An electroencephalography-based human-machine interface combined with contralateral C7 transfer in the treatment of brachial plexus injury

Introduction

Traumatic brachial plexus injury (BPI) is a common nerve injury caused mainly by reverse movement of the head, neck, and shoulder. The brachial plexus can also be damaged by surgery or radiation (Yan et al., 2019). BPI is a severe and devastating condition that is observed in up to 4.2% of all multi-trauma patients, usually affects young adults, and has significant socioeconomic implications (Yan et al., 2019; Estrella et al., 2021). Severe BPI, particularly ipsilateral BPI, discusses the possible mechanism by which the brain-computer interface (BCI) transmits peripheral feedback signals, which optimizes the mechanical response to maximize the rehabilitation effect. The timeline of studies of EEG-based human-machine interface combined with contralateral C7 transfer repair after peripheral nerve injury (PNI) (Wang et al., 2010; Facchini et al., 2021). The reentrant nerve plays a dominant role, it must form an effective reconnection in the cortex (Sturma et al., 2018; Hou et al., 2020). Therefore, satisfactory peripheral nerve regeneration and cortical remodeling are only possible over the long term.

Since 2013, researchers have been applying electroencephalography (EEG) signal-based upper limb control devices to assist with movement, as shown in Table 1. The primary purpose of the brain-computer interface is to accurately identify and extract EEG signals that control limb movement. The signals are translated and amplified by the computer and then transmitted across the PNI site to a robotic arm exoskeleton or distal electrical stimulation device. Unlike existing purely mechanically driven rehabilitation devices, EEG-based devices can actively control distal limb movement to maintain target muscle activity. Early functional exercise not only promotes peripheral nerve rehabilitation, but also accelerates cerebral cortical remodeling. At the same time, it retransmits peripheral feedback signals, which optimizes the mechanical response to maximize the rehabilitation effect. The timeline of studies of EEG-based human-machine interface combined with contralateral C7 transfer for the treatment of BPI is shown in Figure 1.

This review summarizes the application of C7 nerve transfer in treating ipsilateral BPI, discusses the possible mechanism by which the brain-computer interface promotes BPI rehabilitation, and proposes a viable procedure for brachial plexus repair that promotes functional recovery.

Abstract

Transferring the contralateral C7 nerve root to the median or radial nerve has become an important means of repairing brachial plexus nerve injury. However, outcomes have been disappointing. Electroencephalography (EEG)-based human-machine interfaces have achieved promising results in promoting neurological recovery by controlling a distal exoskeleton to perform functional limb exercises early after nerve injury, which maintains target muscle activity and promotes the neurological rehabilitation effect. This review summarizes the progress of research in EEG-based human-machine interface combined with contralateral C7 transfer repair of brachial plexus nerve injury. Nerve transfer may result in loss of nerve function in the donor area, so only nerves with minimal impact on the donor area, such as the C7 nerve, should be selected as the donor. Single tendon transfer does not fully restore optimal joint function, so multiple functions often need to be reestablished simultaneously. Compared with traditional manual rehabilitation, EEG-based human-machine interfaces have the potential to maximize patient initiative and promote nerve regeneration and cortical remodeling, which facilitates neurological recovery. In the early stages of brachial plexus injury treatment, the use of an EEG-based human-machine interface combined with contralateral C7 transfer can facilitate postoperative neurological recovery by making full use of the brain’s computational capabilities and actively controlling functional exercise with the aid of external machinery. It can also prevent disuse atrophy of muscles and target organs and maintain neuromuscular junction effectiveness. Promoting cortical remodeling is also particularly important for neurological recovery after contralateral C7 transfer. Future studies are needed to investigate the mechanism by which early movement delays neuromuscular junction damage and promotes cortical remodeling. Understanding this mechanism should help guide the development of neurological rehabilitation strategies for patients with brachial plexus injury.

Key Words: arm injuries; brachial plexus; brain-computer interfaces; nerve transfer; nerve regeneration; nerve tissue; neurofeedback; neurological rehabilitation; user-computer interface

Table 1

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Conclusions and Future Prospects

In addition, cortical plasticity is a critical factor that affects the success of repair after peripheral nerve injury (PNI) (Wang et al., 2010; Facchini et al., 2021). If the reentrant nerve plays a dominant role, it must form an effective reconnection in the cortex (Sturma et al., 2018; Hou et al., 2020). Therefore, satisfactory peripheral nerve regeneration and cortical remodeling are only possible over the long term.

