



Promoting post-stroke recovery through focal or whole body vibration: criticisms and prospects from a narrative review

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Abstract

Objective Several focal muscle vibration (fMV) and whole body vibration (WBV) protocols have been designed to promote brain reorganization processes in patients with stroke. However, whether fMV and WBV should be considered helpful tools to promote post-stroke recovery remains still largely unclear.

Methods We here achieve a comprehensive review of the application of fMV and WBV to promote brain reorganization processes in patients with stroke. By first discussing the putative physiological basis of fMV and WBV and then examining previous observations achieved in recent randomized controlled trials (RCT) in patients with stroke, we critically discuss possible strength and limitations of the currently available data.

Results We provide the first systematic assessment of fMV studies demonstrating some improvement in upper and lower limb functions, in patients with chronic stroke. We also confirm and expand previous considerations about the rather limited rationale for the application of current WBV protocols in patients with chronic stroke.

Conclusion Based on available information, we propose new recommendations for optimal stimulation parameters and strategies for recruitment of specific stroke populations that would more likely benefit from future fMV or WBV application, in terms of speed and amount of post-stroke functional recovery.

Keywords Chronic stroke · Focal muscle vibration · Whole body vibration · Neurorehabilitation · Post-stroke recovery

Introduction

Stroke is the second leading cause of death after ischemic heart disease and the third leading cause of disability-adjusted life years (DALY) worldwide [1]. Despite the significant decline of stroke mortality rates due to the introduction of new acute stroke therapies and innovative prevention

strategies, the global burden of stroke has progressively increased [2]. Stroke prevalence in 2013 has almost doubled that in 1990, and the absolute number of people affected by stroke has substantially increased worldwide over the same time period, suggesting that global stroke burden continues to increase [3]. A current relevant issue concerns the design of new pharmacological and non-pharmacological strategies to promote post-stroke recovery [4–6]. Among non-pharmacological techniques possibly helpful to promote post-stroke functional recovery, increasing attention has recently been paid to protocols based on muscle vibration.

Muscle vibration was first used in 1892 when Jean-Martin Charcot, who was the most celebrated and powerful clinical neurologist of the nineteenth century, delivered a lecture on the topic of vibratory therapy in neurologic disorders: “Vibration therapeutics: Application of rapid and continuous vibrations to the treatment of certain nervous system disorders” [7]. In his lecture, Charcot summarized the historical background of vibration therapy and then focused on his own clinical experience in patients with Parkinson’s disease (PD).

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Charcot died 1 year later, and although Gilles de la Tourette continued to study vibration therapy, Charcot's observations were largely forgotten [8]. About a century later, Hagbarth and Eklund (1968) studied the motor effects of fMV in patients with various types of central motor disorders, in particular, those associated with spasticity and rigidity [9]. In spastic patients, Hagbarth and Eklund observed that vibration potentiated or reduced voluntary power (and range of movement) depending upon whether the subject tried to contract the vibrated muscle or its antagonist [9]. Later, Bishop studied the neurophysiologic characteristics of the vibratory stimulation and possible associated clinical applications and found a beneficial effect induced by muscle vibration in spasticity disorders (i.e., reduced the strength of spasticity and potentiated weak voluntary movement) [10]. More recently, a growing number of researchers have tested various muscle vibration protocols including focal muscle vibration (fMV) and whole body vibration (WBV) aimed to elicit active modulation of sensory afferent inputs to the central nervous system [11]. Converging evidence from experimental studies raises the hypothesis that fMV and WBV might induce brain reorganization sensorimotor processes in healthy humans [12–20]. Several researchers have also investigated the possible beneficial effect of various fMV and WBV protocols in patients with stroke in order to promote functional recovery through brain reorganization sensorimotor processes. However, whether fMV or WBV protocols can be considered new strategies possibly helpful for promoting post-stroke recovery remains largely unclear.

Here, a workgroup of researchers expert in the field has critically reviewed and discussed 10 years of randomized controlled studies (RCT) investigating the effect of fMV and WBV protocols, in patients with stroke. We focused our attention on the fMV and WBV techniques because these vibration protocols share putative physiological mechanisms possibly able to promote beneficial brain reorganization sensorimotor processes, in patients with stroke. The effect of WBV in patients with chronic stroke has been discussed only in a single previous review [21] thus covering only in part the topic. So far, none have reviewed systematically WBV and fMV studies in patients with chronic stroke in order to clarify the real impact of these vibration protocols on post-stroke motor recovery. Given the significant amount of recent research in the field and the heterogeneity of previous methodologies used and findings reported, the need for a comprehensive and updated review is relevant. We have first summarized the technical aspects and physiological basis of fMV and WBV and then critically re-examined the main methodological aspects and findings achieved in the previous RCT using fMV and WBV in patients with stroke.

