12 | BCIs THAT USE P300 EVENT-RELATED POTENTIALS

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Event-related brain potentials (ERPs) in the EEG are manifestations at the scalp of neural activity that is triggered by, and is involved in the processing of, specific events. The voltages that constitute the ERP are embedded within the general EEG activity recordable from the scalp and are usually quite small relative to the *ongoing* EEG. However, because the ERPs are time-locked to events, and follow a constant time course, they can be extracted by averaging multiple trials of eliciting events. The result is a series of positive and negative voltage deflections that are referred to as *components*. The successive components typically differ in their stimulus rate and amplitude dependence, their topographical distributions, and their relationships to the information processing activities of the brain. The components that can be recorded over the first 150 msec following the eliciting event tend to reflect activity in the primary sensory systems, and their waveforms and scalp distributions vary with the modality of the eliciting stimuli. These are known as the *exogenous* components. Longer-latency components tend to reflect information processing activity that is cognitive in nature and is thus less dependent on stimulus modality and more dependent on the significance of the eliciting event in the subject's concurrent tasks. They are usually referred to as *endogenous* components.

Both early (exogenous) and late (endogenous) components of visual evoked potentials (i.e., VEPs) have been used as signal features for BCIs. The design and operation of BCIs that use endogenous ERP components differ both in principle and practice from those of BCIs that use exogenous ERP components. This chapter focuses on BCIs that use P300, an endogenous ERP component. Chapter 14 discusses BCIs that use exogenous VEP components.

THE P300 ERP AND P300-BASED BCIs

The P300 is a positive deflection that occurs in the scalp-recorded EEG after a stimulus that is delivered under a specific set of circumstances. It was first described by Sutton et al. (1965) and has been widely studied since then to explore higher cortical functions in humans (for review see Bashore & Van der Molen, 1991; Donchin, 1981; Duncan et al., 2009; Fabiani et al., 1987; Polich, 2007; Pritchard, 1981). Although it often occurs at a latency of about 300 msec relative to the eliciting stimulus (hence the designation of P300), this latency may vary from 250 to 750 msec (Comerchero & Polich, 1999; Magliero et al., 1984; McCarthy & Donchin, 1981; Polich, 2007). This variability in latency reflects the fact that the P300 is elicited by the decision, not necessarily conscious, that a rare event has occurred, and the decision latency can, and does, vary with the nature (e.g., the difficulty) of the decision (Kutas et al., 1977). The P300 is usually largest over central parietal scalp and attenuates gradually as distance from this area increases.

In 1988, P300 was first used as the basis for a BCI (Farwell & Donchin, 1988), and a steadily growing number of research groups are currently pursuing its BCI applications. Current P300-based BCIs allow users to select items displayed on a computer screen. Thus, while the process is very different, a P300-based BCI selection is essentially equivalent to a selection by a standard computer keyboard. Because P300-based BCIs are noninvasive, use hardware that is portable and inexpensive, and can provide reliable performance, they are essentially the only BCIs that are currently being used outside of the laboratory by severely disabled people for important purposes in their daily lives, such as communication and environmental control. Furthermore, many different laboratories are exploring possibilities for further increasing the capabilities and usefulness of P300-based BCIs.

The subsequent sections discuss the nature of the P300, address the principles of its BCI usage, review the major areas of P300-based BCI research, summarize current clinical usage of P300-based BCIs, and consider the prospects for their further development.

THE ODDBALL PARADIGM

The specific set of circumstances for eliciting the P300 ERP is known as the *Oddball Paradigm*. This paradigm has three essential attributes (Donchin & Coles, 1988):

- A subject is presented with a series of events (i.e., stimuli), each of which falls into one of two classes.
- The events that fall into one of the classes are less frequent than those that fall into the other class.
- The subject performs a task that requires classifying each event into one of the two classes.

The events that fall into the less-frequent class (i.e., the *oddball* events) elicit a P300. As long as an experimental design

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adopts the three attributes of the oddball paradigm, any stimulus and any classification task can elicit a P300.

It is important to note that, although the two classes are generally two different classes of stimuli, this is not a requirement. As shown by Sutton et al. (1967), a P300 can be elicited by an event that consists of the absence of a stimulus, if that absence satisfies the conditions of the oddball paradigm. That is, a P300 ERP is elicited by rare events that violate the subject's expectations.

Most P300 studies have used visual or auditory stimuli. Figure 12–1 illustrates a typical P300 experiment. The letters *O* and *X* flash on a video screen in a random order at a rate of one per second (i.e., the stimulus onset asynchrony). The *X* occurs infrequently (e.g., 20% of the flashes) and is thus the oddball stimulus, while the *O* occurs frequently (e.g., the other 80% of the flashes). The subject is asked to count the number of times one of the stimuli (e.g., *X*) occurs. Each time a stimulus occurs, a marker is placed in the data file to indicate the identity of the stimulus, *X* or *O*. Each stimulus is presented on the screen for 100 msec, and then the screen is blank for 900 msec (i.e., the interstimulus interval [ISI]) until the presentation of the next stimulus. Figure 12–1A shows the time course of the experimental events.

Figure 12–1B displays the ERPs elicited by the oddball stimulus at midline electrode locations Fz, Cz, and Pz of the 10–20 system (see fig. 12–2) for 800 msec after each stimulus. The three responses show a typical P300 scalp topography: the most prominent potential is a positive component occurring about 350 msec after the *X* stimulus; and it is largest at the Pz electrode and attenuates at more anterior and posterior locations. It should be noted that the results would be essentially the same even if the subject had been asked to count the *O* stimuli rather than the *X* stimuli: P300 is always elicited by the rare events (i.e., the *X* stimuli in this example) (Duncan-Johnson & Donchin, 1977). The next most salient components are the P100 and N200 components, which are considered to be exogenous components even though they can be modulated to some extent by attention (Heinze et al., 1994; Mangun, 1995; Mangun et al., 1993).

