Published in final edited form as:
Muscle Nerve. 2020 June ; 61(6): 702–707. doi:10.1002/mus.26828.

Brain-computer interfaces for amyotrophic lateral sclerosis

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Abstract

A brain-computer interface (BCI) is a device that detects signals from the brain and transforms them into useful commands. Researchers have developed BCIs that utilize different kinds of brain signals. These different BCI systems have differing characteristics, such as the amount of training required and the degree to which they are or are not invasive. Much of the research on BCIs to date has involved healthy individuals and evaluation of classification algorithms. Some BCIs have been shown to have potential benefit for users with minimal muscular function as a result of amyotrophic lateral sclerosis. However, there are still several challenges that need to be successfully addressed before BCIs can be clinically useful.

Keywords

amyotrophic lateral sclerosis; brain-computer interface; neuroprosthetics

1 | VARIETIES OF BRAIN-COMPUTER INTERFACES

Vidal[1] introduced the term “brain-computer interface” (BCI) to describe an apparatus he assembled that allowed users to make simple responses with their electroencephalogram (EEG). Vidal’s system used visual evoked potentials and was based on the focus of the user’s attention. To accomplish this, Vidal used an IBM 360 mainframe system at the UCLA computing center. This was a large system that supported computing for the entire university. As a result, experiments had to be conducted after work hours. Since Vidal’s experiments, computing power has increased exponentially. At the same time, EEG amplifiers have evolved from the use of vacuum tubes, through transistors and integrated circuits, and finally to the current use of microprocessors. These developments allowed for the creation of reasonably priced laboratory systems and, more recently, portable BCIs. Table 1 shows some of the characteristics of several different BCI systems.

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CONFLICT OF INTEREST
The author declares no conflicts of interest.

ETHICAL PUBLICATION STATEMENT
I confirm that I have read the journal’s position on issues concerned with ethical publication and affirm that this report is consistent with those guidelines.

The content of this article was presented in part at the 67th annual meeting of the American Association of Neuromuscular & Electrodiagnostic Medicine, October 17, 2019, Austin, TX.

Farwell and Donchin[2] developed the P300-based BCI. This system was based on a response in the EEG characterized by an enhanced positivity at around 300 milliseconds in the potential evoked by the attended target in an array of flashing letters. Subsequently, a considerable amount of research has been performed with factors such as optimizing stimulus presentation, signal processing, and user applications.[3–5] Most of this work has been done with able-bodied users who do not benefit from the use of a BCI. In addition, by far the most effort has been devoted to the problem of signal processing and classifier learning using archival data.[6]

Wolpaw et al[7] developed the sensorimotor rhythm–based BCI. Sensorimotor rhythms (SMRs) are oscillations in the alpha (9 to 13 Hz) and beta (18 to 25 Hz) bands of the EEG that are reactive to movement, preparation for movement, and imagining movement.[8] Given SMR-based feedback, users can learn to manipulate these signals to control cursor movement in one or several dimensions or the movement of robotic devices.[9,10]

Chapin et al[11] showed that rats could learn to control a robot arm to obtain water reward by modulating the firing rate of single units recorded from within their brains. Taylor et al[12] showed that monkeys could learn to control a virtual cursor in three dimensions using single-unit activity. Single-unit activity has subsequently been used to control devices in human patients.[13]

Birbaumer et al[14] trained two individuals with amyotrophic lateral sclerosis (ALS) to control their slow cortical potentials (SCPs) in order to move a cursor toward one of two targets on a video screen. This EEG feature is a low-frequency potential that varies over a period of seconds. After a number of training sessions, these individuals then used this control to operate a binary spelling device. Their study is the only early BCI report that involved individuals with motor impairments rather than healthy volunteers.

Middendorf et al[15] designed a BCI based on the steady-state visual evoked potential (SSVEP). The SSVEP is typically elicited by a visual stimulus flashing at a fixed rate. This initial SSVEP BCI was used to operate a two-state switch, but subsequent SSVEP-based systems have allowed for much higher information transmission rates by using arrays of visual stimuli flashing at different rates and advanced signal processing methods.[16]

2 | SOME CHARACTERISTICS OF BCIS

There has been much speculation about the neuronal origin of the signals that produce the EEG recorded at the surface.[17] However, understanding the role of various neural elements within complex interacting networks remains a challenge.[18] By and large, the neural circuits that generate the EEG remain unknown. Nevertheless, it is fairly safe to say that the current BCI communication and control systems just discussed are based on intentional use by users and are not based on “mind reading.”

