Artificial Organs

Brain-Computer Interfaces With Multi-Sensory Feedback for Stroke Rehabilitation: A Case Study

*†Danut C. Irimia, ‡Woosang Cho, ‡Rupert Ortner, *Brendan Z. Allison, §¶Bogdan E. Ignat, *Guenter Edlinger, and *‡Christoph Guger

**Guger Technologies OG, Graz, Austria; †"Gheorghe Asachi" Technical University of Iasi, Iasi, Romania; ‡g.tec medical engineering GmbH, Schiedlberg, Austria; §"Grigore T. Popa" Medicine and Pharmacy University of Iasi; and ¶Rehabilitation Hospital of Iasi, Iasi, Romania*

Abstract: Conventional therapies do not provide paralyzed patients with closed-loop sensorimotor integration for motor rehabilitation. This work presents the recoveriX system, a hardware and software platform that combines a motor imagery (MI)-based brain-computer interface (BCI), functional electrical stimulation (FES), and visual feedback technologies for a complete sensorimotor closed-loop therapy system for poststroke rehabilitation. The proposed system was tested on two chronic stroke patients in a clinical environment. The patients were instructed to imagine the movement of either the left or right hand in random order. During these two MI tasks, two types of feedback were provided: a bar extending to the left or right side of a monitor as visual feedback and passive hand opening stimulated from FES as proprioceptive feedback. Both types of feedback relied on the BCI classification result achieved using common spatial patterns and a linear discriminant analysis classifier. After 10 sessions of recoveriX training, one patient partially regained control of wrist extension in her paretic wrist and the other patient increased the range of middle finger movement by 1 cm. A controlled group study is planned with a new version of the recoveriX system, which will have several improvements. **Key Words:** Brain-computer interface—stroke rehabilitation functional electrical stimulation neurofeedback.

In conventional rehabilitation therapy, patients are often asked to try to move the paretic limb, or imagine its movement, while a functional electrical stimulator (FES), physiotherapist, or robotic device helps them perform the desired movement. In conventional therapy, the feedback is often provided when the users are not performing the required mental activity. There is no objective way to determine whether patients who cannot move are actively performing the desired motor imagery (MI) task and thus producing the concordant neural activation. Today, BCI technology can provide an objective tool for measuring MI, creating new possibilities for "closed-loop" feedback. Because the closed-loop feedback is linked with the desired mental activity, it is very important for as every feedback system made possible through MI-based BCI could significantly improve rehabilitation therapy outcomes.

This concurrent sensory feedback with motor intention is an important factor for motor recovery (1,2). Neural networks are strengthened when the presynaptic and postsynaptic neurons are both active. In conventional therapy, when patients receive feedback while they are not performing MI, these two neuronal populations are not simultaneously active. This dissociation between motor commands and sensory feedback may explain why the therapy does not significantly induce the reorganization of the patients' brains around their lesioned area. Nonsimultaneous, dissociated feedback cannot lead to Hebbian learning between two neuronal populations, which underlies the desired improvements from rehabilitation. Thus, conventional therapy may sometimes fail because it relies on open-loop feedback.

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Address correspondence and reprint requests to Woosang Cho, g.tec medical engineering GmbH, Sierningstrasse 14, 4521 Schiedlberg, Austria. E-mail: cho@gtec.at

To complete the feedback loop for paralyzed patients, our system uses visual feedback and FES-induced movements based on their MI (3–5). Research using FES in poststroke patient rehabilitation showed a statistically significant recovery of muscle strength after the therapy (6). FES has also been used for restoring hand grasp and release in people with tetraplegia, and standing and stepping in people with paraplegia (7).

We sought to assess whether a closed-loop BCI system with visual and FES feedback could improve motor function in two chronic stroke patients who did not benefit from conventional therapy. This study presents the measurement procedures and results after 10 BCI training sessions with the first two chronic stroke patients who agreed to participate in our study.

