Science Bulletin 67 (2022) 1932–1934

Contents lists available at ScienceDirect

Science Bulletin

journal homepage: www.elsevier.com/locate/scib

News & Views

Hand surgery in a new "hand-brain" era: change the hand, rebuild the brain

Juntao Feng [a,b], Yudong Gu [a,b,c], Wendong Xu [a,b,c,d,*]

[a] Hand Surgery Department, The National Clinical Research Center for Aging and Medicine, Huashan Hospital, Fudan University, Shanghai 200040, China
[b] Department of Hand and Upper Extremity Surgery, Center for the Reconstruction of Limb Function, Jing'an District Central Hospital, Fudan University, Shanghai 200040, China
[c] Institutes of Brain Science, State Key Laboratory of Medical Neurobiology and Collaborative Innovation Center of Brain Science, Fudan University, Shanghai 200032, China
[d] Research Unit of Synergistic Reconstruction of Upper and Lower Limbs after Brain Injury, Chinese Academy of Medical Sciences, Beijing 100730, China

Amputated hand, and paralyzed hand, are diseases not on the conventional list of the hand surgery world, but now have gradually become the new direction for hand surgeons. A good example is the advancements in treating amputations after traumatic injury of the upper limb. Targeted muscle reinnervation combined with a highly functional bionic arm can greatly compensate for the missing part of the amputated arm [1], which in general satisfies the need for strength and dexterity in daily life. According to the classic cortical homunculus first drawn by Penfield, the hand area occupied nearly-one-third of the sensorimotor cortex [2]. Thus, interventions with the hands enable the modulation of brain function, providing a solution for brain disorders through skillful utilization of brain plasticity. With the recent advancements in neuroscience and biomedical engineering technology, hand surgeons find themselves entering an era with a bigger performance stage than ever before. For paralyzed hand, the most common cause is central neurological diseases such as stroke or cerebral palsy, or paraplegia. Although it is more challenging since surgeons should balance spasticity and motor function at the same time, efforts have been made by hand surgeons around the world, such as hyper selective neurectomy, tendon lengthening or transfer to reduce the spasticity and reconstruct the motor function [3]. Considering the fact that the number of patients with paralyzed hands is over 10 million, which far exceeds the traditional nerve injury entity, this area is the potential further direction of hand surgery. In this article, we will discuss the opportunities and pitfalls in the combination of hand surgery techniques and brain-computer-interface (BCI) in treating paralyzed hands from the perspective of hand surgery development.

The mainstream concept of noninvasive BCI for patients with the paralyzed hand is to collect and analyze the electroencephalograph (EEG) signal pattern of the cortex in order to assist in the rehabilitation of the paralyzed hand. This concept has achieved great success combined with exoskeleton devices in paraplegia patients due to spinal cord injury or subcortical stroke patients, as reported by Wandelt et al. [4]. For patients with cortical injury due to stroke or other cortical injury diseases, the most straightforward signal source is the perilesional cortex (PLC), which shows compensational plasticity for the motor function of the paralyzed limb part with sophisticated mechanism [5]. However, these compensational signals are usually noisy and unstable, which cannot meet the demand for dexterous and flexible demand for hand function in daily life [6]. Inadequate signal of the lesioned hemisphere has become a bottleneck for the current development of BCI devices for paralyzed hand treatment, and thus it is urgent to look for a clean, stable, and accessible signal source to make significant progress for functional replacement or assistance in daily life for hemiplegic patients. Luckily, with the advancements in implanted multichannel electrodes and exoskeleton devices, this has become possible as long as we have a new theoretical model for the signal source.

Because of the uncertainty of the lesioned hemisphere, some researchers have focused on the "other side", the contralesional hemisphere. Previous studies have shown that movement signals of both hands can be detected simultaneously in the primary motor cortex (M1) and premotor cortex of one hemisphere, including kinematic indexes and feedbacks during motor planning and execution [7]. Moreover, the contralesional hemisphere is deeply involved in the post-stroke functional plasticity which is important for the compensation of the paralyzed hand [8]. A team from the United States has already developed an exoskeleton device, called "Ipsihand", which is based on the signal of the contralesional hemisphere and can assist in the rehabilitation and daily use of the paralyzed hand [9]. This is the first device approved by the US Food and Drug Administration (FDA) that utilizes the signal of the contralesional hemisphere, and still has a large space for improvement. The recent research of Ipsihand has discovered some patterns of brain functional reorganization on the network level in the contralesional hemisphere through EEG evaluations [10]. However, the main problem is that the contralesional hemisphere is not able to spontaneously reorganize to independently control the bilateral hands. Therefore, Ipsihand cannot separate the two hands from the signals collected, and thus can only realize the movement of the paralyzed hand but not the coordinate movement of bilateral hands. However, it has made an important step