Since 2013, researchers have been applying electroencephalography (EEG) signal-based upper limb control devices to assist with movement, as shown in Table 1. The primary purpose of the brain-computer interface is to accurately identify and extract EEG signals that control limb movement. The signals are translated and amplified by the computer and then transmitted across the PNI site to a robotic arm exoskeleton or distal electrical stimulation device. Unlike existing purely mechanically driven rehabilitation devices, EEG-based devices can actively control distal limb movement to maintain target muscle activity. Early functional exercise not only promotes peripheral nerve rehabilitation, but also accelerates cerebral cortical remodeling. At the same time, it retransmits peripheral feedback signals, which optimizes the mechanical response to maximize the rehabilitation effect. The timeline of studies of EEG-based human-machine interface combined with contralateral C7 transfer for the treatment of BPI is shown in Figure 1.

This review summarizes the application of C7 nerve transfer in treating ipsilateral BPI, discusses the possible mechanism by which the brain-computer interface promotes BPI rehabilitation, and proposes a viable procedure for brachial plexus repair that promotes functional recovery.

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A summary of electroencephalography (EEG) signal-based prosthesis in brachial plexus injury treatment was introduced in the 1950s. With advances in knowledge and surgical technology, it has become a preferred method for BPI treatment (Feng et al., 2019; Fasce et al., 2021). The spinal accessory, phrenic, supracarpal, axillary, and intercostal nerves as well as the contralateral C7 nerve root may all be used as the donor for nerve transfer (Midha, 2004; Addas and Midha, 2009). A summary of contralateral C7 transfer for various injuries is shown in Table 2. Because isolated C7 nerve root transaction does not lead to obvious motor and sensory deficits, Gu (1992) proposed using the contralateral C7 nerve root as the donor in repair of traumatic brachial plexus avulsion injury. Anatomically, the muscles innervated by C7 are also usually innervated by C6, C8, and T1, and may also play a partial role (Li et al., 2017; Liu et al., 2018). In addition, the C7 nerve root contains more myelinated nerve fibers than other donor nerves, which can provide sufficient power for the transplantation area (Alawieh et al., 2021). In summary, nerve transfer has become a widely used and often successful method to treat BPI. However, surgical repair of complex brachial plexus defects cannot resolve the problems of neuromuscular junction dysfunction and target muscle atrophy.

### Table 1: A summary of electroencephalography (EEG)-based prosthetic function in patients with functional limb loss

| Authors       | Electrode counts (n) | Features                                      | Task/Procedure                | Application significance |
|---------------|----------------------|-----------------------------------------------|-------------------------------|-------------------------|
| Robinson et al., 2013 | 128                  | Regularized wavelet electrode                  | Hand movement                 | High precision control and self-assisted hand mobility device |
| Yi et al., 2013 | 64                   | Multi-class CSE electrode                      | Limb function                 | Medium-precision controlable upper limb mobility device |
| Woo et al., 2015 | 64                   | CSP algorithm                                  | Arm movements                 | Medium-precision controlable upper limb mobility device |
| Jochumsen et al., 2016 | 25                  | Temporal features and spectral features and their combinations | Hand grasping                 | Low-precision controlable hand mobility device |
| Roy et al., 2017 | 29                   | Autoregressive parameter, Hjorth parameter, correlation dimension, Hurst's exponent | Decoding different grasp types | Low-precision controlled upper limb mobility device |
| Iturrate et al., 2018 | 64                  | Temporal and spectral domains                  | R-G actions & variable force  | Medium precision upper limb strengthening device |
| Roy et al., 2018 | 29                   | Correlation dimension in different bands       | Grasp patterns                | Low-precision controlled upper limb mobility device |
| Schwarz et al., 2018 | 61                  | Low-frequency time domain features from 0.3 to 3 Hz | Reach to grasp actions         | Medium-precision prosthetic devices |

**CSP:** Common spatial patterns.

**Search Strategy**

This manuscript systematically reviews the rodent, non-human primate, and human studies of nerve transfer treatment of BPI that have been published between 1990 and 2021. The PubMed and EMBASE databases were searched using the following key words: “brachial plexus injury”, “C7 nerve transfer”, and “peripheral nerve regeneration”. The articles generated by the search were further screened based on titles and abstracts. The databases were also searched for studies of brain-computer interface use in nerve injury repair using the following key words: “arm injuries”, “brachial plexus”, “brain-computer interface”, “nerve transfer”, “nerve regeneration”, “nerve tissue”, “neurofeedback”, “neurological rehabilitation”, and “user-computer interface”.

