

Research paper

Motor and parietal cortex activity responses to mirror visual feedback in patients with subacute stroke: An EEG study



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ABSTRACT

Objective: To elucidate the immediate electrophysiological effects of mirror visual feedback (MVF) combined with or without touch task in subacute stroke.

Methods: Subacute stroke patients and healthy controls were recruited to participate in four grasping tasks (MVF or no MVF, combined with rubber ball or no ball) under electroencephalogram (EEG) monitoring. Event-related desynchronization (ERD) /event-related synchronization (ERS) and the lateralization index (LI) were utilized to observe the electrophysiological effects.

Results: MVF reduced ERD suppression in the contralateral primary motor cortex (M1) of stroke patients. This reduction was observed in the low mu band for the contralateral parietal cortex during pure MVF. The laterality effects in the low mu band under MVF was noted in M1 for stroke patients and in the parietal cortex for all participants.

Conclusions: MVF inhibits the excitability of the contralateral M1 for subacute stroke. MVF inhibit activities in the contralateral M1 and parietal cortex, and reestablished hemispheric balance in the low mu band.

Significance: MVF has an instantaneous effect on subacute stroke by inhibiting the excitability of the contralateral sensorimotor cortex. The attenuated ERD in the low mu band in contralateral M1 and parietal cortex may serve as biomarkers of MVF for stroke rehabilitation.

1. Introduction

Stroke is the predominant cause of adult disability and has emerged as a significant public health concern (Asakawa et al., 2017; GBD 2019 Stroke Collaborators, 2021). In spite of emerging lots of advantaged technology, upper extremity dysfunction remains one of the most challenges in stroke rehabilitation, which raises considerable concern among patients and their caregivers (Pollock et al., 2014b). As a patient-led treatment, mirror visual feedback (MVF) has been studied and applied extensively for upper extremity motor rehabilitation poststroke (Pollock et al., 2014a; Thieme et al., 2018). However, the underlying instant neural effect of MVF is still unknown in patient with subacute stroke.

During the clinical practice of MVF, a plane mirror or mirror box is

positioned in the midsagittal plane, thereby creating an optical superimposition of the mirror image of the unaffected limb onto the affected limb. Previous studies showed that MVF could improve the upper extremity function of stroke patients by remodelling the sensorimotor cortex (Deconinck et al., 2015; Nogueira et al., 2021). However, there is no consensus about the neural mechanism for MVF. A prior study demonstrated that MVF induced a shift in excitability of the precuneus towards the ipsilateral hemisphere of the moving hand (Mehnert et al., 2013). Recent studies demonstrated that visual input alone was not a powerful modulator of the somatosensory cortex, and pure MVF could not induce light touch afferent responses unless the relevant objects were incorporated into the training regimen (Makin, 2021; Arya et al., 2022). The paradigm of MVF combined with task-oriented training, which provided visual and tactile input, had been developed and

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implemented in clinical practice (Chang et al., 2019; Madhoun et al., 2020). Miller and colleagues showed that MVF combined with tool tasks could promote tactile perception (Miller et al., 2017). Despite the widespread clinical application of MVF and task-oriented MVF, the optimal MVF protocol remains to be identified. Elucidating the underlying cortical neural mechanisms associated with MVF is crucial for enhancing clinical practice.

Evidence suggested MVF mediated maladaptive neurophysiological processes, thereby mitigating the “learned non-use” phenomenon observed in the paralyzed limbs on the hemiplegic side (Ramachandran and Altschuler, 2009). Neuroplasticity can be facilitated by reinforcing immediate neurophysiological effects through repeated practice (Kleim and Jones, 2008). One previous functional magnetic resonance imaging (fMRI) study demonstrated that MVF increased activity in precuneus and posterior cingulate cortex, regions implicated in self-awareness and spatial attention (Michielsen et al., 2011). Another functional Near-Infrared Spectroscopy (fNIRS) study indicated that MVF could enhance the activation of the sensorimotor cortex of healthy individuals (Bai et al., 2020). Recently, electroencephalography (EEG), a non-invasive technique for offering superior temporal resolution for detecting transient changes in cortical activity, has been used to elucidate instantaneous brain changes under MVF (Ding et al., 2020; Fong et al., 2021).

The activation and excitation of the cerebral cortex, as evidenced by EEG signals, are commonly characterized by event-related desynchronization (ERD) and event-related synchronization (ERS), which signifies a reduction and an augmentation in the amplitude of the associated cortical activity during a resting state (Pfurtscheller and Lopes da Silva, 1999). An EEG study had previously shown that transient MVF effects were exhibited particularly in the central-parietal region, with the most significant effects observed in the right parietal area’s alpha band (Franz et al., 2016). The alpha band, located near the central sulcus, is also known as the mu band. The ERD of the mu band, referred to as mu suppression, is associated with the activation of the sensorimotor cortex (Neuper et al., 2006). Lee and his colleagues suggested that MVF facilitated cortical activation of mirror neurons and induces alterations in the lateralization index (LI), thereby promoting bilateral hemisphere balance (Lee et al., 2015). One review indicated that MVF enhanced mu suppression over the sensorimotor cortex and might ameliorate inter-hemispheric imbalances resulting from stroke (Zhang et al., 2018). In addition, previous studies have demonstrated that ERD of the low beta band (i.e., low beta suppression) could serve as a neural biomarker for MVF-induced activation of the sensorimotor cortex (Bartur et al., 2018; Fong et al., 2021). Despite numerous studies focusing on the neural mechanisms of MVF, the immediate neural electrophysiological responses of MVF on the sensorimotor cortex during the subacute phase of stroke remain poorly understood. Furthermore, there is a paucity of research examining the neural effects of combining MVF with tactile tasks which provide additional tactile sensory input.

