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An emergency call system for patients in locked-in state using an SSVEP-based brain switch

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Abstract

Patients in a locked-in state (LIS) due to severe neurological disorders such as amyotrophic lateral sclerosis (ALS) require seamless emergency care by their caregivers or guardians. However, it is a difficult job for the guardians to continuously monitor the patients' state, especially when direct communication is not possible. In the present study, we developed an emergency call system for such patients using a steady-state visual evoked potential (SSVEP)–based brain switch. Although there have been previous studies to implement SSVEP-based brain switch system, they have not been applied to patients in LIS, and thus their clinical value has not been validated. In this study, we verified whether the SSVEP-based brain switch system can be practically used as an emergency call system for patients in LIS. The brain switch used for our system adopted a chromatic visual stimulus, which proved to be visually less stimulating than conventional checkerboard-type stimuli but could generate SSVEP responses strong enough to be used for brain-computer interface (BCI) applications. To verify the feasibility of our emergency call system, 14 healthy participants and 3 patients with severe ALS took part in online experiments. All three ALS patients successfully called their guardians to their bedsides in about 6.56 seconds. Furthermore, additional experiments with one of these patients demonstrated that our emergency call system maintains fairly good performance even up to 4 weeks after the first experiment without renewing initial calibration data. Our results suggest that our SSVEP-based emergency call system might be successfully used in practical scenarios.

KEYWORDS

amyotrophic lateral sclerosis (ALS), brain-computer interface (BCI), brain switch, EEG, emergency call system, steady-state visual evoked potential (SSVEP)

1 | INTRODUCTION

There are many patients who cannot communicate with others due to a severe neurological disorder, such as amyotrophic lateral sclerosis (ALS), multiple sclerosis, spinal cord injury, or brainstem stroke (Boillée, Vande Velde, & Cleveland, 2006). Some patients with advanced disease are in a locked-in state (LIS), a condition in which patients have full consciousness but no voluntary muscle movement (Bauer, Gerstenbrand, & Rumpl, 1979). These patients require 24/7 care, especially if they are bedridden and require mechanical ventilation through a tracheostomy because air leakage in the endotracheal tube during mechanical ventilation might result in severe damage unless immediate and proper actions are taken. However, it can be difficult for a guardian to continuously monitor a patients' state, especially when direct communication is not possible. An emergency call system based on brain-computer interface (BCI) technology might be a promising solution to this problem.

BCI technology translates brain signals into commands with which one can communicate with the outside world or control external devices (Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002). In past decades, various kinds of brain signals have been used with the aim of developing practical BCI systems, such as EEG (Galán et al., 2008; Guger et al., 2009; Hong, Guo, Liu, Gao, & Gao, 2009; Hwang et al., 2012; Leeb et al., 2007; McFarland & Wolpaw, 2008; Müller-Putz & Pfurtscheller, 2008; Rebsamen et al., 2007), fMRI (Ramsey, Van De Heuvel, Kho, & Leijten, 2006; Weiskopf et al., 2004), near-infrared spectroscopy (NIRS) (Coyle, Ward, & Markham, 2007; Fazli et al., 2012; Sitaram et al., 2007), MEG (Mellinger et al., 2007; van Gerven & Jensen, 2009), ECoG (Leuthardt, Schalk, Wolpaw, Ojemann, & Moran, 2004; Schalk et al., 2007), and transcranial Doppler ultrasound (TCD) (Aleem & Chau, 2013; Myrden, Kushki, Sejdić, Guerguerian, & Chau, 2011). In particular, EEG-based BCI has been extensively studied, and a variety of EEG-based BCI applications have been developed (Galán et al., 2008; Guger et al., 2009; Hong et al., 2009; Hwang et al., 2012; Leeb et al., 2007; Müller-Putz & Pfurtscheller, 2008; McFarland & Wolpaw, 2008; Rebsamen et al., 2007). However, most EEG-based BCI applications are synchronous systems, which analyze brain signals within a preset time window (Galán et al., 2008; Guger et al., 2009; Hong et al., 2009; Hwang et al., 2012; Leeb et al., 2007; Müller-Putz & Pfurtscheller, 2008; McFarland & Wolpaw, 2008; Nicolas-Alonso & Gomez-Gil, 2012; Rebsamen et al., 2007) and thus can only generate commands or messages at a specified time. In contrast, asynchronous BCI systems can generate commands at user discretion; however, the performances of asynchronous BCI systems are not as high as that of synchronous systems. Researchers have sought to improve performance of asynchronous BCI by adopting various signal processing and pattern classification technologies (Borisoff, Mason, Bashashati, & Birch, 2004; Fatourechi, Ward, & Birch, 2008; Galán et al., 2008; Müller-Putz, Kaiser, Solis-Escalante, & Pfurtscheller, 2010; Müller-Putz, Scherer, Pfurtscheller, & Rupp, 2006; Mason & Birch, 2000; Millán & Mouriño, 2003; Nicolas-Alonso & Gomez-Gil, 2012; Ortner, Allison, Korisek, Gaggl, & Pfurtscheller, 2011; Pan, Li, Zhang, Gu, & Li, 2013; Scherer, Müller, Neuper, Graimann, & Pfurtscheller, 2004). The brain signal-based emergency call system developed in the present study can be regarded as the simplest form of an asynchronous BCI system because it detects specific signal features from continuous EEG signals without any external cues (Mason & Birch, 2000).

