

# Brain–Computer Communication: Unlocking the Locked In

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With the increasing efficiency of life-support systems and better intensive care, more patients survive severe injuries of the brain and spinal cord. Many of these patients experience *locked-in syndrome*: The active mind is locked in a paralyzed body. Consequently, communication is extremely restricted or impossible. A muscle-independent communication channel overcomes this problem and is realized through a brain–computer interface, a direct connection between brain and computer. The number of technically elaborated brain–computer interfaces is in contrast with the number of systems used in the daily life of locked-in patients. It is hypothesized that a profound knowledge and consideration of psychological principles are necessary to make brain–computer interfaces feasible for locked-in patients.

Various neurological diseases restrict both verbal and nonverbal communication. The inability to communicate emotions, thoughts, and needs is one of the most daunting problems for patients with such illnesses. Hemorrhage in the anterior brain stem (mainly in the ventral parts of pons cerebri; see Figure 1) or nonhemorrhagic stroke in the ventral pons can cause a *locked-in syndrome*, which includes tetraplegia and paralysis of cranial nerves (Allen, 1993; Chia, 1991; Patterson & Grabis, 1986). These patients are said to be “locked in” because they are conscious and alert even though they are unable to use their muscles and therefore can communicate neither vocally nor by writing. In the “classic” locked-in syndrome, vertical eye movement as well as eyeblinks remain intact, whereas in the “total” locked-in syndrome, patients lose all ability to move and communicate (G. Bauer, Gerstenbrand, & Rimpl, 1979). Other terms for the same pathological state, such as *pseudocoma* (Xu, Li, Tan, & Zang, 1981) or *Monte-Cristo-*

*syndrome* (Cherrington, Stears, & Hodges, 1976; the character Mr. De Villefort in Alexandre Dumas’s novel suffered from this syndrome), have not been generally accepted. Although locked-in syndrome is usually caused by pontine lesions, it has also been observed after lesions in other brain regions, such as bilateral infarcts of the capsula interna (Chia, 1984). The life expectancy of locked-in patients, depending on the etiology, can exceed 10 years (Cappa & Vignolo, 1982; Thadani et al., 1991). Stroke in the brain stem with locked-in syndrome is not restricted to older age: This pathology is often seen in 20- to 40-year-olds (Patterson & Grabis, 1986). Tumors, encephalitis, and brain injuries localized in the ventral midbrain can also cause locked-in syndrome. Patterson and Grabis found nonvascular lesions in 34 of 139 patients with locked-in syndrome.

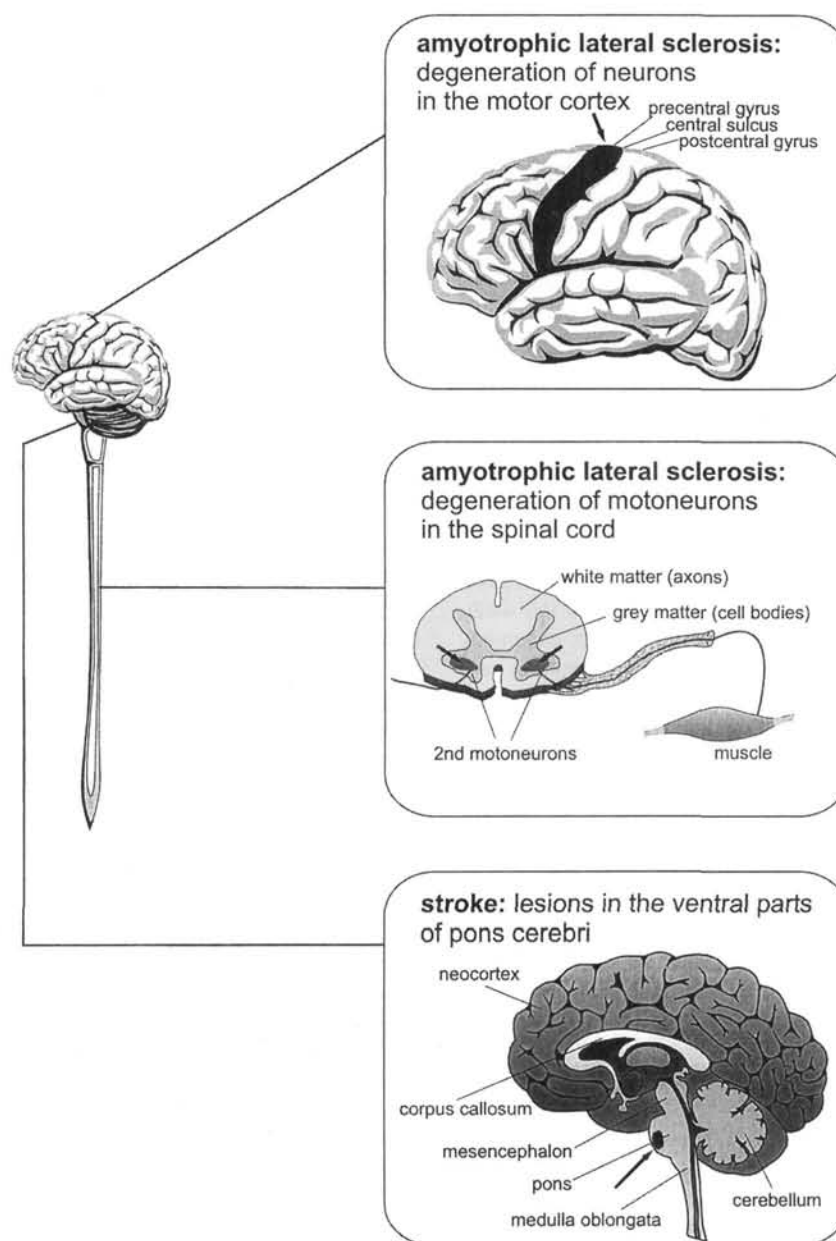
Other causes of total motor paralysis are degenerative neuromuscular diseases, the most frequent being amyotrophic lateral sclerosis, which involves a steadily progressive degeneration of central and peripheral motoneurons (see Figure 1). Usually, but not exclusively, the onset occurs after the age of 30. The etiology of amyotrophic lateral sclerosis remains unclear, and there are no effective therapeutic strategies available (D. B. Williams & Windebank, 1991). Most often, paralysis begins with the lower extremities and then moves on to hands and arms, finally paralyzing breathing and swallowing as well as facial muscles. At the final stage, patients can stay alive only with artificial feeding and ventilation. Sometimes amyotrophic lateral sclerosis begins with bulbar paralysis, followed by a fast-developing tetraplegia. In most people with amyotrophic lateral sclerosis, control of eye muscles, sphincters, and few face muscles is retained up to the end stage of the disease. However, individuals with amyotrophic lateral sclerosis who have absolutely no remaining muscular activity (total locked-in syndrome) have been described by Hayashi and Kato (1989); Harvey, Torack, and Rosenbaum (1979); and Elder, Lashley, and Steck (1982). Gascon et al. (1995) recently reported three exceptional cases of amyotrophic lateral sclerosis in 10- to 15-

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*Figure 1.* Paralysis in amyotrophic lateral sclerosis is caused by degeneration of the 1st and 2nd motoneurons in the spinal cord and neurons in the motor cortex. Paralysis in stroke patients leading to locked-in syndrome is due to hemorrhage in the ventral parts of the pons.

year-old children, and in all three cases the tetraplegia was combined with profound ophthalmoparesis, indicating total locked-in syndrome.

Obviously the problem of communication in patients with total paralysis is of utmost clinical importance. The incidence of amyotrophic lateral sclerosis is about 1.5–2:100,000 (Borasio, 1996) and appears to be growing (Durrleman & Alperovitch, 1989; Murray et al., 1987). In recent years more and more patients with amyotrophic lateral sclerosis have agreed to be artificially ventilated (Borasio, 1996). Because of improvements in resuscitation and rehabilitation medicine, an increasing number of people are resus-

citated after brain stem injury. Because these patients often suffer from hypoxia before resuscitation, they are at risk for brain lesions. The usual strategy used to cope with communication problems in severely paralyzed patients is the use of the remaining motor channels (e.g., Beukelman & Mirenda, 1992). This strategy is useless in those patients without functioning of at least one motor output channel. Communication, however, is an important aspect of the will to live in people with such severe disabilities. In our experience many individuals with amyotrophic lateral sclerosis would not want to continue their life without any possibility of being able to communicate. For instance, Bach (1993) showed that

establishing and maintaining effective communication greatly increased the quality of life in patients with amyotrophic lateral sclerosis.

Existing communication devices, which depend on muscle movement, are not feasible for many locked-in patients. Maintaining communication in such patients requires a communication channel independent of the motor periphery. In this article we describe several strategies underlying communication systems that rely on electrical brain activity only, thus circumventing the motor channel. Despite the somewhat preliminary character of most of these attempts, we present them here because their future development and success will depend more on the application of behavior modification principles than on technological progress.

## Use of Electrical Brain Activity for Communication

### Spontaneous EEG and Event-Related Potentials

Attempts to solve the problem of communication in patients who are paralyzed have led to several strategies that involve direct communication between the brain and a computer. For this methodology the term brain-computer communication is commonly used. Autonomic functions (i.e., heart rate, skin temperature) have also been used as input for computers. Indeed, people with motor disabilities can learn to control these functions to some extent using operant conditioning techniques (Engel, 1977). However, the very slow rate of responsivity (e.g., heart rate, 30 s per trial; R. J. Williams & Roberts, 1988) and the high metabolic noise of some autonomic responses, as well as the high incidence of pathological changes in locked-in patients, make autonomic functions useless for precise and reliable communication. The electrical signals of the brain (electroencephalogram; EEG), with their fast responsivity and covariation with cognitive processes, are more suitable as candidates for nonmotor mediation between person and computer.

The EEG, as the term is commonly used, refers to electrical activity arising from neurons in the cerebral cortex recorded non-invasively from the scalp. This includes spontaneous electrical activity of the cerebral network and the cortical responses to external or internal events. The responses to events are commonly referred to as *event-related potentials*. In general, it is believed that EEG activity results from the summation of excitatory and inhibitory postsynaptic potentials of underlying regions of the cerebral cortex with some contribution of granular and glia cell activity (Speckmann & Elger, 1993). The EEG is usually recorded from the scalp according to the international 10–20 system (Jasper, 1958).

Event-related potentials are electrical brain responses time-locked to physical stimuli or behavioral responses and characterized by their voltage amplitude and their latency in relation to stimulus onset (see Figure 2). The latency and the electrical polarity (positive or negative) are used to label event-related potentials: For example, a prominent negative peak 100 ms poststimulus is called N100; a positive peak 300 ms after stimulus onset is referred to as P300. *Event-related potentials occurring up to 100 ms after stimulus onset are sometimes termed exogenous because they reflect the propagation of activity in the sensory pathways and primary projection areas, thereby reflecting the integrity of those pathways. Exogenous event-related potentials are generally obligatory responses to the presentation of physical stimuli, and they*

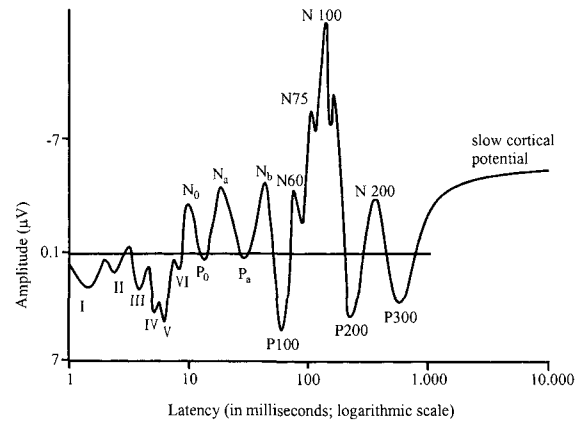


Figure 2. Averaged event-related potentials as responses to acoustic stimuli. The time scale is logarithmic. Waves I to VI are brain stem potentials. Components from  $N_0$  to  $N_{75}$  are *exogenous*, whereas components from 100-ms latency onward ( $N_{100}$ ) are considered *endogenous*. Components after 500-ms latency are referred to as *slow cortical potentials*.

depend more on the physical parameters of the stimulus, such as intensity, rather than on psychological features of the person or the situation. In contrast, the *endogenous* event-related potentials following stimulus onset with a latency in the range of 100 ms up to several seconds depend largely on behavioral and psychological processes related to the event. These potentials are much more determined by the psychological meaning (e.g., attentionally relevant or not; aversive vs. pleasant) for the organism than by the physical quality of the stimulus itself (Rockstroh, Elbert, Canavan, Lutzenberger, & Birbaumer, 1989). Event-related potentials with a latency ranging from 500 ms up to 10 s or more are categorized as *slow cortical potentials* and are discussed in greater detail below.

