Chapter

Orthotic and Prosthetic Management in Brachial Plexus Injury: Recent Trends

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Abstract

The brachial plexus is a network of intertwined nerve that controls movement and sensation in arm and hand. Any injury to the brachial plexus can result in partial or complete damage of arm and hand. The surgery is a common indicative procedure in brachial plexus injury in case of non-spontaneous recovery. The loss of function of hand due to injury can be replaced by using body powered or externally powered devices. Recent development in treatment protocol of prosthetic and orthotic science using artificial intelligence helps in rehabilitating the persons with brachial plexus injury to regain his confidence and perform daily activities. Combination of advancement in surgical procedure along with artificially intelligent devices opens a new array to rehabilitate the person with brachial plexus injury.

Keywords: grasp, artificial intelligence, neural network, assistive technology, external powered device

1. Introduction

Brachial plexus injury (BPI) is one of the common and an unfortunate injury from the patient's perspective, which mostly results from high energy trauma to the neck and upper limbs. Patients with brachial plexus injuries clinically represent devastating injuries and complications with unpredictable outcomes. Stress on the clavicle and adjacent structures including the brachial plexus and subclavian vasa may lead to effectively crippling function in one or rarely both upper limbs. As clavicle is the strongest link in the shoulder area, sudden movements or stress due to trauma can result in the clavicle fracture. Then, all the tensile forces are transferred from the medulla to the neurovascular fibers and nerve roots, which can in turn lead to the upper limb muscle weakness innervated by nerve roots of C5, C6, C7, C8, and T1.

In adults, prevalence of brachial plexus injury shows 89% for male predominantly with a mean age of 29 years and median age of 25 years [1, 2]. Traumatic injuries, such as motorcycle collisions, have the majority in epidemiology of BPI, approximately 44–70% [3, 4]. The most common cause of BPI in children is obstetric brachial plexus palsy (OBPP), with a prevalence rate between 0.38 and 4.6 per 1000 live births [5–7]. Other possible causes for brachial plexus palsy may include iatrogenic injuries, such radiation therapy and as well as those that can occur during surgical and anesthesia procedures.

Patient loses his significant functional ability to perform activity of daily livings (ADL) as well as potential functions in his/her occupation. It is important that this valuable segment of our population should be functionally restored as early as possible to the best of our ability. With modern technology in hand and microsurgery, this is very much feasible provided that the patient is treated in time. There are also treatment techniques available for late clinical referrals, but early treatment brings up a huge difference to the eventual outcome.

The results of brachial plexus injury treatment have considerably improved with the introduction of advanced diagnostic modalities, microsurgical techniques, and magnification. Few years back it was considered a difficult or impossible task to restore a functioning limb in many of the patients with brachial plexus injuries, which just recently microsurgical techniques in neurolysis, nerve repair, nerve grafting, and nerve transfer have made it possible.

This article explains the various orthotic and prosthetic managements, current developments and trends for brachial plexus injuries based on a substantial survey of published peer-reviewed literature, and the insights gained by the author in treating several cases of brachial plexus injuries.

2. Clinical anatomy of brachial plexus complex

The brachial plexus is a supersystem network of nerve fibers that supplies the skin and musculature of the upper extremities. It begins in the root of the neck, passes through the axilla, and runs through the entire upper extremity, usually composed of five roots, three stems, six strands, and three bundles. The brachial plexus is divided into five parts—roots, trunks, divisions, cords, and branches. This complex network is formed by the anterior rami (divisions) of cervical spinal nerves from C5 to C8 and the first thoracic spinal nerve, T_1 (**Figure 1**). The roots of the brachial plexus converge to form three trunks at the back of the neck. A combination of C5 and C6 roots form superior trunk, middle trunk is continuation of C7, and inferior trunk is the combination of C8 and T1 roots. The trunks pass over laterally, crossing the posterior triangle of the neck. Each trunk divides into two branches within the posterior triangle of the neck or above or behind the clavicle. One of them moves anteriorly and the other posteriorly; thus, they are known as the anterior and posterior divisions.

Once both the divisions enter the axilla, they combine to form three cords, named by their positions with respect to the axillary artery. The cords give rise to the major branches of the brachial plexus which mainly control the sensory and motor functions of the upper limbs, shoulder, and chest. The lateral cord is formed by the anterior division of the superior trunk and the anterior division of the middle trunk, and the lateral root of median nerve, musculocutaneous nerve, and lateral pectoral nerve are the main nerve branches. The posterior cord is formed by the posterior division of the superior trunk, the posterior division of the middle trunk, and the posterior division of the inferior trunk, and the subscapular nerve, thoracodorsal nerve, axillary nerve, and radial nerve are the main nerve branches. The medial cord is formed by the anterior division of the inferior trunk, and the main nerve branches are the medial antebrachial cutaneous nerve, ulnar nerve, and medial root of median nerve.

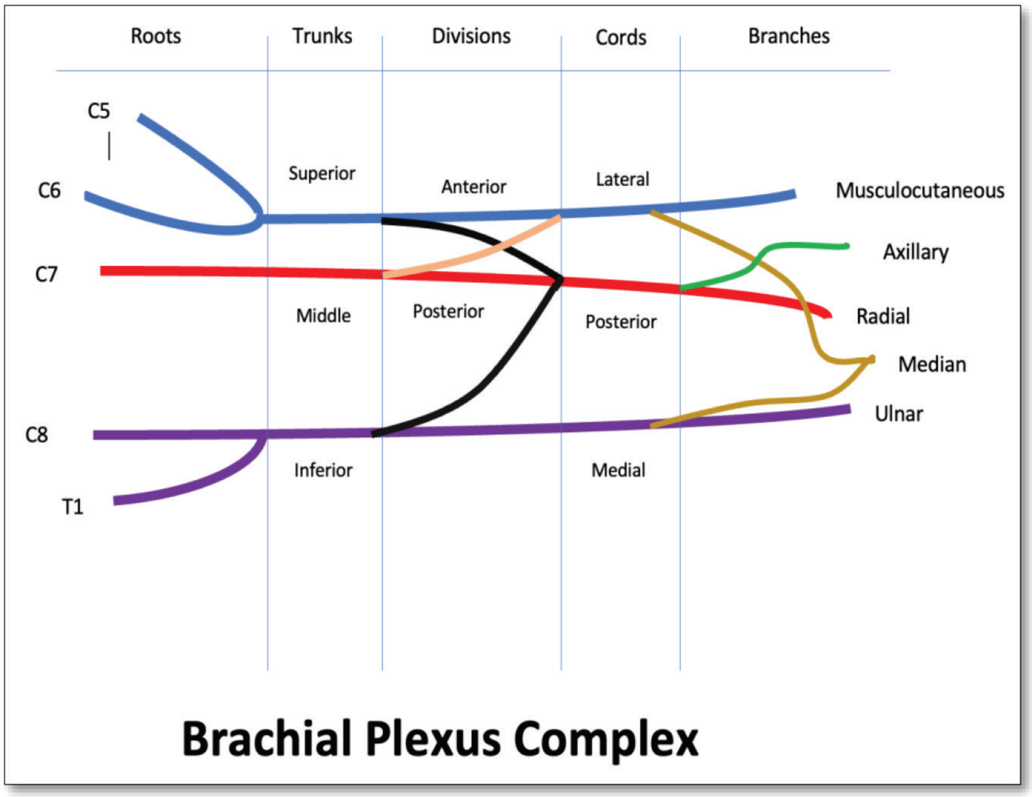

Figure 1.
Diagrammatic representation of course of the brachial plexus.