### Brachial Plexus Injury

**Brachial Plexus Injury Treatment**

BPI can cause loss of shoulder elevation, abduction, and rotation; elbow flexion and extension; and wrist and finger flexion and extension (Sulaiman et al., 2009; Schesslter and McClellan, 2010). As Figure 2 shows, BPI can be classified according to the arm predominantly affected: upper arm (C5–C6 with or without C7 injury), lower arm (C8–T1 injury), and whole arm (C5–T1 injury). Injury treatment mainly consists of surgery, including nerve repair, nerve grafting, nerve transfer, and functional free muscle transplantation to replace original muscle function (Dubuisson and Kline, 2002; Muhedtidjer et al., 2011).

Direct suturing of the adventitia/intima is the most common method of nerve repair and is mainly suited for acute localized injury. The proximal and distal nerve stumps can be directly sutured in tension-free injuries, which include sharp nerve transection and penetrating injury. Nerve transplantation can be used when the nerve defect is too large for tension-free direct suturing. The sural nerve is commonly harvested to use for grafting; other options include the medial brachial cutaneous nerve or the medial forearm cutaneous nerve.

Although these donor nerves do not have a sufficient number of medullary nerve fibers to repair multiple thicker nerves (Garg et al., 2011; Davidge et al., 2021; Hill et al., 2021; Macédo et al., 2021; Rasulíc et al., 2021), nerve transplantation avoids the need for donor region cortical remodeling and provides a sufficient number of motor bundles. However, nerve donor area damage is inevitable, and it cannot fundamentally solve the problems of neuromuscular dysfunction and muscle atrophy.

Functional muscle and tendon transplantation can also partially restore injured limb function. The trapezius muscle is usually preserved in BPI patients and can be transferred to repair the shoulder. Although the superior trapezius muscle has been used to repair shoulder abduction function, results have been mixed (Terzis and Kostopoulos, 2007; Elhassan et al., 2009). As the function of the infraspinatus muscle is closely related to that of shoulder abduction, the repair method in which the infraspinatus muscle is used as the donor has a success rate of greater than 90% (Elhassan, 2014). However, shoulder abduction and rotation require action of multiple muscles (Elhassan et al., 2012) and single tendon transfer cannot completely restore function; therefore, it is often necessary to rebuild multiple functions. Moreover, the outcome of muscle and tendon transplantation is often not ideal and therefore is generally used when neurosurgery has failed or the patient suffers from forearm and hand motor function limitation.

### Realization of Human-Machine Interfaces

**Types of human-machine interfaces**

The invasive human-machine interface includes skeletal muscle implantation and peripheral nerve implantation (Navarro et al., 2005; Christensen et al., 2014; Gelenitís et al., 2021; Hejazi et al., 2021). As shown in Figure 3A and B, the peripheral nerve-implanted electrode and muscle-implanted electrode can collect the local electrical nerve signals of the corresponding area with high precision. This human-machine interface mainly relies on an invasive guide needle or electrode to obtain signals from skeletal, muscle, or peripheral nerves. It's advantage lies in the stability and high intensity of the signal sources. However, the trauma induced by the needle or electrode limits its clinical application. Although some invasive electrodes are designed to promote peripheral nerve growth, regenerative electrodes can only be used in transected peripheral nerves. Regenerated axons grow slowly through the nerve; therefore, this effect cannot be quickly verified by experiments. While it is feasible to use regenerative electrodes to stimulate a small number of regenerated fibers (Spearman et al., 2020), there is no practical way to achieve complete nerve regeneration. The signal source of the non-invasive human-machine interface mainly comes from EEG and electromyography (EMG) (Kuiken et al., 2007; Marchal-Crespo and Reinkensmeyer, 2009).

As shown in Figure 3C and D, the EEG and EMG signals of a non-invasive interface are not determined as accurately as invasive electrode signals. However, they are also difficult to distinguish from confounding signals.
arising from surrounding tissues. Through a series of complex signal processors, functional control signals are extracted, and external flexible exoskeletons or unique robotic arms are directed to assist patients in active recovery. The use of a non-invasive human-machine interface allows complete avoidance of surgical risks. A previous study has shown that a brain-computer interface can perform delicate tasks such as text creation (Marshall and Farah, 2021). Warwick et al. (2003) implanted multielectrode arrays in a healthy subject and achieved bidirectional transmission between the experimental robot arm and the peripheral nervous system. These works have opened many research opportunities in the fields of human-machine interface and activity monitoring (Xiao and Menon, 2019). The signals acquired by the brain-computer interface originate from the cerebral cortex, which is characterized by a complex signal. However, multi-channel high-density electrodes are now available that can accurately acquire signals from different distribution points within a specific area and differentate and integrate them to obtain the desired signal band. After decoding by a computer, a similar effect to that of an invasive human-machine interface can be achieved. Therefore, compared with an invasive human-machine interface, the non-invasive EEG-based interface ensures recognition accuracy, reduces unnecessary trauma, and has better application prospects in promoting nerve injury rehabilitation.