* Corresponding author.
E-mail address: wendongxu@fudan.edu.cn (W. Xu).

https://doi.org/10.1016/j.scib.2022.08.031

in using the signal from the contralesional hemisphere and was appraised as a "breakthrough device" by the US FDA.

We previously established a strategy to exploit the potential of the contralesional hemisphere through peripheral nerve transfer surgery in unilateral spastic arm paralysis patients due to central neurological injuries including stroke, traumatic brain injury, or cerebral palsy. By building an ipsilateral pathway that connects the paralyzed hand with its ipsilateral hemisphere—the contralesional hemisphere—through a peripheral nerve surgery, the "contralateral C7 nerve (CC7) cross transfer" surgery, the paralyzed arm function can be significantly improved [11,12]. A randomized clinical trial study with 18 patients who underwent CC7 cross transfer surgery showed 15.1 points better functional improvement compared to 18 patients who received rehabilitation alone [11]. Recently, a multicenter cohort study in a real-world setting including over 400 patients from China and Republic of Korea verified the safety, effectiveness, and long-term stability of CC7 cross surgery in clinical practice. This study also significantly extended the indications of this surgery in a more inclusive hemiplegia population aged from 4 to 69 years old, male or female, and with chronic cerebral injuries over 1 year or longer [12]. This is an important practical guideline for hand surgeons who want to attempt this surgery around the world.

The research into the mechanism of CC7 cross transfer surgery showed a very special central plasticity pattern corresponding to the recovery of the paralyzed hand. Dynamic functional magnetic resonance imaging (MRI) data from presurgical evaluation to 12 months after the surgery showed that this ipsilateral pathway could induce large-scale functional reorganization in the contralesional hemisphere, including M1, premotor and other areas. A new representational area of the paralyzed hand emerged in the contralesional M1, and established functional control of the paralyzed hand around 10–12 months after the surgery. After large-scale functional reorganization, the contralesional hemisphere established simultaneous control of the paralyzed and intact hand eventually. Their representational areas both appeared in the contralesional hemisphere, although partially overlapped, but can realize the independent and coordinated movement of bilateral hands verified by functional evaluation and daily life activities [11]. These results indicated a new direction in brain plasticity study and provided a new concept for exploiting the potential of the contralesional hemisphere, which was essential for the further study of BCI innovation for the paralyzed hand (Fig. 1).

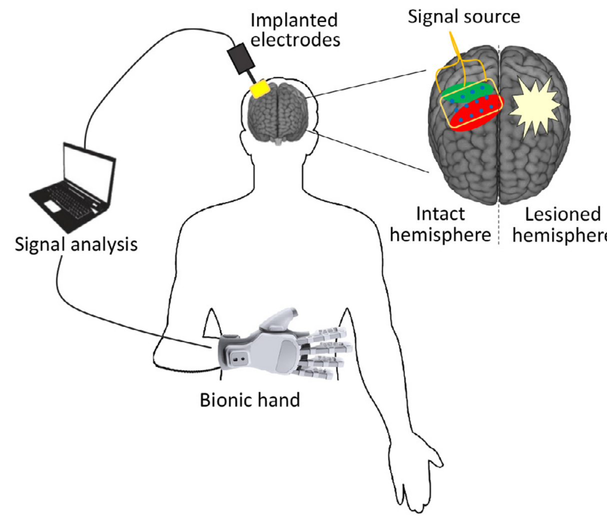

Fig. 1. The concept of BCI driven exoskeleton arm using the signals from the contralesional hemisphere. For patients with unilateral cortical injury (yellow explosive shape) due to stroke, traumatic brain injury, or other diseases, the signal from the contralesional motor cortex is extracted with an implanted multichannel electrode array, and the control of the paralyzed hand (green) and intact hand (red) can be separated through signal analysis to provide stable driving of the exoskeleton arm for the paralyzed hand.

