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Neural and Clinical Variability in Immersive VR–BCI Training: A Case-Series Study with Stroke Patients

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ABSTRACT: Immersive virtual reality–based brain–computer interface (VR–BCI) systems have emerged as promising tools for post-stroke motor rehabilitation, providing embodied feedback and task-specific training. However, reliable neurophysiological predictors of clinical responsiveness remain unclear. This case-series study investigated whether longitudinal modulation of event-related desynchronization (ERD) during VR–BCI training predicts upper-limb motor improvement in individuals with sub-acute and chronic stroke. Five participants completed 12 VR–BCI sessions over four weeks, with clinical assessments conducted pre- and post-intervention. ERD was extracted using individualized frequency bands, and linear mixed-effects models were applied to estimate subject-specific ERD trajectories, including baseline magnitude and session-to-session change. These features were then examined in relation to motor recovery. Robust Alpha ERD was observed across participants, indicating consistent sensorimotor engagement. However, ERD progression across sessions did not significantly predict clinical gains, consistent with prior findings. Finally, BCI accuracy also showed substantial inter-subject variability and was not directly associated with motor improvement.

INTRODUCTION

Stroke remains a major cause of long-term disability worldwide, frequently leading to persistent upper-limb motor impairments that compromise functional independence [1]. Electroencephalography (EEG)-based brain-computer interfaces (BCIs) offer a unique approach by directly translating neural activity into real-time feedback or control signals [2].

Most motor rehabilitation BCIs rely on motor imagery (MI) or motor observation (MO) to modulate sensorimotor rhythms, eliciting event-related desynchronization (ERD) in the Alpha and Beta bands [2, 3]. ERD reflects task-related activation of motor cortical networks and constitutes a core feature for both decoding and neurofeedback paradigms. Meta-analyses indicate that BCI-assisted interventions can yield moderate-to-large improvements in upper-limb motor function after stroke [4]. However, beyond aggregate clinical effects, the BCI field increasingly recognizes substantial inter-individual variability in neural modulation and controllability. More recent critiques argue that such variability often reflects system design and neural diversity rather than user deficits [5], reinforcing the need for personalized and adaptive BCI approaches [6]. Psychological and neurophysiological predictors of sensorimotor rhythms (SMR)-BCI performance further support the relevance of individual differences in baseline neural patterns and learning dynamics [7].

Integration of immersive virtual reality (VR) with BCI training introduces an ecologically rich feedback environment that can enhance embodiment, motivation, and sensorimotor coupling [8]. By closing the sensorimotor loop in a first-person context, VR-BCI systems may reinforce residual motor networks through contingent feedback. Nevertheless, substantial inter- and intra-subject variability in ERD magnitude, modulation stability, and online BCI accuracy remains a persistent challenge [9, 10]. Although stronger and more lateralized ERD patterns, particularly in the ipsilesional hemisphere, have been associated with improved motor outcomes and neuroplastic adaptation after stroke [11, 12], it remains unclear which neural features best characterize responsiveness during longitudinal VR-BCI interventions. In particular, the relative contributions of baseline ERD magnitude, session-to-session modulation dynamics, and online BCI accuracy to overall training responsiveness remain unclear.

While our previous work examined EEG-based predictors of recovery in a larger pilot cohort [13], the present study focuses specifically on neural and clinical variability within an independent case-series sample undergoing immersive VR–BCI rehabilitation. Here, we emphasize subject-specific ERD trajectories, inter-individual differences in BCI controllability, and their exploratory relationship with motor outcomes.

In this context, the present study investigates individ-

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Table 1: Demographic and Clinical Profile of Participants with Stroke. FMA refers to the Fugl-Meyer Assessment for the upper limb (maximum value = 66). ΔFMA is the change between pre- and post-FMA scores, with * indicating minimal clinically important difference (MCID). MPS = months post-stroke.

