Butet *et al.*
Journal of NeuroEngineering and Rehabilitation (2025) 22:67
https://doi.org/10.1186/s12984-025-01598-9

Journal of NeuroEngineering and Rehabilitation

RESEARCH Open Access

EEG-fMRI neurofeedback versus motor imagery after stroke, a randomized controlled trial

Simon Butet[1†], Mathis Fleury[2,3†], Quentin Duché[2,3], Elise Bannier[2,4,5], Giulia Lioi[6], Lou Scotto di Covella[2,3], Emilie Lévêque-Le Bars[1], Anatole Lécuyer[7], Pierre Maurel[2,3*] and Isabelle Bonan[1,2]

Abstract

Neurofeedback (NF), an advanced technique enabling self-regulation of brain activity, was used to enhance upper limb motor recovery in chronic stroke survivors. A comparison was conducted between the efficacy of NF versus motor imagery (MI) training without feedback. We hypothesized that employing a bimodal EEG-fMRI based NF training approach would ensure precise targeting, and incorporating progressive multi-target feedback would provide a more effective mean to enhance plasticity. Thirty stroke survivors, exhibiting partial upper-limb motor impairment with a Fugl-Meyer Assessment Upper Extremity score (FMA-UE) > 21 and partially functional corticospinal tract (CST) were randomly allocated to the NF and MI groups. The NF group (n = 15) underwent a bimodal EEG-fMRI NF training focused on regulating activity in ipsilesional motor areas (M1 and SMA), while the MI group (n = 15) engaged in MI training. Demographic and stroke clinical data were collected. The primary outcome measure was the post-intervention FMA-UE score. Change in bold activations in target regions, EEG and fMRI laterality index (LI) and fractional anisotropy (FA) asymmetry of the CST were assessed after the intervention in both groups (respectively ΔEEG LI, ΔMRI LI and ΔFA asymmetry) and correlated with FMA-UE improvement (ΔFMA). Participants from both groups completed the 5-week training, with the NF group successfully modulating their brain activity in target regions. FMA-UE improvement post-intervention tended to be higher in the NF group than in the MI group ($p = 0.048$), and FMA-UE increased significantly only in the NF group ($p = 0.003$ vs $p = 0.633$ for MI). This improvement persisted at one-month in the NF group ($p = 0.029$). Eight out 15 patients in the NF group positively responded (i.e., improved by at least for 4 points in FMA-UE) compared to 3 out 15 in the MI group. No significant between-group differences were found in the evolution of ipsilesional M1 ($t = 1.43$, $p = 0.16$) and SMA ($t = 0.85$, $p = 0.40$) activation maps. The NF group exhibited a more pronounced lateralisation in unimodal EEG LI ($t = -3.56$, $p = 0.0004$) compared to the MI group, but no significant difference was observed for MRI LI. A non-significant difference in ΔFA asymmetry of the CST between the two groups was found ($t = 25$; $p = 0{,}055$). A non-significant correlation between unimodal ΔEEG LI and ΔFMA ($r = 0.5$; $p = 0.058$) was observed for the NF group. Chronic stroke survivors can effectively engage themselves in a NF task and can benefit from a bimodal EEG-fMRI NF training. This demonstrates potential for NF in enhancing upper-limb motor recovery more efficiently than MI training.

Keywords Stroke, Real-time fMRI, Bimodal neurofeedback, Motor cortex, CST, Upper-limb

[†]Simon Butet and Mathis Fleury have contributed equally to this work.

*Correspondence:
Pierre Maurel
pierre.maurel@irisa.fr
Full list of author information is available at the end of the article

Introduction

Stroke is the leading cause of severe adult acquired disability [1]. Upper limb paresis is highly prevalent after stroke, affecting 55 to 75% of stroke patients, thus comprising autonomy and daily functioning [2]. Consequently, motor recovery emerges as a major rehabilitation issue [3]. While traditional interventions for motor recovery have focused on stimulating upper limb movement, strategies targeting direct modulation of the brain have emerged, including the promising avenue of cerebral training with neurofeedback (NF).

NF aims at guiding the subject to self-regulate brain activity in chosen targets with high potential for motor upper limb (UL) motor recovery, thereby fostering neural plasticity and facilitating functional improvements [4, 5]. Electroencephalography-NF (EEG-NF) has first emerged as a valuable technique for recording brain activity and delivering feedback to patients undergoing UL rehabilitation following stroke [6]. However, this technique is limited by its suboptimal spatial resolution with standard number of electrodes. Conversely, MRI offers high spatial resolution but lower temporal resolution. The combination of these 2 techniques appeared promising. Thus, our research group was among the pioneers in developing a platform enabling simultaneous bimodal EEG-fMRI-NF [7]. This bimodal NF, demonstrated in healthy subjects, elicited increased brain activity in the cerebral target compared to unimodal NF [8]. Encouragingly, three EEG-fMRI-NF studies (including one of our team) involving stroke patients, were identified by recent systematic reviews, all of which have shown promising clinical benefits [9, 10]. However, these studies were limited by small sample size and intensity of their rehabilitation protocols.

Beside the recording of brain activity, selecting the appropriate NF brain target is crucial. Many studies advocate for stimulating activity in the ipsilesional primary motor cortex (M1) as the optimal approach for recovery [11]. Patients who maximally benefit from a stimulation of M1 are those with the strongest potential for recovery [12–14]. In more severely affected patients, outcomes from M1 stimulation are less convincing and the ipsilesional premotor and supplementary motor area (SMA) may offer an effective alternative for motor function relearning [15]. Thus, in a previous study, we implemented a multi-target EEG-fMRI-NF approach guiding patients from SMA to M1 activations, observing promising results specifically in patients with a partially functional cortico-spinal tract (CST) [16]. Consequently, we selected patients with partially functional CST in the present study. Finally, recognizing the necessity for an easily applicable and adequately intensive training regimen, we proposed a protocol comprising alternating bimodal (EEG-fMRI) NF and unimodal (EEG only) NF sessions, tested in a preliminary study with encouraging results [16].

The primary aim of this randomized controlled trial was to assess whether NF training was more effective than MI without feedback in improving UL motricity. To achieve this randomized controlled study, we relied on our previous experiences and implemented the same protocol to our previous experiences, with evolving targets (from SMA to M1) and alternating bimodal EEG-fMRI NF sessions and unimodal EEG NF sessions in chronic stroke patients with preserved CST. This protocol was compared to a training regimen of equivalent duration and intensity based on MI training without feedback, which has previously shown efficacy for upper limb recovery after stroke in combination with traditional rehabilitation [17]. The secondary aim was to compare the effects of training (NF and MI) on cerebral activations and investigate the relationships between changes in cerebral activations and motor recovery.

We hypothesized that our NF protocol would be more effective than MI without neurofeedback for UL motor recovery because NF would prompt participants to self-generate cerebral activity in the ipsilesional M1 and SMA, the most effective targets for patients with preserved CST [18]. Our second hypothesis was that patients who could learn to self-activate SMA and M1 during bimodal NF could be able to utilize their training strategy acquired during the bimodal training when training with unimodal sessions. Finally, we anticipated greater brain activations in the ipsilesional SMA and MI and more globally more pronounced relateralization towards the ipsilesional hemisphere in the NF group compared to the MI group, especially in patients showing motor improvement. Additionally, we assessed changes in fractional anisotropy (FA) asymmetry index of the CST to evaluate structural changes.

Material and methods

CRED-NF checklist is available in supplementary material (CRED NF-checklist [19]).

1. Study design

This simple-blind, single-center, randomized controlled trial (ClinicalTrials.gov: NCT03766113) was conducted from January 2019 to July 2022 at the Physical Medicine and Rehabilitation Department of Rennes University Hospital in France. The trial compared a Neurofeedback (NF) group receiving EEG-fMRI-NF targeting ipsilesional brain motor areas, with a Motor Imagery (MI) group undergoing MI training of hemiplegic upper limb. The primary outcome was the change in upper limb

Fugl-Meyer assessment (FMA-UE) from the beginning to the end of the intervention. Additionally, we evaluated the impact on brain activity, using task-based fMRI and EEG and on brain structure, focusing on the corticospinal tract. The study was approved by the Institutional Review Board. Patients were enrolled by a physician through a secure, web-based centralized data entry system. Randomization was performed by a software module (Ennov-clinical) and was stratified based on age, gender, and Fugl-Meyer Assessment Upper Extremity (FMA-UE) score (more impaired, ≤ 32; less impaired, > 32).

The sample size was calculated based on the main hypothesis that the NF intervention would be superior to MI in improving motor impairment than MI. Using preliminary results [20] comparing the change in the FMA-UE score between the NF and MI groups, with a mean difference in score change of 25 and a variance ratio of 1.5, and assuming an alpha risk of 5% and statistical power of 80%, a total of 36 patients, with 18 participants per group were required.

2. Inclusion criteria

Participants were aged from 18 to 80 years old with unilateral supratentorial stroke occurring more than 6 months prior to inclusion (ischemic or haemorrhagic). They presented no cognitive disorders limiting participation, an upper-limb motor score between 22 and 53 out of 66 on the FMA-UE (defined as poor to notable), and corticospinal tract integrity defined by a fractional anisotropy (FA) asymmetry index > 0.15. [21].

Exclusion criteria included MRI contraindications, major vascular leukopathy on MRI, and a history of previous neurological illness. Participants deprived of freedom or with legal incapacity were not included. Informed consent was obtained from all participants, and procedures followed the guidelines outlined in the Declaration of Helsinki.

3. Study protocol

The training program lasted 5 weeks with 4 assessments at the CHU of Rennes, both groups receiving an equal number of sessions (i.e. 14 training sessions). All participants were allowed to undergo their usual rehabilitation program with their physiotherapist but specific upper limb rehabilitation therapies (constraint induced therapy, mental imagery and mirror therapy) and botulinum toxin injections in the upper limb were not allowed during the protocol. The protocol included 4 assessment visits collecting clinical and brain data:

Inclusion, pre-intervention, post-intervention, and 1-month later (Fig. 1A).

