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REVIEWS

Artificial Feedback for Invasive Brain–Computer Interfaces

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Abstract—During the last two decades, considerable progress has been made in the studies of brain–computer interfaces (BCIs)—devices in which motor signals from the brain are registered by multi-electrode arrays and transformed into commands for artificial actuators such as cursors and robotic devices. This review is focused on one problem. Voluntary motor control is based on neurophysiological processes, which strongly depend on the afferent innervation of skin, muscles, and joints. Thus, invasive BCI has to be based on a bidirectional system in which motor control signals are registered by multichannel microelectrodes implanted in motor areas, whereas tactile, proprioceptive, and other useful signals are transported back to the brain through spatiotemporal patterns of intracortical microstimulation (ICMS) delivered to sensory areas. In general, the studies of invasive BCIs have advanced in several directions. The progress of BCIs with artificial sensory feedback will not only help patients, but will also expand base knowledge in the field of human cortical functions.

Keywords: brain–computer interfaces, implantable multichannel microelectrode, artificial sensory feedback, intracortical microstimulation

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The brain–computer interface (BCI) is a system designed to transmit the intentions of humans to external devices by means of brain signals. Currently, intensive studies on the development and application of BCIs are performed, and the scope of these studies rapidly increases [1]. There are technical, scientific, and social conditions for this. The appearance of inexpensive and powerful computers, mathematical software, and microelectronics has made it possible to process multichannel records of brain signals in real time and to use the results of their processing to manage technical devices. The development of BCIs requires distinguishing stable signs of brain activity corresponding to thoughts and intentions of a person, which contributes to solving the fundamental problem of decoding their functional neural codes. Therefore, the use of BCIs is considered as a new research paradigm in studying the fundamental mechanisms of the brain. A social condition for the BCI development is the need for rehabilitation of patients with various motor and neurological disorders.

There are reasons to assume that the invasive type of BCIs, realized through microelectrodes implanted in the brain, may be the most effective tool to restore the contact with the outer world in the social rehabilitation of patients with a complete loss of motor functions. Naturally, the fundamental problems of the study and development of such BCI are solved in experiments on monkeys, which cannot respond to verbal instructions to perform the required movements and generate brain activity associated with these movements. Therefore, usually they are first trained to perform motor tasks associated with purposeful movements of the arm or with the control of external objects with a joystick and other similar devices.

In the pioneering experiments performed on the primary motor cortex (M1) of awake monkeys, Evarts [2] found that the frequency of individual neurons of M1 was strongly correlated with the strength and torque developed in joints during the movement of animal's arm. It was shown that the temporal and power characteristics of a single-joint movement of monkey's wrist can be predicted sufficiently accurately by using a small population of simultaneously recorded M1 neurons [3]. A landmark study in this field showed that monkeys can arbitrarily control the activity of a single M1 neuron using visual feedback and rewards [4]. A significant contribution to laying the foundations for the development of subsequent BCI research was made by the studies that showed how populations of firing neurons can predict the spatial kinematics of the hand [5, 6]. It was found that M1 neurons exhibit directional sensitivity: the activity of a single neuron reaches a maximum when the hand moves in a direction determined for each neuron and can be characterized by a directionality vector. Accordingly, the hand movement vector at a given time is determined by the sum of vectors of the neurons that are active at this time. Thus, on the basis of data obtained during the performance of a certain motor task by an animal, a program for classifying neuronal activity can be developed, which can transcode neuronal activity into control signals in real time and can be used to control external device instead of using the hand.

In 1999, it was shown that the rat can control the one-dimensional movement of a food-supplying nozzle when the latter was controlled on the basis of decoding multi-electrode recordings of spikes from cortical neurons [7]. Subsequent studies showed the possibility of mental control based on visual feedback in monkeys [8–12], namely, by using a command coming immediately from a population of cortical neurons.

The Need to Introduce an Artificial Sensory Feedback for BCI

In each study, the BCI system consisted of four components: (1) a multi-electrode device, (2) an algorithm for classification of neuronal activity pattern in real time, (3) a controllable device, and (4) a visual feedback.

The development of invasive "brain–computer" interfaces (BCIs) and their study in experiments on monkeys showed that the most important factor in the use of BCIs is the cerebral cortex plasticity, which can improve the arbitrary modulation of neuronal activity and manifests itself when animals are trained using a biofeedback based on visual afferentation [13–15]. The training of monkeys to use BCI actually means the formation of a new visual-motor coordination skill, where a virtual object is used as an executive organ. Meanwhile, in accurate manipulations with objects, the somatosensory feedback is of great importance [16]. Signals from the mechanoreceptors in the skin provide important information on the contact [17] and the forces affecting the skin when grasping an object, especially when the object is shifted relative to the hand or the hand is shifted relative to the object [18]. Without this information, a person either could not hold or would destroy the manipulation object. The importance of proprioceptive afferentation is emphasized by the fact that, in the absence of proprioception, a person lacks the opportunity to plan the movement of the limb [19, 20]. In addition, proprioception gives the sensation that the limb belongs to the body [21, 22].