SUBJECTS AND METHODS

All recording and real-time analysis used recoveriX, which is a complete hardware and software platform that can record, analyze, and utilize electroencephalographic (EEG activity) in real-time. All real-time signal processing and classification methods in this article were implemented in recoveriX. Figure 1 shows the recoveriX system mounted on a patient and the electrode montage. The patients imagine or perform specific movements such as the wrist extension of their paretic limbs. Their corresponding brain activity is acquired by EEG electrodes, then sent to an amplifier. Both a horizontal bar for visual feedback and FES stimuialtion for proprioceptive feedback are provided to patients when the classification algorithm in recoveriX detects correct MI.

Subjects

Two stroke patients in the chronic stage participated in our study. They were both right handed and performed classical poststroke rehabilitation therapy until they joined the study. P1 (female) was 40 years old when the intervention began (5.5 years after stroke) and had severe paralysis in her left hand with no residual movement. She had received conventional therapy for 2 years and no significant functional improvement had been observed before her participation in this study. P2 (male) was 59 years old when intervention began (3.25 years after stroke) and his left arm remained paralyzed, being able to move the middle finger in a range of 0.5 cm. Before participating in our study, in addition to conventional rehabilitation therapy, he performed TMS and mirror rehabilitation therapies, but with no functional improvement. They both participated in 10 recoveriX training sessions at the Rehabilitation Hospital of Iasi, Romania. The study was approved by the Institutional Review Board of the of the Rehabilitation Hospital of Iasi, and both patients signed an informed consent before starting the study.

Stimuli and procedure

The patients were seated in a comfortable chair in front of a computer monitor that presented visual instruction and feedback (see Figs. 1 and 2) with FES pads placed over the forearm of the affected side. FES stimulation stimulation was provided through an 8-channel neurostimulator (MOTIONSTIM8, Krauth + Timmermann GmbH, Germany). For both patients, the first session was a training session, where the subjects were trained regarding the correct MI tasks, and then conducted two practice runs to get familiar with the experience of electrical stimulation and visual feedback.

During all subsequent sessions, after setting up the system, each patient first performed 4 runs to train BCI classifiers and then 2 runs to test onlinc BCI performance. One run contained 40 trials, each eight seconds, with a randomly chosen intertrial interval between 1 and 2 s. Each run required 6 min in total. Each imagination trial started with

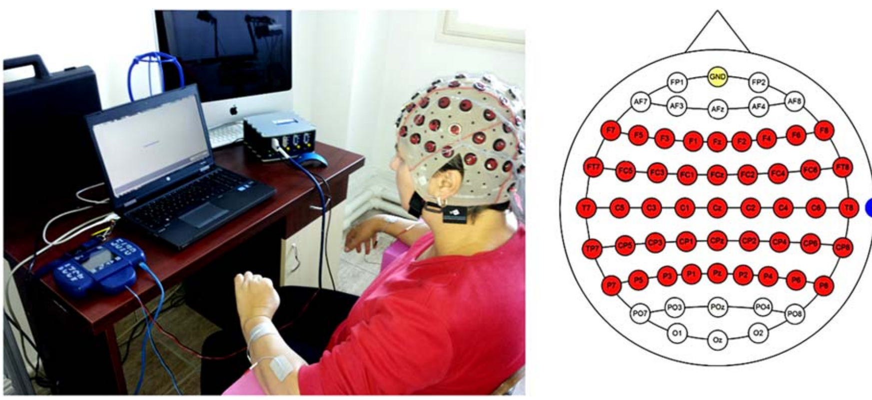

FIG. 1. RecoveriX system mounted on a patient (left) and the EEG electrode placement (right).