Literature research strategy and criteria

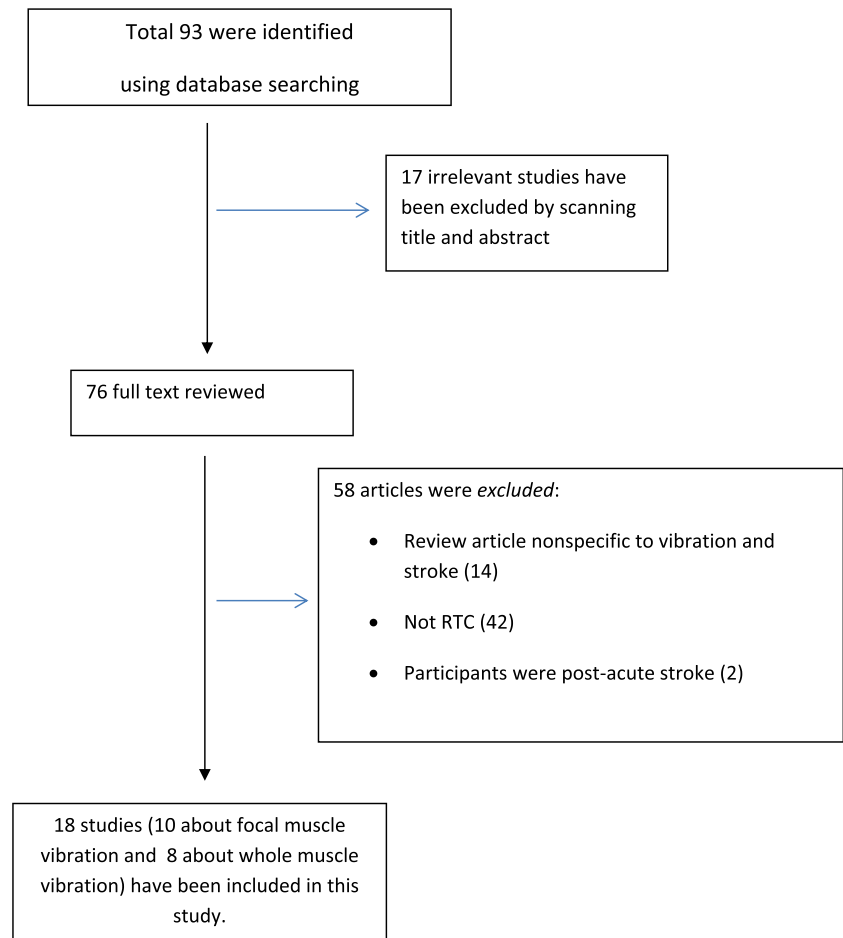
The literature search was performed by means of the following databases: MEDLINE, Scopus PubMed, Web of Science,

EMBASE and the Cochrane Library. Literature criteria included the following terms: “stroke” OR “chronic stroke” AND “vibration,” “stroke” OR “chronic stroke” AND “training,” “stroke” OR “chronic stroke” AND “rehabilitation,” “post-stroke recovery” AND “vibration.” Studies considered for eligibility were only RCTs published from January 2007 to July 2018 implying fMV and WBV for the treatment of patients with chronic stroke. The reference lists of retrieved articles were also manually searched for additional studies. Furthermore, reviews, reports, and unpublished articles were not considered in this study (Fig. 1). Owing to the heterogeneity in methodology used and outcome measures reported in previous studies, we organized a narrative review according to the International Narrative Systematic assessment, INSA tool [22].

Section 1

Focal muscle vibration

Vibration is a mechanical oscillation, i.e., a periodic alternation of force, acceleration over time. During vibration, energy is transferred from an actuator (i.e., the vibration device) to a resonator (i.e., the human body, or parts of it). fMV is commonly achieved using a mechanical stimulation placed over the target muscle using a transducer connected to a control unit; the device and the control unit are able to generate a vibratory stimulus characterized by specific parameters (Fig. 2). The two main parameters to be selected for fMV include amplitude and frequency of vibration. The extent of the oscillatory movement (peak-to-peak displacement in mm) determines the amplitude of fMV, while the repetition rate of the oscillation cycles denotes the frequency of fMV. According to the specific parameters used (e.g., amplitude and frequency) and site of application, fMV can co-activate a mixture of cutaneous mechanoreceptors such as Pacinian and Meissner's corpuscles (rapidly adapting receptors) and Ruffini corpuscle and Merkel's disk [23–25]. In addition, Golgi tendon organs are also responsive to fMV even though this effect likely occurs during muscle contraction, reflecting the threshold for Ib afferents activation [26–28]. However, when fMV is applied over the muscle belly or its tendon, muscle spindle primary endings (Ia fibers) are thought to be the most responsive receptors to fMV [29–31]. Each cycle of the vibratory stimulus is thought to stretch the muscle and selectively excite the primary endings of the muscle spindles causing them to fire once for each cycle of vibration [32]. Most authors seem to agree that the optimum amplitude of the vibratory stimulus is less than 0.5 mm because a greater value tends to lead to an overflow of the stimulus into the surrounding muscles and bone [33]. Hence, fMV given at 0.2–0.5 mm amplitude over a relaxed muscle is a powerful and selective stimulus of activity in Ia afferents by entraining

Fig. 1 Literature search and study selection

the discharge rate of primary muscle spindle endings [25, 30, 34]. fMV at amplitudes lower than 0.5 mm is commonly used also to avoid the Tonic vibration reflex (TVR) first described by Eklund and Hagbarth [35, 36]. In early physiological studies in healthy subjects, Bishop observed that increases in the amplitude of vibration increases the strength of the TVR [10] which has been described as a variant of the classic myotatic reflex in response to a vibratory stimulus of low amplitude (< 3 mm) at a frequency of about of 100 Hz [37]. During fMV, vibration applied at amplitudes < 0.5 mm is currently used to avoid the TVR which may prevent the voluntary tuning of muscle activation, owing to the involuntary muscle contraction. Concerning the frequency of fMV, it is known that the Ia afferent firing rate is entrained linearly with vibration frequencies up to 70–80 Hz, followed by a subharmonic increase at higher frequencies, with sharp falls often observed at frequencies between 150 and 200 Hz [25, 30]. Majority of studies seem to indicate that an increase in the frequency of the vibratory stimulus is accompanied by an increase in the strength of the TVR [29, 38, 39]. Accordingly, most of the authors have used a frequency around 100 Hz and found this to be satisfactory for most applications [34, 40]. During fMV applications, sometimes subjects kept a steady contraction of the target

muscle at 5% of the maximal force, under visual EMG feedback. Voluntary contraction is used because it has been shown that voluntary muscle activity increases response to fMV, most likely through fusimotor co-activation and subsequent increase in spindle discharge [26].

FMV in chronic stroke

Several studies have investigated the clinical application of fMV in patients with chronic stroke in order to promote post-stroke recovery [41]. The four basic indications for focal vibration in neurorehabilitation, regardless of the neurological pathology in question, are (1) to reduce spasticity, (2) to facilitate muscle contraction of functional activity, (3) to stimulate the proprioceptive system to obtain an efficient motor control in functional activities, and (4) to provide a proprioceptive training and restore sensorimotor organization in movement disorders [41].