Recent studies [21, 23–26] suggest that the supply of artificial "sensory" information to the brain through coordinated multi-channel microstimulation of sensory cortical areas will make it possible to realize a brain–computer–brain interface (BCBI), which will provide new opportunities in the basic research into the mechanisms of cortical plasticity and a breakthrough in applied fields such as "natural" anthropomorphic control of multidimensional technical devices and motor rehabilitation of patients with severe injuries of the nervous system. Stimulation of large areas of the brain hampers information processing [27], whereas stimulation of small areas (the so-called microstimulation) can cause motor and sensory effects that mimic the natural activity of stimulated areas [28, 29]. Several studies [30–35] have shown that monkeys can distinguish the amplitude, frequency, and pattern of microstimulation of the area of tactile representation of fingers and palm of the hand in the primary somatosensory cortex and, accordingly, that cortical microstimulation can become the basis of "sensitizing" of a controlled actuator.

Brain Cortex Microstimulation

The effect of microstimulation of different areas of the brain depends on the position of microelectrodes, stimulation parameters, and microstimulation pattern [33, 36]. To minimize the damaging effect of electric current on the brain tissue and the effect of the electrode, which depends on many parameters and can hardly be estimated [37], researchers use stimulation with symmetrical biphasic rectangular pulses starting with the negative phase (usually 2×100 μs) and an amplitude of dozens (rarely more than 100) μA. A poorly controlled microstimulation can lead to an increase in the neuronal activity beyond the computational area [38, 39] as well as affect the excitability of adjacent somatosensory cortical neurons by natural afferent stimuli [40]. The use of an additional pairs of microelectrodes that are subjected to aperiodic random-amplitude microstimulation makes it possible to reduce the threshold of microstimulation supplied as an artificial sensory feedback to another pair of microelectrodes implanted in the primary somatosensory cortex [41]. Another method to reduce the intensity of microstimulation of cortical neurons and, therefore, to decrease the risk of possible damage to the brain tissue is to increase the number of microelectrodes used for stimulation of a certain cortical area, when the current density on each microelectrode is reduced. This technique makes it possible to stimulate neurons with a very high excitability threshold when the number of stimulating microelectrodes significantly increases [42]. This is a solution to the problem when the object of artificial feedback is represented by proprioceptive neurons of area 2 of the primary somatosensory cortex of monkeys, the directional sensitivity of which was shown when the animals ran the cursor using a manipulandum [43]. However, Zaaimi et al. [42] used seven microelectrodes inserted into area 2 of the primary somatosensory cortex. In a more recent study [44], the authors of which used two to four microelectrodes in monkeys, area 3b/1 of the primary somatosensory cortex and a different microstimulation pattern, the effect of increased number of electrodes was negligible; as a result, the authors concluded that this method of artificial proprioceptive feedback realization is not promising and requires high energy costs.

Primary Somatosensory Cortex

To ensure an artificial feedback, intracortical microstimulation of the primary somatosensory cortex (S1) consisting (according to Brodmann) of areas 1, 2, and 3 (the latter, in turn, is divided into area 3a and 3b) is used. These areas are located in the anterior and posterior banks of the central sulcus and the postcentral gyrus surface. In the rostral-caudal direction, these areas are situated as follows: 3a, 3b, 1, and 2. Area 3a receives primary proprioceptive information from the muscle spindles [45] and is projected on areas 3b, 1, and 2, whereas area 3b receives primarily inputs from the skin receptors [46] and is projected on areas 1 and 2 [47–49]. Area 1 receives inputs from areas 3a, 3b, and 2; it is activated by stimulation of skin receptors and sends feedback to area 3b [48]. Area 2 is sensitive to both stimulation of the skin and activation of deep receptors similar to muscle spindles [48]. According to the conventional ideas about the organization of area 3b, the cell responses in this area are determined by the correspondence of receptive fields to individual digits [50]. Recent studies showed a significant interdigital integration in area 3b [51–53] and in area 1 [54]. However, the data obtained have shown that the interdigital integration of tactile information begins with area 3b [55]. The primary somatosensory cortex contains numerous somatotopic maps, which correspond to the skin areas on the contralateral side. Each area S1 contains the complete somatotopic map of the body, located in the mediolateral direction so that the leg is represented by the first one and the face is represented by the last one (most lateral). This order corresponds to the position of parts of the body in the primary motor cortex. The selection of the position of the electrodes for microstimulation depends on the part of the body for which a sensory channel is created. Even fairly small modern matrix multi-microelectrodes, in relation to the cortical representation of the limb and their size in S1, may be incompatible with the objective of their placement (e.g., in the central sulcus). Therefore, reasonable determination of an adequate place for the implantation of multi-microelectrodes at the current level of electrode manufacturing technology becomes crucial [56].