The emergency call system can be implemented using a so-called “brain switch” system that has been developed to help patients in an LIS to turn on or turn off external systems by themselves (Mason & Birch, 2000). Sensorimotor rhythms modulated by motor imagery have been the most widely used brain signals for implementing brain switches (Borisoff et al., 2004; Fatourechi et al., 2008; Müller-Putz et al., 2010; Müller-Putz et al., 2006; Mason & Birch, 2000). Because this kind of brain switch utilizes sensorimotor rhythms that are voluntarily generated, no external stimuli are required to elicit specific brain activity patterns. However, this type of brain switch generally requires long and tedious training sessions for training classifiers (each time prior to using the system), which lead to fatigue for patients in an LIS before they even start using the system (Nicolas-Alonso & Gomez-Gil, 2012). Furthermore, some individuals have difficulty performing motor imagery tasks (Hwang, Kwon, & Im, 2009). According to a study by Vidaurre and Blankertz (2010), 15%–30% of BCI users have “motor imagery illiteracy.” On the other hand, steady-state visual evoked potential (SSVEP) elicited by a visual stimulus flickering or reversing at a specific frequency has also been used as a representative brain signal for implementing brain switches (Ortner et al., 2011; Pan et al., 2013). SSVEP-based BCI paradigms not only showed high performance in terms of true-positive rate (TPR) but also did not require extensive training procedures (Vialatte, Maurice, Dauwels, & Cichocki, 2010) compared with sensorimotor rhythm-based BCI paradigms. In the previous SSVEP-based brain switch studies, flashing or pattern-reversal black-and-white checkerboard stimuli have been mostly used to elicit SSVEP responses (Vialatte et al., 2010); however, these stimuli were so intense that most of the system users suffered from visual fatigue or headache (Vialatte et al., 2010). Although there have been a series of studies on the SSVEP-based brain switches, all of them tested their systems with healthy individuals. Therefore, the clinical value of the SSVEP-based brain switch has not been fully validated.

In this article, we implemented an online emergency call system for patients in an LIS using an SSVEP-based brain switch, with which patients could call their guardians by simply staring at a target stimulus. To reduce the intensity of the visual stimulus, our system adopted a chromatic visual stimulus with isoluminant red-green circular sinusoidal grating, which was previously used for evoking transient visual evoked potential (tVEP) (Lai, Zhang, Hung, Niu, & Chang, 2011) but has never been used to evoke SSVEP. Fourteen healthy participants took part in the online experiments, which were designed to verify whether the chromatic-visual-stimulus-based brain switch outperforms the conventional checkerboard brain switch in terms of both comfortability and BCI performance. Additionally, we tested our emergency call system with three patients with severe ALS to confirm the system feasibility. Among the three patients, one patient used our emergency call system over 4 weeks to validate its test-retest reliability. To the best of our knowledge, this is the first study to apply an SSVEP-based brain switch to LIS patient care.

2 | METHOD

2.1 | Participants and experimental setups

Fourteen BCI-naïve healthy volunteers (six females and eight males, ages 19–29 years) and three patients with ALS (two females and one male; 50, 47, and 53 years old, respectively) were recruited for this study. All healthy participants (denoted by participants H1–H14) had normal or corrected-to-normal vision, and none had a history of neurological, psychiatric, or other severe diseases that might affect the experimental results. Details of the experimental procedures were explained to each participant, and they all provided signed written consent prior to engaging in any research activities. The participants received monetary reimbursement for study participation. All experiments were conducted in the Computational Neuroengineering Laboratory of Hanyang University. The three ALS patients (A1–A3) were diagnosed at 43, 41, and 43 years of age, respectively, and were bedridden with mechanical ventilation through tracheostomy. Neither were they able to move any part of their body; their muscles were severely atrophic. They were alert and had normal sound cognition, and all of them could slowly move their eyeballs. They learned to communicate with their families through subtle eye blinking because their eye muscles were the only facial muscles they were able to move. The symptom scores (ALS-FRS) of all three patients were identically 4. Details of the experimental procedures were explained to the patients and the patients' legal guardians, and signed informed consent was obtained from the patients' guardians prior to the experiments. This study protocol was reviewed and approved by the institutional review board (IRB) of Hanyang University (for healthy participants), by the IRB of the National Rehabilitation Center of Korea (KNRC) (for A1 and A2), and by the IRB of Hanyang University Hospital (A3), and all experiments were conducted according to the declaration of Helsinki.

To acquire EEG signals, three Ag/AgCl electrodes were attached to each participant's scalp (Oz, O1, and O2) according to the extended 10–20 system. Each healthy participant sat in a comfortable armchair and was asked not to move his or her body at any time during the experiment. EEG signals were recorded using a multichannel EEG recording system (WEEG-32; Laxtha Inc., Daejeon, Korea) in a soundproof, dimly lit room. Ground and reference electrodes were placed behind the left and right ears, respectively. An anti-aliasing bandpass filter with cutoff frequencies of 0.7 Hz and 43 Hz was applied prior to sampling. The sampling rate was set at 512 Hz throughout the experiments. For the ALS patients, the same experimental setups were applied, but the experiments were conducted in the patients' houses.

