Brain Topological Correlates of Motor Performance Changes After Repetitive Transcranial Magnetic Stimulation

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Abstract

Repetitive transcranial magnetic stimulation (rTMS) influences the brain temporally beyond the stimulation period and spatially beyond the stimulation site. Application of rTMS over the primary motor cortex (M1) has been shown to lead to plastic changes in interregional connectivity over the motor system as well as alterations in motor performance. With a sequential combination of rTMS over the M1 and functional magnetic resonance imaging (fMRI), we sought changes in the topology of brain networks and specifically the association of brain topological changes with motor performance changes. In a sham-controlled parallel group experimental design, real or sham rTMS was administered to each of the 15 healthy subjects without prior motor-related dysfunctions, over the right M1 at a high frequency of 10 Hz. Before and after the intervention, fMRI data were acquired during a sequential finger motor task using the left, nondominant hand. Changes in the topology of brain networks were assessed in terms of global and local efficiency, which measures the efficiency in transporting information at global and local scales, respectively, provided by graph-theoretical analysis. Greater motor performance changes toward improvements after real rTMS were shown in individuals who exhibited more increases in global efficiency and more decreases in local efficiency. The enhancement of motor performance after rTMS is supposed to be associated with brain topological changes, such that global information exchange is facilitated, while local information exchange is restricted.

Key words: functional magnetic resonance imaging; graph-theoretical analysis; motor performance; repetitive transcranial magnetic stimulation

Introduction

REPEATED APPLICATION OF single transcranial magnetic stimulation (TMS) pulses, the so-called repetitive TMS (rTMS), influences brain activity and connectivity as well as behavior beyond the period of stimulation (Ziemann et al., 2008). Depending on application parameters, especially low or high frequency, rTMS can induce different modulation of cortical excitability ranging from inhibition to facilitation (Maeda et al., 2000b): suppressed and increased cortical excitability was detected in the stimulated area after rTMS at a low frequency (1 Hz) (Chen et al., 1997) and at a high frequency (5–20 Hz) (Pascual-Leone et al., 1994), respectively.

Effects of delivering rTMS to a cortical area have been evaluated with electrophysiological measures, such as motor-evoked potentials (MEPs) and motor thresholds, or neuroimaging. In particular, neuroimaging potentially provides clues to the mechanisms involved in rTMS-evoked changes, overcoming the limitations of other measures (Sieb-

ner et al., 2009). Functional magnetic resonance imaging (fMRI) is a promising neuroimaging modality that has been successfully established in conjunction with rTMS. While a concurrent or interleaved combination of rTMS with fMRI posed technical challenges in its practical application (Bestmann et al., 2003; Bohning et al., 1998), a sequential combination of rTMS with fMRI has been widely implemented.

In the motor domain, a sequential application of fMRI following rTMS over the primary motor cortex (M1) enabled to detect changes in brain activity during a motor task in healthy subjects (Baudewig et al., 2001; Yoo et al., 2008) and patients with stroke (Carey et al., 2010) or Parkinson's disease (Gonzalez-Garcia et al., 2011). Furthermore, plastic changes in interregional connectivity over the motor system were observed in healthy subjects using psychophysiological interaction (Lee et al., 2003) and in stroke patients using dynamic causal modeling (Grefkes et al., 2010). Even though aftereffects of M1 stimulation may not be limited to the motor system, connectivity changes at a wider spatial extent beyond the motor system have not been thoroughly exhibited.

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In this study, using fMRI following rTMS over the M1, we sought changes in the topology of brain networks, and particularly the association of brain topological changes with motor performance changes. Brain networks were assessed using graph-theoretical analysis, which enables to measure topological characteristics of large-scale networks in terms of network parameters. Considering brain stimulation to induce an acute variation in the brain, graph-theoretical analysis would allow us to detect topological changes in brain networks, as shown for various pathological or physiological variations (Bassett and Bullmore, 2009). Among a variety of network parameters, we employed efficiency measures that allow a precise quantitative analysis of the information flow over a network (Latora and Marchiori, 2001).

The data used in this study are part of the data acquired for our previous study (Yoo et al., 2008) in which aftereffects of rTMS on regional activity had been found. In this contribution, we revisited the data with respect to brain topological correlates of motor performance changes following rTMS.

