

Relationship between Event-related Desynchronization and Cortical Excitability in Healthy Subjects and Stroke Patients

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Objective: Relation between cortical excitability and magnitudes of event-related desynchronization (ERD) has not been clarified. This study was investigated that relationship between cortical excitability and ERD magnitudes in healthy subjects and stroke patients.

Methods: Ten healthy subjects and four patients with stroke participated in this study. EEGs were recorded over the sensorimotor cortex (left hemisphere in healthy subjects; damaged hemisphere in stroke subjects) to calculate ERD during motor imagery. Motor-evoked potential (MEP) induced by single-pulse transcranial magnetic stimulation over the primary motor cortex was recorded from the first dorsal interosseus (FDI) muscle at ERD magnitudes of 10% and 30%.

Results: MEP significantly increased at 10% and 30% ERD ($p < 0.01$) than that during rest in healthy subjects. The 30% ERD condition showed significantly higher MEP than that at 10% ERD ($p < 0.05$). In stroke patients, MEP increased with ERD induced by motor imagery, but the change of MEP to ERD amplitude was critically different among the subject.

Conclusion: ERD magnitude corresponds to corticospinal excitability increases in healthy subjects and patients with hemiplegic stroke. BCI based on motor imagery-induced ERD may be a potential rehabilitation strategy for patients with hemiplegic stroke.

Key words: transcranial magnetic stimulation, event-related desynchronization, corticospinal excitability

INTRODUCTION

Patients with hemiparetic stroke initially show severe motor impairments in upper extremities, and approximately 30%–66% of patients will never reacquire upper extremity motor function [1]. Therapeutic interventions for hemiplegic hands include neuromuscular facilitation, electromyographic (EMG) biofeedback, functional electrical stimulation, and constraint-induced movement therapy [2]. However, these therapeutic methods need some voluntary muscle contractions in the paretic arms and are not useful in most patients who are severely impaired with stroke and who lack upper extremity motor function. Brain-computer interface (BCI) based on event-related desynchronization (ERD) transforms thought into action using the electrical activity generated by cortical neurons [3]. This method can be useful for determining motor intent in patients who are severely hemiplegic with undetectable EMG. Using BCI to provide feedback of ongoing sensorimotor cortical activity improved the upper limb function in patients with stroke [4, 5]. Motor imagery-induced ERD during EEG, which is a decrease of specific alpha and beta frequency bands, is often used as a neural marker representing sensorimotor cortex excitability. Enhancing excitability by transcranial current stimulation is

associated with an increase in ERD [6, 7], suggesting that ERD may be a reliable index of excitability. To directly investigate the physiological mechanisms of ERD, we used transcranial magnetic stimulation (TMS) to assess corticospinal excitability in healthy subjects and patients with stroke. We applied TMS when motor imagery-based ERD reached a percentage of the predetermined threshold and assessed ERD-dependent changes in motor evoked potentials. This study was investigated that relationship between cortical excitability and ERD magnitudes in healthy subjects and stroke patients.

METHODS

Participants

Experiment 1

Ten healthy right-handed subjects (5 male, 5 female; mean age, 28.1 ± 8.2 years; range, 22–49 years) with no known neurological disorders or contraindications to TMS [8] participated in this study. The dominant hand was evaluated by the Edinburgh Handedness Inventory [9].

Experiment 2

Four patients with chronic hemiparetic stroke participated in experiment 2. Inclusion criteria consisted of the following: 1) first unilateral subcortical stroke; 2) more than six months from the onset of stroke; and

3) ability to evoke MEPs from the paretic hand muscle when TMS was applied over M1 of the affected hand. Exclusion criteria were as follows: 1) history of major psychiatric or previous neurological diseases including seizure; 2) cognitive impairment precluding informed consent; or 3) use of central nervous system-activating drugs. The mean age of the patients was 63 ± 9.0 years. The duration from the onset of stroke was 46.3 ± 30.2 months. All participants were right handed. Two subjects had lesions in the right hemisphere (respectively thalamus and putamen), and two subjects had lesions in the left hemisphere (both thalamus). Their motor recovery was Brunnstrom's stage 4 or 5. None of the subjects reported severe sensory disturbances. The present study was approved by the Clinical Research Review Committee of the Tokai University School of Medicine and performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects.