- *Enrolment*: FMA-UE and demographic data were collected by a physician (SB). MRI with 3DT1, T2 Flair, blood-oxygen-level-dependent (BOLD) during motor imagery task of hemiplegic upper limb and diffusion-weighted imaging (DWI) was performed. Tractography of the corticospinal tract was performed and the asymmetry index measurement was calculated using MedInria software (RRID:SCR_001462 https://med.inria.fr). Then, if inclusion criteria were met, participants were randomized in NF or MI group (Fig. 1B).
- *Pre-intervention*: FMA-UE and other motor impairment data, activities and autonomy were evaluated. MRI with 3DT1, T2 Flair, BOLD (during NF task) and DWI.
- *Post-intervention*: Same clinical evaluations comprising motor impairment, activities and autonomy were repeated during the week after the NF training MRI: 3DT1, T2 Flair, BOLD (during NF or motor imagery task according to the group) and DWI.
- *1-month later*: Same clinical evaluations were repeated.

In the NF group, the protocol consisted of 5 bimodal sessions involving real-time EEG and functional magnetic resonance imaging (fMRI) NF, along with 9 unimodal EEG-NF sessions. In the MI group, patients underwent 14 sessions of motor imagery (MI) training with EEG recording without NF (Fig. 1B).

4. Interventions

A. Neurofeedback

- Bimodal EEG-fMRI NF sessions (n = 5)

Patients were fitted with a 64-channel MRI-compatible EEG headset (Brain Products GmbH, Gilching, Germany). A conductivity gel was placed in each electrode and impedance was checked. The patient then laid down in the MRI and could view the instructions and the feedback on a screen (for more details about the setup see Paper from Lioi and colleagues [16]).

For each bimodal NF session (NF group), the protocol included a calibration step, where the region of interest (ROI) for the NF was defined [16], and three NF training runs (5 min 20 s each). Each NF run consisted of periods of rest (20 s) alternated with periods of closed-loop NF training (20 s). Instructions for NF oriented the patients towards a technique of kinaesthetic motor imagery, without mentioning a specific strategy. Instructions were repeated before each training session.

The feedback i.e. the NF score was presented online as a vertical gauge. It was computed and updated every

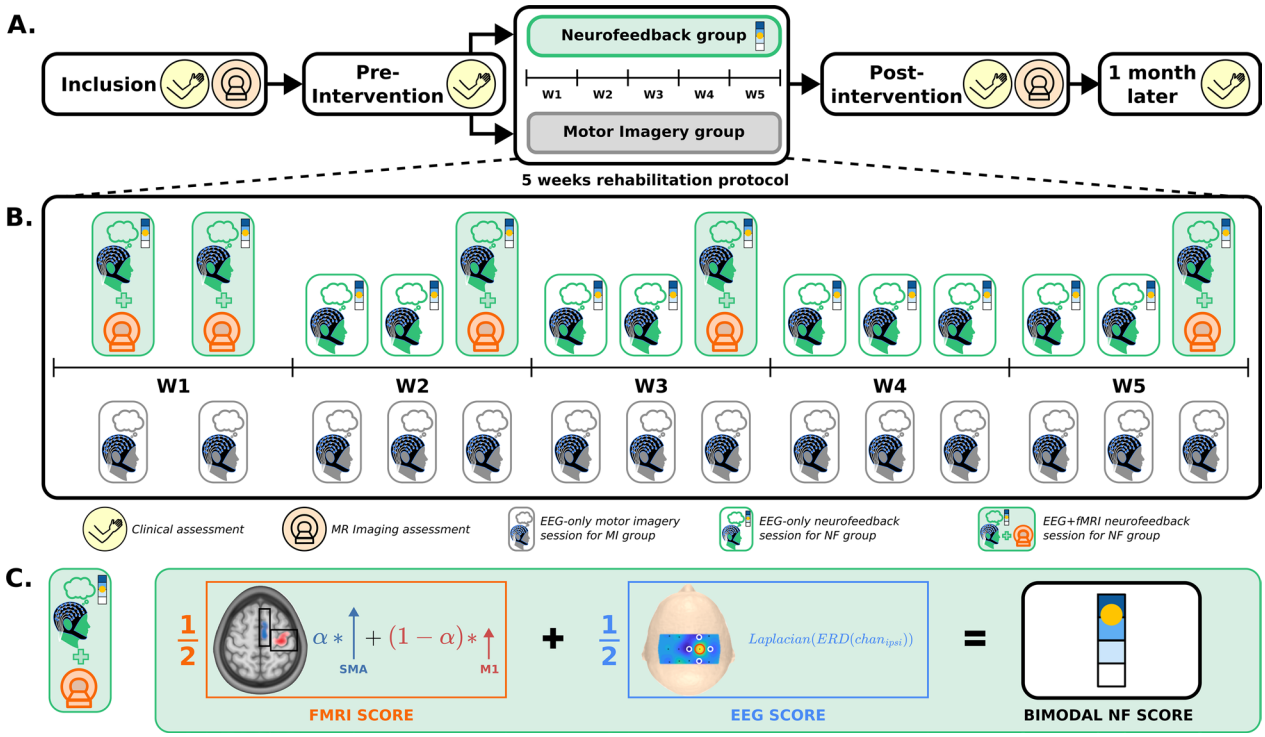

Fig. 1 Study design. **A** Participants had 4 assessment visits: they were recruited and randomly assigned either to the neurofeedback (NF) group or the motor imagery (MI) group. **B** Protocol with 14 training sessions over five weeks for both groups. The NF group alternated between 5 bimodal NF sessions (EEG/MRI) and 9 unimodal sessions (EEG alone). The MI group had 14 identical sessions of motor imagery without feedback. MI patients were equipped with a EEG cap for posterior analysis only. **C** Details regarding the calculation of the NF score in the bimodal NF sessions. The fMRI NF subscore is a weighted (α) sum of brain activity in SMA and in M1 while the EEG NF subscore is the Laplacian of the ERD of the ipsilesional channel. The bimodal NF score is the mean of fMRI and EEG unimodal subscores. The α weight decreases linearly from 0.6 to 0.2 during the protocol to progressively give more importance to the activity in M1 relatively to SMA in the calculation of the feedback

250 ms for EEG and every 1 s for fMRI. It was equal to the average of EEG NF subscore and fMRI NF subscore, computed as follows:

- The fMRI subscore was equal to the weighted sum of BOLD activations in SMA and M1 regions of interest (ROIs). The weights assigned to the two contributions SMA and M1 varied linearly from $\alpha = 0.6$ in the first session favouring SMA activity to $\alpha = 0.2$ in the last session where the fMRI NF score was mainly guided by M1 activity (Fig. 1C).
- The EEG subscore was obtained computing the Event Related Desynchronization (ERD) on a combination of electrodes given by Laplacian filter weights for the two first sessions and then by Common Spatial Pattern (CSP) weights estimated from previous training sessions.

Details about the protocol were identical to those previously published [8, 16].

- Unimodal EEG-NF sessions (n = 9)

Patients were fitted with an 8-channel EEG headset (ANT Neuro, eego mini), in a quiet room, with feedback visualization. Similarly, to the bimodal sessions, the unimodal EEG-NF sessions began by a calibration period followed by three NF runs with a block-design alternating rest and task during 5 min, with an amount of training time and protocol structure equivalent to the bimodal training sessions. The preprocessing steps involved resampling the EEG signals to 512 Hz and applying a band-pass filter with a range of 8–30 Hz. To eliminate interference at 50 Hz, a notch filter was used. Furthermore, potential eye blinks and muscle artifacts were removed from the signals to ensure data quality.

For the online computation of the unimodal NF score, a pipeline was implemented in order to favour changes in laterality of motor brain activity. It involved the extraction of band powers from the ipsilesional and contralesional channels, which were spatially selected (C3 and C4 depending on the lesion side). The channels were then filtered within beta band (12–20 Hz) using a second-order Butterworth IIR filter to avoid phase distortion. The filtered signals were subsequently segmented into epochs

with a duration of 0.5 s and an interval of 0.0625 s. The band powers ($Power_{ipsi}$ and $Power_{contra}$) were computed by calculating the squared Frobenius norm of the epochs for the respective channels. Finally, the NF score was derived by combining the band powers, as the log-normalized ratio $\log(1+Power_{ipsi})-\log(1+Power_{contra})$.

B. Motor imagery (MI) sessions with EEG recording (n = 14)

Patients were fitted with an 8-channel EEG headset, in a quiet room, without feedback visualization (black screen). The session began by a calibration with the same design as for the EEG-NF training. Participants were given the same instructions for performing the kinaesthetic motor imagery.

5. Data acquisition

a. Bimodal NF sessions

EEG and fMRI data were simultaneously acquired [7] on a 3 T Prisma Siemens scanner running VE11C with a 64-channel head coil. Foam pads were installed around the patient's head to avoid motion artifacts. Acquisitions were performed using the product Echo Planar Imaging BOLD sequence with the following parameters: repetition time (TR)/echo time (TE) = 1000/30 ms, Field of View (FOV) 230 mm × 230 mm restricted to motor areas, matrix size = 106 × 106, 16 contiguous 4-mm slices, flip angle = 90°. The fMRI voxel volume was 2.17 × 2.17 × 4 mm^3. In addition, a high-resolution 3D T1 MPRAGE sequence was acquired with the following parameters: TR/TI/TE = 1900/900/2.26 ms, FOV 230 × 230 mm^2, flip angle = 9°.

b. Unimodal NF and MI sessions

We used an 8-channel EEG system (ANT Neuro-eego) integrated with the Mensia Modulo solution. For online EEG processing, the acquired EEG data was preprocessed using the NeuroRT Studio software developed by Mensia Technologies, Paris, France. This software is a complemented and certified version of the OpenViBE software [62] (http://openvibe.inria.fr/).

