

*Original Research*

# Brain oscillatory activity correlates with the relief of post-stroke spasticity following focal vibration

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## Abstract

**Background:** Some evidence has demonstrated that focal vibration (FV) contributes to the relief of post-stroke spasticity (PSS). Although the changes of cortical activity correlating with the relief of PSS induced by FV have been explored using transcranial magnetic stimulation, brain oscillatory activity during the above-mentioned process has not been fully understood. **Objective:** The main purpose of this study is to explore the correlation between the changes in brain oscillatory activity and the relief of PSS following FV. **Methods:** A clinical experiment was carried out, in which FV (87 Hz, 0.28 mm) was applied over the antagonist muscle's belly of the spastic muscle of ten chronic spastic stroke patients. An electroencephalogram was recorded following before-FV and three sessions of FV. Muscle properties to assess the relief of PSS were tested before-FV and immediately after three sessions of FV. **Results:** EEG analysis has shown that FV can lead to the significant decrease in the relative power at C3 and C4 in the beta1 (13, 18 Hz), as well as C3 and C4 in the beta3 band (21, 30 Hz), indicating the activation of primary sensorimotor cortex (S1-M1). Muscle properties analysis has shown that, in the state of flexion of spastic muscle, muscle compliance and muscle displacement of the spastic muscle significantly increased right after FV, illustrating the relief of the spasticity. Moreover, the increase of muscle compliance is positively correlated with the reduction of difference index of the activation of bilateral S1-M1. **Conclusions:** This finding indicated that the relief of PSS can be associated with the activation of bilateral S1-M1 where the activation of the ipsilesional S1-M1 was higher than that of the contralesional one. This study showed the brain oscillatory activity in the bilateral S1-M1 correlating with the relief of PSS following FV, which could contribute to establishing cortex oscillatory activity as a biomarker of the relief of PSS and providing a potential mechanism explanation of the relief of PSS.

**Keywords:** Focal vibration; Post-stroke spasticity; Primary sensorimotor cortex; The relief of spasticity; Muscle compliance

## 1. Introduction

In most countries, stroke, as one of the leading causes of adult mortality and morbidity, led to the loss of patients' motor function and affected the activity of daily living (ADL) [1]. Spasticity, which was characterized by a velocity-dependent increase in tonic stretch reflexes, was a common complication in stroke patients [2]. The incidence rate of post-stroke spasticity (PSS) reached 17% to 42.6% of those in the chronic phase (>3 months poststroke) [3]. The direct costs for 12-month stroke patients with spasticity were four times higher than those for patients without spasticity [4]. Therefore, it was necessary to relieve the PSS. So far, many effective interventions for the treatment of PSS have been reported, including pharmacological interventions, non-invasive brain stimulations, sensory stimulations, etc. [5].

In the past few years, more and more researchers have focused on establishing the connection between changes in the cerebral cortex and the relief of spasticity in order to ex-

plore a potential mechanism of the relief of spasticity at the cortical level using some neuroimaging modalities, including electroencephalogram (EEG) [6], functional magnetic resonance imaging (fMRI) [7,8], and transcranial magnetic stimulation (TMS) [9]. For example, EEG changes over the ipsilesional sensorimotor network in the beta band were associated with the reduction of spasticity following robot-assisted bilateral arm training [6]. Enhanced fMRI activation in the contralesional primary motor and sensory cortex (S1-M1), as well as associative sensory cortex, has been correlated with greater mitigation of PSS following upper extremity motor learning therapy [7].

Several studies have also explored the relationship between changes in the cerebral cortex and the relief of PSS following focal vibration (FV), as one of many sensory stimulation interventions to alleviate PSS [10–12]. Generally speaking, FV was applied over the antagonist muscle's belly of the spastic muscle [12,13]. The choice of stimulation location was mainly based on the cortical reciprocal inhibition between agonist and antagonist muscle [14–16]. In



these studies involving the cortical level, TMS was widely used as the monitor tool and TMS-induced motor-evoked potential (MEP) reflected the motor cortical excitability through electrical signals recorded from the descending motor pathways. The results from these studies have shown that FV can enhance the amplitude of MEP (motor cortical excitability) of the vibrated muscle whilst reducing the amplitude of MEP (motor cortical excitability) of non-vibrated antagonistic muscles in healthy subjects' experiments [14–16]. Based on the potential mechanism of cortical reciprocal inhibition, some clinical experiments' results have also demonstrated that muscle vibration applied over the antagonist muscle belly to spastic muscle can reduce spasticity [10,12,13,17]. The clinical study has further revealed that the differential modulation of excitability in motor cortical circuits induced by FV over the antagonist muscle's belly of the spastic muscle was correlated with the reduction of spasticity [12]. However, MEP was absent for some stroke patients, especially for patients with large cortical lesions involving M1 [18]. Therefore, assessing the changes in motor cortex excitability using MEP was not suitable for all stroke patients during the rehabilitation training.