Methods

Subjects

Thirty healthy subjects (16 females; age 23.1 ± 3.1 years) participated in this study. According to the Edinburgh inventory (Oldfield, 1971), they were all right-handed (Edinburgh inventory score 96.7 ± 5.6). They reported no contraindications to TMS and MRI and had no motor-related dysfunctions. Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki and its later amendments, and the study protocol was approved by the local ethics committee.

Experimental design

The present study was designed as participant-blinded and sham-controlled. Each subject underwent (1) familiarization with the experimental procedure of scanning and behavioral tests; (2) pre-intervention fMRI; (3) location of the hot spot (optimal scalp position) over the right M1 hand area contralateral to the moving hand; (4) subthreshold 10 Hz rTMS over the hot spot; and (5) post-intervention fMRI. More details about the design of the whole experiment are described in our previous study (Yoo et al., 2008).

Real or sham rTMS intervention

Application of rTMS was performed using a Rapid² stimulator (Magstim Company, Carmarthenshire, UK) equipped with a 70 mm figure-of-eight coil over the hot spot, which was identified as the point evoking the maximum motor response in the contralateral first dorsal interosseous (FDI) muscle. Stimulation consisting of a train of 50 pulses at 10 Hz (5 sec) followed by an intertrain interval (25 sec) was repeated 20 times ($30 \text{ sec} \times 20 = 10 \text{ min}$) to deliver a total of 1,000 pulses during a session.

Thirty subjects were pseudorandomly assigned to either a real rTMS group (15 subjects) or a sham rTMS group (15 subjects), matching for age and gender between the two groups. In real rTMS, stimulation intensity was set at 90% of the resting motor threshold, which was defined as the lowest stimulation intensity eliciting at least five twitches (MEPs $\geq 50 \mu\text{V}$ peak-to-peak amplitude in the FDI muscle)

in 10 consecutive trials over the hot spot. Sham rTMS was delivered using a placebo coil at the same frequency and time as those for real rTMS, but without current induction.

Imaging data acquisition and motor performance measurement

Functional images were acquired from a 3.0T FORTE scanner (ISOL Technology, Gyeonggi, Korea). In each fMRI session, a total of 85 whole-brain images were collected with the blood-oxygen-level-dependent contrast in a T2*-weighted single shot echo planar imaging sequence (TR = 3,000 ms, TE = 30 ms, flip angle = 70° , number of slices = 28, slice thickness = 5 mm, matrix size = 64×64 , in-plane resolution = $3.44 \text{ mm} \times 3.44 \text{ mm}$). The second fMRI session started immediately after the intervention to capture the short-lasting aftereffects of rTMS.

In both fMRI sessions, subjects performed the same sequential finger motor task in a block design comprised of four repetitions of a task block (30 sec) followed by a resting block (30 sec). The sequential finger motor task involved pressing buttons in response to a seven-digit number stimulus presented simultaneously on a screen for 3 sec. Subjects were instructed to sequentially push each corresponding button among four numbered buttons as accurately and quickly as possible using left-hand fingers. Each button was labeled with a number indicating which finger should be used: 1, the index finger; 2, the middle finger; 3, the ring finger; 4, the little finger. This kind of sequential finger motor task followed the implementation in previous literature (Kim et al., 2004, 2006).

As measures of motor performance in each session, movement accuracy was defined as the average number of correct responses in one motor task block, and movement time as the average time required for responses to a seven digit number, expressed in milliseconds. To assess different changes in motor performance depending on the type of intervention, that is, the interaction between intervention type (real rTMS vs. sham rTMS) and time point (before vs. after intervention), we performed a repeated-measures ANOVA. Also, motor performance was compared between the two groups at each time point and between the two time points in each group using *t*-tests. Statistical significance was determined at a *p*-value of 0.05.

Imaging data preprocessing and brain network construction

Functional images from each session were preprocessed separately. The first five images were discarded to allow the fMRI signal to achieve equilibrium. Preprocessing of the images were performed using SPM8 (Wellcome Trust Centre for Neuroimaging, University College London, London, UK) in the order of spatial realignment to the mean image, normalization into the same coordinate frame as the Montreal Neurological Institute template brain, and smoothing using a Gaussian filter of 8 mm full width at half maximum.