2.2 | Design of the emergency call system

We used two types of visual stimuli: one is a checkerboard pattern visual stimulus that has been used in many conventional SSVEP-based BCI systems and the other is a chromatic pattern visual stimulus that is known to be more comfortable for the user than the checkerboard stimulus in eliciting transient VEP (Lai et al., 2011). An isoluminant chromatic sinusoidal grating with spatial frequencies of two cycles per degree (cpd) was presented on a 21-inch LCD monitor screen. The monitor refreshing rate was set at 60 Hz, and the resolution of the monitor screen was set to 1,280 × 1,024 pixels. The background color of the screen was gray (RGB: 127, 127, 127), and a fixation cross was located at the center of the screen. The flickering visual stimulus was located at the bottom-right of the screen with a visual angle of 3° (diameter), and a small black dot was located at the center of the concentric stimulus to help the participants focus, as shown in Figure 1. The visual stimulus was located at the corner of the screen simply because the corner is the farthest location from the center, where a fixation dot is located. We tried to prevent the potential disturbance from the flickering stimulus while the study participants were focusing on the center fixation dot.

In our experiments, the participants needed to continuously gaze at a flickering visual stimulus in order to activate the brain switch. From here on, we refer to the time period in which the participant concentrated on the visual stimulus as the "control state." Alternatively, if the participant did not want to turn on the brain switch, he or she was asked to gaze at a fixation cross at the center of the screen; we refer to this period as the "idle state" (during the idle state, the visual stimulus kept flickering). We did not ask the participants to concentrate on the fixation but asked them to simply "gaze at" the fixation so that the experimental conditions can be more realistic. Note that peripheral vision might affect the system performance if the participants do not concentrate on the fixation point. In order to classify whether the participant was in the control state or the idle state, a 2-minute calibration session preceded all tests of the emergency call system (both for healthy participants and patients with ALS). While the participant gazed at either the flicking visual stimulus or the fixation cross for 20 s, three times each, EEG data were recorded from the Oz, O1, and O2 electrodes. Each of the recorded 20-s EEG data was divided into sixteen 5-s epochs with an 80% overlap, and the spectral powers of the stimulation frequency were calculated for each epoch using the fast Fourier transform (FFT). Four thousand ninety-six data points were used to evaluate spectral powers after zero-padding 1,536 zeros to the original 2,560 time samples in each epoch. This process was repeated for three different data sets acquired from the three electrodes. The power values at the stimulation frequency in the three electrodes were used as feature vectors for support vector machine (SVM). We evaluated the power value at the exact stimulation frequency and did not consider higher harmonics. The power

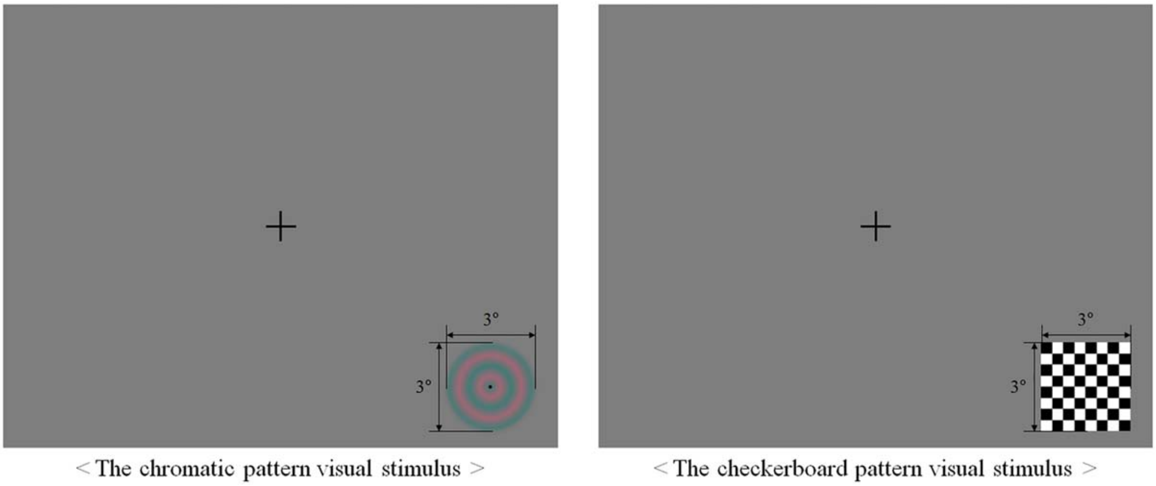

FIGURE 1 The chromatic pattern visual stimulus (left) and the checkerboard pattern visual stimulus (right) adopted in our SSVEP-based brain switch

values for all 96 epochs (16 epochs × 3 sessions × 2 classes) acquired during the calibration session were then used to train the SVM classifier (48 epochs from control state and the other 48 epochs from idle state).

While the emergency call system was operating, the spectral power of the stimulation frequency was consistently calculated at every second using the past 5-s epoch data. At the same time, the SVM classified whether the participant was in the control state (denoted by 1) or the idle state (denoted by 0) based on the spectral power at every second. A newly generated binary result (1 or 0) stacked up behind the previous SVM binary results and yielded a pattern consisting of 10 consecutive binary results (e.g., 0000011001), which was updated every second. The brain switch was turned on when the current SVM result pattern matched one of two predetermined template patterns, "0000011111" or "1111111111," with at least 90% accuracy. The accuracy was defined as the proportion of matched binary elements (0 or 1) in an array (e.g., accuracy of 0000011001 with respect to 0000011111 is 80%). When the brain switch was turned on, it made a call to a predesignated phone using the Skype™ software application.