Compared to other neuroimaging modalities (such as fMRI, Magnetoencephalography), EEG, which was used to record brain oscillatory activities simultaneously in these frequency bands, had the advantage of higher spatial resolution and lower cost. The sensorimotor “mu” rhythms and sensorimotor beta rhythms mainly originated in the somatosensory postcentral gyrus and precentral motor cortex, respectively [19,20]. Some clinical studies have elucidated that EEG brain oscillatory activities (mainly referred to “mu” and beta rhythms) can be acted as a biomarker of motor recovery in stroke patients [21–25]. In these studies, the event-related synchronization and event-related desynchronization (ERS/ERD, referred to the increase/decrease of relative power) overlying sensorimotor cortex in the “mu” and beta band was usually used to assess the activation of the sensorimotor cortex. Based on our previous studies, the beta motor-related power desynchronization (beta-MRPD) was also considered as the activation of the sensorimotor cortex following FV [26,27]. In addition, few studies have so far reported brain oscillatory activities correlating with the relief of PSS following FV.

Currently, Modified Ashworth Score (MAS) was universally accepted in the clinical scale to evaluate the relief of spasticity. Several studies have also used the indexes of muscle properties. These indexes, including muscle tissue's compliance and displacement, reflected the changes in spastic muscle's viscoelastic properties and compliance and assessed the reduction of spasticity [28,29]. It had been demonstrated that the changes in muscle compliance showed a powerful correlation with MAS in patients with spastic cerebral palsy [30] and spastic stroke [31]. In one study, muscle tissue's compliance and displacement were used to evaluate the relief of SPP [29].

Based on these considerations, this study's purpose was to explore the brain oscillatory activity correlating with the relief of PSS following FV by establishing the correlation between the changes of beta-MRPD overlying the sensorimotor cortex and the changes in muscle properties. In the clinic experiment, FV was applied over the antagonist muscle belly to the spastic muscle and EEG was used to monitor the brain activity during FV. All sub-beta MRPD at C3 and C4, including beta1 MRPD (13–18 Hz), beta2 MRPD (18–21 Hz), and beta3 MRPD (21–30 Hz), as well as the difference index of all sub-beta MRPD between C3 and C4, was calculated to evaluate the activation patterns of S1-M1. The relative changes of muscle displacement between the spastic muscle and its antagonist, as well as muscle compliance, were used to evaluate the relief of SPP.

## 2. Materials and methods

### 2.1 Subjects

Ten chronic stroke patients ( $50.8 \pm 17.6$  years) suffering from biceps brachii spasticity were recruited from Beijing Rehabilitation Hospital Affiliated with Capital Medical University and Shenzhen Nanshan District People's Hospital. The clinical features of those patients were shown in Table 1. The inclusion criteria for those patients were included: (1) the age ranging from 18 to 78 years; (2) to have the ability to understand the instruction of the tester; (3) no less than 6 months post-stroke; (4) to have no severe impairment of vision and language; (5) to have no anti-spastic drugs in the last 6 months. The exclusion criteria were included: (1) to have a history of epilepsy and traumatic brain injury; (2) to have other concomitant neurodegenerative diseases; (3) to have serious complications of lung, heart, kidney, and liver. Prior to participating in this study, each subject gave written consent. This study was approved by the Medical Ethics Committee of Beijing Rehabilitation Hospital Affiliated with Capital Medical University and Shenzhen Nanshan People's Hospital.

### 2.2 Experimental setup

Based on this previous study, the changes of muscle displacement and compliance, which have been acquired by the muscle tone intelligence measure system, were used to assess the relief of spasticity quantitatively [29]. In this system, the relationship between muscle tissue displacement and the muscle tissue's resistance to the system (ranging between 0.25 kg and 2.0 kg at the interval of 0.25 kg) induced by external perpendicular compression pressure was established.

EEG signals were recorded using a 64-channel EEG system (ANT Neuro, B.V., Enschede, the Netherlands) with a commercial WaveGuard EEG cap, which was designed according to the international 10-20 system. In this study, the 32 Ag/AgCl electrodes were chosen (Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, M1, T7, C3, Cz, C4, T8, M2, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, O1, POz,

**Table 1. Patient characteristics.**

Subject ID	Sex	Age	Hemiplegic side	Stroke location	Time from stroke onset (months)	MAS
1	Male	26	Right	BG	12	1
2	Female	47	Right	BG	84	2
3	Male	45	Right	BG	6	2
4	Male	27	Right	BG, OL, PL, FL	24	1+
5	Male	67	Right	BG	48	3
6	Male	65	Left	BG, CS, PV	12	1+
7	Female	64	Left	BG, LC	9	1
8	Female	75	Left	BG	29	1
9	Female	34	Left	BG, OL	44	2
10	Female	58	Left	BG	94	1

MAS, Modified Ashworth Scale; BG, Basal Ganglia; OL, Occipital lobe; PL, Parietal lobe; FL, Frontal lobe; CS, Centrum Semioval; PV, Periventricular; LC, Lacunar.