3. Clinical relevance of brachial plexus injury

Generally, BPI can be divided into partial (upper or lower) and complete. The damage of different nerve branches often leads to the dysfunction of corresponding corridor. The clinical representations of upper brachial plexus injury widely referred as Erb's palsy. The forearm is positioned in pronation due to the weakness of biceps brachii. The wrist is weakly flexed due to the weakened wrist extensors, while the wrist flexors are in normal tone. The major characteristics are lack of shoulder abduction, elbow flexion, and an internal and external rotation of the upper extremity, which is often termed as "waiter's tip deformity" [8]. Lower root of the brachial plexus (C8-T1) injury leads to claw hand deformity. Complete injury damages both sensory and motor functions of the limb.

3.1 Manifestations in nerve regeneration after brachial plexus injury

Complete avulsion of the nerve proximal to the dorsal root ganglion or complete avulsion of the nerve root from the spinal cord occurs, and it falls under preganglionic injuries. Injury to the nerve distal to the dorsal root ganglion within the trunk, division, cord, or terminal nerve branches is known as postganglionic injuries. Both preganglionic and postganglionic injury have different yet significant prognostic and therapeutic implications. Preganglionic injuries generally lead to complications such as complete loss of motor and sensation in the distribution of the involved root and denervation of the deep paraspinal muscles of the neck. In postganglionic injuries, i.e., distal to the spinal ganglia, the cell bodies are intact and have more favorable prognosis than is associated with preganglionic injuries. Developments of regenerative microenvironment around the injury, the reinnervation of nerve to target tissue, and axon regeneration are related to the repair process of BPI. At the distal end of the injury, the axons and myelin sheath degenerate and disintegrate into nerve debris. Autophagy reaction is produced by Schwann cells (SCs) followed by Wallerian degeneration at the end of the nerve involved. In the early stage of injury to clear degenerative myelin debris, Schwann cells assist macrophages and also plays a vital role in formation of basement membranes to promote growth and provide channels by secreting laminin, which can guide axons to grow rapidly in the right direction. The proliferating Schwann cells form a solid cell cord (band of Büngner) in the nerve basal lamina enclosed by the basement membrane. This band Büngner has a good guiding effect on the growth of nerve axons, and in addition it not only produces related molecules that promote axon regeneration, but also helps to separate molecules that inhibit regeneration in the endoneurial tube, by which the regeneration and repair of injured nerve can be accelerated [9–11].

Schwann cells, nerve axons, fibroblasts, etc., produce mainly three types of neurotrophic factors (NTFs), which bind with specific receptors on the surface of target cells [12]. In the regeneration and repair of injured brachial plexus, these NTFs play different roles. Neurotrophin, one of the NTF, includes nerve growth factor (NGF) and brain-derived neurotrophin factor (BDNF). NGF can promote the transduction of intracellular signal in damaged nerve, which is an important factor in the acceleration of the growth of axons and the recovery of nerve function. BDNF and its tyrosine kinase receptor B (TrkB) mRNA assist in restoration of neural pathways and enhance regeneration of axons and reconnection of injured muscles. Another NTF neurocytokinin includes ciliary neurotrophic factor (CNTF). Fibroblast growth factor (FGF) and other NTFs such as glial cell line-derived neurotrophic factor (GDNF), insulin-like growth factor (IGF) can enhance and proliferate the axons and Schwann cells of mature spinal cord [13]. Some previous studies have already explained that NTFs can improve regeneration of nerve cell and can accelerate motor nerve conduction velocity [11, 14]. The formation and regeneration of microenvironment is an important factor that not only affects the repair of brachial plexus injury, and in long-term objectives, it is also responsible for resurrection of motor and sensory functions in upper extremity.

4. History of orthotic and prosthetic managements in brachial plexus injury

BPI leads to weakness in upper extremity muscles, hyporeflexia and is commonly associated with upper limb pain. The general principles of upper extremity orthotic and prosthetic managements in BPI are to prevent shoulder joint pain prevent contractures, improve function, e.g., enable positioning of hand in space to allow two handed activities, improve cosmesis and body image, to support the weight of the upper limb, and thus ease the traction forces on the shoulder, and secondarily, such support may assist in edema control.

One of the key goals in rehabilitation and orthotic prescription after BPI is to support the shoulder to prevent subluxation, as impaired innervation to the shoulder girdle leads to inherent instability of the glenohumeral joint, combined with weakening of the shoulder girdle, which in turn causes glenohumeral subluxation. Treatment and prevention of shoulder pain and subluxation is also a common rehabilitative goal in brachial plexus injury patients. **Table 1** represents the orthotic and prosthetic management of brachial plexus injury patients depending on their level of injuries, motor deficits, and functional needs.

Level	Motor deficit	Functional need	Orthotic and prosthetic prescription
C5-C6	Shoulder abduction Shoulder flexion Elbow flexion Wrist extension	Shoulder support Prevent shoulder subluxation Elbow flexion	Wilmer carrying shoulder-elbow-wrist support orthosis, Aeroplane splint, Gunslinger splint, Steeper Stanmore flail arm orthosis, Humeral cuff
C5, C6, C7	Shoulder flexion Shoulder abduction Elbow flexion Elbow extension weakness Wrist extension Finger extension Thumb extension weakness	Shoulder support Prevent shoulder subluxation Elbow flexion Wrist support Finger extension Wrist support Finger extension 1st extension	Wilmer carrying orthosis with arm trough, Functional arm orthosis (FAO), Aeroplane splint, Gunslinger splint
C8, T1	Wrist flexors Finger flexors Thumb flexors Finger extensors Thumb extensors	Wrist stabilization Finger flexion Some amount of finger extension Intrinsics of hand	Static or dynamic wrist hand orthosis, Elbow or wrist driven, tenodesis splint, Knuckle bender splint
C5-T1	Entire ipsilateral upper limb May include scapular motion	Shoulder support Prevent shoulder subluxation Edema control Normal function	Slings, Hemi arm slings, Functional arm orthosis (FAO), Wilmer carrying orthosis with hand support

Table 1.
Orthotic and prosthetic management for BPI depending on the level of injury, motor deficits, and functional needs.

Management of C5, C6, C7 level of injury, a standard shoulder sling can be a simple orthotic aid, which is readily available to support the shoulder, but the concern is the potential development of elbow flexion and shoulder adduction or internal rotation contractures. Even with the return of motor function, the developed contracture may limit functional use of the limb. Other commercially available slings are Bobath sling, static shoulder–elbow sling, Roylan hemi arm sling and humeral cuff (Patterson Medical Holdings, Inc.), etc. Another option that can possibly reduce subluxation and maintain appropriate positioning of the flaccid upper extremity, particularly in patients who are ambulatory, is GivMohr Sling (GivMohr Corporation) [15]. Standard shoulder sling exerts additional upward force from the elbow joint to control shoulder subluxation. An upward force is transferred through the shoulder sling along the length of the forearm, wrist, and hand. The downward weight of the hand and distal forearm pushes the elbow and humerus upward and provides an efficient transmission of force by creating a fulcrum point at the level of the proximal forearm [16]. The shoulder cap fits snugly over the acromioclavicular joint region and applies the fulcrum to the proximal forearm from above, which is a better refinement of preventing shoulder subluxation and shoulder pain compared to slings and hemislings [2, 16, 17]. But the concern is unilaterally functional patients may have difficulty while donning and doffing, because it has more straps and adjustments. Newer design concepts such as Steeper Stanmore flail-arm orthosis have rectified this problem with fewer straps and an adjustable locking device at the elbow. The hemisling and the shoulder caps have certain differentiation in advantages such as hemislings and are commercially available at lower cost with ease of donning and doffing, whereas the shoulder caps have the advantages of greater stability and comfort with respect to hemislings.