ID	Sex	Age	Type	MPS	Side	FMA		
						Pre	Post	Δ
P01	F	29	Hem.	17	R	18	19	1
P02	M	61	Isch.	1	L	4	6	2
P03	M	54	Hem.	64	L	31	33	2
P04	M	62	Isch.	1	R	40	50	10*
P05	F	75	Isch.	27	R	17	17	0

ual learning dynamics during a 12-session VR-BCI intervention in sub-acute and chronic stroke. We focus on subject-specific ERD trajectories and online BCI accuracy to characterize neural controllability and variability across sessions. By examining the relationship between ERD-derived features, BCI performance, and motor outcomes, our objective is to contribute to the identification of neural signatures associated with the responsiveness of VR-BCI and to inform the development of more adaptive and personalized neurorehabilitation systems.

MATERIALS AND METHODS

Participants: Five individuals with stroke in the sub-acute and chronic phases were recruited at the Centro de Medicina de Reabilitação de Alcoitão (CMRA), Portugal. Mean age was 56 years (SD = 17), 3 male and 2 female. Two participants were affected by hemorrhagic stroke and three by ischemic stroke (Table 1). All participants provided their written informed consent in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of the CMRA, with approval no.: 2025/007. Finally, all participants continued their usual therapy; no additional rehabilitation was provided in the study context. Harms were defined as any adverse events or unintended effects related to study procedures (e.g., discomfort, dizziness, anxiety, technical intolerance) and were monitored non-systematically through self-report and investigator observation.

Clinical Outcome Measures: The primary clinical outcome measure included the Fugl-Meyer Assessment for upper extremity (FMA-UE) [14, 15], and all participants with stroke were assessed pre- and post-intervention. The FMA is a standardized Likert-scale assessment widely used to evaluate motor function recovery following stroke-induced hemiplegia and has a maximum score of 66 points [14]. It assesses multiple domains, including motor function, sensation, range of motion, and joint pain. A minimal clinically meaningful improvement following treatment is typically defined as an increase of +4 to +7 points, for chronic stroke, and +10 for sub-acute stroke [16, 17].

Experimental Design: The experimental protocol for this study consisted of a 4-week intervention comprising 12 VR-BCI training sessions. Clinical evaluations were conducted at two distinct time points: (1) before the intervention (pre); and (2) immediately after completing the intervention (post). EEG data were recorded using the Liveamp 32 EEG amplifier (Brain Products GmbH, Gilching, Germany), with a 32-channel setup and a sampling rate of 500 Hz. Visual feedback was delivered through the Pico 4 (Resolution: 2160x2160 per-eye; Refresh Rate: 90 Hz; field of view (FoV): 104° horizontal, 103° vertical; 6 degrees of freedom (DoF) motion tracking) standalone VR system (Figure 1B).

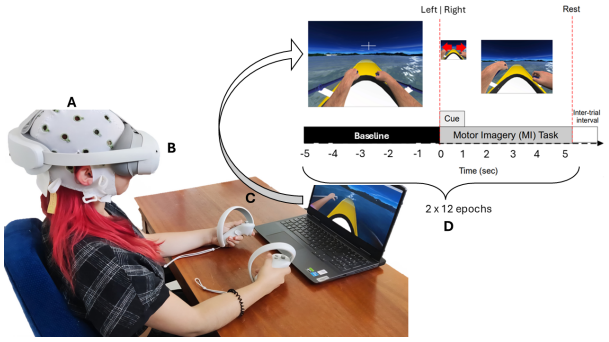

Figure 1: Experimental Setup: A. EEG cap for the System of 32 electrodes; B. HMD for VR feedback; C. VR controllers; D. MI protocol illustrating the epoch length and visual feedback.

The VR-BCI training task used NeuRow, a first-person perspective upper-limb MI and MO paradigm in immersive VR [18]. The protocol involved MI-MO training using embodied feedback rendered via a Head-Mounted Display (HMD). Task-oriented VR environments have been recommended as effective approaches to support ecological validity and patient engagement in MI-based BCI rehabilitation protocols [19].