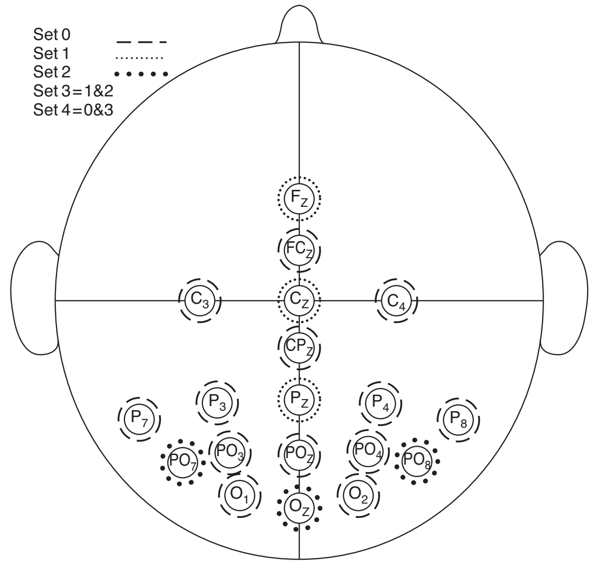

Figure 12.2 Electrode locations evaluated for use in a P300-based BCI by Krusienski et al. (2008). EEG was recorded from 64 electrodes. The sets of electrodes shown here were compared in regard to offline classification accuracy as described in the text.

As noted, P300 latency may vary from 250 to 750 msec (Comerchero & Polich, 1999; Magliero, et al., 1984; McCarthy & Donchin, 1981; Polich, 2007). This variability is thought to reflect differences in the amounts of time it takes to classify

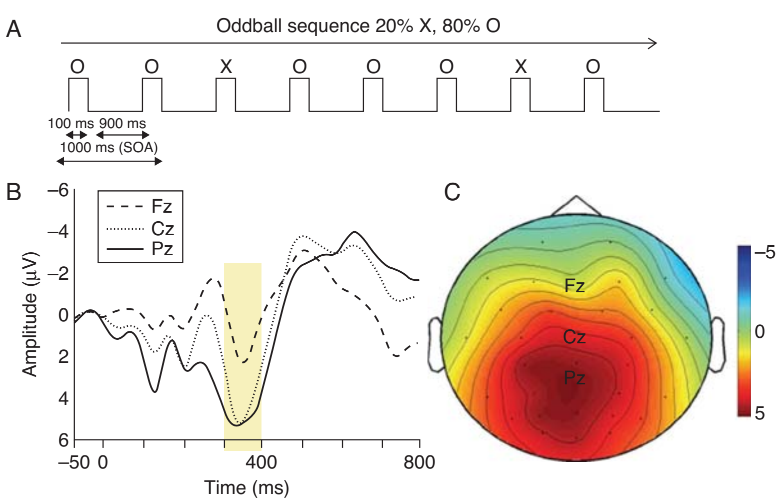

Figure 12.1 (A). Time course of rare (i.e., oddball) and common stimuli in a standard oddball protocol. (B) Average oddball ERPs from a subject for electrode locations Fz, Cz, and Pz, showing a progressively larger positive deflection from frontal, to central, to posterior sites. (C) Topographical distribution of the average ERP amplitude 300–400 msec after the oddball stimulus. The large positive ERP component (i.e., P300) is maximum at Pz and is widely distributed over posterior-parietal regions.

different kinds of events. Kutas et al. (1977) demonstrated the relationship between the latency of the P300 and the difficulty of the classification task.

P300 ORIGIN AND FUNCTION

Some of the most compelling evidence related to the origin of the P300 has been provided by Knight and colleagues through studies in patients with brain lesions. Knight et al. (1989) showed that lesions in the temporal parietal junction abolished the auditory P300 at posterior scalp sites, even though the patients could still discriminate between the stimuli. In contrast, damage to lateral parietal cortex did not impair P300 generation. These results suggest that lateral parietal cortex is not critical in auditory P300 generation. Additional studies have extended these findings. In separate experiments using auditory, visual, or somatic stimuli, Knight and Scabini (1998) showed that prefrontal and lateral parietal lesions had no effect on P300 latency or amplitude. In contrast, temporoparietal junction lesions markedly reduced auditory and somatosensory P300s and reduced visual P300s. Soltani and Knight (2000) provide a comprehensive review of this important work.

Recently, studies that combine the high temporal resolution of EEG with the high topographical resolution of fMRI have provided some additional insight concerning the neural substrate of P300. In a standard auditory oddball task, Mulert et al. (2004) found the P300 to be accompanied by increased fMRI activity in the supplementary motor cortex, the anterior cingulate cortex, the temporoparietal junction, the insula, and the middle frontal gyrus. Furthermore, this fMRI activity was greater and occurred earlier in the right hemisphere than in the left hemisphere (Bledowski et al., 2004; Mulert et al., 2004). In patient studies involving intracranial recording, EEG, and fMRI, Linden (2005) implicated the inferior parietal lobule and the temporoparietal junction in P300 generation. In regard to the fMRI data (see chapter 4 in this volume), it should be noted that blood-flow-related activity measured over several seconds cannot be confidently attributed to an event (i.e., P300) that occurs somewhere in this period and lasts about 100 msec. Thus, fMRI results concerning the area(s) responsible for P300 generation must be interpreted cautiously.

The most comprehensive account of the functional role of P300 is called the *context-updating model* (Donchin, 1981; Donchin & Coles, 1988). Although this model does not make assumptions regarding the actual neural generators of P300, it proposes that the P300 reflects context-updating operations. According to the model, as stimuli are presented and evaluated, the degree to which the events are consistent with the current model of the context is assessed. When an event violates the expectations dictated by the model, and when the violation requires the model to be revised (i.e., *context updating*), a P300 is elicited. The model accounts for many of the salient characteristics of the P300 and is supported by a variety of behavioral and psychophysiological studies (e.g., (Adrover-Roig & Barcelo, 2010; Barcelo & Knight, 2007; Barcelo et al., 2007; Dien et al, 2003; Linden, 2005; Luu et al., 2007).