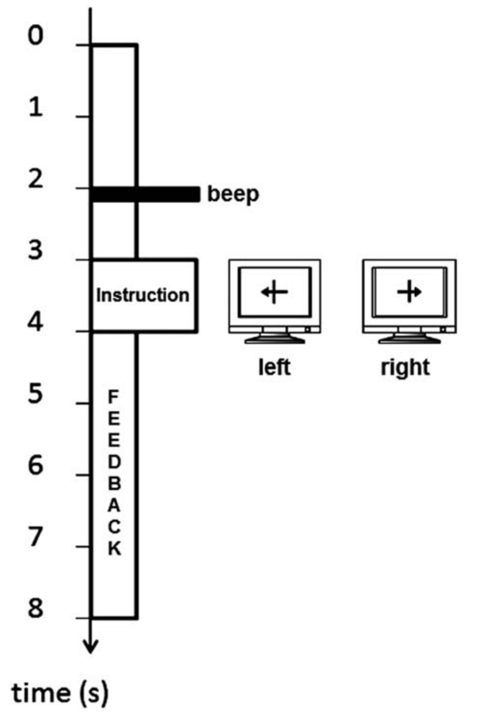

FIG. 2. Time course of a single trial. A fixation cross appears when the trial begins. A short beep is played after 2 s. One second later, a visual instruction is presented. The user receives online feedback based on MI from 4 s until the end of the trial (8 s).

the display of a cross in the center of the monitor. After 2 s, a beep informed the user about the upcoming instruction. The patients were instructed to start imagining the movement of either the left or right hand when an arrow pointing to the left or right side was presented as a visual instruction for 1 s. Both visual and proprioceptive feedback began 0.5 s after the visual instruction ended. A blue bar on the monitor extended to the left or right, indicating both the direction and magnitude of the MI as visual feedback. The FES was activated with a 50 Hz updating rate if the user imagined hand movement on the correct side. The muscle contraction by FES was sufficient enough to cause movement of the affected hand in both patients. The patients had to continue imagining the movement for 4 s after the arrow instruction was presented, after which the feedback and the trial ended. The inter-trial interval was 2 s.

Data acquisition and signal processing

We recorded patients' sensorimotor rhythm using 45 active EEG electrodes (g.LADYbird, g.tec medical engineering GmbH, Schiedlberg, Austria). The electrodes overlaid the sensorimotor area of cortex. Fpz was used as the ground electrode, and a reference electrode was placed on the right earlobe. Figure 3 shows the signal processing chain. EEG signals were transmitted to a biosignal amplifier (g.HIamp, g.tec medical engineering). They were first bandpass filtered (butterworth filter fourth order) between 8 and 30 Hz. Then, common spatial patterns (CSP) (8) were applied to transform the data to a new matrix with minimal variance of one class and maximal variance of the other class. Each class reflects the MI of the according hand versus the motion of the other one. Given N channels of EEG for each left and right trial, the CSP method provides an $N \times N$ projection matrix. This matrix is a set of subject-dependent spatial patterns, which reflect the specific activation of cortical areas during hand MI. With the projection matrix W, the decomposition of a trial X is described by:

$$Z = WX \tag{1}$$

This transformation projects the variance of X onto the rows of Z and results in N new time series. The variance for one class is largest in the first row of Z and decreases in each subsequent row due to the transformation matrix, W. Only first and last two rows ($p = 4$) of W are used to apply the spatial patterns, resulting in four new feature channels: CSP_n, where n represents the number of the row. Next, the

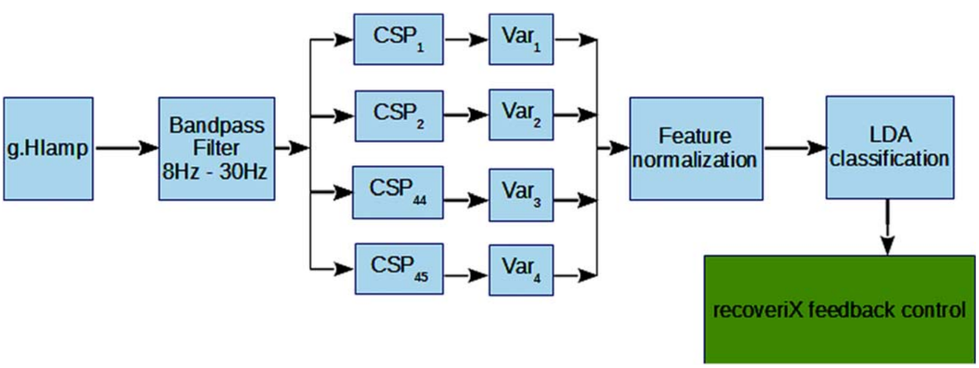

FIG. 3. Schematic view of the signal processing workflow. After acquisition, data is bandpass filtered. Four spatial filters are applied, resulting in four feature vectors. The variance is calculated and normalized. Finally, the LDA classifies the features to drive the recoveriX feedback control.