The demographic data and clinical features of participants are shown in detail in Table 1. A detailed description of purposes, technical aspects of fMV, outcome measures, the timing of follow-up, and finally main results achieved by each of the studies here reviewed are shown in Table 2. The mean age of the patients examined is similar among studies. With



Fig. 2 A representative instrument for the application of focal muscle vibration

the exception of the study of Marconi et al. [15] and Conrad et al. [43], in the remaining studies, the male/female ratio is slightly unbalanced in favor of males [42, 44–50]. The time

interval between stroke onset and fMV application varied significantly among studies since the four studies enrolled patients at a 4–6-month period from the stroke [42, 45–47], whereas the remaining studies applied fMV at least 12 months following stroke. Only four studies have provided information concerning the description of type (ischemic or hemorrhagic stroke), localization (cortical or subcortical, affected hemisphere), and extension of stroke [44, 46, 47, 50]. Only two studies reported stroke localization in detail (lesions detected by CT or MRI were classified as cortical or subcortical, and divided into frontal, fronto-parietal, parietal, fronto-parietal-temporal, or parietal-temporal) [15, 48]. Although the side of the affected hemisphere (left or right) was generally balanced among studies, two studies included patients with predominant left stroke [47, 48], whereas a third study did not report the affected body side [49].

Most of the studies applied fMV over the upper limb muscles with the exception of two studies [42, 46] applying fMV over lower limb muscles. In the upper limb studies, fMV was delivered over different target muscles ranging from a single target muscle [43, 48] to three muscles treated simultaneously by means of a double application of the device such as BB and FR in Marconi et al. [25] and Tavernese et al. [47], and PP and BB in Caliandro et al. [44] and Celletti et al. [50] and then, the third muscle alone. Concerning the specific target muscles, several studies applied fMV over the wrist flexors muscles alone [15, 43–45, 47, 48], or in combination with synergic muscles such as the biceps brachialis [15, 47] or biceps

Table 1 Demographic data and clinical features of patients with chronic stroke in studies applying focal muscle vibration (fMV)

Study	Group	N	Gender (M/F)	Age (years)	Duration of disease	Side (L/R)	Type (I/H)
Paoloni et al. [42]	EG	22	19/3	59.5 (13.3)	1.85 (0.59) year	11/11	N/A
	CG	22	20/2	62.6 (9.5)	1.86 (0.61) year	10/12	N/A
Conrad et al. [43]	EG	10	4/6	55.5 ± 5.35	8.8 ± 6.87 year	7/3	N/A
	CG	5	2/3	56.2 ± 4.2	N/A	2/3	N/A
Marconi et al. [15]	EG	15	9/6	63.6 ± 7.6	39.9 ± 28.8 month	6/9	N/A
	CG	15	8/7	66.3 ± 11.0	40.6 ± 25.1 month	7/8	N/A
Caliandro et al. [44]	EG	28	20/8	57.42 ± 12.79	100.71 ± 82.76 month	14/14	18/10
	CG	21	14/7	61.85 ± 15.74	96.4 ± 66.84 month	12/9	15/7
Noma et al. [45]	EG	12	8/4	57.5 (38–83)	21.5 (8–156) week	7/5	N/A
	CG (rest)	12	8/4	61 (27–83)	16 (7–139) week	4/8	N/A
	CG (stretch)	12	9/3	61.5 (41–83)	16.5 (8–291) week	5/7	N/A
Lee et al. [46]	EG	16	13/3	53.31 ± 8.37	56.94 ± 25.73 month	8/8	10/6
	CG	15	11/4	55.73 ± 8.27	49.93 ± 29.97 month	7/8	9/6
Tavernese et al. [47]	EG	24	21/3	58.9 ± 14.7	19.1 ± 18.9 month	16/8	24/0
	CG	20	18/2	58.3 ± 12.4	25.9 ± 21.8 month	14/6	20/0
Casale [48]	EG	15	9/6	65.13 ± 5.84	N/A	13/2	N/A
	CG	15	9/6	64.2 ± 5.05	N/A	14/1	N/A
Costantino et al. [49]	EG	17	11/6	62.59 ± 15.39	N/A	N/A	N/A
	CG	15	10/5	60.47 ± 16.09	N/A	N/A	N/A
Celletti et al. [50]	EG + RMP	6	4/2	43 (31–68)	6 (2–33) year	3/3	3/3
	EG + CP	6	4/2	43 (30–57)	2.5 (2–4) year	4/2	2/4
	CG	6	4/2	62.5 (46–69)	5.5 (2–7) year	2/4	4/2

Table 2 Characteristics of cited RCT studies regarding focal muscle vibration (fMV) in patients with stroke. EG experimental group, CG control group, FRC flexor carpi radialis, BB biceps brachii, rMV repetitive muscle vibration, RMT resting motor threshold, TMS transcranial magnetic stimulation, SIC1 short-interval intracortical inhibition, ICF intracortical facilitation, MEP motor-evoked potential, PT physiotherapy, WMFT Wolf Motor Function Test, FAS Functional Ability Scale, MAS Modified Ashworth Scale, FMA-UE Fugl-Meyer Assessment of sensorimotor function after stroke for upper extremity, JTT Jebsen-Taylor Hand Function Test, VNRS Verbal Numerical Rating Scale of pain, MI Motricity index