6. Clinical assessment

The evaluations took place in the Physical Medicine and Rehabilitation Department. Demographic information encompassing age, gender, time elapsed since stroke occurrence, affected side, and stroke classification was recorded. The ability to execute motor imagery was scrutinized utilizing the Movement Imagery Questionnaire—Revised Second version score (MIQ-RS) [22]. Clinical evaluations focusing on motor skills, activities, and independence were conducted by a team consisting of physiotherapists (VM, NH, CG) and occupational therapists (MP, MJ, AMV) from the rehabilitation department. All personnel involved possessed significant experience in administering the utilized assessment tools. Evaluators were blinded to the participants' group assignments. The clinical assessments comprised the following:

- Motor impairment was evaluated by FMA-UE [23], Composit Active Range of Motion (CxA) [24], JAMAR [25]. The CxA represents the cumulative active range of motion (AROM) at the shoulder, wrist and fingers joint. Evaluation of active movement was performed according to the measurement modalities described by ref. [26].
- Motor activities were appraised using the Action Research Arm Test (ARAT) [27] and Motor Activity Log (MAL) [28].
- Autonomy in daily life activities was evaluated with Functional Independence Measure (FIM) [29].
- A qualitative questionnaire employing a likert scale was administred to solicit the patients' subjective experiences in both groups one month following the conclusion of the program.
- Offline brain activity analysis
- MRI analysis

Anatomical data were used to segment stroke lesions with an automated method based on an U-net architecture that was trained on a large T1 dataset and fine-tuned on in-house T1 and FLAIR images. BOLD data were processed to obtain NF vs rest normalised individual and group statistical maps. Diffusion data were processed to calculate CST FA asymmetry scores.

More details regarding the pre-processing and processing steps can be found in the Supplementary Material, section 1.

b. EEG analysis

Bimodal EEG data were first corrected using state-of-the-art algorithms to correct for ballistocardiogram and gradient artifacts, using EEGLab tools [30]. Then, both the unimodal and corrected bimodal underwent preprocessing through a classical pipeline for motor-imagery tasks. The event-related desynchronization (ERD) within the refs. [8–30] Hz frequency range was then computed. More details can be found in Supplementary Material, section 2.

c. Laterality Index

The laterality index (LI) was computed for both EEG (LI-EEG) and fMRI (LI-fMRI) modalities with a consistent definition:

$$LI = \frac{A_i - A_c}{A_i + A_c}$$

where A_i and A_c represent respectively the activity in the ipsilesional hemisphere and in the contralesional hemisphere. LI is used as an indicator of the prevalence of activation in one hemisphere relative to the other [31]. The LI ranges from −1 to 1, where a negative LI means contralesional dominance, a positive LI represents ipsilesional dominance, and a value of zero indicates bilateral symmetric activity [32]. The LI-EEG was obtained with the Event-Related Desynchronization (ERD) observed in both C3 and C4. The LI-fMRI was calculated in M1 from individual statistical maps with a threshold-independent method [31].

8. Statistical analysis

All statistical analyses were performed using Python 3.10.12 with the package *scipy* 1.11.2 [33].

a. NF performances

To assess initial success of NF in the NF group, a non-parametric Wilcoxon test was used to compare NF scores between rest and task periods. To evaluate NF learning across sessions, an analysis of variance (ANOVA) was conducted with a fixed effect of session to determine whether NF scores changed significantly over time. Subsequently, pair-wise comparisons were made using paired t-tests to investigate differences in NF scores between the first session (S1) and subsequent sessions (S2, S3, S4, S5) for both EEG-NF and fMRI-NF scores. Additionally, the contributions of EEG and fMRI scores in mediating control over the NF score were assessed using separate ANOVA tests.

b. Clinical scores

The data at inclusion were compared with a student's t-test for quantitative data and a chi2 test for qualitative data. All randomized patients were included in the analysis (intention-to-treat). The within-group clinical scores progressions were evaluated with a paired t-test while the between-group clinical scores changes were compared using a Mann Whitney U test. All statistical tests were performed at the 0.05 level of significance.

At the individual level, we considered as "responder" a patient with an improvement of 4 points or more on the FMA-UE after the protocol [34].

Responses to the qualitative questionnaire were compared using a Student's t-test.

c. MRI-derived metrics

Group NF > rest Z-statistic images were obtained with the *nilearn (Python)* package from the corresponding individual contrast maps computed with SPM12 (Wellcome Department of Imaging Neuroscience, UCL, London, UK). The group statistical maps were thresholded using an uncorrected significance threshold of $p < 0.005$ ($Z > 2.8$). The HMAT atlas [35] was used to perform a ROI analysis (M1 and SMA) where average NF > rest contrast value from each subject and each hemispherical ROI was extracted. Changes in M1 and SMA ipsilesional brain activity were assessed with a Student's t-tests on the ROI data between the first and the last sessions. fMRI LI in M1 were compared between groups and between the first and last timepoint using Student's t-tests. FA was extracted from the stroke-affected and unaffected corticospinal tract (CST) and FA asymmetry was calculated. CST FA asymmetry was calculated as the difference in mean FA between the two CSTs:

$$FA_{asymetry} = \frac{FA_{contralesional} - FA_{ipsilesional}}{FA_{contralesional} + FA_{ipsilesional}}$$

Positive values thus indicate lower FA and more damage in the stroke-affected CST.

d. EEG-derived metrics

To investigate how sessions influence ERD modulation during both bimodal and unimodal paradigms, we conducted an ANOVA with a fixed effect of session. We then compared sessions and groups using Student's t-tests. The analysis of EEG-LI data followed a similar approach as the ERD analysis.

e. Relationships between clinical scores and EEG—fMRI data

In the NF group, MRI analyses (BOLD and laterality index calculation) were compared between pre-intervention and post-intervention (first versus last NF run). In the MI group, MRI analyses were compared between inclusion and post-intervention. For FA analysis, patients of both groups were compared between inclusion and post-intervention.We looked at the differences between the post- and pre-interventional stages for motor

FMA-UE and between the last and the first session for LI measured with both modalities (ΔEEG LI and ΔfMRI LI). Correlations between LI changes and FMA-UE changes were evaluated with Pearson correlation coefficients and were considered as significant for $p < 0.05$.

Additionally, we examined the correlation between changes in the FMA-UE scores and in FA asymmetry scores.

Results

1. Demographic and stroke data

Between January 2019 and July 2022, 221 chronic stroke patients underwent screening through medical file analysis and phone calls to assess eligibility criteria (see Supplementary Fig. 1). Out of these, 46 patients were initially included, but 14 were subsequently excluded for not meeting participation criteria, primarily due to FMA-UE scores outside the inclusion range (26 to 52) or a fraction anisotropy asymmetry index below 0.15. Consequently, 32 patients were randomized into the protocol, with 16 assigned to the NF group and 16 to the MI group (see Table 1). Two participants withdrew from the study before the start of protocol due to COVID-19-related restrictions. Two participants withdrew from the study before protocol initiation due to COVID-19-related restrictions. Ultimately, 30 participants (15 in each group) completed the protocol until the end of NF or MI (primary outcome), with 14 participants in each group completing the study, including the visit one month later. All participants successfully completed the NF training. At baseline, no significant differences between groups were observed, except for a higher MIQRS IV in the MI group ($t = -2.057$, $p = 0.012$).

2. NF Performances

NF patients effectively modulated their brain activity in target regions during bimodal sessions, evidenced by increased EEG-NF and fMRI-NF subscores during task blocks compared to rest (see Fig. 2A). Significant up-regulation of the NF score was observed during the first bimodal session (S1) ($t = 1754.0$, $p = 0.0001$). There was also a significant effect of session ($F = 46.6$, $p = 8.546e{-}12$), with NF scores increasing over sessions (see Fig. 2B). The NF score was mainly driven by the fMRI score ($F = 192.2$, $p = 1.26e{-}43$) rather than the EEG score ($F = 4.3$, $p = 0.03$). Accordingly, we observed a significant increase in fMRI-NF subscore between S1 and subsequent sessions: S2 ($t = -8.3$, $p = 1.4e{-}16$), S3 ($t = -8.86$, $p = 8.5e{-}19$), S4 ($t = -6.5$, $p = 6.1e{-}11$) and S5 ($t = -16.1$, $p = 8e{-}58$), while no significant differences were observed in EEG-NF subscores between sessions.

3. Clinical results

A significant between-group difference was observed in the evolution of FMA-UE between pre-intervention and post-intervention ($p = 0.048$). Notably, there was a significant increase in FMA-UE in the NF group ($t = 3.6$, $p = 0.003$), persisting at one-month post-intervention ($t = 2.45$, $p = 0.029$), which was not observed in the MI group. Responders, defined as patients with an FMA-UE improvement of at least 4 points, were more prevalent in the NF group (8 participants) compared to the MI group (3 participants) immediately post-intervention. Among patients with a baseline FMA-UE score of 40 or higher, a larger proportion of NF patients (8 out of 9) were responders compared to MI patients (2 out of 6). No statistically significant between-group differences were found for other clinical scores (refer to Table 2), except a positive trend in MAL Quant ($p = 0.07$) and MAL Qual ($p = 0.03$) in MI group, but no change in the number of activities, MAL Num ($p = 0.15$). Additionally, there were no significant differences between groups in the evolution of FIM score.

Concerning the patients' perception assessed through a qualitative questionnaire (see Supplementary Table 1), the NF group reported finding the task more challenging ($p = 0.003$) feeling more tired ($p = 0.010$) and perceiving the performance demand as heavier ($p = 0.038$).