variance (VARp) is calculated using a sliding window of 384 samples, which is 1.5 s. For each new sample the sliding window is shifted by one sample to receive four new variance values. These values are normalized and log transformed according to:

$$f_p = \log_{10}\left(\frac{\mathrm{VAR}_p}{\sum_{p=1}^{4}\mathrm{VAR}_p}\right) \quad (2)$$

where f_p ($p = 1{:}4$) are the normalized feature vectors and VAR_p is the variance of p-th spatially filtered signal. These four features are classified with a linear discriminant analysis (LDA) classifier. This LDA classification result drives the BCI feedback block. The classifier used in this article sought to classify left versus right hand MI, but this general approach is widely used.

Training data recorded during the first 4 runs of each session, five sets of spatial filters and classifiers, were calculated from 2-s time windows, shifted in time with a 0.5 Hamming window based on data from the time interval from 4 to 8 s in each trial. The classifier with the highest 10-fold cross-validated accuracy was chosen to provide visual and FES feedback while recording runs 5 and 6. These last 2 runs were used to calculate the online accuracy of the chosen classifier for the current session. To provide feedback during the first 4 runs, we used the spatial filters and classifier calculated in the previous session.

RESULTS

Figure 4 presents the online BCI classification accuracy across 10 sessions for both P1 and P2. The patients reported that they actively participated in MI tasks as instructed. For patient P1, the accuracy in the first two sessions is slightly over the chance level of 50%, and the accuracy of the remaining eight sessions improved substantially. The accuracy dropped to 82.5% in session number 8, which the patient believed resulted from lack of sleep during the previous night. Patient P2 started with a slightly higher accuracy and maintained above 90% from session 4 to the last session. Figure 5 shows results within trials.

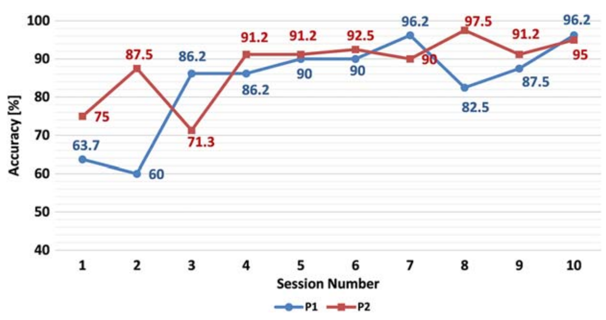

FIG. 4. BCI online classification accuracy across 10 recoveriX training sessions.

