



Localized 100 Hz vibration improves function and reduces upper limb spasticity: a double-blind controlled study

R. CASALE^{1,2}, C. DAMIANI³, R. MAESTRI⁴, C. FUNDARÒ⁵, P. CHIMENTO⁵, C. FOTI²

Background. Physical modalities such as vibration has been suggested as possible non-pharmacological way to control spasticity.

Aims. The hypotheses tested were: 1) can a selective vibration of the upper limb flexor antagonist, triceps brachii, reduce the spasticity of the flexor biceps brachii muscle; 2) is its association with physiotherapy better than physiotherapy alone in reducing spasticity and improving function, 3) can this possible effect last for longer than the stimulation period.

Design. Randomized double-blind study.

Setting. Rehabilitation Institute, inward patients.

Population. Thirty hemiplegic patients affected by upper limb spasticity.

Method. (VIB + PT) group received physiotherapy plus vibration by means of a pneumatic vibrator applied over the belly of the triceps brachii of the spastic side (contact surface 2 cm²; frequency 100 Hz; amplitude 2 mm; mean pressure 250 mBar). (SHAM + PT) group received physiotherapy and sham vibration. Both groups had 60 minutes of physiotherapy (Kabat techniques) for 5 days a week (from Monday to Friday) for 2 weeks. Main Outcome Measure: Ashworth modified scale for spasticity and robot-aided motor tasks changes for functional modifications were evaluated before starting treatment (T0), 48 hours after the fifth session (T1) and 48 hours after the last session (T2).

Results. Fisher's exact test showed a statistically significant greater improvements in the (VIB + PT) group (P=0.0001) compared to in the (SHAM + PT) group after 1 week, as well as after 2 weeks of treatment (P=0.0078) at the Ashworth scale.

Conclusion. 1) 100 Hz vibration applied to the triceps brachii of a spastic upper limb in association with

¹Salvatore Maugeri Foundation, Pavia, Italy

²Doctorate in Advanced Science in Rehabilitation Medicine and Sport

Tor Vergata University, Rome, Italy

³San Raffaele Portuense Tosinvest, Rome, Italy

⁴Department of Biomedical Engineering

"Salvatore Maugeri Foundation", Montescano, Pavia, Italy

⁵Department of Clinical Neurophysiology

Salvatore Maugeri Foundation, Montescano, Pavia, Italy

physiotherapy is able to reduce the spasticity of the flexor agonist, biceps brachii; 2) this association is better than physiotherapy alone in controlling spasticity and improving function; 3) this clinically perceivable reduction of spasticity and function improvement extends (for at least 48 hours) beyond the period of application of the vibration, supporting its possible role in the rehabilitation of spastic hemiplegia.

Clinical Rehabilitation Impact. 100 Hz antagonist muscle vibration, a non-pharmacological treatment, can help physiotherapy to reduce flexors spasticity and improve functions in the rehabilitation of upper limb spasticity

KEY WORDS: Hemiplegia - Muscle spasticity - Rehabilitation.

The control of spasticity in post-stroke patients is a major task and a worldwide priority in neurorehabilitation, not only because of the epidemiological importance of cerebrovascular pathologies and the increasing number of survivors with severe sequelae,¹⁻⁴ but also because of the substantial lack of motor improvement in patients with a severe spastic evolution, especially when involving the upper limb.⁵⁻⁷

Corresponding author: R. Casale, Department of Clinical Neurophysiology and Pain Rehabilitation, Salvatore Maugeri Foundation, via per Montescano, 27040 Montescano, Pavia, Italy.
E-mail: roberto.casale@fsm.it

Rehabilitation programmes are, therefore, often associated with the use of drugs, given systemically or injected locally, to control spasticity. Although generally effective, when given orally such drugs often induce generalised weakness, drowsiness and sedation⁸ and, when injected intrathecally, can cause more severe complications^{9, 10} that sometimes limit their use.

