(c)). The current findings aligned with the existing studies (Camerota et al. 2016; Peppe et al. 2019; Spolaor et al. 2020), which also observed improvements in kinematic parameters. However, these studies noted a transient effect of FV on kinematic parameters in Parkinson's populations, suggesting that the improvements may be short-term rather than sustained.

FV treatment applied in Parkinson's disease involves the highest total number of therapy sessions, reaching up to 44 sessions. Additionally, the utilisation of a high frequency of 9000 Hz and a low amplitude of 0.002 mm in Parkinson's disease treatment distinguishes it from therapies administered for stroke and multiple sclerosis. These distinct variations in treatment parameters underscore the necessity for additional research to understand better the optimal application of FV concerning specific conditions and parameter adjustments. This study aimed to ascertain the impact of vibration parameters such as frequency, amplitude, duration of stimulus sessions, and total therapy sessions on the effect size of FV therapy concerning muscle tone, kinematic parameters, and motor function. The univariate meta-analysis results presented in Table 3 revealed that vibration parameters did not significantly influence the effect size of elbow spasticity. These findings aligned with those of Mortaza et al. (2019), who similarly reported a lack of significant effect of these variables on the primary outcome of functional movement. However, this review found that the total number of therapy sessions significantly affected the effect size in the outcome measures related to upper limb motor function. For instance, Cordo et al. (2009) documented substantial improvement in upper and lower limb motor function among chronic stroke populations after employing six months of Assisted Movement with Enhanced Sensation (AMES). In their study, the treatment protocol involved AMES for 30 minutes daily over a span of 6 months, totalling 180 sessions. The considerable number of repetitions of FV treatment in this context might have triggered a cumulative effect on motor recovery, contributing significantly to the substantial improvement observed. Repeating sessions over consecutive days maximises the consolidation of memory and long-term persistence of training-independent sensory learning (Viganò et al. 2023). The findings from Cordo et al.'s (2022) work underscore the importance of providing adequate therapy sessions to maximise the potential benefits of intervention, particularly in the context of motor function improvement among stroke populations.

Assessing the scientific evidence regarding the effectiveness of FV treatment posed challenges due to the considerable heterogeneity observed in the treatment protocols employed such as the region treated, vibration

parameters and the duration of the treatment. The diverse assessments to evaluate kinematic parameters and motor functions also contributed to the heterogeneity.

In the present study, multivariate meta-regression was not feasible due to the constrained number of studies for each covariate (Higgins et al. 2019; Ravishankar & Sreekumaran Nair 2015). In this review, only six to eight studies were examined due to the scarcity of available research. Encouraging a higher number of studies in this field is vital to facilitate more comprehensive meta-regression investigations. The correlation between covariates, such as the correlation between frequency and amplitude or amplitude and duration of the stimulus sessions, may also have an impact on the effect size. The imputation of the mean and SD of post-FV values based on baseline and change score represented another drawback in this study. The correlation coefficient was considered to be 0.5 in this analysis. Cochrane's handbook's formula for calculating the correlation coefficient should be considered to improve the accuracy of the imputation (Higgins et al. 2019).

CONCLUSION

The results indicate that the use of FV therapy has the potential to effectively reduce spasticity ($P<0.01$), improve kinematic parameters ($P = 0.04$), and enhance motor function ($P = 0.02$) in stroke populations with upper limb impairments. The application of FV therapy has demonstrated significant improvements in kinematic parameters ($P = 0.03$) among those diagnosed with Parkinson's disease and experiencing impairment in their lower limbs. The effect of the vibration on muscle tone in the upper limb for individuals with stroke, as well as the kinematic parameters in the upper and lower limbs for individuals with stroke and Parkinson's disease, was seen to last for a duration of one week but did not exhibit long-term sustainability. It is recommended to establish standardised protocols for FV interventions focused on various neurological disorders. It is essential to have larger sample sizes and varying durations of follow-up in order to accurately evaluate the long-term durability of the effects of FV.

