Steady-state visual evoked potential (SSVEP)-based brain–computer interface (BCI) of Chinese speller for a patient with amyotrophic lateral sclerosis: A case report

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Steady-state visual evoked potential (SSVEP)-based brain–computer interface (BCI) of Chinese speller for a patient with amyotrophic lateral sclerosis: A case report

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ABSTRACT
This study applied a steady-state visual evoked potential (SSVEP) based brain–computer interface (BCI) to a patient in lock-in state with amyotrophic lateral sclerosis (ALS) and validated its feasibility for communication. The developed calibration-free and asynchronous spelling system provided a natural and efficient communication experience for the patient, achieving a maximum free-spelling accuracy above 90% and an information transfer rate of over 22.203 bits/min. A set of standard frequency scanning and task spelling data were also acquired to evaluate the patient's SSVEP response and to facilitate further personalized BCI design. The results demonstrated that the proposed SSVEP-based BCI system was practical and efficient enough to provide daily life communication for ALS patients.

1 Introduction

Amyotrophic lateral sclerosis (ALS) patients in complete lock-in state (LIS) suffer from major dysfunction of muscle control but with their consciousness and cognition remaining intact. Hence, communication is recognized as a primary goal for rehabilitation and functional gains. For those in LIS, communication or motion modalities are severely constrained such that regular outputs, including muscular or verbal signals, are unable to properly express themselves. Current strategies involve eye-tracking techniques that permit target selection on a computer screen by tracking the movement of the pupils. Robust experience of such equipment usually requires careful calibration before or even during use, including stable staring on the target, which may induce visual fatigue after long-time home use. Moreover, eye trackers are susceptible to light conditions, which may limit their applicability in outdoor environments.

Brain–computer interface (BCI) using scalp electroencephalography (EEG) as the communication signal is gaining popularity and research interest in the past two decades due to its
directness, non-invasiveness, and robustness. Over the years, BCI has been proven to be feasible and robust enough to be a communication system for not only healthy subjects but also for LIS patients. Several noteworthy demonstrations of BCI applications on real patients have been published, predominantly using the P300 paradigm. Donchin et al. performed preliminary tests on 3 patients with ALS and concluded promising results [1]. Subsequently, Silvoni et al. and Wolpaw et al. applied a P300 BCI speller on a large cohort (more than 20) of patients, achieving an average accuracy of above 80% [2, 3]. These results show that P300 BCI spellers are practical and can be used as a potential communication method for both clinical and home use for users before entering complete LIS. With more advanced algorithms and systems, P300 control devices have become commercially available, some were even been put into long-time stable home use for painting over two years [4]. However, P300-based BCIs cannot provide accurate and high-speed communication experience for daily conversations, and they are often constrained for generalized utilization due to calibration and inter-subject variabilities.

To obtain direct control and address the abovementioned disadvantages, invasive BCIs attempt to decode neural signals, e.g., motion and articulation preparation signals, by implementing electrode arrays on or in the cerebral cortex to control external devices. Vansteensel et al. and Milekovic et al. managed to operate such experiments on 1 and 6 individuals, respectively [5, 6], which presented a long-term, precise-control, home-use device for using in activities such as web surfing, E-mailing, and other regular internet activities. However, invasive operations seem somehow aggressive or even unnecessary for most patients, considering the potential risks to their health conditions and also financial costs. Nonetheless, the decoding efficiency of neural activities and other factors of invasive BCIs provide a viable high-speed and life-time communication solution, for instance, the subject in study by Vansteensel et al. eventually spelled up to 2 letters per minute after sufficient training [5].

Exploiting periodic EEG response with the same frequencies and its harmonics elicited by an oscillating visual stimulus, steady-state visual evoked potential (SSVEP) emerged as a fast, safe, and robust candidate for the BCI control paradigm. The feasibility of SSVEP-based BCIs has been supported by several clinical applications. For example, Lesenfants et al. demonstrated a gaze-independent SSVEP-based online BCI on 6 LIS patients achieving a positive result [7], which was followed by a similar study on 5 patients but with slightly worse performance in terms of the classification accuracy [8], with less than 5 targets and basic classification algorithms have yet to fully utilize SSVEP-based systems, especially its communication speed. Note that all the BCI spellers mentioned above were implemented for English users, which can cause inconvenience for Chinese users. Consequently, in the present study, considering the unsatisfying communication speed of P300 BCI spellers, the relentless training procedures needed by detection algorithms, and the unfriendly synchronous system design and English interface, we aim to provide an SSVEP-based high-speed asynchronous and training-free BCI speller in Chinese typing interface, which is made readily available for practical home use in a single LIS patient.