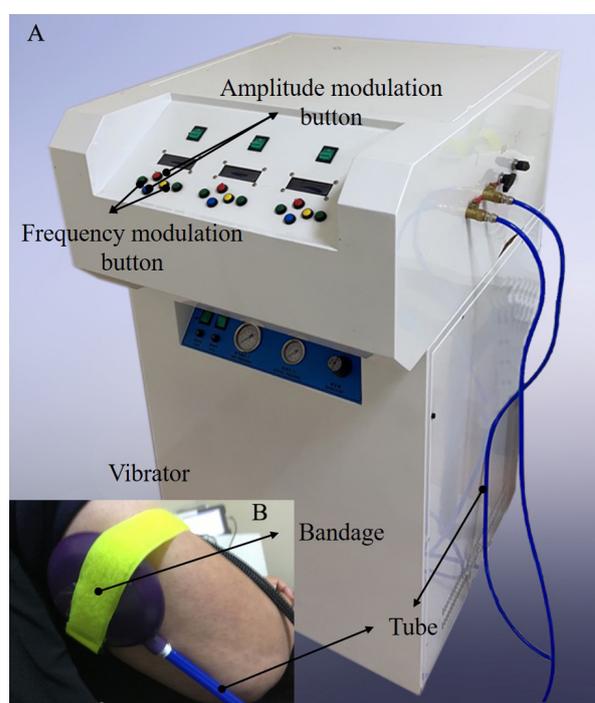
O2, and EOG). Cpz was the reference electrode and the ground electrode was placed between Fz and FPz. The sampling rate was set at 1000 Hz and the electrode impedances were kept below 5 K $\Omega$ . During EEG recording, all the subjects were asked to be seated with upper-limb relaxed and minimize chewing, head movement, eye movement, and body movement.

In this experiment, FV device, in which FV produced by vibrator was driven by air pressure, was used in this study [29], as shown in Fig. 1A. FV at the frequency of 87 Hz and the amplitude of 0.28 mm was applied over the muscle belly of the antagonist's muscle to the spastic muscle (referred to the triceps) for every stroke patient (see Fig. 1B). The experiment was performed by the following procedures: (1) Before-FV (Baseline), the resting state EEG recording for 4 min; (2) the first FV stimulation (S1) with EEG recording for 3 min, during which FV was applied over the muscle belly of the triceps; (3) the second FV stimulation (S2), the same as S1; (4) the third FV stimulation (S3), the same as S2. During each phase, all the patients were asked to keep their eyes closed. Each phase was followed by a pause of about 3 min. The muscle displacement of the biceps and its antagonist in the affected limb of all the patients were measured before and immediately after three sessions of FV. The EEG recording was carried out repeatedly for three trials for all the patients. The diagram of the experimental process was shown in Fig. 2.

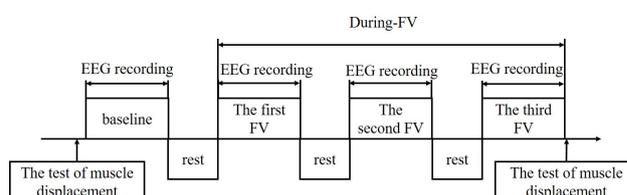
## 2.3 Data analysis

### 2.3.1 EEG analysis

The preprocessing of EEG signals was performed with EEGLAB toolbox 14.0.0b (<http://www.sccn.ucsd.edu/eeglab>). The EEG filter was set between 1 Hz and 45 Hz. The common average reference was chosen and the independent component analysis (ICA) method was used to remove the artifacts. The EEG data were divided into segments of 2 s and the power spectral density (PSD) of each segment was then estimated using Welch method (pWelch algorithm, 0.5 Hz frequency resolution, an overlapping 1-second hanning



**Fig. 1. The diagram of the experiment setup.** FV device (A) and clinical experiment (B).



**Fig. 2. The diagram of the experimental process.**

window, no phase shift). According to our previous studies [26,27], FV led to a desynchronized power at C3 or C4 for stroke patients in these sub-beta bands, including beta1 (13, 18 Hz), beta2 (18, 21 Hz), and beta3 (21, 30 Hz). Therefore, these sub-beta bands above were selected to calculate

the relative power in this study. The relative power was estimated as follows:

$$RP(f1, f2) = \frac{\int_{f1}^{f2} PSD(f1, f2)df}{\int_1^{45} PSD(1, 45)df} \quad (1)$$

where  $RP(f1, f2)$  stood for the relative power of the specified frequency band ( $[f1, f2]$ ), in which  $f1$  and  $f2$  indicated the low and high frequency band respectively. The changes of beta power at C3 and C4 in different FV phases compared to baseline were described as the motor-related power desynchronization (MRPD), which was calculated as follows:

$$MRPD_{\{S1, S2, S3\}} = \frac{RP_{\{S1, S2, S3\}} - RP_{Baseline}}{RP_{Baseline}} \quad (2)$$

