A P300-Based BCI System Using Stereoelectroencephalography and Its Application in A Brain Mechanistic Study

Weichen Huang¹, Peiqi Zhang¹, Tianyou Yu¹, Zhenghui Gu, Qiang Guo∗, Yuanqing Li∗ Fellow, IEEE

Abstract—Stereoelectroencephalography (SEEG) signals can be obtained by implanting deep intracranial electrodes. SEEG depth electrodes can record brain activity from the shallow cortical layer and deep brain structures, which is not achievable through other recording techniques. Moreover, SEEG has the advantage of a high signal-to-noise ratio (SNR). Therefore, it provides a potential way to establish a highly efficient brain-computer interface (BCI) and aid in understanding human brain activity. In this study, we implemented a P300-based BCI using SEEG signals. A single-character oddball paradigm was applied to elicit P300. To predict target characters, we fed the feature vectors extracted from the signals collected by five SEEG contacts into a Bayesian linear discriminant analysis (BLDA) classifier. Thirteen epileptic patients implanted with SEEG electrodes participated in the experiment and achieved an average online spelling accuracy of 93.85%. Moreover, through single-contact decoding analysis and simulated online analysis, we found that the SEEG-based BCI system achieved a high performance even when using a single signal channel. Furthermore, contacts with high decoding accuracies were mainly distributed in the visual ventral pathway, especially the fusiform gyrus (FG) and lingual gyrus (LG), which played an important role in building P300-based SEEG BCIs. These results might provide new insights into P300 mechanistic studies and the corresponding BCIs.

Index Terms—Brain-computer interface (BCI), stereoelectroencephalography (SEEG), P300.

I. INTRODUCTION

Brain-computer interfaces (BCIs) provide a feasible approach for humans to interact with computers without the participation of peripheral nerves and muscles [1]. Event-related potentials (ERPs) are common brain patterns used to examine brain activities and cognitive functions in stimulus-response paradigms and produce control signals in BCIs. P300, one of the ERP components, is evoked by a target oddball stimulus in the auditory, visual, or somatosensory modalities and occurs at a latency of approximately 300 ms, depending on the subject and event-eliciting variables [2]. To date, diverse types of BCI systems have been developed based on P300, such as word spelling [3], prosthetic device control [4], and cognitive assessment for patients with disorders of consciousness [5].

The most common BCI systems to date are based on electroencephalography (EEG) signals. EEG is noninvasive, less technically demanding than other methods, and easy to perform [6]. However, many obstacles hinder the development of EEG-based BCIs. EEG signals are highly mixed and noisy, which may affect the performance of BCI systems [7]. Moreover, EEG cannot record intracranial brain activity and has a limited topographical resolution and frequency range [8], which restricts its use in studies of brain mechanisms.

Stereoelectroencephalography (SEEG), which was developed by Bancaud et al. in the 1960s [9], is becoming a prevalent tool for the surgical treatment of intractable epilepsy. It has played an important role in recent years in seizure prediction and localization of epilepsy [10]. Intracranial SEEG electrodes are very thin cylindrical leads with multiple concentric metal contacts along their length, which are used to acquire signals. Hence, each electrode provides multiple channels of brain signals. These SEEG electrodes can be flexibly inserted into the brain to a stereotactically defined depth and angle [11]. The advantages of SEEG are that its electrodes can record signals in the shallow cortical layer and deeper brain structures, which are not accessible by other implanted recording techniques such as electrocorticography (ECoG) [12]. SEEG signals have a high signal-to-noise ratio (SNR) [13]. Signals from the deeper regions might also help us decode brain activities. Therefore, SEEG provides another potential method of establishing high-performance BCIs. More importantly, these intracranial signals may help to build platforms to explore the neural mechanisms of some cognitive activities.

To date, several BCI systems have been built based on SEEG signals. For instance, Vadera et al. built an SEEG-based BCI to control a 2D cursor through movements of the user’s hands and feet. Two subjects achieved average correlation coefficients of 0.32 in the X-direction and 0.11 in the Y-direction between the target trajectories and actual trajectories [11]. Yamin et al. used an SEEG-based BCI system...
for neurofeedback. Two subjects successfully downregulated their amygdala gamma band activities [14]. Li et al. built an SEEG-based BCI system that enabled users to control a prosthetic hand through hand gestures. Three subjects achieved an average accuracy of 78.70% in three-class predictions [15]. In these studies, only a few subjects were recruited, and further experiments are needed to examine the performance of SEEG-based BCIs.

Krusienski et al. built a P300 speller system containing 36 flashing buttons with an oddball paradigm for row-column intensification using SEEG signals [16]. In their study, the two subjects achieved an average accuracy of 90% and a maximum information transform rate (ITR) of over 20 bits/min based on 16 contacts. This was the first attempt to build an SEEG-based BCI speller system; however, the number of subjects included is far from sufficient to validate the effectiveness of the system, and further study is needed to improve the spelling accuracy and ITR performance. More importantly, the temporal and spatial characteristics of intracranial P300 signals and the underlying neural mechanism of P300 need to be further explored.

