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REVIEW ARTICLE

Neurorestoration: Advances in human brain–computer interface using microelectrode arrays

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ABSTRACT

Neural damage has been a great challenge to the medical field for a very long time. The emergence of brain–computer interfaces (BCIs) offered a new possibility to enhance the activity of daily living and provide a new formation of entertainment for those with disabilities. Intracortical BCIs, which require the implantation of microelectrodes, can receive neuronal signals with a high spatial and temporal resolution from the individual's cortex. When BCI decoded cortical signals and mapped them to external devices, it displayed the ability not only to replace part of the human motor function but also to help individuals restore certain neurological functions. In this review, we focus on human intracortical BCI research using microelectrode arrays and summarize the main directions and the latest results in this field. In general, we found that intracortical BCI research based on motor neuroprosthetics and functional electrical stimulation have already achieved some simple functional replacement and treatment of motor function. Pioneering work in the posterior parietal cortex has given us a glimpse of the potential that intracortical BCIs have to control external devices and receive various sensory information.

1 Introduction

Neural damage, especially spinal cord injury (SCI), amyotrophic lateral sclerosis, and stroke, has long posed a challenge for patients, doctors, and researchers [1–3]. Until now, there has been no good way to help with neural restoration and corresponding functional recovery. Brain–computer interfaces (BCIs), which began in the 1970s [4], offer a new possibility for neural restoration and improving patients' activity of daily living. BCI, sometimes called brain–machine interface, is a direct communication pathway between the brain and external devices. It allows for bidirectional information flow, and it is used for researching, mapping, or enhancing nervous system recovery after neural damage [5].

After reliable results from studies of invasive BCIs in rodents and non-human primates, an array with 68 electrodes was first implanted onto the

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visual cortex of a blinded man in 1978. Since then, more intracortical microelectrode arrays have been implanted in the motor cortex to help patients with hemiplegia or tetraplegia to control robotic limbs in an attempt to assist in the rehabilitation of motor function [6–8]. Moreover, microelectrode arrays have been implanted in other cortical areas to achieve new possibilities in neural rehabilitation [9–11], or even directly control the paralyzed forearm muscles of patients [12].

These advances in human intracortical BCI point to a diverse and promising future in this field. In this review, we focus on human BCI research in movement restoration using microelectrode arrays and summarize the main research directions and the latest results in recent years.

2 Classification of human BCI research

Human BCI research is divided into two categories based on whether external devices are invasive to humans. The original signals of non-invasive BCIs can be obtained from electrooculography, pupil-size oscillation, functional near-infrared spectroscopy, or electroencephalography (EEG). EEG-based BCI has been the most widely used since the emergence of BCI research [13–16]. Although EEG can only receive a rough signal through the scalp, advanced functional neuroimaging like BOLD functional MRI and EEG source imaging has already helped EEG-based BCI demonstrate a great potential in human motor imagery [17, 18]. However, invasive BCI closer to the cerebral cortex, including electrocorticography (ECoG) and microelectrodes, receive neural signals with better temporal and spatial resolution [19]. The electrodes of ECoG are embedded in a plastic pad and placed on the surface of the cortex under the dura mater [20, 21]. Microelectrodes, sometimes called intracortical BCI, are implanted directly into the cerebral cortex to record neuronal signals.

In 1998, Philip Kennedy and Roy Bakay from Emory University, aiming to restore motor function, implanted a neurotrophic electrode into the hand control area of the right motor cortex of a patient who suffered from "locked-in syndrome" [22]. Action potentials from this patient were recorded over months, which were ultimately decoded to control the clicking of a computer mouse [23]. This study laid a good foundation for the development of intracortical BCI clinical research in neural rehabilitation.

3 Intracortical BCI research based on motor neuroprosthetics

Human BCI research is commonly used to help people with tetraplegia restore motor function. Motor neuroprosthetics are the devices that receive the BCI-processed commands and execute the corresponding motion tasks. Motor neuroprosthetics are external devices that replace some aspects of the motor pathway of the nervous system in addition to that of the brain, including robotic arms and computer cursor.