Local treatment of spastic muscles with botulin toxin and phenol¹¹ also has some limitations. Although considered a first-line treatment,¹² their cost/benefit ratio, the development of immune-mediated unresponsiveness and some reported side effects, including unexpected loss of strength and diffuse muscle weakness, can limit the use of botulin toxin in daily clinical practice.¹³⁻¹⁵

It has been suggested that another possible way to control spasticity is to use physical modalities, such as vibration. However, the clinical reports on the use of vibration in the treatment of spasticity are very few and very old^{16, 17} and only recently was mechanical vibration successfully re-proposed to reduce upper limb spasticity in post-stroke patients suggesting a cortical structure and function modification induced by vibration.^{18, 19}

Vibration has been extensively used as a stretch reflex conditioning tool in neurophysiological investigations of spasticity.^{20, 21} Classical neurophysiological experiments have demonstrated that upper limb agonists and antagonists show reciprocal inhibition, that is, when a muscle contracts the antagonist has its activity inhibited and therefore increased motor excitability of a given muscle group can lead to decreased motor excitability in its antagonistic muscle group.²² It has been demonstrated that this reciprocal inhibition is also induced in the agonist muscle when a vibratory stimuli is applied to the antagonistic.²³

The primary endpoints of this clinical study were to test, in a group of hemiplegic patients, the hypotheses that: 1) the application of selective vibration to the upper limb flexor antagonist (*i.e.*, the triceps brachii) associated with physiotherapy can reduce the spasticity of the flexor agonist (*i.e.*, the biceps brachii); 2) the association of 100 Hz vibration with physiotherapy is better than physiotherapy alone in controlling spasticity and improving function; and as a secondary endpoint 3) to confirm the possible utilisation of vibration in reducing spasticity for longer than the stimulus application.

Materials and methods

Study group

Thirty patients of either sex were consecutively selected for this study following application of the inclusion/exclusion criteria (Figure 1). Inclusion criteria were: 1) the presence of a single lesion older more than one year; 2) the presence of a minimal residual voluntary motor activity in the flexion extension elbow movement; 3) the presence of a spasticity rating from 2 to 3 at the Ashworth modified scale;²⁴ 4) lack of improvement in the last six months. The exclusion criteria were: 1) age over 70 and below 18 years old; 2) multiple lesions; detected by CT scan or magnetic resonance imaging; 3) age- and educational level-normalised MMSE score below 22;²⁵ 4) the presence of systemic, bone or joint disorders or tumours or changes in either central or peripheral sensitivity as well as visual impairments able to interfere with the aims and methods of the research; 5) concomitant use of drugs for spasticity; 6) botulin toxin treatment in the last 8 months. The general characteristics of the patients included in the study are reported in Table I.

Study design

The patients recruited were allocated to two different treatment groups using an automated computer randomisation programme. The study was designed as a randomized controlled trial using a double-blind, parallel-group study design. The experimental group received a vibration treatment in addition to physiotherapy (VIB + PT). The control group received physiotherapy alone. In this last group the vibration device was applied in the same way as for the (VIB + PT) group but no vibratory stimulation was delivered (SHAM + PT). The patients and the clinical examiner were blind to the intervention.

PHYSIOTHERAPY

All the physiotherapists involved in the treatment of the patients enrolled in both groups received instruction to guarantee the maximum homogeneity of the administered treatments in terms of treatment protocol to be followed as well as of its duration and sequence. So far both groups had daily sessions of physiotherapy based mainly on Kabat techniques associated with passive and active exercises to reduce spasticity. For both groups each daily session lasted 60 minutes for 5 days a week (from Monday