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DISCLOSURE STATEMENT

The authors report no conflicts of interest.

REFERENCES

Alashram, A.R., Padua, E., Romagnoli, C., Annino, G. 2019. Effectiveness of focal muscle vibration on hemiplegic upper extremity spasticity in individuals with stroke: A systematic review. *NeuroRehabilitation* **45**(4): 471-81.

Alashram, A.R., Padua, E., Romagnoli, C., Raju, M., Annino, G. 2022. Clinical effectiveness of focal

muscle vibration on gait and postural stability in individuals with neurological disorders: A systematic review. *Physiother Res Int* **27**(3): e1945.

Aman, J.E., Elangovan, N., Yeh, I.L., Konczak, J. 2015. The effectiveness of proprioceptive training for improving motor function: A systematic review. *Front Hum Neurosci* **8**: 1075.

Annino, G., Alashram, A.R., Alghwiri, A.A., Romagnoli, C., Messina, G., Tancredi, V., Padua, E., Mercuri, N.B. 2019. Effect of segmental muscle vibration on upper extremity functional ability poststroke: A randomized controlled trial. *Medicine* **98**(7): e14444.

Avvantaggiato, C., Casale, R., Cinone, N., Facciorusso, S., Turitto, A., Stuppiello, L., Picelli, A., Ranieri, M., Intiso, D., Fiore, P., Ciritella, C., Santamato, A. 2021. Localized muscle vibration in the treatment of motor impairment and spasticity in post-stroke patients: A systematic review. *Eur J Phys Rehabil Med* **57** (1): 44-60.

Ayvat, F., Özçakar, L., Ayvat, E., Aksu Yildirim, S., Kilinc, M. 2021. Effects of low vs. high frequency local vibration on mild-moderate muscle spasticity: Ultrasonographical and functional evaluation in patients with multiple sclerosis. *Mult Scler Relat Disord* ***51***: 102930.

Calabrò, R.S., Naro, A., Russo, M., Milardi, D., Leo, A., Filoni, S., Trinchera, A., Bramanti, P. 2017. Is two better than one? Muscle vibration plus robotic rehabilitation to improve upper limb spasticity and function: A pilot randomized controlled trial. *PLoS One* **12**(10): e0185936.

Caliandro, P., Celletti, C., Padua, L., Minciotti, I., Russo, G., Granata, G., La Torre, G., Granieri, E., Camerota, F. 2012. Focal muscle vibration in the treatment of upper limb spasticity: A pilot randomized controlled trial in patients with chronic stroke. *Arch Phys Med Rehabil* **93**(9): 1656-61.

Camerota, F., Celletti, C., Suppa, A., Galli, M., Cimolin, V., Filippi, G.M., La Torre, G., Albertini, G., Stocchi, F., De Pandis, M.F. 2016. Focal muscle vibration improves gait in Parkinson's disease: A pilot randomized, controlled trial. *Mov Disord Clin Pract* **3**(6): 559-66.

Carlsson, H., Gard, G., Brogårdh, C. 2018. Upper-limb sensory impairments after stroke: Self-reported experiences of daily life and rehabilitation. *J Rehabil Med* **50**(1): 45-51.

Casale, R., Damiani, C., Maestri, R., Fundarò, C., Chimento, P., Foti, C. 2014. Localized 100 Hz vibration improves function and reduces upper limb spasticity: A double-blind controlled study. *Eur J Phys Rehabil Med* **50**(5): 495-504.

Celletti, C., Sinibaldi, E., Pierelli, F., Monari, G., Camerota, F. 2017. Focal muscle vibration and progressive modular rebalancing with neurokinetic facilitations in post-stroke recovery of upper limb. *Clin Ter* **168**(1): e33-e6.

