

Cortical Hemispheric Responses to 5 Hz Repetitive Transcranial Magnetic Stimulation in Chronic Stroke: An EEG-Based Study

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This study investigated the effects of 5 Hz repetitive transcranial magnetic stimulation (rTMS) on cortical activation and upper limb function in patients with chronic stroke. Twenty-four patients received 5 Hz rTMS three times per week for four weeks. Electroencephalography (EEG) was used to analyze sensorimotor rhythm (SMR) and the hemispheric asymmetry index (HAI), and upper limb function was assessed using the Fugl-Meyer Assessment (FMA) and the Box and Block Test (BBT). SMR significantly increased in the ipsilesional central regions (C3, C4), while HAI significantly decreased after the intervention ($p < 0.05$), indicating restoration of interhemispheric balance. In addition, FMA and BBT scores showed significant improvement and were positively correlated with EEG indices. These findings suggest that 5 Hz rTMS promotes cortical reorganization and contributes to upper limb motor recovery in patients with chronic stroke.

Keywords : repetitive transcranial magnetic stimulation, electroencephalography, cortical activation, stroke, hemisphere

1. Introduction

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulation technique that delivers brief magnetic pulses through a coil placed on the scalp, generating a strong magnetic field that penetrates the skull and induces electrical currents in cortical neurons [1]. These induced currents flow primarily in a perpendicular direction, depolarizing the axons of pyramidal cells in the cerebral cortex and eliciting action potentials. That is, an externally generated magnetic field induces an electric current that alters the excitability of specific cortical regions [2].

The modulatory effects of rTMS on cortical excitability vary depending on the frequency and intensity of the stimulation. Generally, high-frequency stimulation (≥ 5 Hz) tends to increase cortical excitability, whereas low-frequency stimulation (≤ 1 Hz) induces inhibitory effects

[3]. Owing to these properties, rTMS has been widely employed as a therapeutic intervention to modulate abnormal excitability imbalances in multiple neurological disorders, including stroke, Parkinson's disease, and depression [4]. In particular, patients with stroke often exhibit increased cortical excitability in the ipsilesional primary motor cortex (M1), accompanied by inhibitory effects in the contralesional hemisphere [5].

Recent neuroimaging and electroencephalography (EEG) studies on rTMS have demonstrated that its effects are not limited to the stimulated cortical region, but also extend to the contralateral hemisphere [6]. Functional magnetic resonance imaging (fMRI) and EEG studies have revealed that rTMS enhances interhemispheric functional connectivity and reduces cortical asymmetry, thereby promoting adaptive neuroplasticity that rebalances the activity between the two hemispheres [7].

Although 5 Hz stimulation has been primarily used to enhance cortical excitability in the ipsilesional hemisphere, its effects may also extend to the contralesional hemisphere, thereby modulating interhemispheric interactions [8]. This bilateral response is thought to be mediated by transcallosal connections and network-level plastic reorganization, indicating that the clinical effects of high-frequency

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stimulation are not limited to localized cortical excitation alone [9]. Nevertheless, EEG-based investigations comparing hemispheric activity in patients with chronic stroke remain limited, and the relationship between post-rTMS cortical activation changes and upper limb functional recovery has yet to be clearly elucidated.

Therefore, the objective of the present study was to investigate the changes in cortical activation between the ipsilesional and contralesional hemispheres using EEG following the application of 5 Hz rTMS to the ipsilesional primary motor cortex in patients with chronic stroke. Additionally, we aimed to examine the relationship between these physiological changes and upper limb functional recovery.

2. Materials and Methods

2.1. Subjects

This study was conducted at B Hospital in Gyeonggi Province from February to April 2025. A total of 24 patients with chronic stroke who underwent comprehensive rehabilitation therapy at our hospital were recruited. All participants were diagnosed with either ischemic or hemorrhagic stroke by a rehabilitation medicine specialist using magnetic resonance imaging. Eligibility was limited to individuals whose stroke onset occurred between 6 and 24 months before participation.

All participants were fully informed of the purpose and procedures of the study and provided voluntary consent prior to participation. Inclusion criteria required participants to have sufficient cognitive ability to follow the researcher's instructions, as indicated by a score of ≥ 23 on the Korean version of the Montreal Cognitive Assessment (K-MoCA). Additionally, the participants were required to be able to sit independently and reach at least Stage 3 of the Brunnstrom recovery stage for the upper limb.