In this study, we established a P300-based BCI speller using SEEG signals based on a single-character oddball paradigm. The graphical user interface (GUI) contained 40 buttons corresponding to 40 numbers, which flashed in a random order. Subjects could input a number by focusing on the flashes of the corresponding button. Thirteen epileptic patients participated in our experiment, and the experimental results demonstrated that SEEG was an effective way to construct BCIs. Since the SEEG electrodes can record signals in a stereotactically defined region, the brain regions, which were important for our P300-based SEEG BCI, could be precisely located. Based on the single-contact decoding results, these regions were mainly distributed in the visual ventral pathway, such as the fusiform gyrus (FG) and lingual gyrus (LG). In the future, these brain regions could be directly applied in P300-based SEEG BCI systems. Several electrodes (7 to 13 electrodes; diameter of 0.8 mm; DixiMedical, France) were implanted by a Stereotactic Assistant (ROSA) robotic device (Medtech, France) to localize the seizure origin. Detailed information regarding these subjects is shown in Table I. The subjects were recruited for neurofeedback. Two subjects successfully downregulated their amygdala gamma band activities [14].

| Subject | Sex | Age | Handedness | number of electrodes | number of contacts |
|---------|-----|-----|------------|----------------------|-------------------|
| S 1     | M   | 41  | Right      | 12 (10/2)            | 172 (150/22)      |
| S 2     | M   | 55  | Right      | 12 (12/0)            | 188 (188/0)       |
| S 3     | M   | 22  | Right      | 8 (8/0)              | 122 (122/0)       |
| S 4     | M   | 41  | Right      | 12 (0/12)            | 179 (0/179)       |
| S 5     | M   | 28  | Right      | 7 (7/0)              | 88 (159/0)        |
| S 6     | M   | 35  | Right      | 8 (8/0)              | 132 (132/0)       |
| S 7     | F   | 21  | Right      | 15 (11/2)            | 175 (151/24)      |
| S 8     | M   | 21  | Right      | 11 (0/11)            | 147 (0/147)       |
| S 9     | F   | 38  | Right      | 8 (8/0)              | 120 (120/0)       |
| S 10    | M   | 18  | Right      | 13 (11/0)            | 180 (180/0)       |
| S 11    | M   | 19  | Right      | 13 (11/2)            | 172 (148/24)      |
| S 12    | F   | 26  | Right      | 9 (9/0)              | 118 (118/0)       |
| S 13    | M   | 21  | Right      | 9 (9/0)              | 109 (109/0)       |

The numbers in parentheses represent the number of electrodes or contacts in the left and right hemispheres (left/right).

Section V.

II. METHODOLOGY

A. Subjects

Thirteen patients with epilepsy (average age of 29.7 years old; 10 males and 3 females) participated in our experiment. None of the participants had previously used a BCI system. For each subject, several electrodes (7 to 13 electrodes; diameter of 0.8 mm; DixiMedical, France) were implanted by a Stereotactic Assistant (ROSA) robotic device (Medtech, France) to localize the seizure origin. Detailed information regarding these subjects is shown in Table I. The subjects participated in the experiment one week after the SEEG electrodes were implanted. They all passed examinations to exclude cognitive disturbances and dementia and were able to understand the experimental requirements. All subjects signed informed consent forms before the experiment began. They had no abnormal symptoms, such as epileptic seizures, in the two hours before the experiment. The experiment was supervised by the patients’ families and clinical doctors to prevent the occurrence of a sudden seizure. This study was also approved by the Ethics Committee of Guangdong Sanju Brain Hospital (approval number: 2020-020-072, Guangzhou, China).

B. Data Acquisition

In this study, the data, including SEEG signals and trigger events, were obtained using a Nihon Kohden (Irvine, CA) system. The impedances of all signal contacts were controlled below 5 kΩ. The raw signals were amplified and sampled at 1000 Hz. Then, the signals were filtered by a hardware-based notch filter at 50 Hz. Trigger events were recorded with timestamps that were used to mark the beginning of specific experimental events.

C. Graphical User Interface (GUI) and Experimental Procedure

Before the experiment, the subjects were informed about the procedure of the experiment and were asked to sit on a
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D. Data Analysis

1) Data Preprocessing and Feature Extraction: The raw SEEG signals were first filtered with a tenth-order finite impulse response (FIR) bandpass filter between 0.5 and 20 Hz. Next, for each flash, a series of 600-point data segments (600 ms from the onset of the flash) were obtained based on the filtered data, where each segment was obtained from a contact. For each data segment, we removed the baseline by subtracting the average value of the previous 100 points (100 ms) before the flash onset. Subsequently, we downsampled the data segments from 1000 Hz to 50 Hz. Specifically, we retained the first sample for every 20 samples. Consequently, a 30-dimensional data vector was obtained for each flash and each electrode contact.