**Figure 3 | Types of human-machine interface.**
(A) Peripheral nerve-implanted electrode. Black line: electric wire; black circle: peripheral nerve injury site; (B) Muscle-implanted electrode. Black circle: peripheral nerve injury site; (C) EEG human-machine interface. Black line: electric wire; (D) EMG human-machine interface. Black circle: Peripheral nerve injury site; black box: magnified view of local damage.

**Figure 4 | Schematic diagram of an electroencephalography-based human-machine interface.**
The computer obtains an electrical signal from the cerebral cortex and directly transmits this signal downward to the distal end of the injury with a certain intensity of electrical stimulation. At the same time, the feedback signal is collected and processed by the computer and transmitted back to the cerebral cortex.

The output of EEG signals can be used to control the movement of prosthetics, orthoses, wheelchairs, robots, and computer mice (Hochberg et al., 2012; Gilja et al., 2015; Jarosiewicz et al., 2015). This signal output can also act directly on muscle in the form of electrical stimulation (Plutscholler et al., 2003). The brain response can be fed back as visual (Hochberg et al., 2006; Caria et al., 2012), auditory (Nijboer et al., 2008; Leeb and Pérez-Marcos, 2020), or haptic stimuli that vary according to the measured brain activities (Chatterjee et al., 2007; Lugo et al., 2014). Information about limb position or movement can be used to monitor physical activities or for applications of the human-machine interface (Xiao and Menon, 2019). In addition, a human-machine interface has been used for receiving and translating neural electrical signals in amputation patients to assist with movement (Ortiz-Catalan et al., 2014; Raspopovic et al., 2014; Tan et al., 2014; Oddo et al., 2016; Valle et al., 2018; Petriti et al., 2019) and to feed back touch and proprioceptive sensations from the exoskeleton to the center (Raspopovic et al., 2014; Oddo et al., 2016). Compared with an EMG-based human-machine interface, an EEG-based interface can make full use of the human brain’s computing power without the need for complicated judgment instructions through an external calculator. Such an interface can execute the brain’s motor instructions and transmit feedback signals back to the brain to allow completion of more complex and precise activities. Furthermore, it can receive slow cortical
Review

Numerous Mechanisms for Repairing Brachial Plexus Injury

Remodeling skeletal muscle structure and muscle fiber types

The mechanism of brachial plexus nerve injury repair is shown in Figure 5. Most included studies have shown that denervated muscle mainly manifests as a decrease in wet muscle weight. Reduction in muscle cross-sectional area results from a decline in muscle fiber diameter, loss of cellular nuclei, and cellular apoptosis (Lesenfants et al., 2011). In contrast, the brain-computer interface can promote peripheral muscle activity in the early stage of injury, slow down neuromuscular junction atrophy, and maintain target muscle activity. Simultaneously, the feedback signal benefits the newly developed nerve in terms of remodeling of the cortex and corresponding brain regions (Alvarez et al., 2010). Studies have shown that the precise control of cortical remodeling may be an important factor in repairing PNI and achieving better rehabilitation results. As illustrated in Figure 7, the human-machine interface can help BPI patients achieve better functional outcome by promoting skeletal muscle fiber regeneration, regulating motor neurons, and promoting cerebral cortex plasticity. In summary, applying an EEG-based human-machine interface in BPI patients may improve the surgical outcome of nerve transfer.

Conclusions and Future Prospects

Human neural activity is used as input control in human-machine interfaces. Previous studies have demonstrated the advantages of EEG-based interfaces, which is the most common brain-machine interface used today. Song et al. (2020) proposed an EEG-based human-machine interface to enable paralyzed patients to control an assistive robot. EEG can not only identify working signals, but can also distinguish subtle emotional signals (López-Hernández et al., 2019). Assistive robots can help users with motor actions and provide an exploration of broader applications of human-robot interaction. However, integration of an EEG-based human-machine interface with rehabilitation of surgically repaired PNI has not yet been addressed despite the need for methods to improve rehabilitation outcomes.