4. Offline Brain activity results

a. BOLD data

As shown in Fig. 3, Pre-interventional activity in ipsilesional M1 was low in both groups. At the post-interventional stage, the statistical map showed more focused activations on ipsilesional M1 with less contralesional activity in SMA and PMC for the NF group, while no increase activity in ipsilesional regions was observed in the MI group. However ROI analysis indicated no significant between-group differences in the evolution of ipsilesional M1 ($t = 1.43$, $p = 0.16$) and SMA ($t = 0.85$, $p = 0.40$). Moreover, activation maps indicated a non-significant change in either group for ipsilesional M1 or SMA activity (M1 ($t = 1.2$, $p = 0.23$) and in SMA ($t = 0.7$, $p = 0.47$) for the NF group, and M1 ($t = -0.8$, $p = 0.41$) and SMA ($t = -0.8$, $p = 0.42$) in the MI group).

b. EEG data

Bimodal EEG analysis revealed that there was no effect of session, meaning that there was no

Table 1 Participant Characteristics at inclusion in the neurofeedback (NF) and motor imagery (MI) group

Characteristics	MI Group N=16 Mean±SD	NF Group N=16 Mean±SD	p
Age, y.o.;	59±11	62±13	
Time from stroke to randomization, month;	34±48	22±18	0,377
Sex			
Male (n)	11	10	
Female (n)	5	6	
Stroke Type			
Ischemic (n)	8	12	
Haemorrhagic (n)	8	4	
Hand affected			
Right	8	9	
Left	8	7	
MIQRS			
MIQRS IV	5.42±0.94	4.54±0.92	0,012*
MIQRS IK	4.32±1.38	4.3±0.97	0,979
MIQRS IM	4.87±1.03	4.42±0.83	0,186
Motor function			
FMA	38±11	40±11	0,593
CxA	487.2±122.7	501.8±126.7	0,919
JAMAR (ratio)	0.218±0.26	0.278±0.233	0,522
Motor Activities			
ARAT	19±18	29±18	0,111
MAL (num)	26±2	25±1	0,444
MAL (quant)	1±1.04	1.26±0.98	0,471
MAL (qual)	1.08±1.1	1.27±0.99	0,621
Patient independence			
FIM	113±9	110±11	0,379
Mean FA asymmetry	0.055 ± 0.03	0.06 ±0.048	

Last column: p-value associated with the two-sample t-test for each characteristic; NF group in green and MI group in grey

improvement of ERD across sessions. No difference was found between sessions for both EEG performance during NF and MI, hence meaning an absence of effect of sessions and between sessions.

c. Laterality Index

MRI LI increased non-significantly for both the NF ($t=0.908$, $p=0.37$) and the MI group ($t=1.98$, $p=0.19$) (Fig. 4D), with no significant between-groups differences in LI improvements ($t=-0.25$, $p=0.8$).

Regarding bimodal EEG LI, no significant session effect was identified. However unimodal EEG LI differed significantly between the groups, with the NF group demonstrating greater lateralization ($t=-3.56$, $p=0.0004$), albeit no significant effect of the session was detected ($t=-0.1$, $p=0.9$).

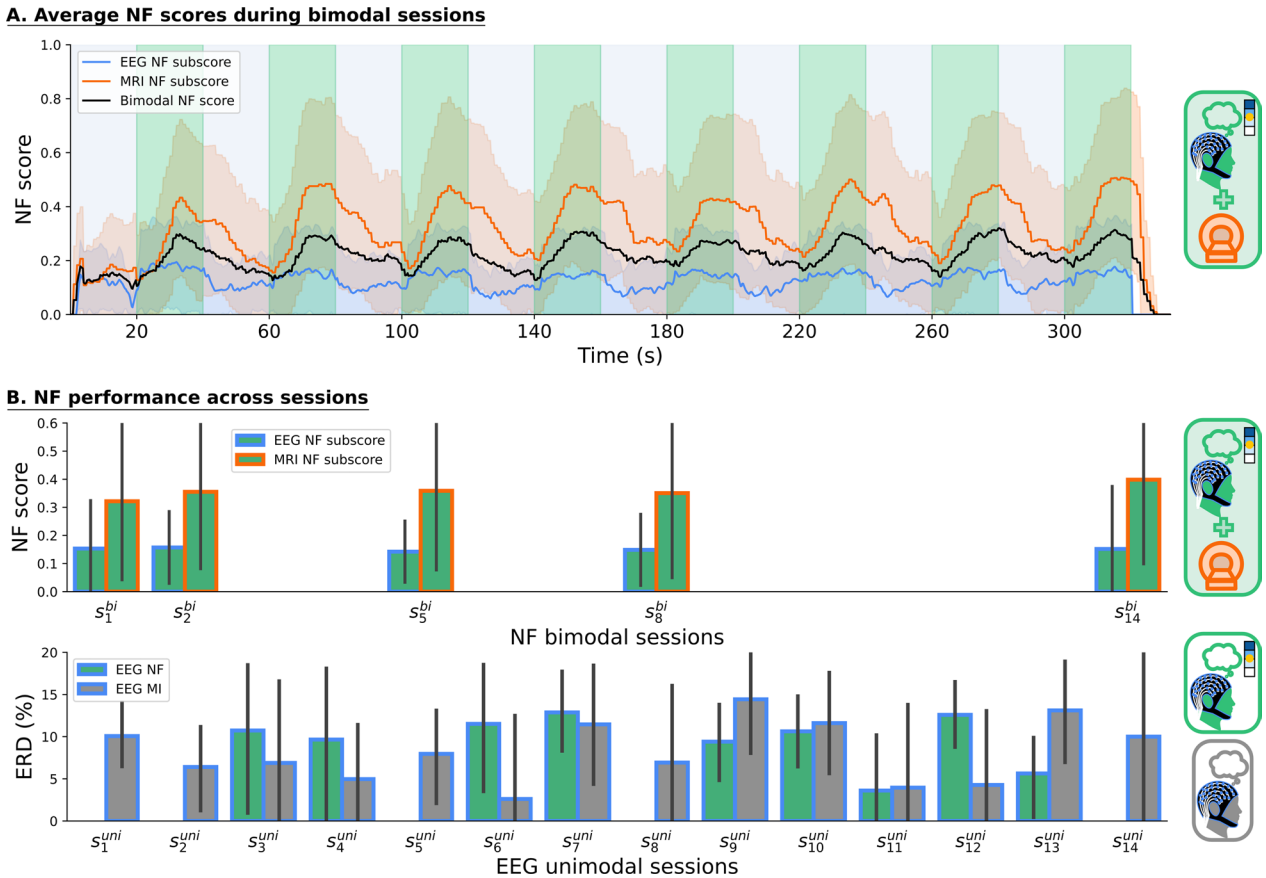

Fig. 2 Neurofeedback (NF) scores and performances. **A** Average NF scores during bimodal sessions. Averaged time-series over sessions and subjects of EEG and fMRI NF subscores (rest blocks: white; task blocks: green) Note that the patients succeeded in activating targeted brain areas during the task and respect the rest. **B** NF performance across sessions. The top panel illustrates the average EEG and fMRI subscores across sessions: both indications from fMRI and EEG were used by the patients during the 5 bimodal sessions. Additionally, there is a significant effect of session (F = 46.6, p = 8.546e−12), implying that NF subscores increased over sessions. The bottom panel represents average ERD evolution recorded by EEG during the unimodal sessions (in grey for MI and in green for NF sessions (9 sessions for the NF group, 14 for the MI group). Patients succeed in activating target brain areas both during unimodal EEG-NF and bimodal fMRI-EEG-NF

d. FA

FA asymmetry index in the CST decreased in the NF group and increased in the MI group (Fig. 5A). A non-significant difference between the two groups was found (Wilcoxon test, $t=25$; $p=0{,}055$). No significant FA changes were detected in either the ipsilesional or contralesional hemisphere (Fig. 5 within both groups when comparing pre-training and post-training scans.

5. Relationships between brain activity and clinical scores

a. Laterality Index

In the NF group, a non-significant positive correlation was observed between unimodal ΔEEG LI and ΔFMA (r = 0.5; p = 0.058). However, no correlations were found between clinical scores and unimodal ΔEEG LI in the MI group, nor were there correlation found between ΔMRI LI and clinical changes in both groups.

b. FA Index

In the NF group, we observed a non-significant negative correlation between ΔFA asymmetry and ΔFMA (r = − 0.1; p = 0.73), while a non-significant positive correlation was observed MI group (r = 0.2; p = 0.48).

Discussion

The objective of this study was to evaluate the efficacy of a bimodal EEG-fMRI NF training alternated with unimodal EEG NF training, targeting ipsilesional SMA and M1, compared to "non-guided" MI training for improving upper limb motricity in chronic stroke survivors

Table 2 Neurofeedback and motor imagery within-group clinical evolutions between consecutive timepoints and between-groups clinical evolutions

Clinical scores	Neurofeedback (NF) group					Motor Imagery (MI) group					NF vs MI	
	Pre	Δ1		Δ2		Pre	Δ1		Δ2		Δ1	Δ2
		$\mu_{\Delta 1}$	p	$\mu_{\Delta 2}$	p		$\mu_{\Delta 1}$	p	$\mu_{\Delta 2}$	p	p	p
FMA-UE	40	3	**0.003**	2.7	**0.029**	38	0.5	0.633	0.3	0.868	**0.048**	0.239
CXA	502	9.8	0.211	3.9	0.702	487	-5.1	0.562	1.1	0.916	0.097	0.505
ARAT	28.7	-0.2	0.890	0.8	0.482	18.5	1.6	0.140	1.5	0.192	0.798	0.729
JAMAR	8.1	0.3	0.779	1.7	0.135	6.9	-0.7	0.366	0.75	0.254	0.255	0.216
MAL QUANT	1.3	0.0	0.844	0.1	0.540	1.0	0.2	0.078	0.24	0.215	0.141	0.730
MAL QUAL	1.3	0.1	0.445	0.2	0.424	1.1	0.2	0.032	0.1	0.432	0.106	1.000
MAL NUM	25.3	0.3	0.610	0.4	0.455	26.1	-0.6	0.156	-0.43	0.212	0.193	0.246

NF: neurofeedback; MI: motor imagery; Δ1: difference between post intervention and pre-intervention stages; Δ2: difference between one month after training and pre-intervention stages; Pre-average score at pre-interventional stage; μΔ1 and μΔ2: average score difference for the corresponding timepoints; p: p-value associated with a Mann Whitney U Test. Bold values: significant difference $p<0.05$; CXA: Composit Active Range of Motion; FMA-UE: Fugl-Meyer Assessment Upper Extremity; ARAT: Action Research Arm Test; JAMAR is a hand dynamometer measuring grip strength; MAL QUANTI; MAL QUALI; MAL NUM: Motor Activity Log; NF group in green and MI group in grey

