HHS Public Access

Author manuscript

Expert Rev Med Devices. Author manuscript; available in PMC 2017 May 01.

Published in final edited form as:

Expert Rev Med Devices. 2016 May ; 13(5): 445–454. doi:10.1080/17434440.2016.1174572.

A review of the progression and future implications of brain-computer interface therapies for restoration of distal upper extremity motor function after stroke

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Abstract

Stroke is a leading cause of acquired disability resulting in distal upper extremity functional motor impairment. Stroke mortality rates continue to decline with advances in healthcare and medical technology. This has led to an increased demand for advanced, personalized rehabilitation. Survivors often experience some level of spontaneous recovery shortly after their stroke event; yet reach a functional plateau after which there is exiguous motor recovery. Nevertheless, studies have demonstrated the potential for recovery beyond this plateau. Non-traditional neurorehabilitation techniques, such as those incorporating the brain-computer interface (BCI), are being investigated for rehabilitation. BCIs may offer a gateway to the brain's plasticity and revolutionize how humans interact with the world. Non-invasive BCIs work by closing the proprioceptive feedback loop with real-time, multi-sensory feedback allowing for volitional modulation of brain signals to assist hand function. BCI technology potentially promotes neuroplasticity and Hebbian-based motor recovery by rewarding cortical activity associated with sensory-motor rhythms through use with a variety of self-guided and assistive modalities.

Stroke background

Stroke, resulting from the cessation of blood flow to cortex as a result of clotting (ischemic stroke) or bleeding (hemorrhagic stroke), is a serious medical emergency that can result in death or substantial neural damage and remains a leading contributor to acquired disability in the United States [1–3]. More than 795,000 individuals are affected by stroke annually [1] and approximately 610,000 [2] are first attacks. The total cost of stroke to the United States is estimated at $34 billion (USD) per year [2]. Despite technological advancements in health care and increased preventative measures such as education and public emphasis on healthy living practices, the incidence of stroke is anticipated to rise annually, increasing by 20% as

Declaration of interest

V. Prabhakaran and J. Williams have a pending US patent on the closedloop neurofeedback used for BCI-facilitated intervention, application number 12/715090. The patent was filed jointly by both V. Prabhakaran and J. 685 Williams. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

early as 2030 [1]. Demographic factors will likely contribute to this trend with an increasing elderly population in America [4]. However, stroke rates have declined significantly in persons 60 years and older, but largely persist in adults aged 45–59 years of age [2]. Mild-to-severe physical, cognitive, and affective impairments are common consequences of stroke insult, and more than half of stroke survivors experience some level of lasting hemiparesis or hemiplegia [5,6]. To meet this increasing public health challenge, it is imperative that effective rehabilitations and treatment methodologies are developed to address each stage of post stroke recovery: chronic and nonchronic (acute and subacute), and adapted to each level of severity of impairment: mild, moderate, and severe.

Stroke often results in a multiplex of motor, sensory, cognitive, and other impairments resulting from damage to neural tissues. Therefore, a successful rehabilitation therapy must increase functional capacities by promoting gradual adaptation of the brain’s remaining neuronal connections [7]. Effective rehabilitation and treatment methodologies would aim to increase the quality of life for individuals after stroke. Brain–computer interface (BCI) therapy offers a unique, multimodal, and multisensory platform for rehabilitative therapy after stroke and will thus be the focus of this review.

BCI principles

The human brain is largely accepted to be a plastic, appetitive, hedonistically driven feedback and feedforward circuit, especially susceptible to punishment or reinforcement and scheduled reward. Even though stroke survivors often present with damaged cortex or disrupted motor connection integrity, noninvasive electroencephalogram (EEG)-based BCIs are still capable of detecting significant and reproducible change.

Potentially relying on the ability of residual motor neurons to fire and facilitate device control, BCIs help to train persisting cortical connections to execute motor output of the hand [4,7,8].

