Development of a Brain-machine Interface for Stroke Rehabilitation Using Event-related Desynchronization and Proprioceptive Feedback

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Abstract We have developed a brain-machine interface (BMI) rehabilitation system for patients with stroke and motor paralysis, which provides proprioceptive feedback upon successful generation of motor-imagery (MI)-induced event-related desynchronization (ERD) and a decrease in mu band (8–13 Hz) activity derived from hand motor imagery. This system consists of an electroencephalogram (EEG) amplifier operated using the MATLAB Simulink software; a pneumatic robotic exoskeleton to provide proprioceptive feedback to the paralyzed hand; and a tablet computer placed over the paralyzed hand to display a hand-action movie to facilitate ERD generation. The EEG amplifier was connected and synchronized via the exoskeleton and tablet computer with an Arduino microcomputer. Nine patients in the subacute stage of recovery after stroke participated in a neurofeedback training experiment, which employed the aforementioned system. During the 4 weeks of this study, the participants received 2 weeks of BMI-based or control interventions in a random and counterbalanced order, in addition to their daily conventional physiotherapy. The control intervention consisted of the same MI training as the BMI-based intervention, but the exoskeleton always provided proprioceptive feedback regardless of the ERD strength. The ERD strength in the affected hemisphere showed a desirable increase with a significant improvement of finger joint spasticity, only after the DMB-based intervention period, and not after the control intervention period. The proposed neurofeedback training can help patients with stroke and movement disorders, because increased ERD strength may lead to recovery of motor function.

Keywords: brain-machine interface, event-related desynchronization, motor-imagery.


1. Introduction

Stroke is a disease resulting from the obstruction or rupture of a blood vessel in the brain, which can cause movement disorders such as hemiplegia. Conventional rehabilitation, such as physiotherapy and occupational therapy, has long been established to reduce motor disability and regain the activities of daily living (ADL) for stroke patients with hemiplegia. Constraint-induced movement therapy is one of the most successful therapies for improving upper extremity function, with confirmed clinical evidence [1]. However, most of the effective conventional therapies to regain functionality of the affected limb are currently applicable to patients with moderate or mild paralysis. Most patients with severe paralysis have to choose a compensatory approach, involving the utilization of residual functions and assistance devices to reduce difficulties in ADL. However, a decade of neuroscience research focusing on the plasticity of the affected motor neural pathway and the reorganization of the motor function of the paralyzed limb has attracted attention, demonstrating the possibility of restoring motor function even in stroke patients with severe movement disorders [2–6]. The brain machine interface (BMI) is one of the promising rehabilitation methodologies to reorganize the affected motor neural pathway, due to its direct detection of motor-related neural activity and its
ability to provide feedback to the patient via visual, auditory, and/or proprioceptive feedback through a robotic orthosis [3, 4]. Motor imagery (MI)-induced event-related desynchronization (ERD) has been employed to detect the motor commands of patients in previously proposed BMI systems for neurorehabilitation [4, 5, 7].

ERD is the attenuation of the power of spontaneous electroencephalograph (EEG) signals in the mu band (8–13 Hz) observed around the motor cortex in synchrony with the intent and/or execution of an exercise. Patients are encouraged to induce larger MI-ERD from the affected side of the motor cortex, and they receive neuro-feedback upon successful generation of MI-ERD, through which the affected motor pathway is reorganized to convey motor intent to the paralyzed limb. Clinical studies show that these neurofeedback systems are beneficial to increase MI-ERD of stroke patients with paralysis and to recover motor function in the affected limb [4, 5, 7]. However, most stroke patients have difficulty with MI. Advanced age and/or higher cognitive dysfunction may impair the patients’ ability to internally simulate the action [8], which may limit the utility of neurofeedback training in such patients. We have therefore developed a novel ERD-BMI rehabilitation device called the Digital Mirror Box (DMB) [9, 10], in which the MI response of the patients is facilitated by placing MI under the observation of a hand-action movie (action observation: AO).

The technical advances of the proposed DMB system over previous BMI rehabilitation systems are summarized by the following two points. First, we adopt a hand action movie for motor imagery cue [9], instead of abstract cues such as verbal instructions [4, 5]. MI with AO (AOMI) has been shown to detect more robust ERD responses in comparison to MI without AO, even in stroke patients with hand paralysis and/or with higher cognitive dysfunction, possibly through stimulation of the mirror neuron system [8]. This contributes to expand the patient populations who could participate in functional recovery training. Second, a temporally and modality congruent feedback, which is a hand movement sensation through an exoskeleton device synchronized with the hand action movie, has superior training effect on ERD strength compared to delayed or abstract feedback [11] and thus contributes to efficiently reconstructing the motor pathways.