3.1 Robotic arm in BCI research

The robotic arm is a programmable mechanical device designed to replace or mimic the function of a human arm. The components of the robotic arm are connected by joints that can be rotated or articulated in certain directions. The robotic arm has been applied to intracortical BCI research with rodents since 1999 [24]. It is the most widely used motor neuroprosthetic in BCI research. With the progress in material innovation and industrial technology, the appearance and function of the robotic arm has become more and more similar to that of a human arm. Thus, they are also commonly used in non-invasive human BCIs such as EEG-based BCIs and steady-state visual evoked potential (SSVEP)-based BCIs [25–27].

There are a number of robotic arms that have appeared in past BCI research. A robotic arm known as DLR Light-Weight Robot Ⅲ, was used in intracortical BCIs [7]. It was developed at the German Aerospace Center, weighed 14 kg, and had seven degrees of freedom [28]. Another robotic arm using intracortical BCI research was invented by DEKA Research and Development Corp. (USA) and is called DEKA Generation 2, which weighs 3.64 kg and has six degrees of freedom [29]. Other robotic limbs including the modular prosthetic limb and a 17-degree-of-freedom robotic limb are also used [8, 10].

3.2 Main intracortical BCI research based on motor neuroprosthetics

Hockberg et al. [6] were one of the first to use neuromotor prostheses for clinical BCI research scholars. They implanted a 96-microelectrode array in the primary motor cortex of a patient with SCI to record the neuronal ensemble activity. They demonstrated that the ensemble activity of these neurons was still decoded to control the opening and closing of a prosthetic hand, although it had been idle for more than three years. Before long, Kim et al. [30] found that in the arm region of the motor cortex, controlling a computer cursor's velocity by neural signals occurred much more accurately and rapidly than controlling the cursor's position directly. They therefore optimized the decoder and replaced the conventional filters with the Kalman filter to further improve the decoding quality. This group at Brown University subsequently demonstrated the accuracy and stability of BCIs using intracortical microelectrode arrays, and the long-term reliability to decode a closed-loop point-and-click behavior [31, 32]. They then used two robotic arm-hand systems for people with tetraplegia to accomplish a reach and grasp task [7], indicating the feasibility for people with a long-standing disability to recreate some useful multidimensional control of motor neuroprosthetics to improve their quality of life.

Another group at the University of Pittsburgh implanted two microelectrodes in the motor cortex of a patient with tetraplegia [8]. They found a high efficiency of the intracortical BCI system to control a motor neuroprosthetic with seven degrees of freedom in a 13-week period, and over a 90% mean success rate at the same time. They further demonstrated the variety of intracortical recording stability in different identified units and subjects [33]. These results underscored the importance of the recording stability to reach a high level of performance so that the BCIs can provide more benefits to their users.

Other groups have performed similar work using intracortical BCIs to control robotic limbs and other motor neuroprosthetics like motor imagery and a computer typing program [10, 34]. The latest research in 2017 successfully used neural signals from the primary motor cortex to manipulate a flight simulator [35].

3.3 New approaches in intracortical BCI research

Recent studies found that the signals extracted from the intracortical microelectrodes were more than spikes. Local field potentials (LFPs) represent another kind of these signals. Researchers demonstrated that LFPs had a higher number of channels and even more accurate target information on intracortical microelectrodes than those of spikes [36]. Certainly, the signal-to-noise ratio of LFPs was not as high as that of spikes, and the decoding performance of multi-channel LFPs was also worse than those of multi-channel spikes. However, other research demonstrated the combined decoding of all LFP performance as well as those of spikes [37]. Over a period of several months, the decreasing trend of the quality of LFP signals and the decoding accuracy were smaller than those in spike signals.

Together, these studies showed that BCI can control motor neuroprosthetics that go far beyond simple computer cursors and three-dimensional robotic arms but can also be used to control more complex systems, which undoubtedly demonstrated the great potential of BCIs for enhancing the activity of daily living and providing new forms of entertainment for people with tetraplegia.

4 Intracortical BCI research based on functional electrical stimulation

Although the motor function pathway is blocked after neural damage, the muscle itself remains intact. Thus, researchers began thinking about establishing a bypass to the muscles to re-enable their use. One technique called functional electrical stimulation (FES), offers a possibility for BCI to achieve this bypass. FES uses low-energy electrical pulses to artificially stimulate muscles in individuals with tetraplegia due to neural injury. It can generate muscle contraction in paralyzed limbs for the individual to produce motor functions such as grasping and walking [38, 39]. Clinically, this technique is often used as a short-term intervention to help individuals with some muscle strength to restore voluntary motor functions.