2 Methods

2.1 Subject

The subject involved in this study was a 38-year-old male diagnosed with ALS for 11 years. His cognitive function is intact, but his motor functions
are mostly damaged. He is not capable of having voluntarily speech, except answering yes or no questions using the left brow and eye muscle movements. He has mainly relied on respiratory and stomach intubation to sustain essential life support.

2.2 Implementation of a non-invasive BCI

This study utilized sampling sinusoidal stimulation methods to provide visual flickers stimulation coded by a joint frequency-phase (JFPM) method on a 60-Hz liquid-crystal display monitor [9]. The SSVEP signals were then triggered by staring at a flickering 40-target virtual keyboard developed using the Psychtoolbox and MATLAB 2018b [10]. Then, the signals were acquired with a sampling rate of 1000 Hz using a wireless EEG amplifier, which were then preprocessed with a 5–100 Hz band-pass filter before classification. The electrode layout followed the standard 10–20 protocol and signals from only 9 channels (Pz, PO5, PO3, POz, PO4, PO6, O1, Oz, and O2) in the occipital region were recorded for recognition during the online free-spelling experiment.

Instead of conforming target recognition to a fixed data length, the applied asynchronous system strategy was programmed to optimize control decision customized by the subject’s signal quality, which renders a more practical and natural spelling experience [11]. The recognition

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**Table 1** Subject information.

|                      |        |
|----------------------|--------|
| Gender               | Male   |
| Age                  | 37     |
| Time since diagnosis | 11yrs  |
| Artificial ventilation| Yes    |
| Limb muscle control  | Absent |
| Eyelid muscle control| Not available |
| Eye movement         | Weak   |
| Communication mode   | Eye movement |

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Fig. 1 Stimulation configuration and keyboard layout.
algorithm of the asynchronous system was the spatial-temporal equalization dynamic window (STE-DW). The algorithm finds an adaptive spatial-temporal equalizer that can equalize the signal in both the spatial and temporal domains to reduce the adverse effects of colored noise. Moreover, it determines the suitable window length to acquire a classification result. More details can be found in Ref. [12].

2.3 Communication and home use

The subject initially performed experiments in October 2018 with an English free-spelling test and continued to use the system for daily communication in Chinese once a week from February to March 2019. The home-use section was composed of mostly free spelling where the subject can express caring requirements and personal feelings. All experimental trials were conducted by qualified experimenters or the patient’s caregiver under precise instructions.

In addition to regular home use, the spelling experiment was also performed in a television studio under a strong electromagnetic field environment in March 2019. The system configuration was the same as that for the home use, but an additional “double-spelling Chinese character spelling strategy” was adopted for simplicity and efficiency.

The double-spelling Chinese character spelling strategy was based on Chinese syllabification. The subject spelled a character by staring at the initial target (consonant), final character in sequence. Considering that the subject had difficulties in moving his sight or eyes, the matching initials and finals for most frequently used characters were put on the same buttons. The double-spelling strategy utilized specific combinations of Chinese initials and finals to reduce the spelling steps for a character and the number of targets. With auto-completion for finals and continuous input for words, the module was able to accommodate the user’s spelling pattern.

2.4 Standard dataset acquisition protocol

Standard dataset protocols were designed to build a benchmark SSVEP dataset for ALS patients, which could facilitate specialized algorithm development for real ALS users and evaluate future ALS-oriented BCI communication systems. The entire acquisition protocol composed of three parts: offline frequency scanning for both narrow band (8.0–15.8 Hz) and whole band (8–60 Hz); online instructed spelling where the subject was requested to spell the given English texts; and online English free spelling.