The negative MRPD value, which was similar to the event-related desynchronization (ERD), reflected the activation of the sensorimotor cortex. In our study, the averaged RP and averaged MRPD in all the FV phases were calculated. To describe the diversity of the activation between the left and the right primary sensorimotor cortex (S1–M1), the difference index of the activation of bilateral S1–M1 ( $\delta_{\{\beta1, \beta2, \beta3\}}$ ) was estimated to be:

$$\begin{aligned} \delta_{\{\beta1, \beta2, \beta3\}} &= MRPD_{\{\beta1, \beta2, \beta3\}}^{C4} - MRPD_{\{\beta1, \beta2, \beta3\}}^{C3} \\ &= MRPD_{\{\beta1, \beta2, \beta3\}}^{Contra} - MRPD_{\{\beta1, \beta2, \beta3\}}^{Ipsi} \end{aligned} \quad (3)$$

where  $MRPD_{\{\beta1, \beta2, \beta3\}}^{Ipsi}$  indicated MRPD of the ipsilesional S1–M1 (also referred to S1–M1 located at the same side as the vibrated limb) and  $MRPD_{\{\beta1, \beta2, \beta3\}}^{Contra}$  indicated MRPD of the contralesional S1–M1 (also referred to S1–M1 located at the same side as the vibrated limb) in the  $\beta1$ ,  $\beta2$ , and  $\beta3$  band. The activation of ipsilesional S1–M1 was higher than that of contralesional S1–M1 according to  $\delta > 0$ , whilst the activation of ipsilesional S1–M1 was lower than that of contralesional S1–M1 according to  $\delta < 0$ .

### 2.3.2 Muscle displacement and compliance analysis

As is well known for us, the coordination of the agonist and antagonist muscles can ensure the smoothness of joint movement. As for patients with PSS, the impairment of motor function was induced by the coexistence of the weakness of the antagonist muscle and the over-activity of spastic muscle. The persistence of this phenomenon would exacerbate spasticity. Therefore, in our previous study, the index, which was used to assess the relief of spasticity, was put forward as follows [29]:

$$\lambda_{\{ext, fle\}}^{AUC\_muscle} = \frac{AUC\_muscle_{\{ext, fle\}}^{biceps}}{AUC\_muscle_{\{ext, fle\}}^{biceps} + AUC\_muscle_{\{fle, ext\}}^{triceps}} \quad (4)$$

$$\lambda_{\{ext, fle\}}^{Compliance} = \frac{Compliance_{\{ext, fle\}}^{biceps}}{Compliance_{\{ext, fle\}}^{biceps} + Compliance_{\{fle, ext\}}^{triceps}} \quad (5)$$

where  $\lambda_{\{ext, fle\}}^{Compliance}$ ,  $\lambda_{\{ext, fle\}}^{AUC\_muscle}$  represented the normalized compliance, AUC\_muscle of biceps muscle following the elbow joint's flexion and extension, respectively. The AUC\_muscle represented the area under the curve for muscle. The muscle compliance, as well as AUC\_muscle, was estimated at the force of 1–2 kg. The changes of  $\lambda_{\{ext, fle\}}^{Compliance}$  and  $\lambda_{\{ext, fle\}}^{AUC\_muscle}$  induced by FV compared to before-FV ( $\Delta\lambda_{\{ext, fle\}}^{AUC\_muscle}$ ,  $\Delta\lambda_{\{ext, fle\}}^{Compliance}$ ) were estimated as follows:

$$\Delta\lambda_{\{ext, fle\}}^{AUC\_muscle} = \lambda_{\{ext, fle\}}^{AUC\_muscle} \Big|_{after-FV} - \lambda_{\{ext, fle\}}^{AUC\_muscle} \Big|_{before-FV} \quad (6)$$

$$\Delta\lambda_{\{ext, fle\}}^{Compliance} = \lambda_{\{ext, fle\}}^{Compliance} \Big|_{after-FV} - \lambda_{\{ext, fle\}}^{Compliance} \Big|_{before-FV} \quad (7)$$