Patients with C5-C6 injury clinically represent with weakness of the shoulder girdle musculature as well as the elbow joint flexion more often than the extension, while because of the relative weakness of the external rotators and abductors, shoulders are internally rotated or adducted. Shoulder internal rotation contractures are found to be the most common. Almost 50–70% of patients may be found with a complications of internal rotation contractures in obstetric brachial plexus palsy [18–20]. In later stages, weakness of the shoulder girdle may have the possibility to cause joint dysplasia over the period and increased glenohumeral instability and subluxation. The patient retains control of hand and wrist movements and some amount of elbow extension as of triceps, if the lower trunk or lower nerve roots (C7, C8, and T1) are preserved. These patients need support of the shoulder and elbow without impeding the wrist and hand movements [21].

Ratchet shoulder abduction orthotic (SAO) devices such as Wilmer carrying orthosis with shoulder-elbow-wrist support, or a Wilmer carrying elbow-wrist-hand orthosis, aero plane splints, gunslinger splints can be indicated, in which shoulder and elbow can be locked in different positions and can be placed in position either by the opposite arm or by leveraging it against a table or other object. A cable-powered device like shoulder-driven elbow-wrist-fingers tenodesis splint or even a myoelectric exoskeletal device, which can be functional by slide input controls by potentiometers, are also prescribed [21, 22]. A cable-controlled elbow functions very similar to control of elbow unit in above-elbow prosthesis by protraction and retraction of the contralateral shoulder. Allowing the elbow movement may lead to loss of control of the glenohumeral joint, and the shoulder may remain subluxed with the additional weight of the orthosis. Mobile arm supports can also be the options for individuals with brachial plexus injury.

C5-T1 injury or the complete brachial plexus injury causes a complete flail arm with both profound hypotonia and hyporeflexia. Orthotic prescription for flail arm is required for potential support and protection for the arm and providing some function to the arm. Essentially, orthoses that immobilize and protect the arm are Wilmer carrying orthosis, gunslinger splint, etc., which are composed of a shoulder support, elbow ratchet, forearm support, and distal trough that can accommodate functional devices. Extending the trough of the shoulder cap all the way to the fingertips also helps to control edema and provides protection to the weak upper extremity. Currently, orthotic management in brachial plexus injury is adding function to the weakened limb. A functional arm orthosis (FAO) can be interpreted to borrow the power from an intact trapezius muscle shrug or from the opposite arm.

Patients with C8-T1 nerve injury or the lower trunk of the brachial plexus injury (Klumpke's palsy) may have shoulder and elbow function preserved with loss of wrist and hand motor control. So, these patients often require orthoses such as the tenodesis splint or dynamic wrist hand orthosis with MCP assist to stabilize the wrist and restore grip and pinch functions rather supporting the shoulder and enhancing the function.

In most severe forms of brachial complex injuries, authors have suggested a more controversial yet functional approach of management that involves immediate prosthetic fitting followed by amputation of the affected extremity above or below the elbow. However, still it is been referred as a controversial approach as the amputation must take place soon after the initial injury to ensure compliance with the prosthesis. But the concern is that the amputation of involved limb is an irreversible procedure, and as we must conduct this early after the injury, the less conservative treatment time and opportunity is available for assessing for any possible neurologic recovery. Therefore, the decision regarding amputation must be made before adequate assessment of any possible recovery of motor and sensory function [23–25].

5. Recent trends in orthotic management of BPI

5.1 Neuromuscular electrical stimulation (NMES) in rehabilitative orthotic devices

NMES is often referred as muscle stimulation that uses an electrical current to produce muscle contractions for the purpose of restoring motor functions in individuals who have muscle weakness or paralysis. NMES creates an electrical field near motor axons of peripheral nerves that is of sufficient strength to depolarize the axonal membranes, and thus, it operates by depolarizing motor axons rather than muscle fibers directly, eliciting action potentials and, consequently, muscle contractions. Neuromuscular electrical stimulation is a modality that involves the application of electrodes connected to a device that provides electrical current to a partially or completely denervated muscle with the goal of promoting functional recovery. NMES has been used in the rehabilitation of multiple central neurological conditions, including stroke, cerebral palsy, traumatic brain injury, multiple sclerosis, and spinal cord injury, with demonstrable success [26]. There have been very less evidence for its effectiveness in peripheral nerve injury and central nervous system injuries. In a randomized study comprising patients with severe median nerve compression, the group treated with postoperative electrical stimulation demonstrated improvements in functional outcomes as compared to the control group [27]. According to Denise Justice et al. [26], NMES studies in the treatment of neonatal brachial plexus palsy did not report loss of motor function, there were reports of improvement in function, and thus, NMES in peripheral nerve therapy was considered reasonable. These results show that there is mixed evidence regarding NMES being associated with improvement in muscle strength, while it can be a vital modality for improving muscle tone [26]. NMES can be applied with surface electrodes on the skin over the targeted muscles or nerves. NMES stimulators range from being capable of delivering a range of a single channel of electrical current to delivering seven to eight independent channels of stimulation. NMES current waveforms are typically characterized by a hierarchy of monophasic or biphasic current pulses. The pulse wave frequency, amplitude, and width or duration of the pulses determine the strength of the muscle contractions elicited. Stimulators are equipped with pattern controllers that allow the patient or clinician to set or adjust some of these stimulation parameters like pulse width, pulse frequency, and the duration and coordination of muscle contractions. Many sophisticated commercially available NMES systems have controllers that receive real-time input from patients, which enables them to adjust the stimulation and elicit subsequent muscle contractions and movements produced. User interfaces with such controllers range from buttons and switches to external or implanted sensors or biopotential recording electrodes [28].

5.1.1 Theory of application of NMES stimulations in brachial plexus injury

Many studies suggest that, by inciting depolarization of cell membrane and opening voltage-gated calcium channels, electrical stimulation can increase intracellular Ca^{2+} transients level, and the increase of Ca^{2+} influx can improve the expression of nerve growth factor (NGF), brain-derived neurotrophin factor (BDNF), and its tyrosine kinase receptor B (TrkB) mRNA, which are the closest transducers for motor neuron regeneration [29], which can also be referred as creating artificial neural network (ANN). Electrical stimulation has also been found effective in promoting reconnection of axons and muscles, accelerate nerve conduction speed, enhance muscle fiber vitality, and followed by restore damaged nerve function. Many research studies show that the main objective of electrical stimulation in downstream pathways is inducing synthetic reactions, so that the use of low frequency stimulation can increase cyclic adenosine monophosphate (cAMP) level in nerve cells and then cAMP can be induced to activate phosphokinase A (PKA).As long as a short electrical stimulation can cause a series of closed loop reactions, it promotes the growth of dorsal root ganglion (DRG) by regulating cell growth-related proteins, cAMP response element binding protein (CREB), and cytoskeleton proteins [30], which in turn activate downstream pathways and increase the expression of BDNF. By inhibiting phosphodiesterase, cAMP can be enhanced and maintained at a certain level, and it elevates BDNF [31].