Seventy-three cortical and subcortical regions over the whole brain were defined based on the automated anatomical labeling brain atlas (Tzourio-Mazoyer et al., 2002). Table 1 lists the 73 brain areas with the acronyms of them, and Figure 1 shows them on the brain. A time series of each brain area was acquired in the same procedure as eigenvariate extraction

TABLE 1. SEVENTY-THREE BRAIN AREAS AND 16 SUBBRAIN REGIONS THAT COMPOSE A BRAIN NETWORK

No.	Brain area	Subbrain region
1/2	Precentral gyrus (PreCG) I/C	Sensorimotor (SM) I/C
3/4	Supplementary motor area (SMA) I/C	
5/6	Postcentral gyrus (PostCG) I/C	Frontal (Frn) I/C
7/8	Paracentral lobule (PCG) I/C	
9/10	Superior frontal gyrus (SFG) I/C	
11/12	Middle frontal gyrus (MFG) I/C	
13/14	Inferior frontal gyrus (IFG) I/C	
15/16	Olfactory cortex (OC) I/C	
17/18	Straight gyrus (SG) I/C	Parietal (Prt) I/C
19/20	Superior parietal gyrus (SPG) I/C	
21/22	Inferior parietal gyrus (IPG) I/C	
23/24	Supramarginal gyrus (SMG) I/C	
25/26	Angular gyrus (AG) I/C	
27/28	Precuneus (Precuneus) I/C	Occipital (Occ) I/C
29/30	Calcarine fissure and surrounding cortex (CS) I/C	
31/32	Cuneus (Cuneus) I/C	
33/34	Lingual gyrus (LG) I/C	
35/36	Superior occipital gyrus (SOG) I/C	
37/38	Middle occipital gyrus (MOG) I/C	
39/40	Inferior occipital gyrus (IOG) I/C	Temporal (Tmp) I/C
41/42	Fusiform gyrus (FG) I/C	
43/44	Heschl gyrus (HG) I/C	
45/46	Superior temporal gyrus (STG) I/C	
47/48	Middle temporal gyrus (MTG) I/C	
49/50	Inferior temporal gyrus (ITG) I/C	
51/52	Insula (Insula) I/C	Limbic/ paralimbic (Lmb) I/C
53/54	Anterior cingulate gyrus (ACG) I/C	
55/56	Median cingulate gyrus (MCG) I/C	
57/58	Posterior cingulate gyrus (PCG) I/C	
59/60	Hippocampus (Hippocampus) I/C	
61/62	Parahippocampal gyrus (PHG) I/C	Subcortical (SC) I/C
63/64	Amygdala (Amygdala) I/C	
65/66	Caudate nucleus (CN) I/C	
67/68	Putamen (Putamen) I/C	
69/70	Thalamus (Thalamus) I/C	Cerebellar (Cbl) I/C
71/72	Cerebellar hemisphere (CH) I/C	
73	Cerebellar vermis (CV) I/C	

Except the cerebellar vermis at the midline, all brain areas and thus all subbrain regions are included as pairs in both hemispheres. The terms in parentheses are abbreviated ones to be presented in figures. C, contralateral to the moving hand; I, ipsilateral to the moving hand.

in SPM8. Voxelwise signals collected from the 80 preprocessed functional images were whitened and high pass filtered at 1/120 Hz, and then singular value decomposed to yield the principal eigenvariate as a representative time series. Seventy-three time series from the 73 brain areas were finally collected, and Pearson's simple correlation between every pair of the time series yielded a 73×73 matrix of correlation coefficients. The correlation matrix was converted to a sparse matrix, or a weighted and undirected network in graph-theoretical terms, by thresholding at a specific correlation coefficient. *Weighted* means that the strength of every suprathreshold connection is kept such that a correlation coefficient surviving the threshold indicates a connection strength. *Undirected* indicates that connections have no directional information.

Efficiency measure computation

At the single connections and brain areas level, interregional efficiency, ε_{ij} , in the communication between a pair of brain areas i and j is defined as the reciprocal of the shortest path length between them (Latora and Marchiori, 2001). Shortest path length is given as the smallest sum of distances, or the smallest sum of inverse connection strengths, assuming that stronger connection implies shorter distance. Epi-regional efficiency, $E(\mathbf{G}_i)$, of a local network, $\mathbf{G}_i$, comprised of neighbor brain areas that have direct connections to a brain area i is defined as the average of interregional efficiency between the neighbors. Diagrammatic description of interregional and epi-regional efficiency is provided in Supplementary Figure S1 (Supplementary Data are available online at www.liebertpub.com/brain).