The combination of BCI and FES technology has spawned a custom-built high-resolution neuromuscular electrical stimulator (NMES). A group at Ohio State University used decoded neuronal activity in the primary motor cortex to control activation of the forearm muscles of a paralyzed individual by NMES in real time [12]. They then collaborated with researchers from Battelle Memorial Institute and demonstrated the possibility of a BCI-FES system to help patients with tetraplegia regain volitional and graded muscle control in the paralyzed limb and even dexterously control seven functional hand movements with over 95% mean accuracy [40, 41].

These results indicated naturalistic and functional control of paralyzed muscles with the BCI-FES system and suggested a further step for this system to extensive clinical applications.

5 Intracortical BCI research based on the posterior parietal cortex

Previous intracortical BCI studies were based on microelectrodes implanted into the primary motor cortex, which is the direct command center for controlling the contralateral limb in the dorsal portion of the frontal lobe. It contains and allocates various motor representations, is responsible for partial motor control, and sends execution instructions to subordinate neurons throughout the body. However, the posterior parietal cortex (PPC), located posterior to the primary somatosensory cortex, receives input from sensory systems and sends the output to the motor cortex. PPC is closely involved in action planning and motor control and may play a high-level role in movements [42, 43].

Therefore, it was speculated whether PPC, as a transit station for sensory and motor functions, could also be used as a database for BCI decoding. A group from the California Institute of Technology realized this idea and implanted two 96-channel microelectrode arrays into the PPC (one in the reach area, another in the grasp area) of a tetraplegic human and successfully decoded motor imagery (including imaged goals, trajectories, and types of movements) from the neuronal ensemble activity in the PPC [10]. Their continued research is a pioneering work in this field, as they implanted two microelectrodes into the primary somatosensory cortex and used an intracortical microstimulation method to repeatedly induce elicitations of sensations in the contralateral arm [11].

These surprising results not only show that the PPC can serve as a rich source of advanced BCI signals including cognitive control but also give us a glimpse of the future of intracortical BCIs that combine sensory and motor feedback patterns in both directions. Sensory feedback to the brain would be a boon for people with motor and sensory disabilities.

6 Discussion

In the past decade, we have seen tremendous advances in the clinical research of intracortical BCIs, which have helped partially paralyzed subjects improve their activities of daily living and brought them new forms of entertainment. We also foresee a future in which the plasticity of this field will be so great that it will no doubt play a much more important role in neural rehabilitation.

With the development of intracortical BCIs, some ethical considerations have emerged. First, intracortical BCI research was designed to help disabled patients recover function, but it is still difficult for this to support millions of large-scale multicenter clinical trials. Second, there would be a benefit-risk ratio for disabilities and commercial interests of doctors and scientists. Thus, it is of vital importance to provide adequate and balanced information for the recipient, and to establish a higher-level ethics committee to approve such clinical trials [44]. Finally, with the expanding sample size of intracortical BCI research, an urgent question remains as to whether the government, the patients, or the researchers will pay for the expensive surgery, care, and equipment. Another question is whether sham surgery should be considered as a placebo effect for BCIs [45, 46]. We would not choose to do so because the BCI recipient can serve as their own controls as the devices can be shut down, and the placebo effect would rather increase the risk of infection than in providing a benefit for paralysis.

However, there remain some unsolved challenges in intracortical BCIs research [47, 48], including: (1) ensure the microelectrodes have a stable, long-term recording of neural signals, (2) optimize the existing decoder to better understand the neural signal and mechanical fitting, (3) develop biocompatible higher motor neuroprosthetic to meet higher decoding requirements.

Today, new technologies have emerged that enable us to solve these problems. These technologies include wireless microelectrodes, new brain imaging techniques, optogenetics, and better biocompatible materials [49–51]. We believe that the combination of these novel technologies and intracortical BCIs will presently help people with paralysis to achieve remarkable and rapid neural rehabilitation.

Conflict of interests

All contributing authors declare no conflict of interests in this work.

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