The amplitude of event-related potentials is usually smaller than the background noise of the spontaneous EEG, which varies randomly across event repetitions, whereas event-related potentials are assumed to remain constant. Therefore, averaging the event-related potentials across numerous event repetitions separates the signal from the background noise and, thus, improves the signal-to-noise ratio.

The spontaneous EEG of the waking adult comprises characteristic bands of different frequencies. Different oscillatory mechanisms are generated in subcortical (i.e., thalamic) and cortical areas underlying diverse psychophysiological states mainly related to sleeping–waking–dreaming cycles and attention (Niedermeyer & Lopes da Silva, 1993). The activity between 8 and 13 Hz is referred to as *alpha* band and is most prominent over occipital, parietal, and posterior temporal regions in the state of relaxed wakefulness with the eyes closed. The  $\mu$  rhythm is defined as arch-shaped 8–12 Hz activity over the sensorimotor cortex. In contrast to the visual alpha rhythm, it is not dependent on vision but is blocked by motor activity, movement preparation, and motor imagery. The *beta* band covers frequencies above 13 Hz, mainly over frontal and central regions. Frequencies from below 8 Hz to 4 Hz form the *theta* band. In the normal waking adult only small amounts of theta frequencies can be recorded in contrast to in infancy and sleep. Frequencies from 0.5–4 Hz are called *delta*

waves, present only in deep sleep or anesthesia. Larger amounts of theta and delta activity in awake adults are abnormal and related to various pathologies as, for instance, neurological diseases. Oscillatory activity above 30 Hz is termed *gamma* activity and has been related to the synchronization of neuronal assemblies involved in the generation of mental representations (Kaiser, Lutzenberger, Preissl, Ackermann, & Birbaumer, 2000; Tallon-Bandry & Bertrand, 1999).

### Brain-Computer Interfaces

The system that translates the electrical activity of the brain into signals controlling external devices is referred to as the *brain-computer interface* (see Figure 3A). Brain-computer interface operation depends on the interaction of three adaptive controllers: first, the electrophysiological activity of the user's brain, which produces the input; second, the interface itself, which translates the electrophysiological activity into signals that control an application; and, third, the application—for example, a program to realize verbal communication. The application has to be adapted to the various needs, performance, and learning progress of the individual user.

One possible way of characterizing brain-computer interface techniques is on the basis of the differentiation between direct and immediate recognition of brain potentials without prior conditioning and the recognition of brain potentials after operant conditioning and self-regulation training. For the direct recognition approaches, it is assumed that confrontation with certain kinds of stimuli (e.g., Farwell & Donchin, 1988) or engagement in certain cognitive tasks (e.g., Keirn & Aunon, 1990a, 1990b) is reflected in specific and detectable event-related brain potentials or EEG power spectra.

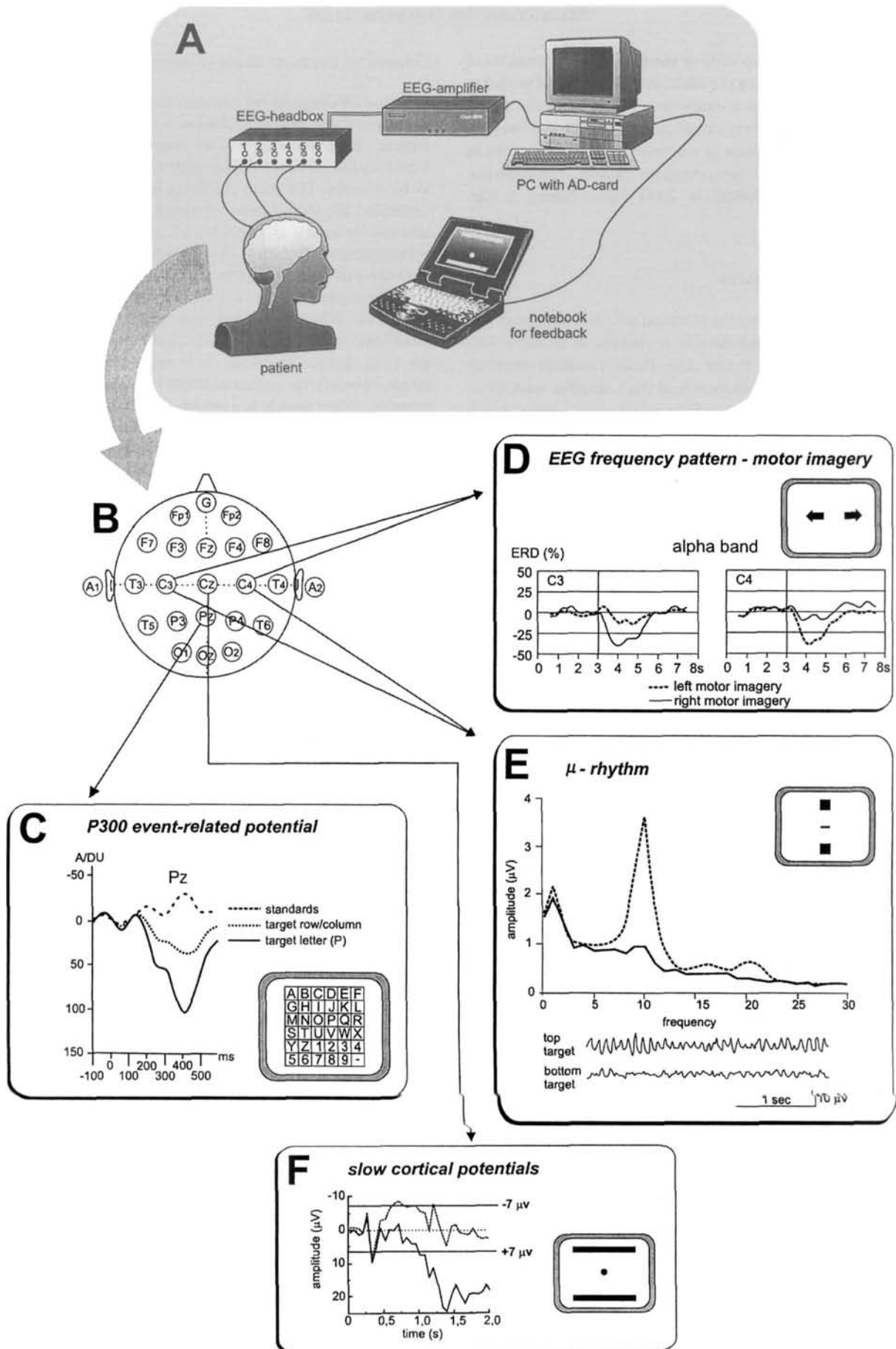
The operant conditioning approach to brain-computer communication establishes control of the target EEG response by means of sensory feedback, positive reinforcement of correct behavior, or both. Many authors have demonstrated operant conditioning and self-regulation of various EEG parameters in animals and humans (Birbaumer, 1977, 1984; Birbaumer, Elbert, Rockstroh, & Lutzenberger, 1981; Kamiya, 1969; Kuhlman, 1978; Plotkin, 1976; Serman, 1977). This is of particular interest because it means that EEG signals can be brought under voluntary control using principles of learning psychology. To construct a direct connection between the brain and a computer on the basis of self-control of brain signals, one must extract EEG components on-line that can be shaped with operant conditioning strategies or cognitive manipulations and develop a design for translation of these EEG responses into a distinct signal capable of controlling external devices (e.g., the movement of a cursor on a computer screen). Patients receive continuous feedback of their target brain response and learn to produce or withhold certain levels of the EEG signal. This may be reflected in the movement of a graphic symbol on a monitor toward a target or in sounds whose frequencies vary according to the amplitude of the brain response. Successful learning using reinforcement and shaping of the response results in the acquisition of a new, nonmotor skill, the voluntary control of the EEG signal.

### Criteria to Evaluate Brain-Computer Interfaces

To use EEG signals for communication, patients should be able to produce these signals rapidly and with high accuracy. These two criteria, speed and accuracy, are commonly used to evaluate the feasibility of a brain-computer interface. The reason for this seems to be obvious. The more rapidly a brain-computer interface is controlled, the more communication is possible in a defined time interval. Accuracy is necessary to avoid unintended and false communication. However, these criteria are not sufficient for the evaluation of brain-computer interfaces. A problem arising from speed as a criterion is how it can be defined in a person who is paralyzed. When compared with speech, all other muscle-controlled devices are slow and most EEG-controlled responses are even slower. Therefore, it is necessary to consider which output channels for communication are available in a particular situation. When speech is available, this is the most suitable way to communicate, at least for communication among individuals in daily life. When speech fails (e.g., because of paralysis of speech muscles) but fingers are available, a keyboard is probably the method of choice, although the communication rate is slow compared with speech. When control over only a few muscles remains (e.g., because of degenerative diseases), communication may only be mediated by a single switch. Compared with speech, the communication rate is reduced, but such a communication is still worthwhile even if it takes much longer to select a letter or a command. Neurological diseases can lead to total motor paralysis that affects even eye movement. For patients with such diseases brain-computer communication is the method of choice, even though the communication rate is further decreased compared with single-muscle switches. However, there is presumably a limit below which the communication rate of a brain-computer interface should not fall. This limit is certainly dependent on the motivation and the patience of individual patients and their social environments and cannot be generally defined.

For the second criterion, accuracy, similar considerations should be taken into account. A lack of accuracy is not a severe problem when mechanisms for error correction are available. We define *accuracy* as percentage of correct responses, that is, correct selections per time interval; *accuracy* does not mean the correctness of the final communicative message. The accuracy of communication using speech or keyboards is far from 100%, but correct communication is possible because errors can be immediately eliminated. To avoid unintended brain-computer communication, the application must be equipped with options to correct wrong selections. It is obvious that less accurate control over the brain-computer interface results in larger numbers of errors; slower error correction; and, consequently, slower brain-computer communication. When speed does not matter, 100% correctness of communication can be attained (by means of error correction) even if accuracy is below 70%. Although this is an open empirical question, one can assume that a brain-computer interface that enables users to select only one correct option every few minutes may not be efficient enough to motivate the patient to use the brain-computer interface. Thus, the challenge is to find the optimal balance between accuracy and speed for the individual user.

Another criterion for the feasibility of a brain-computer interface designed for communication is whether it is actually used by the target group, that is, locked-in patients. The scientific literature



contains many descriptions of brain-computer interfaces using different EEG parameters that have never been used by patient populations (e.g., Anderson, Stolz, & Shamsunder, 1998; Keirn & Aunon, 1990b; Middendorf, McMillan, Calhoun, & Jones, 2000). The fact that these brain-computer interfaces are capable of fast separation and discrimination of EEG frequency patterns does not prove their usefulness to patients. The patient populations in need of brain-computer interfaces have severe neurological or muscular diseases or brain lesions causing extensive changes in EEG power spectra and in the waveforms of event-related potentials. Artificially ventilated patients with amyotrophic lateral sclerosis, for example, show a 1–3 Hz decrease of the spectral peak, and the topography of the different frequency bands is fundamentally different because of tissue damage in motor and frontal areas. Higher background EEG amplitudes caused by pathological brain activity attenuate signal-to-noise ratios and lead to classification errors (Schneider, Heimann, Mattes, Lutzenberger, & Birbaumer, 1992; Schneider, Rockstroh, et al., 1992). The number of sessions needed to learn to produce a particular EEG frequency or a pattern of event-related potentials is usually much higher in patients than in healthy participants; some patterns are even impossible to reproduce. Therefore, any generalization from results obtained with healthy populations to individuals who are paralyzed is problematic.

Despite these and other problems, we do not consider a review of the brain-computer interface literature premature because brain-computer interface research has been ongoing for more than 20 years. The different approaches have never been analyzed and evaluated in terms of their feasibility for locked-in patients. This analysis reveals a great gap between the numerous EEG analysis technologies that have been developed for the purpose of brain-computer communication and the small number of patients who benefit from this means of communication in daily life. The problem is that the technological aspects of brain-computer interfaces (e.g., techniques to extract the useful signal from the “useless” noise) are much better developed than are their psychological aspects: Theories of learning and motivation, ecological aspects of quality of life, and the potentially restricted learning abilities of neurological patients are neglected, ignored, or not considered important. There is a lack of psychological sophistication and insufficient inclusion of behavioral principles. We believe that more psychological theory and experimentation have to be integrated into the development of brain-computer interfaces and considered as important as the technical aspects. Stimulating this integration is the main objective of the present review.

