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Clinical feasibility of brain-computer interface based on steady-state visual evoked potential in patients with locked-in syndrome: Case studies

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Abstract

Although the feasibility of brain-computer interface (BCI) systems based on steady-state visual evoked potential (SSVEP) has been extensively investigated, only a few studies have evaluated its clinical feasibility in patients with locked-in syndrome (LIS), who are the main targets of BCI technology. The main objective of this case report was to share our experiences of SSVEP-based BCI experiments involving five patients with LIS, thereby providing researchers with useful information that can potentially help them to design BCI experiments for patients with LIS. In our experiments, a four-class online SSVEP-based BCI system was implemented and applied to four of five patients repeatedly on multiple days to investigate its test-retest reliability. In the last experiments with two of the four patients, the practical usability of our BCI system was tested using a questionnaire survey. All five patients showed clear and distinct SSVEP responses at all four fundamental stimulation frequencies (6, 6.66, 7.5, 10 Hz), and responses at harmonic frequencies were also observed in three patients. Mean classification accuracy was 76.99% (chance level = 25%). The test-retest reliability experiments demonstrated stable performance of our BCI system over different days even when the initial experimental settings (e.g., electrode configuration, fixation time, visual angle) used in the first experiment were used without significant modifications. Our results suggest that SSVEP-based BCI paradigms might be successfully used to implement clinically feasible BCI systems for severely paralyzed patients.

Descriptors: Brain-computer interface (BCI), Steady-state visual evoked potential (SSVEP), EEG, Clinical feasibility, Locked-in syndrome (LIS), Amyotrophic lateral sclerosis (ALS)

Brain-computer interface (BCI) is a nonmuscular communication method that uses neuronal activity as the input source for controlling external devices (Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002) such as mental spellers (Hwang et al., 2012; Treder, Schmidt, & Blankertz, 2011; Yin et al., 2014), wheelchairs (Diez et al., 2013; Rebsamen et al., 2010), and robotic arms (Palankar et al., 2009; Sakurada, Kawase, Takano, Komatsu, & Kansaku, 2013). BCI has been intensively studied over the last several decades to provide a new method of communication for patients with locked-in syndrome (LIS), which is generally characterized by quadriplegia, anarthria, and preserved consciousness. Among various brain imaging modalities used for BCI, EEG has been most frequently employed because of its portability, noninvasiveness, and reasonable cost (Hwang, Kim, Choi, & Im, 2013).

The feasibility of EEG-based BCI systems has been proven in numerous studies, but most of the early BCI systems were tested with able-bodied subjects, which made it hard to evaluate the clinical feasibility of EEG-based BCI systems. Recently, the number of EEG-based BCI studies performed with patients with LIS has gradually increased, and some studies showed promising results in terms of usability (Kübler & Birbaumer, 2008). For example, a BCI research group at the University of Tübingen applied a spelling device to patients suffering from amyotrophic lateral sclerosis (ALS) and showed that the patients could successfully deliver messages using their brain signals (Birbaumer et al., 1999). Miner, McFarland, and Wolpaw (1998) introduced an EEG-based cursor control system that a patient with ALS could use to answer yes/no binary questions with an acceptable accuracy. Most clinical EEG-based BCI studies have primarily used three characteristic activities: slow cortical potential (SCP), ERP, and sensorimotor rhythm (SMR; Kübler & Birbaumer, 2008).

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Table 1. *Clinical Characteristics of ALS Patients*

		ALS1	ALS2	ALS3	ALS4	ALS5
Gender		Male	Male	Male	Female	Male
Age		45	57	53	46	57
Time since diagnosis		12 years	7 years	10 years	5 years	20 years
Artificial ventilation		Yes	Yes	Yes	Yes	Yes
Limb muscle control[a]		Absent	Very weak (right leg)	Absent	Absent	Absent
Eye movement[a]	Horizontal	Weak	Weak	Weak	Weak	Moderate
	Vertical	Very weak	Weak	Weak	Weak	Moderate
Eyelid muscle control		Very weak	Weak	Weak	Very weak	Moderate
Other muscle control[a]		Not available	Facial muscle (very weak)	Facial muscle (very weak)	Facial muscle (very weak)	Facial muscle (very weak)
Communication mode		Eye movement[b]	Eye movement[b]	Eye movement[b]	Eye movement[b]	Eye movement[c]

[a]The degree of movement is divided into five stages based on a healthy individual as follows: normal/moderate/weak/very weak/absent.
[b]Characters on an alphabet board are pointed out by a caregiver's finger one by one, and the patient makes a certain eye movement when the character the patient wants to select is pointed out.
[c]Each vowel and consonant are spoken by a caregiver, and the patient makes a certain eye movement when the character the patient wants to select is spoken.