The training procedure comprised two phases: (1) Calibration — participants performed cued left- vs right-hand MI synchronized with avatar rowing actions. Each session included 12 randomized trials per hand, with 5 s of baseline and 5 s of MI (Figure 1D). A randomized inter-trial interval (1.25–1.5 s) was applied to prevent stimulus anticipation and carry-over effects. EEG data from calibration were used to extract spatial and spectral features through a common spatial patterns (CSP) filter (4 filters used, in the frequency band of 7 – 25 Hz), which trained a linear discriminant analysis (LDA) classifier, a widely adopted approach for MI-based BCIs [20]. (2) Online training — the trained model then classified MI patterns in real time, enabling participants to control the virtual boat through MI of the cued arm, with the same trial number and duration as in training, and as implemented in previous studies using similar protocols [13, 21]. The online BCI phase was not initiated on the first intervention day, providing participants with an initial familiarization period to adapt to the system and develop an effective neurofeedback control. Patients P01 and P02 started the online BCI phase in session 9, while the rest started in session 7. For each one of the 12 sessions, the number of runs (calibration plus online) was between 2 and 4. Every session where we performed online training, the CSP filters and LDA classifier were trained with

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calibration data from the same session.

EEG Data Analysis: For post-hoc analysis, the EEG signals were processed using MATLAB R2023a (The MathWorks, MA, United States) and EEGLAB toolbox v2023.1. The EEG data preprocessing from the training sessions involved band-pass filtering between 1 and 40 Hz; then, for correct continuous noisy data and for rejecting bad channels, we applied the Artifact Subspace Reconstruction (ASR) method, in two steps, first to identify and interpolate bad channels, and then to reject bad segments. EEG data were subsequently downsampled to 125 Hz. Next, an Independent Component Analysis (ICA) was performed to remove remaining artifactual components in the EEG signals. ICA was computed on data after rejecting bad segments, and the resulting weights were applied to the data before segment rejection. We used the ICLabel [22] method for automatically removing any component classified as "muscle" or "eye" artifact (probability values: $\geq 90\%$). The average number of independent components removed was 3. Further, we performed re-referencing to the common average and then rejected bad trials. Finally, the data were segmented into epochs corresponding to left-hand and right-hand trials, and then time-frequency analysis was performed through the event-related spectral perturbation (ERSP). Since the ERSP values were in decibels, we transformed them into ERD as a percentage decrease, based on the following formula:

$$ERD(\%) = (10^{ERSP/10} - 1) \times 100\% \quad (1)$$

Moreover, since ERD magnitude can differ substantially both across participants and within the same participant over time, we adopted an automatic individualized frequency-band approach to improve the precision of ERD estimation [13]. This strategy enables the analysis to more accurately reflect subject-specific neural oscillatory patterns, particularly given the spectral shifts and altered rhythmic activity commonly observed after stroke recovery [23]. Rather than applying the standard 8-12 Hz Alpha range, we defined a custom frequency window between 6-14 Hz for each participant, electrode, task, and trial. The full implementation of this approach is described further in Valente et al. [13] and it is publicly accessible online [1].

The ERD was extracted from all 32 electrodes, using the same method. Our analysis focused primarily on C3 and C4, as they are positioned over the motor and somatosensory cortices [24], they are also the most commonly analysed in the literature, facilitating comparisons with previous studies.

Statistical Analysis: All analyses were performed in MATLAB R2023a (The MathWorks, MA, United States). Linear mixed-effects models (LMEs) were used to analyze neurophysiological data, accounting for repeated measures and inter-individual variability, including random intercepts per participant. Statistical significance was set at two-tailed $p < 0.05$.