To the best of our knowledge, the template-matching approach used in this study has not been used in any previous SSVEP-based brain switch systems, most of which used predefined threshold criteria based on SSVEP power (Pan et al., 2013; Scherer et al., 2004; Xia et al., 2013). The template pattern-matching program that we implemented turned on the brain switch system only when a binary sequence obtained from 10 successive epochs matched predetermined template patterns with an accuracy of at least 90%. We used two template patterns: "0000011111" and "1111111111." The first template pattern, "0000011111," indicates that the user gazed at the fixation cross for at least 5 s and then changed his or her gaze to the target visual stimulus for 5 s. Note that a user of the system does not initially gaze at the target visual stimulus, and thus the ideal binary sequence in the idle state should be "0000000000." When the user switches his or her gaze to the target visual stimulus, the binary sequence gradually changes from "0000000001" to "0000011111." When this template pattern is solely used and there are some false negatives included in the current sequence pattern, users might not have any more chances to turn on the brain switch system. To prevent this problem, we used one additional template pattern, "1111111111," which indicated that the user was consistently gazing at the target visual stimulus for 10 s. Using this template-matching approach, the users were able to turn on the switch at a minimum time of 4 s because the SVM sequence pattern "0000001111," which can be generated by gazing at the visual stimulus for four seconds, matched the first template pattern "0000011111" with 90% accuracy (note that there can be a longer delay time because, in our experiments, we used a 5-s epoch to evaluate spectral power). We could readily control the TPR and false positive rate (FPR) by adjusting the length of the template patterns or the template-matching accuracy. If the matching accuracy increased and/or if the length of the template patterns was extended, FPRs in both the control and idle states were dramatically decreased, but it took a much longer time to turn on the brain switch, or sometimes the users could not turn on the switch at all because the template-matching program makes its decision conservatively. Because the high TPR for the control state was also an important factor in developing the emergency call system, proper values for the matching accuracy and the length of the template patterns need to be determined.

Ideally, it is desirable to optimize these values for each individual user through repeated experiments, which would be an important topic for future studies.

2.3 | Experimental procedures

Before the main online experiments, a preliminary experiment was conducted with healthy study participants to investigate whether the chromatic visual stimulus was more comfortable than the conventional checkerboard visual stimulus. The participants were asked to gaze at either the chromatic stimulus or a 4×4 square black-and-white checkerboard stimulus, both of which flickered at 6 Hz, for 5 minutes. The flickering frequency of 6 Hz was selected because it is an aliquot of the monitor refreshing rate (60 Hz) and theta frequency band (4–8 Hz) was reported to elicit clear SSVEP responses in most subjects (Hwang et al., 2012). The presentation sequence of each visual stimulus was randomly determined for each participant but artificially counterbalanced. In other words, the checkerboard stimulus was presented first for the half of the participants, while the chromatic stimulus was presented first for the last of the participants. Both stimuli were set up so that they had identically sized focal areas that were located at the bottom-right side of the 21-inch LCD monitor screen; these conditions were repeated in the main experiment. The entire process was repeated twice; thus, four 5-minute sessions were performed for each participant, with a short break between successive sessions. After the preliminary experiments, the participants reported which stimulus was relatively more comfortable to their eyes. We did not use any numerical scale to quantify the comfortability but simply asked each participant to choose one of the following three answers: first stimulus, second stimulus, and no significant difference. There was no EEG recording during the preliminary experiment.

To compare the performance of the brain switches based on either chromatic or checkerboard visual stimulus, online experiments were conducted again with 14 healthy participants. The online experiments were conducted 10 times with a randomly presented chromatic visual stimulus or a checkerboard visual stimulus, each flickering at 6 Hz. Both visual stimuli had identically sized areas and were located on the bottom-right side of the monitor screen, as in the preliminary experiments (see Figure 1). In each trial of the experiment, the participants were asked to gaze at the target visual stimulus to turn on the brain switch (control state) or at a fixation cross on the center of the same screen if they did not want to turn on the brain switch (idle state). We provided verbal instructions as to when the participant needed to gaze at the flickering stimulus. Right after the verbal instruction by an experimenter, a pure-tone beep sound was generated from the computer speaker. The experimenter pushed a keyboard button to generate the beep sound, when the timing was recorded in the computer. The participants were instructed to keep gazing at the fixation cross until a beep sound was presented. When the brain switch was on, auditory feedback was provided using a recorded voice saying "on." We recorded the time each patient required to turn on the brain switch and to maintain the idle state for each trial. The time required to maintain the idle state was defined as the time period from the starting time of each trial to a time when the brain switch system turned on by an unexpected false positive. Wilcoxon signed rank test was used to compare the performances of two brain switch systems with different visual stimuli.

Three patients with severe ALS (A1–A3) were also recruited to further evaluate the feasibility of the online emergency call system. After the initial calibration session, which lasted for 2 minutes, they were asked to gaze at either the visual stimulus or the fixation cross, 10 times each. As with the experiments performed with healthy participants, we provided the patients with verbal instructions as to when to gaze at the flickering stimulus and used the same auditory feedback. For each trial, we measured the time required to turn on the brain switch and the time required to maintain the idle state.

In contrast with the online experiments with healthy participants, the patients were presented with only one visual stimulus (chromatic pattern visual stimulus) because we anticipated it would be too fatiguing for the patients' eyes after a long experimental time. All three patients were given a sufficient break after completing the first online experiment, after which they tried to make three phone calls to their guardians using our emergency call system, which combined the brain switch and Skype™; we only measured the time it took to connect to Skype™ after the presentation of a beep sound. Last, to evaluate the test-retest reliability of long-term use of our system, we had one of the patients (A2) use the emergency call system 20 times over 4 weeks (five times per week) using the initial calibration data acquired during the first experiment.