5.1.2 Patterns of stimulations in NMES stimulator devices

There are three categories of NMES available currently, i.e., cyclic NMES, EMG-triggered NMES, and proportionally controlled NMES. In cyclic NMES, electrodes are placed on the skin over muscle bellies that are targeted for activation. The wrist, finger, and thumb extensors are targeted for the activation of stimulation. A single pair of electrodes may be adequate to produce hand opening and wrist extension. In some patients, elbow extensors or shoulder muscles may also be targeted. Cyclic NMES is considered to be most simple, commercially available, and the most used NMES administering method [32, 33]. Some of the examples of commercially available cyclic NMES units are Myoplus 2 pro (NeuroTrac®), Intelect NMES (DJO Global, Inc.), etc. These units often have two channels. The intensity of stimulation can be adjusted and delivered from each channel to a level that produces comfortable muscle contractions and the desired movement, e.g., hand opening. Stimulation is delivered according to an on–off control pattern, with the timing of the cycle, the number of repetitions, and the maximum intensity of stimulation preset by a therapist. When the pulse stimulation begins, stimulation frequency and duration elicit repeated muscle contractions, therefore arm and hand movement happen, followed by relaxation duration. Cyclic NMES requires no input from the patient. The patient can simply relax his/her limb during the stimulation duration, and let the stimulator activate the muscles, and sometimes patients are also instructed to move the arm or hand in synchrony with the stimulation. Research studies related to cyclic NMES show regimens ranging from 1.5 to 2.5 hours per day for 6–12 weeks [33, 34].

5.1.3 Assistive stimulation control and task-practice training using NMES devices

As the patient is prompted to produce his/her own effort to prompt the movement, EMG-triggered NMES may be more effective in promoting neurologic changes leading to better recovery. Triggered NMES system, e.g., Neuromove, Zynex, etc., elicits repetitive muscle contractions through the EMG-triggered stimulators. As the EMG signal exceeds a preset threshold, the stimulator turns on, and a preset frequency of stimulation is delivered to the target muscle for a preset duration, which is known as stimulation width. After the stimulation turns off, the cycle repeats [35, 36]. NMES is effective when it is used to assist goal-oriented task practice may lead to better outcomes than might be achieved with NMES modalities like cyclic NMES or EMG-triggered NMES, which can be challenging to use in task practice because the timing of the stimulation pattern is preprogrammed [37]. Sensors worn on the body can provide alternative methods of triggering stimulation. A force sensitive resistor on the arm has been used to trigger NMES to the motor points of corresponding muscle when the patient achieves some threshold degree of joint movement while attempting to complete the task [38]. Switch-triggered NMES systems (e.g., NESS H200, Bioness, Inc.) use push buttons to trigger stimulation (**Figure 2**). The push buttons may be operated by a therapist or by the patient. Push buttons give the therapist or patient control of the initiation and duration of stimulation, which makes it more feasible to incorporate NMES into task practice [40, 41].

In proportionally controlled NMES stimulation such as Myoplus 2 pro, NeuroTrac® (**Figure 3**), the intensity of the NMES is not preset, but the patient can regulate intensity by a control strategy that translates his/her desired movement into stimulation intensities, which is being regulated in real time. Thus, proportionally controlled NMES can be differentiated from cyclic and triggered NMES methods.

5.2 Functional electrical stimulation (FES) in orthotic devices

Contralaterally controlled functional electric stimulation (CCFES) is one of the advance functional rehabilitation protocols that can be implemented to enhance the recovery of paretic limb after brachial plexus injury [34, 42]. It uses current pulse width from the contralateral side (non-paretic) upper limb to regulate the intensity of electrical stimulation delivered to the motor unit of the affected upper limb. CCFES treatment is a goal-oriented task practice which can either be in repetitive practice which is self-administered or therapist-guided. The current pulse width stimulation intensity delivered to the affected side is proportional to the degree of respective range of motion of the normal side. It was initially developed at the Cleveland Functional Electrical Stimulation (FES) Center and is a proportionally controlled NMES approach in which the intensity of stimulation to the paretic finger and thumb extensors is proportionally controlled by an instrumented glove worn on the opposite (contralateral) hand (**Figure 4**). CCFES device consists of an instrumented glove, stimulator, and surface electrodes. Up to seven monopolar channels of biphasic current can be delivered by the he stimulator. With the glove, the patient can control the degree of opening of the affected hand and can practice using it in task-oriented therapy. The stimulation intensity can be modulated and delivered as with input from surface electrode, so that each channel can be programmed individually. Also, the individual channel can be programmed automatically by interpreting cyclic stimulation. Pulse duration can be adjusted for specific stimulus channel, so that patterns of stimulation can be customized according to the change in stimulus intensity, which in turn is related either to the function of the input signal from instrumented glove or to the cyclic stimulation pattern. The patient can open their hands (Hand CCFES) or simultaneous reach with hand opening (Arm + Hand CCFES) repeatedly over a midline activities of daily living (ADL) exercise

Figure 2.
Switch triggered stimulation in NESS H200, Bioness, Inc. [39].

Figure 3.
Goal-oriented task practice training of BPI patient by NMES stimulation using Myoplus 2 pro, NeuroTrac$^{®}$.

session of selectable duration by prompting the sound and light ques. MATLAB R2022b can be used to program the stimulator. EMG signals can also be used from the impaired upper limb to deliver proportionally controlled NMES in accordance with the patient's motor intention. In proportionally controlled NMES, the approach capitalizes on the principle of intention-driven movement, linking the patient's motor commands to the stimulated movement and the resulting proprioceptive feedback to the brain.

This pattern of artificial reinstatement of the sensorimotor integration may have the possibilities to enhance Hebbian-type neuroplasticity (i.e., connections between neurons that are simultaneously active and are strengthened), which may

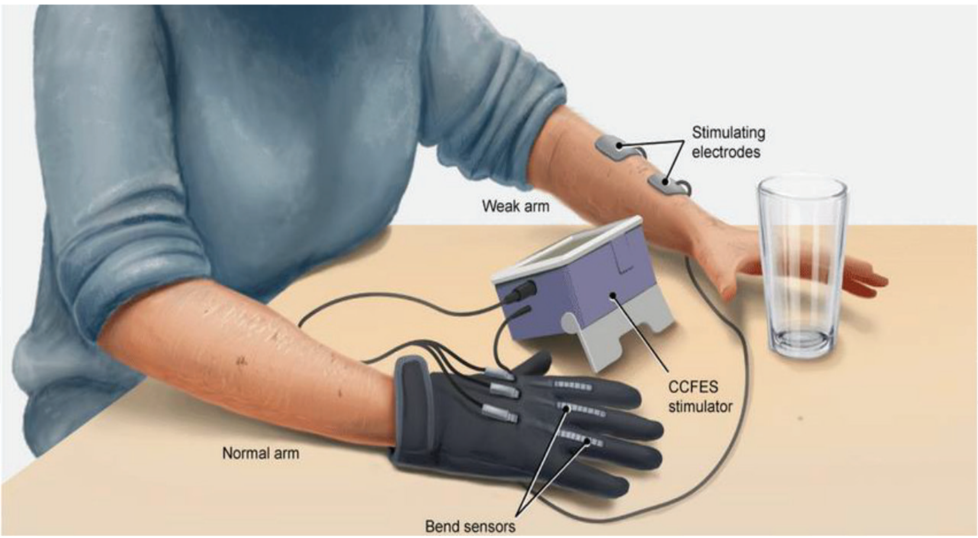

Figure 4.
Illustration of contralaterally controlled functional electrical stimulation (CCFES) [43].