Recently, steady-state visual evoked potential (SSVEP), a periodic brain response to a periodically oscillating visual stimulus, has been widely applied to the field of EEG-based BCI because of its relatively high communication rate compared with other paradigms. Although many SSVEP-based BCI systems have been successfully applied to healthy individuals (Liu, Chen, Ai, & Xie, 2014), they have rarely been tested with the target patients. To our knowledge, it was not until 2009 that an SSVEP-based BCI system was first applied to potential target individuals suffering from Duchenne muscular dystrophy (Parini, Maggi, Turconi, & Andreoni, 2009), followed by increased numbers of patient studies in the last 2 years (Combaz et al., 2013; Daly et al., 2013; Diez et al., 2013; Lesenfants et al., 2014; Lim, Hwang, Han, Jung, & Im, 2013; Sakurada et al., 2013). These clinical BCI studies demonstrated the potential of the SSVEP paradigms in implementing a clinically available BCI system.

However, previous clinical studies did not completely demonstrate the clinical feasibility of SSVEP-based BCI systems for patients with LIS because most of the previous clinical results were obtained from experiments with patients who moderately retained several motor functions such as arm, leg, head, or finger (Combaz et al., 2013; Daly et al., 2013; Diez et al., 2013; Sakurada et al., 2013). To the best of our knowledge, only two BCI studies have investigated the feasibility of using the SSVEP paradigm for patients with LIS (Lim et al., 2013; Lesenfants et al., 2014). Thus, further clinical BCI studies with patients with LIS are required to demonstrate the feasibility of the SSVEP paradigm in real clinical applications.

In this case report, we aimed to provide useful information on the design and implementation of SSVEP-based BCI experiments with patients with LIS as well as to evaluate the clinical feasibility of the SSVEP-based BCI paradigm in patients with LIS. We implemented a four-class online SSVEP-based BCI system and conducted online experiments with five patients with severe ALS. In the online experiments, the patients were asked to focus on one of four visual stimuli, reversing at different frequencies, when their intentions were classified in real time. To further investigate the test-retest reliability of the SSVEP-based BCI system, the online experiment was conducted repeatedly on different days with four patients. Also, the practical usability of the implemented BCI system was tested with two of the four patients on the last visit, when the patients used our SSVEP-based BCI system to answer questions with four choices of answer.

Method

ALS Patients

Five patients with ALS took part in this study (hereafter referred to as ALS1, ALS2, ALS3, ALS4, ALS5). ALS1 had participated in our previous BCI study using the SSVEP paradigm (Lim et al., 2013), but the others were naïve with respect to BCIs. They were all severely paralyzed and bedridden with mechanical ventilation. Their motor functions were almost completely limited to the eyes (eyeball and eyelid) with different degrees of freedom of movement. Movements of facial muscles other than the eyes were virtually zero. The patients were alert and had normal sound cognition. They communicated with their family through slight eye blinking because their other face and tongue muscles were nonfunctional. Detailed descriptions of the ALS patients are presented in Table 1. Before the experiment, all experimental procedures were explained to the patients and their families, and informed consent was obtained from their families under the consent of each patient. A monetary reimbursement was provided for participation after each experiment. This clinical study was approved by the Institutional Review Board (IRB) of the Korea National Rehabilitation Center (for ALS1, ALS4, ALS5) and by the IRB of Hanyang University Hospital (for ALS2, ALS3), and all experiments were conducted according to the Declaration of Helsinki in each patient's home.

Visual Stimulation

A four-class SSVEP BCI system was tested in which four visual stimuli that reversed at different frequencies were presented on a monitor. Since the refresh rate of the monitor was 60 Hz, its divisors were used as stimulation frequencies to precisely elicit corresponding SSVEPs, such as 30, 20, 15, 12, 10, 8.57, 7.5, 6.66, 6, and 5 Hz. In addition, since visual stimuli with lower frequencies including alpha band (8–13 Hz) show relatively higher signal-to-noise ratio (SNR) of SSVEPs than those with higher frequencies (Wang, Wang, Gao, Hong, & Gao, 2006), low-frequency stimuli generally result in higher BCI performance than high-frequency ones (Volosyak, Valbuena, Luth, Malechka, & Graser, 2011). Considering these factors, we empirically selected the four stimulation frequencies of 6, 6.66, 7.5, and 10 Hz, and they were assigned to each of four visual stimuli. A conventional black and white checkerboard pattern was used as a visual stimulus for ALS1, ALS2,

