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Brain–computer interface-assisted pneumatic hand training improves upper limb function after stroke: a randomized controlled trial and EEG characterization

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Abstract

Background

The clinical efficacy of brain–computer interface (BCI)–based rehabilitation after stroke remains uncertain, particularly in the subacute phase, where evidence is limited and clinically meaningful improvement is seldom evaluated. This study aimed to investigate the therapeutic efficacy and electrophysiological mechanisms of BCI-assisted pneumatic hand training in subacute stroke.

Methods

In this prospective randomized controlled trial, 129 patients with stroke were assigned to a BCI group (*n* = 72) or a control group (*n* = 57). Upper limb function was assessed using FMA-UE, ARAT, WMFT, and MBI. Clinically meaningful improvement was evaluated based on minimal clinically important difference (MCID). Resting-state EEG was analyzed for spectral power and topographic distribution.

Results

The BCI group demonstrated greater improvement in FMA-UE scores than the control group (11.57 ± 7.98 vs 5.94 ± 6.13, $p = 0.01$). A higher proportion of patients in the BCI group achieved MCID in FMA-UE, ARAT, and WMFT. EEG analysis revealed increased beta-band power following BCI intervention, predominantly over central and parietal regions. Between-group comparisons showed greater beta-band changes in the BCI group. Post-treatment, no significant differences were observed between the BCI group and healthy controls, suggesting a normalization trend.

Conclusion

BCI-assisted pneumatic hand training enhances upper limb recovery in subacute stroke and is associated with increased beta-band activity, indicating potential neurophysiological mechanisms of motor recovery.

Introduction

Stroke is one of the leading causes of long-term disability in adults worldwide, with up to 85% of survivors experiencing persistent upper limb motor dysfunction beyond the acute phase(1). Given the critical role of the upper limb in activities of daily living (ADL) and occupational tasks, such long-term impairment substantially reduces patients' independence and quality of life(2, 3).Previous studies have demonstrated that timely and effective rehabilitation interventions can partially promote functional recovery and improve activity and participation levels, thereby representing a key strategy for reducing the burden of stroke. In particular, recovery of upper limb function is essential for regaining independence in daily life(4).

Conventional neurorehabilitation strategies largely follow a “periphery-to-central” paradigm, in which peripheral sensory inputs—such as passive physical therapy, functional electrical stimulation (FES), and repetitive task training—are used to facilitate compensatory cortical reorganization. However, for patients with severe motor impairment who are unable to voluntarily initiate motor commands, this approach is often limited by insufficient active engagement, incomplete feedback loops, and plateau effects in rehabilitation outcomes. Clinical evidence suggests that despite receiving multimodal conventional rehabilitation, approximately 40% of patients still exhibit varying degrees of upper limb dysfunction six months after stroke onset(5). Therefore, exploring more effective intervention strategies to overcome the limitations of traditional rehabilitation has become a critical research focus in stroke rehabilitation.

In recent years, advances in neuroengineering and intelligent rehabilitation technologies have led to the increasing application of brain–computer interface (BCI) systems in stroke rehabilitation. BCI provides a novel “central-to-peripheral” rehabilitation paradigm by decoding cortical activity associated with motor intention, such as motor imagery (MI), and translating these signals into control commands for external devices, thereby enabling real-time sensorimotor feedback(6).Previous studies have indicated that BCI training may improve upper limb motor function and promote neuroplasticity in patients with stroke(6–8).However, current evidence regarding its clinical efficacy remains inconclusive. Recent systematic reviews and meta-analyses suggest that the overall effect of BCI interventions on upper limb recovery is modest. Moreover, substantial heterogeneity exists across studies in terms of intervention protocols, training parameters, patient stages, and baseline functional levels. In particular, the effectiveness of BCI in the subacute phase remains unclear, contributing to inconsistencies and potential bias in existing findings(6).

To address these gaps, the present study conducted a prospective randomized controlled trial (RCT) involving 129 patients with subacute stroke. Using a multidimensional assessment framework that incorporates both conventional clinical scales and minimal clinically important difference (MCID), this study aimed to systematically evaluate the clinical efficacy of BCI-assisted pneumatic hand training for upper limb rehabilitation. In addition, by integrating clinical outcomes with electrophysiological measures, we sought to characterize the dynamic changes in EEG rhythms associated with the intervention and to explore the potential neurophysiological mechanisms underlying functional recovery. In addition to efficacy, treatment safety was assessed for participant protection; safety was not defined as a pre-specified study objective, and no formal safety endpoint was analyzed.

Methods

1.1 Study design

This was a single-center, prospective, two-arm, parallel-group randomized controlled trial.Eligible participants were randomly assigned to either the BCI group or the control group using a computer-generated randomization sequence.

A simple randomization method was used. The random allocation sequence was generated by an independent statistician who was not involved in participant enrollment, intervention delivery, outcome assessment, or data analysis. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes, which were opened in the order of enrollment. Participants were enrolled and assigned to their allocated group by a research coordinator according to the envelope order. The research coordinator did not participate in sequence generation, and the enrolling staff had no advance access to the allocation sequence.

Outcome assessors and data analysts were blinded to group allocation. Treating therapists administered the interventions according to group assignment but were not involved in outcome assessment or statistical analysis. Because the BCI device and pneumatic hand were overtly visible, participants and treating therapists could not be blinded to treatment allocation. Blinding of outcome assessors and data analysts was maintained by using coded, de-identified datasets, and all statistical analyses were performed under blinded conditions until the analyses were completed.

Simple randomization was conducted continuously throughout the recruitment period. Therefore, although balanced allocation was intended, the final numbers of participants in the two groups were not exactly equal. The final analysis set included 129 participants, with 72 allocated to the BCI group and 57 allocated to the control group. All participants included in the analysis underwent the same randomization and allocation concealment procedures.

1.2 Participants

A total of 129 patients with stroke admitted to the Department of Rehabilitation Medicine at Beijing Tsinghua Changgung Hospital between January 2024 and March 2025 were consecutively screened and enrolled. All participants met the diagnostic criteria for stroke according to the Chinese Guidelines for the Diagnosis of Major Cerebrovascular Diseases (2019) and had their diagnoses confirmed by cranial computed tomography (CT) or magnetic resonance imaging (MRI).

Inclusion criteria:

1. Diagnosis of stroke based on the above criteria and confirmed by CT or MRI;
2. First-ever stroke, with a disease duration of 7 days to 3 months;
3. Age between 30 and 75 years;
4. Stable vital signs, clear consciousness, and adequate comprehension to follow instructions and complete assessments;
5. No progressive neurological deterioration, with stable conditions of other major organ systems;

6. Willingness to participate and provision of written informed consent.

Exclusion criteria:

1. Disturbance of consciousness;
2. Coexisting neurological disorders;
3. Severe cognitive impairment, psychiatric symptoms, or emotional disorders that would interfere with training or assessment;
4. Severe dysfunction of major organs (heart, lung, liver, or kidney);
5. History of epilepsy or current use of antiepileptic medication;
6. Clinical deterioration, including new infarction or increased hemorrhage;
7. Significant skull defects or other conditions affecting EEG acquisition;
8. Presence of pacemakers, intracranial metal implants, or other implanted metallic devices;
9. Inability or unwillingness to complete the study for any reason.

For the quantitative EEG comparison, an age- and sex-matched healthy control group (n = 24) was recruited from the community and hospital staff volunteers to serve as a reference. Healthy controls had no history of stroke or other neurological or major psychiatric disease, no significant cognitive impairment, and no contraindication to EEG; they underwent the same resting-state EEG acquisition procedure.

1.3 Interventions

1.3.1 Control Group

Participants in the control group received conventional occupational therapy (OT) twice daily, 30 minutes per session, five times per week for 2 weeks. The intervention included proper limb positioning, hand function training, and commonly used neurorehabilitation techniques such as the Bobath concept, proprioceptive neuromuscular facilitation (PNF), Brunnstrom approach, Rood technique, and motor relearning therapy. Training also included activities of daily living (ADL). These interventions represent standard clinical OT practice. All interventions were delivered by registered occupational therapists with clinical experience in neurorehabilitation.