3 | RESULTS

In the preliminary experiment, most healthy participants except only three participants reported that the chromatic visual stimulus was more comfortable for their eyes than the conventional checkerboard visual stimulus, while the other three participants reported experiencing no significant difference in stimulus comfortability. Our results were consistent with a previous study that concluded that chromatic visual stimulus was a comfortable stimulation method for users (Lai et al., 2011). Figure 2 shows an example of SSVEP responses elicited by two different (chromatic and

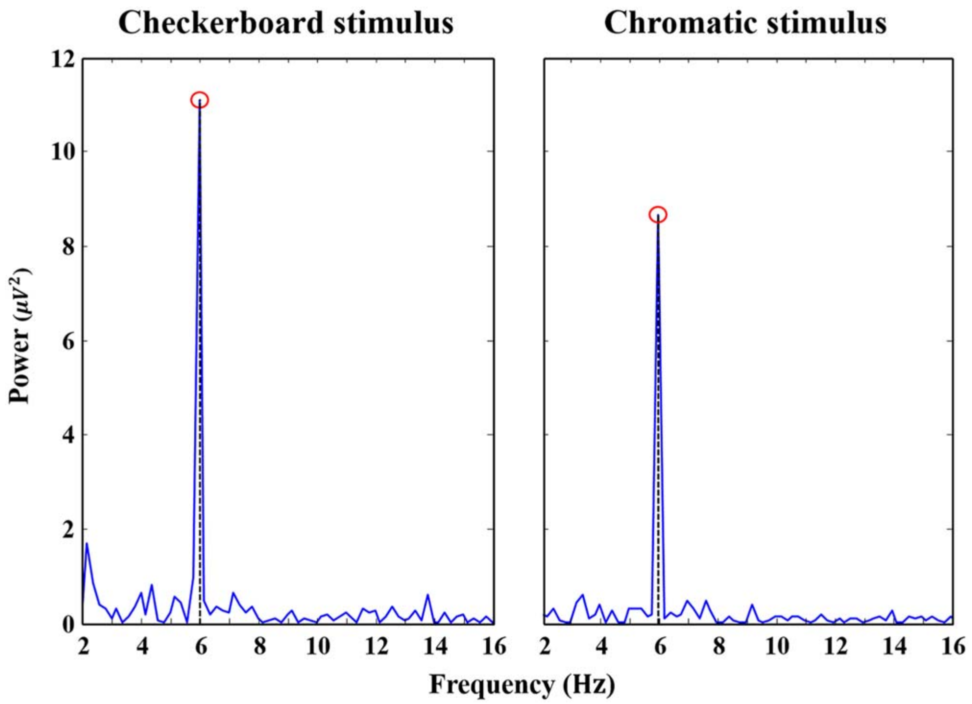

FIGURE 2 An example of power spectra evaluated using a 5-s EEG epoch recorded during "control state." The left and right spectra were obtained while a participant (H6—randomly selected) was staring at checkerboard pattern and chromatic pattern visual stimuli, respectively. Both visual stimuli flickered at 6 Hz. Both spectra show clear SSVEP peaks at the stimulation frequency

checkerboard) visual stimuli flickering at 6 Hz. As seen from the figure, both visual stimuli could elicit clear SSVEP peak at the stimulation frequency, and thus could be used for implementing SSVEP-based brain switch systems.

Table 1 shows the summary of the online experimental results for all healthy participants. The average times needed to turn on the brain switch were 9.9 s and 13.4 s for chromatic stimulus and checkerboard stimulus, respectively ($p = .13$). The average times required to maintain the idle state were 191.9 s and 158.7 s for chromatic stimulus and checkerboard stimulus, respectively ($p = .52$). Although no statistical significance was reported, our results show that the SSVEP-based brain switch system using chromatic visual stimulus is comparable to the conventional system using checkerboard stimulus in terms of BCI performance. The TPR and FPR for our system were 6.06/min and 0.31/min, respectively, which is comparable to results from previous SSVEP-based brain switch studies (Ortner et al., 2011; Pan et al., 2013); however, direct comparison of the results might not be appropriate due to the different experimental conditions and different classification algorithms. We also measured ALS patients' average times for turning on the switch and maintaining the idle state. As previously mentioned, all patients were presented with chromatic visual stimulus. The average time needed for the patients to turn on the brain switch was 11.8 s, whereas that needed for them to maintain the idle state was 101.4 s (Table 2). The results of experiments with patients were worse than those with the healthy participants, as expected.

Figure 3 shows examples of the binary sequences resulting from SVM while a participant (H8) was trying to operate one of the two different types of brain switches. In Figure 3, each of the 5-s EEG epochs was classified as either 1 (control state, depicted as blue or red vertical line) or 0 (idle state, no vertical line). As shown in the figure, participant H8 was only able to turn on the brain switch after he had been gazing at the flickering chromatic visual stimulus for 4 s; this was because the sequence pattern "0000001111" was matched with one of the predetermined template patterns "0000011111" with 90% accuracy. Figure 3 shows that the participant turned on the brain switch more quickly and maintained the idle state longer when a chromatic visual stimulus was used than when a checkerboard stimulus was used. In the figure, the SVM results from the checkerboard stimulus condition included many more false positives and false negatives than those from the chromatic stimulus condition, which might result in differences in the overall BCI performances in the online experiments. It is thought that the checkerboard stimulus was so intense that it sometimes elicited unwanted SSVEP responses due to peripheral vision even when the participants were staring at the central fixation cross.