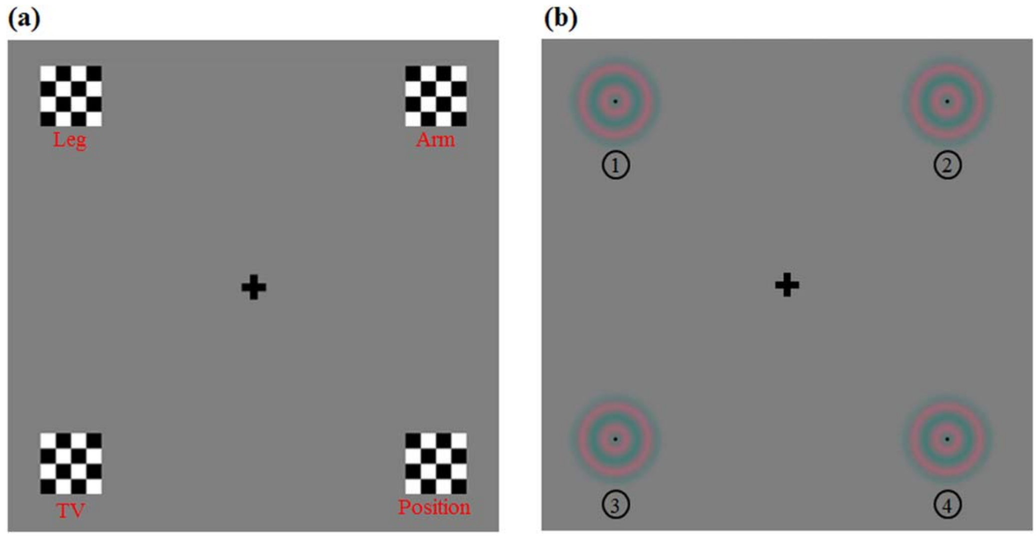

Figure 1. Visual stimuli presented to (a) ALS1, ALS2, ALS3, and ALS5, and (b) ALS4. The four stimulation frequencies of 6, 6.6, 7.5, and 10 Hz are assigned to the top-right, top-left, bottom-right, and bottom-left images, respectively. For ALS5, four checkerboard pattern images shown in (a) were used with the four numbers (1–4) shown in (b), instead of the four words (Leg, Arm, TV, and Position).

ALS3, and ALS5, but a chromatic pattern was used for ALS4 because the patient felt extreme visual fatigue after the initial experiment with a checkerboard pattern. It is known that a chromatic pattern stimulus can be a good alternative to checkerboard patterns in eliciting visual evoked potential (Sui Man, Zhiguo, Yeung Sam, Zhendong, & Chunqi, 2011). Figure 1a,b illustrates the configurations of visual stimuli when the checkerboard and chromatic pattern images were used (see Figure 2 and 3 for the real experimental setup of visual stimuli and examples of SSVEP responses elicited by them, respectively). For the presentation of visual stimuli, we used different-sized computer monitors already installed in each patient's home, and the distance between the monitor and a patient also varied depending on the experimental environment. Therefore, visual angles were slightly different among patients and experimental sessions (see Figure 4 for information on the visual angle of each experiment for each patient).

Experimental Paradigm

Four visual stimuli were consistently reversing at their own frequencies during the entire experiment. The patients were asked to focus on one of the four visual stimuli during a predefined time period (e.g., 6 s) as soon as they were given a cue signal (a short beep sound). Before starting each trial, short verbal instructions were given by an experimenter to the patients to designate which visual stimulus the patients should focus on. Real-time feedback was provided immediately after each trial using computerized voices. In the case of ALS1, ALS2, and ALS3, the real-time feedback was composed