1.3.2 BCI Group

Participants in the BCI group received conventional OT combined with brain–computer interface (BCI) training. Conventional OT was administered once daily (30 minutes per session, five times per week for 2 weeks), with the same content as the control group. In addition, BCI training was performed once daily (30 minutes per session, five times per week for 2 weeks).

To minimize potential effects of training order on outcomes, a randomized alternating sequence design was adopted. The training order was determined using a computer-generated random number table at enrollment and remained fixed throughout the intervention period.

The BCI system used in this study was an active rehabilitation system integrating a brain–computer interface with a pneumatic hand device, developed under the National Key Research and Development

Program of China (Project No. 2022YFC3601100). The system employed a motor imagery (MI)-based paradigm with video-guided and auditory instructions to enhance patient engagement and improve the discriminability of EEG signals. When valid EEG patterns were detected, the pneumatic hand device executed synchronized grasping, extension, and wrist dorsiflexion movements, providing real-time motor feedback.

BCI training paradigm:

Each BCI training session consisted of three levels of difficulty: easy, moderate, and difficult. A 1-minute resting-state EEG recording was obtained before each level. Easy level: Page-turning task, consisting of three steps per action, repeated over five cycles (approximately 6 minutes). Moderate level: Opening a can with one hand, consisting of four steps per action, repeated over five cycles (approximately 8 minutes). Difficult level:%) Grasping a milk cup, consisting of five steps per action, repeated over five cycles (approximately 9 minutes).

Participants were instructed to perform motor imagery of each action step. Successful imagery triggered the pneumatic hand device to execute a grasping movement, providing closed-loop feedback.

BCI training was delivered by therapists and research staff who had completed dedicated training in operation of the brain-computer interface system, including electrode placement, signal-quality checking, system calibration, task instruction, device operation, and management of discomfort or adverse events during the intervention. Interventions were delivered according to predefined standard operating procedures to maintain treatment fidelity, and all sessions were documented. During the trial, both groups received routine inpatient stroke care; concomitant rehabilitation and medications were not restricted during the trial.

1.4 EEG Acquisition and Analysis

Electroencephalography (EEG) signals were recorded using a multi-channel EEG acquisition system (NSM2, Boruikang Technology, Changzhou, China) at a sampling rate of 2000 Hz. An online average reference was applied during acquisition. EEG data were collected using a 32-channel electrode cap arranged according to the international 10–20 system, covering frontal, central, parietal, occipital, and temporal regions. Ag/AgCl electrodes were used, and electrode impedance was maintained below 20 kΩ. Participants were seated comfortably in a quiet environment and instructed to remain awake with eyes open during a 10-minute resting-state EEG recording.

Offline data processing was performed using the MNE-Python platform. Raw EEG data were first imported along with electrode location information. Preprocessing steps included removal of power line noise using a 50 Hz notch filter, band-pass filtering (1–45 Hz), detection and interpolation of bad channels, and artifact correction using independent component analysis (ICA) to remove ocular and other physiological artifacts. Following preprocessing, data were re-referenced to the common average.

For spectral analysis, power spectral density (PSD) was estimated using Welch's method with a window length of 2 seconds, 50% overlap, and a Hamming window. The frequency range analyzed was 1–42.5 Hz. Based on established conventions, frequency bands were defined as delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–42.5 Hz). Spectral power within each band was further normalized to relative power, defined as the proportion of power in each frequency band relative to the total power (1–42.5 Hz), to reduce inter-individual variability in signal amplitude. For spatial analysis, relative power values were projected onto the scalp to generate topographic maps, illustrating the spatial distribution of EEG activity across frequency bands.

All EEG-derived measures were calculated at the individual level and subsequently used for between-group comparisons and pre–post treatment analyses. In addition, functional connectivity metrics were evaluated, and their relationships with clinical outcomes were assessed.

1.5 Clinical Outcome Measures

The primary outcome was the change in FMA-UE score from baseline to the end of the 2-week intervention. Secondary outcomes were the changes in ARAT, WMFT, and MBI scores. All clinical outcomes were assessed at two time points: at baseline (before intervention) and immediately after the 2-week intervention.

1.5.1 Fugl–Meyer Assessment for Upper Extremity

The Fugl–Meyer Assessment for the Upper Extremity (FMA-UE) is a widely used and validated scale for evaluating upper limb motor impairment in patients with stroke. It assesses joint movement, reflex activity, coordination, and the ability to perform isolated movements of the shoulder, elbow, forearm, wrist, and hand. The scale consists of 33 items with a total score of 66 points. Each item is scored on a 3-point ordinal scale (0 = unable to perform, 1 = partially performed, 2 = fully performed), with higher scores indicating better motor function.

1.5.2 Action Research Arm Test

The Action Research Arm Test (ARAT) is a standardized tool for assessing upper limb function in patients with stroke and other neurological disorders. It evaluates functional abilities across four domains: grasp, grip, pinch, and gross movement. The test includes 19 tasks, each scored on a 4-point scale (0–3), yielding a total score of 57 points. Higher scores indicate better upper limb function. The ARAT has demonstrated good reliability, validity, and responsiveness.

1.5.3 Wolf Motor Function Test

The Wolf Motor Function Test (WMFT) is a quantitative measure of upper limb motor function commonly used in patients with central nervous system injuries, including stroke. It consists of 15 functional, task-oriented movements and 2 strength-based tasks. The WMFT assesses both the time required to complete each task (in seconds) and the quality of movement (scored on a 6-point scale from 0 to 5).

Shorter completion times and higher quality scores indicate better motor performance. The WMFT has demonstrated good reliability and validity.

1.5.4 Modified Barthel Index

The Modified Barthel Index (MBI) is used to assess functional independence in activities of daily living (ADL). It consists of 10 items, including feeding, bathing, personal hygiene, dressing, toileting, bladder and bowel control, transfers (bed to chair), ambulation, and stair climbing. Each item is scored based on the level of assistance required, with a total score ranging from 0 to 100. Higher scores indicate greater independence. The MBI has been widely validated and is commonly used in stroke rehabilitation to assess ADL performance.

1.5.5 Definition and Analysis of Minimal Clinically Important Difference

To further evaluate the clinical significance of treatment effects, the minimal clinically important difference (MCID) was applied to the primary outcome measures. MCID is defined as the smallest change in a score that is perceived as beneficial and clinically meaningful by patients. Previous anchor-based studies have suggested that the MCID for FMA-UE is approximately 12.4 points in patients with moderate to severe upper limb impairment during the recovery phase; therefore, this threshold was adopted in the present study(9). For the Action Research Arm Test (ARAT), an MCID of 12 points was applied based on previous anchor-based studies (9). For the Wolf Motor Function Test (WMFT), the MCID was defined as 1.0 points (9). The minimal clinically important difference for the Barthel Index (BI) has been reported as 1.85 points on the original 20-point scale(9). Given that the Modified Barthel Index (MBI) uses a 100-point scoring system, this value corresponds to approximately 9.25 points after linear transformation. Therefore, in the present study, an improvement of approximately 9–10 points in MBI was considered indicative of clinically meaningful improvement.

Based on these thresholds, patients were categorized into two groups: those who achieved MCID and those who did not. The proportion of patients achieving MCID was calculated for each group, and between-group differences were analyzed using the chi-square test. For MCID responder analyses, only participants with complete baseline and post-intervention data for the corresponding outcome measure were included. Therefore, the denominator for each MCID analysis was based on the available complete-case sample for that specific scale. Participants with missing post-intervention data for a given outcome were excluded from the MCID analysis of that outcome but remained included in other analyses when relevant data were available.