2) Single-Contact Decoding and Channel Selection: In the following, we first consider using a single contact for decoding and then choose the best contacts for the online experiment. Forty trials in the calibration run were randomly divided into 10 parts. Then, ten-fold cross-validation was implemented using Bayesian linear discriminant analysis (BLDA). Specifically, by averaging the data vectors comprising the 10 flashes for each button, 36 feature vectors corresponding to target buttons and 1404 feature vectors corresponding to nontarget buttons were obtained for the contact, which were then used to train a binary BLDA classifier. Similarly, for each test trial, 40 feature vectors were obtained for all the buttons, which were used for prediction. For each button, a prediction score was calculated by applying the classifier to the corresponding feature vector. The button with the highest score was identified as the target. In this manner, we performed the decoding based on a single contact and calculated the decoding accuracy. Based on the decoding accuracies of all the contacts, the five electrode contacts with the highest accuracies were selected for the online experiment.

3) Model Training and Online Classification: Before the online experiment, the BLDA classifier was first trained using the calibration dataset from the five selected contacts. Specifically, we concatenated the feature vectors of the five selected contacts and obtained a new 150-dimensional feature vector for each button. Next, we used these feature vectors (40 for the target buttons and 1560 for the nontarget buttons) to train the classifier. During the online process, 40 feature vectors corresponding to the 40 buttons were similarly obtained for each trial and sent to the classifier. The button with the maximum prediction score was thus identified. Then, the number corresponding to the identified button was displayed in the text box.

4) Simulated Online Analysis: Based on the data collected in the online experiment, we performed a simulated online analysis to show the change in performance with respect to the number of repeats of flashes. The simulated online analysis was similar to the online experiment except that we extracted feature vectors by averaging the data vectors of the first n repeats of flashes (n from 1 to 10). Additionally, the simulated online analysis was carried out separately based on each contact and the five selected contacts. In addition, to further assess the performance of our system, ITRs were also calculated for each repeat of flashes based on a single contact and the five selected contacts. The calculation method of the ITR can be found in [1].

5) Permutation Test for Single-Contact Decoding: To identify the contacts with significant decoding accuracies, we implemented a permutation test with 1000 repetitions for each subject. Specifically, for each repetition, we calculated the decoding accuracies using the same method as that used for single-contact decoding, except that the target labels were randomly provided. Then, we identified the maximum decoding accuracy among all the contacts for one subject and began the next repetition. Therefore, we obtained 1000
pseudo-accuracies for each subject. Then, the permutation p-value of each contact was calculated as the proportion of 1000 corresponding pseudo-accuracies greater than or equal to the actual accuracy. Finally, we obtained the contacts with significant decoding accuracies, the permutation p-values of which were less than 0.05 (false discovery rate (FDR)-corrected for multiple comparisons).

6) Electrode Localization: The number of electrodes and contacts for each subject are shown in Table I. To localize the electrodes, we integrated the anatomical information of the brain provided by pre-surgery T1-weighted images and spatial information of electrode positions provided by post-surgery computed tomography (CT) images using Statistical Parametric Mapping software, version 12 (SPM12, http://www.fil.ion.ucl.ac.uk/spm) running in the MATLAB environment (MathWorks, MA, USA). Moreover, we converted the coordinates of the contacts into the Montreal Neurological Institute (MINI) standard space using the ImAGIN toolbox (https://f-tract.eu/software/imagin/) and obtained the brain regions where the contacts were located based on the Automated Anatomical Labeling (AAL) template.

7) Event-Related Potential (ERP) Analysis: The ERP curves were calculated using data recorded in the calibration run when subjects were focusing on the flashing buttons. For each subject, we first averaged the SEEG signals from all the contacts in each brain region to serve as the signal of the corresponding region. Next, for each flash, we cut out a data segment from 200 ms before the onset of the flash to 600 ms after the flash. Then, we averaged the data segments for the flashes corresponding to the target buttons and nontarget buttons, respectively, and obtained the ERP waveforms for each brain region and each subject.