Experimental set-up

Experiments were conducted in a quiet laboratory room at a controlled temperature of $25\text{--}27^\circ\text{C}$. Subjects sat in a comfortable reclining armchair facing a laptop computer monitor placed approximately 0.5 m in front of them at eye level. Upper limbs and hands were at rest. Before starting the experiments, subjects were required to keep their hands and fingers as relaxed as possible and remain awake. An infrared heater was used to maintain hand and forearm skin temperatures $> 32^\circ\text{C}$.

Each trial started with the presentation of the word "rest" on the upper part of the monitor. Subsequently, the word "Ready" was shown for 1 s. Then, the word "Image" was presented for 5 s (Fig. 1). Subjects were instructed to perform motor imagery tasks as described below.

Motor imagery tasks and the method of feedback

Motor imagery tasks involved using the right (dominant; healthy group) or affected (stroke group) hand for a powerful grasp. A third-person perspective of a realistic hand animation was constructed from a picture of the participant's hand, which showed the grasped hand. This animation was recorded as a video prior to the experiment. This hand animation moved according to their ERD strength determined by motor imagery.

EEG recording and quantification of ERD

EEG signals were recorded from the scalp around the sensorimotor cortex using 5 Ag/AgCl surface electrodes (1 cm in diameter; NE-113A, Nihon Kohden corporation, Japan) placed at C3 (defined by the international 10–20 system) and at 20 mm anterior, posterior, right and left positions from C3 in healthy subjects. Electrodes were placed in a similar configuration around the motor cortex of the affected hemisphere in patients with stroke. For all subjects, the reference electrode was placed on the right or left earlobe, and the ground electrode was placed on the forehead.

The EEG signals were amplified (g.USB amp, g.tec medical engineering GmbH, Austria), digitized (600 Hz sampling frequency), and band-pass filtered

(2–100Hz). An additional 50 Hz notch filter was applied to avoid power-line contamination. EEG data analysis was performed using MATLAB (The Mathworks Inc., Natick, MA, USA). All adjacent pairs of EEG bipolar derivations were used to analyze the focal activity of the underlying motor cortex. All trials were segmented into successive 1 s windows with 90% overlap, and the Fourier transformation with the Hanning window was applied for each segment. The power spectrum was calculated in a time-sliding window of 1024 ms with 125 ms overlap. Thus, ERD was calculated every 125 ms at a frequency of 1 Hz according to Eq. 1.

$$ERD(f, t) = \frac{R(f) - A(f, t)}{R(f)} \times 100\% \dots (\text{Eq.1})$$

A is the EEG power spectrum density at time t with reference to the onset of motor imagery at frequency f ; R is the power spectrum in the 3-s reference interval before the word 'Ready' is presented (-4 to -1 s) (Fig. 1). A large positive value indicates a large power decrease during motor imagery compared with the resting condition. The time-frequency ERD/ERS maps of the bipolar pair EEG recordings were calculated for the left and right hemispheres. The largest power decrease in the alpha (8–13 Hz) or beta band (14–30 Hz) during motor imagery was selected. ERD was measured by the frequency band.