The present study aimed to elucidate the electrophysiological activity responses of the motor and parietal cortices to MVF combined with touch task in subacute stroke patients. The mu band is further subdivided into low mu (8–10 Hz) and high mu (10–12 Hz) frequencies, with the low mu band predominantly associated with motor observation and the high mu band primarily linked to motor execution (Frenkel-Toledo et al., 2014). This research would investigate electrophysiological activities by analyzing EEG signals within the low mu, high mu, and low beta bands. Previous studies have demonstrated that the changes in cortical activity were more reliable during whole hand movements, and stroke patients exhibited reduced difficulty and enhanced stability in performance when engaging in grasping tasks (Grefkes et al., 2008; Li et al., 2020). The present study used conventional grasping for manual movement, and a sensory rubber ball grasping for active touch tasks. The study would investigate the instantaneous neural effects of stroke patients and healthy peers under four experimental tasks: (1) normal grasping with a direct view of the active hand (normal grasping), (2)

normal grasping using a sensory rubber ball with a direct view of the active hand (normal ball grasping), (3) normal grasping with a view of the mirror reflection of the active hand (MVF), (4) normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand (MVF-Ball).

2. Materials and methods

2.1. Participants

The enrolled participants included healthy individuals and stroke patients in this study. Stroke patients were recruited from the Department of Rehabilitation Medicine of three hospitals, including Fudan University Affiliated Huashan Hospital, Shanghai Jing’an District Central Hospital, and Fujian Hospital of Fudan University Affiliated Huashan Hospital. The inclusion criteria for eligible patients were as follows: (1) aged 18 to 80 years old, confirmed right-handedness according to the Chinese Classification of Handedness (Li, 1983), with normal vision or corrected vision; (2) confirmed first-time, unilateral cerebral hemorrhage/cerebral infarction by computed tomography (CT) or magnetic resonance imaging (MRI) of the head; (3) onset time between 1 week and six months with stable condition; (4) no cognitive impairment with Montreal Cognitive Assessment (MoCA) score ≥ 22 (Wang et al., 2021); (5) first-time receiving MVF; (6) Brunnstrom stage of the upper extremity and hand between stages I and IV, with the wrist and elbow major flexors muscles, including wrist flexors and biceps brachii muscle tone \leq II, evaluated by Modified Ashworth Scale; (7) able to maintain a seated position for at least 60 min. Patients with the appearance of new infarcts or large-scale cerebral infarction; or who with other severe illnesses, for example, severe coronary heart disease; or who were undergoing other neural regulation modulation techniques, such as brain-computer interface technology and transcranial electrical stimulation technology; or who suffering from metal implants or cranial defects and allergic to any device or component related to the experiment, such as conductive gel, were excluded.

Using convenient sampling for society, age-matched healthy right-handed individuals with normal or corrected-to-normal vision, no previous history of diseases involving the central nervous system, skeletal and muscular system, and other important organ injuries, and no abnormal cognitive and intellectual disabilities were enrolled. Exclusion criteria included individuals who had experienced upper limb trauma or strain disorder within two weeks prior to the experiment, those who were participating in other clinical trials concurrently, and those with allergies to any testing-related equipment or materials, such as conductive gel.

2.2. Sample size

There were no similar studies that provided the effect size. We reviewed all published EEG clinical trials on MT, and the total sample size of most studies ranged from 20 to 40 participants. Thus, the study sets the total sample size at 40, with a 1:1 ratio, including 20 patients and 20 healthy peers.

2.3. Ethics approval and consent to participate

In accordance with the Declaration of Helsinki, informed consent was obtained from all participants prior to the commencement of the experiment. The study protocol received approval from the Ethics Committee of Huashan Hospital, affiliated with Fudan University, and was registered with the Chinese Clinical Trial Registry (Registration No: ChiCTR2200066705) on December 14, 2022.

2.4. Experiment procedures

Before commencing the formal experiment, detailed instructions

were provided to each participant. In order to ensure standard experiment execution, one researcher provided experiment task training for participants prior to the experiment. A sensory rubber ball and a folding mirror box were used for the experiment.

During the experiment, continuous electroencephalography (EEG) was recorded in synchronization with the entire experimental process. All participants were instructed to remain seated and avoid blinking and moving their heads during the EEG recording. To mitigate the risk of inadvertently drawing attention or introducing additional sensory input to the hidden or resting hand, which could complicate data interpretation, electromyography (EMG) was not utilized in this study. Previous studies also showed no EMG signs of activity in the hidden hand of any participant (Debnath and Franz, 2016; Franz et al., 2016). To ensure all participants maintain a relatively consistent mental state, 5 min of rest with eyes closed preceded four experiment tasks. The specific four grasping tasks were as follows: (1) normal grasping with a direct view of the active hand (normal grasping), (2) normal grasping using a sensory rubber ball with a direct view of the active hand (normal ball grasping), (3) normal grasping with a view of the mirror reflection of the active hand (MVF), (4) normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand (MVF-Ball). The four tasks were randomly allocated for each participant to avoid order effects (figure 1). The experiment tasks used a block design. Each task included two sessions, with 30 trials per session (60 trials in total) and a 15-second rest between sessions. Each trial involved an 8-second grasping task with a 5-second close and 3-second open task. During the execution period, participants were asked to use the corresponding hand to naturally grasp the sensory rubber ball or make a grasp without the ball. Between different grasping tasks, participants were allowed a 2-minute rest to relax. During the 2-minute rest time, the researcher would prepare and introduce the next tasks for the participants.

During each grasping task, participants were asked to close and open their unaffected hand (dominant in healthy individuals) without causing any shaking of their bodies and keep their affected hand (non-dominant in healthy individuals) stationary. The grasping tasks required participants to either observe a reflected mirror image or directly view the movement of their unaffected/dominant hand, with the affected/non-dominant hand remaining at rest. Audio instructions to guide the activity tasks were delivered using the Eprime2.0 software (Psychology Software Tools, Inc., V2.0, Sharpsburg, PA, United States). The software drove the loudspeaker, which delivered an auditory prompt for 5 s to instruct participants to move their hand into a closed position, followed by a 3-second prompt to instruct them to open their hand. Upon hearing the command “grasp,” participants naturally executed a grasping motion with the corresponding hand until the closing task was completed. Conversely, when they heard the command “open,” they relaxed and opened their hands.