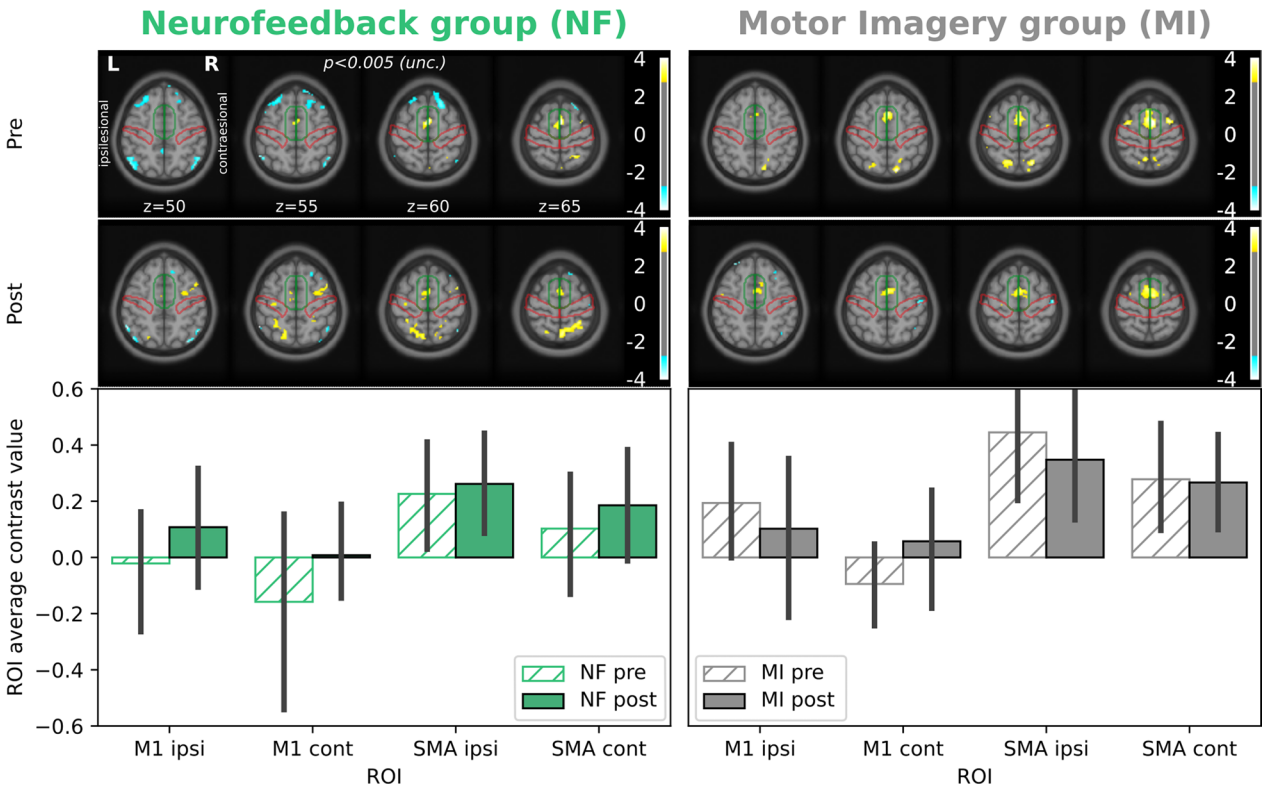

Fig. 3 Group statistical maps ($p < 0.005$ uncorrected) and ROI analysis in ipsilesional and contralesional M1 and SMA for both the neurofeedback (NF) group and the motor imagery (MI) group, both before and after the intervention. Normalised individual contrast maps of patients with right-hemispheric stroke lesions were flipped along the y-axis so that the ipsilesional hemisphere is the left hemisphere for all patients

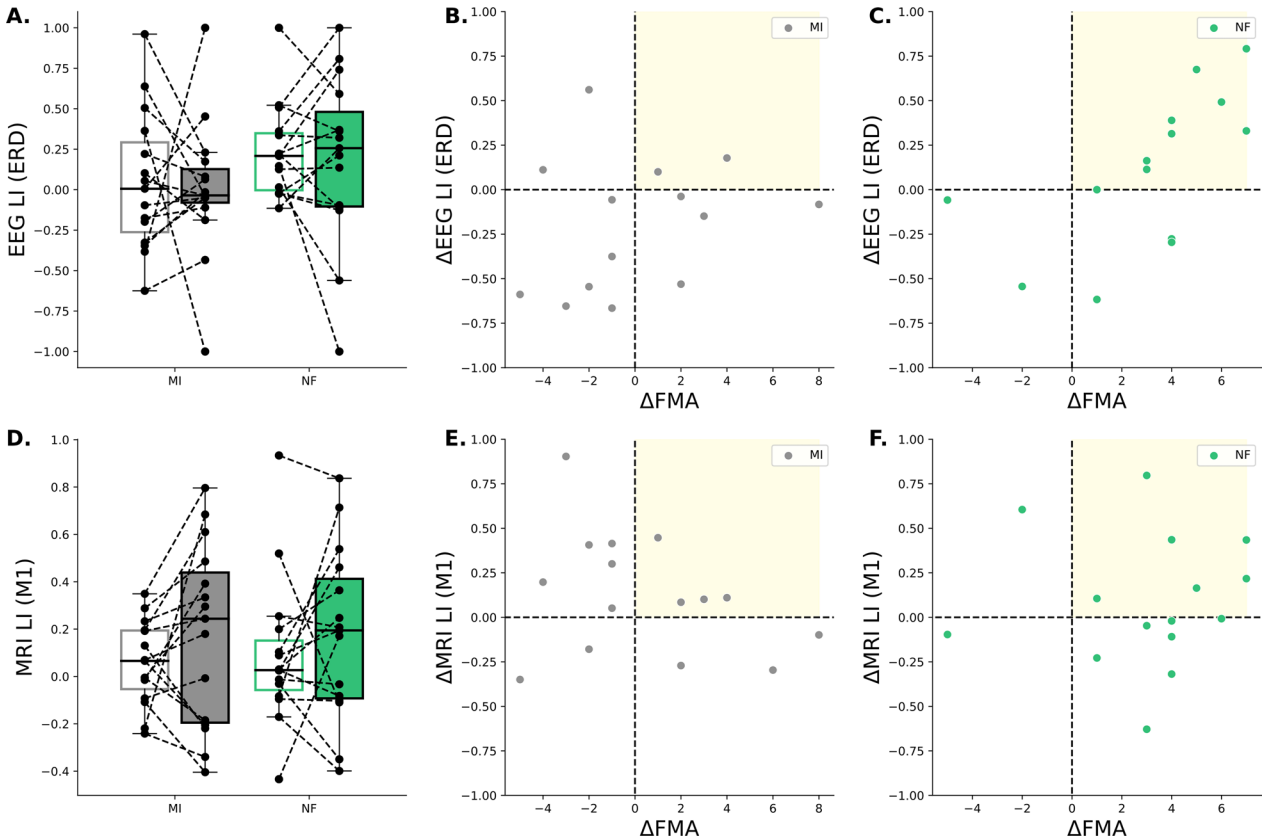

Fig. 4 Laterality Index (LI) scores and association with FMA-UE changes. **A** Boxplots of EEG LI scores for the neurofeedback (NF) and motor imagery (MI) groups. EEG LI scores were calculated for the unimodal sessions. EEG LI changes were greater in the NF group than in the MI group. There was no effect of session for each group. **B**, **C** Scatter plots of EEG LI changes compared to FMA-UE changes for the MI group (**B**) and the NF group (**C**). Each dot represents a participant. There was a non-significant positive correlation ($r = 0.5$, $p = 0.058$) in the NF group between FMA-UE change and EEG LI change, and a trend of positive LI index corresponding to improvement in FMA score is observed (yellow shaded area) **D** Boxplots of fMRI LI scores in the primary motor cortex (M1) for the NF and MI groups. MRI LI scores were calculated during the fMRI NF sessions for the NF group and during the fMRI MI sessions for the MI group. The changes were non-significant in NF ($t = -0.908$, $p = 0.379$) and MI ($t = -1.384$, $p = 0.188$) groups. **E**, **F** Scatter plots of fMRI LI in M1 changes compared to FMA-UE changes for the MI group (**E**) and the NF group (**F**)

with partial motor impairment and preserved CST. We hypothesized that NF, by guiding patients to upregulate cerebral activity in precisely localized motor areas (SMA and M1), would outperform MI training, which involves a similar task but lacks brain activation feedback, in enhancing UL motricity and fostering beneficial cerebral plasticity.

The primary outcome of this randomised controlled trial was UL motricity. Our findings indicate a trend favouring NF over MI in improving UL motricity. Furthermore, significant improvement in FMA-UE scores was observed after NF training but not after MI training. Additionally, a greater proportion of responders was observed in the NF group immediately post-intervention, particularly among patients with initial FMA-UE scores > 40 (see Fig. 6). In the NF group, eight out of nine patients with FMA-UE > 40 demonstrated clear motricity improvements (i.e., were responders), compared to only two out of six in the MI group. Moreover, NF participants maintained motor improvement up to one-month post-intervention, suggesting that participants in the NF group may have gained long-lasting change in brain systems engaged in motor control, thereby facilitating beneficial brain plasticity [36].