TMS and EMG recording

TMS was performed using a Magnetic Stimulator (SMN1200, Nihon Kohden Co., Tokyo, Japan) with a maximal magnetic field strength of 2.2 Tesla equipped with a figure-eight coil with a mean diameter of 9 cm. At the beginning of each experiment, the coil intersection was placed tangentially to the scalp, approximately 2 cm to the left of the Cz according to the International 10–20 system, with the handle pointing backward and laterally at 45° away from the midline. TMS was applied over the left hand motor area in healthy subjects and over the hand motor area contralateral to the paretic hand in patients. Stimulus intensity was initially set at 60% of the stimulator output. The coil was moved over the scalp in 1-cm steps to determine the hotspot. The position over which the magnetic stimulus elicited the largest and fastest MEP was considered to be the hotspot. MEPs were recorded from the right first dorsal interosseus (FDI) in healthy subjects or FDI of the affected hand in patients with stroke using belly-tendon recordings with surface Ag/AgCl disc electrodes (1 cm in diameter) and a band-pass of 5–2 kHz by a Neuropack MEB-2208 (Nihon Kohden Corporation, Japan). A disposable pre-gelled Ag/AgCl ground electrode was placed around the right hand or the affected hand. The resting motor threshold (rMT) was defined as the lowest stimulus intensity to evoke at least 5 of 10 MEPs with an amplitude of at least 50 μV . Stimulus intensity was then set at 120% of rMT.

We performed two sessions of the motor imagery tasks. TMS timing and ERD analysis were simultaneously controlled by the preprogrammed MATLAB software. During the first imagery session (session 1), MEPs were recorded when ERD reached 10% depres-

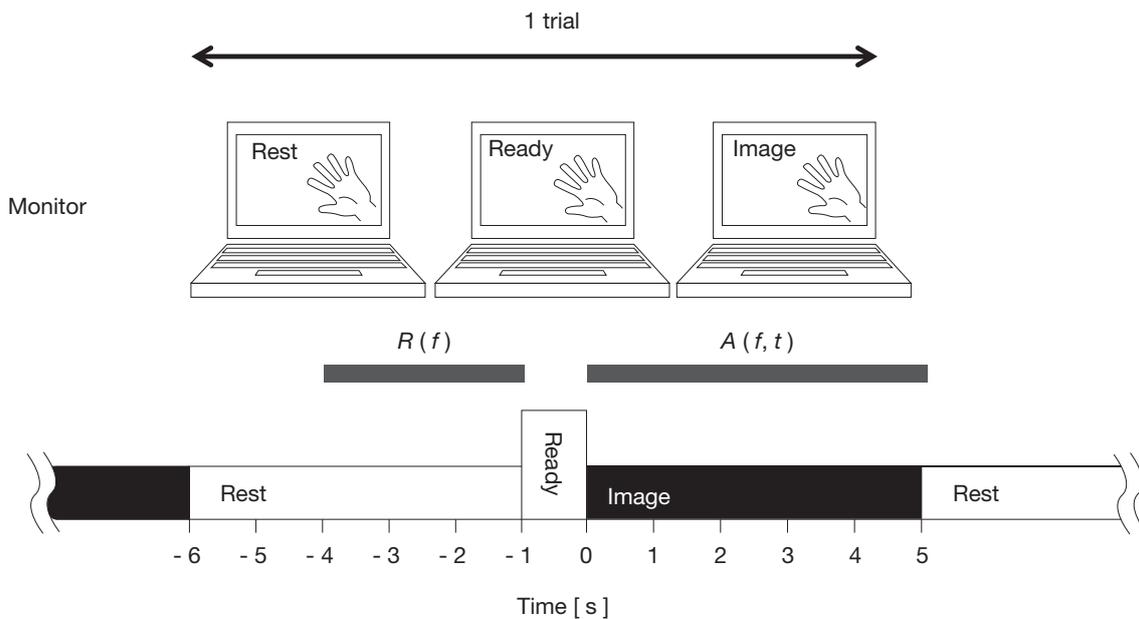


Fig. 1 Experimental set up:

The time course of a single trial consisted of three states: rest, ready, and motor imagery. The instructions were displayed on a monitor in front of the subjects. A trial started with a 6-s period of “rest” during which the word “Rest” was shown at the upper part of the monitor. Subsequently, a 1-s period during which the word “Ready” was shown. The word “Image” was then presented for 5 s, and subjects were instructed to perform a motor imagery task.

sion. During session 2, they were recorded when ERD reached 30% depression. TMS over M1 was delivered when the ERD value was 10% (session 1) or 30% (session 2). TMS was applied 10 times per condition and 10 MEPs were recorded. In addition, 10 MEPs were recorded at rest before each session. The provided MEP was analyzed offline.