Offline acquisition was distinct from online spelling because no feedback was given in this part. The stimulating and recording set up in this section was identical to the previous online non-

Fig. 2  Photo of home use and spelling in a special environment.
invasive BCI experiment discussed in section 2.2 except for during the whole frequency band scanning, the monitor’s refresh rate was increased to 144 Hz. As for the online English spelling task, two pre-designed texts, i.e., “the quick brown fox jumps over a lazy dog” and “the five boxing wizards jump quickly”, were displayed that cover each character in the entire keyboard layout.

All data acquisition for the standard dataset was operated by well-trained experimenters in an ambient home environment using a 64-channel electrode cap and a wireless amplifier. Programs for further signal processing and SSVEP evaluation were built using MATLAB 2018b. The signal-to-noise ratio (SNR) was computed as the most relevant metric of the SSVEP signal quality, which is defined as the ratio of the amplitude of the given frequency and the mean amplitude of signals within the 2-Hz neighboring frequency bands. Another well-acknowledged metric called information transfer rate (ITR) was used to evaluate online BCI performance, which reflects spelling accuracy, character recognition time, and a number of commands.

3 Results

3.1 Communication with assisted home use

On the subject’s intention to spell freely, the proposed system managed to type meaningful words after only 30 s of calibration. The EEG acquired during the calibration time served as the background estimator using the embedded spatial-temporal filter method, which turned out to be a valid and accurate estimation method over EEG traits.

Sequentially, the subject was able to type greetings in Chinese pinyin on an English keyboard layout, showing that our speller interface design was practical and was easy to use on the first attempt. Over the following months, several practices trained the subject to become a veteran in BCI typing and eventually succeeded in spelling randomly picked Chinese poems from TV shows. Continued home use after the show enabled the subject to express personal feelings, suggestions to the existing BCI system, and a variety of texts.

The subject’s comments on the spelling system were generally positive, which can be easily understood from the subject’s responses in the following table. When we asked whether the spelling mechanism was hard for him and whether he felt tired of using this, the subject replied that it was not complicated (“不复杂我都记住啦”) and he did not feel tired (“不累”) in Chinese. He even suggested that we should increase the experiment time and intensity in Chinese (“可以增强度”). Suggestions from the subject mainly concentrated on the integration of our spelling system with Microsoft Word-like applications (“我想用它每天写点东西, 能不能有个沃嘚文档”), which will be discussed in section 4.2.

Statistically, we analyzed the representative text by displaying the spelling contents with its actual inputs and total time, then, concluded that 363 characters were correctly outputted out of a total of 406, which is equivalent to an accuracy of 89.4%. The final ITR was 22.203 bits/min. Other studies argued that to build a BCI for real-life applications, the accuracy has to exceed 70% [13]. Especially for patients with ALS, the importance of accuracy rather than solely pursuing on ITR is what makes the ALS-oriented system efficient. The results presented here indicated that the proposed SSVEP BCI speller not only exceeded the baseline 70% accuracy but also had the best ITR compared to other similar studies [2, 14, 15], to the best of our knowledge. Furthermore, our system did not exhaust the subject with tedious training procedures. Unlike non-invasive P300 spellers and even invasive BCI [5], which could allow spelling of 2 characters per minute after
weeks of training, the BCI proposed in this study was able to spell 1.5–2.5 Chinese characters per minute without any training procedure, which offered the subject a natural spelling experience similar to using a keyboard for the first time. These show that the system was capable of providing relatively efficient, accurate, and natural communication for ALS patients.

A concrete statistical analysis on the subject’s SSVEP signal can be found in section 3.2.3. The subject did not exhibit nor expressed unbearable visual fatigue during usage.

### 3.2 SSVEP signal evaluation

Signal evaluation was conducted to further elucidate the subject’s SSVEP signal’s quality. All results in this section were analyzed from the standard dataset acquired in section 2.4.