Individuals with contraindications to rTMS, such as the presence of metallic implants, cardiac pacemakers, or a history of epilepsy, were excluded. Additionally, patients

with medically unstable conditions, including seizures, cardiovascular disease, or psychiatric disorders, as well as those with unilateral neglect, severe aphasia, or joint contractures that could interfere with task performance, were excluded.

2.2. Experimental Design

This study employed a single-group repeated-measures design to determine the effects of 5 Hz rTMS on cortical activation and upper limb function in patients with chronic stroke. Participants were evaluated at three time points: before the intervention (baseline, T0); immediately after the intervention (post-intervention, T1); and one week after the intervention (follow-up, T2).

The rTMS intervention consisted of 12 sessions, administered three times per week over a four-week period. After completing the baseline assessment (T0), all participants received 5 Hz rTMS. The same assessment procedures were repeated immediately after the intervention (T1) and again one week later (T2).

EEG was performed at all three time points to measure changes in cortical activation, while upper limb function was assessed using the Fugl-Meyer Assessment (FMA) and the Box and Block Test (BBT). Functional evaluations were performed at T0 and T2 (Fig. 1).

2.3. rTMS Protocol

The rTMS device used in this study was the ALTMS® (Remed, Korea, 2018), equipped with a 70 mm figure-eight coil. During stimulation, participants were seated comfortably with their heads supported by a headrest and their arms resting on cushions in a neutral position. The coil was positioned over the ipsilesional primary motor cortex (M1), approximately 2 cm lateral to the midline, with the handle angled 45° posterolaterally [10].

To determine the motor hotspot, the first dorsal interosseous muscle was used as the target, and the resting motor threshold (RMT) was defined as the lowest stimulation intensity eliciting motor evoked potentials

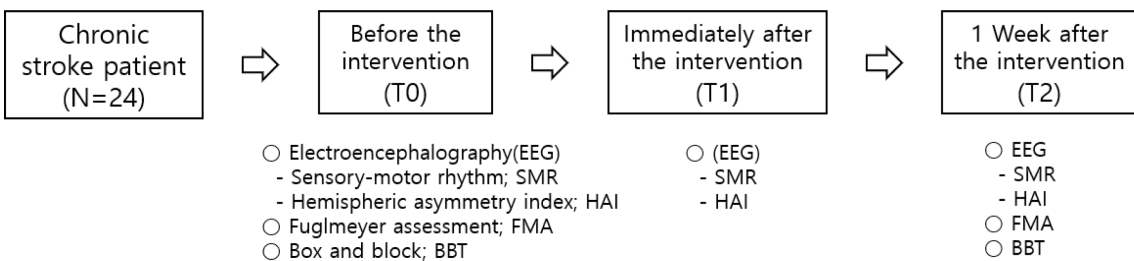


Fig. 1. Study design and assessment timeline. A single-group repeated-measures design was applied. Twenty-four chronic stroke patients received 5 Hz rTMS three times per week for four weeks (12 sessions). EEG (SMR, HAI) was assessed at T0, T1, and T2, and upper limb function (FMA, BBT) was evaluated at T0 and T2.

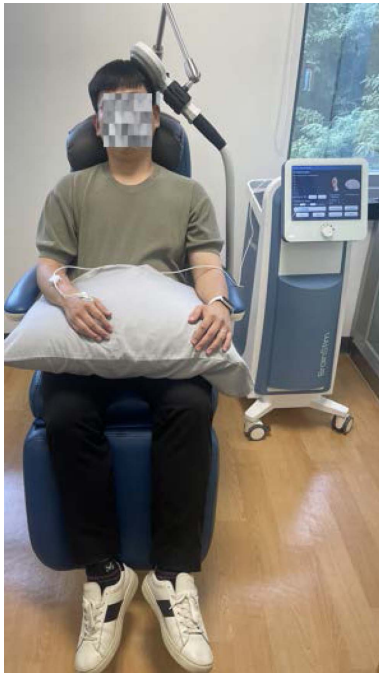


Fig. 2. (Color online) Experimental setup of repetitive transcranial magnetic stimulation (rTMS). A participant is seated comfortably with the head stabilized on a headrest during 5 Hz rTMS using the ALTMS[®] system (Remed, Korea) with a 70-mm figure-eight coil.

exceeding 50 μ V in at least five out of ten trials [11].