1.6 Safety assessment:

Dverse events were defined as any untoward or unintended medical occurrence during the trial, regardless of its presumed relationship to the intervention. Adverse events of interest included, but were not limited to, fatigue, dizziness, headache, skin irritation or discomfort at electrode sites, muscle

soreness, increased spasticity, pain, abnormal blood-pressure responses, falls, and any other unexpected symptoms occurring during or after occupational therapy or BCI training.

A safety stopping guideline was specified, whereby intervention would be discontinued if a serious adverse event occurred. Serious adverse events were defined as events resulting in death, that were life-threatening, that required or prolonged hospitalization, that caused persistent disability, or that were otherwise judged medically important by the investigators.

Adverse events were collected systematically: before and after each session, therapists actively asked participants about any discomfort or new symptoms and monitored their condition during training, and any adverse or unintended event was recorded on a standardized case report form (including date of onset, presentation, severity, duration, management, outcome, and possible relationship to the intervention). Vital signs and tolerance were monitored when indicated, and participants were instructed to report any delayed discomfort occurring outside treatment sessions.

Safety monitoring was performed during every intervention session and at each outcome-assessment visit; all adverse events were reviewed by the study team, and serious adverse events were to be reported promptly in accordance with the requirements of the Institutional Ethics Committee of Beijing Tsinghua Changgung Hospital.

1.7 Sample size calculation

The sample size was estimated using G*Power version 3.1, with the change in Fugl–Meyer Assessment for the Upper Extremity (FMA-UE) score from baseline to post-intervention specified as the primary outcome. Based on previous studies of upper limb rehabilitation after stroke and BCI-assisted interventions, a conservative moderate between-group effect was assumed. The expected between-group difference in FMA-UE change was set at 4.0 points, with a common standard deviation of 8.0, corresponding to a standardized effect size of 0.50. With a two-sided significance level of $\alpha = 0.05$, a statistical power of 80% ($1 - \beta = 0.80$), and an allocation ratio of 1:1, the minimum required sample size was estimated to be 63 participants per group. No formal interim analyses were planned or conducted, however, after accounting for an anticipated dropout rate of 10%, the target sample size was approximately 70 participants per group.

1.8 Statistical Analysis

Clinical outcomes were analysed for all randomized participants with available data for the respective outcome; no imputation was performed for missing data. The number of participants contributing to each analysis is reported with the corresponding result, and denominators for MCID responder analyses reflect the complete-case sample for each scale. No important changes were made to the trial methods after commencement. Recruitment was completed as planned once the target sample size was reached; the trial was not stopped early.

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and Python. Clinical outcomes and baseline characteristics were described according to variable types. Continuous variables were first tested for normality. Data following a normal distribution were expressed as mean ± standard deviation (mean ± SD), and between-group comparisons were performed using independent-samples t-tests. For data that did not meet the assumptions of normality or homogeneity of variance, results were presented as median (interquartile range, IQR), and comparisons between groups were conducted using the Mann–Whitney U test. Categorical variables were expressed as counts (n) and percentages (%), and comparisons were performed using the chi-square test or Fisher's exact test, as appropriate.

EEG spectral analyses were conducted in the Python environment. Within-group comparisons (pre- vs. post-treatment) of relative power in each frequency band were performed using paired t-tests, while between-group comparisons were conducted using independent-samples t-tests. For comparisons among the healthy control, BCI, and conventional treatment groups, one-way analysis of variance (ANOVA) was applied, followed by post hoc pairwise comparisons.

To control for the risk of type I error arising from multiple comparisons across frequency bands, channels, or outcome measures, the Benjamini–Hochberg procedure was applied for false discovery rate (FDR) correction.

Topographic EEG analyses were performed at the channel level. Statistical tests were conducted for each electrode, and corresponding P values were corrected using the FDR method. Only electrodes that remained statistically significant after FDR correction were considered to exhibit meaningful spatial differences.

Correlation analyses were performed using Spearman's rank correlation coefficient to assess the relationships between key EEG metrics and both baseline FMA-UE scores and changes in FMA-UE scores. FDR correction was also applied to these analyses. The significance level was set at $\alpha = 0.05$. A two-tailed $P < 0.05$ or FDR-corrected $P < 0.05$ was considered statistically significant. Figures were generated using GraphPad Prism 8 and Python.

The EEG spectral, topographic, and correlation analyses, as well as the EEG-subgroup comparisons, were exploratory and were not pre-specified as confirmatory endpoints; their P values are interpreted descriptively.

Results

2.1 Baseline Characteristics

No significant differences were observed between the two groups in terms of gender, age, lesion side, time since stroke onset, or stroke type (all $P > 0.05$). In addition, there were no statistically significant

differences in baseline clinical scores between the groups (all P > 0.05). Detailed results are presented in Table 1.

Table 1
Baseline Characteristics of Participants

Variable	BCI Group (n = 72)	Control Group (n = 57)	Statistic	*P* value
Age (years)	57.44 ± 11.64	58.95 ± 12.84	-0.69	0.493
Time since stroke onset(days)	32.25 ± 20.63	33.50 ± 19.80	-0.33	0.740
Sex			0.28	0.598
Male	51 (70.8%)	37 (64.9%)		
Female	21 (29.2%)	20 (35.1%)		
Handedness			2.42	0.120
Right-handed	71 (98.6%)	52 (91.2%)		
Left-handed	1 (1.4%)	5 (8.8%)		
Lesion side			0.82	0.366
Left	41 (56.9%)	27 (47.4%)		
Right	31 (43.1%)	30 (52.6%)		
Stroke type			0.00	1.000
Ischemic stroke	52 (72.2%)	41 (71.9%)		
Hemorrhagic stroke	20 (27.8%)	16 (28.1%)		
* Indicates statistical significance (*P* < 0.05).				

Table 2
Baseline Clinical Assessments

Variable	BCI Group (n = 72)	Control Group (n = 57)	Statistic	*P* value
MMSE	26.10 ± 3.85	26.39 ± 4.33	-0.39	0.698
FMA-UE	23.71 ± 16.45	28.86 ± 19.34	-1.60	0.112
ARAT	14.38 ± 17.17	18.14 ± 17.79	-1.11	0.268
WMFT	28.06 ± 16.02	33.23 ± 17.72	-1.58	0.119
MBI	50.83 ± 19.34	54.81 ± 20.69	-1.11	0.267
* Indicates statistical significance (*P* < 0.05).				

2.2 Comparison of Clinical Outcomes Between the BCI and Control Groups

There were no statistically significant differences in baseline clinical scores between the BCI and control groups (P > 0.05). Analysis of pre–post changes (Δ) showed greater improvements in the BCI group than in the control group across several clinical outcomes. The change in FMA-UE score was significantly greater in the BCI group than in the control group (10.17 ± 7.91 vs. 6.69 ± 5.89; mean difference = 3.38, 95% CI: 0.53–6.24; P = 0.02). Similar between-group differences were observed for ARAT (9.21 ± 9.63 vs. 5.87 ± 5.63; mean difference = 3.34, 95% CI: 0.10–6.58; P = 0.04) and WMFT (10.36 ± 8.25 vs. 7.27 ± 5.95; mean difference = 3.09, 95% CI: 0.14–6.03; P = 0.04). For MBI, the BCI group showed a numerically greater improvement than the control group; however, the between-group difference was not statistically significant (16.31 ± 13.73 vs. 12.30 ± 12.08; mean difference = 2.67, 95% CI: −1.28–9.32; P = 0.14). Detailed results are presented in Table 3.

Table 3
Comparison of Changes in Clinical Outcomes Between Groups

Variable	BCI Group	Control Group	Mean differences (95% CI)	*F* value	Hedges' g	*P* value
Δ FMA-UE	10.17 ± 7.91	6.69 ± 5.89	3.38 (0.53, 6.24)	6.75	0.63	**0.02***
Δ ARAT	9.21 ± 9.63	5.87 ± 5.63	3.34(0.10, 6.58)	14.94	0.46	**0.04***
Δ WMFT	10.36 ± 8.25	7.27 ± 5.95	3.09(0.14, 6.03)	2.68	0.59	**0.04***
Δ MBI	16.31 ± 13.73	12.30 ± 12.08	2.67(-1.28, 9.32)	2.79	0.46	0.14

Δ denotes the change between pre- and post-treatment (post-treatment minus pre-treatment); * indicates statistical significance (*P* < 0.05).