#### 3.2.1 Spatial-temporal analysis

To evaluate the signal quality of the subject’s SSVEP data, we performed spatial-temporal analysis based on the data of the offline frequency scanning paradigm. Fig. 3 shows a temporal waveform of the SSVEP signal from the Oz electrode elicited by a 15-Hz stimulus. The averaged waveform exhibited a distinct periodic coherent brain responses with peaks at 15 Hz with its second, third, or even fourth domain harmonics in the frequency domain. These findings signify a typical SSVEP brain response. They also explain the underlying control mechanism of SSVEP-based BCI speller. Moreover, they crucially provide insights into the feasibility of the subject’s robust

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### Table 2  Chinese spelling contents and performance information.

| Spelling content | Actual input | Total number of inputs | Number of correct inputs | Total spelling time (s) |
|------------------|--------------|------------------------|--------------------------|------------------------|
| 高兴就好        | g 0 g ao x ing 2 jiu h ao 3 2 | 13                      | 12                       | 123.0                  |
| 可以增强度       | k e y 3 z v # o # # z ai # eng jia 2 q # # q iang d u # 6 | 26                      | 20                       | 311.3                  |
| 爸爸速干衣       | b a b 2 s u g # g an 3 y i f 5 # | 21                      | 19                       | 232.7                  |
| 我相写点设计思想用遮盖你们先回避留下姐姐用笔笔记写 | w o x 5 iang 3 x 5 iang 3 x ie d ian 5 2 sh e ji 2 si x iang 2 y ong 1 2 b # zh e g 4 k # n ing # i m 4 x ian 3 h ui 3 d # x ue xiao b # # 7 1 0 # i # iu x i a l ai 2 # j j ie j ie 2 y ong zh 6 # b i j i 6 x i e x i a l uan # 4 e b | 99 | 88 | 1342 |
| 不累            | t b u # e l i 4 4 | 8                      | 7                        | 71.2                   |
| 天命风流你       | t i a n m ing r 3 # f eng l iu 3 3 n i b u # 2 | 20                      | 17                       | 254.9                  |
| 我想用它每天写点东西，能不能有个沃嘚文档 | h w o x 5 5 z # # # x iang 1 x # 2 y ong 2 t 4 m e i t 8 x i e d ian t # 5 2 d ong x i 2 , n eng 2 b u # 2 n eng 2 y ou # ou g 2 w o 5 d e j i # 6 w en d ang 2 | 69 | 61 | 600.8 |
| 怎么找寻，我可以看见别人说话的绿框嘛 | z e n m 2 zh a o x 4 , w o 2 k e h # y 3 k an j 3 b i e r 2 sh uo h ua 2 d e 2 1 v k uang 6 6 m 9 | 42 | 41 | 589.7 |
| 辛苦啦          | x i n k 2 1 3 | 6                      | 6                        | 58.8                   |
| 这个电脑什么牌子雷蛇 | z h e g 2 d ian n a o 2 sh en m ie # 3 p a i z 2 1 e i sh e 3 ch 2 # y # # sh e 9 | 33 | 31 | 319.7 |
| 贵吗            | g 9 # g u i m a r 4 4 # | 11                      | 9                        | 130.3                  |
| 你们回吧         | n # n i m 4 h ui bu 3 # 4 | 13                      | 11                       | 139.2                  |
| 不复杂我都记住啦  | b u 2 2 # f u z 2 w o 2 d ou 4 # d u # ou 2 j i zh u 2 1 3 | 28                      | 25                       | 301.1                  |
| 告诉 36 存文档   | g a o s 3 sh # 3 6 c un 2 w en d ang 4 5 | 17                      | 16                       | 215.3                  |
Fig. 3  Spatial-temporal analysis. (A) SSVEP signal in time domain. (B) SSVEP signal in frequency domain. (C) Topographic maps of SSVEP signals. (D) Topographic maps of SSVEP signals.

close control over the proposed system.

3.2.2 Signal-to-noise ratio analysis

SNR is one of the most useful metrics for estimating signal quality and is directly associated with BCI performance [16].

SNR across the given frequency band reflects the subject's sensitivity to certain frequencies, yielding evidence to adjust a customized system design. The analysis in Fig. 3 shows that there is a decreasing trend from lower to higher frequency bands; this phenomenon is universal and has been reported in healthy demographics. Also, the topography depicted by the SNR in different frequencies shows distinct spatial patterns, which is in agreement with the general frequency response where brain response in lower frequencies tends to be more concentrated in the occipital region rather than being diffused in others.

3.2.3 BCI performance

The theoretical performance of the SSVEP-based BCI in this section is from the online cued English spelling experiment.