2.5. Measurements

One researcher documented the fundamental demographic details of the recruited stroke patients and their healthy counterparts, encompassing gender and age. Furthermore, for the stroke patients, additional clinical information was required, including the duration of the disease, type of stroke, hemisphere of brain injury, specific location of the brain injury, and the Brunnstrom stage of the upper extremity.

2.5.1. EEG acquisition

EEG data were acquired in accordance with the International 10–20 System of Electrode Placement, utilizing a 64-channel Ag/AgCl electrode cap (EasyCap, Brain Products GmbH, Germany) interfaced with a BrainAmp MR Plus amplifier (Brain Products GmbH, Germany). The brainwave signals were sampled at a frequency of 1000 Hz. The ground electrode was positioned at AFz, while FCz served as the reference electrode throughout the recording session. Electrode impedance was maintained below 5 kΩ to ensure optimal signal quality. Prior to the commencement of the experiment, a comprehensive quality check of the EEG signal was performed.

2.5.2. EEG data preprocessing

EEG signals were preprocessed using Matlab R2022b (The MathWorks) in conjunction with the EEGLAB toolbox (Delorme and Makeig, 2004). Initially, the continuous EEG data underwent high-pass filtering at 1 Hz and low-pass filtering at 30 Hz. Electrodes exhibiting poor signal quality were interpolated through a combination of automated algorithms and manual visual inspection. The data were then segmented into epochs of 10,000 ms duration, spanning from 200 ms prior to 8,000 ms following the instruction to initiate grasping. A preliminary artifact removal step was conducted on the EEG epochs, based on the criterion of EEG voltage values exceeding $\pm 500 \mu\text{V}$. Ocular and muscular artifacts were automatically identified and corrected through the application of independent component analysis (ICA). Subsequently, any residual epochs exhibiting EEG amplitudes exceeding $\pm 100 \mu\text{V}$ were eliminated to ensure the acquisition of artifact-free EEG signals. The EEG data were then re-referenced to the whole-brain average. The EEG data from stroke patients with lesions on the left side were flipped so that the right hemisphere was defined as the ipsilateral hemisphere (corresponding to the damaged hemisphere in patients with stroke). Conversely, the left hemisphere was designated as the contralateral hemisphere (corresponding to the undamaged hemisphere in patients with stroke).

2.5.3. EEG parameters analysis

Artifact-free EEG epochs were analyzed in the time–frequency domain. In this study, the event-related spectral perturbation (ERSP), which visualized the change of spectral power relative to the baseline, was initially calculated for subsequent ERD analysis. To be specific, given a total of n trials and $F_k(f,t)$ as the spectral estimation of the k th

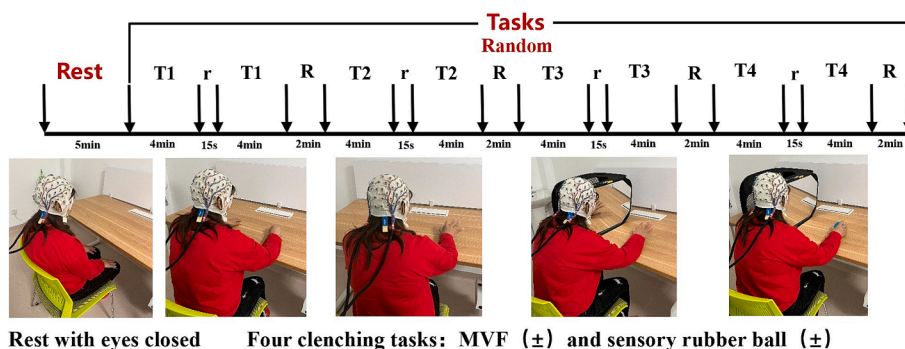


Fig. 1. Synchronous EEG acquisition for the experiment. T1-T4: represents four grasping tasks respectively; r: represents the rest period between two identical tasks; R: represents the rest period between different tasks; Random: represents the random processing of task order.

trail at frequency f and time t , ERSP was computed using the following formula:

$$\text{ERSP}(f, t) = \frac{1}{n} \sum_{k=1}^n (F_k(f, t))^2$$

Event-related desynchronization/synchronization (ERD/ERS) represents the modulation of cortical rhythm amplitude relative to a baseline reference, wherein a more pronounced ERD signifies heightened cortical activity. Conversely, ERS is posited to correspond to an inactive state or inhibition of the relevant neuronal populations (Pfurtscheller, 2001). In this study, the baseline was defined as a 500 ms interval preceding the grasping command in each trial, with the baseline band power designated as R . The time window spanning from 500 to 1500 ms after the grasping command was designated as the interval of interest to capture the execution stage, with the activity frequency band power denoted as A . The ERD/ERS value was calculated by dividing it by the baseline value after baseline subtraction, followed by an average averaging across all included trials. ERD/ERS was computed using the following formula:

$$\text{ERD/ERS} = (A - R)/R \times 100\%$$

According to the aforementioned formula, negative values of ERD/ERS signify a reduction in amplitude, which is manifested as ERD. Conversely, positive values of ERD/ERS indicate Event-Related Synchronization (ERS). This study focused on three specific bands: low mu (8–10 Hz), high mu (10–12 Hz), and low beta (13–16 Hz). Electroencephalographic (EEG) activity was analyzed at the C3/C4 and P3/P4 electrode sites, corresponding to the sensorimotor cortex in both hemispheres (Chang et al., 2023). Specifically, the C3 and P3 channels represented the contralateral primary motor cortex (M1) and parietal cortex (left hemisphere and corresponding to the undamaged hemisphere of stroke), whereas the C4 and P4 channels represented the ipsilateral M1 and parietal cortex (right hemisphere and corresponding to the damaged hemisphere of stroke).

Furthermore, the lateralization index (LI) was computed to characterize the brain lateralization of task effects, indicating the dominance of either the contralateral or ipsilateral hemisphere in specific tasks, as represented by the LI (Lee et al., 2015; Chang et al., 2019). LI was computed using the following formula: $LI = \frac{\text{ERD}_L - \text{ERD}_R}{\text{ERD}_L + \text{ERD}_R}$

ERD_R and ERD_L represent the average ERD within the specified bands of the ipsilateral hemisphere (C4 and P4 channels) and contralateral hemisphere (C3 and P3 channels), respectively. The value of LI ranges from -1 (indicating absolute dominance of the contralateral hemisphere) to 1 (indicating absolute dominance of the ipsilateral hemisphere).