Author (year)	Purpose	Focal vibration (frequency, amplitude, side of the application, time)	Outcome measure	Follow-up	Results
Paoloni et al. [42]	To evaluate if the application of segmental muscle vibration to ankle dorsiflexor muscle can improve walking	All the participants underwent a 50-min general physical therapy session, 3 times a week, over a period of 4 weeks. Participants in the EG alone received additional 12 sessions over 4 weeks over the peroneus longus and tibialis anterior for 30 min per section in trains of 6 s, divided by 1-s pauses; frequency 120 Hz. Amplitude was set at 10 μ m	Gait analysis assessment: time-distance, kinematics and surface electromyography data.	1 month	A significant difference in the EG was observed in gait speed, unaffected side swing velocity, stride length on both the paretic and normal sides, and toe-off percentage on the normal side
Conrad et al. [43]	To test the hypothesis that tendon vibration may improve upper arm tracking performance	70 Hz tendon vibration applied to the skin adjacent to the forearm flexor tendons	Evaluation of the trial focused on hand path kinematics and muscle activity during target tracking.	During the trials	Tracking performance in the hand path length improved and a decrease in the muscle activity during movement was observed
Marconi et al. [15]	To evaluate long-lasting changes of rMV therapy in the upper limb	100 Hz, amplitude range 0.2–0.5 mm applied over the FRC and BB; rMV intervention was applied for 3 consecutive days, 3 times a day, with each application lasting 10 min	Peak-to-peak MEP amplitudes to single pulse TMS; RMT, map area and volume, SIC1 and ICF.	Before, 1 h, 1 week, and 2 weeks after the intervention ended	Reduction in RMT and increase in motor map areas in the vibrated muscles only in the rMV + PT group, with an increase in map volumes for all muscles
Calianandro et al. [44]	To examine the clinical effect of fMV on the motor function of the upper limb	Sinusoidal displacement of 0.2–0.5 mm (peak to peak); forces between 7 and 9 N. Vibration frequency at 100 Hz. Application on the pectoralis minor, biceps brachii and flexor carpi muscles for 3 consecutive days, 3 times a day, with each application lasting 10 min	Improvement of more than 0.37 points in the FAS of the WMFT and MAS.	Before the treatment and 1 week and 1 month after the treatment	A significant difference in the expression of the WMFT FAS scores over time in the EG
Noma et al. [45]	To investigate whether the direct application of vibratory stimuli inhibits spasticity in the hemiplegic upper limbs of post-stroke patients	Rest group: 5 min relax. Stretch group: 5 min of maximal extension of elbow, wrist and fingers EG: 3 or 2 spherical, rubber, vinyl-covered head of 5-cm vibrators (positioned on the hand-and-forearm and on the upper arm) with a frequency of 91 Hz and an amplitude of 1.0 mm applied for 5 min	MAS scores and F-wave.	Before, immediately after and 30 min after each intervention	Reduction of F wave amplitude, F/M ratio, and F-wave persistence after vibration; differences between the two groups
Lee et al. [46]	To investigate the effect of a local vibration stimulus training program on postural sway and gait in stroke patients	Local vibration stimulus training program for 30 min a day, five times a week, for 6 weeks. Two oscillators attached to the heel on the paretic side	A force plate was used to measure postural sway under two conditions: standing with eyes opened and eyes closed. Gait		Postural sway velocity and distance with eyes-open and closed conditions showed a significant decrease in the

Table 2 (continued)

Author (year)	Purpose	Focal vibration (frequency, amplitude, side of the application, time)	Outcome measure	Follow-up	Results
Tavernese et al. [47]	To improve the upper limb motor function	and one oscillator at the achilles and tibialis anterior tendon. Vibration stimulus was provided at an oscillation frequency of 90 Hz and a 15- μ m stimulus amplitude Patients in the EG received 2 weeks of general physical therapy associated with low amplitude vibration therapy at a fixed frequency of 120 Hz over the biceps brachii and flexor carpi ulnaris; vibration amplitude was 10 μ m; 30 min stimulation in trains of 6 s divided by 1-s pauses; total 60 min general session for five times a week for 2 weeks. The CG received 2 weeks of general physical therapy Pneumatic vibrator: contact surface 2 cm ² , frequency 100 Hz, amplitude 2 mm; mean pressure 250 mBar; application on the triceps brachii for 30 min, each session for 5 consecutive days, for 2 weeks	ability was measured using the GAITRite system Kinematic analysis of reaching movement.	At baseline and 2 weeks after treatment	EG; also changes in velocity, cadence, and paretic step length Normalized jerk significantly improved in the EG. Significant improvements for mean linear velocity, mean angular velocity in the shoulder, distance to target at the end of the movement and movement duration
Casale [48]	To evaluate spasticity reduction on flexors and biceps brachii muscle, and whether the effect lasted longer than the stimulation period	12 sessions (3 times per week over 4 weeks) were performed employing vibrations set with a frequency of 300 Hz and amplitude of 2 mm for 30 min on the triceps brachii and the extensor muscles of the upper limb. The paretic upper limb was positioned on a rigid surface and participants were required to maintain isometric contraction of the treated muscle	MAS for spasticity and robot-aided motor tasks changes for functional modification.	48 h after the fifth session and 48 h after the last session	In EG, the values of MAS significantly improved. Traject parameter showed better results in the EG
Costantino et al. [49]	To evaluate the effects of local muscle high frequency mechano-acoustic vibratory treatment on grip muscle strength, muscle tonus, disability and pain in post-stroke individuals with upper limb spasticity	Hand Grip Strength Test with hydraulic dynamometer; MAS; Quick DASH Score FMA-UE; JTT; VNRS.	Hand Grip Strength Test with hydraulic dynamometer; MAS; Quick DASH Score FMA-UE; JTT; VNRS.	At baseline, at the end of treatment (4-weeks)	Improvement of muscle strength and a decrease of muscle tonus, disability, and pain
Celletti et al. [50]	To examine the effect of fMV on the motor function of the upper limb coupled with progressive modular rebalancing rehabilitation approach or associated with conventional therapy versus conventional therapy alone	100 Hz of frequency and 0.2–0.5 mm of amplitude vibration applied in 3 consecutive days over the pectoralis minor and biceps brachii simultaneously (30 min) and over the flexor carpi (other 30 min) for 3 consecutive days, 3 times a day, with each application lasting 10 min	MAS; WMFT; MI for upper limb	Before and after 6 weeks of exercises	Motor function improvement

brachialis coupled with the pectoralis minor [44, 50] or finally in the hand [45]. By contrast, other studies applied fMV over extensor muscles [42, 46, 49] in order to improve flexor muscles spasticity. Again, several studies delivered fMV over a single muscle such as the triceps brachii alone [48] or in association with the *Extensoris carpi radialis* [49]. Studies applying fMV over lower limb muscles implied vibration of the peroneus longus and tibialis anterior [42] or at the Achilles and tibialis anterior tendon [46]. Concerning the simultaneous contraction of the treated muscles, only three studies adopted this paradigm [15, 44, 50].