### 2.4 Statistical analysis

Using SPSS Statistics 20.0 (IBM Inc., NY, USA), the whole statistical analyses were performed. Regarding the relative power, the two-way analysis of variance (ANOVA), in which condition factors (baseline and during-FV) and location factors (ipsilesional S1–M1 and contralesional S1–M1) were considered as within-subjects factors, was carried out in all the sub-beta bands. If the assumption of sphericity checked by the Mauchy's test was significant, the degrees of freedom were adjusted. When the main effect (condition and location) or their interactions (condition  $\times$  location) was significant, post hoc comparisons were carried out to make if FV induced the significant changes in the relative power compared to the baseline phase. The regression analysis was performed to test whether the linear relation between muscle displacement and force existed. The paired-sample  $t$ -test (short for  $t$ -test later) was carried out to make sure if the significant changes in the AUC\_muscle and normalized compliance after FV occurred compared to baseline. Besides, the Pearson's correlation was carried out to determine whether the correlation between the changes in the AUC\_muscle and normalized compliance ( $\Delta\lambda_{\{ext, fle\}}^{AUC\_muscle}$ ,  $\Delta\lambda_{\{ext, fle\}}^{Compliance}$ ) among these indexes of the activation of S1–M1 in all the sub-beta bands, including the difference index of the activation of bilateral S1–M1 ( $\delta_{\{\beta1, \beta2, \beta3\}}$ ), the activation of contralesional S1–M1 ( $MRPD_{\{\beta1, \beta2, \beta3\}}^{Contra}$ ) and the activation of ipsilesional S1–M1 ( $MRPD_{\{\beta1, \beta2, \beta3\}}^{Ipsi}$ ), existed. Due to the robustness of the ANOVA under application of non-normally distributed [32,33], the Shapiro-Wilk test was used to determine whether these metrics were normally distributed when the  $t$ -test and Pearson's correlation analysis were carried out. If these metrics were not normally distributed, the  $t$ -test and Pearson's correlation analysis were replaced by

Wilcoxon signed-rank test and Spearman rank correlation analysis, respectively. The  $p$ -value's significance was set at 0.05.

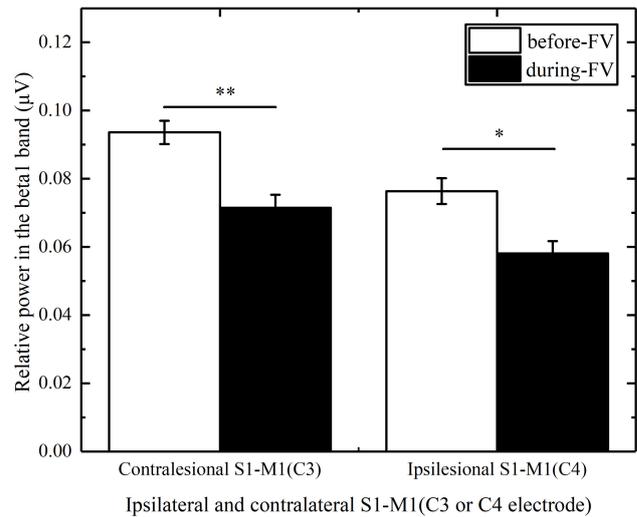
### 3. Results

#### 3.1 Relative power analysis from EEG

Regarding beta1 band, the Shapiro-Wilk test indicated that the relative power of contralateral S1-M1 in the baseline ( $p = 0.587$ ) and during-FV ( $p = 0.559$ ) phase, as well as the relative power of ipsilateral S1-M1 during FV ( $p = 0.066$ ) was normally distributed. However, the relative power of ipsilateral S1-M1 during FV was not normally distributed ( $p = 0.026$ ). Two-way ANOVA showed that the main effect condition ( $F(1,9) = 5.222, p = 0.048$ ) was significant; the main effect location and their interactions location $\times$ condition were not significant. The  $t$ -test showed that FV led to a significant decrease in the relative power of contralateral S1-M1 compared to baseline ( $p = 0.0095$ ), while the Wilcoxon test indicated a significant decrease in the relative power of ipsilateral S1-M1 during FV compared to baseline ( $p = 0.0295$ ) (see Fig. 3). Regarding beta3 band, the Shapiro-Wilk test indicated that the relative power of contralateral S1-M1 in the different phases (baseline,  $p = 0.587$ ; during-FV,  $p = 0.367$ ), as well as the relative power of ipsilateral S1-M1 (baseline,  $p = 0.055$ ; during-FV,  $p = 0.133$ ) were normally distributed. Two-way ANOVA showed that the main effect condition ( $F(1,9) = 7.926, p = 0.02$ ), as well as their interactions location $\times$ condition ( $F(1,9) = 5.775, p = 0.02$ ) was significant; the main effect location was not significant. The  $t$ -test showed that FV led to a significant decrease in the relative power of both contralateral S1-M1 and ipsilateral S1-M1 compared to baseline (ipsilateral S1-M1,  $p = 0.0115$ ; Contralateral S1-M1,  $p = 0.0485$ ) (see Fig. 4B). As for beta2 band, two-way ANOVA showed that the main effect condition ( $F(1,9) = 1.665, p = 0.229$ ), the main effect location ( $F(1,9) = 3.776, p = 0.084$ ), and their interactions location $\times$ condition ( $F(1,9) = 1.042, p = 0.334$ ) was not significant (see Fig. 4A).