8) Functional Connectivity Analysis: Functional connectivity analysis was implemented using the signal segments from all the contacts with significant decoding accuracies in gray matter, because signals were seldom generated and processed in white matter. For each subject, all the contacts with significant decoding accuracies were selected based on the result of single-contact decoding. Furthermore, the SEEG signals of all the significant contacts within each brain region were averaged to serve as the signal of the corresponding region for functional connectivity analysis. For each brain region, the raw signals in the calibration run were first segmented into 40 time series corresponding to 40 trials (0 to 12 s from the onset of each trial). Then, we downsampled these series to 250 Hz. Therefore, a 3000-point signal segment was obtained for each brain region and each trial. Next, we performed a multivariate GC analysis to assess the functional connectivity between different brain regions. Specifically, for each pair of brain regions (e.g., brain regions A and B), we calculated the two GC values using the signal segments of these two regions: one represented the strength of the connection from brain region A to brain region B, and the other represented the strength of the connection from brain region B to brain region A. After obtaining the GC values from all the pairs of brain regions, we implemented a permutation test to estimate the significance of these connections. Specifically, for each pair of brain regions, we subdivided the time intervals of signal segments from these two brain regions into 10 subsegments and randomly permuted the data for these subsegments. Then, we calculated a pseudo-GC value using these permuted data. This process was repeated 1000 times, and we obtained 1000 pseudo-GC values. Then, the permutation p-value of each actual GC value was calculated as the proportion of the 1000 corresponding pseudo-GC values greater than or equal to the actual GC value. Finally, the permutation p-values were thresholded at \( p < 0.05 \) (FDR-corrected for multiple comparisons). We performed GC analysis using the code from the multivariate GC (MVGC) toolbox (https://users.sussex.ac.uk/~lionelb/MVGC/) running in the MATLAB environment [17].

III. RESULTS

A. Online Results

Thirteen subjects participated in our experiment and completed an online experiment of 30 trials. The accuracies achieved by the thirteen subjects in the online experiment are presented in Table II. Using our SEEG-based system, all the subjects achieved online accuracies ranging from 70% to 100%. The average spelling accuracy with a standard deviation of 93.85 ± 9.01% was significantly higher than the random level of 2.5% (\( p < 0.0001 \); \( \chi^2 \) test). These results validate the hypothesis that subjects are able to implement number input through our SEEG-based BCI system.

B. Single-Contact Decoding

We implemented cross-validation using the features from only a single contact and calculated the mean decoding accuracies of all the contacts from 13 subjects in each brain region. As shown in Fig. 2, we list the top six regions that achieved the highest average decoding accuracies, which are the FG, inferior occipital gyrus (IOG), LG, middle occipital gyrus (MOG), inferior temporal gyrus (ITG), and middle temporal gyrus (MTG), respectively. Notably, these brain regions are all in the visual ventral pathway. Although the numbers of contacts were different between brain regions, they had no significant influence on the average decoding accuracy. To further assess the decoding accuracies between these brain regions in the visual ventral pathway, a one-way ANOVA was implemented. From the results, we found that the distributions of decoding accuracies in these six brain regions were significantly different (\( F(5,529) = 38.02 \); Bonferroni-corrected \( p < 0.0001 \)). Specifically, as shown in Table III, the accuracies of the FG and IOG were significantly higher than those of the other four brain regions (Bonferroni-corrected t-test \( p < 0.05 \)). Moreover, the accuracy of the LG was significantly higher than that of the ITG and MTG (Bonferroni-corrected t-test \( p < 0.05 \)).

Moreover, using permutation tests, we found all the contacts with significant decoding accuracies. The locations of these contacts are shown in Fig. 3, and the brain region distribution of these contacts is shown for all subjects in Table V. Excluding the white matter region, the majority of contacts with significant decoding accuracy are distributed in the visual ventral pathway, including the FG, LG, ITG, MTG, IOG, and MOG. Moreover, within each brain region, we calculated...
TABLE II: Spelling accuracies in the online experiment

| Subject | S1 | S2 | S3 | S4 | S5 | S6 | S7 | S8 | S9 | S10 | S11 | S12 | S13 | Mean ± Std |
|---------|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-----------|
| Accuracy (%) | 93.33 | 100 | 90 | 100 | 100 | 83.33 | 90 | 100 | 93.33 | 100 | 100 | 70 | 93.85 ± 9.01 |

TABLE III: P-values for comparisons between decoding accuracies of different brain regions

| MOG | MTG | ITG | IOG | LG | FG |          |          |
|-----|-----|-----|-----|----|----|----------|----------|
|     |     |     |     |    |    | FG       | IOG      |
|     |     |     |     |    |    | 0.0016   | 0.0244   |
|     |     |     |     |    |    | 0.0368   | 0.0453   |
|     |     |     |     |    |    | <0.0001  | <0.0001  |
|     |     |     |     |    |    | <0.0001  | <0.0001  |
|     |     |     |     |    |    | <0.0001  | <0.0001  |
| Mean ± Std | 0.01 ± 0.0 | 0.31 ± 0.0 | 93 ± 9 |

P-values in bold indicate that the corresponding pairs of comparisons are significant (Bonferroni-corrected t-test p < 0.05).

Fig. 2: Distribution of the single-contact decoding accuracies of all the contacts from 13 subjects in the top six brain regions that achieved the highest average decoding accuracies. In each box, the red central mark represents the median decoding accuracy across all the contacts in the same brain region. The bottom and top edges of the box indicate the 25th and 75th percentiles, respectively. The whiskers extend to the most extreme data points not considered outliers, and the outliers are plotted individually using the ‘+’ symbol. FG = fusiform gyrus, MOG = middle occipital gyrus, LG = lingual gyrus, MOG = middle occipital gyrus, ITG = inferior temporal gyrus, MTG = middle temporal gyrus.