In this study, rTMS was delivered at 120% of the RMT, at a frequency of 5 Hz. Each session consisted of 900 pulses per day, administered three times per week for four weeks, totaling 12 sessions (Fig. 2). Participants were continuously monitored for discomfort or adverse effects during stimulation. Throughout the intervention period, participants maintained their routine hospital-based rehabilitation therapy, with no additional neuromodulatory interventions or medication changes permitted.

2.4. EEG Recording and Analysis

In this study, EEG was performed using eight channels (F3, F4, C3, C4, P3, P4, T3, and T4) based on the international 10–20 electrode placement system to analyze changes in motor-related cortical activity [12]. Participants were seated comfortably in a quiet environment and instructed to perform finger tapping when the image on the screen changed. The EEG data were acquired using a computerized EEG system (QEEG-21, LXE5208, Laxtha Inc., Korea) (Fig. 3). Raw EEG data were collected and processed using the real-time data acquisition and time-series analysis software TeleScan (ver. 3.2.9.0, Laxtha Inc., Seoul, Korea) [13].

Independent component analysis was performed to

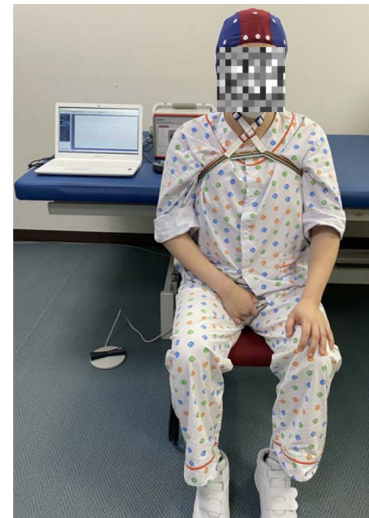


Fig. 3. (Color online) Electroencephalography (EEG) measurement setup. A participant is seated comfortably while EEG signals are recorded using an 8-channel system (TeleScan, Laxtha Inc., Korea). Electrodes are positioned according to the international 10–20 system to measure cortical activity during a finger tapping task.

remove artifacts, and segments contaminated with noise were excluded from the analysis [14]. The sensorimotor rhythm (SMR; 12–15 Hz) band was analyzed, and the relative power was calculated for each channel. EEG power spectra were analyzed under identical conditions at all time points. For the calculation of the hemispheric asymmetry index (HAI), the C3 and C4 channels were reassigned according to the affected side of each participant. Specifically, in patients with right-sided hemiplegia, C4 was defined as the ipsilesional channel and C3 as the contralesional channel, whereas in patients with left-sided hemiplegia, C3 was defined as the ipsilesional channel and C4 as the contralesional channel. This reassignment ensured that the HAI consistently reflected interhemispheric differences between the ipsilesional and contralesional motor cortices across participants [15]. For each participant, the ipsilesional hemisphere was mapped to C3 (left) or C4 (right) depending on the paretic side. Eq. (1)

$$\text{HAI} = (\text{C3} - \text{C4}) / (\text{C3} + \text{C4}) \quad (1)$$

2.5. Upper Limb Function Assessment

To assess changes in upper limb function, the FMA and BBT were performed. Both assessments were conducted before the intervention (baseline, T0) and one week after the intervention (follow-up, T2).

The FMA is a standardized tool used to evaluate motor recovery in patients with stroke. It comprises 66 items,

with a maximum score of 66 points for the upper extremity domain, the focus of this study [16]. The FMA has demonstrated excellent reliability, with a test-retest reliability of 0.98 and an inter-rater reliability of 0.99 in stroke populations [17].

The BBT is designed to measure manual dexterity and gross motor coordination. In this study, the paretic upper limb was assessed while the participants performed the task in a stable seated position, following standardized instructions [18]. The BBT also shows high reliability, with a test-retest reliability of 0.94 and an inter-rater reliability of 0.99 [19].

2.6. Statistical Analysis

All statistical analyses were performed using SPSS Statistics software (version 18.0; IBM Corp., Chicago, IL, USA). To examine changes in EEG parameters and upper limb function, data from three time points (pre-intervention, immediate post-intervention, and one week post-intervention) were analyzed.