P300 AMPLITUDE AND STABILITY

The extensive studies of the past 45 years have defined the characteristics of the P300 in considerable detail. Here we focus on issues of particular importance to P300-based BCIs.

One issue particularly relevant for BCI usage comprises the factors that determine P300 amplitude. P300 amplitude is positively correlated with the time interval between events (i.e., stimuli). All other things being equal, longer interstimulus intervals result in higher amplitude P300s, at least up to intervals of about 8 sec (Polich, 1990; Polich & Bondurant, 1997). Whereas P300 amplitude in a standard oddball experiment is usually 10–20 μV, the P300s produced by BCI applications are usually 4–10 μV. This is presumably due to the rapid stimulus presentation rates used by P300-based BCIs and the resulting overlap of the ERPs to successive stimuli (Marten et al., 2009; Woldorff, 1993). P300 amplitude is also affected by moment-to-moment changes in the probability of the oddball stimulus (Donchin, 1981; Donchin & Isreal, 1980; Horst et al., 1980; Squires et al., 1977). For example, if, by chance, the oddball stimulus occurs two or more times in succession, P300 amplitude is reduced after the first oddball stimulus.

P300 amplitude is also affected by the sum total of the subject's concurrent activities. Thus, when a subject who is performing a task that elicits a P300 is asked to perform a secondary task at the same time, P300 amplitude decreases (Isreal, Chesney, et al., 1980; Isreal, Wickens, et al., 1980; Kramer et al., 1983; Sirevaag et al., 1989). Protocols may be designed that concurrently incorporate two different tasks and two different sets of stimuli and thereby elicit two different P300s. For example, Sirevaag et al. (1989) combined a joystick tracking task with an auditory discrimination task. As the relative difficulty of the two tasks was changed, and the attention each required changed correspondingly, the amplitudes of the two P300s also changed. As one task became more difficult and thus required more attention, the amplitude of its P300 increased, and the amplitude of the P300 associated with the other task decreased. These results and related studies show that attentional allocation and task difficulty affect P300 amplitude. They are relevant for P300-based BCIs since BCI users, in addition to simply watching for the desired stimuli (e.g., the letters they want to spell), are usually engaged in another task as well (e.g., planning the message being written with the BCI).

Another issue of particular importance for P300-based BCI applications is the extent to which P300 amplitude and latency change over time, both within an individual session and across days, weeks, months, and even years. In this area the available literature is mixed. Polich (1986) and Fabiani et al. (1987) showed robust test/retest correlations for peak amplitude and latency across sessions conducted within two weeks of one another. On the other hand, Kinoshita et al. (1996) found significant decreases in P300 amplitude when sessions were spread over several months. A number of studies have reported that P300 amplitude decreases during a session, and P300 latency can display cyclical variations over several hours (Lin & Polich, 1999; Pan et al., 2000; Ravden & Polich, 1999). To a considerable extent, much of the variability in P300 amplitude is due to latency variability (i.e., *latency jitter*). Kutas et al. (1977) showed that changes in P300 latency from trial to trial reduce the amplitude of the averaged P300 and that adjustment for this latency variability eliminates the apparent amplitude variability. Thus, studies that focus on P300 amplitude and do not adjust for latency variability may yield misleading results.

P300-BASED BCIs

The primary advantages of P300-based BCIs are that they are noninvasive, can be parameterized for a new user in a few minutes, require minimal user training, are usable by 90% of people (assuming ability to attend to the stimuli and to perform the classification task), can provide basic communication and control functions, and are relatively reliable. For these reasons, among present-day BCI systems, P300-based BCIs are the type most amenable to independent long-term home usage by people with severe disabilities. This subsection describes the initial P300-based BCI design and then reviews the ways in which this design has been modified and extended to improve or expand the communication and control it provides.

P300-based BCIs incorporate the three essential attributes of the oddball paradigm in a way that serves the needs of a communication and control system; specifically:

- Stimuli representing possible BCI outputs are presented in a random order.
- The stimulus representing each possible output is presented rarely (e.g., with a probability of 1/[number of possible outputs]).
- The BCI user is asked to attend to the stimulus that represents the output he or she desires (i.e., the *target* stimulus).

With a BCI protocol that has these three essential attributes, the stimulus representing the desired BCI output (i.e., the target stimulus) becomes an oddball stimulus and thus elicits a P300 ERP.

THE ORIGINAL P300-BASED BCI STUDY

In 1988, Farwell and Donchin (Farwell & Donchin, 1988) described a P300-based spelling application, which they referred to as a *mental prosthesis*. Their hope was that people who were paralyzed could use it to communicate simple messages. In their first design, all the letters of the alphabet were presented one at a time on a video screen in a random order, and the subject was asked to note when the letter he or she wanted to select (i.e., the target letter) appeared. The target letter did elicit a P300. However, because the letters were presented at a rate of 1/sec, and multiple presentations of each letter had to be averaged to reliably detect the P300, several minutes were required for the subject to select just one letter. Thus, they modified the design to allow selections to be made more rapidly. In the new design, the subject viewed a 6 × 6 matrix of letters and other commands (fig. 12–3A). The stimulus events were flashes of an entire row or column of the matrix. First the rows and then the columns flashed in random order at rates as high as 8/sec. At this rate, the six rows and six columns each flashed once in 1.5 sec. The BCI user was instructed to attend to a given letter and to keep a running mental count of the number of times that letter flashed. Farwell and Donchin (1988) did not ask the subject to foveate (i.e., look directly at) the target letter. They assumed that some BCI users might not be able to control gaze direction (e.g., due to ALS), and thus they relied instead on the evidence of Posner (1980) that attention can be focused away from the gaze fixation point.