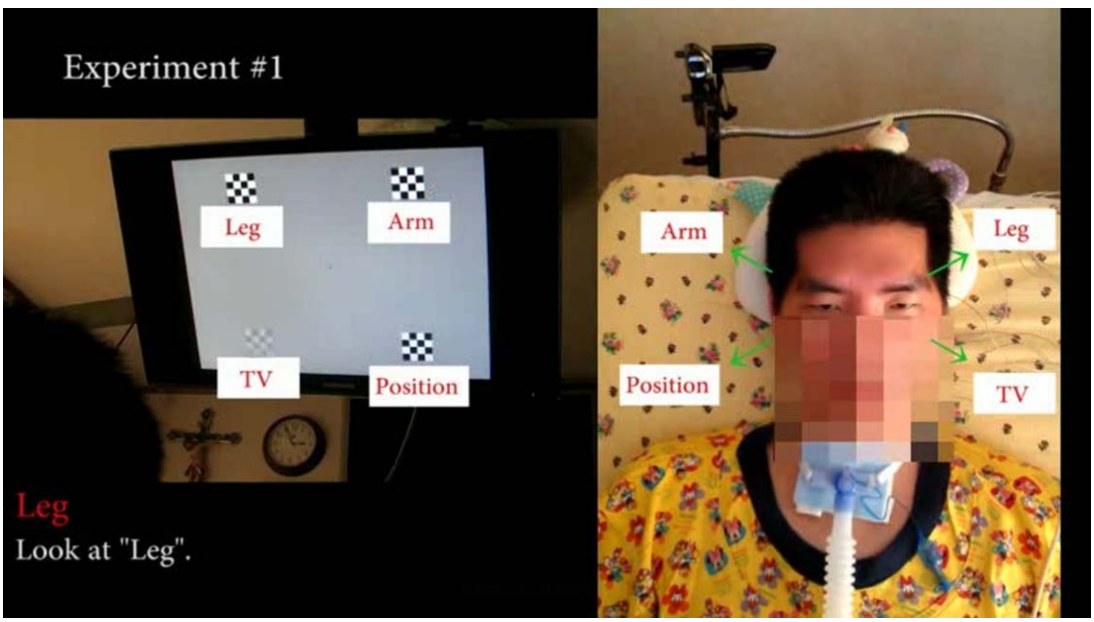

Figure 2. Screen shots of visual stimuli (left) and the patient ALS1 (right) during the online experiment. ALS1 is focusing on the top-left stimulus (Leg) according to the instruction of an experimenter.

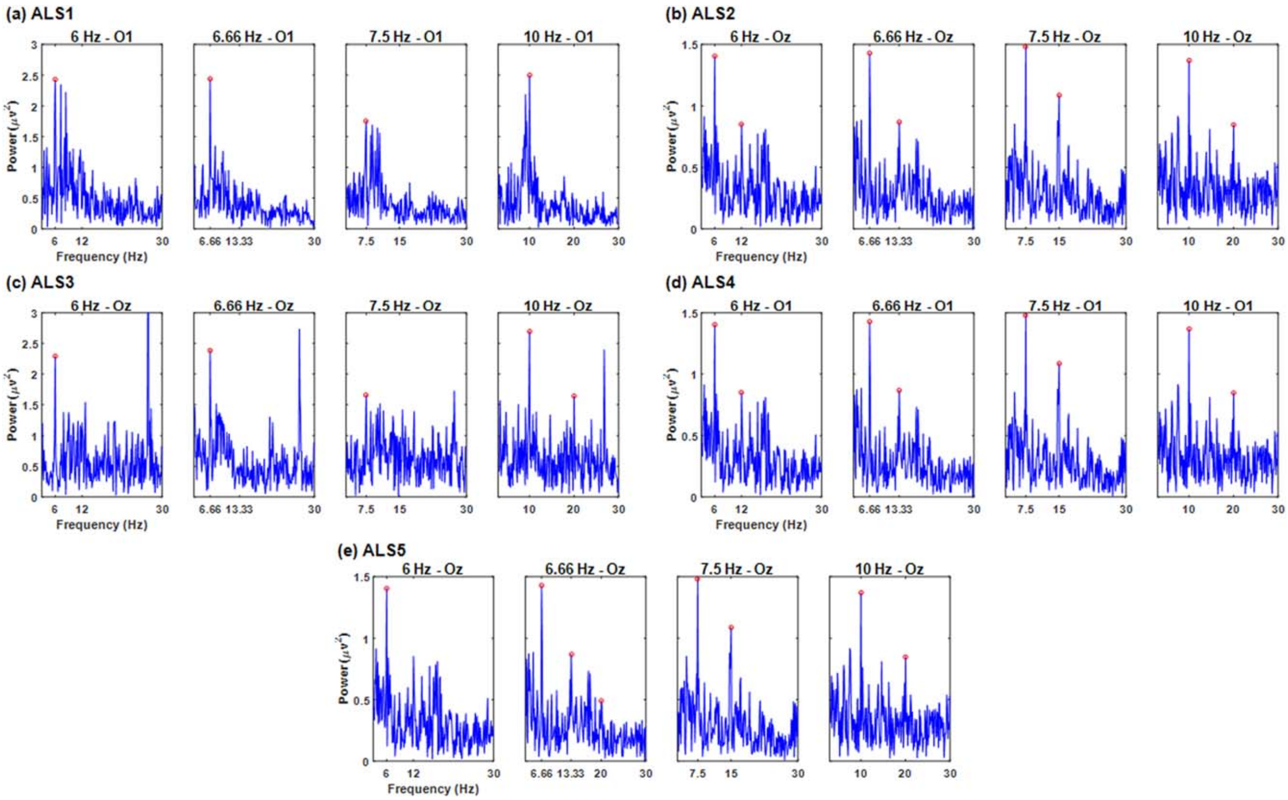

Figure 3. SSVEP responses to four visual stimuli modulated with 6, 6.66, 7.5, and 10 Hz, respectively, for (a) ALS1, (b) ALS2, (c) ALS3, (d) ALS4, and (e) ALS5. The small red circles represent the spectral powers at the fundamental, second, and third harmonic frequencies. The spectral powers at the harmonic frequencies are only marked when they are significantly visible. Of three electrode positions, one electrode showing better and stable SSVEP responses at different stimulation frequencies was individually chosen for each patient by visual inspection (O1 for ALS1 and ALS4; Oz for ALS2, ALS3, and ALS5).