Data analysis

The Statistical Packages for Social Sciences (SPSS 13.0J for Windows; SPSS Inc., Chicago, IL, USA) was used to conduct the statistical analysis.

Experiment 1

MEP amplitude was measured between the negative and positive peak. The averaged amplitude of 10 MEPs was calculated for each session. Wilcoxon signed-rank test was used to compare the MEP amplitude in each session with that at rest. Differences were considered significant at $p < 0.05$. The change in MEP amplitude was expressed as a percentage change of that at rest during each session. Mann–Whitney U tests were used to compare the percentage change in the MEP amplitude at 10% versus 30% ERD.

Experiment 2

MEP amplitudes at 10% and 30% ERD were expressed as a percentage of the average MEP at rest in each respective session. For within-subject comparisons, Wilcoxon signed-rank tests were used to compare the percentage change between the MEP amplitude at ERD and rest. Differences were considered significant at $p < 0.05$. Mann–Whitney U tests were used for between-subject comparisons (rest vs. MEP at each ERD value).

RESULTS

Experiment 1

All subjects showed ERD over the sensorimotor cortex in response to motor imagery. At 10% and 30% ERD, MEP amplitude significantly increased compared with that at rest ($p < 0.01$) (Fig. 2a, 2b).

Percentage change of MEP was significantly higher at 30% ERD than that at 10% ERD ($p < 0.05$). The mean percentage change of MEP amplitude from rest to 10% ERD was 156.0% and that from rest to 30% ERD was 312.7% (Fig. 2c).

Experiment 2

ERD over the sensorimotor cortex was successfully observed in each session for all patients, and MEPs after TMS over the affected M1 was recorded from all FDIs in the paretic hands. The percentage change of MEP amplitude significantly increased in three of the four patients in session 1 and in all of the patients in session 2 (Fig. 3a). MEPs at 30% ERD were significantly higher than those at 10% ERD for all the subjects. MEP amplitudes at 10% and 30% ERD were higher than that at rest, although the difference was not statistically significant ($p = 0.057$) (Fig. 3b).

DISCUSSION

In the present study, the relationship between the strength of motor imagery-induced ERD and TMS-evoked MEPs was investigated. ERD magnitude reflects the change in M1 cortical excitability, and MEP amplitude significantly increased in conjunction with ERD in healthy subjects. In the patient group, MEPs similarly increased along with ERD, although the relationship between MEP and ERD amplitude was critically different among the patients.