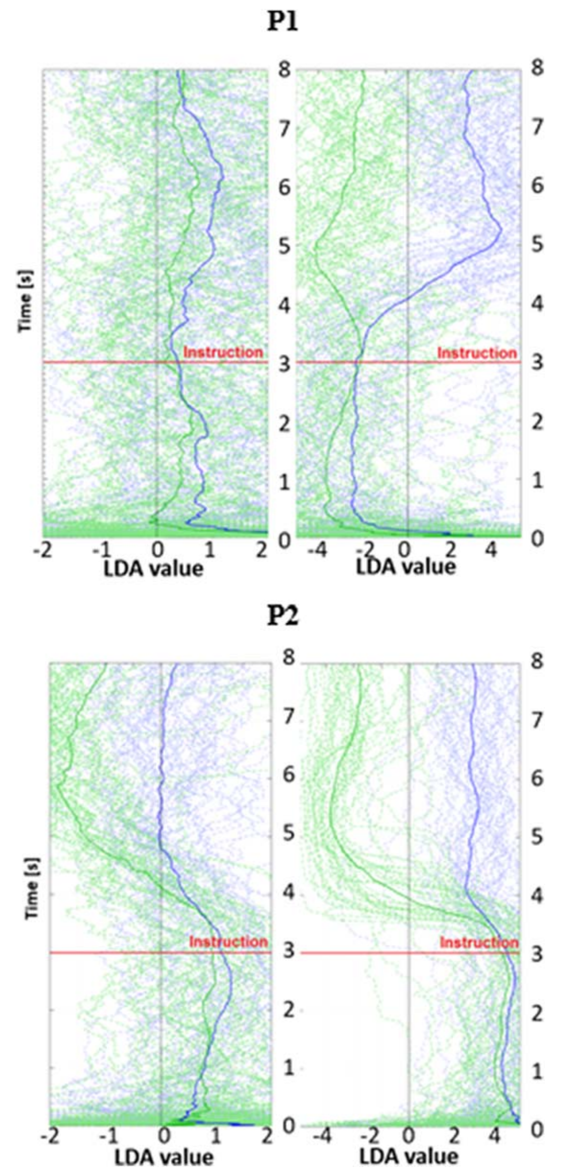

FIG. 5. Linear discriminant analysis (LDA) values of first and last training sessions for both patients are presented in the left and right panels, respectively. The dotted blue lines indicate the LDA values of right motor imagery and the solid blue line shows the average of them. The dotted green lines indicate the LDA values of left motor imagery and the solid green line shows the average of them. Left and right trials were expected to have positive and negative LDA values, respectively. The classification accuracies were calculated with LDA values in the feedback period (4 ∼ 8 s).

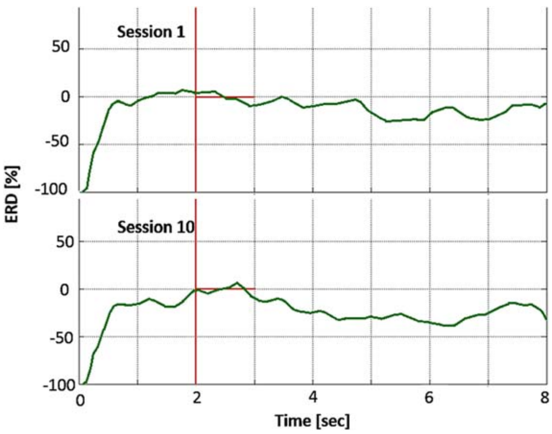

FIG. 6. Event-related desynchronization (ERD) plots of session the first and last (10th) sessions for P1. The plots were produced by g.BSanalyze (g.tec medical engineering GmbH, Schiedlberg, Austria). This averaged ERD plot was based on 8 ~ 12 Hz frequency bands of channel C4, which is located on the lesioned hemisphere. The red vertical line indicates the beep at 2 s, and the red horizontal line reflects the 1-s delay until instructions were presented.

Event-related desynchronization plots also showed that the patients were able to perform the MI tasks. Figure 6 shows two examples of the first and last sessions for P1. ERD is observed in both sessions and statistical comparison between two ERD plots is necessary in the future. However, it is clear that recoveriX training sessions were based on MI tasks. Moreover, Fig. 7 presents the 10-fold cross-validated accuracy plots for sessions 1 and 10, calculated on the classifier training data. The left hand MI data are represented with a yellow line, the right hand MI with a blue line, and the overall accuracy with a green line. These plots also show that P1 started with an overall accuracy of about 60%, accuracy which went above 95% in the 10th session. Patient P2 started with a good accuracy, above 90% even from the first session and it went up to about 95% in the last session.

After 10 training sessions, both patients showed improved motor function. P1, who had no finger and wrist movement, was able to voluntarily relax and extend the wrist of her paretic side. P2 started voluntarily moving all the fingers of the paretic arm, the middle finger movement range increasing from 0.5 cm to approximately 1.5 cm. It was not possible to practice the Nine-Hole Peg Test and measure the electromyogram (EMG) due to complete paralysis of her left hand before the session started, and alternative behavioral measurements are not available in this case study.