For the EEG data, the relative power of the SMR was used as the primary variable. Differences across time points for each EEG channel and the HAI were analyzed using a one-way repeated-measures analysis of variance (ANOVA). The assumption of sphericity for the repeated-measures ANOVA was examined using Mauchly's test. When the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied to adjust the degrees of freedom. When significant differences were detected, Bonferroni-corrected post-hoc tests were performed to identify pairwise differences.

Changes in upper limb function were evaluated by comparing the FMA and BBT scores pre- and post-intervention (T0–T2) using the paired t-test. Pearson's correlation analysis was used to analyze the relationship between changes in EEG parameters and upper limb function. Statistical significance was set at $p < 0.05$.

3. Results

3.1. General Patient Characteristics

A total of 24 patients with chronic stroke participated in this study.

The general characteristics of included patients were as follows: 14 were male and 10 were female; the mean age was 54.82 ± 5.4 years; and the mean duration since stroke onset was 12.62 ± 3.7 months. Regarding stroke type, 13 participants (54.2%) had hemorrhagic stroke, and 11 (45.8%) had ischemic stroke. The side of hemiplegia was evenly distributed, with 12 participants (50.0%) having right-sided hemiplegia and 12 (50.0%) having left-sided

Table 1. General characteristics of subjects (N=24).

Variables	M±SD	
Gender	Male	14(58.3%)
	Female	10(41.7%)
Age		54.82±5.4
Side of stroke	Right	12(50%)
	Left	12(50%)
Type of stroke	Hemorrhage	13(54.2%)
	Infarction	11(45.8%)
Time from stroke to rehab(months)		12.62±3.7
K-MoCA		27.25±2.03

M±SD M: mean SD: standard deviation, K-MoCA: Korean version of the Montreal Cognitive Assessment.

hemiplegia. The mean K-MoCA score was 27.25 ± 2.03 (Table 1).

3.2. EEG Analysis of Cortical Changes

EEG measurements were conducted at three time points: before the intervention (T0), immediately after the intervention (T1), and one week after the intervention (T2). SMR and HAI were analyzed to determine changes in cortical activation.

3.2.1. SMR Relative Power Changes

Changes in SMR relative power elicited distinct patterns across cortical regions.

In particular, areas F3, C3, and C4 exhibited a gradual increase in the relative power of the SMR from T0 to T2, with statistically significant differences ($p < 0.05$). At the C3 site, the SMR increased significantly from 0.075 ± 0.02 at T0 to 0.093 ± 0.01 at T1 and 0.099 ± 0.01 at T2. Similarly, at the C4 site, the SMR rose from 0.074 ± 0.02

Table 2. SMR Relative Power Changes (N=24).

Variables	T0	T1	T2	F	p
F3	0.050±0.02	0.060±0.01	0.071±0.02	5.21	.010*
F4	0.055±0.03	0.060±0.01	0.052±0.01	2.31	.112
C3	0.075±0.02	0.093±0.01	0.099±0.01	4.77	.014*
C4	0.074±0.02	0.085±0.01	0.092±0.01	3.25	.048*
P3	0.085±0.03	0.095±0.01	0.084±0.02	1.94	.158
P4	0.091±0.03	0.098±0.02	0.083±0.01	2.12	.134
T3	0.059±0.01	0.07±0.02	0.071±0.03	0.87	.426
T4	0.070±0.02	0.062±0.01	0.069±0.01	1.11	.336

M±SD M: mean SD: standard deviation, * $p < 0.05$

T0: before intervention, T1: immediately after intervention, T2: one week after intervention

SMR: sensorymotor rhythm

at T0 to 0.085 ± 0.01 at T1 and 0.092 ± 0.01 at T2. At the F3 site, the SMR increased from 0.050 ± 0.02 at T0 to 0.060 ± 0.01 at T1 and 0.071 ± 0.02 at T2, indicating a notable enhancement in cortical activation after rTMS application (Table 2). Conversely, no significant differences were observed at F4, P3, P4, T3, or T4 ($p > 0.05$).