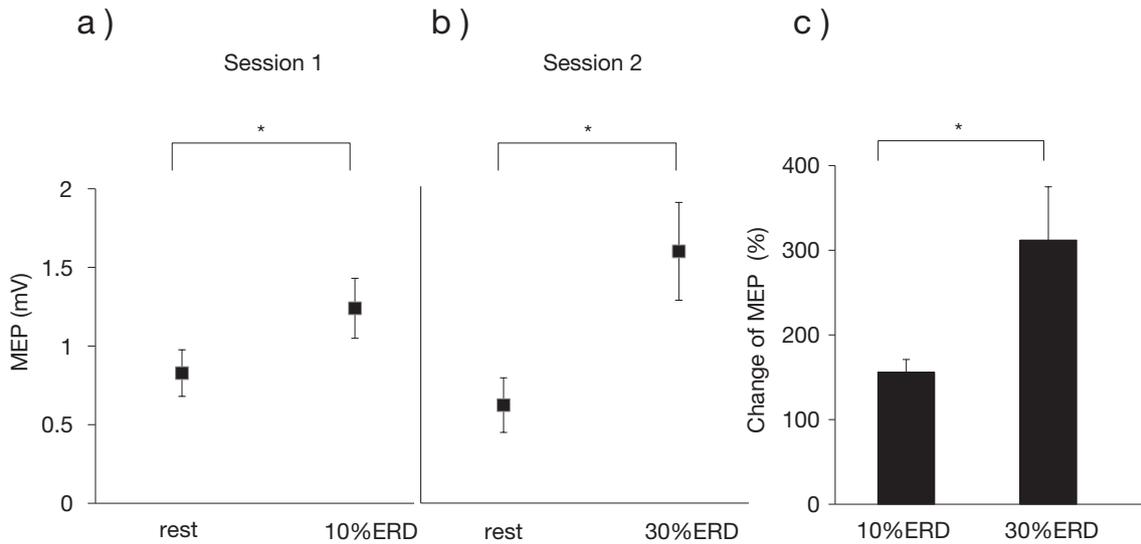


Fig. 2 Change in motor-evoked potential (MEP) amplitude and percentage change of MEP in the healthy subjects at each session: a) The squares show the mean MEP amplitude recorded at rest and at 10% event-related desynchronization (ERD). b) The squares show the mean MEP amplitude recorded at rest and at 30% ERD. c) The bars show the percentage change of MEP in each session from rest. Error bars: SD. * $p < 0.05$.

ERD represents the activation of cortical neurons and is an electrophysiological correlate of increased cortical excitability. Primary sensorimotor cortex and supplementary motor area may have influence on this phenomenon. However detailed origin is unknown. In previous studies, ERD was observed around M1, but cortical excitability was not directly investigated [10]. Therefore, it was unclear whether ERD magnitude reflects the strength of cortical excitability. Simultaneous changes in ERD and MEP were observed during the same motor imagery tasks. Therefore, the present study may be particularly important for showing time resolution of these changes. There is a relationship between ERD in motor preparation and cortical activity detected on functional magnetic resonance imaging, positron emission tomography, or near infrared spectroscopy [11, 12]. Only one report investigated the relationship between MEP amplitude and EEG mu rhythm modulation during motor imagery [13], but the relationship between oscillatory activity and MEP amplitude was still unclear [14–16]. Our results show a relationship between ERD magnitude and MEP amplitude, suggesting that ERD could be a useful index of cortical excitability. Matsumoto *et al.* reported ERD changes in response to anodal transcranial direct current stimulation over M1 [6]. They suggested that there was a relationship between cortical excitability and mu ERD, further supporting our hypothesis.

We obtained both 10% and 30% ERD from patients with stroke in our study. Because patients with stroke suffer neurological damage to their brain, detecting ERD can be difficult. However, Ang *et al.* reported that the capability of operating MI-BCI was not affected by the neurological damage in patients with stroke [17], suggesting that BCI based on ERD can be effective for subcortical strokes. Similar to healthy subjects, MEP increased in relation to ERD strength. Our results demonstrated that BCI objectively assessed M1 performance and increased cortical excitability according to

ERD strength, suggesting that ERD magnitude may become the index of cortical excitability in patients with stroke. Because ERD is the index of cortical activity in the sensorimotor cortex, BCI based on ERD may offer new and promising strategies to modulate neuroplasticity for promoting functional recovery in patients with severe motor disabilities due to stroke. This cortical excitability modulation may be an effective rehabilitation strategy to improve functional outcomes in these patients.

MEPs delivered at 10% ERD did not increase compared with that during rest in one of the four subjects. This may be because MEP amplitude is also affected by spinal excitability and the synchrony of descending volleys. Therefore, the damaged corticospinal tract may not be capable of increasing MEP at this low level of excitation.

There are several limitations to be considered in this study. First, we only studied ERD during rest, 10% ERD, and 30% ERD. Future studies should investigate cortical excitability modulations in detail. Second, the number of patients with stroke was small. Further studies including a higher number of patients will help reveal the relationship between cortical excitability and ERD.

Our results showed a significant relationship between cortical excitability and ERD magnitude. The ERD-based BCI system supported successful motor imagery. Recent studies suggest that information provided by imagination and observation of movements could be useful for motor rehabilitation after stroke [18]. Therefore, these systems obtain the patient's visualization of an image and prove that patients perform an image definitely. These systems improved motor function in previous studies [19, 20], and our results confirmed that those systems increased cortical excitability and contributed to functional improvement.