CONCLUSIONS

We showed that two chronic stroke patients who did not benefit from conventional therapy could improve motor function and brain-computer

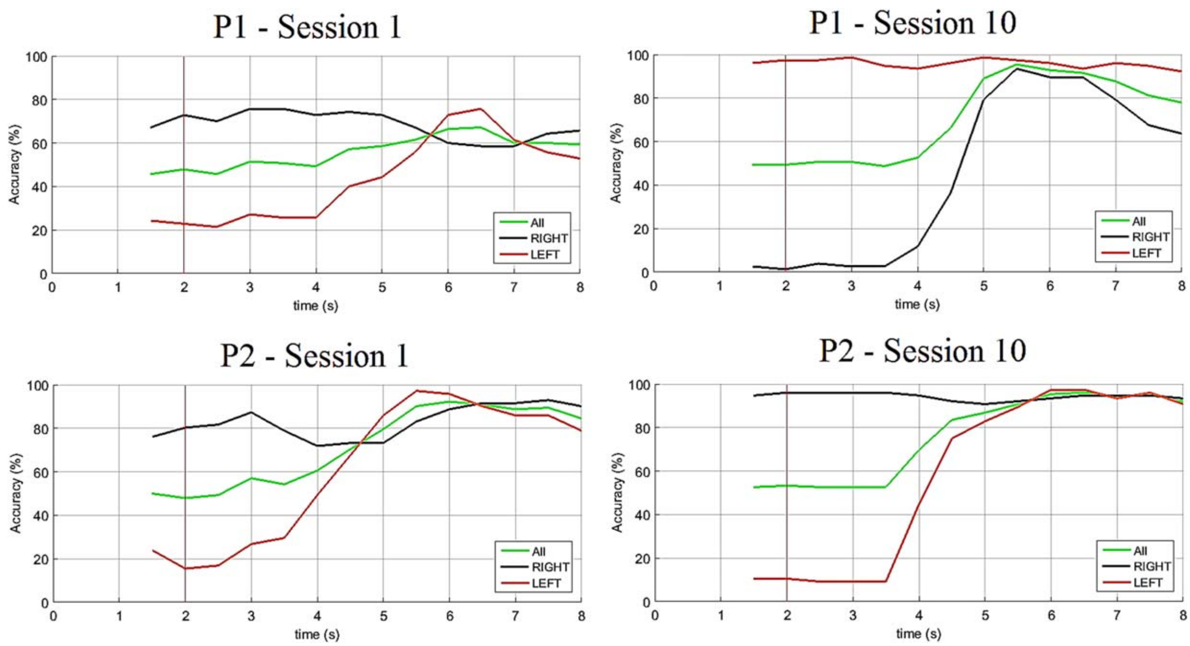

FIG. 7. The 10-fold cross-validated results from the training data of session 1 and session 10 for both patients.

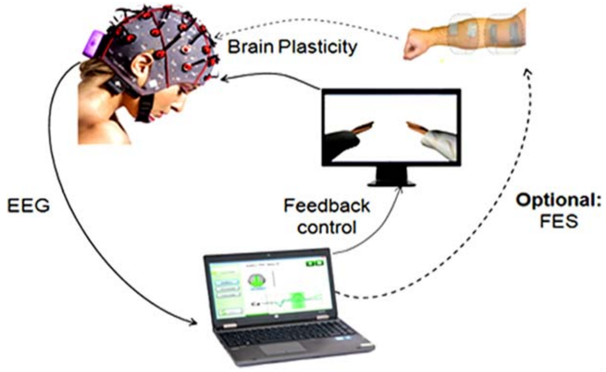

FIG. 8. Schematic illustration of the new recoveriX system to be used in future research.

interface accuracy using a motor imagery-based BCI for rehabilitation. Both patients showed some motor improvement. The higher BCI accuracy and LDA values of later sessions implies that the patients learned to use the BCI effectively. One of the main reasons might be the motivation of the patients. Their enthusiasm to regain voluntary control over their paretic hands motivated them to be very engaged while working with recoveriX.

These initial results extend prior work that has also shown that BCIs using MI can be effective tools for motor rehabilitation (1,2,9–13). However, nearly all prior results focus on patients in the acute or subacute stages, whose conventional therapy improvements may be hard to separate from BCI improvements. The current results suggest that this approach may even benefit patients in the chronic stage who showed no improvement during conventional therapy. As this is only a case study, additional research is needed to explore this suggestion and others presented here.