Choi, W.H. 2017. Effects of repeated vibratory stimulation of wrist and elbow flexors on hand dexterity, strength, and sensory function in patients with chronic stroke: A pilot study. *J Phys Ther Sci* **29**(4): 605-8.

Cordo, P., Lutsep, H., Cordo, L., Wright, W. G., Cacciatore, T., Skoss, R. 2009. Assisted movement with enhanced sensation (AMES): Coupling motor and sensory to remediate motor deficits in chronic stroke patients. *Neurorehabil Neural Repair* **23**(1): 67-77.

Cordo, P., Wolf, S., Rymer, W.Z., Byl, N., Stanek, K., Hayes, J.R. 2022. Assisted movement with proprioceptive stimulation augments recovery from moderate-to-severe upper limb impairment during subacute stroke period: A randomized clinical trial. *Neurorehabil Neural Repair* **36**(3): 239-50.

Costantino, C., Galuppo, L., Romiti, D. 2017. Short-term effect of local muscle vibration treatment versus sham therapy on upper limb in chronic post-stroke patients: A randomized controlled trial. *Eur J Phys Rehabil Med* **53**(1): 32-40.

Dias, S., Welton, N.J., Sutton, A.J., Ades, A. 2014. NICE DSU technical support document 2: A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials. https://www.ncbi.nlm.nih.gov/books/NBK310366/ [25 June 2022].

Dincher, A., Schwarz, M., Wydra, G. 2019. Analysis of the effects of whole-body vibration in Parkinson disease–Systematic review and meta-analysis. *PM&R* **11**(6): 640-53.

Etoom, M., Khraiwesh, Y., Lena, F., Hawamdeh, M., Hawamdeh, Z., Centonze, D., Foti, C. 2018. Effectiveness of physiotherapy interventions on spasticity in people with multiple sclerosis: A systematic review and meta-analysis. *Am J Phys Med Rehabil* **97**(11): 793-807.

Feigin, V.L., Vos, T., Nichols, E., Owolabi, M. O., Carroll, W.M., Dichgans, M., Deuschl, G., Parmar, P., Brainin, M., Murray, C. 2020. The global burden of neurological disorders: Translating evidence into policy. *Lancet Neurol* **19**(3): 255-65.

Geissbühler, M., Hincapié, C.A., Aghlmandi, S., Zwahlen, M., Jüni, P., da Costa, B.R. 2021. Most published meta-regression analyses based on aggregate data suffer from methodological pitfalls: A meta-epidemiological study. *BMC Med Res Methodol* **21**(1): 123.

Gepshtein, S., Li, X., Snider, J., Plank, M., Lee, D., Poizner, H. 2014. Dopamine function and the efficiency of human movement. *J Cogn Neurosci* **26**(3): 645-57.

Gorst, T., Marsden, J., Freeman, J. 2019. Lower limb somatosensory discrimination is impaired

in people with Parkinson's disease: Novel assessment and associations with balance, gait, and falls. *Mov Disord Clin Pract* **6**(7): 593-600.

Hagbarth, K.E., Eklund, G. 1968. The effects of muscle vibration in spasticity, rigidity, and cerebellar disorders. *J Neurol Neurosurg Psychiatry* **31**(3): 207.

Higgins, J.P., Altman, D.G., Gøtzsche, P.C., Jüni, P., Moher, D., Oxman, A.D., Savovic, J., Schulz, K.F., Weeks, L., Sterne, J.A., Cochrane Bias Methods Group, Cochrane Statistical Methods Group. 2011. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 343: d5928.

Higgins, J.P., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J., Welch, V.A. 2019. *Cochrane handbook for systematic reviews of interventions*. New Jersey: John Wiley & Sons.

Jamali, A., Sadeghi-Demneh, E., Fereshtenajad, N., Hillier, S. 2017. Somatosensory impairment and its association with balance limitation in people with multiple sclerosis. *Gait Posture* **57**: 224-9.