It is important to emphasize that this BCI met the requirements of the oddball paradigm and capitalized on its properties. The subject was presented with a random sequence of events. The rare (or oddball) class included the flashes of the row and the column that contained the target letter, while the frequent class included the flashes of the other five rows and five columns. Farwell and Donchin (1988) predicted that only the two rare events would elicit detectable P300s and that once this row and column were identified, the target would be the letter at their intersection.

Figure 12–3B shows the time course of events in the operation of this BCI. Of particular interest is the fact that the rapid rate of stimulus presentation (e.g., every 125 msec) means that two or even three stimuli are delivered before a P300 to the first stimulus can occur. That is, the poststimulus EEG analysis epoch (originally 600 msec) for a given stimulus is still under way when the next several stimulus events occur. Thus, the analysis epoch for each stimulus overlaps those of the several preceding and the several succeeding stimuli. The impact of this overlap on P300 performance, and the measures that might be taken to reduce it (e.g., slower presentation rates), are addressed in a subsequent section.

Using EEG recorded from a single electrode (Pz; referenced to linked ear electrodes) and a 600-msec post-stimulus analysis epoch, Farwell and Donchin (1988) compared four different classification algorithms: stepwise linear discriminant analysis (SWLDA); peak picking of amplitude in the 200- to 400-msec interval; the area under the curve in the same interval; and the covariance between the single trial data and a template representing the standard P300. It should be noted that SWLDA has been used since the 1960s for single trial detection of the P300 (Donchin, 1969; Donchin et al., 1970; Donchin & Herning, 1975; Horst & Donchin, 1980; Squires & Donchin, 1976). In this first P300-based BCI study, Farwell and Donchin (1988) found that the SWLDA and peak picking algorithms provided the highest accuracy in identifying the target stimulus (i.e., the item the user wanted to select). They also found that accuracy was higher for a stimulus presentation rate of 4/sec than for a faster rate of 8/sec. As expected, more stimulus repetitions produced higher accuracy. Accuracy of 80% (with 2.8% [i.e., 1/36] expected by chance) required 20.9 sec per selection; and 95% accuracy required 26.0 sec. These two options gave selection rates of about 3.0 and 2.3 per minute, respectively.

This seminal study of 1988 demonstrated the feasibility of P300-based communication. It has since served as the starting point and the first benchmark for the many P300-based BCI studies that have followed.

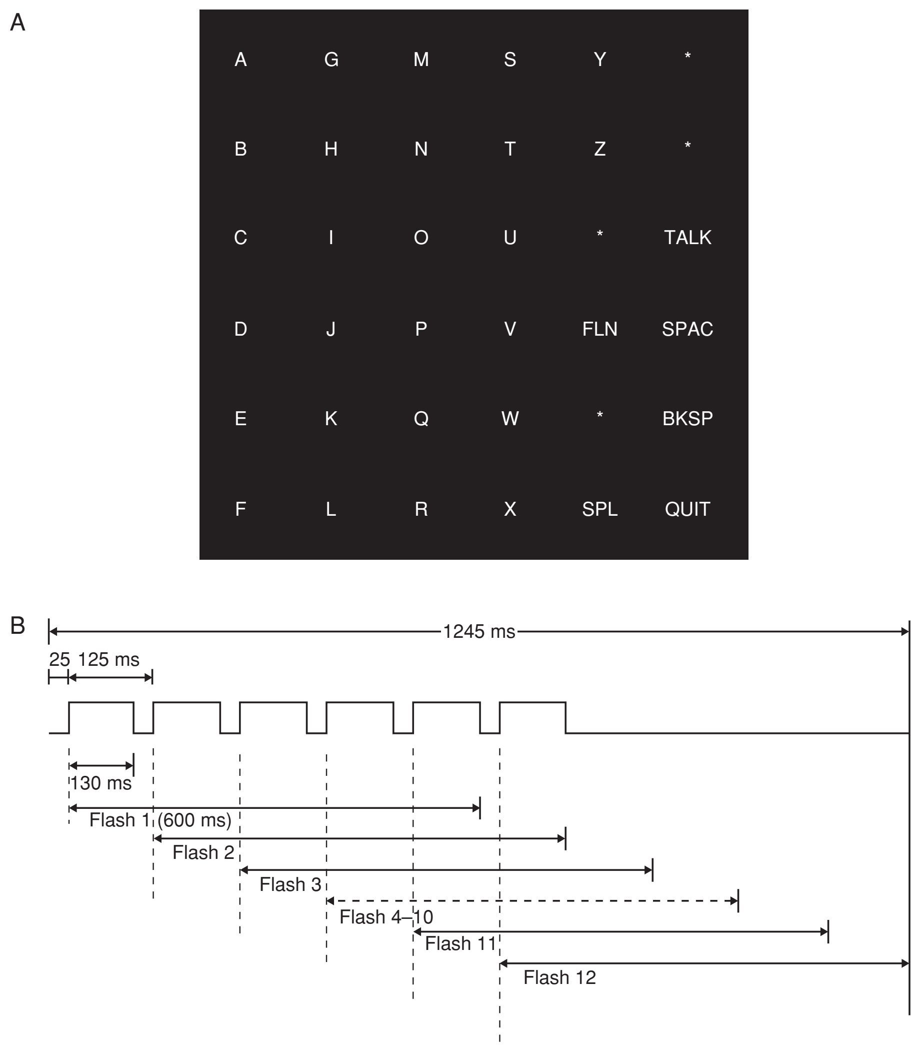

Figure 12.3 (A) The 6 × 6 matrix described by Farwell and Donchin (1988). (B) The time course for a series of 12 flashes with a stimulus onset asynchrony (i.e., time from beginning of one flash to the beginning of the next) of 125 msec. The six columns flashed in a random order and then the six rows flashed in a random order. (Modified from Farwell and Donchin, 1988.)