lead to better motor recovery. Hence, proportionally controlled NMES may be more effective than other NMES stimulations [44]. The command hand glove generally consists of three bend sensors, which are placed on dorsal aspect of 2nd, 3rd, and 4th digits. These use pre-gelled surface electrodes to target small and large muscles in the forearm, hand, etc., which are commercially available in various sizes.

5.2.1 Pattern of stimulation in FES stimulator devices

Cyclic stimulation is generally given at the motor points of individual muscles for gaining the muscle tone and conduction by cyclic pattern involving interrupted galvanic current. Rehastim (Hasomed GmbH, Magdeburg, Germany) is a 8-channel stimulator may be used into the training environment with two bipolar, self-adhesive electrodes (diameter: 40 mm), and applied biphasic square pulse frequency 30 Hz to 50 Hz, pulse width ranging from 300 μs–500 μs. The stimulation of this integrated neuroprosthesis can be updated in a closed-loop, real-time iteration at 50 Hz–60 Hz via a controller area network/universal serial bus (CAN/USB) port using an algorithm. Whenever the brain–machine interface (BMI) classifier output will be positive, NMES can be applied for 5–7 s to the motor points of individual muscles at a joint during respective movement [45]. For example, in Erb's palsy, three fibers of deltoid muscle (anterior, lateral, and posterior) or its motor points. In elbow, stimulation is given to motor point of brachialis muscle and triceps muscle on the anterior aspect and posterior aspect, respectively, just above the elbow region. Thus, for wrist and fingers movements, stimulations are given at the motor points of the flexor and extension muscle groups. Hence, each motor point is stimulated from proximal to distal as one complete stimulation cycle. Each motor point may be stimulated for 10–15 contractions. This cyclic stimulation can be given from 4 to 6 weeks depending on the severity of the injury. As the muscle tone starts to improve, muscle strength also begins to recover, followed by improvement of the conduction. After muscle strength gains approximately 1 or 1+ grade alongside improvement in conduction, the stimulation is shifted from interrupted galvanic current to faradic current to stimulate the muscle in groups, which is otherwise known as faradism. It stimulates for a short duration through interrupted direct current with a pulse width ranging from 300 μs to 500 μs with a frequency of 50–100 Hz. Faradism produces tetanic contraction and relaxation of the muscle, and the pulse frequency and duration can be adjusted [46].

Implantable microstimulator or multichannel implantable pulse stimulation approaches may be recommended for brachial plexus injury patients who have been carefully screened for hypotonia. Emerging technology that uses implanted nerve cuff electrodes to deliver high-frequency stimulus waveforms to nerves may prove capable of generating nerve pulse. Adding such pulse stimulation to an NMES neuroprosthesis could conceivably improve its effect and widen its applicability. Implementing upper limb neuroprostheses in brachial plexus injured patients has been a major challenge over the years, while another major challenge is developing an intuitive method by which patients control stimulation to their affected arm and hand without interfering with the task being attempted. Patient should find neuroprosthesis is easier and more effective than any compensatory strategy already attempted before, and thus, it can be successful [47, 48].

5.3 Implementation of brain-machine interface (BMI) in hybrid neuroprosthesis exoskeleton

Armeo Spring, Hocoma, Volketswil, Switzerland is a commercially available 3D workspace rehabilitation exoskeleton for shoulder, elbow, and wrist joints. It comes with seven degrees of freedom to provide antigravity support for the paretic arm and to provide movement kinematics and grip force. Gravity compensation adjustment is also incorporated into the device, so that patients with severe impairments can perform task-oriented practice with a virtual augmentative environment. There are two springs that are incorporated into the device, by which the unweighing can be realized. The real-time sensor data may be used to display a three-dimensional multi-joint visualization of the user's arm and exoskeleton in virtual reality (**Figure 5**) [49].

To capture the angles of all arm joints and the grip force from a shared memory block, a file mapping communication may be used. The virtual arm software can be programmed in HMD (Kaiser XL50) and SPS framework. Skeletal meshes can be made up of a set of polygons designed to make up the surface of the Skeletal Mesh, VertexBone and VertexSkin engines, etc., or a hierarchy of interconnected bones and joint segments which can be used to animate the vertices of the polygons in the three-dimensional real-time visualization software. The 3D models, rigging, and animations are created in an external modeling and animation application (Unreal engine 4, 3DSMax, Maya, Softimage, etc.) and are then imported into skeletal mesh engines. The bone vertices of the meshed model may be modified according to the degree of freedoms the user can provide in online closed-loop feedback. This can be designed measuring the joint angles and grip forces of the device. The joint angles of the exoskeleton can be directly represented in virtual reality, whereas the grip forces can be augmented to feedback real-time hand function.

Prior to each session, patients must be instructed to perform a natural wrist movement during the assigned tasks aiming at maximum movements, respectively. For an example, the ROM of wrist and elbow movements are calculated as the sum of maximum extension and flexion and can be computed as the mean of each session. The three-dimensional visualization of the fingers and wrist in real-time virtual augmentation software should be applied during each task as implicit online feedback of the respective joint movement. Patient needs to be trained with two exoskeleton sessions: with and

Figure 5.
Integrated neuroprosthesis with a gravity-compensating, seven degree-of-freedom exoskeleton, Armeo Spring exoskleteon, Hocoma, and virtual environment feedback attached to the paretic arm [50].

without BMI-controlled NMES. Both the exoskeleton and the maximum pulse stimulation intensity (S_{max}) are calibrated individually. The exoskeleton is adjusted to provide required gravity compensation for every joint and unrestricted joint movements in three-dimensional space. The S_{max} for individual muscle or each muscle group is determined as the output current approaching the motor threshold but that is still perceived as comfortable. In brachial plexus injury, depending on the severity of upper limb impairment, prolonged supra-motor threshold stimulation may be perceived as painful and was therefore the stimulation intensity and is thus set according to patient's comfort level.

