neural recordings. For microelectrode prosthetics, the ability to identify and track the activity of single neurons has been the feature leveraged to determine the state of the system. As a result, many have investigated the cascade of events that follow chronic implantation of microelectrodes and the degradation in signal quality. This reduction presents increased difficulty for extracting relevant control signatures since the action potentials become buried in the noise.

The results presented here as well as the results presented by others indicate that the inflammatory response and changes in electrode morphological/electrical properties are intimately tied. We would like to caution the reader that we are not claiming that electrode morphological changes are the sole reason for decrease in action potential PPA. The results of this study indicate that there are significant additional electrode structural properties that must be considered.

If conventional microwire electrodes are the recording substrate of choice, a two pronged approach must be taken to achieve long term recordings. At the highest level, the glial response must be controlled. However, once it is controlled, it remains a challenge to preserve the long term wire and insulation properties of the electrode when exposed to the extracellular environment chronically. The results presented here, even over the short duration of four weeks, indicate that the current technology is not sufficient to be robust for the long term. Ultimately, exposure to the extracellular environment may lead to large scale failure in the insulation and metal core making the electrode unusable for single neuron recording.

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Brain–Computer Interface Research at the University of South Florida Cognitive Psychophysiology Laboratory: The P300 Speller

Eric W. Sellers, Andrea Kübler, and Emanuel Donchin

***Abstract*—We describe current efforts to implement and improve P300-BCI communication tools. The P300 Speller first described by Farwell and Donchin (in 1988) adapted the so-called oddball paradigm (OP) as the operating principle of the brain–computer interface (BCI) and was the first P300-BCI. The system operated by briefly intensifying each row and column of a matrix and the attended row and column elicited a P300 response. This paradigm has been the benchmark in P300-BCI systems, and in the past few years the P300 Speller paradigm has been solidified as a promising communication tool. While promising, we have found that some people who have amyotrophic lateral sclerosis (ALS) would be better suited with a system that has a limited number of choices, particularly if the 6 × 6 matrix is difficult to use. Therefore, we used the OP to implement a four-choice system using the commands: Yes, No, Pass, and End; we also used three presentation modes: auditory, visual, and auditory and visual. We summarize results from both paradigms and also discuss obstacles we have identified while working with the ALS population outside of the laboratory environment.**

***Index Terms*—Amyotrophic lateral sclerosis (ALS), brain–computer interface (BCI), P300.**

I. INTRODUCTION

The P300 Speller, first described by Farwell and Donchin [1], adapted the so-called oddball paradigm (OP) as the operating principle of this brain–computer interface (BCI). In an OP, the participant is presented with a Bernoulli sequence of events, each belonging to one of two categories. The participant is assigned a task that cannot be performed without a correct classification of the events. If the participant indeed attends to the sequence, and one of the categories occurs less frequently than the other, events from the rare category elicit the P300 component of the event-related potential (ERP) [2]. In the P300 Speller, the user observes a 6 × 6 matrix where each cell of the matrix contains a character or a symbol. This display serves as a virtual typing keyboard. The columns and rows of the matrix are intensified for approximately 100 ms in a random order. The user's task is to count the number of times the chosen character is intensified. Flashing the 12 elements of the matrix (six rows and six columns) creates an OP with the row and column that contain the chosen character serving as the rare category (see [3] for a complete description of the P300 Speller).

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Farwell and Donchin [1] confirmed that this arrangement does operate as an OP and that it is possible for the computer to correctly identify the chosen character by detecting which row and which column elicit a P300. The detection of the P300 requires, of course, the use of signal averaging, which means that the random sequence of stimuli must be presented several times. In the early work, the need to average reduced the "typing speed" to a maximum of approximately five characters per minute. Further demonstrations and an assessment of the communication speed achieved by such a system were provided by Donchin, *et al.* [3], who tested the system with able-bodied young adults and wheelchair-bound, but otherwise healthy, young adults. They were able to achieve a typing rate up to 7.8 characters a minute. Other researchers have also demonstrated the efficacy of the P300 Speller and have attempted to improve the classification rates of such a system [4]–[6].

Since 2002, our laboratory at the University of South Florida, in collaboration with the Wadsworth Center, has begun to test the P300 Speller with the severely disabled and locked-in individuals for whom the system is intended. In the process, we strive continually to refine the system in order to increase the speed with which the speller can operate. We chose to test the P300 Speller with an amyotrophic lateral sclerosis (ALS) population. As we will demonstrate, many of the patients we tested were able to use the P300 Speller as intended. However, we did encounter many obstacles, and more remain to be overcome as we continue to work with severely disabled individuals. We will describe several of the obstacles we encountered and the solutions we developed while conducting research in a home environment. We shall then review some of the data acquired from the ALS participants. We will then discuss an alternative P300-BCI paradigm, the four-choice paradigm. We will also discuss what we feel are important future directions.