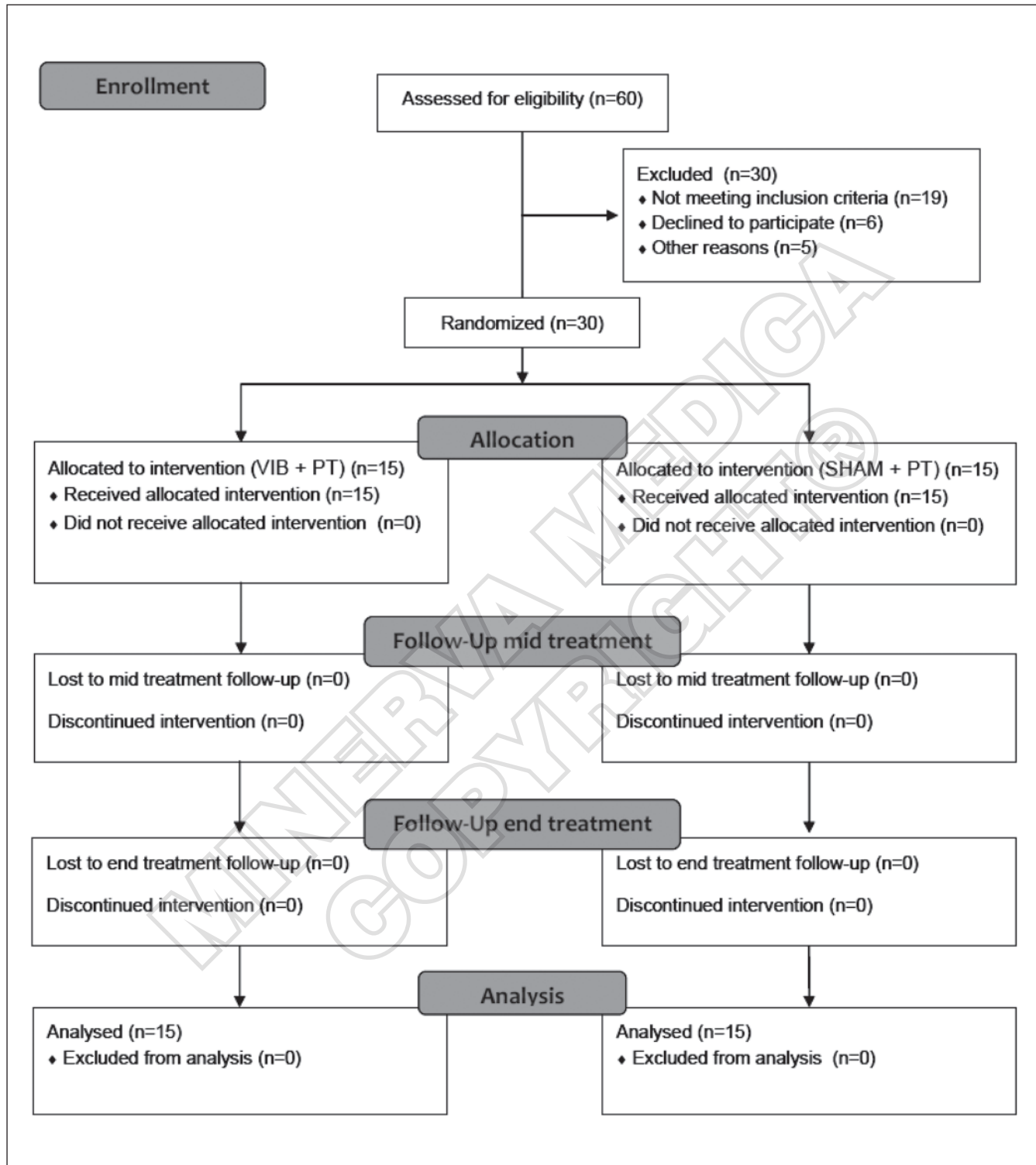


Figure 1.—Randomization flowchart (CONSORT flow diagram).