In this paper, we describe the details of the proposed DMB system, and report the outcome of a preliminary clinical trial in which the effect of two weeks of repetitive DMB-based training of ERD strength was studied in patients in the sub-acute stage of recovery (1–6 months from onset), and with hand paralysis. We focused on patients in the subacute stage of recovery, because the functional remodeling in the remaining nerve tissue is more active in this stage than in the chronic one [12]. The favorable functional outcomes obtained in previous BMI studies targeting chronic stage patients [4, 5] motivated us to test the hypothesis of whether earlier BMI intervention promotes more prominent functional recovery.

2. Overview of the DMB system

The DMB system consists of an EEG amplifier (g.USBamp: g.tec medical engineering GmbH, Austria) with an electrode box operated using the MATLAB Simulink software; an 18.4-in. tablet computer (AiO P1801-T: ASUS, Taiwan) to show a hand action movie; and a pneumatic hand exoskeleton (Power assist hand: Team ATOM, Japan) to provide proprioceptive feedback to the patient (Fig. 1). The exoskeleton device repeatedly inflates and deflates the air bellows around the fingers to provide the bending and stretching motion of the finger joint. Owing to the flexible air bellows placed along the fingers, this device can even be attached to a hand with spasticity and/or contracture. The tablet computer provides a hand-action movie to facilitate MI-ERD response. When the ERD strength exceeds the defined threshold, a proprioceptive feedback is provided to the hand of the patient through the exoskeleton attached to the affected hand. The proprioceptive feedback is provided synchronously with the hand movement in the movie to promote reorganization of the patient sensory-motor pathway. The physiologically congruent proprioceptive feedback, which is linked to the hand action movie, showed a superior effect in inducing ERD strength through repetitive training, compared to other physiologically irrelevant feedbacks, such as auditory feedback, as reported in our previous study in healthy young adults [9]. The hand action movie on the tablet computer screen and the exoskeleton movement are controlled by MATLAB Simulink software (developed in-house) through Arduino UNO microcomputers.

Figure 2 presents the block diagram of the MATLAB
Simulink software developed for the DMB system. The whole system consists of five blocks: (1) EEG acquisition; (2) data storage; (3) online data monitor; (4) data buffer; and (5) ERD strength detection. The ‘Data buffer’ block is used to temporally store a fraction of the EEG data for computing the ERD strength. The following ‘ERD strength detection’ block determines the ERD strength and sends an operating signal to the exoskeleton via the Arduino microcomputer, once the ERD strength exceeds a predetermined threshold value.

2.1 Visual stimulation
The study participant watched a first-person perspective movie on a tablet screen that was placed in front of the hand being tested. The single training block consisted of a movie containing 10 s of rest followed by five repeated clips of a hand moving recording (Fig. 3). Each clip started with 4 s of black fixation on a white screen as a preparation cue, which reminded the participant to relax and pay attention to the side of the screen on which the hand action occurred. This was followed by 10 s of a hand action clip depicting a hand catching and holding a rolling ball. The participant was encouraged to kinesthetically imagine the motion of catching a ball after it appeared on the screen. ERD strength was calculated during this period, and proprioceptive feedback was provided via the exoskeleton device, synchronized with the hand movement depicted in the clip, based on the detected ERD strength.

2.2 Online detection of ERD strength and feedback
EEG signals were recorded continuously at C3 or C4 of the international 10-10 electrode system, corresponding to the hand motor areas of both the affected and unaffected hemispheres, at a sampling rate of 256 Hz with a 0.5–30 Hz band-pass filter. The ground and reference electrodes were placed at AFz and at the ear lobe contralateral to the affected hemisphere, respectively.

ERD strength was determined as the decay ratio in mu band power related to AOMI. We extracted two sub-periods of EEG data, for rest and task. The rest period corresponded to the EEG data recorded 1 s before the ball appeared on the screen (7–8 s in Fig. 3). The task period corresponded to the EEG data recorded for 1 s after the ball appeared on the screen (8.25–9.25 s in Fig. 3), in which the participant was encouraged to imagine the hand motion of catching a ball. EEG data from 8 s to 8.25 s were excluded from analysis, since there was only a shadow of the ball appearing on the screen during that period. The exact timing to detect ERD strength was provided as a 1-kHz tone burst sound trigger embedded in the hand action movie, which was interpreted as an 8-V trigger signal sent to the EEG amplifier through an Arduino microcomputer (‘Trigger signal’ in Fig. 3). The delay in communication between the tablet PC and the EEG amplifier can be as short as 600 μs. We calculated a mean power spectrum for 8–13 Hz for these two sub-periods using the continuous wavelet transform with Morlet wavelet, and defined the ERD strength using the following equation (1):

$$\text{ERD strength} = 100 \times \frac{\mu_{\text{rest}} - \mu_{\text{task}}}{\mu_{\text{rest}}} \%$$

(1)

where $\mu_{\text{rest}}$ and $\mu_{\text{task}}$ denote the mu band spectrum power obtained during the rest and task sub-periods, respectively. If the ERD strength satisfied the predetermined threshold, the exoskeleton provided feedback. Users received proprioceptive feedback via the exoskeleton hand to confirm whether they were able to properly imagine the hand action in the feedback period.