TABLE IV: Distribution of contact with the highest decoding accuracy for each subject

| Subject | Brain Region that Involves the Contact with the Highest Decoding Accuracy |
|---------|--------------------------------------------------------------------------|
| S1      | Inferior Temporal Gyrus                                                 |
| S2      | Fusiform Gyrus                                                           |
| S3      | Middle Occipital Gyrus                                                  |
| S4      | Middle Temporal Gyrus                                                   |
| S5      | Inferior Temporal Gyrus                                                 |
| S6      | Fusiform Gyrus                                                           |
| S7      | Fusiform Gyrus                                                           |
| S8      | Fusiform Gyrus                                                           |
| S9      | Middle Occipital Gyrus                                                  |
| S10     | Fusiform Gyrus                                                           |
| S11     | Fusiform Gyrus                                                           |
| S12     | Fusiform Gyrus                                                           |
| S13     | Fusiform Gyrus                                                           |

the ratio of the number of contacts with significant decoding accuracies to the number of contacts in the same region. The results indicate that this ratio is higher in the visual ventral pathway than in other regions. Furthermore, the FG showed the best performance in both the number and ratio of contacts.

To further determine which brain region(s) are more important for our SEEG-based BCI, we list the brain regions that involve the contact with the highest decoding accuracy for each subject, which is shown in Table IV. We found that the contact with the highest decoding accuracy for 8 subjects was located in the FG, and the contact with the highest decoding accuracy for the remaining 5 subjects was also located in the visual ventral pathway. Taken together, these results demonstrate that the visual ventral pathway, especially the FG, plays a pivotal role in building P300-based SEEG BCIs.

C. Simulated Online Results

We implemented a simulated online analysis of all thirteen subjects using the data recorded in the online experiments. Fig. 4 shows the curves of the average accuracies with their standard deviations and the ITRs, based on the five selected contacts with respect to the number of flash repeats. Specifically, the average spelling accuracy of the thirteen subjects is 93.85 ± 9.01% when the number of repeats is ten, and the maximum average ITR of our system is 54.25 bits/min when the number of repeats of flashes is two. These results validate the feasibility of our SEEG-based speller system using signals from the five selected contacts.

Moreover, we calculated the spelling accuracies and ITRs for each repeat of flashes based on a single contact. Fig. 5 shows the curve of average simulated online accuracies and ITRs based on a single contact with respect to the number of flash repeats. The average accuracy of thirteen subjects is 71.28 ± 22.87% when the number of repeats is 10, while our system achieves a maximum average ITR of 23.19 bits/min when the number of repeats of flashes is three. These results demonstrate that our system can achieve an acceptable performance even when using only a single contact.

D. ERP Waveforms

We present the ERP curves from contacts in the FG and LG, as shown in Fig. 6, whereas there is no significant ERP waveform in the other brain regions. These curves were
Fig. 3: Locations of contacts with significant decoding accuracies in MNI space. Nodes with different colors represent the locations of the corresponding contacts in different brain regions. OT = other grey matter regions, WM = white matter regions. (a) Sagittal view (left hemisphere). (b) Axial view. (c) Sagittal view (right hemisphere).

TABLE V: Distribution of contacts with significant decoding accuracies for all subjects

| Region                     | Number of Contacts with Significant Decoding Accuracies | Ratio of Contacts with Significant Decoding Accuracies |
|----------------------------|--------------------------------------------------------|------------------------------------------------------|
| Fusiform Gyrus             | 42                                                     | 56.76%                                               |
| Lingual Gyrus              | 17                                                     | 24.29%                                               |
| Inferior Temporal Gyrus    | 13                                                     | 13.69%                                               |
| Middle Temporal Gyrus      | 12                                                     | 6.15%                                                |
| Inferior Occipital Gyrus   | 10                                                     | 50.00%                                               |
| Middle Occipital Gyrus     | 6                                                      | 15.79%                                               |
| Postcentral Gyrus          | 4                                                      | 9.52%                                                |
| Superior Temporal Gyrus    | 3                                                      | 3.89%                                                |
| Precentral Gyrus           | 2                                                      | 13.33%                                               |
| Superior Parietal Gyrus    | 2                                                      | 7.41%                                                |
| Inferior Parietal Gyrus    | 2                                                      | 4.76%                                                |
| Rolandic Operculum         | 1                                                      | 4.76%                                                |
| Superior Occipital Gyrus   | 1                                                      | 3.57%                                                |
| Precuneus                  | 1                                                      | 0.90%                                                |
| White Matter               | 17                                                     |                                                      |

The visual ventral pathway includes the FG, LG, ITG/MTG, and IOG/MOG.

calculated using data recorded in the calibration run when subjects were focusing on the target buttons. In each subplot, two curves were obtained by averaging the SEEG signals from all the contacts in the FG/LG corresponding to the target buttons (orange lines) and nontarget buttons (blue lines). Fig. 6(a) and Fig. 6(b) show that P300 can be elicited in the FG or LG, respectively, for the majority of subjects. Although the latency time and amplitude of the P300 wave are not identical in these subjects, the P300 waveforms can be clearly observed in the FG and LG.