It is important to note that the characteristics of these various BCIs vary considerably. For example, McFarland et al[19] compared data recorded from individuals using SMR and P300 BCIs in terms of whether adaptation to changing signal statistics was useful. Adaptive normalization of the features and classifier weights improved performance for the SMR data but not for the P300 data. These results probably reflect the fact that learned control of SMR features occurs over an extended period of time, whereas the acquisition of the skills necessary for the use of the P300 is more rapid. BCIs also differ in terms of information transfer rates. For example, a series of studies showed that most healthy individuals could learn to use either a SMR, P300, or SSVEP BCI system.[20–22] However, the speed and accuracy of performance with these three BCIs differed considerably. The SSVEP-based BCI had the highest information transfer rate followed closely by the P300-based BCI.

BCIs also differ in the nature of the artifacts that can appear to be correct EEG-based performance. The P300 has similar spectral characteristics to eye blinks. As a result, classifiers trained to identify the EEG response to targets may also be sensitive to eye blinks. However, true P300 responses differ in terms of the topology of the response, showing peak amplitudes over central (eg, Cz) and slightly more posterior (eg, Pz) electrodes. In contrast, eye blinks show peak amplitudes at the most anterior electrodes. Thus, careful inspection of the EEG features that control selection can allow the investigator to rule out the potential role of artifacts in determining performance. Although the spectral characteristics of SMRs do not overlap greatly with eye blinks, they do overlap with the wide-band activity of muscles (electromyography, or EMG). However, true SMRs differ from EMG in that they have relatively narrow spectral peaks located over central scalp regions in relatively narrow alpha and beta bands.[23]

It can be argued that individuals with limited voluntary motor capacities could benefit from whatever signal a system is sensitive to. However, failure to rule out the involvement of non-EEG artifacts limits the applicability of results obtained with healthy volunteers to those individuals who could most benefit from BCI usage. This is particularly important as much of the BCI research to date involves offline evaluation of data collected from healthy volunteers. For example, Palaniappan[24] reported that including gamma band activity (ie, EEG activity in the 24- to 37-Hz band) improved the accuracy of classifying archival data from healthy subjects. However, Pope et al[25] found that scalp-recorded activity in this band was virtually eliminated in subjects who volunteered to be given a paralytic drug. This issue may also be a problem for studies investigating BCIs using other frequency bands in view of the broadband nature of EMG activity and difficulty in interpreting the meaning of the weights from multivariate classifiers.[26,27]

There has been extensive research with classification algorithms, many of which are evaluated offline.[6] This may reflect a tendency of researchers in the machine-learning community to seek practical applications for those algorithms that are currently popular. To be useful for communication or control a device must by necessity operate online in real time. Most of the published classification algorithms have not actually been used in functioning BCI devices.

Development of sensor technology may be of greater importance than refinement of classification algorithms. Improved sensors could be made easier to apply by caregivers without the need for extensive training, be more comfortable for the user, and produce signals with a better signal-to-noise ratio.[28] Methods for EEG recording were simplified considerably by the introduction of cloth caps that hold the electrodes in place. These caps made application of electrodes easier and quicker, although the process still requires some time and expertise. In addition, the pressure of individual electrodes against the scalp may vary due to individual variations in head shape. Too much pressure may be uncomfortable for the user, whereas insufficient pressure affects the quality of the recording. Users have found that the jell used with typical wet electrodes is unpleasant, but dry electrodes may not yet produce comparable results.[29,30] BCI performance would be improved by a better signal-to-noise ratio than that produced by current sensor technology.

3 | REAL-TIME APPLICATIONS OF BCIS WITH DISABLED USERS

Although most BCI research has been done with data from healthy volunteers, a number of studies have examined performance in patients with ALS. For example, the study by Birbaumer et al[14] with slow cortical potentials involved two individuals who were using mechanical ventilation. Likewise, Kubler et al[31] showed that four individuals with ALS could learn to operate a BCI with EEG rhythms recorded over the sensorimotor cortex. However, most BCI studies in individuals with ALS have used the P300.[5,32–34] Of interest is the fact that most of these studies used relatively standard signal-processing methods, in contrast to many of the studies examining archival data that tended to evaluate more novel and complex methods.

In a review of BCI studies with ALS patients, Kübler and Birbaumer[35] concluded that communication was possible prior to individuals being completely locked-in (ie, having no means of communication). However, they found no evidence that patients with completely locked-in syndrome (CLIS) could use a BCI system. This conclusion was also supported by a more recent review of the literature.[36] Kübler and Birbaumer[35] suggested that CLIS individuals may have undergone extinction of goal-directed thinking due to a lack of normal sensorimotor feedback. Other explanations for the lack of evidence for successful BCI use in CLIS include “BCI illiteracy,” cognitive impairment, and problems with vision.[36]

Extinction of goal-directed thinking presumably relates to the lack of perceived relationships between intent and effects on the environment in CLIS patients. This view implies that maintaining the relationship between intent and effects on the external environment (eg, through BCI-based technologies) would prevent this extinction of goal-directed thinking. An alternative notion is that the progression of neuropathology in ALS results in BCI illiteracy or cognitive impairment, conditions that would not be preventable by maintaining contingencies between thought and the environment.