2.6. Statistical analysis

Statistical analysis was conducted utilizing SPSS 25.0 for Windows (IBM SPSS Inc., USA), with GraphPad Prism 8 employed for statistical graph plotting, and the EEGLAB toolbox used for generating time–frequency plots. For clinical behavioral analysis, the Shapiro-Wilk test and Q-Q plots were applied to assess the normality of continuous data. In this study, the age variable followed a normal distribution, and descriptive statistics were presented as $\bar{x} \pm s$. Independent sample t -tests were conducted to compare two groups of age. Gender data were presented as n , and group comparison was conducted using the chi-square test (χ^2).

A three-way repeated measures analysis of variance (ANOVA) was performed independently for the low mu, high mu, and low beta bands to examine the differences in ERD/ERS and LI across the four tasks. The within-subject factors were defined as MIRROR (mirror vs. no mirror) and BALL (ball vs. no ball), while the between-group factor was defined as GROUP (stroke patients vs. healthy controls). The assumptions of normality and homogeneity of variances were evaluated using the

Shapiro-Wilk test and Levene's test, respectively. The Mauchly test is employed to assess the violation of the sphericity assumption in all ANOVA models. In instances where the sphericity assumption is rejected, adjustments are made using the Greenhouse-Geisser correction. A significance level of 0.05 was established, and post-hoc comparisons were conducted utilizing the Bonferroni correction to account for multiple comparisons.

3. Results

The study recruited twenty stroke patients and twenty healthy controls between December 2022 and April 2023. All participants completed the experiment. Following the preprocessing of EEG data, the data from one healthy participant were excluded due to insufficient clean epochs for further analysis. Consequently, the study included twenty stroke patients (mean age: 56.70 ± 14.89 years; male: female ratio = 15:5) and nineteen healthy controls (mean age: 55.58 ± 7.44 years; male: female ratio = 10:9) for the final analysis. There was no difference in age and sex between both groups. The basic and clinical information of the enrolled stroke patients was presented in Table 1.

After excluding trials with abnormal energy amplitudes, the average total number of included trials for healthy subjects in the tasks of normal grasping, normal ball grasping, MVF, and MVF-Ball were 57.32 ± 1.06 , 57.74 ± 1.15 , 57.47 ± 0.91 , and 57.11 ± 0.74 , respectively. A one-way ANOVA analysis revealed no significant differences in the number of trials between these tasks for healthy subjects. Similarly, for stroke patients, the average total number of included trials in the aforementioned tasks were 57.60 ± 1.00 , 57.55 ± 1.23 , 57.50 ± 1.85 , and 56.90 ± 2.34 , respectively, with no significant differences in trial numbers between tasks observed. According to the independent-sample t -test, there was no difference between stroke patients and healthy peers in the same tasks.

3.1. ERD/ERS results

The ERSP changes for M1 (C3 and C4 channels) and parietal cortex (P3 and P4 channels) were present in figure 2 and figure 3, respectively.

3.1.1. Primary motor cortex

The mixed-effects ANOVA of ERD/ERS on M1 was presented in supplemental table 1, and the value was shown in figure 4. For the contralateral M1, the mixed effect ANOVA showed that significant interaction effects of MVF*Group existed in the low mu, high mu and low beta bands, and significant main effects for Group and Ball conditions existed in high mu and low beta suppression ($P < 0.05$ for all). In addition, the mixed-effects ANOVA for high mu suppression revealed a significant interaction effect of MVF*Ball on the contralateral M1 ($P < 0.05$). Further analysis revealed that, in the contralateral M1, compared to the absence of MVF, ERD of all bands was significantly decreased during MVF tasks for stroke patients; when compared to the healthy, ERD on MVF tasks was decreased in stroke patients ($P < 0.05$ for all). Compared to normal grasping, high mu suppression was significantly reduced during normal ball grasping in no MVF tasks ($P = 0.001$); under no ball tasks, high mu suppression decreased during MVF compared to normal grasping ($P = 0.001$). In the contralateral M1, low beta suppression during normal ball grasping was diminished relative to normal grasping ($P < 0.05$).

For the ipsilateral M1, a mixed-effect ANOVA on high mu suppression revealed a main effect of the Ball condition and an interaction effect of MVF*Group on ipsilateral M1 ($P < 0.05$ for all). A mixed-effects ANOVA on low beta suppression demonstrated a significant main effect for the Ball condition and a significant interaction effect of MVF*Ball*Group ($P < 0.05$ for all). Subsequent significant analysis indicated that, compared to healthy individuals, stroke patients exhibited decreased high mu suppression under MVF conditions ($P < 0.05$). Compared to a normal clench, the high mu suppression observed during a normal ball clench was significantly decreased ($P < 0.05$).

Table 1
The basic and clinical information of the enrolled stroke patients.

Number	Sex	Age (years)	Disease course (months)	Stroke type	Lesional side	Lesional site	arm/hand ^a
1	male	29	3	hemorrhage	left	basal ganglia	III/III
2	male	69	6	hemorrhage	right	basal ganglia	III/IV
3	male	50	3	hemorrhage	right	basal ganglia	I/I
4	female	77	5	ischemia	left	basal ganglia	II/II
5	female	59	3	ischemia	right	corona radiata	I/I
6	male	43	3	ischemia	right	basal ganglia	IV/IV
7	male	46	3	hemorrhage	left	basal ganglia	I/I
8	male	30	6	ischemia	left	basal ganglia	III/III
9	male	77	3	ischemia	left	brainstem	II/II
10	male	54	1	ischemia	right	basal ganglia	III/I
11	female	61	1	ischemia	left	basal ganglia	III/III
12	female	55	1	ischemia	left	basal ganglia	III/III
13	male	71	2	ischemia	left	frontal/temporal/insular	III/II
14	male	76	1	ischemia	right	lateral ventricle	III/II
15	male	42	6	hemorrhage	left	basal ganglia	III/III
16	female	70	1	ischemia	left	basal ganglia	II/II
17	male	73	3	ischemia	left	thalamus	IV/IV
18	male	47	3	hemorrhage	left	basal ganglia	IV/IV
19	male	55	3	ischemia	right	basal ganglia	IV/IV
20	male	50	6	hemorrhage	right	basal ganglia	III/III

^a Brunnstrom stage of the upper extremity.