In the era of intelligence, what is the opportunity for hand surgery development in the innovation of new BCI devices for the paralyzed hand? Here are a few thoughts from a perspective of a hand surgeon.

First, it is important to enrich the knowledge of brain regions from the bilateral hemisphere and their plasticity mechanism that participated in the compensatory control of the paralyzed hand after stroke. It will provide new ideas for surgical innovation. Previous research about the role of the contralesional hemisphere in the control of the paralyzed hand points out a potential direction for BCI research, further research needs to focus on how different movements of the bilateral hand are coded by neuron population and the key brain regions participated in [5]. After understanding these mechanisms so can we simulate the neuron activity patterns to provide a calculating model for BCI devices with flexible control under different contexts. To accomplish this, we need to collect more signals directly from the neurons at a population level in the motor cortex. Implantable multichannel electrodes and electrocorticogram in epilepsy patients have provided valuable evidence for elucidating the motor coding in M1 and premotor cortex [13]. Further, understanding the different plasticity mechanisms after CC7 cross transfer surgery will provide more valuable indications on how to exploit the potential of the contralesional hemisphere. The key difference after CC7 cross transfer surgery is that the control of the paralyzed hand is established by the contralesional hemisphere and separated from the intact hand. The functional MRI in patients and neural circuit tracking in disease animal models including monkeys and rodents are both needed, while the former can provide information about key brain regions participated in this process, and the latter can give insights on how these regions accomplish the process through functional reorganization.

Second, cooperation between hand surgeons and engineers will greatly accelerate the development and clinical use of BCI devices. Iteration of new devices and intervention techniques focuses on the efficiency and accuracy of the movements. As hand surgeons have a deeper and more systematic understanding of patients' demands for hand function, we can look into new surgical techniques that rebuilt more signals in the brain and the peripheral pathway to facilitate the signal needed for driving BCI devices. On the other hand, optimizing algorithm of the neural dynamics is still a popular research field for computing science. Hand surgeons can also make the signals more approachable by performing peripheral nerve transfer surgery such as TMR. For collection devices, a higher signal-to-noise ratio, more portable, and less invasive is still needed for the large patient population, considering their physical condition and willingness to wear the electrodes. Besides the devices, cooperation with therapists is also very important. According to previous studies, appropriate rehabilitation is related to better functional improvement after CC7 cross transfer [12,14]. Therefore, it is hopeful that developing a BCI-driven rehabilitation mechanical arm combined with an interactive interface can provide an immersive training experience and visual feedback, which can further improve the motor function of the paralyzed hand [15].

Finally, to more precisely induce the plasticity of the contralesional hemisphere, more selective peripheral nerve transfer surgeries can be supposed, such as CC7 nerve root to C5 to improve should function, CC7 to C8 for hand function, or combination with nerve branch transfer. These surgeries aim to induce central plasticity of a certain area of the limb representation more selectively in the motor cortex, therefore establishing the motor control of the paralyzed limb. These explorations should be done with caution not to damage the residual motor function of the upper limb. Besides surgical innovation, developing interventions directly applied to the brain to facilitate plasticity is also very important. Current noninvasive interventions including transcranial magnetic stimulation, and electrical stimulations can be based on the new concept. Invasive cortical stimulation can provide more specific stimulation to the brain. For example, as sensory feedback plays an important role in motor recovery [16], direct cortical electrical stimulation makes it possible to construct artificial sensory feedback, and implantable electrodes to the sensory cortex can simulate the sensory feedback of the upper limb. This provides a better opportunity for the development of a closed-loop bidirectional brain-computer interface.

The diagnosis and treatment of central and peripheral nerve injury have been well developed in the field of nerve repair, and further direction needs to fully embrace the brain-computer interface. As a hand surgeon, mastering these latest frontier technologies and understanding the relevant principles of brain plasticity related to exercise control is an important part of maintaining a leading industry. The application of brain-computer interface in hand surgery, starting from the new continent of the "contralesional hemisphere", will provide a particular opportunity for the large number of patients with paralyzed hands.