THE AIMS AND LIMITATIONS OF SUBSEQUENT P300-BASED BCI STUDIES

The central goal of almost all these subsequent studies has been to improve the speed, accuracy, capacity, and/or clinical practicality of P300-based BCIs so that they can provide important new communication and control options for people whose severe motor disabilities prevent them from using conventional (i.e., muscle-based) assistive communication technology.

In considering these efforts to improve the performance of P300-based BCIs, it should be remembered that the core of the evaluation should be the improvement that the BCI can make to the quality of life of users with severe disabilities. In this regard, the fact that the BCI can restore a measure of independent communication may be more important than the BCI's exact accuracy or bitrate (i.e., speed). Furthermore, it is not possible to conclude that a new design is superior to previous ones until it has been evaluated and validated in actual use by people with severe disabilities. These caveats must be emphasized as we proceed to discuss the extensive work exploring possible improvements in P300-based BCIs.

Most P300-based BCI studies have focused on offline analyses of data previously collected. Although offline analysis can enable very efficient comparison of different alternatives, it can only predict how the alternatives *may* perform in actual online usage. Even with leave-one-out cross-validation, offline analysis cannot reveal exactly how future performance may change when a method is actually used online. To the extent that the new method changes the classification, and thus the feedback provided to the BCI user, it may affect subsequent EEG and thereby affect subsequent performance in ways only assessable by online testing. The critical importance of online validation of new methods was discussed in greater detail in chapter 8 of this volume. In sum, while offline analysis is the workhorse of BCI research, online testing must be considered the gold standard. About 25% of the studies that have used offline analyses to evaluate alternative P300-based BCI methods have also included online validation of their results.

ALTERNATIVE ELECTRODE MONTAGES

As reviewed in Fabiani et al. (1987), P300 has traditionally been recorded from electrodes Fz, Cz, and Pz, according to the 10–20 electrode system (Jasper, 1958). Figure 12–2 shows examples of several electrode montages that have been used in P300-based BCI studies (Krusienski et al., 2008). The original Farwell and Donchin (1988) study used only the EEG recorded from electrode Pz. Studies since then have explored other recording montages: three or four midline electrodes, Fz, Cz, Pz, or Oz (Piccione et al., 2006; Sellers & Donchin, 2006; Serby et al., 2005); the International 10–20 system (Citi et al., 2008); a set of 10 midline and parietal/occipital electrodes (Kaper et al., 2004; Lenhardt et al., 2008); a set of 11 electrodes (Neshige et al., 2007); and a set of 25 central and parietal electrodes (Thulasidas et al., 2006).

Krusienski et al. (2008) compared the performances of SWLDA classification algorithms based on the EEG from: locations Fz, Pz, and Cz; locations PO7, PO8, and Oz; or all six of these locations. These locations are shown in figure 12–2. The algorithms that used either set of three EEG electrode locations achieved accuracies of about 65% on the 6x6 matrix, whereas the algorithm that used all six locations achieved an accuracy of 90%. At the same time, they also found that SWLDA classification was not further improved by using a still larger set of 19 electrodes that included the original 6 electrodes. The high performance of these six EEG electrodes in offline analyses was also confirmed in online testing.

These results are supported by the results of Hoffmann et al. (2008), who investigated the 4 midline electrodes, a set containing four additional parietal electrodes, as well as sets that included 16 and 32 electrodes. In general, the set using the midline and parietal electrodes performed as well as the 16- and 32-electode montages. Meinicke et al. (2002) also examined the effects of various numbers of electrodes on the resulting classification. They found that with one or three electrodes, 30 sec were needed to achieve 85% accuracy; in contrast, 7 or 10 electrodes reached accuracy above 95% after 15 sec.

ALTERNATIVE SIGNAL-PROCESSING METHODS

Numerous studies have evaluated and compared the performances of a variety of different classification algorithms, for example:

- Independent components analysis (chapter 7, this volume) (Beverina et al., 2003; Khan et al., 2009; Li et al., 2009; Serby, et al., 2005)
- Support vector machines (chapter 8, this volume) (Beverina, et al., 2003; Garrett et al., 2003; Guo et al., 2010; Hong, Guo, et al., 2009; Hong, Lou, et al., 2009; Kaper, et al., 2004; Krusienski et al., 2006; Lal et al., 2004; Lenhardt et al., 2008; Lima et al., 2010; Meinicke, et al., 2002; Olson et al., 2005; Qin et al., 2007; Salvaris & Sepulveda, 2009; Salvaris & Sepulveda, 2007; Serby et al., 2005; Thulasidas et al., 2006)
- Stepwise linear discriminant analysis (SWLDA) (see chapter 8, this volume) (Bianchi et al., 2010; Brouwer & van Erp, 2010; Dias et al., 2007; Garrett et al., 2003; Hoffmann et al., 2008; Krusienski et al., 2006; Nijboer et al., 2008; Sellers & Donchin, 2006; Sellers et al., 2006; Townsend et al., 2010)
- Fisher's linear discriminant (see chapter 8, this volume) (Babiloni et al., 2001; Gutierrez & Escalona-Vargas, 2010; Hoffmann, et al., 2008; Nazarpour et al., 2009; Salvaris & Sepulveda, 2009, 2010)

In an extensive offline analysis, Krusienski et al. (2006) compared classification by SWLDA, linear support vector machines, Gaussian support vector machines, Pearson's correlation method, and Fisher's linear discriminant analysis. Although all five methods performed reasonably well, the SWLDA and Fisher's linear discriminant methods were significantly better than the other three (approximately 88% accuracy vs. 80–83% accuracy). Meinicke et al. (2002) also compared three different classification methods: area; peak picking; and SVMs. They used electrode Pz and showed that the SVM solution reached about 78% accuracy in 30 sec, whereas the area and peak picking methods reached about 78% accuracy in 1 min.