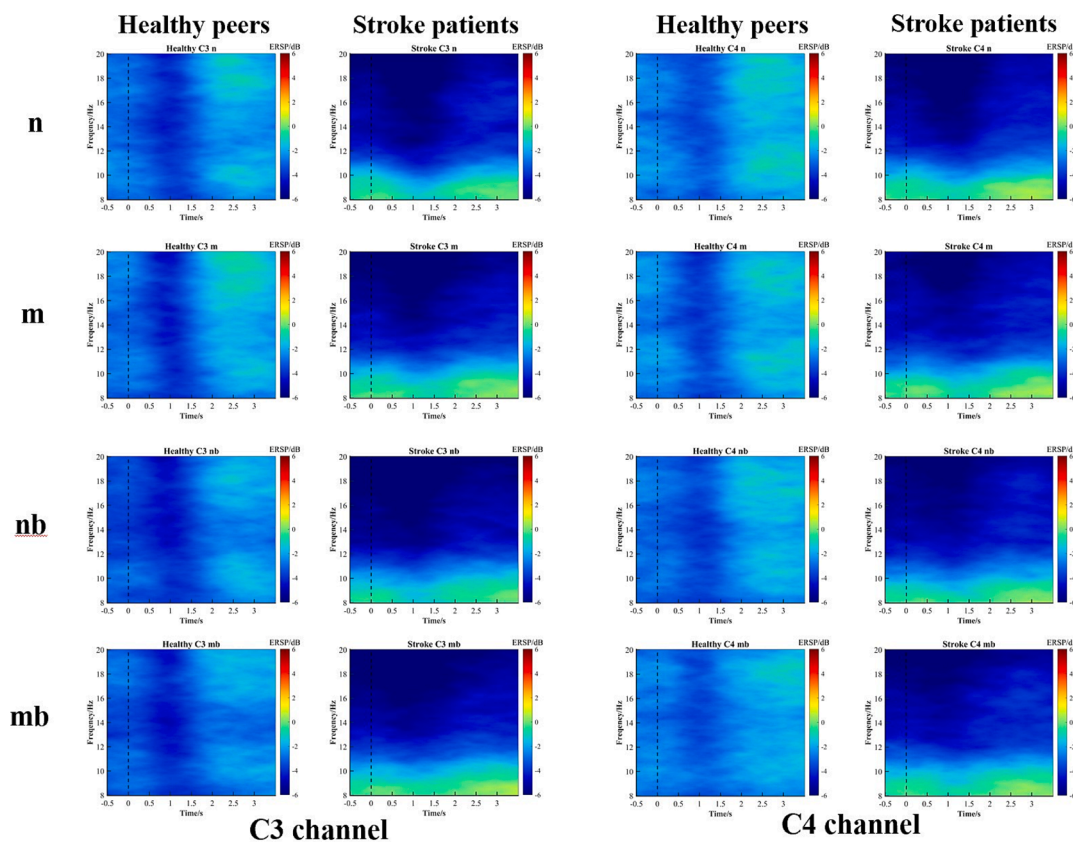


Fig. 2. The ERSP changes of the primary motor cortex (C3 and C4 channels) under four grasping tasks. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

3.1.2. Parietal cortex

The mixed-effects ANOVA of ERD/ERS on the parietal cortex were presented in [supplemental table 2](#), and the value was showed in [figure 5](#). There were no significant effects were found in the ipsilateral parietal cortex for all bands. For the contralateral parietal cortex, the mixed-effects ANOVA indicated a significant interaction effect of MVF*Group*Ball on the contralateral parietal cortex concerning low mu suppression, and significant main effects of Group were observed in high

mu and low beta suppressions ($P < 0.05$ for all). In addition, the mixed effect ANOVA on low beta suppression showed significant main effects on Ball condition ($P = 0.045$). Further analysis of the low mu suppression identified significant two-factor interaction effects within the stroke patient, normal grasping and MVF conditions, respectively ($P < 0.05$ for all). Subsequent analysis revealed that, in comparison to normal grasping, stroke patients exhibited elevated ERD/ERS values during MVF, and this metric was also elevated when compared to healthy