E. Functional Connectivity Analysis

To determine the connection among different brain regions when subjects were receiving visual oddball stimuli, we implemented GC analysis for all the contacts with significant decoding accuracies in gray matter regions. Because white matter conveys information between gray matter regions and signals are seldom generated and processed in white matter regions, we did not use signals from white matter regions. For each subject, we obtained the mean signal for each brain region by averaging the SEEG signals of all the significant contacts in the corresponding region. According to the results of single-contact decoding, we focused on the brain regions in the visual ventral pathway: the FG, LG, ITG, MTG, IOG, and MOG.

1) Connectivity Between the Visual Ventral Pathway and Other Regions: We calculated the GC values of the 22 causal flows between 6 brain regions in the visual ventral pathway and the other regions outside of the visual ventral pathway. Specifically, there are 6, 5, 2, 3, 4, and 2 causal flows associated with FG, LG, IOG, MOG, ITG, and MTG, respectively. The results are shown in Fig. 7. We found that all 22 causal flows from the visual ventral pathway to other regions are significant through permutation tests, whereas only 12 of those flows are significant in the reverse direction. Moreover, we calculated the average GC value between 6 brain regions in the visual ventral pathway and the regions outside of the visual ventral pathway. As shown in Fig. 7(b), we found...
that the GC values of causal flow from the visual ventral pathway to the other regions were higher than those from the other regions to the visual ventral pathway. Specifically, the GC values of causal flow from the FG and LG to the other regions were significantly higher than those for the opposite direction (\( p = 0.0356 \) for FG, \( p = 0.0366 \) for LG; paired t-test). These results might imply that brain regions outside of the visual ventral pathway were influenced by the visual ventral pathway, especially the FG and LG, when subjects were receiving visual oddball stimuli.

2) Connectivity Within the Visual Ventral Pathway: To further explore the connectivity of the FG and LG, we similarly calculated the GC values within the visual ventral pathway. Specifically, the GC values of 24 causal flows between the FG and the other regions in the visual ventral pathway and 22 causal flows between the LG and the other regions in the visual ventral pathway were calculated. The results are shown in Fig. 8. The connectivity between the LG and MOG was not analyzed because only one subject had implanted contacts with significant decoding accuracy located in both regions. We also calculated the average GC values between the FG/LG and the other regions. The results showed that the GC values of causal flow between regions within the visual ventral pathway did not show significant differences between the two directions. Moreover, 22 causal flows of a total of 24 flows between the FG and the other regions in the visual ventral pathway were significant in both directions through permutation tests, while 19 causal flows of a total of 22 flows between the LG and the other regions in the visual ventral pathway showed significance in both directions. These results imply the existence of strong connectivity in the visual ventral pathway, and brain networks within these regions were activated when subjects were receiving visual oddball stimuli.

IV. DISCUSSION

In the present study, we developed a P300 speller BCI system based on SEEG signals. Thirteen subjects demonstrated that our BCI system was able to achieve high performance. The online results and offline analysis showed the feasibility of our BCI system. Moreover, further offline analysis might reveal the location of important brain regions for building P300-based BCIs. The following discussion is divided into four parts. First, we show the performance of our SEEG-based BCI speller. Second, we show the performance and significance of single-contact decoding. Third, we discuss some brain activities related to P300 that might be useful to build P300-based SEEG BCIs. Finally, we present the limitations of this study and our future work.

A. Performance of our SEEG-Based BCI

To date, the majority of P300 speller BCIs have been built based on EEG signals. With the development of novel stimulus methods and P300 detection algorithms, the performance of EEG-based BCIs has improved in recent years. Conversely, since SEEG-based BCI spellers were proposed, few studies have been implemented to improve the performance in recent years. In our study, we established an SEEG-based BCI speller system using signals from just five contacts, and we compared the performance of our system with that of several BCI speller systems from previous studies in which similar stimulus GUIs and protocols were implemented.

The results of the online test (Table II) and simulation online test (Fig. 4) demonstrated that all the subjects, who were new users of the BCI system, achieved excellent performance in terms of both spelling accuracy and ITR. To further evaluate the performance of our system, we show some existing benchmark P300 speller systems, as summarized in Table VI. The paradigms of these systems are similar to ours. The results show that our system demonstrates an equivalent performance in terms of both spelling accuracy and ITR compared with some benchmark EEG-based speller systems, and it achieves
a substantial improvement in the ITR compared with the previous SEEG-based BCI system.