In addition to the kinds of studies described above, several Internet-based BCI data competitions (e.g., Blankertz, 2005; Blankertz et al., 2004; Blankertz et al., 2006; Bradshaw et al., 2001; Rakotomamonjy & Guigue, 2008) have motivated many research groups from all over the world to try to develop better P300-based BCI algorithms. Although a number of the new algorithms may achieve small improvements in performance, the overall result of now fairly extensive studies is that various signal-processing methods, when properly employed, provide roughly similar performance in offline analyses. At the same time, some algorithms are likely to be easier than others to use in online applications. Taken as a whole, these studies suggest that individual differences among BCI users may be a more critical determinant of performance than the exact choice of classification algorithm, provided that the algorithm is properly parameterized (see chapter 8, this volume). This overall result implies that major improvements in the current performance of P300-based BCIs are likely to come from other kinds of changes, as addressed in subsequent subsections.

ALTERNATIVE STIMULI AND STIMULUS PRESENTATION PARAMETERS

A number of studies have focused on the standard visual matrix with row/column presentation and explored the impact of variations in basic parameters such as item size and number, the rapidity of row/column flashing, flash duration, and the number of repetitions per selection (Salvaris & Sepulveda, 2009; Sellers et al., 2006).

For example, Sellers et al. (2006) compared two different values of stimulus onset asynchrony (i.e., the time from the beginning of one stimulus to the beginning of the next), 175 msec and 350 msec, as well as two different matrices (3×3 and 6×6). In contrast to the findings of Farwell and Donchin (1988), but consistent with the findings of Meinicke et al. (2002), they found that the higher stimulus rate yielded higher classification accuracy regardless of whether the conditions were matched for the number of stimulus presentations or the time per selection was held constant. In addition, P300 amplitude was larger with the 6×6 matrix than with the 3×3 matrix. This is consistent with the many studies showing that P300 amplitude is inversely related to target probability (e.g., Allison & Pineda, 2003, 2006; Duncan-Johnson & Donchin, 1977). On the other hand, Guger et al. (2009) compared the 6×6 matrix format to a single-item presentation format. Although P300 amplitude was higher with the single-item format, the matrix format yielded higher accuracy and higher bit rate (chapter 8, in this volume).

Using the Farwell and Donchin matrix format, other studies have explored other variations in the presentation. Takano et al. (2009) varied the contrast between the stimuli and the background. They compared a white/gray pattern (luminance condition); a green/blue isoluminance pattern (color condition); and a green/blue luminance pattern (luminance/color condition). In online testing the third condition (luminance/color) provided higher accuracy. Salvaris and Sepulveda (2009) varied the item/background colors, the item size, and the distance between items. Although a white background yielded the best performance, and small items yielded the lowest performance, no single option was best for all subjects.

Perhaps the most important practical implication of these and other studies of basic format parameters is that the optimal parameter settings vary across users, and thus they should be optimized for each new BCI user (Sellers & Donchin, 2006).

Other researchers have explored modifications in the nature of the visual stimulus. In an effort to reduce the impact of the overlapping analysis epochs associated with rapid stimulus presentation rates, Martens et al. (2009) tested an apparent-motion paradigm in which the matrix items were in rectangles and the stimulus was a sudden 90° rotation of the rectangle. The user's task was to count the number of times the rectangle containing the desired item rotated. This paradigm showed a statistical improvement in performance for two of six subjects. In a similar effort, Hong et al. (2009) explored a stimulus designed to elicit a motion-specific ERP component (i.e., N200) that is most prominent at parietal electrodes P3 and P7. Although offline analyses found performance similar to that of the standard P300-based BCI format, the results suggested that the new design might reduce the number of scalp electrodes needed.

Several studies have addressed two problems associated with the row/column stimulation format. First, the desired item (i.e., the target stimulus) will sometimes flash twice in succession (once as part of a column and once as part of a row). As a result, the P300 ERP evoked by the second flash is likely to be attenuated (Squires et al., 1976); and, because their analysis epochs overlap, the two ERPs may distort each other (Martens et al., 2009; Woldorff, 1993). Furthermore, depending on the subject and particularly with higher stimulus-presentation rates, the subject may not even notice the second flash of the target. Another problem is that, with the row-column format, it is the target's row or column, not the target alone, that evokes the P300 ERP. As a result, although items not in the target's row or column are seldom selected by mistake, items that are in the target's row or column are selected by mistake much more often (Donchin et al., 2000; Fazel-Rezai, 2007).

To address these two problems, Townsend et al. (2010) developed a format in which groups of items (e.g., six items from an 8×9 matrix of alphanumeric symbols and commands) were presented simultaneously. The groups were selected to satisfy two constraints. First, no item could be presented a second time until at least six intervening groups of flashes had occurred. Second, two adjacent items were never presented at the same time. This *checkerboard* presentation format eliminated the two problems of successive target presentations and adjacent item presentations. In an online comparison in 18 subjects that took into account the need to correct for any errors that occurred, the checkerboard format performed significantly better than the standard row/column format. In addition, most users, including several people with ALS, reported that they liked the checkerboard format better. Further explorations of alternative presentation formats are likely to produce further improvements.

THE POSSIBLE ROLE OF GAZE DIRECTION IN P300-BASED BCI PERFORMANCE

As described above, the P300 is evoked by stimuli of special significance. In the case of P300-based BCIs, the special significance is that the stimulus represents the BCI output desired by the user. Thus, P300 elicitation does not require that the user look directly at (i.e., fixate) the stimulus, and P300-based BCIs should be usable by people with limited or even absent eye movements, such as many of those with late-stage ALS. At the same time, some recent evidence suggests that the performance of P300-based BCIs that use a matrix format may depend to some extent on the user's ability to fixate the desired item.