At the whole-brain level, the average of interregional efficiency between every pair of brain areas over the whole brain is termed *global efficiency*, E_{glob} , since it exhibits the efficiency in transporting information at a global scale between generic brain areas. The average of epi-regional efficiency for every local network over the whole brain is termed *local efficiency*, E_{loc} , since it displays the efficiency in exchanging information around a generic brain area. Global and local efficiency is interpreted to measure the efficiency in transporting information over a whole-brain network at global and local scales, respectively (Latora and Marchiori, 2001).

Having defined connection density as the ratio of the number of existing connections to the number of connections in the fully connected network with the same number of brain areas, we determined a range of sparsity in terms of connection density. That is, we used the approach based on fixing connection density to extract a sparse matrix from a correlation matrix. Since the brain is known to be a small-world network (Bassett and Bullmore, 2006), we assessed global and local efficiency only across a range of connection densities where small-world properties were satisfied. Considering a small-world network as the system that communicates efficiently at both global and local scales (Latora and Marchiori, 2003), small-world properties of a brain network can be formulated in terms of efficiency, specifically as having higher local efficiency than that of the randomized brain network.

Supplementary Figure S2 shows comparison between E_{loc} of brain networks and local efficiency of matched random networks, $E_{\text{loc,rand}}$ at connection density from 0.05 to 0.50. The matched random networks were considered as 100 instantiations generated by randomly rewiring the connections of brain networks at each connection density, preserving the strength of every connection. Commonly for before and after the intervention in the real and sham rTMS groups, E_{loc} was higher than $E_{\text{loc,rand}}$ at connection density from 0.05 to 0.35, so that this range of connection density was chosen as the range of interest for further investigation.

We performed a repeated-measures ANOVA to assess the interaction between intervention type (real rTMS vs. sham rTMS) and time point (before vs. after intervention) for each of E_{glob} and E_{loc} . Also, we carried out Pearson's partial correlation to assess the association of changes in each of E_{glob} and E_{loc} with changes in motor performance, after controlling for motor performance before the intervention since it could affect the degree of motor performance changes after the intervention. We compared correlation coefficients, after

FIG. 1. Seventy-three brain areas displayed on the brain. The location and extent of each brain area was defined based on the automated anatomical labeling brain atlas. The left panel is a coronal view from posterior to anterior, the middle panel a sagittal view from right to left, and the right panel a transverse view from superior to inferior. Color images available online at www.liebertpub.com/brain

a Fisher's z transformation, between the real and sham rTMS groups. Statistical significance was determined at a p -value of 0.05.

When significance was found from the inferences regarding E_{glob} and E_{loc} , we searched for contributions at subbrain levels toward the significance at the whole-brain level. That is, we followed the approach considering a series of hierarchical functional networks composed of the whole brain or components of the whole brain, which was introduced previously (Park et al., 2012). At the low subbrain level, inferences were made for the regional global efficiency between and within subbrain regions and the regional local efficiency within subbrain regions. Table 1 lists a total of 8 subbrain regions in each hemisphere, each of which was comprised of 1–7 brain areas among the 36 brain areas in one hemisphere, excluding the cerebellar vermis at the midline. Regional global efficiency was acquired as the average of interregional efficiency over connections between a pair of subbrain regions or within a subbrain region, and regional local efficiency as the average of epi-regional efficiency over brain areas within a subbrain region. At the high subbrain level, inferences were made for the hemispheric global efficiency between and within hemispheres and the hemispheric local efficiency within hemispheres. Hemispheric global efficiency was acquired as the average of interregional efficiency over connections between a pair of hemispheres or within a hemisphere, and hemispheric local efficiency as the average of epi-regional efficiency over brain areas within a hemisphere. Statistical significance was determined at a p -value of 0.05, with false discovery rate corrections for multiple comparisons of the components at each subbrain level.

Results

Changes in motor performance

After the intervention, average movement accuracy increased from 90.20 ± 18.76 to 98.87 ± 14.63 in the real rTMS group and from 89.00 ± 17.90 to 93.27 ± 14.26 in the sham rTMS group. Average movement time decreased from 356.13 ± 59.17 ms to 309.93 ± 35.47 ms in the real rTMS group and from 362.00 ± 61.55 ms to 342.53 ± 49.31 ms in the sham rTMS

group. However, even though the real rTMS group showed higher movement accuracy [$t(14) = 2.8381$, $p = 0.0132$] and shorter movement time [$t(14) = -5.0072$, $p = 0.0002$] than that of the sham rTMS group after the intervention, the interaction between intervention type (real rTMS vs. sham rTMS) and time point (before vs. after intervention) was not found.