Lee, S.W., Cho, K.H., Lee, W.H. 2013. Effect of a local vibration stimulus training programme on postural sway and gait in chronic stroke patients: A randomized controlled trial. *Clin Rehabil* **27**(10): 921-31.

Marconi, B., Filippi, G. M., Koch, G., Giacobbe, V., Pecchioli, C., Versace, V., Camerota, F., Saraceni, V.M., Caltagirone, C. 2011. Long-term effects on cortical excitability and motor recovery induced by repeated muscle vibration in chronic stroke patients. *Neurorehabil Neural Repair* **25**(1): 48-60.

McGlone, F., Reilly, D. 2010. The cutaneous sensory system. *Neurosci Biobehav Rev* **34**(2): 148-59.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., PRISMA Group 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* **6**(7): e1000097.

Mortaza, N., Abou-Setta, A.M., Zarychanski, R., Loewen, H., Rabbani, R., Glazebrook, C.M. 2019. Upper limb tendon/muscle vibration in persons with subacute and chronic stroke: A systematic review and meta-analysis. *Eur J Phys Rehabil Med* **55**(5): 558-69.

Noma, T., Matsumoto, S., Shimodozono, M., Etoh, S., Kawahira, K. 2012. Anti-spastic effects of the direct application of vibratory stimuli to the spastic muscles of hemiplegic limbs in post-stroke patients: A proof-of-principle study. *J Rehabil Med* **44**(4): 325-30.

Önal, B., Sertel, M., Karaca, G. 2022. Effect of plantar vibration on static and dynamic balance in stroke patients: A randomised controlled study. *Physiotherapy* **116**: 1-8.

Paoloni, M., Giovannelli, M., Mangone, M., Leonardi, L., Tavernese, E., Di Pangrazio, E., Bernetti, A., Santilli, V., Pozzilli, C. 2013. Does giving segmental muscle vibration alter the response to botulinum toxin injections in the treatment of spasticity in people with multiple sclerosis? A single-blind randomized controlled trial. *Clin Rehabil* **27**(9): 803-12.

Paoloni, M., Mangone, M., Scettri, P., Procaccianti, R., Cometa, A., Santilli, V. 2010. Segmental muscle vibration improves walking in chronic stroke patients with foot drop: A randomized controlled trial. *Neurorehabil Neural Repair* **24**(3): 254-62.

Peppe, A., Paravati, S., Baldassarre, M.G., Bakdounes, L., Spolaor, F., Guiotto, A., Pavan, D., Sawacha, Z., Bottino, S., Clerici, D., Cau, N., Mauro, A., Albani, G., Avenali, M., Sandrini, G., Tassorelli, C., Volpe, D. 2019. Proprioceptive focal stimulation (Equistasi®) may improve the quality of gait in middle-moderate Parkinson's disease patients. Double-blind, double-dummy, randomized, crossover, Italian multicentric study. *Front Neurol* **10**: 998.

Ravishankar, N., Sreekumaran Nair, N. 2015. Meta-regression: Adjusting covariates during meta-analysis. *Int J of Adv Res* **3**(2): 899-904.

Rocchi, L., Suppa, A., Leodori, G., Celletti, C., Camerota, F., Rothwell, J., Berardelli, A. 2018. Plasticity induced in the human spinal cord by focal muscle vibration. *Front Neurol* **9**: 935.

Roll, J., Vedel, J., Ribot, E. 1989. Alteration of proprioceptive messages induced by tendon vibration in man: A microneurographic study. *Exp Brain Res* **76**(1): 213-22.

Salter, K., Campbell, N., Richardson, M., Mehta, S., Jutai, J., Zettler, L., Moses, M., McClure, A., Mays, R., Foley, N., Teasell, R 2013. Outcome measures in stroke rehabilitation. Evidence Reviews. https://www.ebrsr.com/evidence-review/20-outcome-measures-stroke-rehabilitation [27 June 2022].