BCI therapies take advantage of the brain’s ability to associate novel and independent stimuli and the goal-directed nature of motor execution to create an environment in which motor skills can be trained, performed, and reinforced. Learning results from a change in behavior dependent on punishing or rewarding experiences. BCIs capitalize on the brain’s natural instinct to discern adaptive from maladaptive, or unsuccessful, strategies over time [7,9,10], due to the scheduled reinforcement provided by the BCI task.

EEG-based BCIs function by establishing a closed-loop neural interface. A BCI uses raw functional cortical activity recorded by the EEG and translates it into a classified device command designed to circumvent or aid neuromuscular efferents potentially compromised by stroke [4]. Signal input is amplified and processed by a regression model [11–15] that extracts particular amplitude changes or features and accounts for signal noise. Specific features of the signal recorded from the subject’s scalp are selected against this noise, and information from the input data is selected and classified using an algorithm and parameters specified in the programming of the BCI device. With this real-time processing, the reduced representation of brain activity is effectively translated into an output or feedback modality, often one that allows a desired task to be performed more easily. EEG electrodes placed over the sensorimotor regions provide the most localized and reliable functional cortical activation changes relevant to the hand's motor function and are most often selected to control the external device. When considering BCI use with additional modalities, lesion location and integrity of remaining neural pathways may limit the potential for normal function as well as the potential for recovery.

EEG-based BCI is one of the most studied and popular BCI systems currently on the market. EEG-based BCI is most commonly used because it is cost-effective, noninvasive, portable, and has shown to be effective in improving motor function post-stroke [16,17].

Multiple studies have observed significant increases in the Fugl-Meyer Assessment (FMA) of Motor Recovery after Stroke and the Action Research Arm Test (ARAT) following EEG-based BCI therapy [11,18,19]. Treatment time in these studies varied greatly, suggesting that a minimal amount of EEG-BCI could create noticeable results in participants.

While EEG-BCI appears to create noticeable improvements in upper extremity (UE) motor function in participants, learned nonuse is a phenomena which presents in stroke patients that offers an example of how environmental conditions might limit or allow for motor recovery. It is plausible that learning to associate movement intention with the successful completion of a BCI task or behavioral output is a possible means for recruitment of vestigial neuronal pathways preserved after insult or disease. Such pathways are very small remnants of neuronal pathways that were once much larger and are the compromised neurological and neuroanatomical profiles of typical BCI users that may exist following the neurological trauma which resulted in the user's distal motor impairment. The possible recruitment of these vestigial pathways has the potential for the restoration of functional motor capacities, selection of letters from an array [2,20], or movement of a virtual cursor [7,12,21–26].

Furthermore, BCIs provide real-time feedback to the user and reward consistent production of neural features concordant with hand motor function. Therefore, apparent changes in functional cortical activation patterns may persist after therapy when attempting tasks similar to those trained with BCI therapy [7,11,27,28]. This theoretical knowledge supports the possibility of inducing lasting brain changes through BCI system and regimen. The necessary functional connectivity changes induced in stroke patients with lasting recovery of hemiparesis remain unclear, though mechanisms and strategies have been proposed [4].

Learning mechanisms

Therapies that incorporate BCI devices can be explained by conventional learning theories and replication of the BCI-driven motor learning outcomes observed in the healthy brain [7,12,29]. Reinforcement of motor behaviors is a key mechanism evident in the training and use of BCI therapies. Simple Pavlovian conditioning, or learning a new behavior through association and reinforcement, is a primary mechanism for developing associations and expectations common to us as humans. This Pavlovian conditioning allows a BCI user to fully integrate themselves with the neural interface. The basic theoretical design of BCI paradigms operate on the principle that targeted functional cortical activation of the motor areas should result in task completion or facilitated motor output, and insufficient activation should not produce any significant change in the BCI's behavior. Sufficient and targeted functional cortical activation is programmed to generate a successful manipulation of the BCI paradigm and activation of an assistive or augmentative device. The intrinsic reward of success is expected to guide motivation and behavior, the same way a developing brain might learn to interact with a novel environment to manipulate or engage with what is contained within that environment. Furthermore, motivation is important for motor reeducation as it assists in the recruitment of functional and residual neural pathways.