#### 3.2 Muscle compliance and displacement analysis

The results from the regression analysis showed that the relationship between biceps' muscle displacement and resistance force was linear significantly following the elbow joint's flexion and extension. The Shapiro-Wilk test showed that AUC\_muscle and muscle compliance following elbow joint's flexion and extension in the before-FV and after-FV phases were normally distributed. The  $t$ -test indicated that a significant increase in the biceps' AUC\_muscle following elbow joint's flexion ( $p = 0.0055$ ), as well as  $\lambda_{fle}^{Compliance}$  ( $p = 0.0305$ ), occurred after FV (see Fig. 5). No significant changes in the biceps'  $\lambda_{ext}^{AUC\_muscle}$  and  $\lambda_{ext}^{Compliance}$  occurred after FV compared with baseline by the  $t$ -test.



**Fig. 3. The relative power of ipsilateral and contralateral S1-M1 in the beta1 band in the following two phases: before-FV and during-FV. \*** indicated  $0.01 < p < 0.05$ , \*\* indicated  $p \leq 0.01$ .

#### 3.3 The correlation analysis between the activation of S1-M1 and, muscle displacement and compliance

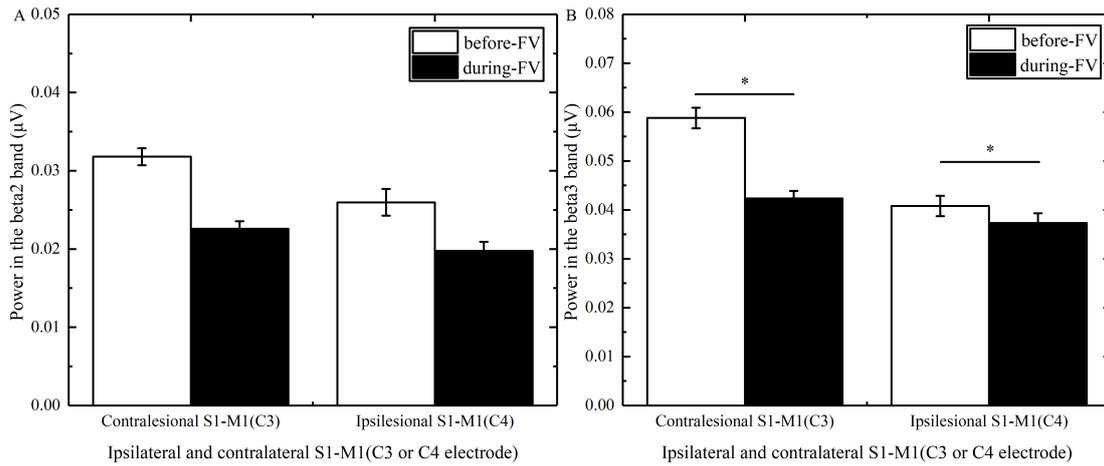
The Pearson's correlation analysis confirmed that the difference index in the beta3 band ( $\delta_{beta3}$ ) ( $r = 0.654, p = 0.02$ , see Fig. 6), had a significantly positive correlation with the changes of  $\lambda_{fle}^{Compliance}$ . The Pearson's correlation analysis also confirmed that the activation of ipsilateral S1-M1 in the beta3 band ( $MRPD_{beta3}^{Ipsi}$ ) had a significantly positive correlation with the changes of  $\lambda_{fle}^{Compliance}$  ( $r = 0.618, p = 0.0285$ ) (see Fig. 7). Besides, the Shapiro-Wilk test indicated that difference index in the beta3 band ( $p = 0.061$ ), the changes of  $\lambda_{fle}^{Compliance}$  ( $p = 0.198$ ) and  $MRPD_{beta3}^{Ipsi}$  ( $p = 0.505$ ) was normally distributed. No other significant results were found while performing the Pearson's correlation analysis.

### 4. Discussion

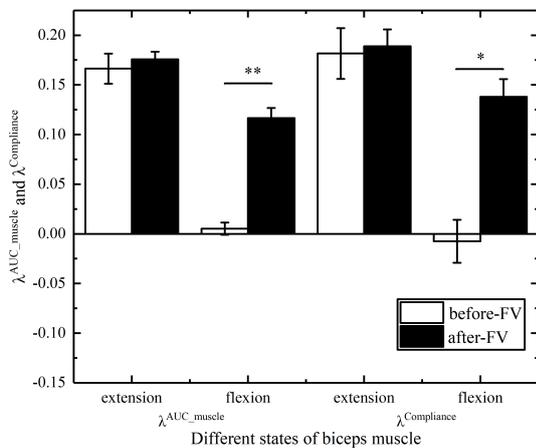
This study has explored the brain oscillatory activity correlating with the relief of spasticity following FV. The clinical experiment showed that the activation of bilateral S1-M1, as well as the increase of AUC\_muscle and muscle compliance, was induced following FV (frequency: 87 Hz; amplitude: 0.28 mm) over the antagonist muscle's belly to spastic muscle in chronic stroke patients. Importantly, the difference index of the activation of bilateral S1-M1 has a positive correlation with the increase of muscle compliance.