Brunner et al. (2010) and Treder and Blankertz (2010) compared P300-based BCI performance when the user fixated a central point to that when the user fixated the target. In both studies, performance was better when the user fixated the target. However, as noted previously, it is well established that the P300 amplitude is decreased when the subject is assigned a second task (Donchin, 1987b; Fowler, 1994; Gopher, 1986; Kramer et al., 1986; Kramer et al., 1983; Kramer et al., 1985; Sirevaag et al., 1989; Wickens et al., 1983; Wickens et al.,1984). By asking that the subject fixate a point other than the target during BCI use, Brunner et al (2010) and Treder and Blankertz (2010) essentially imposed a second task. Thus, although accuracy was significantly higher in the fixate condition, it is not surprising that the gaze requirement yielded lower P300 amplitude and reduced accuracy. Although Brunner et al. (2010) conclude that the higher classification accuracy in the fixate condition indicates that P300-based BCI performance depends on the subject's ability to fixate the target character, it is evident from their results that classification does not require fixation. Moreover, using a paradigm similar to that of Treder and Blankertz (2010), Liu et al. (2010) reported mean accuracy higher than 96% for a covert attention task. These results demonstrate that optimizing the presentation paradigm can yield highly accurate results even when the subject does not fixate the target.

Nearly all P300-based BCI studies since 2004 have incorporated relatively short-latency (e.g., 150–250 msec) features recorded from occipital scalp locations (i.e., over visual cortex). The clear value of such early-latency posterior scalp features suggests that the responses elicited by the matrix P300-based BCI, and the accuracy of the classification they achieve, may depend to some degree on occipital visual evoked potentials (e.g., P100 and N200 see The Oddball Paradigm above), in addition to the P300. On the other hand, it should be noted that occipital VEP components are affected by attention (Eason, 1981; Harter et al., 1982; Hillyard & Munte, 1984; Mangun et al., 1993). It has also been noted that P300-related activity occurring in the temporal-parietal cortical junction may contribute to the EEG recorded from occipital electrodes (Dien et al., 2003; Polich, 2007).

The practical implications of these results for the clinical usefulness of P300-based BCIs are not clear. Whereas P300-based BCI performance may depend to some degree on the user's ability to look directly at the desired item, the importance of this factor in determining the usefulness of these BCIs for people with eye-movement impairments remains to be determined. In this regard it is relevant to note that one person with ALS who could no longer use his eye-tracker communication device was able to use a P300-based BCI very effectively (Sellers et al., 2010). In a more general sense, it should be appreciated that the performance of any BCI that depends on the user's vision is likely to be affected by loss of eye-movement control. For example, a sensorimotor-rhythm-based BCI (see chapter 13, this volume) that controls cursor movement is likely to perform less well when the user's gaze cannot follow the moving cursor. This practical reality brings us to the next section.

P300-BASED BCIs THAT USE AUDITORY STIMULI

Many of the people who need the basic communication capacity that a P300-based BCI could provide may find it impractical or impossible to use a system that requires vision. For example, in addition to weak eye-movement control, people with advanced ALS may have visual difficulties due to diplopia (double vision), ptosis (drooping eyelids), or dry eyes. In response to this problem, several research groups have begun developing P300-based BCIs that use auditory stimuli instead of, or in addition to, visual stimuli (Hill, 2005; Nijboer et al., 2008; Pham et al., 2005). The major limitation of these paradigms is the low number of possible selections (e.g., two or four) compared to the much higher number available with standard visual P300-based BCIs (e.g., $6 \times 6 = 36$). Thus, the rate of communication is necessarily slow. Nevertheless it might still be extremely valuable for people who lack other effective options.

In an effort to improve the bitrate, several studies have presented auditory stimuli that map onto a visual matrix. Furdea et al. (2009) used a 5×5 visual matrix in one condition, and a 5×5 auditory (i.e., the spoken words "one" to "ten") and visual matrix in another condition. The auditory stimuli mapped to the five rows and five columns of the matrix, which were labeled 1–10. Nine of 13 subjects were able to use the auditory and visual matrix with accuracy of 70% or higher. In contrast, all 13 subjects achieved accuracy of 75% or higher in the visual condition, and 11 of the 13 were above 95%. In a similar design, Klobassa et al. (2009) used a 6×6 matrix and presented environmental sounds that correspond to the rows and columns. This study showed that subjects were eventually able to use the system with the auditory stimuli alone. However, the communication rates were still relatively low next to those of visual P300-based BCIs.

These early studies have established the feasibility of auditory P300-based BCIs. This achievement, combined with the clinical need for such systems, should encourage their further development.

PROSPECTS FOR IMPROVING P300-BASED BCIs

Current P300-based BCI designs provide relatively modest rates of communication. Many research groups are working to improve P300-based BCIs by exploring new electrode selection methods, presentation paradigms, and applications.

Cecotti et al. (2011) introduced a new electrode selection algorithm to reduce the number of electrodes necessary for a given person to use a P300-based BCI. Electrode selection, more specifically reduction, will be a valuable asset in terms of cost, convenience, and portability as more people begin to use BCIs. In theory, a small number of electrodes should be sufficient for P300-based control; however, due to individual differences, it may be advantageous to start with a somewhat larger array and then prune it to as few electrodes as possible.

Other studies have explored variations in contrast and color (Salvaris & Sepulveda, 2009; Takano et al., 2009), overlapping stimuli and apparent (Martens et al., 2009) or actual (Hong et al., 2009) motion, stimulus presentation modifications (Jin et al., 2011; Townsend et al., 2010), suppressing characters that surround the target during calibration (Frye et al., in press), and using mindfulness induction to increase attentional resources (Lakey et al., in press). Schreuder et al. (2010) designed a five-choice auditory BCI by giving each stimulus a unique tone and a unique spatial location. The study showed that the system produced speed and accuracy comparable to some visual P300-based BCIs. Brouwer and van Erp (2010) showed that a tactile P300-based BCI using stimulating electrodes placed around the waist can achieve speed and accuracy similar to that of most auditory BCIs.