Santisteban, L., Térémetz, M., Bleton, J.P., Baron, J.C., Maier, M.A., Lindberg, P.G. 2016. Upper limb outcome measures used in stroke rehabilitation studies: A systematic literature review. *PLoS One* **11**(5): e0154792.

Schwarzer, G., Schwarzer, M. G. 2012. Package 'meta'. *The R foundation for statistical computing* **9**: 27.

Seo, N.J., Enders, L.R., Fortune, A., Cain, S., Vatinno, A.A., Schuster, E., Ramakrishnan, V., Feng, W. 2020. Phase I safety trial: Extended daily peripheral sensory stimulation using a wrist-worn vibrator in stroke survivors. *Transl Stroke Res* **11**(2): 204-13.

Seo, N.J., Woodbury, M.L., Bonilha, L., Ramakrishnan, V., Kautz, S.A., Downey, R.J., Dellenbach, B. H.S., Lauer, A.W., Roark, C.M., Landers, L.E., Phillips, S.K., Vatinno, A.A. 2019. TheraBracelet stimulation during task-practice therapy to improve upper extremity function after stroke:

A pilot randomized controlled study. *Phys Ther* **99**(3): 319-28.

Spina, E., Carotenuto, A., Aceto, M.G., Cerillo, I., Silvestre, F., Arace, F., Paone, P., Orefice, G., Iodice, R. 2016. The effects of mechanical focal vibration on walking impairment in multiple sclerosis patients: A randomized, double-blinded vs placebo study. *Restor Neurol Neurosci* **34**(5): 869-76.

Spolaor, F., Romanato, M., Guiotto, A., Peppe, A., Volpe, D., Sawacha, Z. 2020. Changes in muscular and postural control after proprioceptive focal stimulation with Equistasi® device in middle-moderate Parkinson's disease. *Gait Posture* **81**: 350-1.

Tavernese, E., Paoloni, M., Mangone, M., Mandic, V., Sale, P., Franceschini, M., Santilli, V. 2013. Segmental muscle vibration improves reaching movement in patients with chronic stroke. A randomized controlled trial. *NeuroRehabilitation* **32**(3): 591-9.

Toscano, M., Ricci, M., Celletti, C., Paoloni, M., Ruggiero, M., Viganò, A., Jannini, T. B., Altarocca, A., Liberatore, M., Camerota, F., Di Piero, V. 2020. Motor recovery after stroke: From a vespa scooter ride over the roman sampietrini to focal muscle vibration (FMV) treatment. A 99mTc-HMPAO SPECT and neurophysiological case study. *Front Neurol* **11:** 567833.

Veroniki, A.A., Jackson, D., Viechtbauer, W., Bender, R., Bowden, J., Knapp, G., Kuss, O., Higgins, J.P., Langan, D., Salanti, G. 2016. Methods to estimate the between-study variance and its uncertainty in meta-analysis. *Res Synth Methods* **7**(1): 55-79.

Viganò, A., Celletti, C., Giuliani, G., Jannini, T. B., Marenco, F., Maestrini, I., Zumpano, R., Vicenzini, E., Altieri, M., Camerota, F., Di Piero, V. 2023. Focal muscle vibration (fMV) for post-stroke motor recovery: Multisite neuroplasticity induction, timing of intervention, clinical approaches, and prospects from a narrative review. *Vibration* **6**(3): 645-58.

Yin, L., An, Y., Chen, X., Yan, H. X., Zhang, T., Lu, X.G., Yan, J.T. 2022. Local vibration therapy promotes the recovery of nerve function in rats with sciatic nerve injury. *J Integr Med* **20**(3): 265-73.

Zhao, L., He, L., Huang, S., Gong, L., Lv, Y., Qian, Z. 2014. Protection of dopamine neurons by vibration training and up-regulation of brain-derived neurotrophic factor in a MPTP mouse model of Parkinson's disease. *Physiol Res* **63**(5): 649-57.