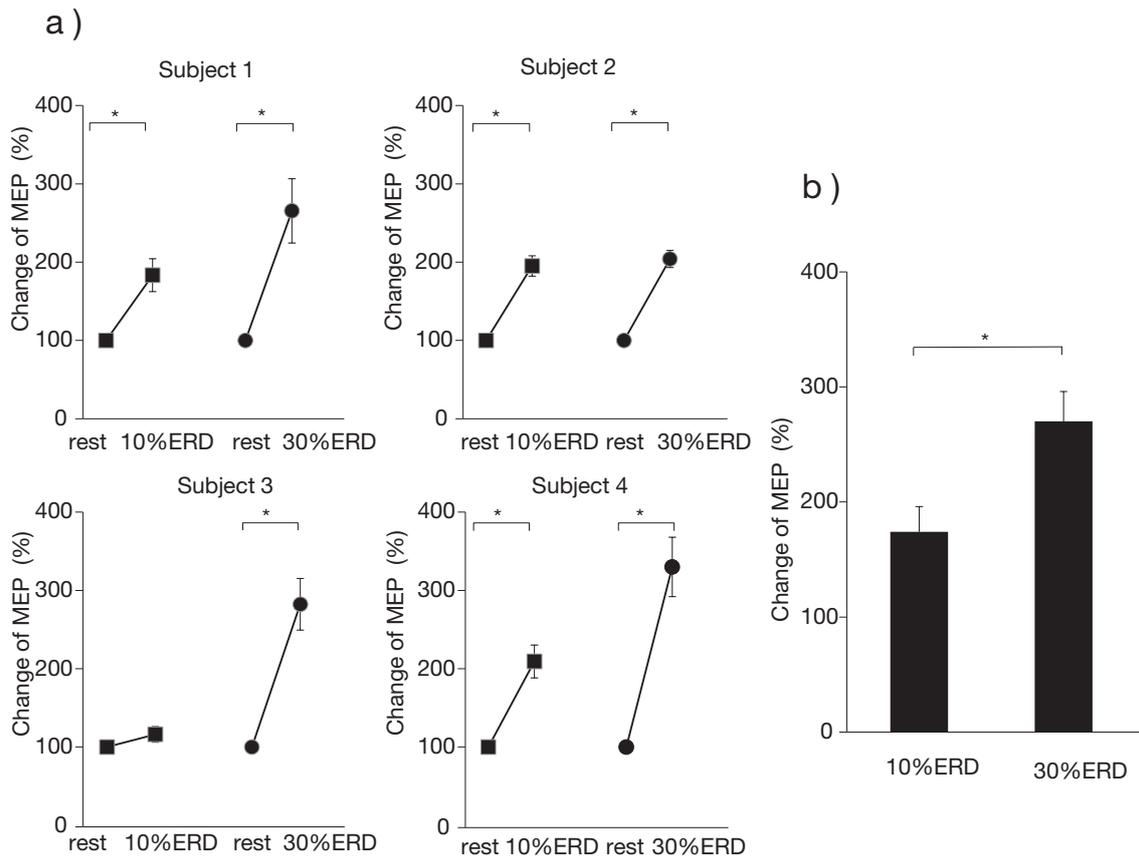


Fig. 3 Percentage change of motor-evoked potential (MEP) in patients with stroke =at each session: a) The black square shows the percentage change of MEP amplitude at rest and at 10% event-related desynchronization (ERD). The circles show the percentage change of MEP amplitude at rest and at 30% ERD. Each panel shows each subject's results. b) The bars show the percentage change of MEP during each session.

CONCLUSION

The ERD magnitude may be related to corticospinal excitability observed in both healthy subjects and patients with hemiplegic stroke. Therefore, the development of a visual feedback system using ERD as a monitor of motor imagery strength may be useful for either chronic or acute phase rehabilitation.

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