The threshold value of ERD strength was adapted and adjusted so that the participant could gradually increase the strength of ERD strength through neurofeed-
back training. All participants started the first block with a threshold value of 10%, indicating that the exoskeleton moved once the ERD strength exceeded 10%. Upon completion of the first block, the threshold value for the next block was adjusted according to the following rules: (1) the threshold value was increased by 10 pt (percent point) if the patient was able to operate the exoskeleton hand more than 3 times in the previous block; (2) threshold value was decreased by 10 pt if the patients failed to operate the exoskeleton when the threshold was set at 10%, the threshold value was maintained at 10%. In all remaining cases, the same threshold value as in the preceding block was employed.

3. Preliminary clinical trial of DMB-based rehabilitation

3.1 Participants
Nine hospitalized stroke patients in the subacute stage of recovery with hand paralysis (left paralysis: 4, right paralysis: 5, average age: 64.3 ± 3.1 years) participated in this study (Table 1). Participants were fully informed about the purpose of this study prior to participation. The study was approved by the Institutional Review Board of each participating institution, and written informed consent was obtained from all participants.

3.2 DMB-based Neurofeedback training
All study participants received DMB-based or control interventions continuously for 14 days each, alternately in a random and counterbalanced order (Fig. 4), on top of their conventional rehabilitation. Participants were confirmed to have stable vital signs (body temperature, blood pressure, and heart rate) every morning before the intervention. A therapist monitored the participants during the whole intervention session, to detect potential neurological problems considered common in the subacute stage of recovery, such as seizures [13], although these problems did not occur in the current study.

During the period of DMB-based intervention, the participants were trained using the DMB prior to their daily hour of physiotherapy. During the period of control intervention, participants performed the same AOMI training prior to their daily physiotherapy, in the same manner as the DMB-based intervention, but the exoskeleton provided hand movements for all hand action movies regardless of their ERD strength. Participants conducted five training blocks (25 trials) per day. For each intervention, the AOMI-related ERD strength of the participant was evaluated three times during the study: before starting the intervention (‘Pre’ in Fig. 4), at the end of first 14 days of DMB-based/control intervention (‘Middle’ in Fig. 4), and at the end of both interventions (‘Post’ in Fig. 4). All participants successfully generated ERD responses while observing the hand action movie during DMB-based intervention, starting from the first day of the intervention. We also evaluated the spasticity [mean modified Ashworth scale (MAS) scores of all finger joints] and function [Fugl-Meyer assessment (FMA); total score of the affected hand] before and after each intervention period. In this paper, we mainly report the ERD response results. Details for other clinical outcomes are presented elsewhere [14].

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical characteristics of participants.</th>
</tr>
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<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>64.3 ± 9.7</td>
</tr>
<tr>
<td>Time from onset, days, mean ± SD</td>
<td>104 ± 24</td>
</tr>
<tr>
<td>Sensory function evaluated by stroke impairment assessment set (SIAS), 0/1/2</td>
<td>2/4/3</td>
</tr>
<tr>
<td>Brunnstrom recovery stage, II/III/IV</td>
<td>2/2/5</td>
</tr>
<tr>
<td>Gender, men/women</td>
<td>6/3</td>
</tr>
<tr>
<td>Type of stroke, ischemic/hemorrhagic</td>
<td>2/7</td>
</tr>
<tr>
<td>Paretic side, right/left</td>
<td>5/4</td>
</tr>
<tr>
<td>Lesion, C/S/CS</td>
<td>1/8/0</td>
</tr>
<tr>
<td>Higher cognitive dysfunction, +/− (unilateral spatial neglect, attention and/or executive function disorder, aphasia, apraxia, etc.)</td>
<td>8/1</td>
</tr>
</tbody>
</table>

SD: standard deviation; C: cortical; S: subcortical; CS: cortical and subcortical

Fig. 4 Experimental design. DMB-based and control interventions were alternated every 14 days.
3.3 Evaluation data measurement
During measurement of evaluation data, participants were encouraged to imagine a kinesthetic hand movement while watching the hand action movie, as in the DMB-based/control intervention. Similar to the DMB-based/control intervention, participants placed their paralyzed hands on the back of the tablet and watched the movie five times. Regardless of the ERD response, this measurement did not provide feedback.