of four sentences corresponding to the most frequently used requirements in the patient's daily life, which were "My legs are uncomfortable," "My arms are uncomfortable," "Turn on the TV," and "Change my body position" as determined based on the interview with ALS1's family. The four commands were written below each visual stimulus as "Leg," "Arm," "TV," and "Position," respectively (see Figure 1a). For ALS4 and ALS5, numbers from 1 to 4 were used for the real-time feedback, during which the numbers were presented under each visual stimulus (see Figure 1b). The four numbers were used instead of the four words so as to test whether our SSVEP-based BCI system could be used in another practical situation (i.e., answering a questionnaire survey with four options).

Experimental Procedure

ALS1 performed six experimental sessions (denoted by D1/S1–D1/S6 in Figure 4a), each of which consisted of four trials, except that six trials were tested in the third session (D1/S3). This first experiment was prepared as a preliminary experiment to confirm the possibility of SSVEP-based BCI in patients with LIS and to investigate the influence of various experimental conditions on the BCI performances. All six sessions were conducted in a single day (denoted by D1). In the first three sessions (D1/S1–D1/S3), the distance between the patient and the monitor was 70 cm, and the distance between the nearest visual stimuli was set to 23.33 cm, resulting in a visual angle of 18.92° × 18.92°. Time periods required to gaze at a target were set as 6, 4, and 5 s for the first three sessions, respectively, to investigate the effect of the time period on BCI performance. In the last three sessions (D1/S4–D1/S6), the time period was fixed at 6 s, while the visual angle of the stimulus was reduced to 15.18° × 15.18° in order to investigate the influence of the visual angle on the BCI performance. Since a time period of 6 s showed a better performance in the experiment with ALS1, this time period was used for experiments with the other patients. For ALS2 and ALS3, the same experiment conducted with ALS1 was conducted on two different days while keeping all experimental conditions unchanged over the 2 days. Four experimental sessions composed of 8–12 trials were performed on each day, and thereby a total of 64 and 72 trials were tested for ALS2 and ALS3, respectively. Visual angles were set to 15.53° × 15.53° and 16.26° × 16.26° for ALS2 and ALS3, respectively. In the first visit of ALS4 (D1/S1 in Figure 4d), we only confirmed SSVEP responses to each visual stimulus, and then conducted four experimental sessions each with six trials in the next visit (D2/S1–D2/S4). To further investigate the feasibility of the four-class SSVEP BCI system in a practical situation, in the last visit (D3/S1) we asked ALS4 to answer a questionnaire regarding BCI technology using our SSVEP BCI system. One example question and its four-answer candidates are as follows: Do you think that BCI technology can be helpful for your life?—(1) Yes, both invasive and noninvasive technology can, (2) Yes, noninvasive BCI technology can, (3) Yes, invasive BCI technology can, (4) No, neither invasive nor noninvasive BCI technology can. A full list of questionnaire items and responses (both true answers and BCI outputs) is provided in online supporting information Appendix S1. Each question and its four possible answers were spoken by an experimenter, and then