Concerning fMV parameters, vibration amplitude varied significantly among studies ranging from 10 μm [42, 47], 15 μm [46], 0.2–0.5 mm [15, 44] to 2 mm [48, 49]. A single study did not clarify the amplitude of fMV [43]. The frequency used in the studies varied from 70 to 120 Hz except for Costantino [49] who used a frequency of 300 Hz. The duration of fMV and the number of sessions also varied among studies, ranging from a single session [43, 45], to three consecutive days [15, 44, 50] or even more (about 10–12 sessions in four studies) [42, 47–49]. Finally, a single study applied fMV repeatedly for 30 times [46].

Outcome measures varied among studies, ranging from clinical evaluation made by standardized clinical scales (spasticity) to experimental environments including behavioral measurement (kinematics and gait analysis), and finally neurophysiological measures including TMS and EMG. For the upper limb, evaluations were done by analyzing reaching movements. Tavernese et al. [47] evaluated the reaching movement variation before and after fMV, while Conrad et al. [43] evaluated the hand kinematics and muscle activity during target tracking not only before and after but also during vibration. Interestingly, Marconi et al. [15] evaluated vibration effects on cortical activity using TMS. For the lower limbs, the evaluation was done on gait parameters by using a gait analysis system [42] or in association with postural and balance measures [46]. All the other studies used a clinical outcome scale in order to evaluate spasticity [44, 45, 48, 50] or hand function [44, 48–50]. Noma et al. [45] used also F wave parameters to evaluate spasticity. A detailed description of the main results achieved by the fMV studies reviewed is shown in Table 2.

Section 2

Whole body vibration

WBV consists of a mechanical stimulus characterized by an oscillatory movement portrayed by specific parameters such as amplitude, frequency, and finally magnitude

(acceleration) of oscillations. The magnitude of oscillations is commonly reported in g or g -force values according to the following formula: $g = [D (2\pi \times \text{Hz})^2] / 9.81$, where D indicates the displacement of the platform (amplitude of WBV) [51, 52]. WBV is practically delivered by means of a vibrating platform where participants stand in a static position or move dynamically (Fig. 3). Two different types of WBV have been reported. The first type of WBV is achieved by means of a platform that vibrates in a predominantly vertical direction with 4-mm peak-to-peak amplitude. Differently, the second type of WBV is given through a platform able to rotate around an antero-posterior horizontal axis. Contrarily from the first type of WBV, the second type of WBV implies an asynchronous application of vibration to the left and right foot and thus an asymmetric perturbation of the legs [53]. Given that, as for fMV, also WBV is thought to entrain muscle spindles and subsequently, alpha-motoneuron firing rate possibly leading to the TVR [51], several authors have investigated the possible beneficial effects of WBV to boost muscle strengthening and improving proprioception control in healthy athletes [51]. The frequencies used for exercise range from 15 to 44 Hz and displacements range from 3 to 10 mm. Acceleration values range from 0.3 to 15 g (where g is the Earth's gravitational field or 9.81 m/s²) [51, 52]. Thus, vibration provides a perturbation of the gravitational field during the time course of the intervention [51, 52].



Fig. 3 A representative instrument for the application of whole-body vibration

WBV in chronic stroke

In the present section, we review the RCT studies applying WBV in patients with chronic stroke with the aim of promoting post-stroke recovery. The demographic data and clinical features are shown in detail in Table 3. A detailed description of purposes, technical aspects of WBV, outcome measures, timing of follow-up, and finally main results achieved by each of the studies here reviewed are shown in Table 4.

The age of patients recruited in all the previously published WBV studies is generally comparable with a rather balanced proportion of males and females in two studies [55, 59] but not in the other six studies (unbalanced with a majority of males). Although all patients enrolled in the WBV studies have been classified as chronic stroke patients, the exact time interval between stroke and WBV application varied significantly. All the studies enrolled patients at least 6 months following a stroke except for Brogårdhet et al. [54] who did not clarify the time interval from stroke and WBV application. A limitation of the WBV studies concerns the lack of a clear and detailed description of the type (ischemic or hemorrhagic stroke), localization (cortical or subcortical, affected hemisphere), and extension of stroke.

Concerning the specific parameters used during WBV, there was a variety of protocols with frequencies ranging from 5 to 40 Hz [55, 56, 59, 61] and amplitudes ranging from 0.44 mm to 6 mm. Ranges of accelerations applied during WBV have been not clarified. The duration of WBV also varied significantly among studies ranging from 30 s to 2.5 min. Moreover, most of the WBV studies planned repeated sessions of WBV ranging from 17 [59] to 30 [61] with the exception of two studies [57, 58] who evaluated the effect of a

single WBV session. Liao [61] investigated the effect of low-intensity and high-intensity WBV with respect to sham stimulation.