2.3 Comparison of MCID Achievement Between the BCI and Control Groups

MCID responder analyses were conducted using complete-case samples for each outcome measure. Accordingly, the denominators varied slightly across analyses depending on the availability of complete pre- and post-intervention data. Analysis of minimal clinically important difference (MCID) demonstrated higher responder rates in the BCI group across multiple outcome measures. For FMA-UE, the proportion of patients achieving MCID was significantly greater in the BCI group than in the control group (40.3% [29/72] vs. 9.6% [5/52]; OR = 6.34, 95% CI: 2.25–17.85; P = 0.01). For ARAT, a significantly higher MCID achievement rate was observed in the BCI group (23.6% [17/72] vs. 7.7% [4/52]; OR = 3.71, 95% CI: 1.17–11.78; P = 0.02). For WMFT, the proportion of patients achieving MCID was also significantly greater in the BCI group (80.6% [58/72] vs. 50.0% [26/52]; OR = 4.14, 95% CI: 1.87–9.20; P = 0.01). For MBI,

although the MCID achievement rate was higher in the BCI group than in the control group (62.5% [45/72] vs. 48.1% [25/52]), the between-group difference did not reach statistical significance (OR = 1.80, 95% CI: 0.87–3.71; P = 0.14).

2.3.1 Baseline Characteristics of the EEG Subgroup

The EEG subgroup was a pre-specified subset: from the 129 enrolled patients, consecutive participants meeting predefined EEG criteria were included, independent of treatment response or outcome. Recordings that did not meet the predefined EEG quality-control standards (e.g., excessive artefacts, poor electrode contact, marked myogenic or ocular contamination, or insufficient task completion) were excluded. To assess the representativeness of the EEG subgroup relative to the overall clinical sample, baseline characteristics were compared between the EEG and non-EEG groups. No statistically significant differences were observed between the two groups with respect to treatment allocation, sex, time since stroke onset, handedness, lesion side, stroke type, baseline MMSE scores, or baseline clinical outcome measures (FMA-UE, ARAT, WMFT, and MBI) (all P > 0.05). A significant difference was identified in age, with the EEG subgroup being younger than the non-EEG group (53.68 ± 11.83 vs. 59.34 ± 12.02; P = 0.031).

These findings indicate that the EEG subgroup was broadly comparable to the overall clinical cohort in most demographic and clinical characteristics, supporting its representativeness. However, the observed age difference should be considered when interpreting the results. Detailed results are presented in Tables 5 and 6.

Table 5
Comparison of Baseline Characteristics Between the EEG Subgroup and the Non-EEG Group

Variable	**EEG Subgroup (n = 28)**	**Non-EEG Group (n = 101)**	**Statistic**	***P* value**
Age (years)	53.68 ± 11.83	59.34 ± 12.02	t = -2.18	0.03
Time since stroke onset(days)	60.43 ± 34.21	75.62 ± 40.15	t = -1.42	0.16
Sex			χ^2 = 0.08	0.78
Male	20 (71.4%)	68(67.3%)		
Female	8 (28.6%)	33 (32.7%)		
Handedness			χ^2 =2.42	0.12
Right-handed	26 (92.9%)	90 (89.1%)		
Left-handed	2 (7.1%)	11(10.9%)		
Lesion side			χ^2 = 0.01	0.91
Left	13 (46.4%)	49 (48.5%)		
Right	15 (53.6%)	52 (51.5%)		
Stroke type			χ^2 = 0.11	0.74
Ischemic stroke	24 (85.7%)	84 (83.2%)		
Hemorrhagic stroke	4 (14.3%)	17(16.8%)		
* Indicates statistical significance ($P < 0.05$).				

Table 6
Comparison of Baseline Clinical Assessments Between the EEG Subgroup and the Non-EEG Group

Variable	**EEG Subgroup (n = 28)**	**Non-EEG Group (n = 101).**	**Statistic**	***P* value**
MMSE	25.21 ± 3.15	25.47 ± 3.02	-0.39	0.69
FMA-UE	32.54 ± 14.62	30.12 ± 13.98	0.82	0.41
ARAT	18.73 ± 16.45	12.94 ± 13.02	1.88	0.06
WMFT	30.61 ± 12.38	28.47 ± 11.96	0.89	0.37
MBI	58.21 ± 19.45	57.36 ± 18.92	0.17	0.86
* Indicates statistical significance ($P < 0.05$).				

Baseline characteristics were compared between the BCI and control groups within the EEG subgroup. No statistically significant differences were observed in demographic variables, including age, sex, time since stroke onset, handedness, and lesion side, or in stroke type. Baseline clinical scores, including MMSE, FMA-UE, ARAT, WMFT, and MBI, did not differ significantly between the groups (all P > 0.05). Comparisons with the overall cohort are presented in Tables 7 and 8.

Table 7
Comparison of Baseline Characteristics Between the BCI and Control Groups Within the EEG Subgroup

Variable	BCI Group (n = 16)	Control Group (n = 12)	Statistic	*P* value
Age	51.2 ± 10.1	57.0 ± 13.5	-1.25	0.226
Time since stroke onset	27.4 ± 18.5	29.8 ± 17.0	-0.34	0.735
Sex (Male/Female)	12 / 4	6 / 6	0.94	0.243
Handedness (Right/Left)	16 / 0	10 / 2	0.91	0.175
Lesion side (Right/Left)	9 / 7	5 / 7	0.15	0.703
Stroke type (Ischemic/Hemorrhagic)	12 / 4	7 / 5	0.28	0.432
* Indicates statistical significance (*P* < 0.05).				

Table 8
Comparison of Baseline Characteristics Between the BCI and Control Groups Within the EEG Subgroup

Variable	BCI Group (n = 16)	Control Group (n = 12)	Statistic	*P* value
MMSE	24.4 ± 4.3	26.2 ± 5.0	-0.96	0.349
FMA-UE	19.2 ± 13.4	29.7 ± 17.7	-1.70	0.104
ARAT	8.7 ± 14.0	13.9 ± 16.0	-0.88	0.391
WMFT	22.4 ± 14.2	35.0 ± 17.5	-1.99	0.062
MBI	49.0 ± 14.6	56.2 ± 21.7	-0.99	0.336
* Indicates statistical significance (*P* < 0.05).				

2.3.2 Whole-brain QEEG Spectral Analysis

Pre-treatment whole-brain QEEG spectral analysis showed abnormal spectral patterns in the patient groups compared with healthy controls. After Benjamini–Hochberg correction for multiple comparisons, relative theta-band power was significantly higher in both stroke groups than in healthy controls (all P_FDR < 0.001), whereas relative beta-band power was significantly lower (P_FDR < 0.05). No significant differences were observed in relative alpha- or gamma-band power between the patient groups and

healthy controls (all P_FDR > 0.05). Within the patient cohort, no significant differences in pre-treatment relative power across frequency bands were observed between the BCI and conventional therapy groups. Detailed results are presented in Table 9.

Post-treatment comparisons with healthy controls showed that relative theta-band power remained significantly higher in both the BCI and conventional therapy groups (P_FDR < 0.01). In the beta band, relative power was lower in the conventional therapy group than in both the BCI group and healthy controls, whereas no statistically significant difference was observed between the BCI group and healthy controls. Detailed results are presented in Table 10.