TABLE I.—*Demographic and treatment assignment data of the patients.*

Subjects ID	AGE	Gender	Lesion side	Left/right handed	% Disability (Barthel)	Treatment
1	70	F	Left FT	Right	35%	SHAM + PT
2	69	F	Left T	Right	50%	VIB + PT
3	65	F	Right TO	Left	40%	VIB + PT
4	58	M	Left T	Right	45%	SHAM + PT
5	68	M	Right FT	Left	35%	SHAM + PT
6	68	M	Left T	Right	45%	SHAM + PT
7	70	M	Left PO	Right	50%	VIB + PT
8	66	M	Left PO	Right	40%	SHAM + PT
9	68	M	Left TP	Right	50%	VIB + PT
10	69	F	Left TP	Right	45%	VIB + PT
11	61	M	Left TP	Right	35%	SHAM + PT
12	66	M	Right TO	Left	40%	VIB + PT
13	70	F	Left T	Right	50%	VIB + PT
14	58	M	Left T	Right	40%	VIB + PT
15	68	M	Left TP	Right	35%	VIB + PT
16	48	M	Left TP	Right	45%	VIB + PT
17	68	M	Left TP	Right	35%	VIB + PT
18	70	F	Left TP	Right	35%	SHAM + PT
19	61	M	Left PO	Right	40%	VIB + PT
20	66	M	Left TFP	Right	50%	VIB + PT
21	63	F	Left FT	Right	40%	VIB + PT
22	70	M	Left FT	Right	35%	SHAM + PT
23	65	M	Left T	Right	40%	SHAM + PT
24	68	F	Right PO	Left	45%	VIB + PT
25	61	M	Left T	Right	40%	SHAM + PT
26	65	F	Left TP	Right	35%	SHAM + PT
27	63	F	Left TP	Right	50%	SHAM + PT
28	67	F	Left FT	Right	45%	SHAM + PT
29	54	M	Left TP	Right	35%	SHAM + PT
30	57	F	Left TP	Right	35%	SHAM + PT

SHAM + PT: sham vibration and physiotherapy; VIB + PT: vibration and physiotherapy; TFP: temporo fronto-parietal; PO: parieto occipital; FT: fronto temporal; T: temporal; TO: temporo occipital; TP: temporo parietal.

to Friday) for the 2 weeks of the trial at approximately the same time of the day (morning).

VIBRATION

Patients in the experimental group (VIB + PT), in addition to the daily sessions of physiotherapy, also received treatment with vibration. A pneumatic vibrator powered by compressed air²⁶ was utilized [VIBRA, @Circle]^a. A 100 Hz vibration thus produced, was applied over the belly of the triceps brachii muscle of the spastic side by means of so that the amplitude of vibration was approximately 2 mm with a mean pressure of 250 mBar. The patients in the VIB + PT group received vibration sessions of 30 minutes each for 5 consecutive days for 2 weeks at approximately the same time of the day (afternoon). With the

same technique and time of application a cup-shaped transducer with a contact surface of 2 cm² was also applied to the triceps brachii of the control group (SHAM + PT) but no stimuli were delivered.

Spasticity and motor function evaluation

In both groups the spasticity of the biceps brachii was evaluated using the modified Ashworth scale (MAS)²⁴ while to assess upper limb motor function, the residual motor activity was assessed by means of a robot-aided device [Armeo@spring, Ocoma]^b suitable to provide information on reaching movements induced by the presentation of a visual task at a defined level of difficulty in terms of percentage of completed tasks (Task, %), time to complete tasks (Time, sec) and normalised deviation from the

TABLE II.—Values of all outcome variables in the two groups (VIB + PT) (SHAM + PT) before (T0), after 1 (T1) and 2 (T2) weeks of treatment.

Variables	N1	SHAM + PT	N2	VIB + PT
MAS-T0	15	2.20±0.9	15	2.30±0.6
MAS-T1	15	2.13±0.8	15	1.50±0.8
MAS-T2	15	1.90±0.9	15	1.27±0.8
Task-T0	15	0.69±0.1	15	0.74±0.1
Task-T1	15	0.70±0.1	15	0.77±0.1
Task-T2	15	0.72±0.1	15	0.79±0.1
Time-T0	15	107.13±14.3	15	105.00±13.1
Time-T1	15	105.73±12.1	15	97.00±12.9
Time-T2	15	102.07±12.9	15	92.33±12.3
Traject-T0	15	2.11±0.4	15	1.92±0.5
Traject-T1	15	2.04±0.4	15	1.69±0.5
Traject-T2	15	1.95±0.5	15	1.57±0.5

MAS: modified Ashworth scale; SHAM + PT: sham vibration and physiotherapy; VIB + PT: vibration and physiotherapy.