Accuracy, defined as the proportion of correct trials, is the most direct evaluation criterion used in BCI systems, especially those designed for ALS patients' communication. An accurate system guarantees robustness and feasibility. Fig. 4(D) reflects the confusion matrix of the online English free-speller experiment result, where the X-axis is the stimulus frequency and the Y-axis is the resulting frequency. In general, the output is related to the system input and 10 specific frequency stimulation results were correct. However, we cannot ignore the fact that mistakes appeared and the frequencies corresponding to the mistaken output are mostly lower than the actual stimulation frequency. The mean accuracy of the 7-block experiment was 75.1%, the maximal accuracy was 95.9%, and the minimum was 61.1%.

Besides accuracy, the average recognition time is also an essential index to judge the system performance. It is usually believed that the average recognition time is relevant to the signal's quality. As shown in Fig. 4, the online English speller experiment's results indicate that the average time for different frequency stimulations is different. In total, the mean detection time of the 7-block experiment was 4.69 s, the maximum was 8.1 s, and the minimum was 3.41 s. In 223 correct trials, the detection times of 3 trials were higher than 10 s. It can be inferred from Fig. 4(A) that the detection times of major trials were below 6 s. Moreover, the distribution of the average detection time and the stimulation frequency are shown in Fig. 4(B), which demonstrates that the subject has different sensitivities toward...
distinct frequency stimulations. These show that the dynamics strategy can successfully yield output characters in flexible and reasonable time.

Taking the two aforementioned essential factors together, we then analyze the ITR, which is the most authoritative and quantitative evaluation criterion used in non-invasive BCIs [17]. For the whole 7 blocks, the maximum ITR was 77.90 bits/min and the minimum was 21.34 bits/min. In general, the average ITR of the online English test was 46.70 bits/min, which was significantly higher than that of the online free spelling, which could be explained by the effects of distinct experiment configurations. To the best of our knowledge, the ITR covered in this case has not been reported in other non-invasive and patient-oriented BCI studies, and further indicates that the patient using this system can communicate rapidly and correctly.

We could, if necessary, modify the system configuration further to boost the BCI’s performance in terms of ITR. Two assumptions have been made prior to system design, which could lead to underwhelming performances if not achieved. Firstly, the human brain has different SSVEP response intensities to stimuli of different frequencies [18]. Secondly, spontaneous EEG signals are not completely white noise [19]. For example, alpha-band frequency components will influence the SNR of similar frequency components and easily arouse error judgments. Hence, diversity of response intensities exists in practical system applications. A more effective and convenient system can be achieved when we know the
subject’s response characteristics in section 3.2.1 and 3.2.2. For instance, we could assign the most frequently used character to be the frequency response with the highest SNR.

4 Discussion

The analysis showed no differences in the ALS patient’s SSVEP signals compared to healthy subjects. ALS patients suffer from motor function disabilities with the rest of the brain intact, including the visual system. Consequently, the relatively low SNR indicates merely demographic variability and is susceptible to the patient’s mental state, fatigue, willingness to participate, and others. Hence, the feasibility of SSVEP-based BCI speller needs to be validated on a larger patient population to provide long-term, stable, and robust evidence for its use. In practice, from both the patient’s feedback and our observation, improvements in the system have been made to improve user experience. Therefore, we discuss comparisons between the proposed speller and other communication modalities for ALS patients, as well as further describing potentials for improving user experience.

4.1 Comparison with current studies

4.1.1 SSVEP BCIs with other BCIs

SSVEP-based BCIs are significantly better than P300-based BCIs in terms of ITR. Compared to current ALS-oriented BCIs, which are predominantly P300 BCI spellers, the typical ITR for a patient with ALS was reported to be 5.89–19 bits/min [2, 14, 15] (mostly under 15 bits/min), whereas the ITR for SSVEP BCI speller was 22.5 bits/min. Despite the insignificant difference between the SSVEP signal of the patient and healthy demographics, the ITR concluded in this case was indeed dramatically lower than the highest communication speed of typical SSVEP spellers, which we suspect is because of our choice of a much more conservative parameter setting to guarantee accurate typing for the patient. Nonetheless, this comparison implies that our SSVEP-based BCI speller is dominantly efficient than BCIs based on the P300 paradigm. Besides, to the best of our knowledge, none of the aforementioned studies have implemented Chinese in their spelling settings, which we did here using an efficient double-spelling strategy.