New applications are also emerging. For example, Mussinger et al. (2010) showed that a P300-based BCI can be used as a creative tool as well as a communication device. Subjects performed copy-spelling, copy-painting, and free-painting tasks. We have seen advances toward a P300-based Internet browser (Bensch et al., 2007; Mugler et al., 2008; Mugler et al., 2010) and also how a predictive spelling program can increase throughput (Ryan et al., 2011).

INDEPENDENT HOME USE OF P300-BASED BCIs

Because P300-based BCI systems are noninvasive, relatively portable and inexpensive, and perform reliably, they are the first BCIs being taken out of the laboratory and used independently by severely disabled people in their daily lives for basic communication and environmental control. Although the first report of in-home testing is provided in Farwell and Donchin (1988), the concept was first described earlier by Donchin in a 1985 lecture (see Donchin, 1987a, for a transcript of the lecture). Birbaumer et al. (1999) reported the first long-term home usage of a BCI system by a man with ALS. However, it is only recently that a larger-scale effort to implement home use independent of close oversight by a research team has begun (Sellers et al., 2010; Vaughan et al., 2006). Even though the system is slow compared to conventional means of communication, it should be noted that, for severally disabled users, communication speed is often less important than accuracy and reliability and the fact that the BCI restores a measure of independence (Kubler & Neumann, 2005; Nijboer et al., 2008; Sellers & Donchin, 2006) (although most BCI users would presumably opt for faster communication if it were available).

These first efforts have encountered, described, and begun to address the myriad difficult issues that arise when a new technology is taken out of the simple, highly controlled laboratory environment and placed into the complex, changing, and unpredictable environments in which people, including those with severe disabilities, actually live. These issues include (but are certainly not limited to) the capacities, expectations, and desires of the prospective users and their caregivers; the need for extremely simple and robust hardware and software and for simple and convenient usage procedures; the difficulty of evaluating prospective users who currently can communicate very little if at all; the impact of the user's disease process on P300 generation; the selection of the proper point in the disease process to introduce BCI usage; the physical and mental state of the user; the physical and social features and stability of the home environment; the presence of electromagnetic noise or instability; the need for prompt and effective technical support; the impact of other illnesses; and the practical and ethical issues that arise if and when disease progression degrades BCI performance. These many issues are addressed more fully in chapters 20 and 24 of this volume. Indeed, although the subject of chapter 20 is the clinical usage of BCIs in general, its substance is of necessity drawn almost entirely from experience with P300-based BCIs.

One issue important for home use is addressed here because it applies to P300-based systems specifically. That issue is the extent to which long-term intensive home use (i.e., many hours per day over months and years) will degrade performance. The amplitude, form, or stability of the P300 might conceivably degrade over the hours of use within a day and/or over many days and weeks of use. For example, habituation, or decreased amplitude with repeated stimulus presentation, occurs with many ERP phenomena (Kinoshita et al., 1996; Ravden & Polich, 1998, 1999). The initial results for P300-based BCI use are encouraging. Sellers and Donchin (2006) showed reliable use of the P300-based BCI by six people, three with ALS, over a period of 10 weeks. Most notably, despite frequent lengthy daily use over 3 years, P300-based BCI performance by a person with ALS did not deteriorate (Sellers et al., 2010). The amplitude and form of the target and nontarget ERPs remained stable. Furthermore, even though the SWLDA algorithm was reparameterized periodically, the optimal parameters changed very little over time.

One important finding from efforts to provide the P300-based BCI to people who are very severely disabled is that it is useful to conduct an initial test of the extent to which the person can generate a P300 in the simplest and most straightforward form of the oddball paradigm, such as a protocol in which a succession of two pictures (e.g., a zebra or an elephant) are presented, with one appearing 80% of the time and the other 20%. If the rare event fails to elicit a P300, it is very unlikely that the person will be able to use a visual P300-based BCI. A recent innovation is the development of a screening method to evaluate more thoroughly within a few sessions whether a severely disabled person has the ability to use the P300-based BCI (McCane et al., 2009).

SUMMARY

An *event-related potential* (ERP) is a distinctive pattern of voltage changes that is time-locked to a specific event. The most prominent ERP BCI is the P300-based BCI. The P300 is a positive potential that occurs over central-parietal scalp 250–700 msec after a rare event occurs in the context of the *oddball* paradigm. This paradigm has three essential attributes:

- A subject is presented with a series of events (i.e., stimuli), each of which falls into one of two classes.
- The events that fall into one of the classes are less frequent than those that fall into the other class.
- The subject performs a task that requires classifying each event into one of the two classes.

In 1988, Farwell and Donchin described a BCI based on the oddball paradigm. The rows and columns of a 6 × 6 matrix of letters and commands flashed rapidly, and the target events were the row and column that contained the item the subject wanted to select. This P300-based BCI provided relatively slow but effective communication.

Over the past two decades, the original P300-based BCI design has provided a robust basis for continued development by many groups. It has been further refined through studies of alternative recording sites, signal-processing methods, and stimulus presentation parameters and formats; and P300-based BCIs that use auditory rather than visual stimuli have been described.

Because P300-based BCIs are noninvasive, relatively simple and inexpensive, and provide stable performance, they are the first BCIs being taken out of the laboratory and used independently by severely disabled people for basic communication and control in their daily lives. This clinical translation effort is revealing, and spurring solutions to, the many problems associated with moving BCI systems from the laboratory to the home.

The relatively slow communication rates of current P300-based BCIs mean that they are likely to be useful mainly for people whose severe disabilities largely preclude their use of other assistive communication technologies. Further exploration of promising new options may substantially increase the speed of P300-based BCIs and thereby expand their communication and control applications and their user populations.

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