We next introduce seven approaches to brain-computer interfaces. The approaches are separated into two groups according to

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*Figure 3.* A: A typical arrangement of a brain-computer interface. The user sits in front of a PC or notebook, which provides him or her with a matrix or a task or with feedback of his or her brain responses. A PC with an analog-digital (AD) card transfers the analog electroencephalogram (EEG) activity into digital signals, which control the application (for instance, a matrix with symbols). The EEG is recorded from the user's skull with electrodes and is amplified. B: The electrodes are usually placed on the skull according to the international 10–20 system. As the shape of skulls varies across individuals, it is impossible to determine absolute sites for electrode placement. Consequently, the electrodes are positioned in relative distances (10% and 20% of the total scope of the individual skull). The capital letters refer to the lobes of the brain (F = frontal; T = temporal; P = parietal; O = occipital). Electrodes placed on the left hemisphere are marked with odd numbers, those on the right with even numbers, and those sagittal with z. C = central; G = ground; A = auricular (behind the earlobes). C–F show EEG activity used as target signals in four brain-computer interfaces. C: The P300 brain-computer interface. Bottom right, the matrix with 36 cells. Counting how often the cell with the target letter flashes leads to a clearly distinguishable P300 event-related potential (solid line), whereas the positive shift in response to the target row or column is reduced (dotted line). Flashing of nontarget rows or columns does not elicit a P300 (dashed line). A/DU = analog/digital units. Pz is the electrode location where the P300b component is recorded. From “The Mental Prosthesis: Assessing the Speed of a P300-Based Brain-Computer Interface,” by E. Donchin, K. M. Spencer, and R. Wijesinghe, 2000, *IEEE Transactions on Rehabilitation Engineering*, 8, p. 176. Copyright 2000 by IEEE. Reprinted with permission. D: The brain-computer interface using EEG frequency patterns related to motor imagery. An arrow on the screen (top right) indicates whether the user should imagine left- or right-hand movement. Imagery of left-hand movement leads to a desynchronization in the alpha band over the right hemisphere at the electrode position C4, whereas at C3 synchronous EEG activity in the alpha band is maintained. ERD = event-related desynchronization. From “Current Trends in Graz Brain-Computer Interface (BCI) Research,” by G. Pfurtscheller, C. Neuper, C. Guger, W. Harkam, H. Ramoser, A. Schlögl, B. Obermaier, and M. Pgegenzer, 2000, *IEEE Transactions on Rehabilitation Engineering*, 8, p. 216. Copyright 2000 by IEEE. Reprinted with permission. E: The screen (top right) shows targets toward which the cursor has to be moved. Top graph:  $\mu$ -rhythm voltage recorded over C3 and C4. A high  $\mu$ -rhythm amplitude (dashed line) moves the cursor toward the top target, and low amplitude, toward the bottom target (solid line). Bottom graph: Sample EEG traces accompanying top or bottom targets. The  $\mu$ -rhythm is prominent with the top target and minimal with the bottom target. From “Brain-Computer Interface Research at the Wadsworth Center,” by J. R. Wolpaw, D. J. McFarland, and T. M. Vaughan, 2000, *IEEE Transactions on Rehabilitation Engineering*, 8, p. 224. Copyright 2000 by IEEE. Reprinted with permission. F: The screen (right) shows the top and bottom targets. The course of slow cortical potentials during feedback in the Thought Translation Device is illustrated. Cortical negativity moves the cursor in the top target (top line, dashed), and cortical positivity does so in the bottom target (bottom line, solid). When a threshold of 7  $\mu$ V is surpassed, the computer counts a hit.

whether learning to self-regulate an EEG response is necessary to use the brain-computer interface or not.

### On-Line Classification of Cognitive and Sensory Brain Potentials and EEG Power Spectra

Several brain-computer interfaces use EEG pattern recognition techniques under the assumption that specific mental operations and responses to specific sensory stimuli result in reproducible EEG frequency or event-related potential patterns. The EEG patterns are identified by the brain-computer interface and used for selection of communication symbols. These approaches focus on the identification of algorithms to detect the chosen signal in the EEG for communication. The brain-computer interfaces of, for example, Farwell and Donchin (1988); Donchin, Spencer, and Wijesinghe (2000); Bayliss and Ballard (2000); Sutter (1992); and Middendorf et al. (2000) use event-related potentials as the target signal. In contrast, for example, Keirn and Aunon (1990a, 1990b), Penny, Roberts, Curran, and Stokes (2000), and Pfurtscheller et al. (2000) used patterns of spectral power in the EEG related to different cognitive tasks as the target signal. In the following sections three brain-computer interfaces based on on-line recognition of EEG patterns are described: The first is controlled by the P300 event-related potential, the second uses visual event-related potentials, and the last relies on the detection of patterns of spectral EEG power.

#### *The P300 Event-Related Potential*

The P300 is an endogenous event-related potential with a peak latency of 300–400 ms after stimulus onset. It is a well-documented EEG response to a rare task-relevant event measured, usually, in the so-called oddball paradigm: The participant is presented with a sequence of frequent and rare events. In addition, the participant is asked to perform a task that makes categorization of the events necessary. Given these circumstances, the rare event elicits the P300 event-related potential. The less probable the eliciting event, the larger the P300 (Donchin, Spencer, & Wijesinghe, 2000). The P300 consists of two components: an earlier prefrontal P300a, indicating novelty, and a later parietal P300b. Various hypotheses about the functional significance of the P300 exist, linking it to specific steps in the flow of information processing (Donchin & Coles, 1988). The most dominant and agreed-on view associates the P300b with the updating of representations in working memory (Donchin, 1981; Fabiani, Gratton, Karis, & Donchin, 1988). For the purpose of brain-computer communication, individuals do not have to learn to produce this response, as it is elicited involuntarily by the rare task-relevant event. The P300b is most prominent over parietal regions and is recorded at the electrode location Pz (see Figure 3B).

Farwell and Donchin (1988) and, subsequently, Donchin et al. (2000) tested a variation of the oddball paradigm for brain-computer communication. The authors presented the user with a  $6 \times 6$  symbol matrix, which contained the alphabet, numbers, and a space symbol, resulting in a square containing 36 cells (see Figure 3C). Visual stimuli consisted of the flashing of one row or one column of the matrix in random order. To select a letter, the user had to focus attention on the cell containing the target letter he or she wanted to select and count the number of times the row or

column with that cell flashed. In each trial, each of the six columns and each of the six rows were illuminated once for a period of 100 ms. Therefore, one trial consisted of 12 events (sequential illumination of six rows and six columns). As the participant had to count how often one single cell flashed (the cell containing the target letter), only 2 events out of 12 possible events were task-relevant and rare compared with all other events—characterizing the design as an oddball paradigm. Each illumination of the target cell elicited a P300b. The response to all other flashes (rows and columns that did not contain the target cell) did not elicit a P300 (see Figure 3C).

The event-related potential pattern was measured on-line after each flash—namely, in the time window from 100 ms prior to the flash to 500 ms after the flash (see Figure 3C). A successful hit was scored whenever the system detected a P300 that was significantly larger than all other event-related potentials in that latency range. Detection and measurement of the P300 requires averaging of the EEG signal as described above. The quality of the detection of the P300 and, consequently, the accuracy of letter selection increased with the number of trials included in the signal averaging. According to Donchin et al. (2000), an average of 40 trials in 60 s led to perfect accuracy. Therefore, perfect letter selection within the P300 brain-computer interface would be achieved if a total of 60 s to communicate each character was an acceptable speed. The authors, however, considered this communication speed “unacceptably slow” (p. 175). If an individually optimized on-line algorithm to extract the P300 event-related potential from the background noise was used and if an accuracy of less than 100% was accepted, the time needed to select a character could fall below 60 s. With 80% accuracy, a speed of 7.8 characters per minute was predicted.

Donchin et al. (2000) tested 4 participants with disabilities (3 with complete, 1 with incomplete paraplegia, all wheelchair users) from the university community in one training session. In all 4 participants, the P300 was detected as reliably as in 10 participants who did not have disabilities.

The P300 brain-computer interface uses a cognitive event-related potential as a control signal. In contrast, the brain-computer interfaces described in the next section rely on sensory components of event-related potentials.

#### *Visual Event-Related Potentials*

Visual event-related potentials are elicited by visual stimuli such as flashes or flickering illumination. They can be recorded throughout the visual system. The amplitude and frequency of visual event-related potentials can be used to control a brain-computer interface (Middendorf et al., 2000; Sutter, 1992; Sutter & Tran, 1990; Vidal, 1973). Participants are presented with a screen that offers different items for selection (as described in the next paragraph). The user has to fixate his or her eyes on the item he or she wants to select. The items on the screen are activated sequentially to elicit a visual event-related potential. The brain-computer interface detects the visual event-related potential elicited by the fixated item, which then leads to the selection.

Sutter and Tran (1990) and Sutter (1992), for example, confronted participants with a matrix of eight columns and eight rows (a total of 64 cells) that contained characters, words, or keys. The cells of the matrix were activated (by flickering illumination) in a



pseudorandom sequence. Participants had to fixate the cell containing the character or key they wanted to select. The matrix cell that elicited the largest visual event-related potential amplitude over the occipital cortex was considered as the target cell that the participant wanted to select. The authors reported successful communication using this method in 60 participants who did not have disabilities. In patients with neurological impairments, communication problems due to large muscular artifacts from neck muscles interfering with the visual event-related potential recording were described by these authors. Success was also limited in patients with cerebral palsy because of artifacts caused by involuntary athetoid movements, as it was in patients with amyotrophic lateral sclerosis, where artifacts were caused by fasciculations. In an attempt to overcome these problems, the authors implanted an electrode between the dura mater and the skull of one amyotrophic lateral sclerosis patient. This patient was given the communication system for use and evaluation in his home. The authors reported a very high communication rate of 10–12 words per minute. It should be noted that the brain–computer interface on the basis of visual event-related potentials requires that the user be able to control gaze direction.

### *EEG Power Spectra Related to Motor Imagery or Cognitive Tasks*

Another approach to brain–computer communication is based on the assumption that different cognitive tasks (e.g., solving a multiplication problem or imagining a finger movement) lead to distinct, task-specific distributions of EEG frequency patterns over the scalp. These patterns of spectral power could be used to encode several commands of a patient. For example, EEG during mental rotation of a three-dimensional geometric figure after imagined left-finger movement could turn on the TV, or imagined left-finger movement followed by imagined right-finger movement could turn off the TV.

Pfurtscheller and his colleagues have shown in a series of studies that imagination of specific movement of arms, fingers, or legs leads to characteristic EEG frequency patterns, which could be used to control a brain–computer interface (Guger, Schlögl, Walterpacher, & Pfurtscheller, 1999; Kalcher, Flotzinger, Neuper, Göllly, & Pfurtscheller, 1996; Pfurtscheller, Neuper, Schlögl, & Lugger, 1998). Extensive off-line analysis revealed that classification accuracy improves when features like electrode position and frequency range are optimized individually for each user (Pregener, Pfurtscheller, & Flotzinger, 1996). Characteristically, at electrode positions over the central motor cortex (C3 and C4; see Figure 3B), an event-related desynchronization of the EEG was recorded over the hemisphere contralateral to the imagined movement, whereas synchronization of the EEG was present over the ipsilateral hemisphere (see Figure 3D). This difference in the EEG frequency patterns over both hemispheres was used to control a cursor on a computer screen in one dimension (Pfurtscheller et al., 2000). Currently, the brain–computer interface is used by a patient experiencing tetraplegia following a spinal cord injury. An apparatus to open and close his hand, referred to as an *orthosis*, was connected to the interface. The patient learned to control the orthosis in 62 training sessions over 5 months. Accuracy was between 90% and 100% (Pfurtscheller et al., 2000).

Keirn and Aunon (1990a, 1990b) and, subsequently, Anderson et al. (1998) used EEG frequency patterns related to other mental tasks, namely, (a) thinking of nothing in particular (baseline task), (b) solving a multiplication problem, (c) mentally rotating a complex three-dimensional block figure (participants studied a drawing of a figure for 30 s, and after the drawing was removed, participants were instructed to visualize the object being rotated around its axis), (d) mentally writing a letter to a friend without vocalization, and (e) visualizing numbers being written on a blackboard sequentially, with each number being erased before the next is written. In Keirn and Aunon's studies, off-line classification of the distribution of spectral power resulted in accuracy levels as high as 80%–90%. Accuracy was defined as successful classification of the EEG power spectra characteristic for the different cognitive tasks. The data were obtained from healthy participants.

### Operant Learning of Brain Responses

Brain–computer interfaces that operate without prior conditioning of a specific EEG response do not require that users undergo a sophisticated learning procedure. External stimuli or mental tasks evoke the specified EEG pattern, and thus the system learns to detect and identify the brain signal. However, it seems probable that long-term use of these signals for brain–computer interface operation will cause changes in them that may be adaptive or maladaptive. Alternatively, brain–computer interfaces that make use of operant learning require patients' control over the target EEG signal, such as the slow cortical potential amplitude (Birbaumer et al., 1999) or the power of the 8–12 Hz frequency band ( $\mu$  rhythm; Wolpaw & McFarland, 1994; Wolpaw, McFarland, Neat, & Forneris, 1991).