#### 4.1 The changes in brain oscillatory activities overlying S1-M1 induced by FV

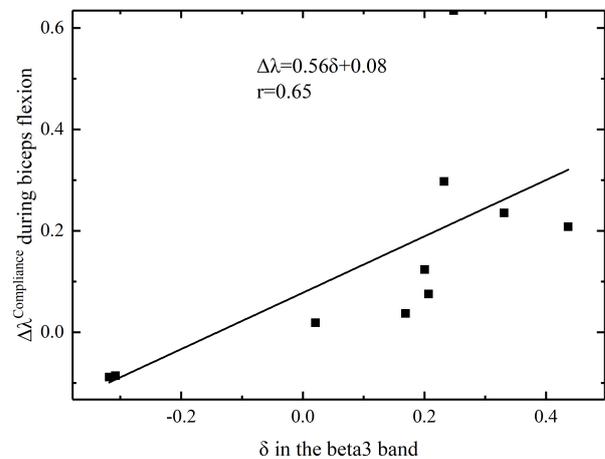
Our study has shown that FV led to the significant decrease of relative power at C3 and C4 in the beta1 band, as well as C3 and C4 in the beta3 band, which has indicated the activation of S1-M1 in several EEG-fMRI studies [19,20].



**Fig. 4.** The relative power of ipsilesional and contralateral S1-M1 in the different frequency bands: beta2 (A) band and beta3 (B) band. \* indicated  $0.01 < p < 0.05$ , \*\* indicated  $p \leq 0.01$ .



**Fig. 5.** The biceps'  $\lambda^{AUC\_muscle}$  and  $\lambda^{Compliance}$  following elbow joint's flexion and extension. \* indicated  $0.01 < p < 0.05$ , \*\* indicated  $p \leq 0.01$ .



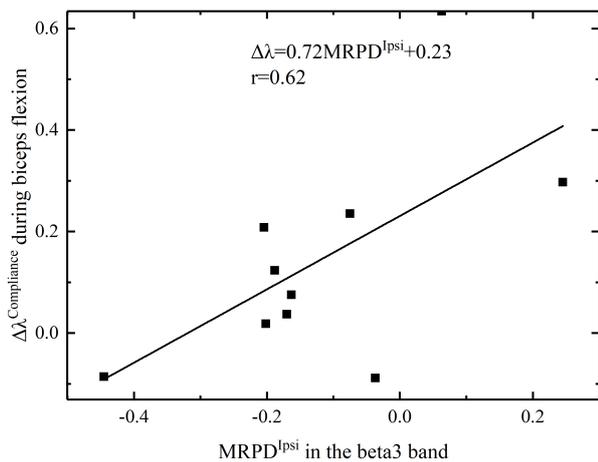
**Fig. 6.** The correlation between the difference index of the activation of bilateral S1-M1 ( $\delta$ ) and the changes of compliance ( $\Delta\lambda^{Compliance}$ ) during biceps flexion in the beta3 band.

The result was similar to the previous studies which have shown that FV can activate the S1-M1 in subacute stroke patients [26,27]. Our study further demonstrated that FV can induce the activation of bilateral sensorimotor cortex in chronic stroke patients, which has also been observed during the movement of affected hand or thumb-to-index tapping using PET [34,35], voluntary movement of the paretic limb using fMRI [36], knee flexion-extension using fMRI [37], motor imagery supination movement using EEG [38], passive movement of the affected hand using fMRI [39], the movement of the paretic hand using fMRI [40]. Especially for stroke patients with spasticity, the activation of the bilateral sensorimotor cortex was induced during imaginary finger movement with the impaired hand using fMRI [41], the passive movement of the paretic hand using EEG-fMRI [42], sequential finger movement using fMRI [43], imagery of finger movements using fMRI [44]. Therefore, FV, as a sensory stimulus, was similar to the motor task. They both

generated a proprioceptive afferent drive to induce the activation of the contralateral and ipsilesional sensorimotor cortex. The latter could be caused by the recruitment of the uncrossed corticospinal tract.

#### 4.2 The relief of PSS caused by FV

In this study, the AUC\_muscle and compliance of spastic muscle tissue increased following FV, which indicated the relief of spasticity. On one hand, non-spastic muscle's compliance and displacement were higher than that of the contralateral spastic muscle for chronic spastic stroke patients [28,45,46]. The increase in muscle compliance had also been related positively to the reduction in the MAS [30,31], which was the current standard for clinical assessment of extremity spasticity. On the other hand, muscle stiffness was the inverse of AUC\_muscle and muscle compliance [28,31]. Muscle stiffness showed a powerful correlation with the muscle tone following upper-extremity reha-



**Fig. 7. The correlation between ipsilesional S1-M1 (MRPD<sup>Ipsi</sup>) in the beta3 band and the changes of compliance ( $\Delta\lambda^{\text{Compliance}}$ ) during biceps flexion.**

bilitation programs [46]. Therefore, it could be inferred that the ease in the muscle compliance and AUC\_muscle was associated with the reduction of spasticity, although a direct clinical measurement of spasticity after antagonist stimulation is needed in further studies.