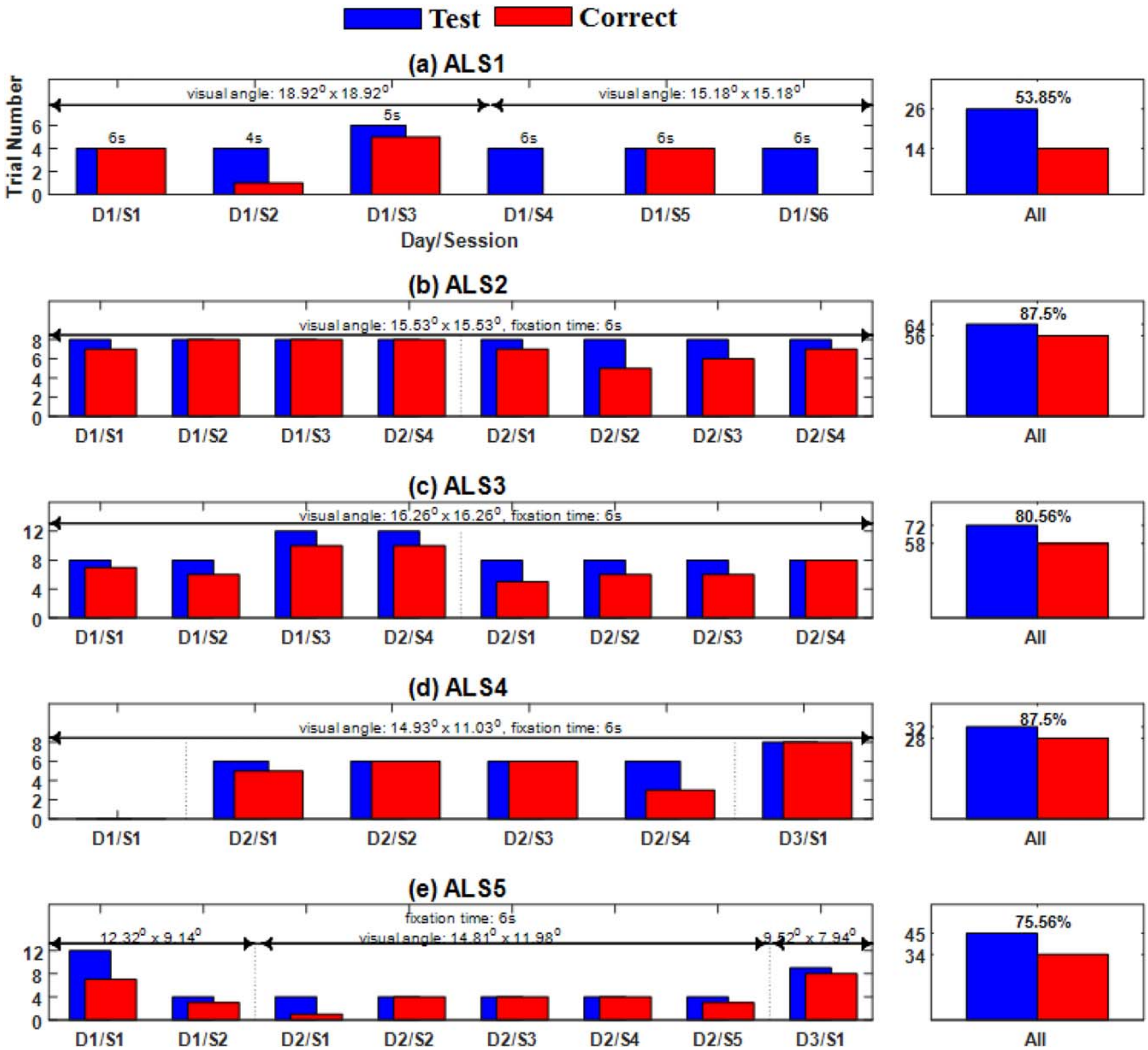

Figure 4. Online experimental results of all patients. The blue and red bars represent the numbers of tested and correctly classified trials, respectively. The information of visual angles and time periods used for a single trial is given for each session, together with the corresponding online results. *D* and *S* denote *day* and *session*, respectively. ALS1, ALS2, ALS3, ALS4, and ALS5 participated in the online experiment for 1, 2, 2, 2, and 3 days, respectively. Because some questions in the questionnaire experiment (D3/S1 in ALS4 and ALS5) had subsequent subquestions depending on the answer, the numbers of questions used for ALS4 and ALS5 were slightly different (eight questions for ALS4 and nine questions for ALS5).

ALS4 answered each question using our BCI system. Afterward, we repeated the questionnaire survey experiment without using BCI to evaluate the accuracy of our four-class BCI system. For this patient, a visual angle of 14.93° × 11.03° was used for all experiments. The same experiment performed with ALS4 was also conducted for ALS5 on three different days (denoted as D1/S1–D3/S1 in Figure 4e), but in contrast to ALS4, online experiments were conducted from the first visit to the patient's home (D1/S1–D1/S2). Because ALS5 asked us to set a different monitor distance from him on each experimental day in order to see the visual stimuli as comfortably as possible, we used slightly different visual angles ranging from 7.94° to 14.81°. Except for the experiments performed with the questionnaire, the number of trials for each session was controlled depending on the patients' condition, and was also balanced in such a way that each visual stimulus was tested as equally as possible. Figure 2 shows a screenshot of visual stimuli (left) and ALS1 (right) taken while ALS1 was focusing on the top-left stimulus (Leg) according to the instruction of an experimenter. A movie taken during the experiment with ALS1 can be found in the online supporting information.