4.1.2 SSVEP BCIs with eye-tracking speller

Eye-tracking devices are currently used by patients with ALS for communication. Recent comparisons have suggested that eye-tracking spellers can communicate with a speed of 86 bits/min [20]. After calibration, subjects using eye-tracking devices can have natural and rapid computer control spelling, and commercially available devices using eye-tracking as an alternative cursor inherited various applications that not only enable necessary commination but also engage users in active social life. The spelling performance of the SSVEP speller and eye-tracking devices should be further compared in a larger population, especially for patients with a disability; however, in this study, we found that the SSVEP speller could not match the performance of an eye tracker in terms of communication speed. We do emphasize that comparisons between different modalities are difficult to evaluate; hence, further studies need to be conducted in this regard.

Many studies have argued that communication for patients with a disability should first prioritize accuracy and user experience rather than performance. The patient in our study reached an acceptable online spelling accuracy of 89.4%; however, we were unable to measure the accuracy of the eye tracker so direct comparisons cannot be made. Nonetheless, a comparison of the accuracy of c-VEP and eye tracker showed no
systematic difference across subjects. As for user experience, subjects using both eye trackers and SSVEP spellers suffer from visual fatigue after long-term use, which worsens the experience and possibly impedes daily communication. Yet in this study, the patient did not complain about such discomfort, instead, relentlessness and unstable eye-tracking calibration bothered the patient the most in daily use. This observation was also supported by the study of Nezamfar et al. showing that eye trackers are susceptible to slight head movement [20]. On the contrary, the BCI speller used in this study was not constrained by complicated and unstable calibration, thus it has more usability. In conclusion, the communication rate of eye-tracking devices was found to be higher than the speller. Eye trackers provided a sophisticated platform created on various computer applications, which is what SSVEP-based BCI is missing currently. Nevertheless, the eye tracker’s susceptibility to head movement affects the user experience during long-term use, which the SSVEP speller has an advantage on.

4.2 Toward a user-friendly device

4.2.1 User-friendly interface

Complicated acquisition and speller interface are designed for academic use and not for home use. The patient’s caregivers mentioned that independent operations on the proposed system are excessively difficult for them to operate, especially because they seldom use a personal computer. This emerged as the major obstacle for long-term home use.

Consequently, more effort should be devoted to develop a user-oriented system interface and discard unnecessary set-up procedures.

4.2.2 Convenient setting procedure

Non-invasive BCIs have always had the problem of inconvenient preparation routine especially impedance fitting. This problem is more evident for ALS patients because most of them in LIS are constrained in a fixed position, i.e., sitting on a wheelchair or laying on the bed, which inevitably requires excessive effort in the preparation step.

Luckily, in this case, we reduced the size of the electrode cap to 9 channels (reference and ground channels are not included), covering the entire occipital area. During home use, this montage allowed the whole preparation to be completed in under approximately 20 min by an experienced experimenter. In practice, impedance fitting appeared to not cause significant complications to untrained caregivers. Therefore, our experiment montage permits a reasonably setting practice even for inexperienced experimenters and caregivers.

However, to diminish further inconvenience for patients and their caregivers, improvements on dry electrodes and other long-term stable recording techniques need to be developed in the future.

4.2.3 Sophisticated software development

The current BCI system offers only a text input proxy, while the affiliated software developments are still in absence, which is needed to engage users; especially real patients in daily use. Applications like E-mail and social media are critical extensions of the communication. In this case, the patient has been strongly expressing the intention of communicating on social media using this system. Therefore, such developments should be made in the future.

5 Conclusion

Here, we showed the feasibility and efficiency of an SSVEP-based BCI for communication of an ALS patient. The patient was able to communicate practically and rapidly under complicated environments for various means, with the help
of a calibration-free asynchronous speller system. The free-spelling experiment demonstrated that our system is robust and productive enough to facilitate communication for ALS patients and can be further modified according to the SSVEP standard dataset.

**Conflict of interests**

The authors declare no conflict of interests in this work.

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