Three elements are important for successfully learning to self-regulate a physiological parameter that usually cannot be consciously perceived (e.g., blood pressure, skin temperature, EEG activity): first, real-time feedback of the physiological parameter—in the case of a brain–computer interface, the specific EEG activity; second, positive reinforcement of correct behavior; and, third, an individual shaping schedule in which progressively more demanding tasks are rewarded (Kübler et al., 1999; Kübler et al., in press; Taub et al., 1994).

Usually, participants are provided with visual feedback of the to-be-controlled EEG response. The EEG signal is transformed into movement of a graphic symbol on a computer screen informing the patient continuously about his or her specific EEG activity (Birbaumer et al., 1994; Rockstroh, Birbaumer, Elbert, & Lutzenberger, 1984; Rockstroh et al., 1993). Communication using a brain–computer interface requires at least a binary (yes–no) signal. The simplest case is to select or reject a letter, word, or item that is presented on the screen for selection. For a binary signal, which allows one-dimensional cursor movement, the user has to produce voluntarily two clearly distinguishable EEG responses. For this reason participants have to perform two different tasks, for example, to move the cursor toward the bottom or the top of a computer screen by alterations in the specific EEG response. The target in each trial (e.g., top or bottom of the screen) is indicated by the computer. At the end of each trial, participants are informed as to whether they accomplished the task.

To use brain–computer interfaces that rely on operant learning and feedback, participants are trained to self-regulate a specific



EEG response. The obvious disadvantage is that a long training period may be required before the self-regulation skill can be used for communication (Kübler, 2000). Successful brain-computer communication is possible only if the learning capacity and motivational status of a patient and his or her environment are considered individually.

Brain-computer interfaces operating on the basis of operant learning are explained in the following sections. First, a brain-computer interface using the activity of single neurons as the specific to-be-controlled signal is described. Second and third, brain-computer interfaces using synchronous activity of larger brain areas are introduced: a system that uses the 8–12 Hz  $\mu$  rhythm and another using slow cortical potentials as the target EEG response.

### *Self-Control of Action Potential Firing Rate*

The action potential of a neuron is an all-or-none signal of constant amplitude. Information is encoded in the action potential frequency or firing rate. If patients with locked-in syndrome were able to learn self-control over the action potential firing rate of neurons in the central nervous system, this ability could be used to operate a brain-computer interface. Because action potentials cannot be recorded from the scalp, electrodes have to be inserted into cortical tissue.

Kennedy and Bakay (1998) used the action potential firing of cortical neurons. An electrode containing “proprietary neurotrophic factors” (p. 1707) was implanted surgically into cortical tissue (Kennedy, Bakay, & Sharpe, 1992). The neurotrophic factors stimulated adjacent neurons to grow into the tip of the glass electrode. The electrode then measured neuronal activity directly from the cortical tissue. The authors showed in studies with monkeys that the implanted electrode can remain active in the brain for 15 to 16 months (Kennedy & Bakay, 1997). A patient diagnosed with amyotrophic lateral sclerosis who had close to total locked-in syndrome was the first human participant to undergo this treatment. Two electrodes were implanted in the hand area of the right motor cortex, and 16 days after implantation action potentials were recorded. The patient was trained to increase or decrease the firing rate to produce a binary signal. The patient received both visual and auditory feedback of the neural activity. Unfortunately, this patient died before she was able to use the brain-computer interface for communication. A second patient communicated with the brain-computer interface at a maximum rate of three letters in 60 s on the 423rd day after electrode implantation (Kennedy, Bakay, Moore, Adams, & Goldwithe, 2000).

### *Cursor Control With the $\mu$ Rhythm*

The ability to control the  $\mu$  rhythm has been demonstrated in humans (Kuhlman, 1978; Serman, 1977) and cats (Wyrwicka & Serman, 1968). Wolpaw et al. (1991) recorded the  $\mu$  rhythm in healthy participants who had to move a cursor into a target either at the top or at the bottom of a video screen. The voltage of this frequency (8–12 Hz) determined vertical cursor movements across the screen. Increased  $\mu$ -rhythm amplitude moved the cursor toward the top target, and decreased  $\mu$ -rhythm amplitude moved the cursor toward the bottom target (see Figure 3E). After several weeks of training, healthy participants reached an accuracy of

about 90%. Further studies demonstrated that self-control of the  $\mu$  rhythm could also provide graded one-dimensional cursor control (McFarland, Neat, Read, & Wolpaw, 1993) and two-dimensional cursor control (Wolpaw & McFarland, 1994).

In subsequent studies of the same group, parameters that affect the accuracy and speed of the brain-computer interface were investigated and improved. For instance, it was determined individually at which electrode sites the  $\mu$  rhythm was most pronounced (McFarland, McCane, David, & Wolpaw, 1997; Pfurtscheller, Flotzinger, Pregenzer, Wolpaw, & McFarland, 1996; Wolpaw, Flotzinger, Pfurtscheller, & McFarland, 1997).

Recently Wolpaw, Ramoser, McFarland, and Pfurtscheller (1998) investigated whether communication accuracy could be improved when a given response had to be confirmed or canceled. This method was referred to as response verification. A response verification procedure allowed a reduction in target selection errors and partially eliminated the impact of spontaneous variation in EEG voltage. In this procedure each outcome was determined by cursor movement into opposite directions during two subsequent trials (for the one-dimensional control: toward the top and bottom of the screen; for the two-dimensional control, in addition, to the left and right margin of the screen). Participants had to confirm the selection of a target by moving the cursor into the opposite hemifield of the screen, and in case of misses they had to cancel the trial by moving the cursor into the same hemifield again. This procedure increased accuracy; for example, a patient who achieved 90% accuracy was able to achieve a response verification accuracy of more than 99%. This improvement occurred at the expense of the speed of the system. However, if accuracy is more important than speed, response verification is useful.

In these studies of  $\mu$ -rhythm control both healthy participants and participants with disabilities such as amyotrophic lateral sclerosis and spinal cord injury have attended the training. The attained accuracy was 90% or more.

### *Cursor Control With Slow Cortical Potentials*

There are a number of reasons why slow cortical potentials have been used for the brain-computer interface referred to as the Thought Translation Device. First, their neurophysiological basis is well understood; second, they are universally present in cortical cell assemblies; and, finally, learning rules for the acquisition of slow cortical potential self-control are known (Birbaumer, Elbert, Canavan, & Rockstroh, 1990). Intensive research has been conducted to clarify the neurophysiology underlying slow cortical potential generation and its relation to behavior.

The vertical arrangement of pyramidal cells in the cortex is essential for the generation of slow cortical potentials. Most apical dendrites of pyramidal cells are located in Cortical Layers I and II. Depolarization of the apical dendrites giving rise to slow cortical potentials is dependent on sustained afferent intracortical or thalamocortical input to Layers I and II (see Figure 4) and on simultaneous depolarization of large pools of pyramidal neurons. The slow cortical potential amplitude recorded from the scalp depends on the synchronicity and intensity of the afferent input to Layers I and II (Speckmann, Caspers, & Elger, 1984).

The depolarization of cortical cell assemblies reduces their excitation threshold. Firing of neurons in regions responsible for specified motor or cognitive tasks is facilitated. Whenever a task-

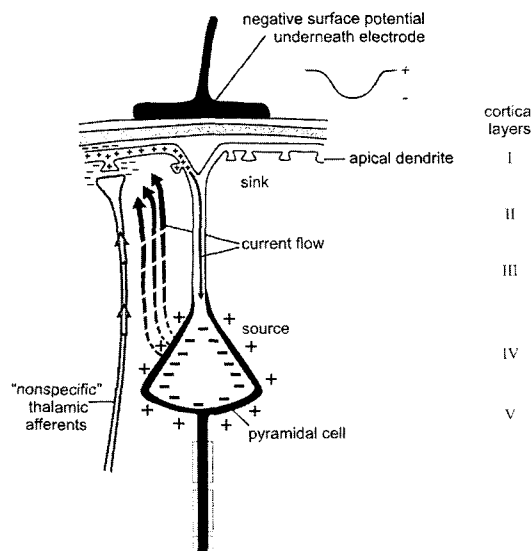


Figure 4. Negative slow cortical potentials at the surface of the cortex originate from afferent thalamic or cortical input to the apical dendrites in Layers I and II. The extracellular surrounding of the dendrites is electrically negative, leading to current flow into the cell mediated by positive sodium ions (sink). Intracellularly, the current flows toward the soma (source). This fluctuation of ions generates field potentials that can be recorded by electrodes on the scalp.

relevant event is expected, cortical excitation thresholds are lowered in the corresponding cortical cell assemblies to facilitate neuronal firing. Negative slow cortical potential amplitude shifts can be recorded in the EEG using experimental paradigms that elicit cognitive or motor mobilization (Birbaumer et al., 1990; Rockstroh et al., 1989). Negative amplitude shifts grow with increasing attentional or cognitive resource allocation.

A strong relationship between self-induced cortical negativity and reaction time, signal detection, and short-term memory performance has been reported in several studies in humans and monkeys (Birbaumer, Elbert, Lutzenberger, Rockstroh, & Schwarz, 1981; Lutzenberger, Elbert, Rockstroh, & Birbaumer, 1979, 1982; Lutzenberger, Roberts, & Birbaumer, 1993; Rockstroh, Elbert, Lutzenberger, & Birbaumer, 1982). Tasks requiring attention are performed significantly better when presented after spontaneous or self-induced cortical negativity. For instance, Lutzenberger et al. (1982) trained their participants in slow cortical potential self-regulation by providing feedback and positive reinforcement of correct responses. Participants were also presented with arithmetic tasks. In trials in which arithmetic tasks had to be solved, no feedback (transfer trials) was provided; participants were only asked to produce cortical negativity or positivity as in feedback trials. The arithmetic tasks were solved significantly faster after a preceding negative slow cortical potential shift. Self-induced cortical positivity usually reduces cognitive and motor performance.

Studies by Birbaumer and coworkers (Birbaumer, 1984; Birbaumer et al., 1990; Birbaumer, Elbert, Rockstroh, & Lutzenberger, 1981), as well as other investigators (H. Bauer, 1984; Serman, 1981), have demonstrated that healthy participants and patients with neurological conditions (epilepsy and amyotrophic lateral sclerosis; Kübler et al., 1998; Rockstroh et al., 1993) can

attain reliable control over their slow cortical potential amplitude at central, frontal, and parietal locations with operant learning. Moreover, participants can learn to control slow cortical potential differences between the left and right hemispheres and differentially at frontal, central, and parietal sites (Birbaumer et al., 1988; Kotchoubey, Schleichert, Lutzenberger, Anokhin, & Birbaumer, 1996; Rockstroh, Elbert, Birbaumer, & Lutzenberger, 1990). This capability could be used for two-dimensional cursor control in a brain-computer interface.

In the first study using the Thought Translation Device, healthy participants were trained to self-control their slow cortical potential amplitude at electrode locations Cz, C3 (right-hand region), and C4 (left-hand region; Kotchoubey, Schleichert, Lutzenberger, & Birbaumer, 1997). All healthy participants attained significant (i.e., better than chance) control of their slow cortical potential amplitude at Cz during the first training session (10 min). Control over interhemispheric slow cortical potential amplitude differences, that is, between C3 and C4 (see Figure 3B), was more difficult but was achieved in further training sessions by 4 of the 5 participants and was subsequently replicated (Kotchoubey et al., 1996). As it was more difficult for healthy participants to achieve reliable control over the interhemispheric slow cortical potential asymmetry than over the slow cortical potential amplitude at Cz, training with locked-in syndrome and amyotrophic lateral sclerosis patients was initiated with one-dimensional cursor movements. Thus, the patients had to control their slow cortical potential amplitude at Cz only.

With the Thought Translation Device participants observe two rectangles, one at the top and one at the bottom of the screen, and a cursor informs the patients of their slow cortical potential amplitude (see Figure 3F). Participants were not instructed in how to move the cursor. They were only advised to be attentive to the feedback and to find the most successful mental strategy.

The patients' task was to move the cursor in the highlighted target. Whenever a rectangle was hit according to the task requirement, it flashed and a smiling face appeared as a positive reinforcement. The criterion for the slow cortical potential amplitude necessary to move the cursor into a rectangle (the hit amplitude) was set individually according to the patients' performance. For instance, when a patient produced slow cortical potential amplitude shifts of  $10 \mu\text{V}$  only, the criterion for a hit was lower (in voltage) than for a patient who produced slow cortical potential amplitude shifts of  $20 \mu\text{V}$  (Kotchoubey et al., 1996, 1997; Kübler et al., 1999). A minimal amplitude shift of  $3 \mu\text{V}$  had to be surpassed in all patients. Whenever the slow cortical potential amplitude shift exceeded the corresponding threshold, the cursor touched the rectangle, and the computer counted a hit.