II. OBSTACLES AND SOLUTIONS

The obstacles fall largely into three classes: technical, practical, and empirical. The technical challenges relate to recording quality. In moving from a laboratory environment to a home setting we encountered many sources of noise that must be reduced if we are to have adequate recordings. When working with people who rely on respirators to breathe, two distinct types of artifacts have been observed. First, a respirator may introduce electrical or mechanical artifacts. Second, the respirator may produce subtle movements of the persons head. Such disturbances may manifest as high-frequency noise or low-frequency drift. Most of the high-frequency noise can be controlled through proper grounding and setting of the ground and reference electrodes. The low-frequency drift can typically be controlled by careful attention to the person's position. For example, sponge pads placed under the Fp1 and Fp2 electrodes provided enough cushion to exacerbate the movement produced by the ventilator; by removing these pads artifacts can be significantly reduced. The recording environment can also be a significant source of electrical noise, and the home environment is naturally much less controlled than the laboratory. We encountered such challenges as the activation of air conditioners or refrigerators, the ringing of telephones, the automatic opening of garage doors, and the occasional wandering pet who disturbs the connector cable; this is but a partial list. In many of these cases it is easy to find a solution; however, each instance requires a solution, and each environment provides a new set of challenges.

Another class of problems is related to practical issues while conducting studies with severely disabled or locked-in individuals. The most basic question we confront when working with locked-in individuals concerns their perceptual and cognitive abilities. Examples include the following questions: Is the person attentive? Can the person see the display? Did the person attend to the correct character? What is the person's level of cognitive ability? In part, we have addressed these questions by preceding the use of the P300 Speller by a standard, "classical" OP, in which two very distinct stimuli are presented, one of the two being rare [2]. If the rare events elicit a standard P300 in locked-in individuals, we can assume that the person was able to understand the instructions and attend to the task. Furthermore, this test establishes that the person does have the mechanism and processing that underlie the elicitation of the P300. In contrast, if a P300 is not elicited, we cannot make the converse assumption. In addition, the fact that a user does not exhibit a particular response may not have a bearing on whether or not they are able to perform a particular task; however, it may, or may not, preclude them from using a P300-BCI.

In practice, all that is needed to use a P300-BCI is a differential response to the target and nontarget stimuli [7]. Therefore, even if individuals suffering from ALS produce less typical ERPs than age-matched peers in a standard OP [8], [9], they may still be able to use a BCI. What is potentially more troubling is that the cognitive abilities of the ALS population have been questioned [8]–[10]. However, preliminary results of verbal and nonverbal working memory tasks collected at the University of Tübingen indicate higher working memory scores as the person's motor skills become more impaired (unpublished data). Regardless of these conflicting results, if participants are unable to understand task instructions, or to perform the cognitive operations required by the task, they will not be able to use the BCI.

Other important difficulties in working with locked-in individuals include determining whether or not they are able to see the computer display. It is possible to make assumptions about whether or not a user can see the display by measuring responses to auditory and visual stimuli. However, it is more difficult to determine whether or not a user intended to focus on a particular stimulus. For example, when conducting studies with able-bodied participants, if a user makes a mistake and focuses on the wrong character he has the ability to notify the experimenter. A locked-in person does not have this option, and the resulting data may be misinterpreted. Unfortunately, there is no way to correct such an error because, by definition, a locked-in person cannot communicate. In this case, until the locked-in person is provided with a functioning BCI system, one must assume that such errors will not be detected.

III. EARLY RESULTS WITH AN ALS POPULATION

In collaboration with the BCI group at the Wadsworth Center and the BCI group at the University of Tübingen we have tested 15 people with ALS and one person who had a brainstem stroke, with the P300 Speller. Nine of the people were able to reach accuracy levels above 75%. The remaining people were unsuccessful using the P300 Speller ($\text{accuracy} < 50\%$); however, all seven unsuccessful users were either locked-in at the time of testing, or they could only communicate with their primary caregivers. In addition, two of the participants performed at accuracy levels $>90\%$ for up to 20 sessions (100% in some sessions), and two participants continue to use the P300 Speller on a regular basis, with accuracy levels up to 100%. Fig. 1 shows, in each row, averaged waveforms for the target and nontarget stimuli for each of two ALS participants. One session includes 2040 target intensifications and 10 200 nontarget intensifications. For each user, the duration between the two sessions is approximately six weeks. Each user's waveforms appear quite different from one another. This is not uncommon, as waveform morphology in an oddball task is known to vary from individual to individual [2]. In contrast, each user's waveforms are quite similar over time. This illustrates that the responses do not habituate and that the waveform morphology remains stable for over the duration of many weeks [11]. These results are encouraging; however, the people who need the system most, people who are locked-in, have not been able to use the system for communication. To date, we have not worked with