Pairing a stimulus with reinforcement or punishment is integral to human learning. The most efficient known mechanism to facilitate such learning is persistent and repeated transmission between pre- and postsynaptic cells. 'BC I-induced Hebbian neural recovery' [4,19,24,30] posits that the amount of reinforcement and the timing or schedule of reinforcement can significantly impact the efficiency and specificity of learning [31]. This basic mechanism of synaptic plasticity can be assumed to operate in stroke afflicted brains similar to the way it operates in the healthy brain [32]. In fact, neuroimaging studies using functional magnetic resonance imaging (fMRI) have shown increased cortical activation in areas damaged by stroke following BCI therapy and training [4,7,12,31,33]. Specifically, Hebbian learning may facilitate rehabilitation in stroke survivors by retraining or recreating synaptic connections necessary for the functional cortical activity essential for smooth and controlled motor output [4,7,12,19,24,30,31,33,34]. This mechanism may offer predictive indications about the relative likelihood of extinction or retention of the newly learned behavior [16,27,31,33–36]. Because motor output is cued by the BCI paradigm, facilitative therapy can be administered as soon as the necessary cortical activity is recognized by the BCI classifier.

Proprioceptive feedback and stimulation are associated with eliciting UE motor and hand function. It is understood that the reward of these 'targeted activations' acts to improve the likelihood of functional cortical activation, BCI task completion, and subsequent reinforcement provided by the task's parameters. Presumably, even in trials where little or no motion is realized or facilitated, individuals might experience recovery of functional cortical activity or augmentation of existing functionality, attributable to BCI system therapies. If a reward does not present itself immediately (i.e. hitting the virtual target), the participant may still experience a positive effect because of the sensory input to their hand. This rehabilitation regimen serves the purpose of real-time reinforcement of satisfactory cortical oscillations for motor output and assisted completion of a rehabilitative task to expedite and focus the user's motor learning as a means of maximizing the therapeutic and rehabilitative effect of the therapy session.

The better a user's movement intention is paired with assistive therapy, as executed by the BCI, the more likely cortical plasticity changes will occur, according to the Hebbian, 'fire together, wire together' rule [4]. As stated, this is particularly evident in BCI-based therapies incorporating functional electrical stimulation (FES) or other modalities for rehabilitation of motor function. When a feature signal is detected over the sensorimotor region of the cortex, stimulation of the distal hand muscles facilitates physical muscle contraction [12,24,37–40].

The appropriate moment for administration of facilitative therapy can be inferred by the BCI and administered in an iterative process because motor output is cued by the user's direct neural input to the BCI paradigm. Pairing of stimulation with activation, as inferred by the BCI, acts to close the feedback loop of a normal motor program. A normal motor program includes planning of motor intent, initiating movement, monitoring progress, and ending with the recognition of successful execution. As indicated by the literature reviewed herein, such targeted paradigms result in recovery when administered to patients presenting with hemiparesis [19,24,30].

BCI technology for rehabilitation

BCI technology is well suited for neural rehabilitation post stroke as it utilizes the user's direct neural input for the purpose of manipulating a peripheral component, such as a user's hand. Similar to the way the central nervous system operates the hand through physiological circuitry of the peripheral nervous system, the BCI executes similar actions via a device command. Noninvasive 'hijacking' of the brain's residual functional connections by a BCI may be used to support the recovery of functional capacities in the brain such as voluntary motor function through goal-directed practice and training. Such connections have the potential to increase voluntary motor function, as BCI invokes the same neural mechanisms that control volitional movement of a hand.

By encouraging motor-related functional cortical activity for the completion of a defined rehabilitation task, BCIs invoke the same neural mechanisms that control volitional movement of a hand. Utilizing BCI to mediate the user's intention to move their hand and subsequent output acts to close the neural feedback loop that is potentially compromised after the stroke insult. BCI-mediated therapy can recruit the brain's natural explicit and procedural learning mechanisms along with memory mechanisms to enhance functional capacity of a hand. BCIs can be used to train a patient to maximize the potential recovery of functional motor movement in their paretic hand.