Notably, our SEEG-based BCI speller achieved these performances using signals from only five channels for data processing during the online spelling experiment. Generally, the use of fewer channels reduces both the hardware and signal processing costs. For invasive BCIs, fewer channels (electrodes) might cause less cerebral injury in users, which is preferable.

B. Single-Contact Decoding

In our study, we also analyzed the performance using the signal from a single contact. From the results of the simulation online test (Fig. 5), we found that our SEEG-based system performed well even when using a single signal channel. The thirteen subjects achieved a maximum average ITR of 23.19 bits/min. Moreover, the average spelling accuracy of all thirteen subjects was 71.28 \pm 22.87\%, and four of them even achieved a spelling accuracy greater than 90\%. These results indicate that online speller tasks can be achieved by using only one contact. However, few previous studies on P300-based BCIs used a single channel for data acquisition and processing. Our study demonstrates that the construction of P300-based BCIs using a signal channel is an attainable goal.

Nevertheless, the majority of SEEG contacts are useless for building a P300 BCI system. Our offline analysis results (Fig. 2, Table V, and Table IV) show that only a small portion of contacts achieved significant decoding accuracies, which are distributed mainly in the ventral visual pathway, including the FG, LG, ITG, MTG, IOG, and MOG. In particular, the contacts in the FG achieved excellent performance in our analysis. These findings reveal that the electrode (contact) distribution is important in the performance of SEEG-based BCI systems. Our experimental results might provide guidelines for electrode placement, and the ventral visual pathway (especially the FG) can be directly applied in P300-based SEEG BCIs in the future.

C. Network Perspective of P300 Activity

It has been suggested that P300 is generated from neuronal activities related to the processing of various types of information [2]. P300 plays an important role in building BCI systems for both healthy people and patients with different diseases. This ERP component is considered to be a neural signature of cognitive processes, such as attention, memory updating, and the peripheral stimulus response [23]. Therefore, investigating underlying brain mechanisms related to P300 may aid the design of a more suitable paradigm to evoke P300 and build highly efficient BCIs.

Based on our results, the ventral visual pathway, including the FG and LG, are important for building P300-based BCIs. The ventral visual pathway is a recurrent and highly interactive occipitotemporal network that connects early visual areas and the anterior inferior temporal cortex, and visual information is processed through multiple routes along this network [24], [25]. In our study, strong bidirectional causal flows were observed within these regions, including the FG and LG (Fig. 8). These causal flows might result from the activation of the visual processing network, suggesting that large information exchanges occurred in these regions. More importantly, the FG and LG are involved in processing higher-level visual information [26]. The functions of the FG include perceiving the shape of pictures, words, and even human faces [27], [28]. The LG plays a role in color perception and processing focal attention-related activities [29], [30]. Based on the results of ERP waveforms (Fig. 6), the P300 component is observed in these two brain regions, but it is not significantly found in other regions. According to previous studies, the P300 component reflects the cognitive capacity invested in task-relevant or significant events [31]. In this regard, we suggest that the P300 component in the FG and LG reflects the processing of color and shape information of our visual stimulus and stimulus-driven visual attention. Other regions in the ventral visual pathway also participate in visual information processing and might also result in P300 components. Although these P300 components are not apparent in these regions, they are still sufficient for our BCI to achieve good performance.

Moreover, a minority of significant contacts are distributed outside the visual ventral pathway, such as the precentral gyrus, parietal gyrus, and precuneus (Table V). Results of the GC analysis (Fig. 7) show that more causal flows are significant from the visual ventral pathway (especially the FG and LG) to the regions outside of the visual ventral pathway than those from the reverse direction, which suggests that more information has been transmitted from the visual ventral pathway to the other regions. Therefore, the FG and LG might influence brain regions outside of the visual ventral pathway when subjects were receiving visual oddball stimuli. Nevertheless, according to previous studies, these regions outside of the visual ventral pathway might also participate in cognitive activities related to P300. Specifically, the superior/inferior parietal gyrus and precentral gyrus have been suggested to be more active in the processing of visuospatial short-term memory and spatial attention [32]. The process of working memory has also been shown to activate the LG, precentral gyrus, and occipital-parietal regions, including the precuneus and superior/inferior parietal gyrus [33]. These brain activities have been suggested to result in the generation of the P300 component [34], [35]. Therefore, contacts in these regions also achieve acceptable performances for our BCI.