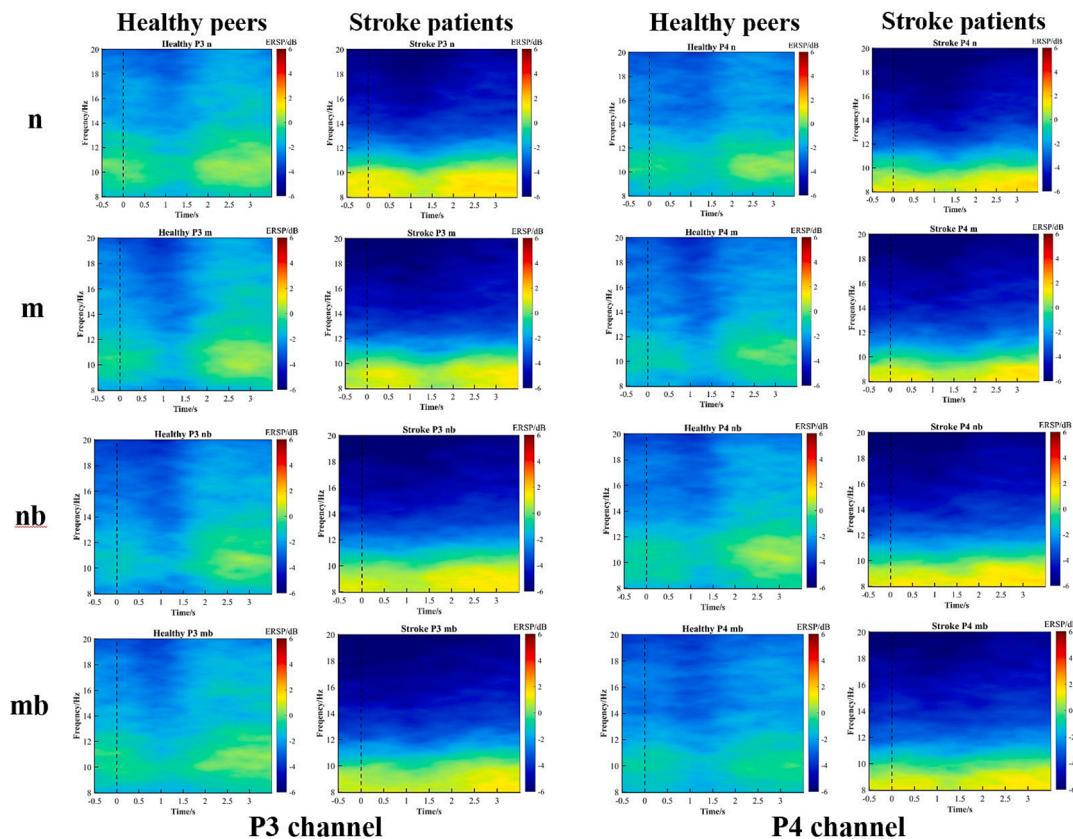


Fig. 3. The ERSP changes of the parietal cortex (P3 and P4 channels) under four grasping tasks. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

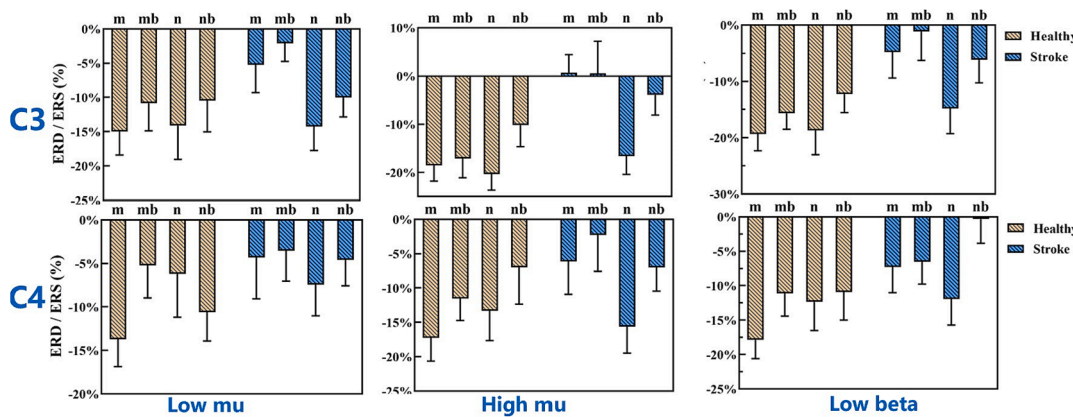


Fig. 4. ERD/ERS value in the motor cortex for grasping tasks. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

controls ($P < 0.05$ for all). Compared to the healthy, high mu and low beta suppressions of the contralateral parietal cortex were decreased in stroke patients ($P < 0.05$ for all). Compared to normal grasping, a decline of low beta suppression was found when participants received normal ball grasping ($P < 0.05$).

3.2. Lateralization results

3.2.1. Primary motor cortex

The mixed-effects ANOVA of LI on the M1 were presented in [supplemental table 3](#), and the value was showed in [figure 6](#). The analysis of

LI for the M1 revealed a significant interaction effect on $MVF \times Group$ in the low mu band ($P = 0.043$). Post-hoc Bonferroni analysis indicated that, compared to no MVF, stroke patients showed a statistically significant change in LI from negative (LI = -0.162) to positive (LI = 0.099) when receiving MVF tasks ($P = 0.032$).

3.2.2. Parietal cortex

The mixed-effects ANOVA of LI on the parietal cortex were presented in [supplemental table 4](#), and the value was showed in [figure 7](#). The mixed effect ANOVA showed that significant main effect of MVF and interaction effect of Ball \times Group were existed in the low mu band, and an

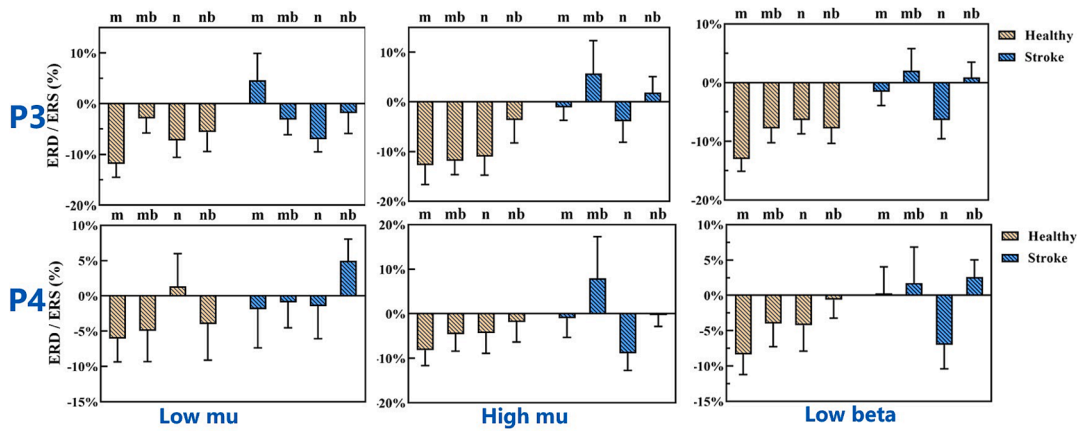


Fig. 5. ERD/ERS value in the parietal cortex for grasping tasks. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