To sum up, the scope of hand surgery is expanding, and a new "hand-brain" era is coming. By exploiting this hand-brain connection, hand surgeons will be wiser in dealing with medical puzzles about the brain, by "changing the hand".

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (82021002, 81830063, and 82072539) and the CAMS Innovation Fund for Medical Sciences (2019-I2M-5-007). We would like to thank the President of International Federation of Societies for Surgery of the Hand (IFSSH), Prof. Daniel J Nagle of Northwestern Memorial Hospital for his insightful comments on the manuscript.

References

[1] Ortiz-Catalan M, Mastinu E, Sassu P, et al. Self-contained neuromusculoskeletal arm prostheses. N Engl J Med 2020;382:1732–8.
[2] Penfield W, Boldrey E. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 1937;60:389–443.
[3] Leclercq C, Perruisseau-Carrier A, Gras M, et al. Hyperselective neurectomy for the treatment of upper limb spasticity in adults and children: a prospective study. J Hand Surg Eur 2021;46:708–16.
[4] Wandelt SK, Kellis S, Bjånes DA, et al. Decoding grasp and speech signals from the cortical grasp circuit in a tetraplegic human. Neuron 2022;110:1777–87.
[5] Khanna P, Totten D, Novik L, et al. Low-frequency stimulation enhances ensemble co-firing and dexterity after stroke. Cell 2021;184:912–30.
[6] Gallego JA, Makin TR, McDougle SD. Going beyond primary motor cortex to improve brain-computer interfaces. Trends Neurosci 2022;45:176–83.
[7] Bundy DT, Leuthardt EC. The cortical physiology of ipsilateral limb movements. Trends Neurosci 2019;42:825–39.
[8] Alawieh A, Tomlinson S, Adkins D, et al. Preclinical and clinical evidence on ipsilateral corticospinal projections: implication for motor recovery. Transl Stroke Res 2017;8:529–40.
[9] Bundy DT, Souders L, Baranyai K, et al. Contralesional brain-computer interface control of a powered exoskeleton for motor recovery in chronic stroke survivors. Stroke 2017;48:1908–15.
[10] Humphries JB, Mattos DJS, Rutlin J, et al. Motor network reorganization induced in chronic stroke patients with the use of a contralesionally-controlled brain computer interface. Brain-Computer Interfaces 2022;9:179–92.
[11] Zheng M-X, Hua X-Y, Feng J-T, et al. Trial of contralateral seventh cervical nerve transfer for spastic arm paralysis. N Engl J Med 2018;378:22–34.
[12] Feng J, Li T, Lv M, et al. Reconstruction of paralyzed arm function in patients with hemiplegia through contralateral seventh cervical nerve cross transfer: a multicenter study and real-world practice guidance. EClinicalMedicine 2022;43:101258.
[13] Willett FR, Deo DR, Avansino DT, et al. Hand knob area of premotor cortex represents the whole body in a compositional way. Cell 2020;181:396–409. e26.
[14] Li J, Ying Y, Su F, Chen L, Yang J, Jia J, et al. The Hua-Shan rehabilitation program after contralateral seventh cervical nerve transfer for spastic arm paralysis. Disabil Rehabil 2022;44:404–11.
[15] Rodgers H, Bosomworth H, Krebs HI, et al. Robot assisted training for the upper limb after stroke (RATULS): a multicentre randomised controlled trial. Lancet 2019;394:51–62.
[16] Flesher SN, Downey JE, Weiss JM, et al. A brain-computer interface that evokes tactile sensations improves robotic arm control. Science 2021;372:831–6.

Juntao Feng obtained his M.D. degree from Hand Surgery department of Huashan Hospital, Fudan University, and now he is an attending doctor and associated research fellow. His main research area is in the brain functional reorganization and clinical appliance of contralateral C7 nerve cross transfer surgery in spastic arm paralysis patients due to central neurological injury.

Wendong Xu is the President of Chinese Society for Surgery of the Hand and the Past President of International Wrist Arthroscope Society, the Vice President of Huashan Hospital and the Executive Deputy Director of National Clinical Research Center for Aging and Medicine. He is the pioneer in the new area of "creatively using the peripheral nerve surgery in treating the central nervous system diseases".