The concept of BCI illiteracy clarifies the fact that not all users can successfully use this technology.[37] This difficulty is present in a proportion of apparently healthy individuals and implies that it is a characteristic of the individual that prevents successful use. ALS-associated neuropathology may compromise neural systems that are the basis for the signals used by a given BCI. For example, SMR-based BCIs use signals associated with the motor cortex, a neural system compromised in ALS. Likewise, the P300 response is typically attenuated in many forms of dementia.[38] As discussed by Allison and Neuper,[37] improvements in BCI technology (eg, signal processing or task design) may be one possible solution to BCI illiteracy. They also suggested switching to a different BCI approach that uses a different neural signal. The authors further implied that BCI illiteracy may actually be due to a shortcoming in BCI technology rather than a problem with the individual.[37]

The development of cognitive impairments in a proportion of ALS patients is well documented.[39] In more severe cases, patients with ALS meet criteria for frontotemporal dementia. One of the characteristic symptoms of frontotemporal dementia is development of progressive aphasia.[40] Clearly, difficulty with language would be problematic when using any assistive communication device. The possibility that poor BCI performance is due to cognitive or linguistic factors is difficult to assess given the problems in assessment of patients with CLIS, and even those who still have limited communication abilities.

Some researchers have attempted to develop BCI-based methods for cognitive assessment. For example, Poletti et al[41] developed a P300-based system for assessment of executive functions and found reduced processing speed in ALS patients when compared with healthy controls. However, when using BCI technologies to assess cognitive status, there is inherent ambiguity as to whether performance deficits reflect cognitive status or proficiency in BCI use. This is particularly apparent when assessing constructs such as speed of information processing. Possible increased demands on cognitive resources associated with difficulty in BCI use could also compromise assessments. An alternative approach could involve screening for genetic risk factors. For example, Geronimo et al[42] found an association between poor P300 BCI performance and abnormal repeat expansion, which has a high prevalence in ALS and frontotemporal dementia.

McCane et al[43] examined the ability of 25 ALS patients to use a visual P300-based BCI. Seventeen patients had an average performance of over 70% correct, which is adequate for communication. The remaining patients averaged 12% correct, which would not support effective communication despite the fact that chance performance was 3%. This has been demonstrated with simulations showing that error-corrected performance is not produced in a reasonable amount of time unless performance is about 70% or better.[44] Performance in the McCane et al[43] study did not vary with extent of disability, as assessed using ALS Functional Rating Scale—Revised (ALSFRS-R) scores. However, all patients with poor performance had problems with vision (eg, nystagmus, diplopia, ptosis).

Pasqualotto et al[45] compared performance of ALS patients using an eye-tracking system with that for a P300 BCI system. They found that information transfer rates and usability ratings were both higher for the eye-tracking system. In contrast to findings by McCane et al,[43] they also reported that P300 BCI performance correlated positively with ALSFRS-R score. Whether an individual patient finds an eye-tracking device superior to a P300 BCI may depend on the characteristics of both the patient and the BCI. Vaughan et al[46] described an ALS patient who found a visual P300 speller to be superior to his eye-gaze system. He used the BCI 4 to 6 h/day for several years for email and other tasks. I was involved in home visits with this patient and was told by caregivers that the eye-tracking system he had been using was no longer functioning satisfactorily. In contrast, the patient was quite pleased with the P300 system. Although eye-tracking systems depend solely on precise control of eye movements, the P300 system can also involve implicit attention.[47] Thus, there may be a subset of ALS patients who can benefit from visual BCIs at some point in the progression of their disease.

Researchers have sought to develop BCI systems that use alternative sensory modalities given potential vision problems in ALS patients. Kubler et al[48] compared auditory and visual versions of P300-based BCIs in paralyzed ALS patients. They found reduced accuracy for the auditory system when compared with the visual system. Heilinger et al[49] found that ALS patients could use a P300 system based on vibrotactile stimuli.

Individuals with ALS have also used BCI systems based on intracortical recordings, which involve sharp electrodes that penetrate and reside in brain tissue. One problem with invasive recordings concerns the permanence of the implants. Over time, the quality of recordings declines due in part to the brain’s response to the presence of foreign objects.[50] Jarosiewicz et al[51] studied several methods that aimed to reduce such effects, including tracking the statistics of the signals and updating the classifier periodically. Milekovic et al[52] described results from home use over a 138-day period that did not require calibration. This was due to the “decoder” being calibrated from data recorded over a long duration (ie, up to 42 days) and based on spectral analysis of local field potentials rather than neuronal spikes. This ALS patient could speak, was able to eat, and had an ALSFRS-R score of 16 out of 48.