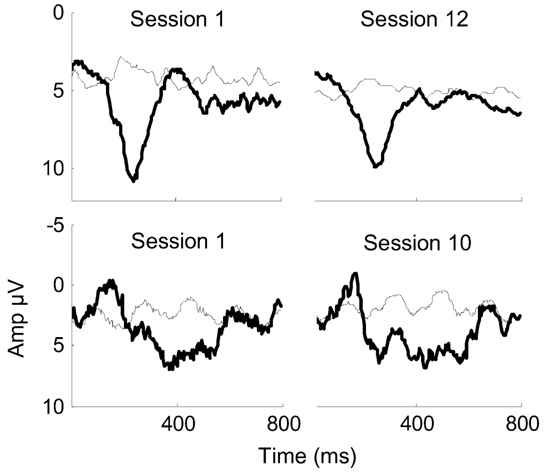

Fig. 1. Averaged waveforms for two sessions of 6 × 6 Speller data recorded from two people with ALS (Pz electrode). Thick waveforms represent target stimuli; thin waveforms represent nontarget stimuli. Each row presents data from different user.

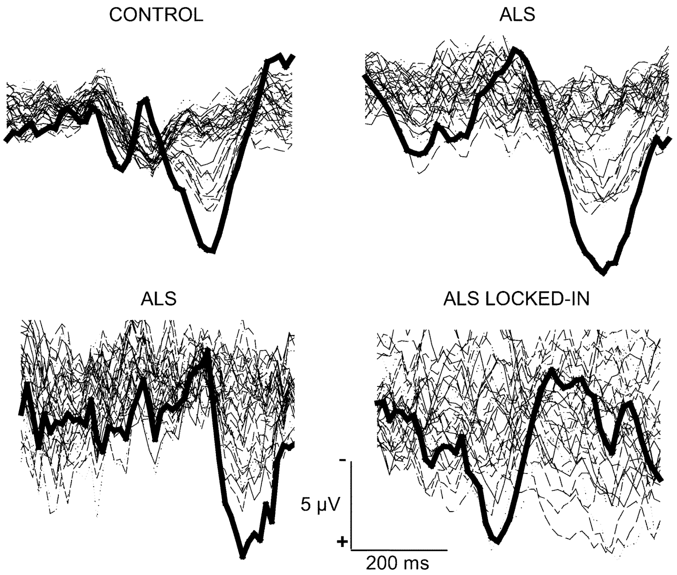

Fig. 2. Average waveforms for each of 36 cells of 6 × 6 matrix (Cz electrode) for four participants. Thick waveform indicates target cell. Each row and each column was intensified 15 times. Each waveform represents average of row/column intersection.

a participant who successfully used a P300-BCI and then progressed into the locked-in state. Thus, we are unable to determine the ultimate usefulness for the locked-in population at this time.

One of the largest obstacles we have encountered while using the P300 Speller is the variability of the data acquired from locked-in individuals. Fig. 2 shows data for all 36 cells of the 6 × 6 matrix overlaid for each of four participants. The thick waveform indicates the target cell. The figure clearly shows a substantial difference between the target cell and the nontarget cells; however, this is not true for the locked-in participant. While it appears that a P300 response may be present to the target item, the other 35 cells contain a substantial amount of variability that obscures the response. The reason for the increase in variability is unclear. It is possible that as ALS progresses the electroencephalogram (EEG) response becomes generally more variable; this is suggested by Paulus *et al.* [9], who showed that 12 of 16 ALS patients produced abnormal P300 responses. Because of the difficulties some ALS users have had in using the P300 Speller, and the difficulties for the locked-in users, we decided to modify the paradigm in an attempt to make the system easier to use.

IV. FOUR-CHOICE PARADIGM

The four-choice OP allows the user to respond to "yes/no" questions (for a complete description of the paradigm and experimental results see [7]). While this mode of communication is far more limited than that provided by a full text writing system, it does not tax the person to the same degree, and, in the setting of the severely paralyzed individual, enables very useful communication. The four-choice system, while still utilizing the OP principles, reduces the total number of stimuli employed in an attempt to reduce the amount of variability between stimulus types. The user is presented with a sequence of four events (the words "Yes," "No," "Pass," and "End"). The user's choice of one of the words creates an OP with the target category appearing 25% of the time. We tried this system using three presentation modalities: auditory, visual, or concurrent auditory/visual presentation. The user's task is to attend to the sequence and count the number of times the target stimulus flashes. The target stimulus is defined as the word that answers a given question. Three non-ALS participants and three ALS participants were included in this study to investigate some basic questions: Can a BCI based on a four-choice oddball sequence serve as a communication device? Does the presentation mode affect classification values? Are the responses of ALS users stable across time? All six users participated in ten experimental sessions that presented each of the three stimulus modes in each session, using a counter-balanced design [7]. The users took 4–6 weeks to complete the experimental sessions.