Table 9
Baseline Comparison of Whole-Brain QEEG Spectral Power Across Frequency Bands Among Groups

Frequency Band	BCI Group	Control Group	Healthy Group	*F* value	*P* value	*P_FDR*
δ	**1.729 ± 0.387**	**1.902 ± 0.298**	**1.903 ± 0.341**	**1.95**	**0.15**	**0.24**
θ	2.386 ± 0.828*	2.181 ± 0.552*	1.629 ± 0.534	8.44	0.01	0.01
α	3.183 ± 1.060	3.245 ± 0.761	3.204 ± 0.838	0.03	0.97	0.97
β	0.523 ± 0.196*	0.532 ± 0.157*	0.648 ± 0.169	3.69	0.03	0.04
γ	0.156 ± 0.063	0.144 ± 0.064	0.178 ± 0.053	1.91	0.16	0.24
* Indicates statistical significance (*P* < 0.05).						

Table 10
Post-treatment Whole-Brain QEEG Spectral Power Across Frequency Bands Among Groups

Frequency Band	BCI Group	Control Group	Healthy Group	*F* value	*P* value	*P_FDR*
δ	**1.951 ± 0.268**	**1.918 ± 0.457**	**1.903 ± 0.341**	**0.11**	**0.90**	**0.90**
θ	2.288 ± 0.694*	2.185 ± 0.653*	1.629 ± 0.534	7.43	0.00	0.00
α	3.078 ± 1.007	3.429 ± 0.870	3.204 ± 0.838	0.81	0.45	0.52
β	0.528 ± 0.188	0.449 ± 0.150*	0.648 ± 0.169	5.35	0.01	0.02
γ	0.170 ± 0.061	0.163 ± 0.066	0.178 ± 0.053	3.15	0.05	0.09
* Indicates statistical significance (*P* < 0.05).						

2.3.3 Topographic Analysis

In the theta band, the topographic findings were consistent with the spectral analysis. At baseline, stroke patients exhibited widespread increases in theta activity over the frontal and central regions, whereas healthy controls showed a relatively uniform and lower distribution. Following treatment, both patient groups maintained similar spatial patterns, suggesting stability of the theta-band abnormality. Difference

topographic maps demonstrated widespread positive deviations in the frontal and central regions in the patient groups relative to healthy controls.

In the beta band, topographic analysis further refined the between-group differences observed in spectral results. At baseline, both patient groups showed reduced beta activity across the scalp. After treatment, the conventional therapy group continued to exhibit broadly reduced beta power, predominantly over the central and surrounding regions, remaining clearly different from healthy controls. In contrast, the BCI group showed partial recovery of beta activity, with distributions in the central and portions of the parietal regions trending toward those of healthy controls. Difference maps indicated widespread negative deviations in the central and parietal regions in the conventional therapy group compared with healthy controls, whereas the extent of negative deviation was smaller in the BCI group. Maps of between-group changes further demonstrated more pronounced positive changes in the BCI group over the central and parts of the parietal regions in the beta band.

In the gamma band, although spectral analysis did not reach statistical significance, topographic maps suggested a consistent trend. The conventional therapy group continued to show relatively reduced gamma activity after treatment, primarily over the central and parietal regions, whereas the BCI group exhibited relatively increased gamma activity in localized areas. Detailed spatial distributions are shown in Figs. 4 and 5.

2.4 Safety results

No adverse events or unintended events were reported in either group during the treatment interventions.

Discussion

4.1 BCI Combined with Pneumatic Hand Training Enhances Clinically Meaningful Upper Limb Recovery

Existing systematic reviews and meta-analyses indicate that most BCI-related studies have predominantly focused on chronic stroke populations, whereas randomized controlled evidence in subacute stroke remains limited. Moreover, substantial heterogeneity in intervention paradigms, training parameters, and patient characteristics contributes to uncertainty in effect estimation and increases the risk of bias, thereby limiting the generalizability of current evidence(10–12).

Against this background, the present prospective randomized controlled trial systematically evaluated the clinical efficacy of brain–computer interface (BCI) combined with pneumatic hand training in patients with subacute stroke. Compared with conventional therapy, the BCI group demonstrated greater improvement in FMA-UE scores, with consistent benefits also observed in ARAT and WMFT outcomes. These findings suggest that BCI-assisted training combined with occupational therapy may confer

additional benefits for upper limb motor recovery, particularly in grasping, object manipulation, and task-oriented motor performance. This study further incorporated minimal clinically important difference (MCID) analysis to evaluate the clinical relevance of treatment effects. While mean score changes reflect statistical differences at the group level, they do not necessarily indicate whether individual patients achieve functionally meaningful improvement. MCID provides a more clinically interpretable threshold, reflecting changes that are perceptible and meaningful to patients(9).In this study, the BCI group showed higher MCID achievement rates for FMA-UE, ARAT, and WMFT, indicating that BCI-related improvements were not only statistically significant but also more likely to translate into clinically meaningful functional gains at the individual level. These findings therefore extend current evidence for BCI-based upper limb rehabilitation in subacute stroke from both statistical and clinical significance perspectives.

4.2 Beta-Band Oscillatory Activity as a Potential Electrophysiological Marker of BCI-Induced Modulation

At the electrophysiological level, the present study identified characteristic alterations in resting-state EEG rhythms in stroke patients at baseline, manifested as increased relative power in the theta band and reduced activity in the beta band, reflecting a shift toward enhanced low-frequency and attenuated high-frequency oscillatory activity. Consistent with prior literature, post-stroke EEG has been widely characterized by a global slowing pattern, with increased relative power in low-frequency bands (theta and delta) and decreased power in higher-frequency bands (alpha and beta). Such alterations are thought to reflect cortical slowing, disrupted neuronal synchrony, and impaired sensorimotor network integrity following stroke(13–15). Accordingly, the baseline findings observed in the present study are in line with the canonical electrophysiological profile reported in stroke populations.

Following intervention, these abnormalities persisted to a certain extent in both patient groups. Subgroup analysis revealed that relative theta power remained elevated in both the BCI and conventional therapy groups compared with healthy controls, with no significant between-group differences, suggesting that low-frequency abnormalities may be relatively resistant to short-term modulation. In contrast, the beta band demonstrated a more differentiated pattern: while the conventional therapy group remained significantly different from healthy controls, the BCI group no longer showed a statistically significant difference, indicating a tendency toward normalization of beta activity following BCI intervention. Topographical analyses further contextualized these spectral findings. At baseline, theta enhancement was predominantly distributed over frontal and central regions, whereas reduced beta activity was primarily localized to central and parietal areas. Post-intervention, the spatial distribution of theta abnormalities remained largely unchanged; however, the BCI group exhibited relative enhancement of beta activity in central and parietal regions, whereas persistently reduced beta activity was observed in the conventional group. Given that central regions correspond to primary sensorimotor cortices and parietal regions are implicated in sensory integration and motor planning, these findings may indicate modulation of sensorimotor cortical dynamics following BCI training.

Previous studies have suggested that short-term rehabilitation or neuromodulatory interventions can induce changes in alpha and beta oscillations within sensorimotor networks; however, the extent to which such local oscillatory changes translate into stable large-scale network reorganization remains contingent upon factors such as intervention duration, training intensity, and analytical approaches(16).Beta oscillations, in particular, have been consistently associated with motor preparation, execution, and sensorimotor integration, and are regarded as key electrophysiological markers of motor system function after stroke. Indeed, studies in subacute stroke populations have reported associations between resting-state beta activity and upper limb function measures such as FMA-UE and ARAT, suggesting that beta oscillations may partially reflect motor functional status(17).Nevertheless, no significant association was observed between changes in beta activity and clinical improvement in the present study after correction for multiple comparisons. This discrepancy may, in part, be attributable to differences in analytical frameworks. Prior studies have predominantly examined cross-sectional relationships between electrophysiological measures and behavioral performance at a single time point, whereas the present study evaluated correlations between longitudinal changes. Such change–change associations are inherently more susceptible to inter-individual variability, baseline functional heterogeneity, recovery trajectories, and differential responsiveness to intervention.