Pels et al[53] reported consistent performance over a 3-year period in an ALS patient using an implanted electrocorticography (ECoG)-based BCI. ECoG systems use arrays of electrodes implanted subdurally that do not penetrate the brain tissue and thus may be less susceptible to deterioration by the brain’s response to foreign objects. The authors did not report on the level of physical and cognitive functioning of the subject other than describing her as late stage. However, an article they cited described that she was ventilated and could use an eye-tracking system at the time of implantation.[54] Pels et al[53] noted that their patient used the ECoG system at home.

Wolpaw et al[55] described a study involving five Veterans Administration medical centers, each managing several patients with ALS. After a screening of 37 patients to determine usability, P300-based spellers were placed in the homes of 27 patients for periods of 12 to 18 months. Of these, 14 patients completed the study while the remaining patients left the study due to disease, death, or loss of interest. Patients completing the study used the BCI mainly for communication via a text program as well as other applications such as email and an internet news reader. Ratings by patients and caregivers indicated that BCI benefit exceeded burden. Seven patients continued to use the BCI after the end of the study. Maintenance of BCI home use with this system required training of the patient’s caregiver in the application of an electrode cap and operation of the system, in addition to responding to occasional technical support from researchers. The study demonstrated that a subset of ALS patients could use a noninvasive BCI system in their homes if given external support. Having been involved in the study, I would add that success depended on the particular study site as well as the motivation of both caregiver and patient.

4 | PROSPECTS FOR WIDESPREAD USE OF BCIS

Current BCI technology can improve the lives of a limited number of individuals who are both severely physically weakened and retain sufficient mental abilities. In order to do so, however, it is also necessary to have trained and motivated caregivers and technical support personnel. This greatly limits the potential population of individuals who can actually benefit from BCI use. The number of potential BCI users could increase if there are further improvements in this technology. At present, however, BCI use remains in the domain of research and development.

The marketing of direct-to-consumer neurotechnologies is on the rise despite the fact that the efficacy and safety of these products has not been established.[56] Many of these devices are marketed as tools to enhance mental states, but some also claim that they can help individuals with mobility restrictions (eg, ALS) regain independence.[57] At this point, it is probably best to thoroughly investigate the basis of any such claims before considering their use.

There has been considerable media coverage of BCI research. Gilbert et al[58] analyzed the content of this coverage and found that a substantial amount of it was overly positive and did not portray the state of the art realistically. They documented many instances of unsubstantiated claims. These include overly optimistic assessments of the utility of current BCI technologies for the disabled, suggestions that BCI technologies may enhance the abilities of able-bodied users, and the idea that BCI technologies are enabling us to “read the minds” of users. Rinaldi[59] suggested that both scientists and journalists are responsible for the sensationalization of scientific research. For the scientist, overly optimistic portrayal of research can result in favorable institutional and financial support. For the journalist, there is the tendency to publish articles that will “grab the reader’s attention.” These tendencies can result in unrealistic expectations on the part of the public. BCI research is by no means unique in this sense.

Widespread clinical use of BCI systems will require development of accurate, portable, reliable, and user-friendly devices.[60] One problem with the commercialization of these devices is that the number of people who need the limited capabilities of current BCIs is relatively small by marketing standards. Several tech firms have expressed interest in developing BCI technologies.[61] Although these efforts draw considerable media attention, to date workable solutions have not appeared.

BCI technology promises to provide a new means of communication and control for individuals with severely limited motor function. To date, research has only established proof of principle. Further technological improvements are necessary if BCIs are to become practical for individuals who can actually benefit from their use.

Funding information

National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health, Grant/Award Number: 1P41EB018783

Abbreviations:

ALS	amyotrophic lateral sclerosis
ALSFRS-R	Amyotrophic Lateral Sclerosis Functional Rating Scale—Revised
BCI	brain-computer interface
CLIS	completely locked-in syndrome
ECoG	electrocorticography
EEG	electroencephalogram
EMG	electromyography
SCP	slow cortical potential
SMR	sensorimotor rhythm

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TABLE 1

Some characteristics of several different BCI systems

BCI system	Signal	Invasiveness	Training required
P300	Evoked potential	Noninvasive	Minimal
SMR	“Spontaneous” rhythms	Noninvasive	Extensive
Single unit	Neuronal spikes	Invasive	Extensive
SSVEP	Evoked oscillations	Noninvasive	Minimal

Abbreviations: BCI, brain-computer interface; SMR, sensorimotor rhythm; SSVEP, steady-state visual evoked potential.