The outcome variables measured to clarify the possible beneficial effects of WBV included clinical, neurophysiological, and behavioral data. Some authors evaluated the severity of spasticity by means of the Modified Ashworth scale [56, 58], others calculated the H/M ratio [58], while some measured balance [59] or muscle strength [54, 55, 57, 60, 61]. Outcome measures also included serum level of specific collagen proteins [56] or ultrasound evaluation of muscle structure [59]. The effect of WBV on all these clinical, neurophysiological, and behavioral measures is rather inconsistent. Pang [56] found differences in the severity of spasticity, whereas Tankisheva et al. [55] did not. However, a beneficial effect of WBV on muscle strength in patients with chronic stroke was reported by both studies. Chan et al. [58] found a significant reduction of spasticity clinically tested by means of the Modified Ashworth scale and by using the H/M ratio. Other studies, however, did not confirm the effect of WBV on muscle strength in patients with chronic stroke [54, 59, 60]. Studies evaluating balance before and after WBV found no beneficial effect in chronic stroke patients [59]. Similarly, measures of clinical functional evaluation in chronic stroke patients such as the 6 Minute Walking Test [60, 61], Timed Up and Go test [57], and Berg Balance Scale [62] revealed non-significant effects of WBV. Concerning the exact timing of clinical, neurophysiological, or behavioral evaluations before and after WBV, many studies have made the evaluation before and soon after WBV [54, 57–59, 61] or at 1 month [56, 60] and 6 weeks following WBV [55]. A detailed description of

Table 3 Demographic data and clinical features of patients with chronic stroke in studies applying whole body vibration (WBV)

Study	Group	N	Gender (M/F)	Age (years)	Duration of disease	Side (L/R)	Type (I/H)
Brogårdhet et al. [54]	EG	16	13/3	61.3 + 8.5	37.4 + 31.8 months	9/7	14/2
	CG	15	12/3	63.9 + 5.8	33.1 + 29.2 months	7/8	13/2
Tankisheva et al. [55]	EG	7	4/3	57.4 + 13	7.71 + 8.6 years	4/3	6/1
	CG	8	6/2	65.3 + 3.7	5.28 + 3.6 years	4/4	5/3
Pang et al. [56]	EG	41	26/15	57.3 + 11.3	4.6 + 3.5 years	20/21	20/21
	CG	41	32/9	57.4 + 11.1	5.3 + 4.2 years	14/27	21/20
Silva et al. [57]	EG	28	19/9	60.75 + 11.8	40.85 + 68.76 months	17/11	25/3
	CG	10	8/2	58.1 + 8.14	39.6 + 63.55 months	7/3	8/2
Chan et al. [58]	EG	15	10/5	56.07 + 11.04	30.4 + 25.8 months	12/3	10/5
	CG	15	11/4	54.93 + 7.45	38.87 + 38.22 months	7/8	5/10
Marin et al. [59]	EG	11	6/5	62.3 + 10.6	4.3 + 2 years	5/6	10/1
	CG	9	5/4	64.4 + 7.6	4.3 + 3 years	5/4	7/2
Lau et al. [60]	EG	41	26/15	57.3 + 11.3	4.6 + 3.5 years	20/21	20/21
	CG	41	32/9	57.4 + 11.1	5.3 + 4.2 years	14/27	21/20
Liao et al. [61]	EG LWBV	28	20/8	60.8 ± 8.3	8.5 ± 5.2 years	20/8	12/16
	EG HWBV	28	18/10	62.9 ± 10.2	8.1 ± 4.2 years	19/9	12/16
	CG	28	24/4	59.8 ± 9.1	9.0 ± 4.6 years	12/16	11/17

Table 4 Characteristics of the cited RCT studies regarding whole body vibration (WBV). *CTs* C-telopeptide of type I collagen cross-links, *BAP* bone-specific alkaline phosphatase, *MAS* Modified Ashworth Scale, *BBS* Berg Balance scale, *VAS* visual analogic scale, *TUG* Timed Up and Go test, *6MWT* 6-Minute Walk Test

Author (year)	Purpose	WBV (frequency, amplitude, side of the application, time)	Outcome measure	Follow-up	Results
Pang [56]	To investigate the effect of WBV on bone turnover, leg muscle strength, motor function and spasticity	The device that generates vertical WBV. Frequency range 20–30 Hz and amplitude from 0.60–0.44 mm. Three times per week for 8 weeks (total 24 sections) of training following a specific protocol preceded by 15 min of warm-up exercises	Serum level of (CTs) and (BAP). Concentric knee flexion and extension power. MAS	Baseline, immediately after 24 session program and 1 month after the termination of training	No significant effect on serum levels of CTx and BAP A significant time effect in the concentric knee flexion power Significant knee difference in knee MAS score
Tankisheva et al. [55]	To investigate the effect of a 6-week WBV training program	Vertical vibration platform, 3 times a week for 6 weeks. Progressively increasing the intensity by increasing the frequency (35 to 40 Hz) or the amplitude (1.7 and 2.5 mm) Sessions 1–12: 5 bounds × 30 s Sessions 13–18: 17 bounds × 60 s	Ashworth scale (score 0–4) applied on the gastrocnemius, soleus, quadriceps, hamstrings, adductors, and psoas muscles Knee extension and flexion strength with an isokinetic dynamometer Sensory organization test for postural control	Baseline, after the intervention period of 6 weeks and after 6 weeks of follow-up	No significant differences in the Ashworth scale; a significant difference in isometric knee extension strength
Marin et al. [59]	To analyze the effects of WBV on lower limb muscle architecture, muscle strength, and balance	Vibration platform with an increase in frequency (from 5 to 21 Hz), sets (from 4 to 7), and time per set (from 30 to 60 s) during 17 sessions. Amplitude ranged between 4 and 6 mm peak to peak	Ultrasound evaluation of muscle architecture. BBS. Muscle strength	Before and after treatment	Increased muscle thickness observed in both groups. No statistically significant difference observed in the BBS and in muscle strength
Chan et al. [58]	To investigate the effect of a single session of WBV training on ankle plantar flexion spasticity and gait performance	A single session of vertical WBV with a magnitude of 12 Hz and an amplitude of 4 mm Subjects were positioned on the platform in semi-squat position and the time course included two 10-min periods of vibration with a 1-min rest interval	MAS. Subject experience of the influence of ankle spasticity on ambulation was scored by VAS. The maximal amplitude of H reflex and the Hmax/Mmax ratio to assess ankle spasticity. The time up and go test. A force plate was used to measure foot pressure	Before and after treatment	Hmax/Mmax ratio significantly decreased in the EG Time up and go significantly improved in EG MAS and VAS showed a significant difference between EG and CG
Brogardh et al. [54]	To evaluate the effects of WBV training	12 sessions of WBV training (twice weekly during 6 weeks) on a vibrating platform The EG trained on a vibrating platform with an amplitude of 3.75 mm The CG trained on a vibrating platform with an amplitude of 0.2 mm. The frequency on both platforms was set to 25 Hz	Isokinetic and isometric knee muscle strength (primary outcome measures), muscle tone, balance, gait performance, and perceived participation (secondary outcome measures) were assessed during 2 h before and after the WBV training	Pre- and post-training	No significant differences were found in any outcome measures between the EG and CG after 6 weeks
Liao et al. [61]	To investigate the effects of different WBV intensities on body functions/structures	Patients were randomly assigned a low-intensity WBV (frequency 20 Hz 1 mm amplitude), high-intensity WBV	Knee muscle strength (isokinetic dynamometry), knee and ankle joint spasticity with MAS, balance (Mini Balance	At baseline and post-intervention	Significant time effect for muscle strength, TUG distance, and oxygen consumption rate achieved during the 6-MWT, the