Moreover, no significant alterations in functional connectivity were detected. This finding does not negate the neuromodulatory effects of BCI but rather suggests a potential temporal dissociation between clinical recovery, local oscillatory modulation, and large-scale network reorganization. Post-stroke network reorganization is widely regarded as a dynamic, stage-dependent process influenced by lesion characteristics, recovery phase, and intervention intensity. Consequently, short-term functional gains may not be accompanied by detectable changes in resting-state functional connectivity(18).Compared with network-level metrics, local oscillatory activity—particularly within the beta band—may represent a more sensitive marker of early neurophysiological responses to intervention. Prior work has demonstrated that beta oscillations are associated with motor performance and responsiveness to training, supporting the interpretation that the observed enhancement of beta activity in central and parietal regions reflects early-stage modulation of sensorimotor cortical function(18).Clinical recovery is a multifactorial process influenced by spontaneous recovery, training-induced adaptation, compensatory strategies, and baseline functional status. These factors may weaken the direct linear coupling between electrophysiological changes and behavioral outcomes.

No significant changes in EEG functional connectivity or its association with clinical improvement were observed in the present study. This finding may, at least in part, be attributable to methodological factors. Specifically, the relatively limited sample size of the EEG subgroup may have reduced the statistical power to detect connectivity effects. In addition, EEG functional connectivity measures are highly sensitive to signal-to-noise ratio, preprocessing pipelines, and the choice of connectivity metrics, and different analytical strategies may yield divergent results. Previous systematic reviews have also highlighted substantial heterogeneity in both methodology and findings across EEG/MEG network studies in stroke. Therefore, the absence of detectable functional connectivity alterations and their

associations with clinical outcomes under the current sample size and analytical conditions appears methodologically plausible.

The present findings support a framework in which local oscillatory modulation may precede stable large-scale network reorganization. Short-term BCI intervention may primarily influence sensorimotor cortical dynamics, particularly beta-band activity over central and parietal regions, whereas the emergence of consistent brain–behavior relationships and global network reconfiguration may require longer intervention periods, larger sample sizes, and extended follow-up.

Conclusion

This study demonstrates that BCI-assisted pneumatic hand training effectively promotes upper limb functional recovery in patients with subacute stroke and leads to a higher proportion of clinically meaningful improvements compared with conventional therapy. Electrophysiological findings suggest that increased beta-band activity over central and parietal regions may represent an early neurophysiological response to BCI intervention and serve as a potential electrophysiological indicator of sensorimotor cortical modulation.

Limitations

Several limitations should be acknowledged. First, EEG analyses were conducted in a relatively small subgroup, which may have limited statistical power, particularly for detecting functional connectivity changes and EEG–clinical associations. Second, the intervention period was relatively short (2 weeks), and the follow-up duration was limited, such that the findings may primarily reflect early neurophysiological changes and short-term functional improvements rather than long-term network reorganization and stable brain–behavior relationships. Third, EEG analyses in this study mainly focused on spectral power and its spatial distribution. Although functional connectivity analysis was performed, no significant findings were observed. Future studies incorporating multimodal neuroimaging approaches (e.g., fMRI or DTI) and more advanced network analysis methods may provide a more comprehensive understanding of the neural mechanisms underlying BCI intervention. Finally, the study population consisted of individuals with subacute stroke, and the generalizability of the findings to other stages of stroke recovery requires further validation in larger and more diverse cohorts.

Declarations

During the preparation of this manuscript, the authors used ChatGPT (OpenAI, San Francisco, CA, USA) to assist with language editing and proofreading. After using these services, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Beijing Tsinghua Changgung Hospital (approval number 23323-0-02). Participants were not involved in the design, conduct, or reporting of this study. Participants took part only as study subjects and provided written informed consent before enrollment; during the trial they were informed of the study procedures, potential benefits, and risks, and their tolerance and adverse events were monitored throughout the intervention. All procedures were conducted in accordance with the Declaration of Helsinki and relevant institutional guidelines.

Trial registration

Chinese Clinical Trial Registry (ChiCTR), ChiCTR2400079594, https://www.chictr.org.cn, registered on 13/09/2020.

Consent for publication

Not applicable

Availability of data and materials

The raw data supporting the findings of this study are available from the corresponding author upon reasonable request, provided that such requests align with ethical guidelines, institutional policies, and any applicable data protection regulations.

The full trial protocol is provided as a peer-review file accompanying this submission. **Competing interests**

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' contributions

Xiang Cheng: Conceptualization, neuroimaging analysis, statistical modeling, and original draft preparation.

Xiang Yu Deng: Clinical study design interpretation of clinical findings, and manuscript drafting and revision.

Ming Chen Zheng: Data acquisition and technical support for the image processing pipeline.

Yun Guo: Clinical data collection, lesion segmentation, and data curation.

Run Qiu: Clinical data collection.

XueYi Ni: Clinical data collection.

Wei Bei Dou: Project supervision, methodology refinement, and critical revision of the manuscript.

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The full trial protocol is provided as a peer-review file accompanying this submission.

Competing interests

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Table 4

Table 4 is available in the Supplementary Files section.