BCI can be coadministered with established interventions or paired with more novel, research-based, home-written, or home-brewed tasks. BCI therapies can incorporate various therapeutic interventions in conjunction with traditional EEG-based BCIs or as adjuvants including: virtual reality [20,22,28,35], constraint-induced movement [9,11,41,42], robot-assisted movement therapy [8,30,43–45], and FES [5,12,24,39]. BCI therapy tasks are designed to recruit multiple sensory systems, such as visual and tactile. For example, the combination of a visual display along with the tongue display unit (TDU) provides tactile and visual input, making it an immersive multisensory intervention [46]. They provide an environment that reinforces successful motor intention and output by priming or cueing a motor intention, which encourages formation and execution of a motor plan. Implementing relevant behavioral outcome assessments, such as ARAT, 9-Hole Peg Test, FMA, and others, can establish the efficacy of BCI therapies on functional outcomes and quality of life [7,22,27]. Additionally, future studies utilizing pre- and post-therapy functional neuroimaging scans, fMRI and DTI for example, are ideal for a more comprehensive understanding of the cortical plasticity mechanisms by which BCI therapies affect change in recovering stroke patients. Neuroimaging measures are principal for distinguishing post stroke changes, such as those in functional activation and connectivity, gray matter and white matter structural integrity, and perfusion. In this review, various BCI treatment modalities are considered and compared with respect to restoration of UE motor impairment as a result of stroke.

Efficacy in stroke rehab

Various studies have demonstrated clinical efficacy and support for use of BCI in stroke rehabilitation (see Table 1). Early clinical BCI studies showed evidence for the feasibility and potential efficacy of BCI combined with FES and motor imagery (MI)-based BCI in combination with physiotherapy and robotic orthoses for motor recovery post stroke [22,38,43,44,47,48]. Because BCIs using FES and other modalities close the neural feedback loop, proper neural signals can be reinforced through the assisted execution of the user's motor plan. Recent studies have found similar outcomes regarding BCI effectiveness as the earlier BCI studies. The effectiveness of BCI-mediated interventions was reviewed as a progression from self-guided movement (MI-based BCI) to assisted movement (BCI-FES and BCI with orthoses).

MI utilizes self-guided movement (i.e. the user's imagination) of their paretic limb. MI has yielded promising results when used in conjunction with BCI. MI-based BCIs act to facilitate rehabilitation of UE motor function through the pairing of MI with completion of a simple motor task [13,22]. In many BCI therapies, MI-based BCI is used as a training condition or as a means for setting up control signals and classifiers for subsequent therapy conditions or administrations [10,16,17,32,38,48]. A review by Teo and Chew suggests that combining MI with BCI is a feasible intervention for improving hand motor function in the post stroke population, particularly with those in the chronic phase of stroke with mild-to-moderate severity [49].

While recent evidence supports the potential efficacy of MI based BCI in use with mild-to-moderate stroke for distal UE motor function, there are mixed findings on the effectiveness of MI combined with BCI for improving distal UE motor function in individuals with severe stroke, when used in solidarity. It is suggested that those with severe stroke may need more assistance to produce functional UE movement. A recent study by Ang et al. examined the efficacy of a MI-BCI system combined with a Haptic-Knob robotic hand interface (BCI-HK) in restoring UE motor function for individuals with chronic stroke and moderate to severe UE impairment. The outcomes indicated significant motor function gains in FMA of Motor Recovery after Stroke (FMMA) scores for both the proximal and distal UE, suggesting BCI-HK therapy is effective for improving UE motor impairment in individuals with chronic stroke when combined with therapist-assisted UE mobilization [50]. In addition, Ang et al. examined the efficacy of a MI-BCI system combined with shoulder–elbow robotic feedback (BCI-Manus) in restoring UE motor function for individuals with chronic stroke. The findings indicated significant motor function gains in FMMA scores, suggesting BCI-Manus therapy is effective for improving UE motor impairment in individuals with severe, chronic stroke [8]. Though this study was specific to proximal UE rehabilitation, systems for robotically guided distal UE movement may be similarly effective for severe stroke distal UE rehabilitation.