EEG Data Recording and Analysis

EEG signals were recorded using a multichannel EEG acquisition system (WEEG-32, Laxtha Inc., Daejeon, Korea), with the reference attached on the left mastoid and the ground attached on the right mastoid. All EEG electrodes used in this study were attached on the scalp using conductive gels. In order to check whether EEG electrodes were stably attached during the experiment, we checked increments of alpha power when the patients closed their eyes, and SNRs of SSVEPs elicited when the patients focused on each visual stimulus for 10 s. If alpha power increased with eyes closed, and the SNR exceeded 2, we assumed that the EEG electrodes were properly attached. This procedure was performed before the experiments and whenever the patients took a rest. Sampling rate was set at 512 Hz, and an antialiasing band-pass filter with cutoff frequencies of 0.7 and 50 Hz was applied before the sampling. Three occipital locations (Oz, O1, O2) were selected for the EEG recording based on our previous SSVEP studies showing good performance with the same electrode configuration (Hwang, Kim, Han, & Im, 2013; Hwang et al., 2012; Lim, Lee, Hwang, Kim, & Im, 2015). This simple electrode setting also allowed us to reduce the experimental preparation time. Nevertheless, an optimal electrode configuration needs to be determined for each patient based on a preliminary test for the long-term daily use of BCIs. For the online data analysis, on-going EEG signals were segmented from onset time to the end of a predefined period for each trial, and the spectral powers for each electrode were evaluated using fast Fourier transform (FFT). When the time period used for one target detection was 6 s, spectral powers at the four stimulation frequencies (6, 6.66, 7.5, 10 Hz) could be precisely estimated using FFT with a frequency resolution of 1/6 Hz. Only for ALS1, time periods of 4 and 5 s were tested, where the FFT window size was set to 6 s using zero padding (1,024 and 512 zeros were added for 4- and 5-s EEG data, respectively). The spectral powers at four stimulation frequencies (6, 6.66, 7.5, 10 Hz) and those at their second harmonics were summed over all three channels, and the frequency showing the highest power value was selected (Hwang, Kim, Han & Im, 2013; Hwang et al., 2012; Lim et al., 2015).

Results

Figure 3 shows examples of SSVEP responses of each patient for each of four visual stimuli modulated with different frequencies. In Figure 3, the red circles indicate the spectral powers at the fundamental stimulation frequencies and harmonic frequencies. Harmonic frequencies were marked only when they were clearly observed. Dominant spectral powers at each stimulation frequency were observed in ALS1 and ALS3, as shown in Figure 3a,c, but harmonic SSVEP responses were not clearly observed. Spectral peaks at both fundamental and harmonic frequencies were observed in ALS2, ALS4, and ALS5 (Figure 3b,d,e). Before the main experiments with patients, we always checked whether the SSVEP responses had an SNR high enough to be used to implement SSVEP-based BCI applications. The criterion was SNR of 2. In cases when harmonic responses are not clearly shown in the power spectra (SNR < 2), we did not use the power spectral densities at harmonic frequencies as the candidate features for classification.

Figure 4 shows a summary of the experimental conditions and the corresponding online experimental results for each patient, where the blue and red bars represent the number of test trials and correctly identified trials, respectively. ALS1 showed a good online performance for the first session (D1/S1), but the performance decreased dramatically when the time period given to the patient to attend to a target stimulus was reduced from 6 s to 4 s (D1/S2). When the time period increased by 1 s, the performance was almost recovered (D1/S3). From these experimental sessions, we confirmed that the time periods might need to be customized individually. In the last three sessions performed after reducing the visual angle, the BCI performances fluctuated from 0% to 100% (D1/S4–D1/S6). The overall accuracy of our test experiments with ALS1 was 53.85% (chance level: 25%). The online experiments with the other four ALS patients showed more stable and better performances than with ALS1, reporting mean classification accuracies of 87.5%, 80.56%, 87.5%, and 75.56% for ALS2, ALS3, ALS4, and ALS5, respectively. In particular, these patients showed fairly stable online performance over different days/sessions (D1: 96.88% and D2: 78.13% for ALS2; D1: 82.5% and D2: 78.13% for ALS3; D1: 83.33% and D2: 100% for ALS4; D1: 62.5%, D2: 80%, and D3: 88.89% for ALS5). Also ALS4 and ALS5 showed good online performance in the questionnaire survey experiments that simulate a practical interactive communication situation (see D3/S1 for ALS4 and ALS5 in Figure 4).

Discussion

Many EEG-based BCI studies have been conducted in patients with LIS, in which SCP, ERP, and SMR paradigms have been employed to modulate discriminable brain signals in patients (Kübler & Birbaumer, 2008). In recent years, SSVEP has attracted growing attention in the BCI community because SSVEP-based BCI systems can provide relatively high communication rates and require little training and fewer electrodes compared to systems based on other paradigms (Liu et al., 2014; Vialatte, Maurice, Dauwels, & Cichocki, 2010). Some SSVEP-based BCI studies showed acceptable system performances (Combaz et al., 2013; Daly et al., 2013; Diez et al., 2013; Lesenfants et al., 2014; Lim et al., 2013; Parini et al., 2009; Sakurada et al., 2013), but the clinical feasibility of the SSVEP paradigms is still questionable for patients with LIS, who are the main targets of BCI technology, because most previous clinical results were obtained from "incomplete" LIS patients who still have moderate motor functions. In the present study, we applied a four-class SSVEP-based BCI system to five patients with advanced ALS in order to provide information on the clinical feasibility of an SSVEP paradigm in patients with LIS. For this purpose, the reliability and practical applicability of the implemented SSVEP-based BCI system were investigated over multiple days in a realistic communication situation.