#### 4.3 The short-term effect of FV on the brain oscillatory activities correlating with the relief of PSS

The difference index of the activation of bilateral S1-M1 had a positive correlation with the changes in muscle compliance. Therefore, the short-term relief of PSS induced by FV was attributed to the cortical activation patterns. The patterns referred to the activation of bilateral S1-M1 where the activation of the ipsilesional S1-M1 was higher than that of the contralesional one. The result corresponded with one study, which showed that the increase in the activation of the bilateral sensorimotor cortex was associated with the reduction of spasticity after repetitive arm cycling following botulinum toxin injections [47]. Another study also found that the activation of the bilateral cerebral cortex for several patients was associated with the improvement of spasticity after robot-assisted arm training [6]. This further supported the viewpoint that a learning effect in bilateral cortex sensorimotor representations induced by FV contributed to improving the maladaptive cortical plasticity of spasticity, thus mitigating the spasticity for chronic stroke patients. Besides, the activation of ipsilesional S1-M1 in the beta3 band had a positive correlation with the increase of muscle compliance, which meant that the activation of ipsilesional S1-M1 contributed to the relief of spasticity. The phenomenon above also was in accord with the result from our present study.

However, some researchers have drawn different conclusions. For example, several studies have confirmed that the reduction of spasticity can be associated with the activation of the sensorimotor cortex in an “alleviating” dif-

ference direction, including a decrease in the excitability of contralesional sensorimotor cortex [41], an increase in the excitability of ipsilesional sensorimotor cortex [43,48], and a higher decrease in the excitability of contralesional sensorimotor cortex than that of the ipsilesional sensorimotor cortex [49]. The relief of spasticity could be attributed to the rebalance of abnormal interhemispheric interaction between contralesional and ipsilesional sensorimotor cortex (e.g., the increased inhibitory effect of the unaffected hemisphere on the affected hemisphere). This contributed to functional recovery after stroke [50]. However, the opposite conclusion has also appeared: the relief of spasticity correlated with the activation of sensorimotor cortex in an “aggravating (or clear)” difference direction, including an increase in the excitability of contralesional sensorimotor cortex [7], a decrease in the excitability of ipsilesional sensorimotor cortex [51], and the coexistence of the first two cases [8]. This was due to the potentially supportive evidence that increased activation in contralesional S1-M1, as an additional source of cortical organization, has played an important role in the recovery of motor function [52]. Our study combined the two explanations above: FV rebalanced interhemispheric interactions (inhibition and facilitation) by inducing the activation of bilateral S1-M1 in which the activation of ipsilesional S1-M1 was higher than that of contralesional one. This provided a new treatment guideline for stroke rehabilitation. Especially for TMS, facilitation of bilateral S1-M1, where the facilitation of the ipsilesional S1-M1 was stronger than that of the contralesional one, appeared a new effective option for motor recovery post-stroke.

The small sample size and the short duration of the experiment were limitations of this study. A large sample longitudinal study will be carried out to explore the brain oscillatory activity correlating with the relief of PSS following FV in the future.

## 5. Conclusions

To summarize, this study has demonstrated that FV over the antagonist muscle belly to the spastic muscle has a short-term positive effect on the relief of the PSS, which was evaluated by muscle properties, including AUC\_muscle and normalized compliance. These changes in these muscle properties have been correlated positively with the difference index of the activation of bilateral S1-M1. The “alleviating” difference index referring to the activation of bilateral S1-M1, where the activation of the ipsilesional S1-M1 is higher than that of the contralesional one, can be the potential mechanism of the short-term relief for chronic stroke patients. This study not only demonstrate the correlation between brain oscillatory activity and the relief of PSS, but also indicate brain oscillatory activity as a potential biomarker of the relief of PSS. The future study will focus on investigating the changes of cerebral activity correlating with the reduction of PSS following long-term

FV using EEG, which can provide a new explanation of the long-term mechanism of FV on the relief of PSS.

## Abbreviations

FV, focal vibration; PSS, post-stroke spasticity; S1-M1, primary sensorimotor cortex; ADL, activity of daily living; EEG, electroencephalogram; fMRI, functional magnetic resonance imaging; TMS, transcranial magnetic stimulation; MAS, modified Ashworth Score; ERS/ERD, event-related synchronization/desynchronization; MRPD, motor-related power desynchronization; ICA, independent component analysis; PSD, power spectral density; AUC\_muscle, area under the curve for muscle.

## Author contributions

WL, CL, and LJ designed the research study. WL and FL performed the research. QX, AL, and LM provided help and advice on the clinical experiment. WL, FL, and QX analyzed the data. WL and CL wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

This study was approved by the local ethics committees named Medical Ethics Committee of Shenzhen Nanshan People's Hospital (2018-0210-2) and Beijing Rehabilitation Hospital Affiliated with Capital Medical University (209bkkj-028). All the subjects gave written consent before participating in this study.

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## Conflict of interest

The authors declare no conflict of interest.

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