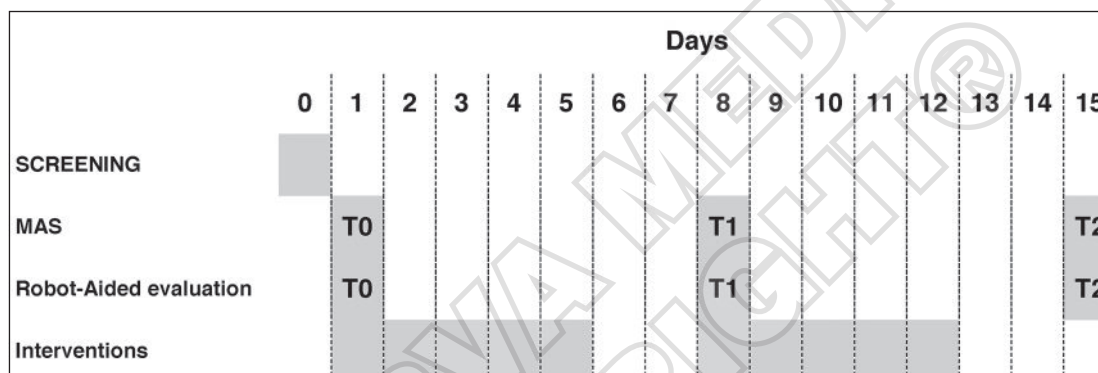


Figure 2.—Study protocol (GANTT diagram). Clinical and instrumental examination at T0, T1 and T2 were done in the morning, while interventions were always provided in the afternoon.

shorter trajectory (Traject) to reach it. Both spasticity and motor function were evaluated before starting treatment (T0), 48 hours after the fifth session (T1) and 48 hours after the last session of vibration (T2) by two different doctors unaware of the purpose of the research or the type of treatment applied. Table II reports the timing of the various elements of the research protocol (GANTT Diagram, Figure 2).

Statistical analysis

Descriptive statistics are given as mean \pm SD. The Shapiro-Wilk statistic was used to test the normality of the distribution of all variables.

To investigate the primary end points, we assessed the effect of vibration as adjunctive treatment on all outcome variables with a two-factor analysis of variance, where the first factor was treatment

(physiotherapy, SHAM + PT, *versus* physiotherapy + vibration, VIB + PT) and the second factor was time (three measurements, T0, T1, T2), with repeated measurements in the time factor.

Within-group comparisons were carried out by paired t-tests or by a Wilcoxon's matched pairs test in case of violation of the normality assumption.

The frequency of patients who improved their score at the MAS scale in the two groups was compared by Fisher's exact test. A P value <0.05 was considered statistically significant.

All analyses were carried out using the SAS/STAT statistical package, release 9.2^c.

Ethical issues

The protocol followed the Helsinki recommendations on non-pharmacological biomedical research involving

TABLE III.—Distribution of the global effects (improved/unchanged) after 2 weeks of treatment (T2).

	VIB + PT	SHAM + PT	Total
Improved	13	5	18
Unchanged	2	10	12
Total	15	15	30

VIB + PT: vibration and physiotherapy; SHAM + PT: sham vibration and physiotherapy.

human subjects and was approved by the Institute's Ethical Committee. All the subjects received a careful explanation of the aims of the study and methods used and agreed to participate in the study. Before their enrolment they gave signed, informed consent. Subjects were free to withdraw from the study at any time.

Results

Patients in the two groups had similar age (64.7 ± 5.4 vs. 65.1 ± 5.8 years) and sex ratio (male to female ratio around 3:2). The values of all outcome

variables at T0, T1 and T2 are reported in Table III for both groups of patients.

Figure 3 shows the time course of respectively MAS, Task, Time and Traject at the observation times in the group of patients who underwent physiotherapy + vibration (VIB + PT, circles) and in the control group (SHAM + PT, squares).

We found a significant ($P < 0.01$) time-treatment interaction in the analysis of variance for all outcome measures except Traject ($P = 0.08$). This result indicates that the time course of MAS, Task and Time over the observation period was different in patients who underwent physiotherapy + vibration com-