For patients with preserved CST, several studies have shown that, the best substitute network for plasticity is anatomically and functionally close to the initial damaged network [37–39]. In such cases, reorganization relies on perilesional direct motor tracts (e.g., M1 and ipsilesional premotor areas) [40]. However, for more severely affected patients, M1 stimulation alone is less convincing. The inclusion of SMA in our approach was driven by several factors: (1) SMA is more likely to remain intact in ischemic stroke due to its location within the anterior cerebral artery territory; (2) SMA projections to CST fibers suggest a role in restoring motor function through

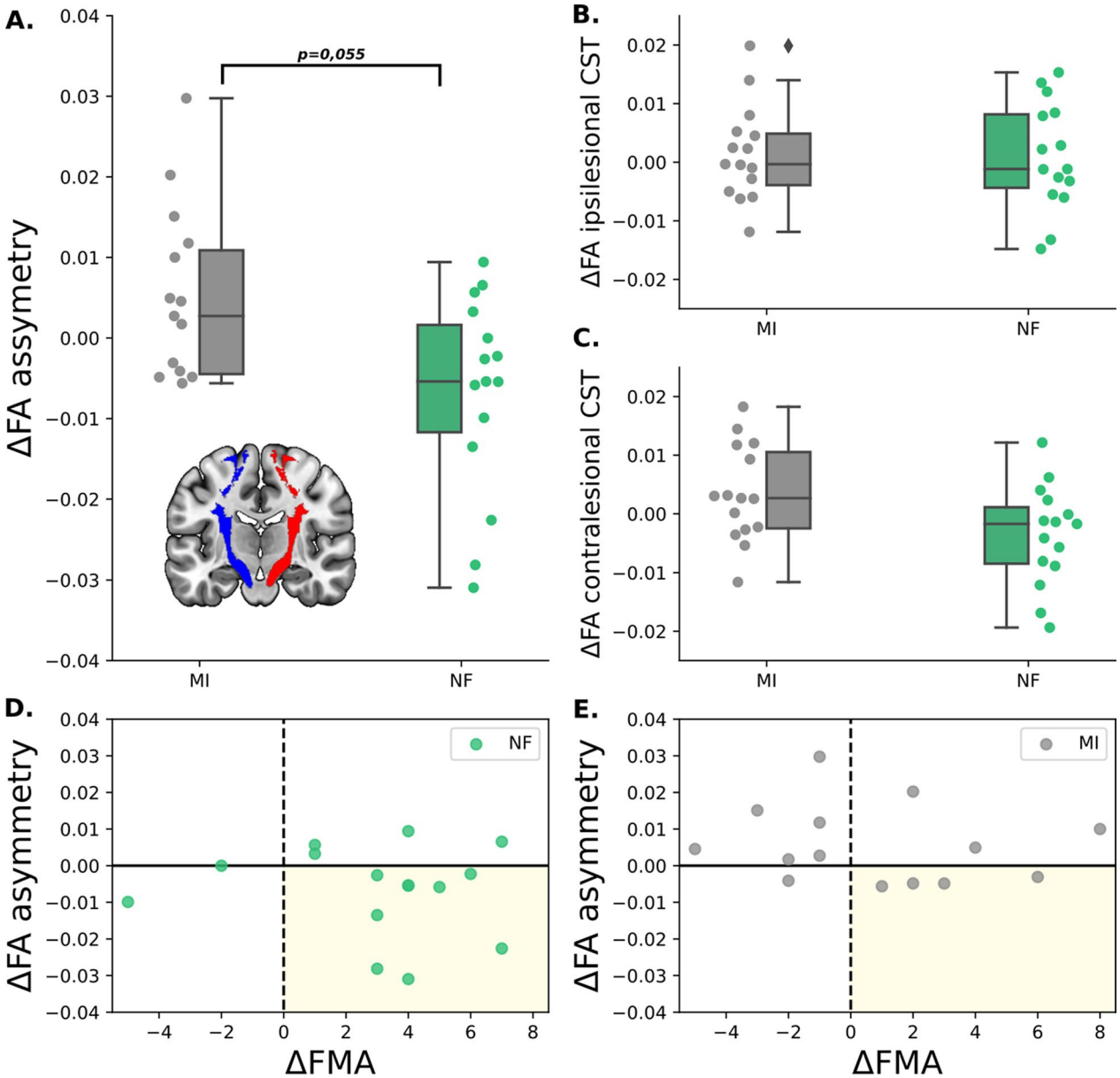

Fig. 5 White matter integrity changes in the corticospinal tract (CST). **A** Changes in Fractional Anisotropy (FA) asymmetry pre-post in the CST for the neurofeedback (NF) and motor imagery (MI) groups. **B**, **C** FA changes in both contra- and ispsi- lesional CST for the NF and MI groups. **D**, **E** Fractional anisotropy asymmetry changes and relationship with FMA-UE changes for the NF and MI groups. CST FA asymmetry is the difference in mean FA between the two CSTs (Unaffected – Affected)/(Unaffected + Affected), positive values indicate lower FA/more damage in the stroke-affected CST. A non-significant difference was found between the NF group and the MI group (Wilcoxon test, t = 26 p = 0.055)

adaptive re-mapping after stroke [41]; and (3) SMA is more easily engaged during motor imagery than M1 [42, 43], as demonstrated by prior studies [44–46].

Our results support the hypothesis that guiding patients to both SMA and M1 would be interesting. Patient engagement during NF training was evident through the alternating increases and decreases in NF scores during task and rest periods (see Fig. 2). Patients successfully activated target brain areas (SMA and M1) guided by the NF score during the NF sessions. They were able to regulate the NF score from the first session. Furthermore, we observed an improvement in the fMRI NF score modulation across sessions, demonstrating that they improved their capacity to self-activate the targeted brain area (SMA and M1) throughout the sessions. Qualitative analysis of patient questionnaires revealed that

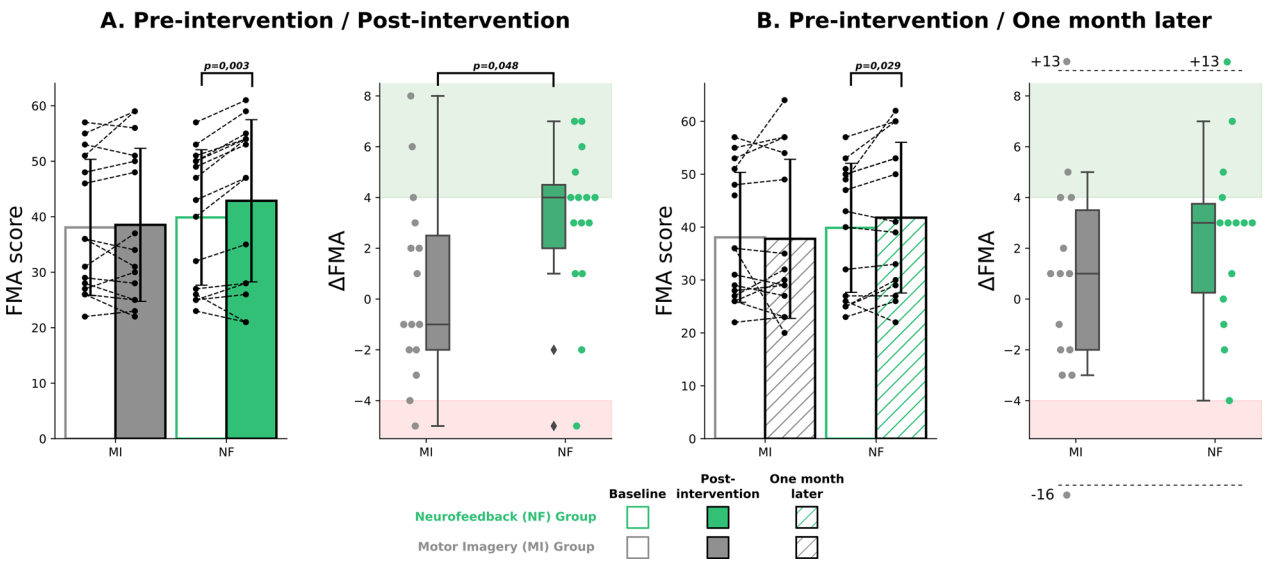

Fig. 6 Comparison of motor outcome (FMA-UE) evolution between the neurofeedback (NF) and motor imagery (MI) groups after the training (**A**) and at one month later (**B**). The green shaded area corresponds to the responders (ΔFMA ≥ 4) while the red area depicts individuals with a significant decrease (ΔFMA ≤ 4). **A** Effect of the training protocol. The NF group improved between pre- and post- intervention (paired t-test, t = − 3.6, p = 0.003). FMA-UE improvement was greater in the NF group compared to the MI group (Mann Whitney U test, t = 160.5, p = 0.048). There were 8 responders in the NF group and 3 in the MI group. In the subset of patients with an initial FMA-UE ≥ 40, there were 8/9 responders in the NF group and 2/6 in the MI group. **B** Effect of the training protocol at distance. The NF group improved between pre-intervention and 1 month after the protocol (paired t-test, t = − 2.5, p = 0.029). Participants with extreme ΔFMA scores were represented after the black dashed line

NF training was perceived as more challenging and tiring than MI, underscoring its demanding nature. Nonetheless, patients' compliance was excellent regardless of group. All participants completed the 5-week intensive training protocol. Even patients with low Motor Imagery Questionnaire scores successfully engage in the NF protocol [47].

As described above, we found an improvement in the online NF score. In addition, we observed promising trends in offline metrics derived from EEG and MRI, particularly within the NF group. Specifically, we observed a tendency for increased bold activity in the ipsilesional M1 and SMA in the NF group only, along with improvement in LI measured by EEG. However, no such improvement was noted for LI MRI, as bilateral activity increases were observed in both M1 and SMA. Furthermore, change in LI appeared to be associated with motor improvement. LI, commonly used to quantify inter-hemispheric activation comparison comparisons, assumes that optimal motor recovery follows a shift in brain activity toward the ipsilateral cortex [36]. A positive correlation between unimodal EEG LI and FMA-UE (r = 0.5, p = 0.058) was identified. Our finding aligns with previous findings [48], where a correlation between LI values and motor function of the upper limb was demonstrated.

We also noted a trend toward reduced FA asymmetry of the CST in the NF group compared to the MI group, suggesting structural changes in the CST induced by NF training ([36]; Zolkefley et al.). Interestingly, nine out of thirteen participants who showed FMA-UE score improvements also exhibited greater reductions in FA asymmetry (Fig. 5). This suggests enhanced ipsilesional motor pathway function in approximately two-thirds of NF responders, consistent with the findings of Sanders et al. [36]. Our results further support the evidence that NF can induce structural changes in white matter tracts in the chronic stroke survivors, as previously shown in healthy subjects [49]. Altogether, the sustained improvements in motricity observed up to one-month post-training, combined with changes in brain activity and CST structure, highlight the beneficial and long-lasting brain plasticity induced by NF training [16, 50–52, 60].

Setting up a bimodal NF platform presented challenges [7, 8]. We developed a protocol alternating bimodal and unimodal sessions to increase training intensity. A key question concerns the added value of including unimodal EEG sessions alongside bimodal sessions. Our results indicate that the bimodal mode enhances training by combining the high spatial resolution of MRI with the temporal resolution of EEG. Indeed, patients successfully activated target brain areas during both unimodal EEG-NF and bimodal fMRI-EEG-NF sessions, with the NF score predominantly driven by fMRI signals. This finding supports the hypothesis that bimodal sessions

amplify the effectiveness of unimodal sessions. Alternating bimodal NF (which is more resource-intensive) with unimodal NF (which is easier to perform and less costly) appears to be a promising strategy for achieving sufficient rehabilitation intensity to improve recovery.