Previous studies have also underscored that the classical scalp P300 component is related to multiple cognitive activities with a distributed network in different brain regions, such as frontal cortices [23], occipital cortices [36], temporal cortices [37], and subcortical structures involving the amygdala, hippocampus, and thalamus [38]–[42]. These brain regions might be used to build P300-based BCIs in the future. However, it is still unclear whether the brain also decodes P300 for cognitive functions and whether P300 itself has a functional role in actual neural processing. The results in this study also cannot answer these important questions. Therefore, a panoramic description of the P300-related cognitive activities still requires further exploration, and it is also a promising topic for future study. Existing P300 studies are based mainly on EEG signals and other functional neuroimaging methods.
Fig. 6: ERP waveforms were obtained by averaging the SEEG signals from all the contacts in the FG/LG corresponding to the target buttons (orange lines) and nontarget buttons (blue lines). (a) ERP waveforms in the FG for 7 subjects (S1, S5, S7, S8, S9, S11, and S12) corresponding to the target buttons (orange lines) and nontarget buttons (blue lines). (b) ERP waveforms in the LG for 7 subjects (S1, S3, S4, S6, S9, S12, and S13) corresponding to the target buttons (orange lines) and nontarget buttons (blue lines).

TABLE VI: Results obtained from our SEEG-based system and several other P300 speller systems

| P300 Speller System | Signals | Number of Channels | Number of Buttons | Online Spelling Accuracy | Maximum Average ITR |
|---------------------|---------|--------------------|------------------|--------------------------|---------------------|
| Lin et al. [20]     | EEG     | 16                 | 36               | 79.00%                   | 20.256              |
| Lenhardt et al. [21]| EEG     | 10                 | 36               | 87.50%                   | 32.17               |
| Gu et al. [19]      | EEG     | 12                 | 40               | 94.32%                   | 50.26               |
| Speier et al. [22]  | EEG     | 32                 | 36               | 94.80%                   | 59.39               |
| Krusienski et al. [16]| SEEG   | 16                 | 36               | 95.00%                   | *23                 |
| Our system          | SEEG    | 5                  | 40               | 93.85%                   | 54.25               |

The ITRs are measured in bit/min.
* The specific maximum ITR was not provided in this study; 2 subjects achieved an average maximum ITR of approximately 23 bits/min after 4 rounds of flashing, according to Fig. 4 in the original article [16].
Fig. 7: The functional connectivities between the visual ventral pathway (FG, LG, IOG, MOG, ITG, and MTG) and other regions. (a) Red nodes: brain regions in the visual ventral pathway. Green nodes: brain regions outside the visual ventral pathway. Blue edges: connections from the visual ventral pathway to other regions (a total of 10 connections). Orange edges: bi-directional connections (a total of 12 connections). For uni-directional connections, the width of an edge reflects the GC value of the causal flow in the corresponding direction. For bi-directional connections, the width of an edge reflects the average GC value of the causal flows in two directions. (b) Average GC value of causal flows between brain regions in the visual ventral pathway and other regions. The blue bars represent the GC values of causal flow from the brain regions in the visual ventral pathway to the other regions, while the orange bars represent those for the reverse direction. (* \( p < 0.05 \))

Fig. 8: The functional connectivities between the two regions (FG, LG) and the other regions in the visual ventral pathway. The width of an edge reflects the average GC value of all causal flows between the corresponding regions.

In our study, the SEEG-based BCI provides a new method for localizing the brain regions that are vital for P300-based BCIs. SEEG electrodes can be implanted in the shallow cortical layer and deeper brain structures to record high-quality intracranial signals, which is preferable when exploring brain mechanisms and corresponding BCIs.

D. Limitations and Future Work

Three main limitations of this work are apparent. First, similar to other invasive approaches, SEEG-based BCIs are highly demanding in terms of the electrode distribution. Different tasks require electrodes covering different brain regions; otherwise, the efficiency of the system will be significantly affected. Therefore, SEEG-based BCI systems have restrictive conditions for subject recruitment. It is difficult to conduct large-scale experiments, but we will increase the number of subjects in the future to validate our experimental results. Second, the relationship between EEG and SEEG signals is still unclear. We will also attempt to record SEEG and EEG signals simultaneously and determine their relationship by network analysis or source localization. Third, SEEG is a promising technique for other clinical applications in addition to epilepsy detection and treatment. Further exploration of the design of the SEEG-based real-time BCI system may aid in the diagnosis, prediction, and rehabilitation of patients with other brain/mental diseases.

V. CONCLUSION

In this study, we presented a P300 BCI system based on SEEG signals. Thirteen subjects with epilepsy participated in our experiment, and the experimental results demonstrated the validity of our SEEG-based BCI system. The subjects achieved an average online spelling accuracy of 93.85±9.01% and a maximum average ITR of 54.25 bits/min using signals from 5 contacts. Moreover, our system achieved an acceptable performance even when using only a single contact. More importantly, through our offline analysis, we found that brain regions in the visual ventral pathway were important for our BCI, especially the FG and LG. In the future, these regions could be directly applied in building P300-based SEEG BCIs.
These findings might be useful for understanding the P300 brain mechanisms and the corresponding BCIs.

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