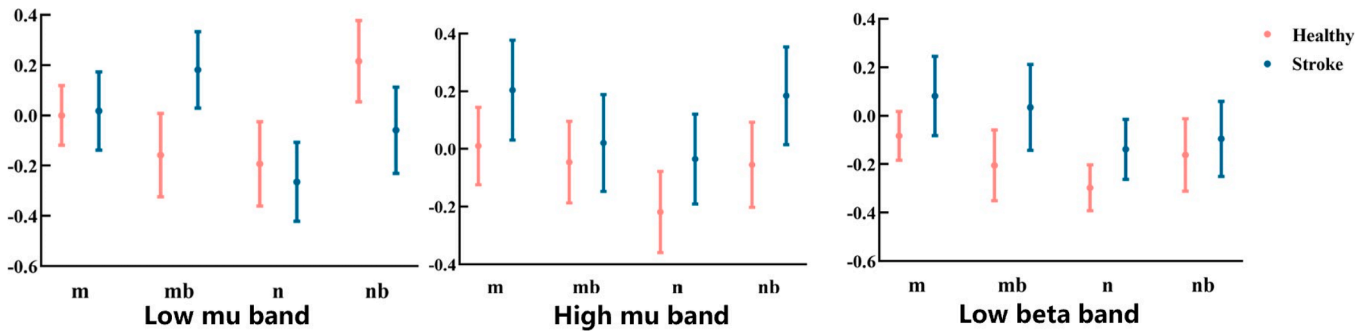


Fig. 6. LI in the primary motor cortex. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

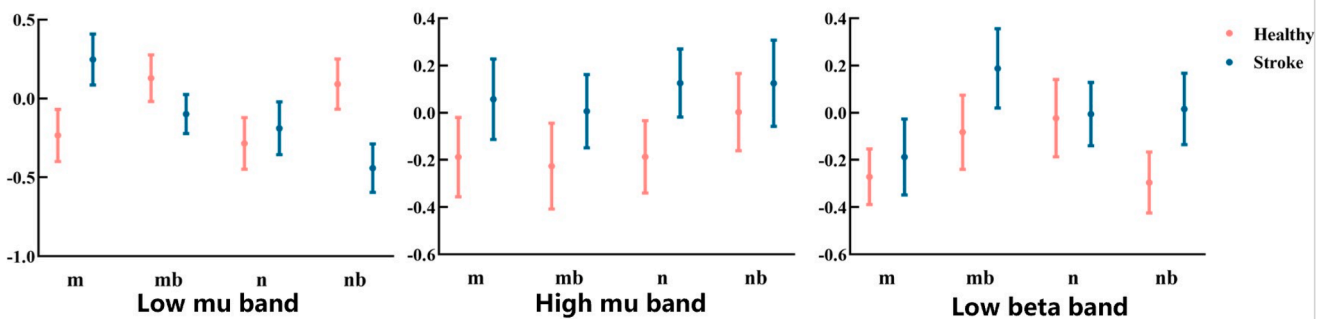


Fig. 7. LI in the parietal cortex. n: represents normal grasping with a direct view of the active hand; m: represents normal grasping with a view of the mirror reflection of the active hand; nb: represents normal grasping using a sensory rubber ball with a direct view of the active hand; mb: represents normal grasping using sensory rubber ball with a view of the mirror reflection of the active hand.

interaction effect of Mirror*Ball was detected in the low beta band for the parietal cortex ($P < 0.05$ for all). The post-hoc Bonferroni analysis showed that compared to no MVF, the LI of MVF tasks changed from negative (LI = -0.206) to positive (LI = 0.011) within the low mu band ($P = 0.027$) with significance ($P < 0.05$). In the low mu band, healthy subjects exhibited a significantly higher LI (LI = 0.110) during normal ball grasping tasks compared to stroke patients (LI = -0.270). Additionally, in healthy subjects, there was a statistically significant alteration in LI from negative (LI = -0.259) to positive (LI = 0.110) during normal ball grasping tasks as opposed to normal grasping ($P < 0.05$).

4. Discussion

The present study investigated the instantaneous electrophysiology effects of low mu, high mu, and low beta bands in the M1 and parietal cortex during four grasping tasks between stroke patients and healthy counterparts. The findings revealed significant MVF effects in stroke patients, which inhibited the excitability of the contralateral M1 across all bands, as well as the contralateral parietal cortex specifically in the low mu band. The current study demonstrated the phenomenon of lateralization in the low mu band during MVF, characterized by a shift in M1 activation towards the affected hemisphere and an enhancement of

parietal cortex activation towards the ipsilateral hemisphere across all participants.

Stroke is a type of vascular-induced localized brain damage that affects neurons in areas adjacent to or distant from the injured region via changes in their neuronal networks, consequently resulting in diverse motor control impairments (Platz et al., 2000; Shimizu et al., 2002). One previous review showed that the EEG signals of stroke patients during motor preparation and execution exhibited significant differences compared to those of healthy individuals (Monge-Pereira et al., 2017). Many studies showed that compared to the healthy, stroke patients exhibited less bilateral brain activation when performing tasks (Stępień et al., 2011; Chang et al., 2019). The results of the present study were similar to these previous observations. Specifically, this study revealed that stroke patients, in contrast to their healthy counterparts, exhibited diminished high mu suppression in the affected M1 during MVF, and showed decreased excitability in the affected M1 during normal ball grasping. These phenomena may be attributed to alterations in neuronal function within the brain regions compromised by the stroke. Furthermore, stroke patients demonstrated diminished activation in the unaffected parietal cortex, specifically in the high mu and low beta bands, relative to healthy controls during ipsilesional hand activities. Additionally, during MVF tasks, stroke patients exhibited decreased low mu suppression in the unaffected parietal cortex and reduced excitability across three bands in the unaffected M1 compared to healthy individuals. The attenuated ERD observed in stroke patients suggested reduced cortical activity in the unaffected hemisphere relative to healthy individuals. This phenomenon might be linked to the minor dysfunction observed in the ipsilesional hand post-stroke and warranted further investigation (Metrot et al., 2013; van Dokkum et al., 2018).