[1] https://github.com/LaSEEB/Individualized-ERD

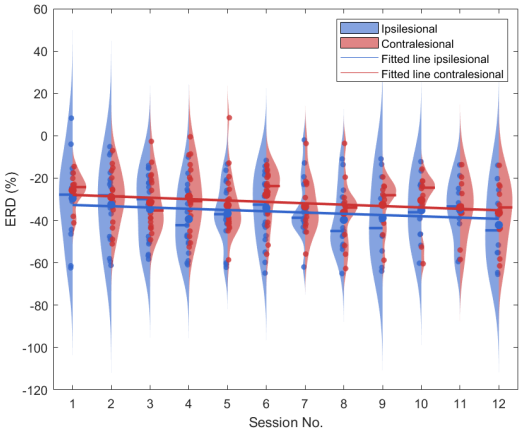

Figure 2: Ipsilesional and contralesional ERD distributions across VR–BCI training sessions for each participant. For each session, each participant had between 2 and 4 runs, which we use here, instead of only one value per participant per session. Fitted lines represent linear regression trends.

To examine the relationship between longitudinal predictors (ERD progression across training sessions) and cross-sectional clinical outcomes (ΔFMA), we implemented a two-stage modeling approach, used in previous studies [23, 25]. LME models were selected because they provide robust regression estimates while accounting for subject-specific variability.

In the first stage, an LME model was fitted to estimate individual ERD trajectories (from the affected side) over the intervention period using the following formula:

$$\text{mean\_erd} \sim \text{sessions} \times \text{stroke\_type} + (\text{sessions} \mid \text{subjects}) \quad (2)$$

This model included time (sessions) and subjects as random effects, allowing subject-specific variability in baseline ERD (intercept) and ERD progression over time (slope). The extracted intercept and slope represent each participant's baseline ERD level and the rate of change in ERD throughout the intervention.

In the second stage, the extracted ERD *intercepts* and *slopes* were then incorporated into a linear regression model to predict clinical motor recovery, measured by ΔFMA:

$$\text{delta\_fma} \sim \text{slope} \times \text{intercept} \quad (3)$$

RESULTS

Clinical Outcomes: Considering the upper-limb impairment level according to FMA-UE scores in pre-assessment, participants P03 and P04 presented mild impairment, and participants P01, P02, and P05 presented severe impairment. At post-assessment, one participant (P04) showed an improvement ($\Delta FMA = 10$), corresponding to the minimal clinical importance difference for the sub-acute population. In contrast, the remaining participants demonstrated improvements ranging from 0 to 2, below significant values (Table 1).

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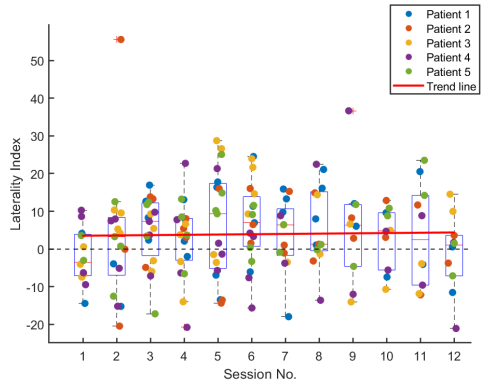

Figure 3: ERD LI across VR–BCI training sessions for each participant. Fitted line represents linear regression trend.

ERD Dynamics Across Sessions: ERD was consistently observed across sessions in both ipsilesional ($y = -0.595x - 32.088$) and contralesional ($y = -0.658x - 27.276$) sensorimotor regions (Figure 2). ERD values remained strongly negative throughout the intervention, typically ranging between approximately -20% and -60%, indicating sustained suppression of sensorimotor rhythms during motor imagery training.

Laterality Index Analysis: In terms of ERD hemispheric patterns, LI values showed substantial variability across sessions and participants, with distributions centered around zero (Figure 3). Linear trend analysis revealed a small positive slope ($y = 0.079x + 3.441$), suggesting a mild shift toward ipsilesional dominance.