Four patients with severe or total paralysis were trained with the described version of the Thought Translation Device (Kübler et al., 1998, 1999). Three men diagnosed with amyotrophic lateral sclerosis were tetraplegic and unable to speak; 2 had been artificially fed by tube and ventilated by tracheostoma (invasive artificial ventilation) for at least 3 years (referring to the beginning of the studies) and had only unreliable control over eye movement. The female patient was locked-in after an infarct of the arteria basilaris. All patients were trained at home or in a nursing home while lying in bed or sitting in wheelchairs. After 20 to 40 sessions (2 to 4 weeks) all patients were able to self-regulate their slow cortical potential amplitude according to the task requirement. Overall

accuracy (percentage of correct responses) in self-regulation training varied between 65% and 90% (Kübler et al., 1998, 1999).

For verbal communication patients were provided with the Language Support Program (Perelmouter, Kotchoubey, Kübler, Taub, & Birbaumer, 1999). In the Language Support Program patients were presented with the identical screen design as in the slow cortical potential training, but the rectangles were now also used for letter presentation. Patients were able to spell words. Average time needed to select a letter varied over training sessions and patients. Provided with a set containing 16 letters, patients' time per session to select a letter varied between 12 and 192 s (Kübler et al., 1999).

Two patients have been using the Language Support Program for free communication with the whole set of 32 symbols—the German alphabet including umlaut, space (–), and punctuation marks (, .)—for 24 months (Birbaumer et al., 1999). The time to select a letter in the Language Support Program with perfect slow cortical potential control and a trial length of 4 s was 20–40 s depending on the position of the letter in the German alphabet. Across sessions, however, the time to select a letter varied from 20 s to 390 s. Thus, performance varied markedly from day to day.

### Limitations of Brain–Computer Interfaces

All brain–computer interfaces have limitations, namely: (a) habituation, (b) interference and distraction, (c) impaired visual system, (d) instability of EEG frequency bands, and (e) invasive recording. Not all limitations are present in all brain–computer interfaces.

#### *Habituation*

Participants in the studies of Farwell and Donchin (1988) and Donchin et al. (2000) had to write only a few letters in a single session. The P300 event-related potential is well known to habituate with repeated stimulation (Polich & McIsaac, 1994). It is not clear whether the P300 habituates if patients have to perform hundreds of trials day after day, week after week, year after year. Habituation may restrict the feasibility of brain–computer interfaces that rely on detecting EEG responses elicited by external events. The long training periods in the  $\mu$ -rhythm brain–computer interface and the Thought Translation Device revealed that the corresponding brain responses do not habituate; EEG responses remain the same for weeks, months, and years.

#### *Interference and Distraction*

Interference and distraction may be potential problems that arise when patients have to use the brain–computer interface for daily communication in the social environment and not only for selecting a few letters given by the experimenter or for moving a cursor into targets on the screen. In the P300 brain–computer interface interference may occur between counting the number of flashes of the matrix cell that contains the target letter and simultaneously concentrating on the characters, words, and sentences to be communicated. This situation entails divided attention. The imagery associated with the different cognitive tasks that the patient performs to produce specific EEG frequency patterns may interfere with the thoughts the patient intends to communicate, and vice

versa. Strategies to self-regulate an EEG response may interfere with thinking of words to communicate and of how to spell these words. The performance of 2 patients who used the Language Support Program of the Thought Translation Device decreased during the transfer from simple cursor movement training to copying words presented by the trainer and again after transfer from copying to free communication, indicating interference. The performance of both patients returned to high levels after continuation of training for several weeks (Birbaumer et al., 1999).

#### *Impaired Visual System*

Brain–computer interfaces relying on visual event-related potentials raise another important problem. Patients have to fixate the matrix cell on the screen that contains the key or word they want to select (Sutter, 1992). Whenever the patients move their eyes, a communication error occurs because a false target is fixated. For the P300 brain–computer interface attention is focused on the target cell and the flashes must be counted. Therefore, visual attention is crucial. Both visual attention and the visuomotor system may be compromised in patients who are paralyzed. Furthermore, the locked-in syndrome may be accompanied by eye muscle paralysis: Patients lose control over horizontal and vertical eye movement and voluntary movement of the eyelid. Visual impairment may also be caused by decreasing eyesight. Brain–computer interfaces that use visual event-related potentials as control signals are not feasible for patients with an impaired visual system. Brain–computer interfaces should not rely on visual stimulation alone. The brain–computer interfaces based on operant learning have to provide another feedback modality besides vision. The use of auditory signals implies that feedback of the EEG response, the task requirement, and the reward for correct responses have to be presented acoustically. The Thought Translation Device using slow cortical potentials is equipped with an auditory and a tactile feedback mode. However, the Language Support Program presenting the verbal choices still relies on the visual modality.

#### *Instability of EEG Frequency Bands*

Instability of EEG frequency bands related to cognitive tasks may restrict their correct classification. The literature (e.g., Niedermeyer & Lopes da Silva, 1993; Rockstroh et al., 1989) indicates that EEG frequency patterns vary during the performance of the same cognitive task even within short periods of time. For instance, Flor et al. (1996) demonstrated that even in a very simple aversive classical conditioning paradigm EEG patterns changed substantially in less than 1 hr. This may lead to several problems concerning the use of pattern recognition algorithms for EEG classification. First, as the EEG frequency patterns vary over time, they may not match the pattern recognition algorithm, and therefore EEG classification may not be stable. Keirn and Aunon (1990a, 1990b) reported that classification 2 weeks after the first experiment was poor. They concluded that the classifier has to be trained before each session. Second, to function effectively for communication, the pattern recognition algorithm has to distinguish between single trials, so that the trials can be identified as belonging to a particular task. This is possible only if the EEG frequency pattern for a cognitive task is stable at least for the time

period during which the same pattern recognition algorithm is used. It is possible that the EEG frequency patterns are affected by the actual use of the brain-computer interface, but again stability is mandatory for long-term use by locked-in patients. It also remains unclear whether the power of the EEG frequencies of an individual patient change with the use of the system.

### *Invasive Recording*

Most brain-computer interface techniques entail noninvasive recording from the scalp. The brain-computer interface used by Kennedy and Bakay (1998) and Kennedy et al. (2000), which operates with the action potential firing rate, is the only brain-computer communication technique that requires a surgical intervention. Even if the possible costs and risks of this operation were low, the gain would not be clear. There is no evidence that the signal-to-noise ratio for electrical responses recorded directly from the brain are higher than for those recorded from the scalp. Actually, the contrary may be true: Scalp EEGs' smearing may constitute a "natural" filter of single-cell noise despite the large amplitudes of the electrocorticogram. Moreover, it is unclear whether the operant control of firing rates of single units is easier than the control of summated synchronous activity. The tissue growing into the electrode following the attraction of the nerve growth factor may not be functional, which would explain the long training period in both cases (Kennedy & Bakay, 1998; Kennedy et al., 2000). The axons growing into the electrode do not participate in the sensorimotor firing patterns of the surrounding tissue. Extensive work on brain plasticity has shown that a plastic change in the adult nervous system through learning is possible only if the respective neuronal circuit participates functionally in the physiological tasks of that circuit (Buonomano & Merzenich, 1998). Behavioral training changes the firing properties of neuronal representation only if the operantly trained movement leads to a positive reinforcement for a functional behavioral or physiological response. Reinforcement and feedback of noisy single-cell firing may lead to superstitious conditioning of random firing patterns not under voluntary control.

### Clinical Evidence From Locked-In Patients

The 4 patients described above were the first trained with the Thought Translation Device. Since those first reports (Birbaumer et al., 1999; Kübler et al., 1998, 1999), 8 other patients have been trained and many parameters of the Thought Translation Device have been changed (Hinterberger, 1999; Kübler, 2000; Kübler et al., in press). Training these patients at home or in nursing homes for weeks, months, or years has revealed not only technical or physical restrictions but also problems that arose from the individual patients' life history and current social and psychological situation. Some examples may illustrate this issue.

The young woman who was locked in after a brain stem infarct and trained with the Thought Translation Device was able to move her left eyelid after a few weeks. On being provided with a spelling table, she asked first, and to the surprise of her therapists, "Why do I wear such an ugly shirt?" From a healthy person's perspective one might expect another expression after several months without communication. When the menu containing desires and needs was shown to her, she missed the "paint fingernails" option, which was

not available in the menu. This example demonstrates that a brain-computer interface and its applications can only be optimized together with the individual patient.

Patient 002 (Birbaumer et al., 2000), with end-stage amyotrophic lateral sclerosis with weak and unreliable control of eye muscles, was able to use the Language Support Program for free communication and liked to use the program. Unfortunately, none of his family or friends were interested in communicating with him. After several weeks of communication he terminated further use. Maintaining patients' ability to communicate means providing them not only with a brain-computer interface but also with a social environment in which there are people to whom the communication can be addressed.

Patient 003 (Birbaumer et al., 2000) learned to use the Language Support Program in a few weeks with an accuracy rate of above 90%. However, when he was transferred to free communication, it became apparent that his reading and writing skills would not permit the use of self-selected letters. Therefore, he was provided with a menu containing simple phrases of different categories (e.g., turn on and off the TV set, thirsty, hungry, pain, etc.). Although helpful, this leads to restrictions, because only those wishes and needs included in the menu can be communicated.

An important issue in training is contingent reward of correct behavior, provided both by the brain-computer interface and by the trainers. Trainers usually comment on the performance of the patient. A patient diagnosed with infantile cerebral paresis exhibited involuntary muscle spasms (Kübler, 2000). When the patient was reinforced verbally by the trainer, muscle spasms increased, leading to a displacement of electrodes.

Training locked-in patients to use a brain-computer interface leads inevitably to an involvement in their private life and psychological as well as physical problems. This offers the possibility of including more psychological aspects in the training schedule.

### Comparison of Brain-Computer Interfaces

The goal for brain-computer communication is that the patients use the system permanently in daily life without the aid of their attendants. Clearly, brain-computer interface research is far from this goal. The "use" of brain-computer communication is restricted to several hours per week. An overview of how brain-computer interfaces meet several criteria is given in Table 1. As can be seen, none of the brain-computer interface techniques is doing well on all of the criteria. In offline analysis, Donchin et al. (2000) reported an impressive speed of 7.8 characters per minute, but the system has not been used by locked-in patients. Wolpaw, Ramoser, McFarland, and Pfurtscheller (1998) reported an accuracy of 98–99%, but this performance was achieved during sessions in which the cursor had to be moved into targets and no letter selection occurred. Patients of Birbaumer et al. (2000) are using the system, but speed and accuracy vary substantially within and between patients. Nevertheless, the Thought Translation Device is used by locked-in patients, who have communicated many messages (see Figure 5 for an example) (Birbaumer et al., 1999, 2000; Kübler, 2000).

The most thorough and continuous research on the development of a brain-computer interface has been conducted by Wolpaw's group ( $\mu$ -rhythm brain-computer interface) and by Birbaumer and coworkers (Thought Translation Device). Both brain-computer

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Table 1  
Results of the Brain-Computer Interfaces on Several Criteria

Brain-computer interface	Authors	Speed	Accuracy	Use	Training duration	Experience with patients
P300	Donchin, Spencer, and Wijesinghe (2000)	7.8 characters per minute	80%	No	—	4 patients with disabilities, using wheelchairs, one session in the lab
Visual event-related potential	Sutter (1992)	10-12 words per minute	Not reported	No details available	Not reported	1 amyotrophic lateral sclerosis patient at home
EEG frequency patterns—motor imagery	Pfurtscheller et al. (2000)	No letter selection, but orthosis	90%–100%	Yes	5 months	1 tetraplegic patient at home
EEG frequency patterns—cognitive tasks	Keirn and Aunon (1990a, 1990b)	Not reported	70%–90%	No	—	None
Action potential firing rate	Kennedy, Bakay, Moore, Adams, and Goldwaite (2000)	3 characters per minute	Score of 4 (0 = highest accuracy, 18 = lowest accuracy)	Yes	> 1 year	1 amyotrophic lateral sclerosis patient in a hospital
μ-rhythm	e.g., Wolpaw, Ramoser, McFarland, and Pfurtscheller (1998)	No letter selection	~90%	No	—	Several patients with disabilities, with different diagnoses, in the lab
Slow cortical potentials	e.g., Kübler et al. (1999)	0.15-3 characters per minute	65%–90%	Yes	Several weeks to > 1 year	12 patients with severe or total paralysis, with different diagnoses, at home or in nursing homes

ICH-WEISS-NICHT, WAS-SOLL-ES-BEDEUTEN, DASS-ICH-SO-SCHWANKEND-BIN.-ICH-VERSUCHE-EINE-ETWAS-ANDERE-STRATEGIE-BEIM-NEGATIVIEREN.-STATT-ANSpannung-UND-ENTSPANNUNG-VERSUCHE-ICH-EINFACH-NICHTS-ZU-MACHEN.-NUR-DARF-ICH-NICHTS-DABEI-DENKEN, INSBESONDERE-NICHT-DARAN, OB-ICH-TREFFE-ODER-NICHT. NATÜRLICH-DRÄNGEN-SICH-AB-UND-AN-GEDANKEN-AUF. ICH-DARF-SIE-NUR-NICHT-SO-WICHTIG- NEHMEN.-

Figure 5. Message communicated by Patient 004: "I do not know what it means [the preceding phrase is a quotation from the famous poem "Lorelei" by Heinrich Heine] that I am so inconsistent. I am trying a slightly changed strategy to produce cortical negativity. Instead of tension and relaxation, I try to do nothing. It is important that I do not think about it, especially not about whether I am going to select a letter or not. Of course, sometimes thoughts impose themselves. I just must not care about them."

interfaces have been tested over an extended period of time with the same participants. This is a very important point because a brain-computer interface is meant to be used by locked-in patients for months and years. Both techniques were reported in several versions with healthy participants and patients with paralysis. The Thought Translation Device was evaluated with locked-in patients and has been used for communication. The data have been replicated in several experiments.