An earlier study by Mihara et al. found greater functional gains on the hand/finger subscale of the FMA following six sessions of mental practice with near-infrared spectroscopy (NIRS)-mediated MI of the distal UE in addition to standard rehabilitation. A significant effect of neurofeedback was also found in those severely impaired, suggesting MI plus NIRS could be useful for a wide variety of stroke impairment [51]. A study by Naseer and Hong found enhanced performance of MI wrist classifiers in developing a BCI, demonstrating the feasibility of a functional NIRS (fNIRS)-based BCI [52]. These studies suggest that fNIRS-mediated MI-BCI therapies in adjuvant to standard rehabilitation may be more effective in addressing severe distal UE motor impairment than MI-based BCI alone.

In addition to self-guided movement, BCI can be paired with assistive movement such as FES and orthoses. FES utilizes real-time feedback of BCI signal input to selectively administer therapeutic feedback responses only when the correct brain signals are detected [7,12,24,39,40,53,54]. The FES is cued by the BCI in response to its recognition of classified cortical activation features [7,24,39]. Further evidence for the effectiveness of BCI-FES in improving distal UE motor function has emerged recently. Biasiucci et al. found improvements in finger extension in the FMA after 10 sessions of FES –controlled BCI for individuals in the chronic phase of stroke [39]. Another study using FES -controlled BCI along with tongue stimulation found clinically significant improvements on behavioral measures including ARAT and the Stroke Impact Scale hand function domain after 18–30 h of treatment [37]. However, one requirement for FES to be effective is the user's capacity for residual movements, which is not always plausible for individuals with severe motor impairments [55]. Due to this limitation, the use of hand orthotics is becoming increasingly used in conjunction with BCI-FES interventions.

Orthotics combined with BCI are showing promising results for distal UE function. Shindo et al. used orthotics with BCI to elicit finger extension resulting in increased function and decreased spasticity. These findings also corresponded to increased excitability in the brain, which reflect the BCI principles of impacting brain plasticity through learning mechanisms to elicit improved motor function [17]. Similarly, Ramos-Murguialday et al. used hand and arm orthoses in severe stroke patients and found clinically significant improvements in FMA scores that correlated with plasticity changes in the brain [56]. Another study comparing different feedback types found that somatosensory feedback through an orthosis was more effective at improving finger motor function than animated visual feedback on a computer screen for individuals with chronic stroke. Although both groups had enhanced brain activation following BCI treatments, the difference in functional UE motor scores suggest that certain types of sensory feedback may better facilitate motor reorganization in the brain [57].

While BCI interventions have shown to be effective with both self-guided movement (i.e. MI) and assistive movements (i.e. FES and orthotics), some studies have found that BCI interventions have not shown distinct improvements as effectively within the stroke population. Ang et al. found that a 2-week BCI-MI intervention with transcranial direct current stimulation did not elicit significant motor improvements within a stroke population that included both acute and chronic survivors. However, although not significant findings, the researchers found that participants had better accuracy in the BCI-MI task and increases in laterality coefficients, reflecting cortical activation related to motor planning [58]. The short length of the study may be the reason behind the lack of physical motor improvements, but these findings show promise for future directions BCI research may take due to changes in brain activation.

Other studies have raised the question of pre requirements and individual characteristics needed for BCI to be effective. A review by Ahn and Jun explored the idea of 'BCI-illiteracy,' referring to certain users that have more difficulty in controlling the BCI system due to variabilities in physiological and psychological characteristics. One such finding suggests that individuals that are successful BCI performers are better at recruiting MI-related brain networks and those that are 'BCI-illiterate' have less developed networks to recruit from. Other variables contributing to BCI performance success include motivation and the use of tactile and visual feedback modalities. Together, these elements may contribute to a user's level of concentration, which may lead to greater BCI success [59].