We do plan to conduct this research. The recoveriX system and current training paradigm will be updated and studied with a larger patient population in comparison with a control group for meaningful statistical outcomes. A new FES device will replace the current FES device for an easier interface with the software. The bar feedback will be replaced with a three-dimensional forearm using virtual reality for a more immersive environment. We will reduce the number of channels to reduce cost and setup time. EEG will be wirelessly transmitted using a much smaller amplifier via g.Nautilus, as seen in Fig. 8. We will also introduce improved classifier software and new paradigms for training different limb movements.

Overall, the current initial results further support mounting evidence that BCI-based therapy can yield better results than conventional therapy, for different types of stroke patients. Future work might incorporate haptic systems, EMG and other multimodal signals, noninvasive brain stimulation, and/or devices to facilitate lower limb rehabilitation.

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Author Contributions: DCI: data collection and analysis; WC: data analysis and manuscript preparation; RO: software development and data analysis; BZA: manuscript preparation and editing; BEI: ethical protocol design and supervision of the data collection procedure; GE: system development; CG: study design.

REFERENCES

1. Silvoni S, Ramos-Murguialday A, Cavinato M, et al. Brain-computer interface in stroke: a review of progress. *Clin EEG Neurosci* 2011;42:245–52.
2. Ortner R, Irimia D-C, Scharinger J, Guger C. A motor imagery based brain-computer interface for stroke rehabilitation. *Stud Health Technol Inform* 2012;181:319–23.
3. Guger C, Edlinger G, Harkam W, Niedermayer I, Pfurtscheller G. How many people are able to operate an EEG-based brain-computer interface (BCI)? *IEEE Trans Neural Syst Rehabil Eng* 2003;11:145–7.
4. Wolpaw J, Wolpaw E-W. *Brain–Computer Interfaces: Principles and Practice*. Oxford, United Kingdom: Oxford University Press, 2012.
5. Brunner C, Birbaumer N, Blankertz B, et al. BNCI Horizon 2020: towards a roadmap for the BCI community. *BCI* 2015;2621:1–10.
6. Glanz M, Klawansky S, Stason W, Berkey C, Chalmers TC. Functional electrostimulation in poststroke rehabilitation: a meta-analysis of the randomized controlled trials. *Arch Phys Med Rehabil* 1996;77:549–53.
7. Triolo RJ, Bogie K. Lower extremity applications of functional neuromuscular stimulation after spinal cord injury. *Top Spinal Cord Inj Rehabil* 1999;5:44–65.
8. Blankertz B, Tomioka R, Lemm S, et al. Optimizing spatial filters for robust EEG single-trial analysis. *IEEE Signal Process Mag* 2008;25:41–56.
9. Xu R, Jiang N, Mrachacz-Kersting N, et al. A closed-loop brain-computer interface triggering an active ankle-foot orthosis for inducing cortical neural plasticity. *IEEE Trans Biomed Eng* 2014;61:2092–101.
10. Belda-Lois J-M, Mena-del Horno S, Bermejo-Bosch I, et al. Rehabilitation of gait after stroke: a review towards a top-down approach. *J Neuroeng Rehabil* 2011;8:66.
11. Ang KK, Guan C, Phua KS, et al. Brain-computer interface-based robotic end effector system for wrist and hand rehabilitation: results of a three-armed randomized controlled trial for chronic stroke. *Front Neuroeng* 2014;7:30.
12. Ortner R, Ram D, Kollreider A, Pitsch H, Wojtowicz J, Edlinger G. Human-computer confluence for rehabilitation purposes after stroke. In *Lecture Notes in Comput Science*

(including Subseries *Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics*) 2013;8022 LNCS PART 2;74–82., Springer Link
13. Mattia D, Pichiorri F, Molinari M, Rupp R. Part II: devices, applications and users brain computer interface for hand motor function restoration and rehabilitation. In: Allison ZB, Dunne S, Leeb R, Del J, Millán R, Nijholt A, eds. *Towards Practical Brain-Computer Interfaces: Bridging the Gap from Research to Real-World Applications*. Berlin, Heidelberg: Springer Berlin Heidelberg, 2013;131–53.