Research on the brain-computer interface technique based on visual event-related potentials developed by Sutter (1992) was not continued. The P300 brain-computer interface technique exhibits a gap of 12 years between the first (Farwell & Donchin, 1988) and the second (Donchin et al., 2000) publication. This underlines the necessity of continuous technical, physiological, and psychological research into brain-computer communication. Some of the behavioral questions important for further development and application of brain-computer interfaces are addressed in the next section.

### Psychological Principles and Brain-Computer Interfaces

#### Behavioral Analysis

It is crucial for the success or failure of any brain-computer interface to conduct a thorough behavioral analysis with the patient and his or her significant others before and during training that includes reinforcement history and future resources for positive reinforcement (Kanfer & Saslow, 1976). One of the main reasons for the lack of brain-computer interface use by patients is that research has primarily focused on technical and electrophysiological aspects rather than on learning principles and motivational-ecological factors. The brain-computer interface has to be embedded in a behavioral program of improving the patients' psychological condition, and the training has to be subdivided into small steps of increasing difficulty (Kübler et al., in press) to avoid frustration of the patient, which may lead to termination of training (Kübler, 2000). Following Kanfer and Saslow's S-O-R-C guide to behavior analysis, situational context (stimuli S); stable enduring variables such as personality traits, motivation, and physiological predispositions (organism, O); responses (R) to the particular situations; and available and actual positive and negative consequences (C) should be continuously analyzed. Because of the extreme social restrictions characteristic of locked-in patients with a chronic, progressing disease, the usual psychological and psychophysiological assessment instruments are not applicable or

have to be modified. Even the simplest questionnaires, such as the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), contain some items that cannot be answered by a patient who is severely paralyzed. For example, an artificially fed patient cannot be asked about his appetite (BDI Item 18: "My appetite is no worse than usual"), and a patient who is paralyzed is not able to "work as well as before" (BDI Item 15), but this is no reason to conclude that he or she is depressed. However, the use of modified illness behavior questionnaires and measures of life events and daily hassles, disability, and suffering developed for chronic pain and illness may be useful to guide behavior analysis (for a review of those instruments, see Turk & Melzack, 1992). The number of potentially available positive reinforcers for patients who are severely paralyzed is obviously reduced compared with that for healthy participants. A list of 150 items subdivided into seven groups (solving, hearing, seeing, watching, reading, smelling, other) was presented to the patients of Kübler et al. (1998, 1999) and Birbaumer et al. (2000). Although the scope of locked-in patients is extremely restricted, positive reinforcers remained. The patients differed in terms of what they like to watch on TV or to listen to on the radio, but some items were generally considered very important and pleasant: to experience ease and peace, to make a profit, to be well-informed, to sleep well, and to get a massage. It remains to be tested how positive reinforcers could be integrated into a training schedule. Several negative reinforcers such as relief of painful body or limb posture, saliva, disturbing body odors, daily or weekly toilet rituals, and personal hygiene cannot be manipulated in an operant schedule for improving learning of brain-computer interface control.

### *Extrinsic Rewards and Intrinsic Motivation*

For continuous application of a brain-computer interface independently of continuous presence and praise of trainers, intrinsic motivation for the task is necessary in the face of a markedly reduced availability of positive reinforcers. In human participants straight application of schedules of reinforcement developed in the animal literature is not always possible and may even be detrimental (Deci, Koestner, & Ryan, 1999; Leslie, 1996). Cognitive evaluation of the reinforcing feedback stimuli changes during training; external attribution of control of reinforcement to the computer or to the trainer eliminates reinforcer attractiveness; and, most important, subjective attribution of loss of free choice and self-efficacy may attenuate the effectiveness of the contingency. No systematic research on this particular patient population is available to guide schedules of reinforcement and shaping. Being vitally dependent 24 hr a day on the continuous presence and care of others amplifies the reinforcement value of free choice and privacy of communication. Two patients requested a secret code in their Language Support Program to store and send out communication without access by caregivers and experimenters.

Environmental control is often cited as an important option for brain-computer interfaces: It is considered a strong positive reinforcement if patients regain at least some control over their environment. With a binary signal, different response sequences could be used to command a combination of environmental devices such as TV sets, signal to call the attendant, and so on. Patients using the Thought Translation Device were provided with an environmental control program. Seven different applications could be connected

to the Thought Translation Device. However, the patients indicated a preference for continuing with the spelling training. For these patients verbal communication was more important and rewarding than environmental control. This may be due to the circumstance that patients who are paralyzed and artificially ventilated are usually dependent on 24-hr care. So long as eye movement is available, patients are often able to communicate simple needs to caretakers by, for example, glancing in the direction of the window, thereby signaling to open it.

### *Perceptual Awareness of Brain Responses*

Speed of learning to self-regulate physiological responses depends—among other factors—on the perception of the target response. Whether this perception has to be conscious or not is a matter of dispute (Brener, 1974). There is, however, agreement that at least for the initial phases of brain self-regulation, instruction and awareness of the target response is useful. Birbaumer et al. (1988) trained two groups of healthy participants to self-regulate their slow cortical potentials: Group 1 received the instruction to imagine scenes with motor preparation (e.g., waiting for the return of the ball in a tennis game) to enhance cortical negativity. Group 2 received no instruction except to carefully follow the feedback provided by the computer. The results showed that instruction improved learning speed during the initial 4 training sessions. At Session 5 both groups achieved an equal success rate. Muscular activation during imagery did not affect the cortical response curves.

Furthermore, Kotchoubey, Kübler, Strehl, Flor, and Birbaumer (2000) demonstrated in a group of 22 patients with intractable epilepsies trained to reduce cortical negativity that only those patients who achieved reliable long-term control of their cortical responses were able to indicate after 30 training sessions whether they had produced a negative or positive cortical potential at a given trial. Thus, perception of the electrocortical changes is obviously related to the control of these changes. Roberts, Birbaumer, Rockstroh, Lutzenberger, and Elbert (1989) and Elbert, Rockstroh, Lutzenberger, and Birbaumer (1980) demonstrated in groups of healthy students trained to self-regulate slow cortical potentials that imagery accompanied by muscular or visceral activation did not improve task performance. Only subjective reports describing cognitive strategies such as "concentration," "autosuggestion," "thought stopping," and "mental motor preparation" covaried with improvement, whereas strategies such as "muscular relaxation," "respiration changes," and "strong feelings" interfered with the acquisition of cortical self-control.

A careful descriptive analysis of subjective reports of the cognitive strategies used by the few locked-in patients trained resulted in highly variable cognitive strategies; all strategies were kept over months and sometimes years of training. Patient 001 (Birbaumer et al., 2000) used imagery of "electrifying the brain." In contrast, Patient 002 of the same study could not report any systematic mental strategy. Patient 003 selected words by giving the cursor the "order" to move toward the bottom of the screen. Patient 004 (Kübler et al., 1999) imagined himself carrying something heavy up a hill and letting it loose at the top. These highly stable descriptions strengthen the argument that cognitive and not visceral-muscular strategies assist cortical self-regulation. None of

the successful patients reported strategies using emotional, visceral, or motor responses.

### Attentional Factors

Visual evoked potentials, P300 amplitude,  $\mu$  rhythm, event-related desynchronization, and slow cortical potentials all reflect different types of attentional modulation (Hillyard, Mangun, Woldorff, & Luck, 1995; Niedermeyer & Lopes da Silva, 1993). Therefore, knowledge of the diverse attentional strategies involved and systematic experimental manipulations of those strategies may improve instructional control or stimulus control of self-regulation of brain responses.

A fundamental problem inherent in all brain-computer interface applications represents the passage from controlled to automatic attention (Shiffrin & Schneider, 1977) during the course of training and the necessity for divided attention during selection of symbols. Although automatic, nonconscious strategies of successful self-control are highly desirable, they may not be possible for most of the brain signals used. Pauli, Lutzenberger, Birbaumer, Rickard, and Bourne (1996) and Pauli et al. (1994) demonstrated that even after thousands of repetitions of simple arithmetic tasks, a substantial amount of attentional response allocation was present at the cognitive-motor level, expressed in reaction time, and at the cortical level, indicated by a highly stable prefrontal amplitude of the processing positivity of the event-related brain potential during task presentation. This may also apply to brain self-regulation tasks and fits the clinical experience that patients and healthy individuals report mental exhaustion after 2–3 hr of training with the brain-computer interface. In addition, all brain-computer interface systems published require a substantial differentiation between baseline measures of the respective brain response and the actual response used to select letters or symbols. This differentiation implies permanently increased attentional responding and impedes automation. In the case of the  $\mu$  rhythm, the attentional allocation is targeted on the motor system, and in the case of the P300 and visual event-related potentials, on the perceptual system, asking for permanent activation of novelty modules in the posterior cortex (Ravden & Polich, 1998). In the case of negative slow cortical potentials, motor or cognitive preparatory responses have to be maintained (Rockstroh et al., 1989), and for positive slow cortical responses, probably interruption of ongoing processing (thought stopping) is necessary, again asking for attentional resource mobilization (Birbaumer et al., 1990). Without automation, the voluntary regulation of cortical responses through manipulation of selective attention and simultaneous selection of a letter or word held in working memory calls for division of attention between the two tasks. Preliminary measurement of the blood oxygen level dependent response in functional magnetic resonance imaging during self-regulation of slow cortical potentials indicates increased blood flow during self-regulation in brain areas responsible for selective attention: prefrontal areas, anterior cingulate, and cortical areas involved in the idiosyncratic imagery strategy (H. Bauer, Birbaumer, & Rösler, 1997). Neuroimaging of cortico-subcortical areas, together with a thorough assessment of cognitive-emotional strategies for physiological self-control and perception of cortical changes, will certainly improve our understanding of the underlying psychophysiological and neural mechanisms. Knowledge of the neuroanatomical circuits responsible for

divided attention between physiological self-regulation and simultaneous brain-computer communication may be useful for improvement of the behavioral procedures.

### Conclusions

Different brain-computer interface technologies with sophisticated methods of EEG analysis exist. Speed, accuracy, and usage by patients served as evaluation criteria for brain-computer interfaces in this review. The systems differ substantially in the extent to which they met the criteria, and none of the brain-computer interfaces fitted all well. The brain-computer interface relying on visual evoked potentials (Sutter, 1992) has not been further developed, and the system using EEG frequency patterns related to cognitive tasks (Keirn & Aunon, 1990a, 1990b) has never been tested with locked-in patients. Their contribution to the further development of brain-computer communication may be questionable. The brain-computer interfaces based on the P300 event-related potential (Donchin et al., 2000) and EEG frequency patterns related to motor imagery (Pfurtscheller et al., 2000) promise high accuracy and were tested in patients with paralysis. For both systems more experience with locked-in patients is necessary to decide whether they are feasible for the target population. The brain-computer interface using the action potential firing rate as a control signal (Kennedy et al., 2000) requires a surgical intervention, which we consider a disadvantage compared with noninvasive systems because a gain in accuracy and speed, which might justify an operation, is not discernible. The brain-computer interfaces based on operant learning to self-control the  $\mu$ -rhythm voltage (Wolpaw et al., 1991) and the slow cortical potential amplitude (Birbaumer et al., 1999) feature long-term research on the target EEG signal, and healthy volunteers and patients were trained for extended time periods. The  $\mu$ -rhythm brain-computer interface obtained a high accuracy, but no locked-in patient is using the system. In contrast, despite a great variability in accuracy, the Thought Translation Device is used for communication by locked-in patients (Birbaumer et al., 1999; Kübler, 2000; see Figure 5). Either of the two systems meets, largely, one of the criteria: accuracy and usage. Therefore, a combination of the  $\mu$ -rhythm brain-computer interface with the Thought Translation Device may lead to progress in brain-computer communication technology and is currently under development.