For all of the non-ALS participants and two of the three ALS users, the stimuli in the four-choice OP study elicited responses that were classified accurately enough to control the BCI. The third ALS user was only able to achieve 62% averaged across all sessions. While this accuracy level is well above change (25%), it may be frustrating to use a system that does not reach an accuracy level of at least 70% [12]. Averaged across all experimental sessions, the auditory stimuli were classified most accurately for two ALS users and the auditory and visual combined stimuli were classified most accurately for the remaining user, average accuracy of 80%, 73%, and 62%, respectively [7]. In addition, the waveforms were fairly stable across sessions, which is important for long-term BCI use. Fig. 3 shows target and nontarget waveforms for each of the three ALS patients in session 1 and session 10 of the Sellers and Donchin [7] study. Each row shows one user's data. Similarities between the waveforms in each session regarding shape and latency are evident, most notably for the users presented in rows 2 and 3.

V. FUTURE DIRECTION AND CONCLUSION

The ultimate goal in BCI research is to make systems as fast and accurate as possible. However, it is important to realize that for locked-in users, speed of communication is not as important as the reliability of the communication and its very existence. When one has virtually no way to communicate, even one selection a minute can make a significant difference in the quality of life [13]. As we conclude this phase of the exploration of the P300-BCI, it seems likely that the system will be able to serve locked-in individuals. Several directions for future research are evident. In the first place, additional detection and classification algorithms can be explored. Recent studies have examined and compared classification algorithms based on maximum likelihood and independent component analysis [6], continuous wavelet transformations [14], and support vector machines [4], [5]. In addition, there is no reason that classifiers based on other algorithms should not be empirically tested and used online if they prove more effective than the current classification methods.

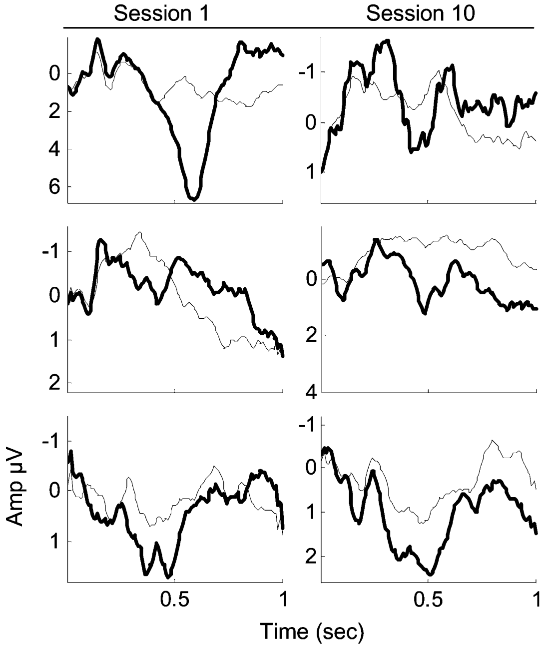

Fig. 3. Averaged waveforms for two sessions of four-choice data recorded from three people with ALS (Pz electrode). Thick waveforms represent target stimuli; thin waveforms represent nontarget stimuli. Each row presents waveforms for different user. Row 1 = visual data, Rows 2 and 3 = auditory/visual data.

It is also clear that there are various ways in which adaptive logic can be introduced to increase the system's speed and reliability. Recent work by Sellers *et al.* [15] indicates that the detectability of the P300 can be enhanced by using different matrix sizes and different inter stimulus intervals. These results suggest that the system can be tailored to each user's pattern of EEG and ERP activity. While there is no "best" classification method or preprocessing technique, it is advantageous to test many different methods. Krusienski *et al.* [16] tested many different variables related to preprocessing within the stepwise discriminant analysis framework, and their results suggest that an optimal channel set should include at least six electrode locations (i.e., Fz, Cz, Pz, Oz, PO7, and PO8).

In summary, a growing body of literature has demonstrated the efficacy of P300-BCI systems. As the technique becomes more refined, and more research is conducted with severely disabled individuals, the method will produce faster and more reliable communication.

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