Changes in global and local efficiency

No interaction between intervention type (real rTMS vs. sham rTMS) and time point (before vs. after intervention) was found for either E_{glob} or E_{loc} . Indeed, both E_{glob} and E_{loc} were not different between the real and sham rTMS groups at either time point (Supplementary Fig. S3) as well as between the two time points in either group (Supplementary Fig. S4).

Correlation of efficiency changes with motor performance changes

In the real rTMS group, changes in E_{glob} positively correlated and changes in E_{loc} negatively correlated with changes in movement accuracy across a wide range of connection density (Fig. 2). For both E_{glob} and E_{loc} , correlation coefficients were different across most of the range of connection density between the real and sham rTMS groups. With changes in movement time, no correlation of changes in E_{glob} and E_{loc} was found in either group and no difference in correlation coefficients was shown between the two groups across the range of connection density considered (Supplementary Fig. S5). It is notable that the association of changes in E_{glob} and E_{loc} was not shown even with changes in movement accuracy when we carried out Pearson's simple correlation, without controlling for movement accuracy before the intervention.

Contribution of subbrain levels toward the whole-brain level

For the correlation of E_{glob} changes with movement accuracy changes at the whole-brain level, Figures 3a and 4a exhibit contributions of subbrain components such that correlation was significant in the real rTMS group as well

FIG. 2. Correlation of changes in (a) global and (b) local efficiency with changes in movement accuracy after the intervention of real or sham rTMS. It is displayed as a function of connection density across the range from 0.05 to 0.35 with an increment of 0.01. A red circle represents significant correlation in the real rTMS group, and an asterisk indicates significant difference in the correlation between the real and sham rTMS groups. rTMS, repetitive transcranial magnetic stimulation. Color images available online at www.liebertpub.com/brain

as significantly different between the two groups across over half of the range of connection density considered. In the similar way, for the correlation of E_{loc} changes with movement accuracy changes at the whole-brain level, Figures 3b and 4b display contributions of subbrain components.

At the hemispheric level, the real rTMS group exhibited positive correlation of hemispheric global efficiency changes with movement accuracy changes between the two hemi-

spheres and in the hemisphere ipsilateral to the moving hand (Fig. 3a). Moreover, the real rTMS group displayed negative correlation of hemispheric local efficiency changes with movement accuracy changes in both hemispheres (Fig. 3b). Correlation at the hemispheric level was supported hierarchically by correlation at the 8 subbrain regional level (Fig. 4). The sham rTMS group showed no correlation both at the hemispheric level and at the 8 subbrain regional level.

FIG. 3. Correlation of changes in (a) hemispheric global and (b) local efficiency with changes in movement accuracy after the intervention of real rTMS. Red and blue mean positive and negative correlation, respectively, which are significant in the real rTMS group as well as significantly different in relation to the sham rTMS group across more than half of the range of connection density from 0.05 to 0.35. It has to be noted that hemispheric local efficiency is defined for within hemispheres, so that any significant correlation is shown only through the diagonal of the square. Hemi C, hemisphere contralateral to the moving hand; Hemi I, hemisphere ipsilateral to the moving hand. Color images available online at www.liebertpub.com/brain

FIG. 4. Correlation of changes in (a) regional global and (b) local efficiency with changes in movement accuracy after the intervention of real rTMS. In the upper panels, red and blue mean positive and negative correlation, respectively, which are significant in the real rTMS group as well as significantly different in relation to the sham rTMS group across more than half of the range of connection density from 0.05 to 0.35. It has to be noted that regional local efficiency is defined for within subbrain regions, so that any significant correlation is shown only through the diagonal of the square. In the lower panels, the same results are displayed on a transverse view of the brain from superior to inferior. The abbreviated terms of subbrain regions conform to those presented in Table 1. C, contralateral to the moving hand; I, ipsilateral to the moving hand. Color images available online at www.liebertpub.com/brain

Discussion

A combined application of rTMS and fMRI is useful to assess plastic reorganization of the brain. In our previous study, with that combined application, we showed that rTMS over

the M1 induced increases in activity over the frontal, temporal, and parietal cortices beyond the motor system during the sequential finger motor task (Yoo et al., 2008). In the current study, using the same data and instead employing graph-theoretical analysis, we could not find changes in the topology

of brain networks after M1 stimulation, but we presented the association of brain topological changes with motor performance changes at a wide extent over the brain.