Table 4 (continued)

Author (year)	Purpose	WBV (frequency, amplitude, side of the application, time)	Outcome measure	Follow-up	Results
	activity, and participation	(frequency 30 Hz, 1 mm amplitude), or CG	Evaluation Systems Test), mobility (TUG), walking endurance (6MWT), balance self-efficacy (Activities-specific Balance Confidence scale), participation in daily activities (Frenchay Activity Index), perceived environmental barriers to societal participation (Craig Hospital Inventory of Environmental Factors), and quality of life (Short-Form 12 Health Survey)		Mini Balance Evaluation Systems Test, the Activities-specific Balance Confidence scale, and the Short-Form 12 Health Survey physical composite score domain
Silva et al. [57]	To investigate the acute effects of WBV on motor function	One session of WBV (frequency of 50 Hz and amplitude of 2 mm) comprising four 1-min series with 1-min rest intervals between series in three body positions: bipedal stances with the knees flexed to 30° and 90° and a unipedal stance on the paretic limb	Simultaneous electromyography of the affected and unaffected tibialis anterior and rectus femoris muscles bilaterally in voluntary isometric contraction; the 6MWT; the Stair-Climb Test; and the TUG	Before and after vibration therapy	No effects on the group and time interaction relative to variables affected side rectus femoris, unaffected side rectus femoris, affected side tibialis anterior, unaffected side tibialis anterior, and the Stair-Climb Test
Lau et al. [60]	To examine the efficacy of WBV in optimizing neuromotor performance and reducing falls	The EG received 9–15 min of WBV (vertical vibration; frequency = 20–30 Hz amplitude = 0.44–0.60 mm, peak acceleration = 9.5–15.8) while performing a variety of dynamic leg exercises on the vibration platform. The CG performed the same exercises without vibration. The subjects underwent their respective training three times a week for 8 weeks	Balance (BBS), mobility (10-m walk test and 6MWT), knee muscle strength (isokinetic dynamometry), and fall-related self-efficacy (activities-specific balance confidence scale)	At baseline, immediately after the 8-week training and at 1-month follow-up	Significant improvement in balance, mobility, muscle strength, and fall-related self-efficacy measures in both groups after the 8-week treatment period

the main results achieved by the WBV studies is shown in Table 4.

Discussion

Muscle vibration seems to be a safe method possibly helping to improve the outcome of stroke patients. Despite the growing amount of literature in this research field, a relevant number of issues remain still unsolved. First, to analyze the role of a rehabilitative intervention in stroke patients, it should be mainly taken into account that stroke is a heterogeneous

condition, thus entailing different degrees of damage with different recovery mechanisms. In this view, there is a lack of RCTs designed to investigate how the potential for stroke recovery and the benefit from rehabilitation strategies vary according to stroke (lesion) characteristics. Indeed, most of the studies that analyzed the effects of fMV/WBV on stroke recovery did not report subgroup analysis focused on the different lesion localizations, or yet extent and number of brain lesions. It is known that the global burden and persistence of post-stroke functional deficit crucially reflect infarct size and lesion location (e.g., cortical or subcortical stroke). Patients with cortical stroke are known to manifest worse baseline

National Institute of Health Scale/Score (i.e., stroke severity) on average than patients with subcortical lesions. Conversely, a single subcortical white matter damage would result in cortical differentiation causing widespread cortical dysfunction or severe motor impairment and poor motor recovery [63, 64]. Hence, when evaluating the effect of fMV/WBV on post-stroke recovery, it should be taken into account that the efficacy would depend on the specific pattern of brain damage [62]. Only a few sporadic case series have been carried out specifically on this issue. A single study from Marconi [15] reported that fMV-induced effects on 31 chronic stroke patients varied depending on whether the stroke was cortical or subcortical. However, further RCTs with larger cohorts of subjects are needed to verify these observations. Beyond cortical and subcortical stroke localization, other clinical features would influence the degree of post-stroke recovery such as stroke severity upon admission [65], hemispheric lateralization, stroke volume, number of lesions and patients' characteristics such as gender and age [66], and presence of aphasia or visual field deficit [66].

A further aspect concerns the optimal timing of intervention. Motor recovery is thought to be almost completed within 10 weeks by stroke occurrence, and stroke recovery reaches a plateau 3 to 6 months after stroke onset [67]; accordingly, most of the post-stroke rehabilitation guidelines suggest to begin the rehabilitation program in the very early phase of acute stroke. Since the very first hours after stroke, the role of changes in perilesional and remote brain regions triggered by the focal brain lesion, and the role of the recruitment of remote or secondary brain structures might play a role in the various degrees of motor recovery [68, 69].