The study results demonstrated significant effects of MVF on stroke patients. Specifically, during MVF tasks, the ERD/ERS values in three frequency bands—low mu, high mu, and low beta—within the C3 channel were elevated in stroke patients compared to conditions without MVF. This increase suggested that MVF might inhibit the excitability of the contralateral M1 in stroke patients. The interhemispheric competition model suggested that stroke-induced damage to one hemisphere disrupted the equilibrium of hemispheric interactions. It further hypothesized that inhibiting activity in the unaffected hemisphere might enhance recovery by alleviating the pathological inhibition exerted on the affected hemisphere (Jones et al., 2013; Di Pino et al., 2014). Previous studies showed that the contralateral brain was in a state of hyperactivation in the acute and subacute stroke (Manganotti et al., 2002; Shimizu et al., 2002; Bütefisch et al., 2003), which has been found a negatively correlation with poststroke motor recovery (Ward et al., 2003). Additionally, the patients included in the study had experienced stroke onset within the past six months and were all in the subacute phase of stroke. Thus, the inhibition of MVF on the activation of the contralateral hemisphere might be advantageous for stroke rehabilitation. A recent study demonstrated that MVF elicited significant mu suppression in both the ipsilateral M1 and parietal lobe (Chang et al., 2023). However, our findings diverged from those of the aforementioned study. This discrepancy may be attributed to the fact that the majority of patients in the previous study were in the chronic phase of stroke, whereas our study primarily included patients in the subacute phase. Additionally, variations in MVF paradigms could have influenced neural activation outcomes.

The present study significantly observed reduced low mu suppression under MVF conditions. In comparison to conventional grasping, stroke patients exhibited a diminished low mu suppression in the contralateral parietal cortex during MVF. Additionally, within the low mu band, MVF facilitated the activation of the M1 towards the ipsilateral hemisphere in stroke patients and induced lateralized activation of the parietal cortex across all subjects. These findings indicate that MVF inhibited the suppression of low mu band in the contralateral motor and parietal cortices, thereby promoting a balance in hemispheric interactions. Previous EEG studies have demonstrated that MVF facilitated

the equilibrium of bilateral hemispheric activity, which was advantageous for stroke rehabilitation (Bartur et al., 2018; Zhang et al., 2018). Our results were similar to the aforementioned results. The ERD attenuation in the low mu band within the contralateral hemisphere may serve as a biomarker for MVF effects in subacute stroke patients. Saleh et al. demonstrated that the activation of the motor cortex during MVF may be attributed to the engagement of the action observation network (Saleh et al., 2017). The low mu suppression was considered to be associated with motor observation (Frenkel-Toledo et al., 2014), indicating that motor observation significantly contributed to the neural mechanisms underlying MVF.

The study showed neurophysiological effects associated with ball grasping tasks. The findings indicated a general reduction in ERD suppression of bilateral M1 in the low beta and high mu bands during these tasks, compared to normal grasping. This phenomenon may be attributed to the constraints imposed by the rubber ball used in the tasks. Furthermore, the ball grasping tasks provided active tactile sensory input, which is believed to enhance motor preparation and control, thereby facilitating task execution (Beudel et al., 2011; Arbuckle et al., 2022). A prior study demonstrated that the integration of subthreshold vibration stimulation with motor training led to a reduction in ERD suppression within the primary motor cortex and enhanced manual dexterity activities in stroke patients, with a significant correlation observed (Schranz et al., 2022). Previous researches have demonstrated that increased ERD in the sensorimotor cortex during activities in stroke patients was associated with elevated demands on pyramidal neuron concentration and excitatory drive. This finding implies that increased ERD was correlated with the complexity and successful execution of task performance (Platz et al., 2000; Monge-Pereira et al., 2017). In the parietal cortex, normal ball grasping tasks, as compared to standard grasping tasks, resulted in a reduction of low beta band suppression on the contralateral side and promoted an activation bias towards the ipsilateral hemisphere in the low mu band in healthy subjects. These observations suggest that normal ball grasping tasks may induce alterations in excitability across both hemispheres of the parietal cortex. Moreover, the observed variations in ERD suppression across different bands during the ball grasping task may reflect intricate neural dynamics within the sensorimotor cortex. This underscores the necessity for further research to elucidate their potential implications for upper extremity motor rehabilitation following stroke.

The study showed that a significant interaction effect of MVF*Ball was found in the LI within the low beta band. The interaction effect might suggest that MVF had an impact on the tactile sensation, which deserves further investigation. In contrast to MVF, the MVF-Ball paradigm offers an additional tactile stimulus. However, no difference was found in post-hoc Bonferroni analysis, which indicated that compared to MVF, no additional neural effects associated with MVF-Ball. A prior study demonstrated that incorporating functional electrical stimulation with MVF resulted in greater activation of the sensorimotor cortex compared to MVF alone (Wang and Luo, 2022). Furthermore, our previous research has indicated that multisensory integration facilitated by MVF can augment the subjective perception of embodiment (Ding et al., 2020). The results of this study were different with those of previous research. The lack of statistically significant differences may be attributable to the relatively small sample size employed in this study.

The present study had several limitations. Firstly, the sample size was relatively small, potentially restricting the generalizability of the findings. Consequently, the results should be interpreted with caution. Secondly, the study did not account for hemispheric differences in the analysis of ERD suppression, as this was beyond the scope of the current investigation. Future research should address this aspect to provide a more comprehensive understanding. Finally, as a cross-sectional study, our investigation was limited to observing the immediate neural activation effects of MVF in patients with subacute stroke. Nonetheless, the implications of this activation, particularly the potential role of neural markers in long-term stroke rehabilitation and prognosis, warrant

further exploration.

5. Conclusions

In summary, the present study demonstrates that MVF inhibits the excitability of the contralateral M1 in patients with subacute stroke. MVF inhibits activities in both the contralateral M1 and the parietal cortex, and promote hemispheric balance in the low mu band for stroke patients. The findings underscore the attenuation of ERD in the low mu band within both the contralateral M1 and the parietal cortex during MVF, which may be biomarkers for subacute stroke rehabilitation.

CRediT authorship contribution statement

Jie Jia was involved in the initial study design; Jinyang Zhuang and Xiyuan Lei participated in the experiment intervention and assessment; Jinyang Zhuang, Xiyuan Lei and Xiaoli Guo were involved in data acquisition and analysis; Jinyang Zhuang wrote the main manuscript text; Xiyuan Lei, Xiaoli Guo, Li Ding and Jie Jia reviewed and edited the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cnp.2024.12.004>.

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