We conducted additional online experiments to further validate the practicality of our emergency call system with

TABLE 1 Summary of online experimental results for all healthy participants. "Control" represents the average time required to turn on the brain switch system, while "Idle" represent the average time for maintaining idle state without false positives. "SD" represents the standard deviation

Stimulus type	Chromatic visual stimulus (s)		Checkerboard visual stimulus (s)	
Participant ID	Control (SD)	Idle (SD)	Control (SD)	Idle (SD)
H1	6.8 (1.1)	111.8 (115.8)	9.4 (3.4)	101.2 (66.6)
H2	9.6 (5.5)	159.6 (99.4)	9.8 (10.8)	88.6 (63.8)
H3	4.2 (0.8)	236.4 (114.7)	17.0 (14.6)	176.2 (88.1)
H4	10.2 (13.3)	109.0 (70.8)	11.0 (5.3)	140.2 (82.1)
H5	5.4 (1.1)	364.0 (119.1)	22.4 (11.1)	123.4 (91.3)
H6	12.2 (4.0)	80.8 (61.9)	26.4 (13.8)	261.6 (65.0)
H7	8.6 (2.1)	300 (0.0)	12.8 (14.2)	68.0 (48.2)
H8	22.4 (10.7)	88.0 (97.3)	9.6 (1.5)	189.6 (104.7)
H9	6.2 (1.3)	300 (0.0)	6.6 (1.9)	125.2 (63.6)
H10	18.0 (20.8)	212.4 (115.3)	8.4 (2.5)	267.6 (72.4)
H11	10.2 (2.3)	158.8 (99.6)	7.6 (1.3)	261.2 (73.6)
H12	8.8 (4.1)	167.0 (113.1)	31.8 (26.9)	73.6 (78.2)
H13	6.6 (2.1)	232.0 (100.9)	7.0 (2.0)	203.0 (101.6)
H14	9.4 (1.7)	272.4 (55.8)	8.2 (3.3)	142.6 (105.3)
Average	9.9	191.9	13.4	158.7

three patients (A1–A3). These patients could always make phone calls to their guardians in average times of 7, 6.67, and 6 s, respectively. Figure 4 shows a series of snapshots taken during the online experiments, when one of the patients (A1) called her husband using our emergency call system. A sample movie of this experiment can be found online (https://youtu.be/DQQR8MgRo6M) as well as in the attached supplementary movie file. Table 3 shows the results of the following test-retest reliability experiments, which clearly demonstrate that patient A2 was able to use our system with the initial calibration data without needing additional training sessions for 4 weeks. Although there was a sudden drop in the performance of the system in the third week, the performance was recovered in the fourth week to the performance level of the second week. These online experimental results showed that the SSVEP-based brain switch system has the potential to be used successfully in practical scenarios. Nevertheless, the system will benefit from further improvements, which will be discussed in the Discussion section.

TABLE 2 Summary of online experimental results for all ALS patients

Participant ID	Control (SD)	Idle (SD)
A1	18.3 (11.9)	75.3 (32.3)
A2	7.6 (2.7)	109.0 (44.7)
A3	9.7 (2.1)	120 (0)
Average	11.8	101.4

4 | DISCUSSION

Herein, we present findings from evaluations of a brain switch–based emergency call system that we developed for patients in an LIS. This system allows patients to call their guardians or caregivers by simply staring at flickering visual stimulus for a short period of time. We adopted chromatic visual stimulus flickering at a specific frequency, which had not been used to elicit SSVEP prior to this study. We compared the performances of the SSVEP-based brain switches using a chromatic visual stimulus versus the conventional checkerboard visual stimulus. According to our experimental results, the average time needed to turn on the brain switch