Approaches to Creating an Artificial Sensory Feedback

An artificial feedback signal should not be functionally different from the natural feedback signals: it should provide the necessary sensory information and allow multisensory integration with the visual channel to reduce the variability of movement when both signals are used. Currently, there are two approaches to creating such an artificial sensory feedback [22, 57]: biomimetic, when microstimulation of brain structures should correspond to the existing anatomical and physiological knowledge, and "adaptive," which is based on the cortical plasticity and the learning process and requires creating a "map" between the sensors and the brain microstimulation patterns, but without the limitations characteristic of the biomimetic approach. In particular, when the biomimetic approach is used, the problem of using the hand as an artificial feedback from proprioceptors becomes rather difficult because microstimulatory pulses should be transmitted directly to the proprioceptive representation of the hand, which is often located at the fundus of the central sulcus [58, 59]. The authors of a series of papers [60–63] developed an approach in which this problem does not arise because in these studies the integration of the two sensory signals (proprioceptive and visual) depends primarily on the spatiotemporal correlation between the two signals, which allows the underlying neurons to learn to recognize the common causative factor (e.g., the position of the hand) rather than on the neuronal activity patterns for coding spatial information.

The "brain–computer–brain interface" (BCBI) ideology has led to the emergence of fundamentally new potential possibilities of mental control of external objects. The authors of a modeling study performed under the supervision of Mussa-Ivaldi [64] attempted to assess the possibility that the behavior of the part of the central nervous system in a closed-feedback system consisting of a BCI and an artificial sensory channel may differ from the combination of the properties of neuronal and artificial components of this system. A question was raised whether it is possible to simultaneously regulate the bidirectional brain–computer communication so that the desired dynamic behavior of the combined system would form. Using the bidirectional connection between the sensory and motor areas of the brain of an anesthetized rat and a virtual dynamic object with programmable properties, the authors of this study showed that the interaction between the brain activity and the state of the external object generated a family of movement trajectories of the object, which converge at the selected point of equilibrium regardless of the initial position. Thus, the bidirectional interface makes it possible to determine not only an individual trajectory of movement but also the whole family of trajectories, including those resistant to unexpected disturbances.

Mathematical modeling showed [65] that the sensorimotor interaction realized in BCBI gives an idea of both a three-dimensional environment and the scheme of the body, even in the case of a relatively simple model of the human consisting of a tactile-sensitive body and a proprioceptive-sensitive hand with many degrees of freedom.

Electrodes for Recording Electrical Signals and Cortical Microstimulation

One of the major factors hampering the development of BCI is the problems associated with the technology and stability of recording of electrical signals of the brain [66]. Each type of the used signals (spike activity of individual neurons, multiunit activity, and low-frequency cortical field potentials) has its advantages and disadvantages [15, 67–70]. Existing studies often lead to inconsistent conclusions in comparing the amount of information in these signals based on the basis of the accuracy with which they could be used to reconstruct the kinematics of movement of the arm to the target and grasping it in two- and three-dimensional space. The inconsistencies could be caused by the differences in the motor tasks used, in the areas of registration, in the decoding algorithms or in the number of spikes per channel, which characterized each of the studies [71–75].

The consequences of long-term chronic recording of the electrical activity of the brain or its microstimulation with electric current with the use of microelectrodes are the major constraint to the real introduction of neurointerfaces into the clinical practice. The accumulated experience showed that the work with multichannel chronic electrodes significantly differs from the use of an electrode in an acute experiment [76]. In microstimulation of brain tissues, the strongest impact is caused by the electric current as such, which in the absence of compliance with the safety regulations [37] may cause injury of the patient [77]. At the same time, changing the frequency and amplitude of current pulses of a certain form and the duration of supply of these pulses can allow reflecting the touch force variability or surface roughness of the study objects [21, 78, 79]. In this regard, a significant number of research groups including various specialists work to improve the material of electrodes, their coating and structure, and the methods of their implantation into the brain [80]. The results of a recent study on a long-term microstimulation of the primary somatosensory cortex in three rhesus monkeys using chronically implanted electrodes are encouraging [81]. Stimulation was performed for 4 h per day for 6 months using various microstimulation patterns. It was found that the range of variation of the impedance and voltage of the electrode, characterizing the electrode–tissue surface state, decreased and stabilized after 10–12 weeks of stimulation. The magnitude of this decrease depended on the amplitude of the current and, to a lesser extent, on the duration of pulses. Moreover, there were no disturbances in the fine motor control.