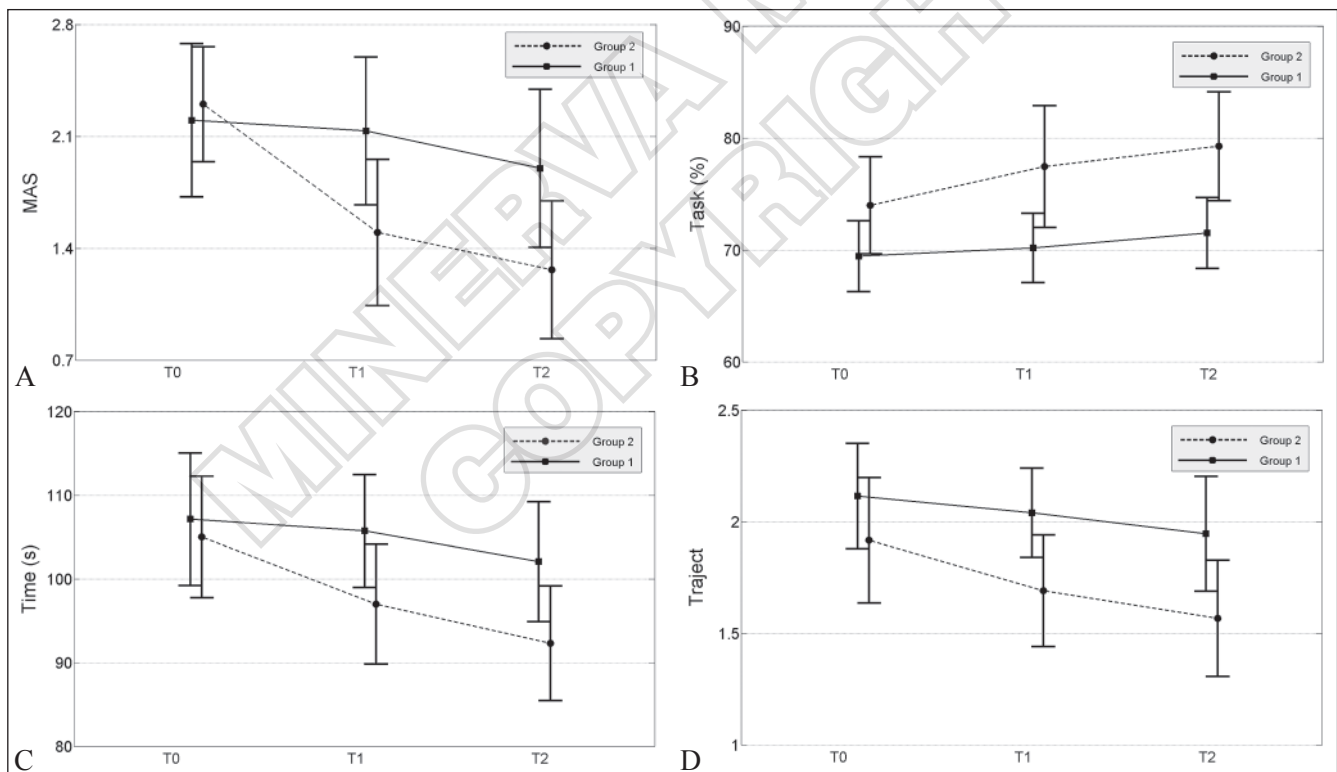


Figure 3.—A-D) show the time course of respectively MAS, Task, Time and Traject at the observation times in the group of patients who underwent physiotherapy + vibration (VIB + PT, circles) and in the control group (SHAM + PT, squares).

pared to control patients. Hence, separate paired t-tests (two for each group of patients) were carried out to compare these variables at T1 *vs.* T0 and T2 *vs.* T0.

In patients who underwent physiotherapy + vibration, the values of MAS significantly improved at T1 and T2 with respect to T0 ($P < 0.0001$ both), while in control patients the improvement reached statistical significance only at T2 ($P = 0.33$ T1 *vs.* T0 and $P = 0.023$ T2 *vs.* T0).

Similar results were found for Time ($P < 0.0001$ both comparisons in VIB + PT group, $P = 0.56$ T1 *vs.* T0 and $P = 0.042$ T2 *vs.* T0 in SHAM + PT group) and for Task ($P < 0.0001$ T2 *vs.* T0, $P = 0.0006$ T1 *vs.* T0 in VIB + PT group, $P = 0.26$ T1 *vs.* T0 and $P = 0.041$ T2 *vs.* T0 in SHAM + PT group).