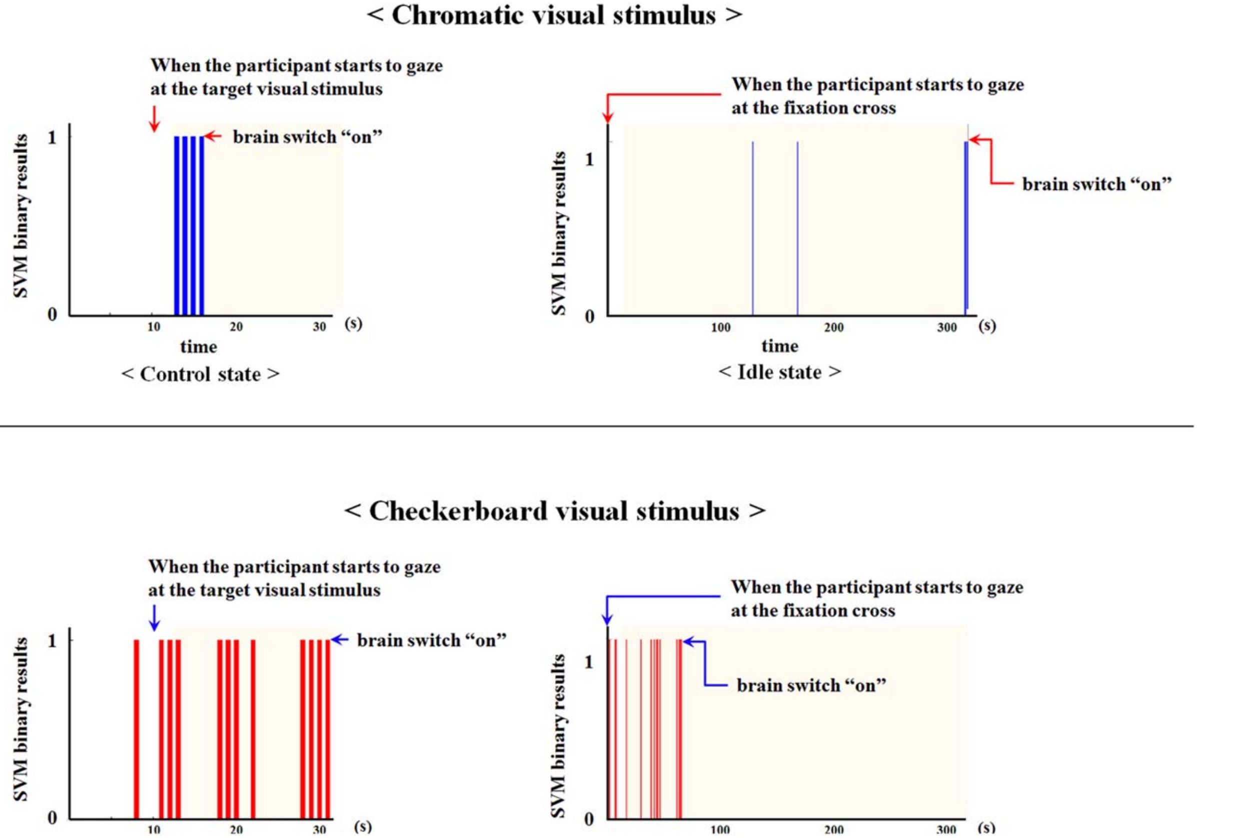

FIGURE 3 Examples of the binary sequences resulting from SVM while a participant (H8, male) operated two different types of brain switches with chromatic or checkerboard visual stimulus. In the figures, "control state" represents time-varying classification results while the participant switched his attention from a fixation cross to the flickering visual stimulus at 10 s (marked with a vertical red arrow), while "idle state" represents the classification results while the participant gazed at a fixation cross at the center of the screen all the time

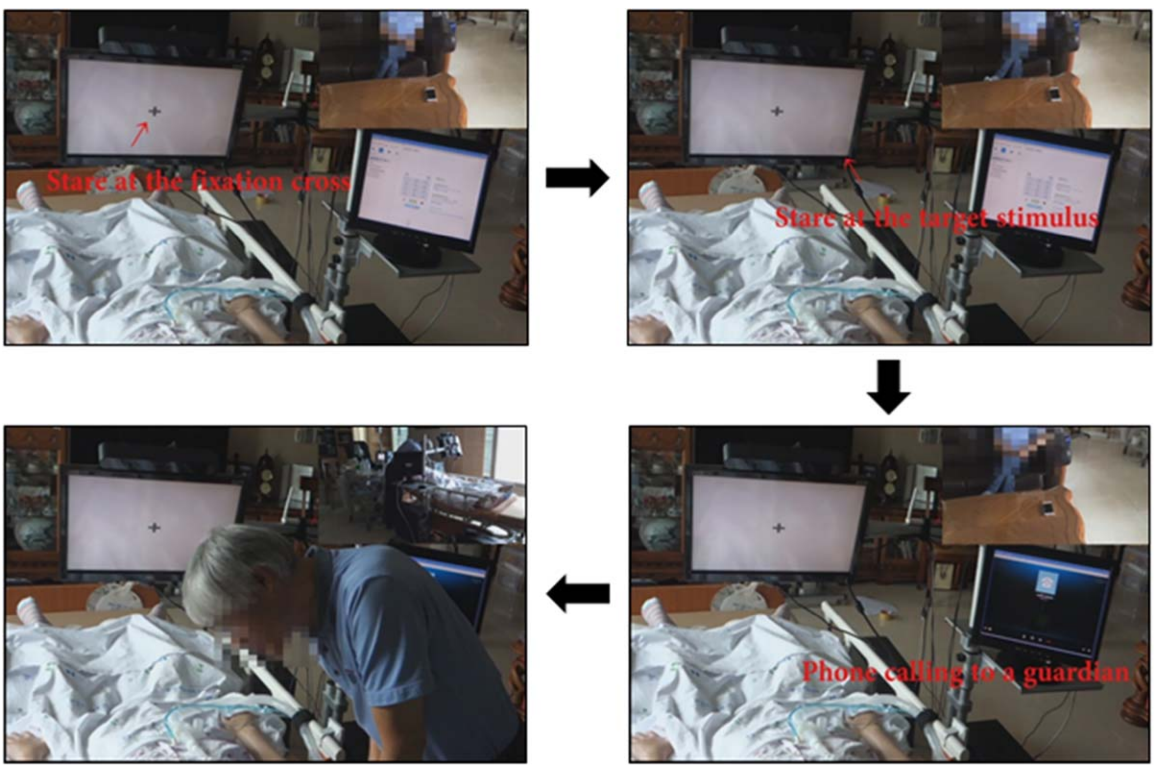

FIGURE 4 A series of snapshots from the online experiment taken while a participant (A1) called her husband using our emergency call system

TABLE 3 Results of the test-retest reliability experiment

	1st week		2nd week		3rd week		4th week	
Trial	Control	Idle	Control	Idle	Control	Idle	Control	Idle
1	6	187	6	194	10	180	6	61
2	7	80	5	42	24	118	20	65
3	8	90	19	85	130	24	7	18
4	12	105	11	171	43	180	7	180
5	5	83	12	31	23	180	9	126
Average	7.6	109.0	10.6	104.6	46.0	136.4	9.8	90.0

with the chromatic visual stimulus was 9.9 s, and the average time to maintain the idle state was 191.9 s with healthy participants. We found that, overall, the performance of the chromatic stimulus was comparable to that of the checkerboard stimulus in terms of BCI performance. Considering that more participants reported that the chromatic stimulus was less stimulating to their eyes, the use of chromatic visual stimulus would be a new additional option for SSVEP-based brain switch systems. Note that the conventional checkerboard stimulus was still better for some participants, and thus we used the phrase "a new additional option" instead of "a new alternative." One of the most important contributions of our study might be the estimation of the test-retest reliability of the emergency call system when used by a patient with severe ALS; our results showed good system performance with up to 4 weeks of consecutive use.