To promote the feasibility of brain-computer interfaces for locked-in patients, researchers must take into account psychological factors along with improvement of EEG analysis. A behavioral analysis of the patients' social and psychological situation during training is necessary to adapt the application controlled by the brain-computer interface to the patients' motivation and learning capacities. Usage of the brain-computer interface has to be rewarding. For this reason, the individual's needs and interests must be analyzed and reinforced. More neuroscientific research is necessary to understand the neuroanatomical basis of divided attention to find strategies for automatizing control of the brain-computer interface, so that attention can be focused on communication itself. We believe that the promising field of brain-computer communication is doomed to failure unless more psychological theory and experimentation is integrated into the development of brain-computer interfaces and is considered to be as important as technical aspects. Thus, the development of brain-computer interface



technology for use by locked-in patients is an interdisciplinary challenge demanding the knowledge of psychologists, neuroscientists, physicists, and engineers.

## References

- Allen, C. M. C. (1993). Conscious but paralysed: Releasing the locked-in. *The Lancet*, *342*, 130–131.
- Anderson, C. W., Stolz, E. A., & Shamsunder, S. (1998). Multivariate autoregressive models for classification of spontaneous electroencephalogram during mental tasks. *IEEE Transactions on Biomedical Engineering*, *45*, 277–286.
- Bach, J. R. (1993). Amyotrophic lateral sclerosis—Communication status and survival with ventilatory support. *American Journal of Physical Medicine & Rehabilitation*, *72*, 343–349.
- Bauer, G., Gerstenbrand, F., & Rimpl, E. (1979). Variables of the locked-in syndrome. *Journal of Neurology*, *221*, 77–91.
- Bauer, H. (1984). Regulation of slow brain potentials affects task performance. In T. Elbert, B. Rockstroh, W. Lutzenberger, & N. Birbaumer (Eds.), *Self-regulation of the brain and behavior* (pp. 216–226). Berlin, Germany: Springer.
- Bauer, H., Birbaumer, N., & Rösler, F. (1997). Slow scalp recorded brain potentials, sensory processing and cognition. In P. Laming, E. Sykova, A. Reichenbach, G. I. Hatton, & H. Bauer (Eds.), *Glial cells: Their role in behavior* (pp. 267–290). Cambridge, England: Cambridge University Press.
- Bayliss, J. D., & Ballard, D. H. (2000). A virtual reality testbed for brain-computer interface research. *IEEE Transactions on Rehabilitation Engineering*, *8*, 188–190.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, *4*, 561–571.
- Beukelman, D. R., & Mirenda, P. (1992). *Augmentative and alternative communication: Management of severe communication disorders in children and adults*. Baltimore: Brooks.
- Birbaumer, N. (1977). Operant enhancement of EEG-theta activity. In J. Beatty & H. Legewie (Eds.), *Biofeedback and behavior* (pp. 135–145). New York: Plenum.
- Birbaumer, N. (1984). Operant control of slow brain potentials: A tool in the investigation of the potential's meaning and its relation to attentional dysfunction. In T. Elbert, B. Rockstroh, W. Lutzenberger, & N. Birbaumer (Eds.), *Self-regulation of the brain and behaviour* (pp. 227–239). Berlin, Germany: Springer.
- Birbaumer, N., Elbert, T., Canavan, A. G. M., & Rockstroh, B. (1990). Slow potentials of the cerebral cortex and behaviour. *Physiological Reviews*, *70*(1), 1–41.
- Birbaumer, N., Elbert, T., Lutzenberger, W., Rockstroh, B., & Schwarz, J. (1981). EEG and slow cortical potentials in anticipation of mental tasks with different hemispheric involvement. *Biological Psychology*, *13*, 251–260.
- Birbaumer, N., Elbert, T., Rockstroh, B., & Lutzenberger, W. (1981). Biofeedback of event-related potentials of the brain. *International Journal of Psychology*, *16*, 389–415.
- Birbaumer, N., Ghanayim, N., Hinterberger, T., Iversen, I., Kotchoubey, B., Kübler, A., Perelmouter, J., Taub, E., & Flor, H. (1999). A spelling device for the paralysed. *Nature*, *398*, 297–298.
- Birbaumer, N., Kübler, A., Ghanayim, N., Hinterberger, T., Perelmouter, J., Kaiser, J., Iversen, I., Kotchoubey, B., Neumann, N., & Flor, H. (2000). The thought translation device (TTD) for completely paralyzed patients. *IEEE Transactions on Rehabilitation Engineering*, *8*, 190–193.
- Birbaumer, N., Lang, P., Cook, E., Elbert, T., Lutzenberger, W., & Rockstroh, B. (1988). Slow brain potentials, imagery and hemispheric differences. *International Journal of Neuroscience*, *39*, 101–116.
- Birbaumer, N., Rockstroh, B., Elbert, T., Wolf, P., Dürting-Röth, A., Reker, M., Daum, I., Lutzenberger, W., & Dichgans, J. (1994). Biofeedback of slow cortical potentials in epilepsy. In J. G. Carlson, A. R. Seifert, & N. Birbaumer (Eds.), *Clinical applied psychophysiology* (pp. 29–42). New York: Plenum.
- Borasio, G. D. (1996). Amyotrophe Lateralsklerose (ALS): Molekulare Pathogenese und experimentelle Therapie [Molecular pathogenesis and experimental therapy]. *Neuroforum*, *4*, 5–13.
- Brener, J. (1974). A general model of voluntary control applied to the phenomena of learned cardiovascular change. In P. A. Obrist, A. H. Black, J. Brener, & L. V. DiCara (Eds.), *Cardiovascular psychophysiology* (pp. 365–391). Chicago: Aldine.
- Buonomano, D. V., & Merzenich, M. M. (1998). Cortical plasticity: From synapses to maps. *Annual Reviews of Neuroscience*, *21*, 149–186.
- Cappa, S. F., & Vignolo, L. A. (1982). Locked-in syndrome for 12 years with preserved intelligence. *Annals of Neurology*, *11*, 545.
- Cherrington, M., Stears, J., & Hodges, J. (1976). Locked-in syndrome caused by a tumor. *Neurology*, *26*, 180–182.
- Chia, L. G. (1984). Locked-in state with bilateral internal capsule infarcts. *Neurology*, *34*, 1365–1367.
- Chia, L. G. (1991). Locked-in syndrome with bilateral ventral midbrain infarcts. *Neurology*, *41*, 445–446.
- Deci, E. L., Koestner, R., & Ryan, R. M. (1999). A meta-analytic review of experiments examining the effects of extrinsic rewards on intrinsic motivation. *Psychological Bulletin*, *125*, 627–668.
- Donchin, E. (1981). Surprise! . . . Surprise? *Psychophysiology*, *18*, 493–513.
- Donchin, E., & Coles, M. G. H. (1988). Is the P300 component a manifestation of context updating? *Behavioral and Brain Sciences*, *11*, 357–374.
- Donchin, E., Spencer, K. M., & Wijesinghe, R. (2000). The mental prosthesis: Assessing the speed of a P300-based brain-computer interface. *IEEE Transactions on Rehabilitation Engineering*, *8*, 174–179.
- Durrlleman, S., & Alperovitch, A. (1989). Increasing trend of ALS in France and elsewhere: Are the changes real? *Neurology*, *39*, 768–773.
- Elbert, T., Rockstroh, B., Lutzenberger, W., & Birbaumer, N. (1980). Biofeedback of slow cortical potentials. *Electroencephalography and Clinical Neurophysiology*, *48*, 293–301.
- Elder, S., Lashley, J. K., & Steck, C. G. (1982). Amyotrophic lateral sclerosis: A challenge for biofeedback. *American Journal of Clinical Biofeedback*, *5*(2), 123–125.
- Engel, R. R. (1977). Methodological and technological issues in biofeedback research. In J. Beatty & H. Legewie (Eds.), *Biofeedback and behavior* (pp. 47–57). New York: Plenum.
- Fabiani, M., Gratton, G., Karis, D., & Donchin, E. (1988). The definition, identification and reliability of measurement of the P300 component of the event-related brain potential. In P. K. Ackles, J. R. Jennings, & M. G. H. Coles (Eds.), *Advances in psychophysiology* (pp. 1–78). Greenwich, CT: JAI Press.
- Farwell, L. A., & Donchin, E. (1988). Talking off the top of your head: Toward a mental prosthesis utilizing event-related brain potentials. *Electroencephalography and Clinical Neurophysiology*, *70*, 512–523.
- Flor, H., Birbaumer, N., Roberts, L. A., Feige, B., Lutzenberger, W., Hermann, C., & Kopp, B. (1996). Slow potentials, event-related potentials, “gamma-band” activity, and motor responses during aversive conditioning in humans. *Experimental Brain Research*, *112*, 298–312.
- Gascon, G. G., Chavis, P., Yoghmour, A., Stigsby, B., Shums, A., Ozand, P., & Siddique, T. (1995). Familial childhood primary lateral sclerosis with associated gaze paresis. *Neuropediatrics*, *26*, 313–319.
- Guger, C., Schlögl, A., Walterpacher, D., & Pfurtscheller, G. (1999). Design of an EEG-based brain-computer interface (BCI) from standard components running in real-time under Windows. *Biomedizinische Technik*, *44*, 12–16.
- Harvey, D. G., Torack, R. M., & Rosenbaum, H. E. (1979). Amyotrophic