As regards Traject parameter, patients in the VIB + PT group had better results than those in the SHAM + PT group, however the statistical analysis ($P = 0.08$) does not allow to reject the null hypothesis that both groups of patients had the same time course. Taken as a whole, the patients improved their performance both at T1 ($P = 0.012$) and at T2 ($P < 0.0001$) with respect to T0.

Finally, at T1, 1 patient in the SHAM + PT group and 12 in VIB + PT group had improved MAS with respect to basal value (Fisher's exact test $P < 0.0001$) while at T2, 5 patients in SHAM + PT group and 13 in VIB + PT group had improved MAS with respect to basal value (Fisher's exact test $P = 0.0078$).

Discussion

The physiopathology of spasticity in hemiplegic patients is not completely understood²⁷ and this lack of complete knowledge is reflected in the field of rehabilitation by the poor control of spasticity. In particular, upper limb rehabilitation of hemiplegic patients is all too often unsatisfactory because of various degrees of spasticity masking any possible motor recovery. Several methods of controlling spasticity are used, including systemic and local administration of antispastic drugs such as botulin toxin,⁸⁻¹² but their side effects, low cost/benefit ratio and the absence of controlled study in arm/hand function can limit their clinical utility.¹³⁻¹⁵ This lack of controlled studies can also be a reflection of the difficulty in the clinical and instrumental assessment of arm/hand function before and after a given treatment. In

this research an effort was made to overcome the criticism present in literature on the use of the MAS for spasticity.^{5, 24, 28, 29} In this context both the difficulty in finding reliable tests for the upper limb, like the simple six-minute walking for the lower limb, and the substantial lack of positive results in the management of the spastic upper limb in hemiplegic patients has been taken into consideration.⁵⁻⁷ Recently the use of robot device has been convincingly proposed in the rehabilitation of the upper limb in post stroke patients, not only as a tool to improve upper limb movement but also as a mean to provide functional measures in clinic.³⁰⁻³² In our study we used a robotic device (Armeo®spring, Hocoma) able to record and quantify some motor parameter to objectively evaluate the possible therapeutic efficacy of vibration.

It is worth mentioning that the literature on vibration is indeed quite scattered, encompassing whole body vibration or localized applications of different devices. Localized vibration ranges from mechanical (the so-called "ball" stimulator,^{18, 19} cylinder²⁰⁻²³ etc.) to mechanoacoustic devices that use sound waves to activate mechanoreceptors.²⁶ Differences in frequencies were also used. Moreover the most important differences between techniques are the sites of application both in normal and in pathological conditions. Application exists where vibration was applied to the antagonist muscle group^{23, 33} as well as to the agonist/spastic muscle group^{18, 34, 35} showing quite evidently different action mechanisms, but almost equal clinical results. The explanation of the above mentioned critical factors is beyond the aim of this limited research paper.

This clinical study had as a primary endpoint to assess whether in a group of hemiplegic patients the application of localised 100 Hz vibration to the upper limb flexor antagonist (*i.e.*, the triceps brachii) associated with physiotherapy was able to reduce the spasticity of the flexor agonist (*i.e.*, the biceps brachii). Consequently, the other and more important primary endpoint was to assess if its association with physiotherapy was better than physiotherapy alone in controlling spasticity and improving function. A third and secondary endpoint was to confirm the possible utilisation of vibration in reducing spasticity for longer than the stimulus application.

Our results: 1) indicate that a 100 Hz vibration applied to the triceps brachii of a spastic upper limb in association with physiotherapy is able to reduce

the spasticity of the flexor agonist, biceps brachii in a group of hemiplegic patients; 2) point out that the combined use of a vibratory stimulation within a traditional physiotherapy approach can provide better and faster results not only decreasing spasticity but more important, improving motor functions; 3) confirm that this clinical functional perceivable reduction of spasticity of the biceps brachii extends (for at least 48 hours) beyond the period of application of the vibration, supporting the existing pilot data on the possible role for this strategy in the rehabilitation of spastic hemiplegia.¹⁹ We also suggest that, among other more centrally located mechanisms,³³ vibration applied to an antagonistic muscle may exert its action also by means of the agonist/antagonist reciprocal inhibition at a spinal level.