In general, it is difficult to achieve a high TPR in the control state while maintaining a low FPR in the idle state because of the large temporal variability of the brain signal (Pan et al., 2013). To circumvent this problem, Pan et al. (2013) proposed a pseudo-key-based approach for the SSVEP-based brain switch. In the Pan et al. (2013) study, a target key and additional pseudo-keys were displayed on the monitor screen, and the SSVEP powers of the target key and the pseudo-keys were compared to improve the discrimination rate of the control and idle states. On the other hand, Cao, Li, Ji, and Jiang (2014) proposed a hybrid brain switch that combined motor imagery-based sensorimotor rhythms and SSVEP to control the direction and speed of a wheelchair. Both of the previous studies concluded that their approaches were more efficient and accurate than the conventional SSVEP-based brain switches although they did not test their systems with patients. In comparison to the previous studies that tried to achieve high TPRs for the control state and low FPRs for the idle state with an SSVEP-based brain switch, we did not use any additional (pseudo) targets or additional brain rhythms. Instead, we adopted a template pattern-matching method that can potentially manipulate the TPR and FPR by adjusting some control parameters used in the pattern-matching process, which will be explained in the following paragraph.

Conventional brain switches changed the system state not only from the "off" state to the "on" state, but also from the "on" state to the "off" state (Müller-Putz et al., 2006). In our study, the brain switch did not include a function to turn off the system because our emergency call system did not need such a function. Nevertheless, it is expected that our brain switch system can be readily applied to other BCI applications that require a "turning-off" function, such as P300-based mental spelling systems and sensorimotor rhythm–based wheelchair/robot-arm controllers, with merely a slight modification. In order to implement the "turning-off" function in our brain switch system, new template patterns "1111100000" and "0000000000" can be used instead of "0000011111" and "1111111111."

In our study, we used a 5-s epoch to evaluate spectral power, which is relatively long compared to the conventional SSVEP-based BCI studies. We used such a long epoch length to increase the accuracy of the SSVEP detection because reliability of the emergency call system was thought to be more important than the response time. Nevertheless, adopting a better feature extraction method such as canonical correlation analysis (CCA) would be considered in future studies to enhance the overall performance of our emergency call system because the use of CCA features enhanced the overall BCI performance in many recent SSVEP-based BCI studies (Wang et al., 2016; Wieser, Miskovic, & Keil, 2016; Zhang et al., 2013, 2014, 2015, 2017). In addition, we asked the participants to gaze at the fixation cross during the idle state; however, this condition might not be realistic because many patients with ALS generally spend time watching TV. Considering more realistic experimental conditions would be another topic that needs to be further investigated in future studies.

To the best of our knowledge, no previous SSVEP-based brain switches have been applied to patients with severe ALS, with complete loss of function and atrophy of muscles (except the ocular muscles). 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 in LIS, who are more suitable targets for BCI system applications. There are some experimental conditions of our study that were particularly important considerations when conducting online experiments with LIS patients. For example, the total experimental time should be carefully controlled, and an appropriate break time needs to be added between trials/sessions, in consideration of the fact that patients cannot directly express whether they feel mental or physical fatigue during online experimentation. Additionally, because patients in an LIS are generally bedridden and require mechanical ventilation through a tracheostomy, the experimenters should pay particular attention while they are attaching the electrodes to patients' occipital areas. We used a doughnut/ring-shaped cushion to secure space between the electrodes and the bed (Hwang et al., 2016).

Clinical feasibility of SSVEP-based BCI systems has been seamlessly questioned since early 2000s (Wolpaw et al., 2002) because the development of camera-based eye trackers can provide very sensitive and accurate estimations of gaze directions (Cecotti, 2016; Kim, Kim, & Jo, 2015; Pasqualotto et al., 2015). Modern eye trackers exhibited nearly 100% recognition accuracy in two-class communication paradigm when each single trial takes 8 s (Kathner, Kubler, & Halder, 2015), or showed a typing speed as fast as 1.5 letters per second (Naqvi, Arsalan, & Park, 2017). Nevertheless, if the performance of SSVEP-based BCI systems can be further improved, the SSVEP-based BCI would be a promising alternative to the eye-tracker system, because the current eye tracker–based communication device also has its own limitations such that the camera occludes a part of the user's view and its performance is highly influenced by surrounding illumination (Morimoto & Mimica, 2005).

5 | CONCLUSIONS

In this study, we implemented an emergency call system based on an SSVEP-based brain switch that can be used by patients in an LIS to call their guardians. We tested a visually less stimulating chromatic visual stimulus as an alternative to the conventional checkerboard stimulus, and we applied a template-matching approach for the implementation of the brain switch system. A series of online experiments performed with 14 healthy participants showed that the SSVEP-based brain switch with the chromatic visual stimulus was better than that with the conventional checkerboard visual stimulus with regard to comfort, while the overall BCI performances of both approaches were not significantly different. Online experiments with three patients in an LIS showed that they could successfully call their guardians in an average time of 6.56 s using our emergency call system. Additionally, our test-retest reliability experiment results showed that the implemented emergency call system can be used up to at least 4 weeks without changing the initial calibration data, which is another contribution of our study.

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SUPPORTING INFORMATION

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

Movie S1

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