5.3.1 Electroencephalographic (EEG) signal acquisition

Since many years, any brain disorders can be easily diagnosed by visual inspection of EEG signals. In healthy adults, the amplitudes and frequencies of such signals change from one state to another of the human, such as simple situations like wakefulness and sleep. The characteristics and amplitudes of the waves also change in accordance with age. Five major brain waves have been distinguished into five bandpass by their different frequency ranges, from low to high frequencies, respectively, are called alpha (α), theta (θ), beta (β), delta (δ), and gamma (γ). In 1929, Berger introduced the alpha and beta waves. In 1938, Jasper and Andrews used the term "gamma" for the waves of above 30 Hz. The delta refers to all low frequency waves below the alpha range and the theta waves as those having frequencies within the range of 4–7.5 Hz [51]. A beta wave rhythm varies within the range of 14–26 Hz, while amplitude normally under 30 μV and is found in normal adults (**Figure 6**). Usual waking rhythm of the brain like active thinking, active attention, solving concrete problems, etc., is associated with beta rhythm, and when a person is in a panic state, the corresponding rhythm may be acquired. Mainly over the frontal and central regions of the brain, beta wave rhythm can be encountered. A central beta rhythm is related to the Rolandic alpha or sensory-motor rhythm (SMR) and can be influenced by motor activity or tactile stimulation [52]. The gamma rhythm, often referred as fast beta wave, has frequencies above 30–45 Hz. The gamma wave band has also been proved to be a good indication of event-related synchronization (ERS) of the brain, and the gamma wave has been considered to be a good indication [53].

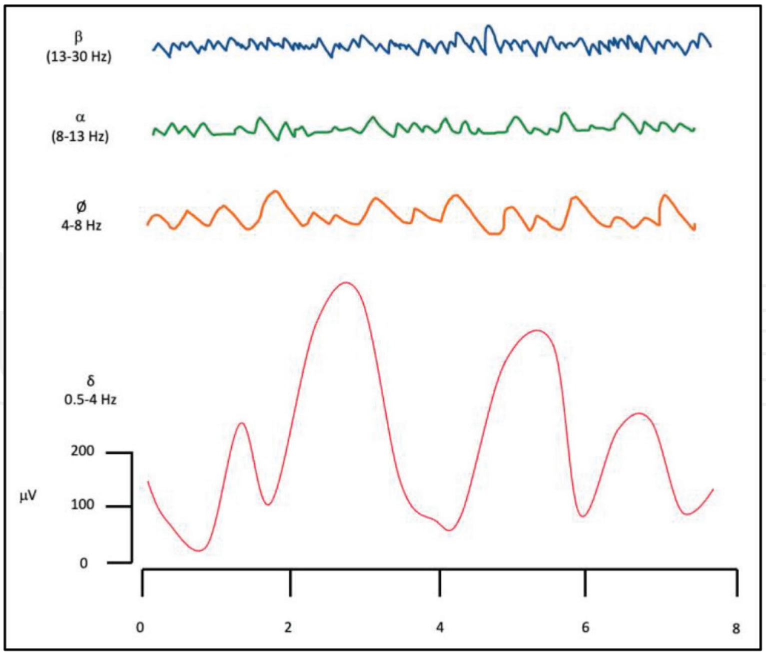

Figure 6.
Normal beta (β), alpha (α), theta (θ), and delta (δ) rhythms in order of high to low frequencies.

5.3.2 Classification and feature extraction of recorded EEG signals

Electroencephalographic (EEG) signals can be recorded with Cerebair (Nihon Kohden, Japan), Sienna Ultimate (EMS Biomedical, Austria), BrainAmp DC amplifiers, and anti-aliasing filter (BrainProducts, Munich, Germany) from approximately 21 Ag/AgCl scalp disposable gel-less and pre-gelled type electrodes over central and frontal regions of the brain. Each signal is sampled with up to 16 bits and is very popular in many commercially available EEG recording systems. Therefore, it is essential to store the archived signal masses in memory volumes. However, the memory size for archiving the EEG signals is often much lesser than that used for archiving radiological images.

A calculation procedure indicates that for a 1 hour recording from disposable electrodes (gel-less, and pre-gelled types) with an amplification rate of 1000 Hz in accordance with international 10–20 system.

$$N_E x \text{ seconds } x \text{ minutes } xfx\ b \approx \text{GB}. \tag{1}$$

GB = memory size, N_E = numbers of electrodes, f = frequency of amplification rate, b = bits.

Thus, a memory size of 21 × 60 × 60 × 1000 × 16 ≈ 1.20 Gbits ≈ 0.15 Gbyte is required. In today's technology of SSDs, hard drives, optical disks, CDs, and zip disks, there should be enough storage facilities for a large group of patients. EEG reading formats can easily be converted to spreadsheets that will be readable by most signal processing software packages such as MATLAB for different EEG machines.

Since electrode impedance often exceeds the frequency range of the physiological signals, ambient noise may compromise the recordings. Therefore, the high frequency noise must be avoided during this period so that all potential sources of electrical noise from the sampling environment can be removed and aliasing error can be avoided [54–59].

Since EMG may contaminate via compensatory movements with EEG, it may implicit artifacts that can compromise EEG-based BMI training [60]. In order to avoid or minimize these artifacts, the patients must be instructed to avoid blinking, chewing, and any head and body movements other than the joint movements. Also, the clinician should conduct visual inspection and feedback so that alternative BMI control can be prevented. After receiving the raw EEG signal, the data is filtered through bandpass, and DC notch filters and then spanning for visual artifact rejection are performed. Using EEGLAB-Toolbox (MATLAB Central, MathWorks), each session of event-related spectral perturbation (ERSP) of the feedback electrodes is calculated [49].

Surface electromyography (EMG) of the individual muscle or each muscle group is to be recorded with a Butterworth high bandpass filter and a sampling rate of 500–1000 Hz. An individual EMG threshold is set to calibrate the EMG classifier. The activity of the bipolarized EMG channels is measured and analyzed followed by discrimination between movement, and rest need to be performed.

The waveform length (λ)

$$\lambda(t_1) = P_t \left| x(t_o + 1) - x(t_o) \right| \tag{2}$$

$$\text{whereas } P_t = t_1 + t_o \tag{3}$$

$$t_o = t_1 - w + 1 \tag{4}$$

is calculated for each bipolarized EMG channel within a sliding window of w (ms). To correct for a delayed response of the subject to the cues, we calculated the cross- correlation of a vector L = $\lambda(t_1)$ containing the waveform length feature with a vector P = $P_{(t1)}$ which encodes the trial phase, where $P_{(t1)} = 1$ if t1 is part of the movement phase, otherwise $P_{(t1)} = 0$.

To improve the assignment of the waveform length to the movement or rest class (M_λ or R_λ, respectively), latency of the maximum of the cross-correlation sequence can be used as an offset. With a receiver operating characteristic (ROC) analysis, the threshold for the discrimination between the two distributions M_λ and R_λ is set. The criterion for threshold selection may be set as such that the false-positive rate must be lower than 5% to ensure high specificity of the classifier.

5.3.3 Desynchronization of BMI and NMES classifiers

As event-related desynchronization (ERD) is correlated to movement in the beta (β) band gets detected by EEG in the ipsilateral hemisphere of the brain (**Figure** 7). The brain-machine interface (BMI) environment stimulates EMG recordings of patient's joint during the movement [58, 61]. Once both the EMG and EEG classifier gives a positive output, NMES stimulation may be triggered. The same EMG filtering and feature extraction procedure can be used during the NMES session. Then, the samples of each data packet from these channels can be joined together to form a wavelength, which is to be computed, summed up for bipolar channels, and compared to the threshold for movement detection. As soon as it crosses the threshold, the EMG classifier will give a positive output.