Reflex transmission changes in the pathways involved in the maintenance of the motor drive as well as in the pathological changes that occurs in spasticity, may depend both on an altered supraspinal drive and on changes at cellular level in the spinal cord.³⁴ It was recently demonstrated that the application of a vibratory stimulation on a muscle induces an enhanced inhibition/ reduced excitability of corticospinal activity resulting in a reduction of flexor muscle spasticity^{18, 19} reconfirming the important role of the motor cortex in the treatment of spasticity. However in case of a cortical lesion with a reduction of the cortical motor drive, the spinal cord becomes the pivotal structure in the genesis/ maintenance of an altered muscle tone.³⁴ Indeed before reaching the cortical level, where it prolongs the cortical silent period,³³ vibration impinges the spinal cord where agonists and antagonists muscles are linked by the so-called reciprocal inhibition.^{22, 34, 35} Reciprocal inhibition happens also in case of a spinal cord injury where the application of a vibratory stimulus is still able to modify reflexes without the involvement of supra spinal structures.³⁶ In the normal subject a combined clinical consequence of this reciprocal inhibition is the smooth execution of movements while in the presence of a upper motor neurone lesion, *i.e.*, in presence of a flexor spasticity, residual movements can be further blunted and the movement becomes impossible or not graded in the strength of the muscular contraction.³⁷ In this case when a vibration is applied to the antagonist muscle, the increased sensory barrage, inhibits the activity of the spastic agonist muscle and better regulates reciprocal Ia inhibition according to the require-

ments of a voluntary movement.³⁷ In the present research this is clinically demonstrated by the reduction of spasticity and by the unveiling of possible residual voluntary movement of the antagonist with a functional improvement better than physiotherapy alone. Percentage and Time of reaching (Figures 3A-C) and, even if not statistically significant, Traject improvement (Figure 3D) demonstrate a better agonist antagonist coupling. These improvements in flexor spasticity and upper limb function were statistically better in the VIB + PT group both at T1 and T2 suggesting not only a better but also a faster results when physiotherapy is associated with a vibratory stimulation of the antagonist muscle group.

The secondary endpoint of this study was to determine whether 100 Hz vibration can induce a clinical modification of spasticity extending beyond the period of application of the vibration. In our study we found that upper arm flexor spasticity remained reduced and functions improved as measured by a clinical score and robot aided functional assessment, for 48 hours after the vibration sessions. This was confirmed both at T1 and T2. It was recently demonstrated that high frequency vibration can induce neural modifications lasting far longer than the period of application of vibration.²⁶ The choice of a selective stimulation along with the use of a 100 Hz vibration frequency, specific for Ia fibers could account for the early changes obtained with only 10 sessions of 30' each. Selectivity of the stimulation site and frequency of vibration chosen could also account for the durable effects on spasticity and function that we recorded 48 hours after the last vibration session. This is in line with other reports suggesting the possible clinical relevance for the use of direct and localised muscle vibration.^{19, 38}

Conclusions

The present paper should be viewed as providing supporting evidence of a functional improvement of the spastic upper limb when 100 Hz vibration, applied to the antagonistic muscle, is associated with conventional physiotherapy and to a possible use of a robotic device to help the clinician to evaluate the results of a treatment.³² Although we used a ICF body function scale, *i.e.*, the MAS, other important aspects of ICF such as participation, personal and environmental factors were not considered in

this study.³⁹ This is certainly a point of weakness that should be amended with further studies. Indeed even if a robotic-aided assessments is “a good supplement to standard clinical assessments as they provide objective, sensitive, and detailed information about a subject’s motor ability” a clinical as well as an ICF evaluation is needed.³² The parallel recording of any improvements in movement, which could be assessed by robotic devices or movement analysis systems and ICF participation, personal and environmental factors scales, would improve the possibility to have objective as well as ecologic parameters in the evaluation of upper limb rehabilitation in hemiplegia. These results should be confirmed by further studies for longer period of observation — data herein reported are limited to a 48 hours span — and with outcome measures as much as possible covering all domains of ICF.³⁹ Moreover, due to differences in vibration frequencies^{26, 40} and different sites of application,^{18, 23, 33-35} further studies with specific experimental models are needed to ascertain the best frequency and site of application.

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