Collectively, current research demonstrates that BCI has the potential to harness the reserve of recovery potential left after stroke insult [60]. A powerful platform for motor recovery post-stroke has been created through a combination of individual learning mechanisms, BCI principles, and various modalities such as FES and MI.

Limitations

Several themes emerged in review of previous studies on BCI therapies. Several studies studied the chronic stroke population, disregarding the mild-to-moderate stroke population. This has implications for the potential for recovery. In addition, several studies investigated BCI as an adjunct to traditional physiotherapy. When studying BCI in conjunction with traditional physiotherapy, it is difficult to discern the outcomes as resulting from BCI alone, traditional physiotherapy alone, or a combination of the two treatments.

While the implications of BCI appear promising, one major limitation of BCI is underpowered studies due to small sample sizes [4,9,22,25,26,34,38,39,61,62]. Additional studies with larger and more heterogeneous samples are required to determine if adults' post-stroke can successfully use BCI for motor learning and in particular using Hebbian-type learning [4,9,22,26,34,38,61,62]. More rigorous RCTs are required for BCI to have increased impact and power on the field of stroke neurorehabilitation. While BCI technology appears impactful on improving motor control for individuals post-stroke, there are more methodological studies on healthy individuals than individuals with stroke. In addition, many BCI methods studies focus on upper limbs and few targeting the lower limbs [63]. Therefore, the efficacy of BCI treatment should be examined in future studies. Recent studies have found that structured, task-oriented rehabilitation programs and EEG-biofeedback systems (neurofeedback) do not significantly improve UE motor function or recovery in adults' post-stroke compared to conventional rehabilitation [64,65]. In addition, the efficacy of BCI combined with conventional therapy is unclear due to difficulty discriminating between outcomes due to BCI and outcomes due to conventional therapy [63].

Determining the optimal treatment dosage is another area that will require future BCI research. Currently, recommendations for treatment dosage vary greatly across studies. Previous studies have implemented treatment across 11–22 sessions [7,12,31,37,47], while others have found successful outcomes from fewer than 10 sessions [38]. More research on the frequency of BCI treatment is needed to determine the optimal amount to best promote UE motor rehabilitation. Additionally, these variations in study design have created inconclusive findings on the lasting effects of BCI therapy, in the absence of frequent motor rehabilitation [47]. Further, the generalizability of findings are inconclusive based on low participant numbers and varied dosing and study designs [11,62].

Expert commentary

BCI systems are likely advantageous over standard stroke interventions due to their ability to engage multiple learning modes. Based in Pavlovian conditioning and facilitating Hebbian learning mechanisms, BCI therapies use the goal-directed nature of motor execution and the brain's ability to associate novel and independent stimuli to create an environment in which motor skills can be trained, performed, and reinforced. In addition, BCI technology seems well suited for neural rehabilitation post-stroke as it utilizes the user's direct neural input for the purpose of manipulating a peripheral component, creating a closed-loop feedback system between the CNS and PNS. Noninvasive reading of the brain's residual CNS activity, commonly through an EEG cap, paired with external sensory (visual, tactile) input to the PNS may be used to support the recovery of functional capacities in the brain such as voluntary motor function.

BCI can be coadministered with established intervention therapies as well as more novel tasks, including biofeedback or constraint-induced movement therapy. To date, research suggests various modalities used in conjunction with a BCI system are effective for UE stroke rehabilitation, including coadministration with FES, TDU, and MI. Certain studies are also beginning to incorporate neuroimaging systems such as fMRI. Currently, laterality index and activation maps are some of the most commonly studied fMRI data. BCI may be used to support the recovery of functional capacities in the brain such as voluntary UE and hand motor function through goal-directed practice and training, which in turn in is thought to improve quality of life.

Ongoing research to evaluate the effectiveness of BCI-based stroke rehabilitation for hand therapy is currently in progress and must be a priority now and in the future. There is a demand for larger randomized control trials and clinical-based trials with BCI-based interventions. There is room for potential use of BCI-based interventions on a smaller, more personalized scale as technology improves and allows for increased portability and compatibility. This may lead to the use of BCI interventions in clinics or homes in the near future. With increased accessibility to these therapies, a more neurologically diverse population may have the opportunity to experience an increased quality of life from the outcomes of BCI interventions.