Figures

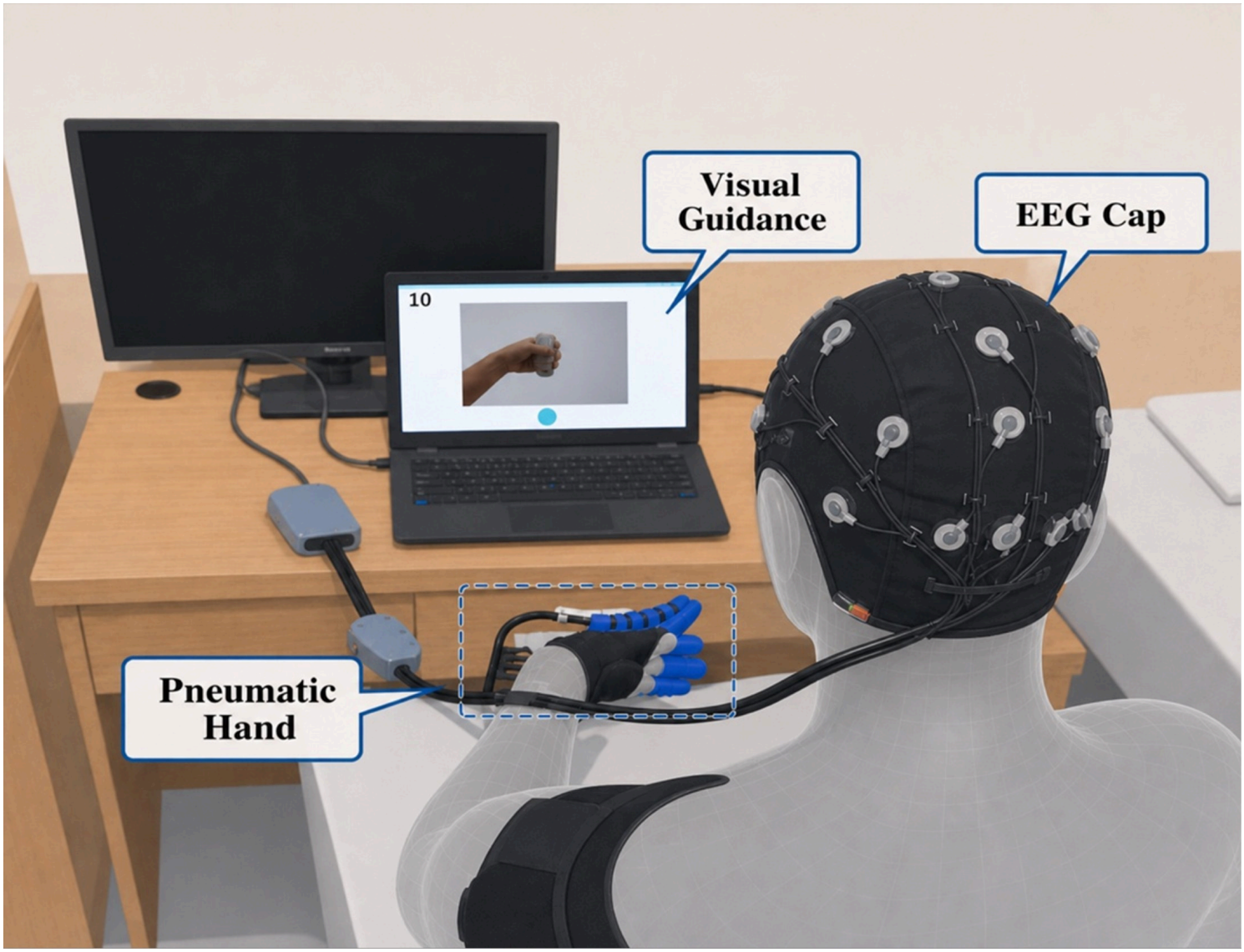


Figure 1

Schematic Diagram of the BCI-Based Rehabilitation System

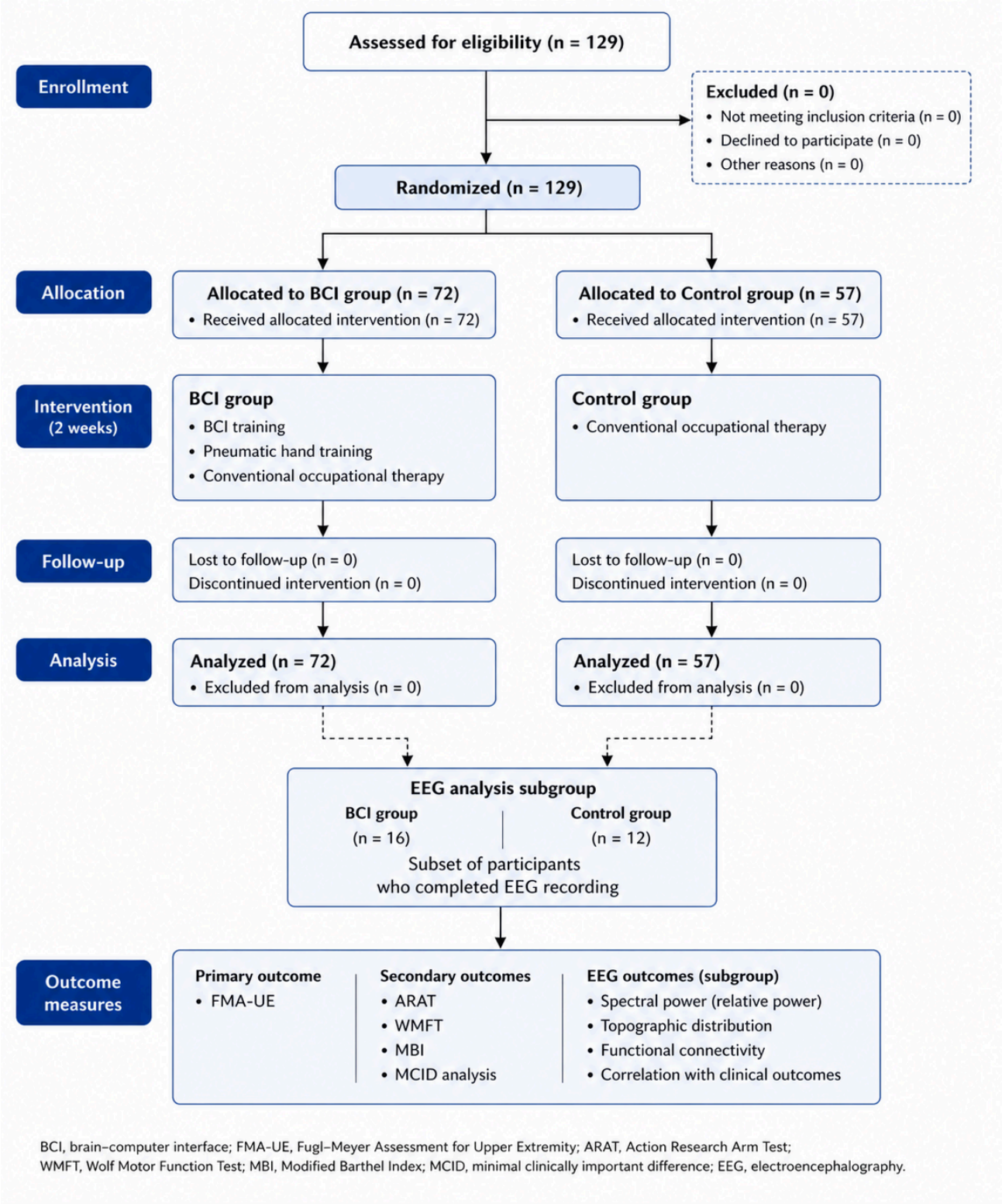


Figure 2

Study Flow Diagram

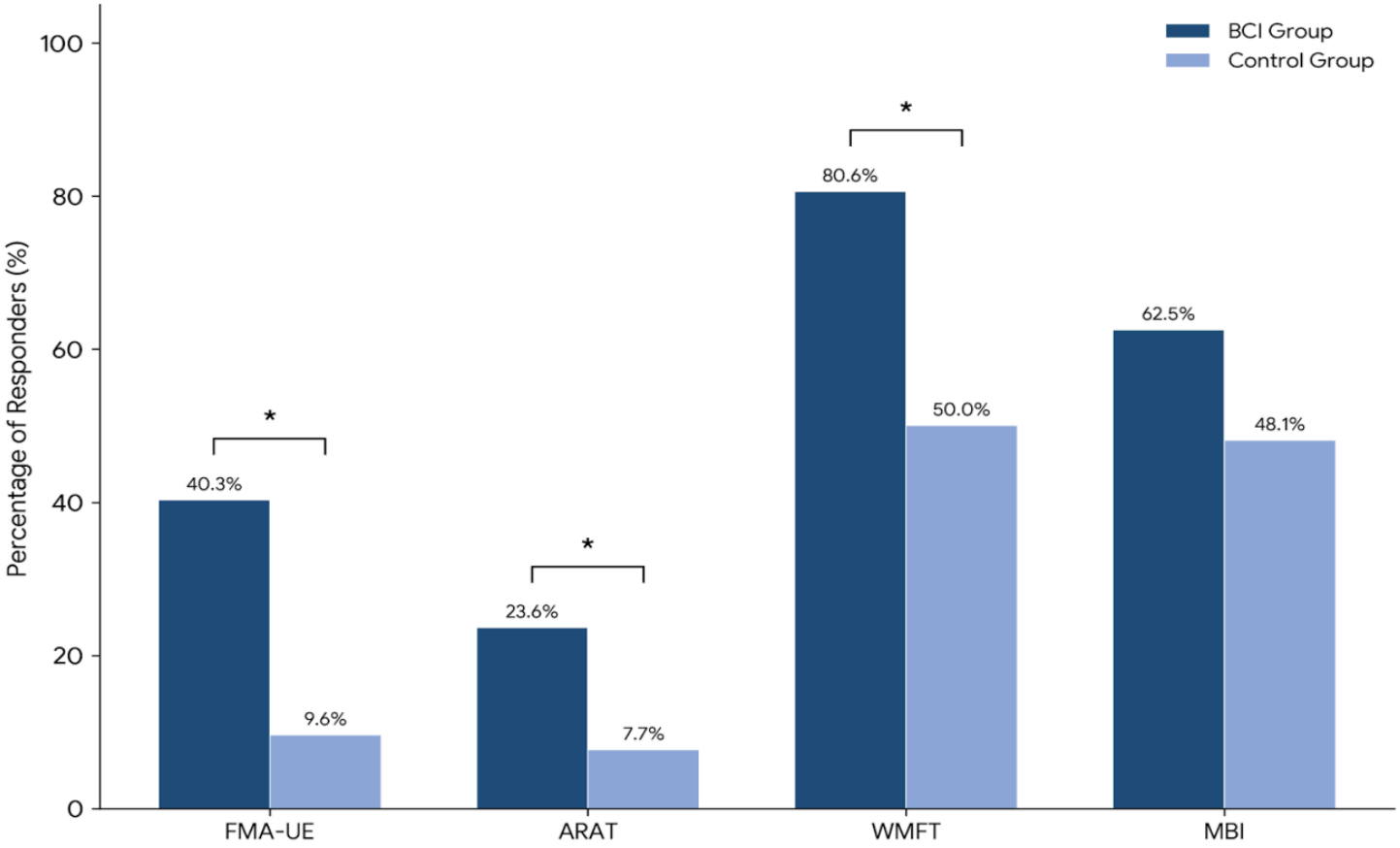


Figure 3

Comparison of MCID Achievement Rates Between Groups

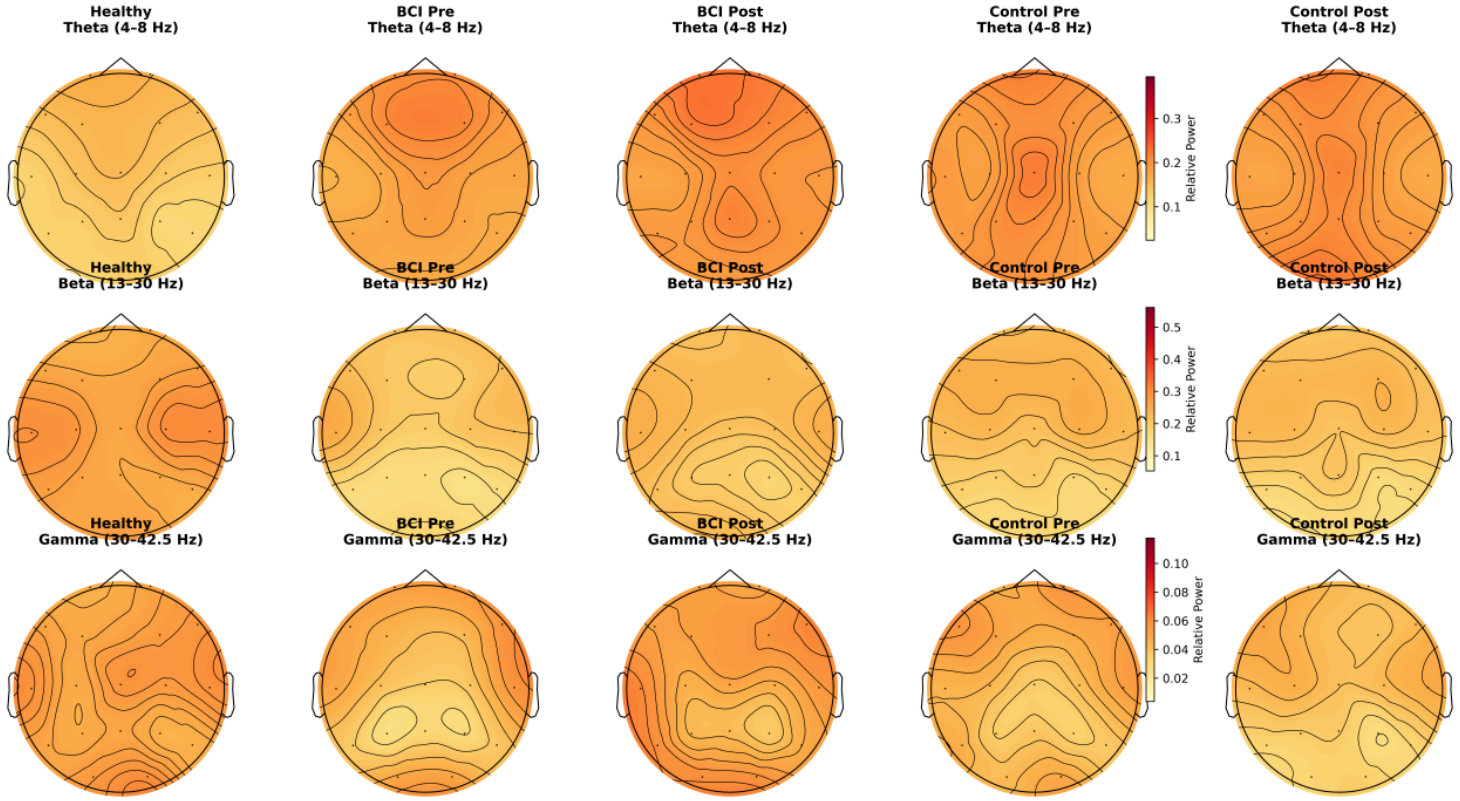


Figure 4