3.2.2. Changes in HAI

Analysis of changes in the HAI across time points revealed significant differences among the three measurements ($p < 0.05$). At T0, the HAI value was -0.072 ± 0.10 , indicating greater activation in the contralesional hemisphere. However, the value shifted to $+0.048 \pm 0.09$ at T1 and remained stable at T2 ($+0.048 \pm 0.09$), suggesting a sustained increase in ipsilesional cortical activation following rTMS intervention (Table 3).

3.3. Changes in Upper Limb Function

Upper limb function was assessed using the FMA and the BBT at T0 and T2.

The FMA score increased significantly from 36.257 ± 5.06 at T0 to 38.124 ± 5.98 one week after the intervention ($p < 0.05$). Likewise, the BBT score improved from 5.352 ± 1.71 to 6.015 ± 1.77 ($p < 0.05$), indicating a significant enhancement in upper limb motor performance in both assessments (Table 4).

3.4. Correlation Between EEG and Upper Limb Function

Pearson correlation analysis was performed to examine the relationship between changes in EEG indicators and improvements in upper limb function (Table 5).

Changes in the SMR relative power at the C3 site

Table 3. Hemispheric Asymmetry Index (HAI) Changes (N=24).

Variables	T0	T1	T2	F	p
HAI(C3-C4)	-0.072 ± 0.10	0.048 ± 0.09	0.048 ± 0.09	4.17	.021*

M±SD M: mean SD: standard deviation, * $p < 0.05$

T0: before intervention, T1: immediately after intervention, T2: one week after intervention

HAI: hemispheric asymmetry index

Table 4. Changes in Upper Limb Function (N=24).

Variables	T0	T2	t	p
FMA	36.257 ± 5.06	38.124 ± 5.98	2.54	.018*
BBT	5.352 ± 1.71	6.015 ± 1.77	2.35	.025*

M±SD M: mean SD: standard deviation, $p < 0.05$ *

T0: before intervention, T2: one week after intervention

FMA: fugl-meyer assessment, BBT: box and block test

Table 5. Correlation between EEG and Upper Limb Function (N=24).

Variables	SMR(C3)	SMR(C4)	HAI(C3-C4)	FMA	BBT
SMR(C3)	1				
SMR(C4)	.412*	1			
HAI(C3-C4)	.458*	.431*	1		
FMA	.521**	.405	.492**	1	
BBT	.382	.463**	.478**	.617**	1

M±SD M: mean SD: standard deviation, * $p < 0.05$, ** $p < 0.01$

SMR: sensorymotor rhythm, HAI: hemispheric asymmetry index, FMA: fugl-meyer assessment, BBT: box and block test

showed a significant positive correlation with the FMA scores ($r = 0.521$, $p < 0.01$). Likewise, changes in SMR at the C4 site moderately correlated with both FMA ($r = 0.405$) and BBT scores ($r = 0.463$, $p < 0.01$). Furthermore, the HAI demonstrated significant positive correlations with FMA ($r = 0.492$, $p < 0.01$) and BBT ($r = 0.478$, $p < 0.01$). Additionally, a strong positive correlation was observed between FMA and BBT scores ($r = 0.617$, $p < 0.01$).

4. Discussion

This study investigated the relationship between changes in interhemispheric cortical activation and improvements in upper limb function following the application of 5 Hz rTMS in patients with chronic stroke, using EEG as an objective measure.

The results demonstrated that SMR activity in the C3 and C4 regions increased both immediately and one week post-intervention, while the HAI decreased, indicating a reduction in cortical asymmetry between the hemispheres. In the present study, the observed decrease in the HAI indicates a restoration of interhemispheric balance, reflecting a relative normalization of cortical activation between the ipsilesional and contralesional motor cortices. This finding suggests that 5 Hz rTMS may reduce excessive contralesional activity while facilitating ipsilesional cortical excitability, thereby promoting more balanced interhemispheric interactions. Furthermore, these EEG changes showed statistically significant positive correlations with improvements in FMA and BBT scores, suggesting that the enhanced cortical reorganization induced by 5 Hz rTMS contributed to functional recovery of the upper limb.