Five-year view

Ongoing research to evaluate the effectiveness of BCI-based stroke rehabilitation for hand therapy continues in earnest. Thus, it is important to direct development toward necessary improvements in BCI methodologies to address efficacy, reproducibility, and the identification of the specific mechanism of therapeutic action. Improvements and revisions, including relevant behavioral outcome measures and pre- and post-therapy fMRI, in future investigations are essential to enhancing device performance and improving the rehabilitative impact of each therapy session.

Future BCI intervention studies will need to incorporate stroke patients from a wide range of neurological and demographic profiles. In addition, future research must focus on BCI methodology with use of subjects with stroke, rather than solely healthy individuals. Future research populations must differ in chronicity, severity, lesion location, as well as number of stroke insults to better formulate generalizable trends and outcomes. Further addressing different subpopulations could elicit clarification in the relationship between BCI therapy and the nature of neuroplasticity, which could allow for eventual tailoring of individual neurorehabilitation programs for stroke patients to realize maximal recovery. In the future, these paradigms may include those with different neurological impairments such as quadriplegia, which often manifest as exclusion criteria for many prior BCI studies [29,31,66]. Severely impaired patients previously unable to engage will experience continually improving interpersonal interactions. Moreover, it may be possible to improve BCI device design through further comparisons between spatial and frequency patterns of neural activity derived from task performance among different subpopulations. Future research exploring the multiple impacts of BCI on a wider range of severity will explore the different impacts BCI therapy has on individuals with varying levels of severity. For example, BCI may have different impacts on individuals with mild motor impairments compared to individuals with more severe motor impairments.

To date, an increasing number of studies successfully explore various modalities with which to use a BCI system as a neurorehabilitation device for stroke. Such modalities, such as fMRI, EEG, EMG-triggered orthotics, and FES, aim to increase function and quality of life for individuals unable to engage in tasks due to CNS damage. Several examples demonstrate the flexibility of BCIs as a dynamic therapy. For example, a case study discussed by Reiss et al. [9] demonstrated how noninvasive BCI allowed individuals experiencing locked-in syndrome, due to a brainstem stroke, to produce messages. This important innovative function of BCI provided autonomy for these survivors, although they often required assistants from a health-care provider and at least some level of persisting ocular motor or musculoskeletal control. Such examples demonstrate the flexibility of BCIs as a dynamic therapy for stroke survivors, a patient population often presenting with a multiplex of impairments and comorbidities.

Neuroimaging measures, such as NIRS, fMRI, and real-time fMRI, hold promise for maximizing BCI treatments by measuring and representing the rehabilitative capacities of BCI therapy on a patient-to-patient basis. Neuroimaging of functional brain organization will be used by therapists to make personalized adjustments to the BCIs in order to maximize the therapeutic effect of treatment. Simultaneous fMRI-EEG technology may be incorporated with BCIs in the future to image brain changes in an increased temporally relevant manner. This proposed methodology takes advantage of the spatial resolution of fMRI with the temporal resolution of EEG. Simultaneous EEG-fMRI should be studied further to establish validity and to reduce its cost. Advancements in neuroimaging measures are still forthcoming and their incorporation with emerging technologies such as BCI may provide a dynamic approach for establishing the 'best fit' therapy for a patient. Furthermore, future studies investigating EEG-fMRI must investigate if the neural changes centrally coexist with functional outcomes peripherally. Future studies must investigate the interaction between neural changes, functional outcomes, and self-efficacy in adults' post-stroke after using BCI.