Linear Mixed-Effects Modeling: Finally, to formally examine longitudinal ERD dynamics, the LME model revealed a significant negative intercept ($\beta = -37.97$, $p < 0.001$), indicating strong overall ERD suppression across participants during the intervention. However, session progression was not statistically significant ($\beta = 0.07$, $p = 0.89$), suggesting that ERD magnitude remained relatively stable across training sessions. Stroke type (ischemic vs hemorrhagic) also did not significantly influence ERD trajectories ($\beta = 7.34$, $p = 0.46$), and the interaction between session and stroke type was not significant ($\beta = -0.07$, $p = 0.93$). Random-effects estimates indicated substantial between-subject variability in baseline ERD ($\sigma^2 = 9.95$), whereas variability in session-related slopes was comparatively small ($\sigma^2 = 0.61$) (Table 2). A second-stage linear regression analysis examined whether ERD baseline magnitude (intercept) and ERD progression (slope) predicted motor recovery (ΔFMA). The model explained 27% of the variance in ΔFMA but was not statistically significant ($R^2 = 0.27$, $F = 0.123$, $p = 0.935$), indicating that neither baseline ERD nor longitudinal ERD modulation reliably predicted clinical improvement in this cohort (Table 3).

BCI Accuracy: BCI accuracy showed marked inter-subject variability across sessions (Figure 4). Participant P02 achieved the highest performance, reaching near-ceiling accuracies in the later sessions (95.8–100%). In contrast, participants P01 and P03 remained close to chance level throughout the intervention (approximately

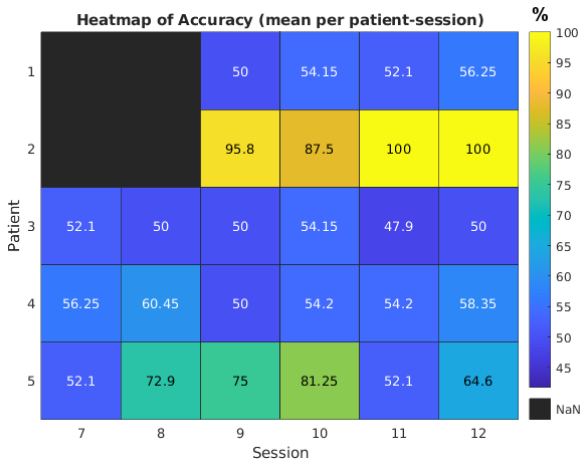

Figure 4: Heatmap of mean BCI accuracy per online session for each participant. For sessions with two runs, accuracy represents the mean across runs.

50–56%). Participants P04 and P05 demonstrated intermediate performance, with accuracies generally ranging between 50–70% and showing moderate fluctuations across sessions. The highest accuracy values occurred in sessions in which participants appeared to combine MI with slight overt motor intent or minimal limb movement. Such behavior can increase the separability of sensorimotor EEG patterns and consequently improve classification performance. Finally, the relationship between high BCI accuracy (ΔAcc) and clinical improvement (ΔFMA) showed no significant relationship ($r = 0.06, p = 0.92$).

DISCUSSION

This case-series study extends our prior randomized pilot by testing the same ERD extraction and mixed-effects trajectory framework in an independent five-patient cohort [13]. Consistent with the larger study, ERD engage-

Table 2: Fixed and random effects estimates from the LME Model analyzing ERD progression over sessions and stroke types.

Fixed Effects	**β (95% CI)**	**t**	**p**
Intercept	-37.97 [-50.53, -25.41]	-5.97	1.4×10^{-8}
Sessions	0.07 [-0.99, 1.14]	0.14	0.89
Stroke Type	7.34 [-12.42, 27.09]	0.73	0.46
Sessions × Type	-0.07 [-1.74, 1.59]	-0.09	0.93
Random Effects	**Var (95% CI)**		
Subject (Intercept)	9.95 [4.71, 21.02]		
Session (Slope)	0.61 [0.13, 2.86]		
Residual	12.85 [11.52, 14.34]		

Table 3: Second-stage regression linking ERD features to ΔFMA.