In our study, participants underwent 14 sessions over five weeks (three sessions per week), comprising five bimodal and nine unimodal sessions. This rehabilitation schedule was informed by previous studies suggesting that 30 min of training three times per week is necessary to achieve effectiveness after stroke [53]. As suggested by Thibault et al. in a previous review [54] on fMRI-NF, the number of training sessions likely the sustainability of motor improvements [55].

The control group underwent MI training rather than sham NF training, as MI has previously been shown to be effective [17]. Using a sham NF approach could potentially have influenced changes in bold self-regulation [56] and could have exacerbated the motor function deficits of patients in the control group [57]. Despite the challenge of choosing an effective training as a control group, we observed consistent positive effects in the NF group. The MI group was structured similarly to the NF group, utilising an EEG headset and undergoing a training protocol of identical duration and intensity. Analysis of qualitative questionnaires revealed similar treatment beliefs between the two groups, underscoring the robustness of the comparison.

Limitations

The primary limitation of our study was the reduced sample size of patients (32 out of 36 attempted), which decreased the study's statistical power. The trial was suspended from March 2020 to January 2021 due to the COVID-19 pandemic, and financial and organizational constraints necessitated the discontinuation of the protocol before completion.

A second limitation concerns the selection criteria. Unlike some preliminary studies that included very selectively chosen patients, we did not exclude patients based on premorbid status and included stroke patients regardless of the characteristics of their stroke lesions. The impact of patients' premorbid status (e.g., age, diabetes) on limiting brain structural reserve may partly explain non-responder patients [58]. Additionally, stroke-related variability (type of stroke, location and size of lesion, post-stroke delay, and amount of rehabilitation received before) may have contributed to the difficulty in establishing a correlation between motor improvement and changes in brain activity. Nevertheless, this broad inclusion criteria also strengthens the generalizability of our results to patients regardless of their premorbid status and stroke lesion [59]. Individual data could be studied in the future considering these considerations.

The third limitation is technical. The echo-planar imaging (EPI) BOLD sequence covered the motor cortex but not deeper brain regions. This limitation stemmed from the need to balance a relatively high temporal resolution, i.e., a low Repetition Time (TR) of 1 s, with the finite number of slices attainable within the constraints of the imaging protocol using the standard BOLD sequence, which at the time did not include multiband options. This limitation precluded our ability to observe certain networks, such as the default mode network or other networks intricately associated with NF [55]. However, in another previous work (Lioi et al. 2021), we conducted an analysis of changes in motor networks after NF training that revealed, consistent with the results of this study, a decrease in ipsilesional self-inhibitory connections corresponding to an increase in activation during the NF motor task.

Significance and perspectives

In this study, we highlight the benefits of using a bimodal NF protocol to train patients with preserved CST to self-activate their SMA and M1 and improve UL motor function following stroke. Our findings suggest that participants with a Fugl-Meyer score greater than 40 derive the greatest benefit from this rehabilitation approach. To improve the logistical feasibility, reduce the cognitive demands of the protocol, and minimize the time spent in MRI, which is both limited and costly, it may be possible to utilize the data collected in this study to develop a predictive model that reduces MRI reliance for future patients [61]. Furthermore, providing feedback in a format that enhances mental imagery, such as combining visual and haptic interfaces, could help lower the cognitive demands of the training [9, 62].

For more severely affected patients with damaged CST, identifying alternative targets beyond the primary motor pathway is crucial. These targets could be tailored to each patient based on the extent of motor pathway damage and may involve regions in the contralateral hemisphere or extrapyramidal accessory motor circuits [63, 64]. In such cases, MRI is particularly valuable for accurately identifying these new targets due to its superior spatial resolution. Combining fMRI with EEG remains essential to implement effective and practical neurofeedback.

Conclusion

We present the first randomized controlled trial involving simultaneous EEG-fMRI NF training in stroke survivors. This study demonstrates that this innovative NF rehabilitation program, which proposes brain targets evolving throughout the protocol and alternates

between bimodal and unimodal sessions, is feasible and appears to be more effective in enhancing UL motricity compared to an MI training protocol in participants with partially functional CST. The results indicate that improvements in motor outcomes are sustained one month after the end of the protocol, suggesting the maintenance of brain changes beyond the training period. The combination of EEG and fMRI offers the advantage of allowing precise definition of brain targets and delivering intensive training. In the future, it will be necessary to adapt the training for more severely affected patients and personalize brain rehabilitation programs based on the lesion location and extent.

Abbreviations

ARAT	Action Research Arm Test
CST	Corticospinal tract
CxA	Composite Active Range of Motion
FA	Fractional anisotropy
LI	Laterality Index
M1	Primary motor cortex
NF	Neurofeedback
MI	Motor imagery
FMA-UE	Fugl-Meyer Assessment for Upper-Extremity

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12984-025-01598-9.

Supplementary Material 1: Supplementary Table 1. Questionnaire results. Supplementary Figure 1. Flow chart. Supplementary Figure 2. Stroke lesions heatmaps for the neurofeedback (NF) group, the motor imagery (MI) group and all patients. Supplementary Figure 3. Comparison of motor outcome (CXA) evolution between the neurofeedback (NF) and motor imagery (MI groups during the training (A) and at distance (B). A. Effect of the training protocol. The NF group shows a non-significant improvement between pre- and post- intervention (ΔCXA=+9.8, paired t-test, t=1.31, p=0.211) while the MI group decreased the CXA score (ΔCXA=-5.1, paired t-test, t=-0.59, p=0.562). B. Effect of the training protocol at distance. The NF group improved between pre-intervention and 1 month after the protocol (ΔCXA=+3.9, paired t-test, t=0.39, p=0.702) while the MI group decreased its CXA score (ΔCXA=+1.1, paired t-test, t=0.11, p=0.916).

Acknowledgements

MRI data acquisition was supported by the Neurinfo MRI research facility from the University of Rennes I, University Hospital of Rennes, Inria, CNRS and the Rennes Cancer Center. Neurinfo was also supported by the European Research Council (FEDER), the French State, the Brittany Council, Rennes Metropole, Inserm and GIS IBISA. Neurinfo is also supported by the Brittany Council, Rennes Metropole and GIS IBISA. The authors would like to thank the physiotherapists and occupational therapists: Vincent Mayer, Noëlla Halet, Coralie Gastine, Anne-Marie Voisin, Manon Perrier and Maxime Jaffré as well as the MR technologists Stéphanie Chhoa, Vanessa Even, Marithé Desclos, Catherine Guillemot, Gwenola Morrisse and Lucille Patier and Prof. Jean-Christophe Ferré for their support. Additionally, we would like to thank Francesca Galassi and Stéphanie Leplaideur for their help in segmenting stroke lesions, and Sébastien Cordillet for providing advice on statistical analysis. The authors are thinking in particular of Christian Barillot, who was the visionary initiator and "daddy" of this study, and who steered the HEMISFER project until his sudden death in 2020.

Author contributions

S.B. and M.F. wrote the main manuscript text. S.B., M.F., and Q.D. prepared all figures. M.F. and Q.D. performed all analyses and wrote the code. S.B., M.F., Q.D., E.B., G.L., A.L., P.M., and I.B. interpreted the data. S.B., M.F., E.B., G.L., L.S., and E.L. participated in the acquisition of the data. S.B., M.F., Q.D., E.B., G.L., A.L., P.M., and I.B. conceptualized the study design. All authors reviewed the manuscript.

Funding

This study is supported by CominLabs and the Fondation pour la Recherche sur les AVC.

Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Our Local Ethic Committee approved the study. All the patients gave their written informed consent to study participation.

Consent for publication

All the patients gave their written informed consent for publication of any individual person's data in any form.

Competing interests

The authors declare no competing interests.

Author details

[1]Physical Medicine and Rehabilitation Department, CHU Rennes, Hôpital Pontchaillou, 2 rue Henri Le Guilloux, 35033 Rennes Cedex 9, France. [2]Univ Rennes, INRIA, CNRS, INSERM, IRISA, EMPENN ERL U1228, 35000 Rennes, France. [3]Unité Empenn U1228, INSERM, INRIA, Université Rennes I, IRISA, UMR CNRS 6074, Campus de Beaulieu, 35042 Rennes, France. [4]Radiology Department, CHU Rennes, Rennes, France. [5]Plateforme Neurinfo, Unité Empenn U1228, Service de Radiologie – IRM RdC CHU Rennes, Université Rennes 1, Hôpital Pontchaillou, 2, rue Henri Le Guilloux, 35033 Rennes, France. [6]BRAIn Team, Lab-STICC, IMT Atlantique, UMR CNRS 6285, Atlantique Bretagne-Pays de La Loire Campus de Brest Technopôle Brest-Iroise CS 83818 29238, Brest, France. [7]INRIA, Univ Rennes, CNRS, IRISA, Campus Universitaire de Beaulieu, 35042 Rennes, France.

Received: 15 October 2024 Accepted: 1 March 2025
Published online: 25 March 2025

References

1. Lecoffre C, et al. National trends in patients hospitalized for stroke and stroke mortality in France, 2008 to 2014. Stroke. 2017;48:2939–45.
2. Emerson JR, Binks JA, Scott MW, Ryan RP, Eaves DL. Combined action observation and motor imagery therapy: a novel method for post-stroke motor rehabilitation. AIMS Neurosci. 2018;5:236.
3. Broussy S, et al. Sequelae and quality of life in patients living at home 1 year after a stroke managed in stroke units. Front Neurol. 2019;10:471826.
4. Le Franc S, et al. Toward an adapted neurofeedback for post-stroke motor rehabilitation: state of the art and perspectives. Front Hum Neurosci. 2022;16:917909.
5. Cervera MA, et al. Brain-computer interfaces for post-stroke motor rehabilitation: a meta-analysis. Ann Clin Transl Neurol. 2018;5:651–63.
6. Baniqued PDE, et al. Brain–computer interface robotics for hand rehabilitation after stroke: a systematic review. J Neuroeng Rehabil. 2021;18:1–25.
7. Mano M, et al. How to build a hybrid neurofeedback platform combining EEG and fMRI. Front Neurosci. 2017;11:249134.
8. Perronnet L, et al. Unimodal versus bimodal EEG-fMRI neurofeedback of a motor imagery task. Front Hum Neurosci. 2017;11:1–15.
9. Fleury M, Figueiredo P, Vourvopoulos A, Lecuyer A. Two is better? Combining EEG and fMRI for BCI and neurofeedback: a systematic review. J Neural Eng. 2023. https://doi.org/10.1088/1741-2552/AD06E1.
10. Ciccarelli G, et al. Simultaneous real-time EEG-fMRI neurofeedback: a systematic review. Front Hum Neurosci. 2023;17:1123014.