- lateral sclerosis with ophthalmoplegia: A clinicopathologic study. *Archives of Neurology*, 36, 615–617.
- Hayashi, H., & Kato, S. (1989). Total manifestations of amyotrophic lateral sclerosis: ALS in the totally locked-in state. *Journal of the Neurological Science*, 93, 19–35.
- Hillyard, S. A., Mangun, G. R., Woldorff, M. G., & Luck, S. J. (1995). Neural systems mediating selective attention. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 665–681). Cambridge, MA: MIT Press.
- Hinterberger, T. (1999). *Optimierungsmethoden für die Kommunikation durch Selbstkontrolle langsamer kortikaler Potentiale* [Methods for optimizing the communication mediated by self-control of slow cortical potentials]. Tübingen, Germany: Schwäbische Verlagsgesellschaft.
- Jasper, H. H. (1958). Report of Committee on Methods of Clinical Investigation of EEG. Appendix: The ten twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology*, 10, 371–375.
- Kaiser, J., Lutzenberger, W., Preissl, H., Ackermann, H., & Birbaumer, N. (2000). Right-hemisphere dominance for the processing of sound-source lateralization. *Journal of Neuroscience*, 20, 6631–6639.
- Kalcher, J., Flotzinger, D., Neuper, C., Göllly, S., & Pfurtscheller, G. (1996). Graz brain–computer interface: II. Toward communication between man and computer based on on-line classification of three different EEG patterns. *Medical & Biological Engineering & Computing*, 34, 382–388.
- Kamiya, J. (1969). Operant control of the EEG alpha rhythm and some of its effects on consciousness. In C. T. Tart (Ed.), *Altered states of consciousness* (pp. 489–501). New York: Wiley.
- Kanfer, F. H., & Saslow, G. (1976). Verhaltenstheoretische Diagnostik. [Diagnosis according to behavioral theory]. In D. Schulte (Ed.), *Diagnostik in der Verhaltenstherapie* (pp. 24–59). Munich, Germany: Urban & Schwarzenberg.
- Keirn, Z. A., & Aunon, J. I. (1990a). Man–machine communications through brain-wave processing. *IEEE Engineering in Medicine and Biology Magazine*, 9, 55–57.
- Keirn, Z. A., & Aunon, J. I. (1990b). A new mode of communication between man and his surroundings. *IEEE Transactions on Biomedical Engineering*, 37, 1209–1214.
- Kennedy, P. R., & Bakay, R. A. E. (1997). Activity of single action potentials in monkey motor cortex during long-term task learning. *Brain Research*, 760, 251–254.
- Kennedy, P. R., & Bakay, R. A. E. (1998). Restoration of neural output from a paralyzed patient by a direct brain connection. *NeuroReport*, 9, 1707–1711.
- Kennedy, P. R., Bakay, R. A. E., Moore, M., Adams, K., & Goldwaithe, J. (2000). Direct control of a computer from the human central nervous system. *IEEE Transactions on Rehabilitation Engineering*, 8, 198–202.
- Kennedy, P. R., Bakay, R. A. E., & Sharpe, S. S. (1992). Behavioral correlates of action potentials chronically recorded inside the cone electrode. *NeuroReport*, 3, 605–608.
- Kotchoubey, B., Kübler, A., Strehl, U., Flor, H., & Birbaumer, N. (2000). *Learning to perceive brain states*. Manuscript submitted for publication.
- Kotchoubey, B., Schleichert, H., Lutzenberger, W., Anokhin, A. P., & Birbaumer, N. (1996). Self-regulation of interhemispheric asymmetry in humans. *Neuroscience Letters*, 214, 91–94.
- Kotchoubey, B., Schleichert, H., Lutzenberger, W., & Birbaumer, N. (1997). A new method for self-regulation of slow cortical potentials in a timed paradigm. *Applied Psychophysiology and Biofeedback*, 22, 77–93.
- Kübler, A. (2000). *Brain–computer communication—Development of a brain–computer interface for locked-in patients on the basis of the psychophysiological self-regulation training of slow cortical potentials (SCP)*. Tübingen, Germany: Schwäbische Verlagsgesellschaft.
- Kübler, A., Kotchoubey, B., Hinterberger, T., Ghanayim, N., Perelmouter, J., Schauer, M., Fritsch, C., Taub, E., & Birbaumer, N. (1999). The Thought Translation Device: A neurophysiological approach to communication in total motor paralysis. *Experimental Brain Research*, 124, 223–232.
- Kübler, A., Kotchoubey, B., Salzmann, H. P., Ghanayim, N., Perelmouter, J., Hömberg, V., & Birbaumer, N. (1998). Self-regulation of slow cortical potentials in completely paralyzed human patients. *Neuroscience Letters*, 252, 171–174.
- Kübler, A., Neumann, N., Kaiser, J., Kotchoubey, B., Hinterberger, T., & Birbaumer, N. (in press). Brain–computer communication: Self-regulation of slow cortical potentials for verbal communication. *Archives of Physical Medicine and Rehabilitation*.
- Kuhlman, W. N. (1978). EEG feedback training: Enhancement of somatosensory cortical activity. *Electroencephalography and Clinical Neurophysiology*, 44, 290–294.
- Leslie, J. C. (1996). *Principles of behavioral analysis*. Amsterdam: Harwood Academic.
- Lutzenberger, W., Elbert, T., Rockstroh, B., & Birbaumer, N. (1979). The effects of self-regulation of slow cortical potentials on performance in a signal detection task. *International Journal of Neuroscience*, 9, 175–183.
- Lutzenberger, W., Elbert, T., Rockstroh, B., & Birbaumer, N. (1982). Biofeedback produced slow brain potentials and task performance. *Biological Psychology*, 14, 99–111.
- Lutzenberger, W., Roberts, L. E., & Birbaumer, N. (1993). Memory performance and area-specific self-regulation of slow cortical potentials: Dual-task interference. *International Journal of Psychophysiology*, 15, 217–226.
- McFarland, D. J., McCane, L. M., David, S. V., & Wolpaw, J. R. (1997). Spatial filter selection for EEG-based communication. *Electroencephalography and Clinical Neurophysiology*, 103, 386–394.
- McFarland, D. J., Neat, G. W., Read, R. F., & Wolpaw, J. R. (1993). An EEG-based method for graded cursor control. *Psychobiology*, 21, 77–81.
- Middendorf, M. S., McMillan, G., Calhoun, G., & Jones, K. S. (2000). Brain–computer interfaces based on the steady-state visual evoked response. *IEEE Transactions on Rehabilitation Engineering*, 8, 211–214.
- Murray, T. J., Cameron, J., Heffernan, L. P., MacDonald, H. N., King, D. B., Bedwell, S. R., Scott, M., Patil, J., Shears, S., & Malik, H. G. (1987). Amyotrophic lateral sclerosis in Nova Scotia. *Advances in Experimental Biology and Medicine*, 209, 345–349.
- Niedermeyer, E., & Lopes da Silva, F. (1993). *Electroencephalography: Basic principles, clinical applications, and related fields* (3rd ed.). Baltimore: Williams & Wilkins.
- Patterson, J. R., & Grabois, M. (1986). Locked-in syndrome: A review of 139 cases. *Stroke*, 17, 758–764.
- Pauli, P., Lutzenberger, W., Birbaumer, N., Rickard, T. C., & Bourne, L. E., Jr. (1996). Neurophysiological correlates of mental arithmetic. *Psychophysiology*, 33, 522–529.
- Pauli, P., Lutzenberger, W., Rau, H., Birbaumer, N., Rickard, T. C., Yaroush, R. A., & Bourne, L. E. (1994). Brain potentials during mental arithmetic: Effects of extensive practice and problem difficulty. *Cognitive Brain Research*, 2, 21–29.
- Penny, W. D., Roberts, S. J., Curran, E. A., & Sokes, M. J. (2000). EEG-based communication: A pattern recognition approach. *IEEE Transactions on Rehabilitation Engineering*, 8, 214–215.
- Perelmouter, J., Kotchoubey, B., Kübler, A., Taub, E., & Birbaumer, N. (1999). A language supporting program for thought-translation-devices. *Automedica*, 18, 67–84.
- Pfurtscheller, G., Flotzinger, D., Pregenzer, M., Wolpaw, J. R., & McFarland, D. (1996). EEG-based brain computer interface. *Medical Progress Through Technology*, 21, 111–121.
- Pfurtscheller, G., Neuper, C., Guger, C., Harkam, W., Ramoser, H., Schlögl, A., Obermaier, B., & Pregenzer, M. (2000). Current trends in

- Graz brain-computer interface (BCI) research. *IEEE Transactions on Rehabilitation Engineering*, 8, 216–219.
- Pfurtscheller, G., Neuper, C., Schlögl, A., & Lugger, K. (1998). Separability of EEG signals recorded during right and left motor imagery using adaptive autoregressive parameters. *IEEE Transactions on Rehabilitation Engineering*, 6, 316–324.
- Plotkin, W. B. (1976). On the self-regulation of the occipital alpha-rhythm: Control strategies, states of consciousness, and the role of physiological feedback. *Journal of Experimental Psychology: General*, 195, 66–99.
- Polich, J., & McIsaac, H. K. (1994). Comparison of auditory P300 habituation for active and passive conditions. *International Journal of Psychophysiology*, 17, 25–34.
- Pregenzer, M., Pfurtscheller, G., & Flotzinger, D. (1996). Automated feature selection with a distinction sensitive learning vector quantizer. *Neurocomputing*, 11, 19–29.
- Ravden, D., & Polich, J. (1998). Habituation of P300 from visual stimuli. *International Journal of Psychophysiology*, 30, 359–365.
- Roberts, L., Birbaumer, N., Rockstroh, B., Lutzenberger, W., & Elbert, T. (1989). Self-report during feedback regulation of slow cortical potentials. *Psychophysiology*, 26, 392–403.
- Rockstroh, B., Birbaumer, N., Elbert, T., & Lutzenberger, W. (1984). Operant control of EEG, event-related and slow potentials. *Biofeedback and Self-Regulation*, 9, 136–160.
- Rockstroh, B., Elbert, T., Birbaumer, N., & Lutzenberger, W. (1990). Biofeedback-produced hemispheric asymmetry of slow cortical potentials and its behavioral effects. *International Journal of Psychophysiology*, 9, 151–165.
- Rockstroh, B., Elbert, T., Birbaumer, N., Wolf, P., Dürchting-Röth, A., Reker, M., Daum, I., Lutzenberger, W., & Dichgans, J. (1993). Cortical self-regulation in patients with epilepsies. *Epilepsy Research*, 14, 63–72.
- Rockstroh, B., Elbert, T., Canavan, A., Lutzenberger, W., & Birbaumer, N. (1989). *Slow cortical potentials and behavior*. Baltimore: Urban & Schwarzenberg.
- Rockstroh, B., Elbert, T., Lutzenberger, W., & Birbaumer, N. (1982). The effects of slow cortical potentials on response speed. *Psychophysiology*, 19, 211–217.
- Schneider, F., Heimann, H., Mattes, R., Lutzenberger, W., & Birbaumer, N. (1992). Self-regulation of slow cortical potentials in psychiatric patients: Depression. *Biofeedback & Self-Regulation*, 17, 203–214.
- Schneider, F., Rockstroh, B., Heimann, H., Lutzenberger, W., Mattes, R., Elbert, T., Birbaumer, N., & Bartels, M. (1992). Self-regulation of slow cortical potentials in psychiatric patients: Schizophrenia. *Biofeedback & Self-Regulation*, 17, 277–292.
- Shiffrin, R. M., & Schneider, W. (1977). Controlled and automatic human information processing: II. Perceptual learning, automatic attending and a general theory. *Psychological Review*, 84, 127–190.
- Speckmann, E.-J., Caspers, H., & Elger, C. W. (1984). *Neuronal mechanisms underlying the generation of field potentials*. Berlin, Germany: Springer.
- Speckmann, E.-J., & Elger, C. E. (1993). Introduction to the neurophysiological basis of the EEG and DC potentials. In E. Niedermeyer & F. Lopes da Silva (Eds.), *Electroencephalography—Basic principles, clinical applications, and related fields* (3rd ed., pp. 15–26). Baltimore: Williams & Wilkins.
- Serman, M. B. (1977). Effects of sensorimotor EEG feedback training on sleep and clinical manifestations of epilepsy. In J. Beatty & H. Legewie (Eds.), *Biofeedback and behavior* (pp. 167–200). New York: Plenum.
- Serman, M. B. (1981). EEG biofeedback: Physiological behavior modification. *Neuroscience and Biobehavioral Reviews*, 5, 405–412.
- Sutter, E. E. (1992). The brain response interface: Communication through visually-induced electrical brain responses. *Journal of Microcomputer Applications*, 15, 31–45.
- Sutter, E. E., & Tran, D. (1990). Communication through visually induced electrical brain responses. *Schriftenreihe der Oesterreichischen Computer Gesellschaft*, 55, 279–288.
- Tallon-Bandry, C., & Bertrand, O. (1999). Oscillatory gamma activity in humans and its role in object representation. *Trends in Cognitive Science*, 3, 151–162.
- Taub, E., Crago, J. E., Burgio, L. D., Groomes, T. E., III, Cook, E. W., DeLuca, S. C., & Miller, N. E. (1994). An operant approach to rehabilitation medicine: Overcoming learned nonuse by shaping. *Journal of the Experimental Analysis of Behaviour*, 61, 281–293.
- Thadani, V. M., Rimm, D. L., Urquhart, L., Fisher, L., Williamson, P. D., Enriquez, R., Kim, J. H., & Levy, L. L. (1991). 'Locked-in syndrome' for 27 years following a viral illness: Clinical and pathological findings. *Neurology*, 41, 498–500.
- Turk, D. C., & Melzack, R. (1992). *Handbook of pain assessment*. New York: Guilford Press.
- Vidal, J. J. (1973). Toward direct brain computer communication. *Annual Reviews of Biophysics and Bioengineering*, 2, 157–180.
- Williams, D. B., & Windebank, A. J. (1991). Motor neuron disease (amyotrophic lateral sclerosis). *Mayo Clinic Proceedings*, 66, 54–82.
- Williams, R. J., & Roberts, L. E. (1988). Relation of learned heart rate control to self-report in different task environments. *Psychophysiology*, 25, 354–365.
- Wolpaw, J. R., Flotzinger, D., Pfurtscheller, G., & McFarland, D. J. (1997). Timing of EEG-based cursor control. *Journal of Clinical Neurophysiology*, 14, 529–538.
- Wolpaw, J. R., & McFarland, D. J. (1994). Multichannel EEG-based brain-computer communication. *Electroencephalography and Clinical Neurophysiology*, 90, 444–449.
- Wolpaw, J. R., McFarland, D. J., Neat, G. W., & Forneris, C. A. (1991). An EEG-based brain-computer interface for cursor control. *Electroencephalography and Clinical Neurophysiology*, 78, 252–259.
- Wolpaw, J. R., McFarland, D. J., & Vaughan, T. M. (2000). Brain-computer interface research at the Wadsworth Center. *IEEE Transactions on Rehabilitation Engineering*, 8, 222–226.
- Wolpaw, J. R., Ramoser, H., McFarland, D. J., & Pfurtscheller, G. (1998). EEG-based communication: Improved accuracy by response verification. *IEEE Transactions on Rehabilitation Engineering*, 6, 326–333.
- Wyrwicka, W., & Serman, M. B. (1968). Instrumental conditioning of sensorimotor cortex EEG spindles in the waking cat. *Physiology and Behavior*, 3, 703–707.
- Xu, X. H., Li, S. W., Tan, M. X., & Zang, X. (1981). Locked-in syndrome (pontopseudocoma): Report of three clinical and pathological cases. *Chinese Medical Journal*, 94, 821–826.

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