As the behavioral outcome of rTMS over the M1, motor performance was not enhanced after real rTMS as compared to after sham rTMS, in terms of both movement accuracy and time. Furthermore, the topology of brain networks was not changed after real rTMS as compared to after sham rTMS, in terms of both global and local efficiency. These nonsignificant changes in the motor performance and efficiency measures reflect interindividual variability of rTMS effects. The subject-to-subject variability of the effects of rTMS over the M1 on motor responses was repeatedly exhibited (Maeda et al., 2000a; Sommer et al., 2002), and thus more reliable and stable rTMS protocols have been searched for (Paulus, 2005). Each individual's optimum motor responses may depend on various stimulation parameters, including the frequency (Rounis et al., 2005), intensity, and coil type (Lang et al., 2006). Moreover, the degree of modulation of the brain is likely to be different depending on the functional state of the targeted cortex at the time of stimulation (Bestmann et al., 2008).

Under the interindividual variability of rTMS effects, we showed that there was an association between brain network changes and motor performance changes in the individuals. The higher the individuals' movement accuracy, the more reorganized their brain networks in such a way that global information flow was facilitated, while local information flow was restricted. As the association with movement time changes was not shown in this study, the association of changes in cortical excitability, as measured by MEPs, was exhibited only with movement accuracy changes, but not with movement time changes, in the previous study in which the same kind of sequential finger motor task was employed (Kim et al., 2006). Between movement accuracy and time, movement accuracy may be a more sensitive motor performance measure in reflecting the relation to changes of the brain.

Alterations in how efficiently information is transferred over the brain appear to reflect an acute shift of the brain state induced by rTMS. In motor performance, lower efficiency in global information flow suggested a brain state in association with aging (Park et al., 2012); higher efficiency in local information flow indicated a brain state in connection with spinal cord injuries (Fallani et al., 2010). Thus, contrary to the brain state of impaired motor function, increases in the efficiency in global information flow and decreases in the efficiency in local information flow could reflect the brain state of intact or enhanced motor function. The effectiveness of rTMS for motor function may be related to the shift of the brain state toward an emphasis on global information exchange, with a restriction on local information exchange.

The association of brain network changes with motor performance changes was exhibited at a wide extent over the brain, beyond the stimulation site and motor system, at sub-brain levels. Increases in the efficiency in global information flow associated with motor performance changes were displayed between the two hemispheres and also in the hemisphere ipsilateral to the moving hand (Fig. 3a), and supportive results were shown at the low subbrain level (Fig. 4a). It is notable that brain topological correlates at the whole-brain level were dominantly contributed at sub-

brain levels by the connections between the two hemispheres and particularly in the unstimulated (ipsilateral) hemisphere, rather than the stimulated (contralateral) hemisphere. Decreases in the efficiency in local information flow associated with motor performance changes were exhibited over both hemispheres at different subbrain levels (Figs. 3b and 4b), still beyond the stimulated hemisphere. Changes in the pattern of connectivity in the unstimulated hemisphere were likely to be derived through connections between the unstimulated and stimulated hemispheres. Changes in inter-hemispheric connectivity following brain stimulation were shown even for other stimulation modalities such as transcranial direct current stimulation (Polanía et al., 2011).

Considering interindividual variability of rTMS effects caused by various factors, characteristic changes of the brain exhibited in individuals with greater motor improvements following rTMS may be informative for developing noble rTMS protocols for greater specificity and efficacy as well as for understanding the mechanisms of rTMS effects. Even though significant changes after the intervention were not shown for the motor performance and efficiency measures we employed, the association of brain topological changes with motor performance changes provides an alternative perspective on the brain-behavior relation modulated by rTMS.

Conclusion

In connection with motor performance changes toward improvements, application of rTMS appears to reinforce the brain to integrate information between distant brain areas, while imposing a restriction on local information exchange. At subbrain levels, brain topological correlates were exhibited at a wide extent over the brain, beyond the stimulation site and motor system.

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Author Disclosure Statement

No competing financial interests exist.

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