11. Favre I, et al. Upper limb recovery after stroke is associated with ipsilesional primary motor cortical activity: a meta-analysis. Stroke. 2014;45:1077–83.
12. Bonkhoff AK, Grefkes C. Precision medicine in stroke: towards personalized outcome predictions using artificial intelligence. Brain. 2022;145:457–75.
13. Guggisberg AG, Koch PJ, Hummel FC, Buetefisch CM. Brain networks and their relevance for stroke rehabilitation. Clin Neurophysiol. 2019;130:1098–124.
14. Byblow WD, Stinear CM, Barber PA, Petoe MA, Ackerley SJ. Proportional recovery after stroke depends on corticomotor integrity. Ann Neurol. 2015;78:848–59.
15. Plow EB, Cunningham DA, Varnerin N, Machado A. Rethinking stimulation of brain in stroke rehabilitation: why higher-motor areas might be better alternatives for patients with greater impairments. Neuroscientist. 2015;21:225.
16. Lioi G, et al. A multi-target motor imagery training using bimodal EEG-fMRI neurofeedback: a pilot study in chronic stroke patients. Front Hum Neurosci. 2020;14:497414.
17. Monteiro KB, et al. Effects of motor imagery as a complementary resource on the rehabilitation of stroke patients: a meta-analysis of randomized trials. J Stroke Cerebrovasc Dis. 2021;30:105876.
18. Grefkes C, Fink GR. Connectivity-based approaches in stroke and recovery of function. Lancet Neurol. 2014;13:206–16.
19. Ros T, et al. Consensus on the reporting and experimental design of clinical and cognitive-behavioural neurofeedback studies (CRED-nf checklist). Brain. 2020;143:1674.
20. Pichiorri F, et al. Brain-computer interface boosts motor imagery practice during stroke recovery. Ann Neurol. 2015;77:851–65.
21. Stinear CM, Barber PA, Petoe M, Anwar S, Byblow WD. The PREP algorithm predicts potential for upper limb recovery after stroke. Brain. 2012;135:2527–35.
22. Loison B, et al. Translation and validation of the French Movement Imagery Questionnaire-Revised Second version (MIQ-RS). Ann Phys Rehabil Med. 2013;56:157–73.
23. Fugl Meyer AR, Jaasko L, Leyman I. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. Scand J Rehabil Med. 1975;7:13–31.
24. Bayle N, Maisonobe P, Raymond R, Balcaitiene J, Gracies JM. Composite active range of motion (CXA) and relationship with active function in upper and lower limb spastic paresis. Clin Rehabil. 2020;34:803–11.
25. Mathiowetz V, et al. Grip and pinch strength: normative data for adults. Arch Phys Med Rehabil. 1985;66:69–74.
26. Gracies JM, et al. Five-step clinical assessment in spastic paresis. Eur J Phys Rehabil Med. 2010;46:411–21.
27. Yozbatiran N, Der-Yeghiaian L, Cramer SC. A standardized approach to performing the action research arm test. Neurorehabil Neural Repair. 2008;22:78–90.
28. Uswatte G, Taub E, Morris D, Light K, Thompson PA. The Motor Activity Log-28: assessing daily use of the hemiparetic arm after stroke. Neurology. 2006;67:1189–94.
29. Keith RA, Granger CV, Hamilton BB, Sherwin FS. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil. 1987;1:6–18.
30. Warbrick T. Simultaneous EEG-fMRI: what have we learned and what does the future hold? Sensors. 2022;22:2262.
31. Brumer I, de Vita E, Ashmore J, Jarosz J, Borri M. Implementation of clinically relevant and robust fMRI-based language lateralization: choosing the laterality index calculation method. PLoS ONE. 2020;15: e0230129.
32. Nam CS, Jeon Y, Kim YJ, Lee I, Park K. Movement imagery-related lateralization of event-related (de)synchronization (ERD/ERS): Motor-imagery duration effects. Clin Neurophysiol. 2011;122:567–77.
33. Virtanen P, et al. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods. 2020;17(3):261–72.
34. Page SJ, Fulk GD, Boyne P. Clinically important differences for the upper-extremity Fugl-Meyer Scale in people with minimal to moderate impairment due to chronic stroke. Phys Ther. 2012;92:791–8.
35. Mayka MA, Corcos DM, Leurgans SE, Vaillancourt DE. Three-dimensional locations and boundaries of motor and premotor cortices as defined by functional brain imaging: a meta-analysis. Neuroimage. 2006;31:1453–74.
36. Sanders ZB, et al. Self-modulation of motor cortex activity after stroke: a randomized controlled trial. Brain. 2022;145:3391.
37. Werhahn KJ, Conforto AB, Kadom N, Hallett M, Cohen LG. Contribution of the ipsilateral motor cortex to recovery after chronic stroke. Ann Neurol. 2003;54:464–72.
38. Fridman EA, et al. Reorganization of the human ipsilesional premotor cortex after stroke. Brain. 2004;127:747–58.
39. Johansen-Berg H, et al. The role of ipsilateral premotor cortex in hand movement after stroke. Proc Natl Acad Sci USA. 2002;99:14518–23.
40. Cirillo C, et al. Post-stroke remodeling processes in animal models and humans. J Cereb Blood Flow Metab. 2020;40:3–22.
41. Schulz R, et al. Assessing the integrity of corticospinal pathways from primary and secondary cortical motor areas after stroke. Stroke. 2012;43:2248–51.
42. Sharma N, Baron J-C. Does motor imagery share neural networks with executed movement: a multivariate fMRI analysis. Front Hum Neurosci. 2013;7:564.
43. Mehler DMA, et al. The BOLD response in primary motor cortex and supplementary motor area during kinesthetic motor imagery based graded fMRI neurofeedback. Neuroimage. 2019;184:36–44.
44. Berman BD, Horovitz SG, Venkataraman G, Hallett M. Self-modulation of primary motor cortex activity with motor and motor imagery tasks using real-time fMRI-based neurofeedback. Neuroimage. 2012;59:917–25.
45. Chiew M, LaConte SM, Graham SJ. Investigation of fMRI neurofeedback of differential primary motor cortex activity using kinesthetic motor imagery. Neuroimage. 2012;61:21–31.
46. Blefari ML, Sulzer J, Hepp-Reymond MC, Kollias S, Gassert R. Improvement in precision grip force control with self-modulation of primary motor cortex during motor imagery. Front Behav Neurosci. 2015;9:129872.
47. Malouin F, Richards CL. Clinical applications of motor imagery in rehabilitation. Multisens Imagery. 2013;9781461458791:397–419.
48. Calautti C, et al. The relationship between motor deficit and hemisphere activation balance after stroke: a 3T fMRI study. Neuroimage. 2007;34:322–31.
49. Marins T, et al. Structural and functional connectivity changes in response to short-term neurofeedback training with motor imagery. Neuroimage. 2019;194:283–90.
50. Bezmaternykh DD, et al. Application of fMRI and simultaneous fMRI-EEG neurofeedback in post-stroke motor rehabilitation. Bull Exp Biol Med. 2021;171:379–83.
51. Savelov AA, et al. Prospects of synchronous fMRI-EEG recording as the basis for neurofeedback (exemplified on patient with stroke sequelae). Bull Exp Biol Med. 2019;166:390–3.
52. Zatorre RJ, Fields RD, Johansen-Berg H. Plasticity in Gray and White: neuroimaging changes in brain structure during learning. Nat Neurosci. 2012;15:528.
53. Kwakkel G, et al. Effects of augmented exercise therapy time after stroke: a meta-analysis. Stroke. 2004;35:2529–36.
54. Thibault RT, MacPherson A, Lifshitz M, Roth RR, Raz A. Neurofeedback with fMRI: a critical systematic review. Neuroimage. 2018;172:786–807.
55. Ros T, et al. Closed-loop brain training: the science of neurofeedback. Nat Rev Neurosci. 2016;18:86–100.
56. Ninaus M, et al. Neural substrates of cognitive control under the belief of getting neurofeedback training. Front Hum Neurosci. 2013;7:55644.
57. Paret C, et al. Current progress in real-time functional magnetic resonance-based neurofeedback: methodological challenges and achievements. Neuroimage. 2019;202:116107.
58. Paul T, et al. The role of corticospinal and extrapyramidal pathways in motor impairment after stroke. Brain Commun. 2022;5: fcac301.
59. Stinear CM. Stroke rehabilitation research needs to be different to make a difference. F1000Res. 2016;5:1467.
60. Giulia L, et al. The impact of neurofeedback on effective connectivity networks in chronic stroke patients: an exploratory study. J Neural Eng. 2021;18:056052.
61. Cury C, Maurel P, Gribonval R, Barillot C. A sparse EEG-informed fMRI model for hybrid EEG-fMRI neurofeedback prediction. Front Neurosci. 2020;13:1451.

62. Le Franc S, et al. Influence of virtual reality visual feedback on the illusion of movement induced by tendon vibration of wrist in healthy participants. PLoS ONE. 2020;15: e0242416.
63. Ward NS, Carmichael ST. Blowing up neural repair for stroke recovery: preclinical and clinical trial considerations. Stroke. 2020;51:3169–73.
64. Buetefisch CM. Role of the contralesional hemisphere in post-stroke recovery of upper extremity motor function. Front Neurol. 2015;6:214.

Publisher's Note