Mean ERD strength was determined offline by the following analysis. First, trials with EEG amplitude exceeding ± 100 μV were excluded from analysis, as they were likely to be contaminated by motion or blink artifacts. The remaining EEG data were subjected to time frequency analysis using the Morlet mother wavelet, and the ERD strength was calculated for each trial according to equation (1). The mu band power during rest period (μrest) was defined as the mean power of mu-band activity 1 s prior to the ball appearing on the screen. The mu band power during task period (μtask) was defined as the mean power spectrum during the 1-s interval within the first 2 s time window starting from the appearance of the ball on the screen, in which the lowest spectral intensity of the mu band was obtained. The adaptive time window for calculation of μtask was used to determine the maximum ERD strength for each individual only in offline analysis, as the required calculation time is too long to provide online feedback during the intervention.

3.4 Statistics
Statistical analysis was performed using EEG data obtained from nine patients. However, the data of post evaluation from two participants each in DMB-based and control interventions were excluded, due to technical problems during EEG measurement or large artifacts observed throughout the evaluation sessions. For both DMB-based and control interventions, the changes in ERD strength, MAS, and FMA at the post-intervention evaluation relative to the pre-intervention evaluation (ΔERD, ΔMAS, and ΔFMA) were analyzed using the Wilcoxon signed-rank test. We considered P < 0.05 as statistically significant.

4. Results
Throughout the two interventions, the participants received proprioceptive feedback 350 and 122.3 ± 12.7 times in total during the control and DMB-based interventions, respectively. Figures 5 and 6 show the results comparing the mean ΔERD in DMB-based and control interventions. The median increase in ERD strength of the affected side after DMB-based interventions was 22.9%, while no improvement was observed after control interventions (−12.5%). There was a strong tendency of increase in ΔERD on the affected side, showing the superior effect of the DMB-based intervention over the control intervention in facilitating MI-related motor cortical activity in stroke patients with paralysis (P < 0.08). However, the median ΔERD on the unaffected side after control and DMB-based interventions were 0.85 and −4.55%, respectively, with no significant difference (P = 0.89). Finger joint spasticity showed significant improvement after DMB intervention, while no change was observed after control intervention (median finger extension ΔMAS = −0.4 vs. 2.0 (DMB vs. control), P = 0.02; median ΔFMA = 1 vs. 0, P = 0.75).

5. Discussion
We propose a novel neurorehabilitation system for stroke patients with hand paralysis, using action observation and proprioceptive feedback to facilitate reorganization of the affected motor cortical activity. Fourteen days of continuous DMB-based intervention resulted in a strong tendency of increase in ERD strength on the affected side of the patients in the subacute stage of stroke recovery, while the ERD strength on the unaffected side was unchanged. These results suggest the promotion of remaining motor neurons on the affected hemisphere and the suppression of the hyperactivity of the unaffected hemi-
sphere, which is considered to be an ideal reorganization of the motor pathway, leading to better prognosis [4]. In fact, the DMB-based intervention showed superior effect in reducing finger joint spasticity compared to the control intervention. Conversely, the same duration of control intervention showed less effect on ERD strength changes, especially on the affected side, even though the number of proprioceptive feedbacks upon MI was larger than in the DMB-based intervention. This result suggests that the neurofeedback accurately reflects the ERD strength of the participants. The mere movement of the hand not linking to brain activities cannot play a significant role in inducing neural plasticity in the affected motor area.

ERD is considered to be an active state of the motor cortex [15]. Although the restoration of activity in the affected motor cortex has been reported to be a good predictor of functional recovery in stroke patients [16], these patients tend to have lower ERD strength in the affected motor cortex [17]. Our proposed DMB-based rehabilitation may help stroke patients regain ERD strength, and facilitate the activity of the affected motor cortex for improved functional recovery. Concurrent improvement in MAS score also support the notion that the unwanted activity of motor neurons causing spasticity could be suppressed by DMB-based rehabilitation.

Our results also showed the usefulness of neurofeedback training as an early intervention for stroke patients in the subacute stage of recovery. Although outcomes from studies with different patient profiles and neurofeedback protocols should not be directly compared, our approach apparently showed better functional outcomes, especially in reducing muscle spasticity, compared to previous studies performed in chronic stage patients [4, 5]. Future research with a larger number of patients is needed to confirm the significance of DMB rehabilitation in accelerating motor functional reorganization during the subacute stage of recovery.

6. Conclusion

In stroke patients in the subacute stage of recovery, ERD-BMI rehabilitation with proprioceptive neurofeedback demonstrated a superior effect in promoting motor-imagery related motor cortical activity in the affected hemisphere, compared to passive hand movement therapy not incorporating motor cortical activity. As DMB can be administered simultaneously to multiple patients with simple preparations (wearing of EEG caps and exoskeletal gloves), it can provide patients with additional rehabilitation opportunities and promote their functional recovery. Further studies with a larger patient population is required to examine the longitudinal impact of DMB on functional recovery of stroke patients.

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References


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