Another relevant point concerns the putative physiological mechanisms responsible for the beneficial effect induced by vibration protocols. Several studies in animals and in humans have demonstrated that experimental modulation of proprioceptive inputs to the CNS can re-shape cortical mapping in the

sensorimotor region, owing to use-dependent plasticity processes [70–73]. For instance, limb immobilization can deteriorate cortical motor representation of the target body region, reduce cortical excitability, and degrade motor learning [70, 71]. Hence, it might be argued that the fMV/WBV-induced selective stimulation of muscle spindles might elicit changes in afferent sensory inputs to the CNS possibly leading to beneficial cortical/subcortical brain reorganization sensorimotor processes in various neurological conditions imposing limb immobilization such as stroke. It is known that in patients with stroke, the severity of motor deficit reflects two main pathophysiological processes: (1) loss of function due to neuronal loss and (2) maladaptive use-dependent plasticity in survived cortical/subcortical regions operating in both the affected and unaffected hemisphere [74]. Stroke-induced limb immobilization would, therefore, imply reduced afferent inputs to the CNS driving to low activation of cortical/subcortical motor maps coupled with increased inhibition from survived brain regions. As a result, reduced use-dependent cortical plasticity would further deteriorate the motor outcome and delay significantly the timing of post-stroke functional recovery [74]. Hence, we speculate that fMV/WBV would, in theory, promote post-stroke functional recovery by enhancing proprioceptive inputs to the CNS and inducing beneficial cortical and subcortical reorganization processes based on re-balancing and shaping of cortical and subcortical sensorimotor representations.

A final comment concerns the direct comparison between the amount of after-effects induced by fMV and WBV, in terms of post-stroke motor recovery. The experimental and clinical data coming from the RCT studies point to the fragility of the WBV after-effects when compared to fMV, in patients with stroke. The inconsistent results observed in previous WBV studies in stroke would reflect a number of methodological reasons including the relevant variability in the stimulating parameters and experimental design used. A possible

Table 5 Recommendation for optimal technical application of focal muscle vibration (fMV) and whole body vibration (WBV)

fMV	Frequency	70–120 Hz [19,29, 46–48, 50–54, 85]
	Amplitude	10 μ m–1 mm [19, 45, 47, 51–53, 59]
	Target muscle	Upper limb: flexor muscles [19, 45, 47, 50, 51, 59] Lower limb: less clear, preferentially extensor muscles [52, 53]
	State of the muscle during the intervention	Mild tonic contraction [19, 45, 47, 50, 52]
	Duration	10–30 min [19, 42, 45–47, 52, 53, 59]
	Design	Repetitive sessions [19, 42, 45–47, 52, 53, 59]
	WBV	Frequency
Amplitude		1–4 mm [56–58, 60, 63, 64]
Acceleration		Not clear, presumably between 0.3 and 15 g [62]
State of the muscle during the intervention		Mild tonic contraction [56–58, 60, 62–65]
Duration		Variable between maximum 10–15 min [58,61–65]
Design		Repetitive sessions [56–58, 60, 65]

future scenario would also imply different target stroke populations for the two muscle vibration techniques. Repetitive sessions of fMV would be more suitable for neurorehabilitative applications in patients with post-stroke. By contrast, stroke patients manifesting gait and balance impairment would, in theory, benefit from repetitive WBV applications due to the possible beneficial effect of perturbation of the gravitational field [51, 52].

Based on the currently available experimental and clinical data here examined, through this narrative review, we propose a new recommendation for optimal technical application of fMV and WBV in patients with stroke (Table 5). Our recommendation also includes new proposed strategies for the recruitment of specific cohorts of patients with the aim to increase the likelihood for a vibration-induced beneficial symptomatic effect in terms of post-stroke motor recovery. Future studies with fMV/WBV should be designed in patients with cortical rather than subcortical strokes that may imply more severe white matter lesions which in turn preclude motor recovery after stroke [74]. In addition, fMV and WBV should be applied in patients with acute or subacute stroke rather than in chronic stroke thus increasing the likelihood for the occurrence of cortical reorganization processes (cortical plasticity), well-known crucial mechanisms underlying motor recovery after stroke [74]. It should be taken into account that optimal response to muscle vibration would require active target muscle contraction during the intervention (Table 5). Accordingly, future studies should recruit patients with consistent and residual muscle force and exclude those with severe muscle weakness.

In conclusion, we suggest that future studies should be designed in clinically homogeneous cohorts of patients with stroke taking into account our proposed recommendation for optimal technical application of fMV and WBV. Moreover, besides the evaluation of patient's clinical features by means of clinical scales, future studies should also include standardized outcome measures based on more advanced and objective technologies. This study design would finally allow a better comparison between fMV and WBV in terms of symptomatic improvement in patients with stroke.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Abbreviations BAP, bone-specific alkaline phosphatase; BB, biceps brachii; BBS, Berg Balance Scale; CG, control group; CTs, C-telopeptide of type I collagen cross-links; DALYs, disability-adjusted life-years; EG, experimental group; FAS, Functional Ability Scale; FMA-UE, Fugl-Meyer Assessment of sensorimotor function after stroke for upper extremity; fMV, focal muscle vibration; FRC, flexor carpi radialis; ICF,

intracortical facilitation; JTT, Jebsen-Taylor Hand Function Test; MAS, Modified Ashworth Scale; MEP, motor-evoked potentials; MI, Motricity index; PT, physiotherapy; RMT, resting motor threshold; rMV, repetitive muscle vibration; SICI, short-interval intracortical inhibition; TMS, transcranial magnetic stimulation; TUG, Timed Up and Go test; VAS, visual analogic scale; VNRS, Verbal Numerical Rating Scale of pain; WBV, whole body vibration; 6MWT, 6

Minute Walk Test; WMFT, Wolf Motor Function Test

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