Baseline Whole-Brain QEEG Spectral Topographic Maps Across Frequency Bands

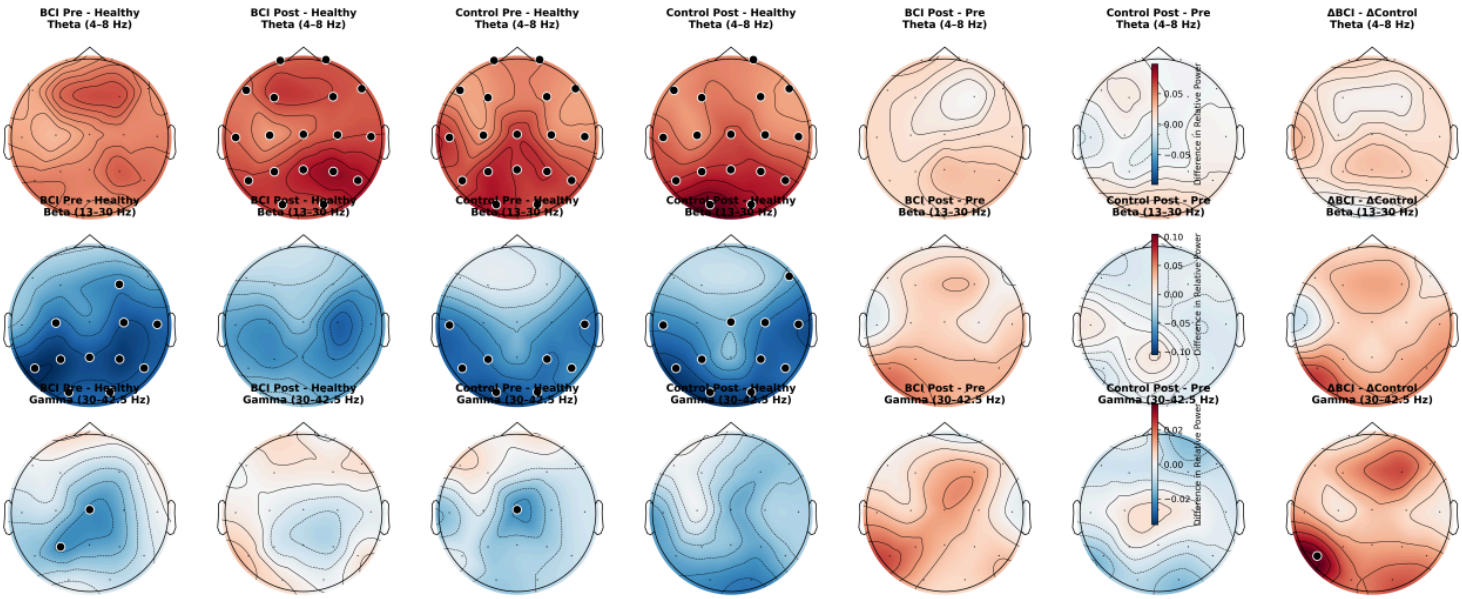


Figure 5

Difference Topographic Maps of Whole-Brain QEEG Spectral Power Across Frequency Bands with FDR-Corrected Significant Electrodes

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2025editablechecklist.docx
- WHOformatresearchprotocolfinal.docx
- Table4.docx