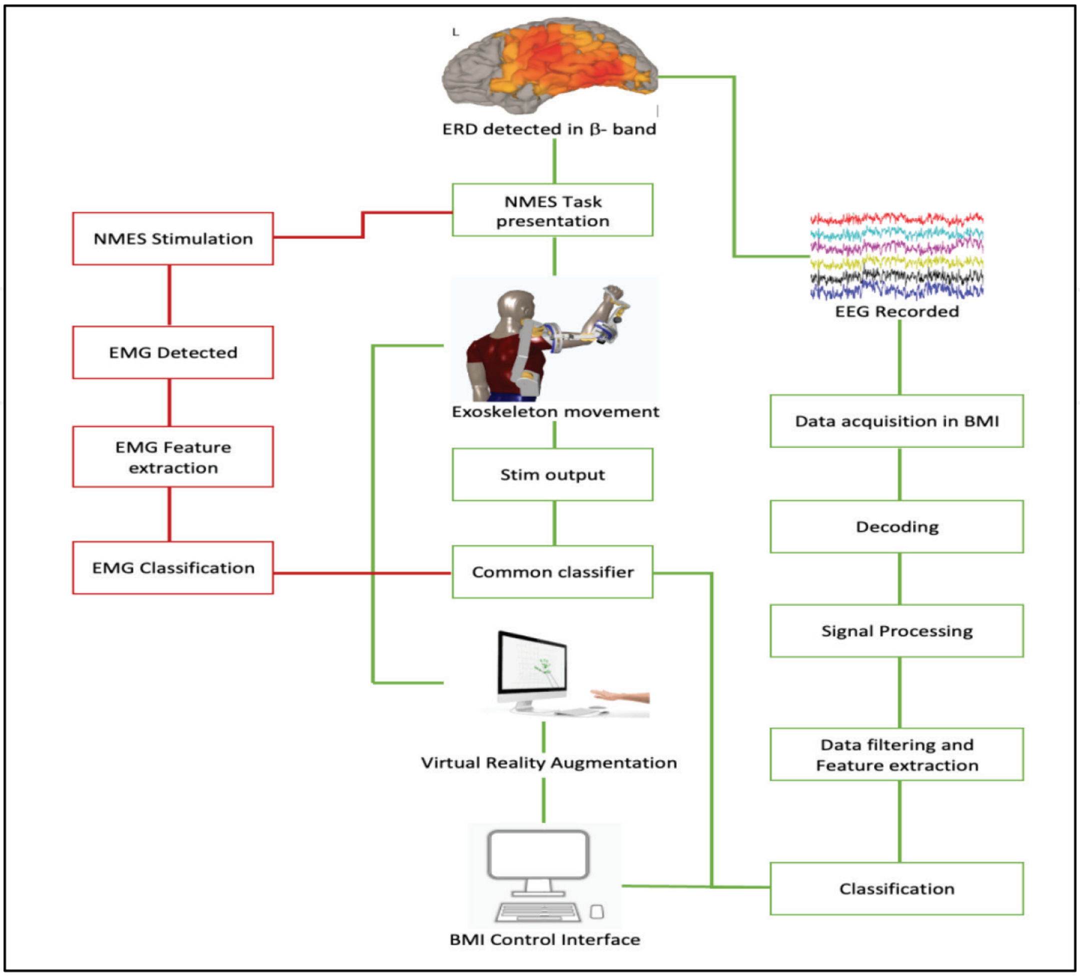

Figure 7.
Illustration of the flowchart of closed loop environment for hybrid brain-machine interface.

The sensitivity and specificity of the classifier of a linear discriminant analysis (LDA) are indicated by the true-positive rate (T_p) and the true-negative rate (T_n), respectively, while N is the total number of sample blocks in either during the movement or rest period. The positively and negatively classified sample blocks are ${}_pN$ and ${}_nN$, respectively.

$$\text{The false} - \text{positive rate}\left(F_p\right) = 1 - T_n.$$

TPR and TNR are calculated by

$$T_p = \frac{pNm}{Nm} \tag{5}$$

$$T_n = \frac{pNr}{Nr} \tag{6}$$

For the different classifier modalities, i.e., EEG, EMG, and hybrid EEG/EMG, the classification accuracy (X) of a BMI system is computed by

$$\mathrm{X} = \left(\frac{Tp + Tn}{2}\right) x\,100 \tag{7}$$

The correct response rate (C_R) is calculated by the ratio between the number of BMI-controlled NMES assistance (N_{NMES}) and the number of trials (N_t).

$$\mathrm{CR} = \frac{Nnmes}{Nt}\,\mathrm{x}\,100 \tag{8}$$

The feasibility of integrating a hybrid BMI approach based on EEG/EMG into an integrated neuroprosthesis exoskeleton followed by neurofeedback training by stimulating NMES involving virtual environment increases the stability of classification and data extraction and can be expected that using BMI + NMES with neuroprosthesis exoskeleton can be more effective on ROM and ERD than the implementation of exoskeleton alone [62].

6. Recent trends in prosthetic management of BPI

6.1 Surface electromyographic (sEMG) virtual reality augmentative biofeedback in prosthetic (bionic) hand reconstruction

Hand reconstruction has seen many new approaches to replace the non-functioning plexus limb. The bionic hand/myoelectric/hybrid prosthetic hand uses the myoelectric signal from the electrical voltage generated during muscle contraction to control some movement. In patients with brachial plexus injury, this type of prosthesis uses the rest of the human body's neuromuscular system to control flexion/extension of the elbow, supination/pronation of forearm (rotation), or inhibiting functional grasps [2].

Bionic reconstruction can be recommended for patients with failed surgical treatment alternatives (i.e., nerve repair, nerve transfers, and secondary reconstructions resulting in futile upper limb function). Patients with simultaneous central nervous system injury, unstable fractures of the affected limb, untreated or resilient mental health problems, lack of compliance and commitment to adhere to a long-lasting rehabilitation program cannot be adequate candidates for a biofeedback training in bionic hand reconstruction. Tinel signs are suggested to be eliminated along the neural axis of the major peripheral nerves indicating the presence of viable axons suitable for nerve transfer surgery. Multidisciplinary team consisting of experienced prosthetists, reconstructive surgeons, orthopedic surgeons, physiatrists, psychologists, and physiotherapists should be formed for the assessment of the patients whether they are fit into the reconstruction procedure and explain to the patient that the functionality of a myoelectric prosthesis. Other interventions, such as psychological support, posture training, and/or strengthening of the remaining muscles, are also indicated [25].

Surface electromyographic signals (sEMG) electrodes are generally used on the exact skin position, where muscle contraction can be palpated with the finger, e.g., 5 cm distal to the elbow joint on the dorsal extensor compartment when the patient is asked to think of extending his/her wrist and fingers. While the sEMG electrode is moved to the volar aspect of the forearm, placing it on the pronator teres muscle, ask the patient to attempt pronating his/her forearm. Patient's movements can be assessed and evaluated while the signal being observed on the computer screen. When the patient thinks of this movement, the amplitude repeatedly increases [63]. In some cases, sEMG signals are not found. In these cases, nerve and muscle transfer need to be performed to establish new EMG signal sites, which delay signal training for 6–9 months. At least two separate EMG signal sites are needed for dexterous control of prosthetic hand.