Predictor	**β**	**t-statistic**	**p-value**
Intercept	14.39	0.51	0.70
ERD Slope	-35.73	-0.49	0.71
Baseline ERD	0.24	0.38	0.77
Slope × Baseline	-0.93	-0.48	0.71
Model Fit			
$R^2 = 0.27$			p = 0.94

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ment was robust, but longitudinal ERD progression did not emerge as a reliable predictor of motor gains. Further, previous work investigating ERD dynamics during stroke recovery, reported that patients with favorable recovery trajectories exhibited a progressive increase in ipsilesional ERD modulation accompanied by a decrease in contralesional activity during the acute phase after stroke [26]. In contrast, the present cohort of chronic stroke participants showed relatively stable ERD magnitudes across sessions, with only a mild shift toward ipsilesional dominance reflected in the LI. These differences may reflect the later stage of recovery in our cohort, where neural engagement patterns may already be stabilized and less sensitive to longitudinal modulation during training.

Clinical Implications: From a clinical perspective, only one participant (P04) achieved a clinically meaningful improvement in FMA-UE ($\Delta FMA = 10$), exceeding the minimal clinically important difference. Taking into account the higher baseline assessment of participant P04 ($FMA - UE = 40$), corresponding to a lower impairment level, these findings suggest that differences in baseline motor function may have influenced clinical outcomes. These results are consistent with prior BCI rehabilitation studies where baseline FMA-UE ≤ 30 has been associated with poorer recovery outcomes [27].

ERD Dynamics During VR–BCI Training: Across sessions, VR–BCI training consistently elicited robust ERD over sensorimotor areas. ERD values remained strongly negative throughout the intervention, indicating reliable engagement of motor-related cortical networks during the training task. However, ERD magnitude showed minimal longitudinal modulation. LME model indicated that ERD remained relatively stable across sessions, suggesting that participants were able to engage sensorimotor rhythms early in the intervention rather than progressively increasing ERD magnitude over time.

Hemispheric Variability: Analysis of the LI revealed heterogeneous hemispheric recruitment patterns. Although a slight shift toward greater ipsilesional dominance was observed across sessions, LI values remained widely distributed around zero, indicating that both hemispheres contributed to motor imagery engagement. Such variability is consistent with prior studies showing that stroke recovery may involve either ipsilesional reactivation or compensatory contralesional recruitment depending on lesion characteristics and recovery stage ([12, 26]).

Longitudinal ERD Trajectories: The two-stage modeling approach further indicated that ERD features alone were not sufficient to explain clinical improvement. While baseline ERD and slope explained a modest portion of the variance in motor recovery, the regression model was not statistically significant. These findings suggest that simple ERD magnitude or linear progression metrics may not capture the complex neural adaptations underlying functional recovery in VR–BCI interventions.

BCI accuracy and recovery outcomes: BCI accuracy also showed substantial variability across participants. Notably, decoding performance did not correspond to clinical improvement, reinforcing the dissociation between BCI classification accuracy and functional recovery outcomes ([28, 29]).
Together, these findings emphasize the importance of considering inter-individual neural variability when interpreting BCI rehabilitation outcomes, and the importance of personalized and patient-centered VR–BCI rehabilitation paradigm [19].

Limitations: Several limitations should be acknowledged. First, the small sample size limits statistical power and the generalizability of the findings. Further, heterogeneity in stroke chronicity and baseline motor impairment likely contributed to the variability observed in both neural and behavioral outcomes. Future studies with larger cohorts and longer longitudinal protocols will be necessary to better characterize intra-individual neural dynamics and their relationship with motor recovery during VR–BCI rehabilitation.

CONCLUSION

This case-series study investigated neural and clinical variability during immersive VR–BCI rehabilitation in individuals with chronic stroke. The results show that VR–BCI training reliably elicited sensorimotor ERD, confirming consistent engagement of motor-related cortical networks during motor imagery. However, longitudinal ERD modulation did not significantly predict motor recovery, and substantial inter-individual variability was observed in both neural activity and clinical outcomes. These findings suggest that simple ERD magnitude or linear ERD progression may not fully capture the neural mechanisms underlying functional recovery in VR–BCI interventions. Instead, recovery may involve more complex neurophysiological adaptations beyond mean ERD measures. Overall, this work highlights the importance of considering neural variability when interpreting ERD-based biomarkers and supports the need for more personalized approaches in VR–BCI neurorehabilitation.

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