The performance of ALS1 significantly varied across sessions as a result of changes in experimental conditions such as visual angle and time period. In particular, only one out of four trials was correctly classified in the second session (D1/S2) because of the shorter time period (4 s). Also, no trials were correctly identified in the fourth (D1/S4) and sixth (D1/S6) sessions, both of which were performed immediately after reducing the visual angle. In patient ALS1, focusing on one of four visual stimuli became harder after the fourth session because of peripheral vision from other stimuli that were much more closely placed in a reduced visual angle, and after the sixth session the patient was completely fatigued. As a result, the experiment was stopped after the sixth session. Although the overall performance of ALS1 was lower than that of the other patients, it was still significantly higher (53.85%) than the chance level of 25%. It is expected that ALS1 might achieve better performance if the experimental condition was stabilized as for the other patients. The other four patients (ALS2–ALS5) showed good online performances in fixed experimental conditions (ALS2 87.5%, ALS3 80.56%, ALS4 87.5%, ALS5 75.56%).

The test-retest reliability of the implemented BCI system was investigated with four patients (ALS2–ALS5) on different days.

The patients showed stable performances over different days and sessions, demonstrating the good test-retest reliability of the SSVEP-based BCI system. As mentioned earlier, ALS1 participated in our previous study using a two-class SSVEP-based BCI system, in which a classification accuracy of 80% was reported (Lim et al., 2013). Even though the experimental conditions of our previous SSVEP-based BCI study were different from those of the current study, it might be reasonable to assume that the test-retest reliability of an SSVEP-based BCI system was indirectly verified for ALS1. Also, ALS4 and ALS5 could successfully use our BCI system as a communication tool in a question-answer situation, confirming the practical usability of the SSVEP-based BCI system. Together, these results suggest that the SSVEP paradigm could be potentially used to develop a clinically available BCI system for patients with LIS. However, further clinical studies with a larger population of patients should be performed to definitively address the clinical feasibility of the SSVEP paradigm.

The clinical symptom severity of the five ALS patients who participated in our study was generally much worse than that of patients recruited in previous clinical BCI studies based on SSVEP (Combaz et al., 2013; Daly et al., 2013; Diez et al., 2013; Lesenfants et al., 2014; Parini et al., 2009; Sakurada et al., 2013). The four limbs of our patients were totally paralyzed except ALS2, who showed a very weak movement of right leg, and all patients were artificially ventilated. Fortunately, all patients maintained residual eye movements to different extents ranging from very weak to moderate, which was their only means of communication (see Table 1). In contrast, most patients in previous clinical SSVEP-based BCI studies had other communication options (e.g., head or finger movement), and some could even perform oral communication (Combaz et al., 2013; Lesenfants et al., 2014). In this sense, the results of our study seem particularly meaningful because the potential clinical feasibility of an SSVEP-based BCI system was verified with patients with LIS, who are more suitable targets for BCI system applications.

Strong SSVEPs are generally observed over the occipital lobe because this brain area is responsible for visual information processing, and therefore recording electrodes are generally placed around the occipital area to measure high-quality SSVEPs. However, this unfortunately reduces the clinical practicality of SSVEP-based BCI systems because it is difficult to access the occipital area for severely paralyzed patients lying face up with mechanical ventilation. In fact, our patients were all bedridden with mechanical ventilation through tracheostomy. Therefore, we had to be very careful when lifting the patient's head to attach electrodes on the occipital area because this might result in an emergency situation if the head movement affected the position of a ventilation hose during the electrode attachment. Also, recording electrodes attached on the occipital area were pressed down between the patient's head and a pillow during the experiment, which could cause artifacts in EEG signals. In fact, noise components were observed in a form of relatively strong powers at several nonstimulation frequencies, as shown in Figure 3. Recently, one study provided a potential solution to this practical problem by showing that reasonable SSVEPs can be measured from nonhair-bearing areas (e.g., forehead, face, neck areas), even though they were relatively weak compared with those measured from the occipital areas (Yu-Te, Yijun, Chung-Kuan, & Tzyy-Ping, 2012). However, it was not clear how accurately distinct SSVEPs measured from nonhair-bearing areas can be classified, and this would be an important future topic to be addressed in order to significantly improve the clinical practicality of an SSVEP-based BCI system. On the other hand, development of a specially designed dense electrode array that can be readily attached to the patient's occipital area would be useful for enhancing the efficiency and accuracy of the SSVEP-based BCI systems.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Appendix S1: Questionnaire on brain-computer interface technology and questionnaire for preferable technology of brain-computer interface.

Movie: Application of an SSVSP-based BCI system to an ALS patient.