As soon as two or more EMG signals have been identified, sEMG-guided signal training should be given to patient to get acquainted with adjustment of the voltage gain of each signal independently to achieve a similar signal amplitude threshold for all signals during training, which will make signal separation and comprehension easier during the training of the patient. But during training phase relaxation should be allowed as muscle strength may decrease faster in patients with complex nerve injuries and faint myoactivity. Depending on the number of available EMG signals and the degrees of freedom of the bionic hand, it is necessary to use methods for switching between these degrees of freedom through pattern recognition software. One frequently used method of switching between degrees of freedom is via the simultaneous contraction of two muscles, also known as co-contraction.

Hybrid hand fitting and prosthetic training are needed to be given with individually tailored socket onto or below the functionless plexus hand (**Figure 8**). Strength training for elbow flexors and shoulder muscles should be performed, if co-activation of the muscles used for prosthetic control is observed while lifting the arm. Simple grasping tasks, such as picking up manipulating small objects, boxes, signal independency should be improved through strength training, simple tasks of daily living, and co-activation of signal amplitude training. As the patient must lift the weight of his/her own hand in addition to the hybrid prosthetic hand, the device might feel rather heavy.

It should be noted that many tasks might be restricted since the paralyzed hand gets in the way and phase relaxation should be allowed in-between. Direct visualization of this muscle activity is vital for patient as it allows him/her to mentally grasp the pattern of myoelectric hand control and follow the training progress more consciously.

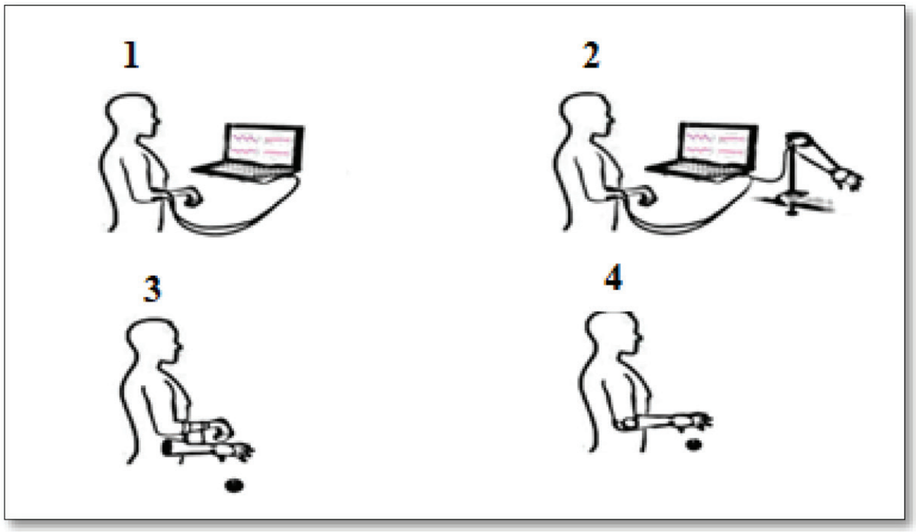

Figure 8.
(1) To identify the highest EMG amplitude over a specific target muscle, several motor commands may be attempted with virtual augmentation, and different signal positions can also be compared. (2) The EMG activity in a patient's arm is directly translated into prosthetic function after using a tabletop prosthesis. (3) Patient can visualize and embrace the use of future prosthetic hand, after the fitting and training with a hybrid prosthetic hand. (4) EMG signals can be trained and optimized either with sEMG biofeedback or with the prosthetic hand itself, after prosthetic reconstruction [64].

6.1.1 Elective amputation of affected limb and prosthetic hand replacement

Depending on the availability of site of the various EMG signals, the level of amputation (transradial, transhumeral, or, in rare cases, glenohumeral) should be precisely planned by the multidisciplinary team consisting of the patient's psychologist, prosthetist, physiotherapist, and the surgeon responsible for the amputation so that patient's expectations can be familiarized with everyone and unresolved questions regarding the planned amputation and clear communication regarding decision of amputation can be made; otherwise, it will result in irreversible and life-altering surgery. Elective amputation is to be performed as described previously followed by post-operative wound healing, and patient should be trained adjacent joints for improved upper limb mobility. The EMG signal training and selection of EMG electrodes' site should be followed up after 4–6 weeks of post-operative wound healing. These electrode positions and motor commands might differ slightly from the ones found before amputation. The prosthetist must design the prosthesis which may consist of prosthetic socket, hook/hand, silicone liner, and sEMG electrodes depending on the sites of EMG signals and co-contraction of muscles. Then, the procedure must follow post-prosthetic training from open/close the prosthetic hand without any co-contraction with weight of the prosthetic device being supported, followed by prosthetic movements on different arm positions such as the elbow flexion or extension. Patient should be trained for simple grasping tasks simultaneously with activities of daily living training staring with rather simple tasks as opening a door to slowly adding complexity and tasks that the patient considers relevant for his/her specific life adaptation or function.

7. Conclusion

Brachial plexus injuries have shown an upward trend in recent years with the frequent occurrence of accidental injuries such as car accidents, fall from heights, and external force pulling. Over the years it is been an absolute challenge for the prosthetists and orthotists to facilitate functions in BPI patients. Advancement in the field of brain–machine interface, artificial intelligence and replication of anatomical movements with prosthetic arm have emerged as excellent and effective treatment protocols for BPI. The interpretation of BMI with neuromuscular stimulation with exoskeleton assistive device has shown impressive effects on ROM, cortical modulation, and pain. In the future, novel restorative framework may be implemented while retaining their voluntary effort in BMI-NMES training goal-oriented training sessions. Additionally, due to the reduced neuromuscular interface in BPI affected patients, it is not clear whether currently commercially available prosthetic arm systems designed for otherwise healthy amputees can significantly enhance the prosthetic function in patients with brachial plexus injury, and hence, novel technologies for prosthetic control may be explored in future. Future studies should evaluate the applicability and benefits of the listed novel technologies as controlled trials with higher patient numbers will demonstrate the positive effects of the current rehabilitation protocols of patients with severe brachial plexus injuries.

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Conflict of interest

The authors declare no conflict of interest.

Nomenclature

BPI	brachial plexus injury
OBPP	obstetric brachial plexus palsy
ADL	activities of daily living
SCs	Schwann cells
NTF	neurotrophic factors
NGF	nerve growth factor
BDNF	brain-derived neurotrophin factor
TrkB	tyrosine kinase receptors
mRNA	messenger ribonucleic acid
CNTF	ciliary neurotrophic factor
FGF	fibroblast growth factor
GDNF	glial cell line-derived neurotrophic factor
IGF	insulin-like growth factor
LMN	lower motor neuron
SAO	shoulder abduction orthosis
FAO	functional arm orthosis
NMES	neuromuscular electrical stimulation
ANN	artificial neural network
cAMP	cyclic adenosine monophosphate
PKA	protein kinase A
DRG	dorsal root ganglion
CREB	cyclic-AMP response binding protein
EMG	electromyographic
CCFES	contralaterally controlled functional electrical stimulation
FES	functional electrical stimulation
BMI	brain-machine interface
EEG	electroencephalogram
ERD	event-related desynchronization
sEMG	surface electromyographic

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