These findings are consistent with previous reports suggesting that high-frequency rTMS enhances excitability in the ipsilesional motor cortex while simultaneously suppressing hyperexcitability in the contralesional cortex,

thereby contributing to the restoration of interhemispheric balance [20, 21]. Notably, the SMR has been associated with cortical stability during motor execution and motor learning processes [22]. Importantly, the observed increase in SMR should not be interpreted solely as an enhancement of cortical excitation. The SMR has been widely regarded as a neurophysiological marker associated with the stabilization of motor control and the recovery of inhibitory regulation within the sensorimotor cortex. In the context of stroke rehabilitation, increased SMR activity is thought to reflect improved cortical efficiency and refined motor output, rather than excessive excitatory activation. Therefore, the enhancement of SMR observed in this study may indicate a normalization of inhibitory control mechanisms that contribute to more stable and coordinated upper limb motor performance following 5 Hz rTMS. In the current study, the observed increase in SMR, which was closely linked to improvements in upper limb function, may reflect the recovery of inhibitory regulation within the motor cortex, supporting the normalization of cortical excitability after rTMS intervention.

Moreover, the decrease in the HAI suggests that functional reorganization between the two hemispheres occurred after the intervention. rTMS has been reported to suppress excessive activation in the contralesional sensorimotor cortex and enhance activation in the ipsilesional hemisphere, thereby normalizing the interhemispheric cortical interactions in patients with stroke [23]. Similarly, in this study, the application of 5 Hz rTMS enhanced SMR within the ipsilesional central region (C3) and reduced interhemispheric asymmetry, which can be interpreted as a neurophysiological mechanism underlying upper limb motor recovery.

Meanwhile, the results of the upper limb function assessments revealed notable improvements in both FMA and BBT scores, supporting the clinical efficacy of rTMS in promoting upper limb motor recovery and aligning with previous research findings [24].

The robust correlation between FMA and BBT scores indicates that both assessments consistently reflect improvements in motor performance. Furthermore, the parallel trends observed between functional recovery and changes in EEG parameters suggest that rTMS may facilitate functional recovery through cortical plasticity, reinforcing its role in promoting neurophysiological reorganization post-stroke.

The relevance of this study lies in its quantitative analysis of cortical changes using EEG-based indices following rTMS application, as well as in demonstrating that these neurophysiological changes are directly associated with clinical functional improvements.

Importantly, the SMR and HAI serve as key indicators of cortical activation and may be valuable tools for evaluating the neurophysiological effects of rehabilitation interventions in future research.

Nevertheless, several limitations of this study should be acknowledged. First, this study employed a single-group repeated-measures design without a control or sham stimulation group. Therefore, it is not possible to definitively attribute the observed changes in cortical activation and upper limb function solely to the effects of 5 Hz rTMS. Spontaneous recovery, placebo effects, or the influence of concurrent conventional rehabilitation therapy cannot be completely excluded. In addition, the absence of a control group limits the ability to compare the magnitude of rTMS-induced effects with natural recovery trajectories or alternative interventions. Future studies should incorporate randomized controlled or sham-controlled designs to establish stronger causal relationships between rTMS-induced cortical modulation and functional recovery. Second, the small sample size restricts the generalizability of the findings. Additionally, because the C3 and C4 electrode positions may represent either the ipsilesional or contralesional hemisphere, depending on the side of the hemiplegia, future studies should incorporate analyses that account for hemispheric lateralization. Third, repeated statistical analyses across multiple EEG channels may increase the risk of statistical errors, which should be considered a limitation of this study.

However, this study provides important evidence that 5 Hz rTMS positively influences cortical activation and functional recovery in patients with chronic stroke. These findings further support the potential utility of EEG-based assessments for verifying cortical reorganization and upper limb motor recovery following neuromodulatory interventions.

5. Conclusion

This study investigated the effects of 5 Hz rTMS on cortical activation and upper limb functional recovery in patients with chronic stroke. The findings revealed a considerable increase in SMR following rTMS, accompanied by a decrease in the HAI, indicating restoration of interhemispheric balance in cortical activity. Furthermore, these cortical changes showed a marked correlation with improvements in upper limb function.

Overall, the findings suggest that 5 Hz rTMS facilitates the excitability of the ipsilesional motor cortex while modulating hyperexcitability in the contralesional cortex, thereby enabling positive interhemispheric interaction and enhancing motor recovery.

EEG-based measures, such as SMR and HAI, appear to be valuable neurophysiological biomarkers for objectively evaluating the effects of rTMS interventions in stroke rehabilitation.

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