Limitations and advantages

Development of an effective human-machine interface for PNI rehabilitation requires in-depth cross-disciplinary collaboration between science, engineering, and medicine. The multi-dimensional combined approach proposed in this study has not yet been implemented in the clinic, and the development and approval cycle for a rehabilitation system can be long. However, brain-computer interface-based prosthetics are a reality and have great potential to improve rehabilitation outcomes after C7 nerve transfer for severe BPI.

Several points deserve particular attention. Future work and reliable replication of previous studies are required to ensure that EEG can be assimilated in automated human-machine interfaces. In addition, engineering quality is equally important. Most existing external brain-machine interface-controlled exoskeleton devices are only in the laboratory stage; eventually, they must be durable enough to allow long-term clinical use. Accuracy of dynamic recognition of EEG signals is another major factor that limits the stable provision of services. The rates of correct recognition by existing algorithms range between 40.5% and 92.7% in previous reports, which should be improved. New density sensors show great potential for use in human-machine interfaces, such as the latest high-density EEG collectors, which have extremely high resolution and the ability to acquire multi-conductor electrical potentials (Kübler et al., 2001), sensorimotor rhythms, P300 event-related potentials (Kühler et al., 2009; Halder et al., 2010), steady-state visual evoked potentials (Lesenfants et al., 2014), and error-related negative evoked potentials (Chavarriaga and Millan Jdel, 2010). To reduce muscle atrophy and maintain muscle function as much as possible, intervention should be performed in the early stage of injury. The influence of the human-machine interface on motor learning offers exciting new prospects for retaining skills after neural injury.

Motor neuron regulation

After PNI, the speed and number of regenerated axons are disturbed, mainly by neurotrophic factors. Exercise is effective for functional recovery after spinal cord injury in rodents and cats (Alluin et al., 2011), which may be related to neurotrophic factors induced by exercise. Both motor neuron nucleolar area and rate of protein synthesis increase in rats that undergo treadmill training (Kang et al., 1995; Boeltz et al., 2013). Neuronal anterograde and retrograde transport of axonal proteins also increases, which promotes an increase in dendrites (Shin et al., 2014). This positive promoting effect may be realized through the human-machine interface.

Promoting cerebral cortex plasticity

Changes in the cerebral cortex occur after PNI. As nerves regenerate and axons regrow into target organs, the afferent nerves can gradually transmit signals to the center. Afferent stimulation can improve cortical cell activity and induce cerebral cortex reorganization (Hickmott and Merzenich, 2002). As shown in Figure 6, cerebral cortex remodeling after PNI repair can provide sufficient motor and plasticity and can improve motor function.

Figure 5 | Mechanisms of brachial plexus injury repair.

Figure 6 | Central remodeling of the cerebral cortex caused by peripheral nerve reconnection.

Figure 7 | Flowchart for neurological rehabilitation after peripheral nerve injury using an electroencephalography-based human-machine interface.
signals in specified areas. Such collectors should provide a basis for precise acquisition and control of human-machine interfaces. In the early stages of rehabilitation after C7 nerve transfer for BP, full use of the brain’s computing potential and activity of external mechanical aids for functional exercise can greatly contribute to better outcomes. In the long term, it can prevent disuse atrophy of muscles and target organs and maintain neuromuscular junction effectiveness. Cortical remodeling also becomes important for recovery as the brain re-establishes effective pathways.

Innovation and comments

This review advocates integrating a human-machine interface into the rehabilitation process after PNI repair and argues for a recovery that does not rely solely on surgery to heal massive injuries. Active, controlled, and safe functional exercise at a later stage is equally important. The unique feedback coordination mechanism of the human-machine interface further enhances control of function through rehabilitation processes. In contrast to conventional manual rehabilitation, the interface has potential to maximize user initiative, regenerate peripheral nerves, and promote cortical remodeling for better and faster recovery.

Conclusion and prospects

The method proposed in this study suggests a possible direction for the future development of human-machine interfaces as a feasible solution to BP, a difficult clinical problem. In the future, the application of artificial intelligence technology in the field of human-machine interface will make it possible to achieve excellent rehabilitation results with BP.

Although remarkable progress has been made in BP repair, in the future, human-machine interfaces will also play a critical role in recovery from nerve injury. In each rehabilitation method, the disintegration of the neural junction effectiveness. Cortical remodeling also becomes important for recovery after C7 nerve transfer for BP. An EEG-based human-machine interface shows excellent potential to improve surgical outcomes after brachial plexus repair.

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