Simultaneous Recording of Electrical Signals of the Cortex and Its Microstimulation

The location of the recording electrodes of BCI, which are characterized by a very high sensitivity, and the stimulating electrodes in electrically conductive brain tissue leads to the distortion of recorded neural signals of BCI when attempting to directly use artificial feedback with the aid of microstimulation [79]. The most obvious and common solution is to block the inputs of amplifiers of BCI recording channels for the period of microstimulation, which is performed as pulse spikes of a certain duration. However, the inevitable occurrence of transient processes associated with switching on and off in electrical circuits, this method leads to the loss of information about the neuronal activity of the brain structure used in the BCI [79]. A better solution is to filter the occurring artifact to restore the original signal. This method was first successfully used in the combination of EEG with transcranial magnetic stimulation [82] and then in the experiments on monkeys performing the task of running a computer cursor [83].

The Use of S1 Microstimulation in Experiments on Monkeys

Currently, there is no data indicating whether the microstimulation of S1 areas in monkeys causes any (and which exactly, if any) sensations. It is only known that animals can perceive microstimulation as a guide to action and can differently respond to microstimulation patterns with different parameters [78]. In another study [84], monkeys were able to distinguish the amplitude of microstimulation effects simulating the indentation of the skin on digits to different depths. The animals equally well distinguished both the indentation depth and the corresponding microstimulation amplitudes; i.e., they perceived both types of stimuli in a similar manner. In the study with the use of a combination of BCI and an artificial sensory feedback [79], monkeys were trained to active examination of two visually identical targets on the display screen with a joystick controlling a symbolic image of the hand. When the hand symbol got on one of the targets, it caused microstimulation of the area of tactile representation of digits and palm of the hand in the primary somatosensory cortex by sending a pulse with a constant frequency. The second target caused microstimulation with the same mean frequency of pulses but with a disturbed periodicity. When holding the hand symbol on the target that caused a pulsed stimulation at a constant rate for the required period of time, the monkey received reinforcement with juice and gradually learned to significantly discriminate between the targets. Thus, it was shown that a certain change in the cortical microstimulation pattern becomes sensorily significant for the monkey. Combinations of changes in the amplitude, frequency, and pattern of microstimulation are quite sufficient to reconstruct a wide variety of tactile sensations.

CONCLUSIONS

In general, invasive BCIs are developing in several directions. These efforts will not only help patients but also expand the fundamental knowledge of the functional mechanisms of the human cortex, which, in turn, should help to increase the BCI efficiency. The study and analysis of the formation of BCI for the visual feedback closure can provide ample material for understanding the processes of training of motor skills, on the one hand, and help to create the next generation of neuroprostheses, on the other [85]. In other words, the potentials of the existing BCIs are limited by the insufficient fundamental knowledge about the brain function rather than by the restrictions in the power of computers and characteristics of electronic devices [1]. In particular, the neuronal mechanisms of control and adaptation of hand movements are not quite clear partly because the connection between the activity of neurons in many areas of both the frontal and parietal cortex and the resulting movement of the hand is almost always indirect and difficult to identify [86]. Transcoding programs in BCIs set a unique connection between the activity of recorded neurons and the movements of the effector. Therefore, the use of BCIs provides a unique technology for studying motor control and its adaptation [25]. An example of this was the study on monkeys [87], in which 10–15 neurons in the M1 area, stably recorded for many days during the implementation of the cursor running task by the monkey, were selected. After calibration of the transcoder for the activity of the selected neurons, the monkey was transferred into the BCI operation mode with a closed feedback and then trained to a sufficiently high level of task implementation. Then, significant changes were made in the transcoder program, which did not allow the monkey to perform the task, although the animal coped with the first transcoder was used. The new achievement of the same high level of the task implementation by the animal within several days gave a unique material on the learning of a new pattern of activity by a certain limited number of neurons. In another study in monkeys [88], which were trained to run the cursor using a BCI in a three-dimensional visual space, the researchers changed the random sample of recorded neurons and turned the map of the directional patterns of their activity by 90 degrees. In the first sessions performed after these changes, the monkeys moved the cursor at an angle to the desired direction and then gradually partially (approximately by 25%) compensated for the mistake after a long period of training. Thus, information on the neuronal activity before, during, and after adaptation as well as comprehensive information about the algorithmic conversion of signals make it possible to study the mechanisms of motor learning. Similarly, the use of BCI and artificial sensory feedback with parameters that are changed in the course of the study can become a method for studying the mechanisms of sensory rearrangements.

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