A recent study found those with hand paresis after stroke improved more when they had combined EMG-triggered electrical stimulation with task-oriented training [67]. While EMG-triggered electrical stimulation is not driven by a traditional BCI, there is an emphasis on the potential for recovery when combining various modalities. The combination of BCI therapies with a wearable 'smart glove' orthotic is of particular interest. 'Smart gloves' are wearable biofeedback devices that record kinematic data associated with movements of the hand, wrist, and digits and can be used along with virtual reality to retrain motor patterns. Such devices and therapeutic combinations have been found to decrease levels of motor impairment and increase quality of life [68].

Administration of such a BCI-FES therapy may allow for rehabilitation of the upper and lower extremities as well as improve a patient's posture and gait [24]. Coordinated by a BCI-FES system, the user is provided with a tactile, proprioceptive sense of their movements. It is also possible that impaired muscle groups will receive focused and timed electrical stimulation to facilitate contraction of dynamic muscle groups to perform complex motor tasks. Synchronized by a BCI, such FES pulses may be used to assist abated movement or augment normal contraction. Recent evidence, also reviewed herein, suggest BCI-FES can potentially induce neural improvements associated with motor function. Through this combination, BCI has future implications in motor recovery and muscular reeducation for those neurological deficits caused by stroke, as well as other neurological conditions.

When considering what devices to combine with BCI, initially, it is important to consider feasibility and cost, as individuals are less likely to use treatments that are expensive or cumbersome to operate [69]. As research in the field progresses, the authors are hopeful that BCI therapy will become available as an affordable and effective in-home treatment. The authors suggest that development of a portable BCI system for in-home use will primarily consist of a laptop computer or tablet-like device containing appropriate software connected to a 16-channel (or fewer) EEG system with a stable, robust, and durable electrode array and amplifier.

Human–device interaction might be realized as an augmentative implementation of BCIs as BCI-system software advance over time to become more standardized and user friendly. It may soon be feasible for stroke survivors to dial phone numbers, answer correspondences, or even operate home appliances with the help of a BCI. To ensure reliability and safety in the usage of in-home treatments, it is initially suggested that health-care professionals and eventually caretakers, such as family members or hospice staff, are trained to oversee the BCI therapy operations and to ensure proper regulatory compliance is adhered to.

BCI technology provides patients with a range of impairments and across a spectrum of stroke chronicity the opportunity to benefit from a professionally prescribed, clinically designed, and individualized neurorehabilitation regimen. The authors believe that the most significant advancements over the 5 years following this review will be the transfer of noninvasive BCI intervention therapies from clinics and research labs to in-home and increasingly personalized treatments. These efforts are essential for continuing the advancement of BCI technologies toward improving the quality of life and sense of autonomy for stroke survivors in their daily living activities. This review suggests rich promise for the future of BCI technology as a treatment modality for distal UE motor impairment following stroke insult.

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Key issues

- Despite advances in medical practice and technology, stroke incidence remains a leading cause of major disability and death worldwide.
尽管医疗与技术在不断进步，中风发病率仍然是全球残疾和死亡的主要原因之一。
- Though stroke mortality is declining, stroke incidence is increasing and so too are the health care costs associated with treatment and patient rehabilitation.
尽管中风的死亡率有所下降，但由于发病率的上升，病人治疗和康复的医疗费用也在增加。
- BCIs offer a non-invasive, closed-loop neural interface with an option to include a prosthetic device, robot, or other machine to further facilitate rehabilitation therapy.
BCIs提供一种非侵入式的闭环神经接口，可以借助假肢、外骨骼等机械来促进康复治疗。
- BCI-mediated therapy offers the personalizable and adaptable therapy platform required of a modern restorative physiotherapy.
BCI提供了一种现代康复物理疗法所需的个性化和适应性的治疗平台。
- BCIs operate by direct integration of the brain and an external computer or other devices for the purpose of rehabilitation of hand and other upper extremity motor impairments.
BCIs通过将大脑和计算机等设备直接整合来实现手或其他上肢运动障碍的康复。
- BCI's method of action is to train controlled neuromodulation via psychophysiological integration of motivation, learning mechanisms, motor plan rehearsal, proprioceptive feedback, and reward systems in order to restore and orchestrate intentional movement of hemiparetic distal extremities. BCI的方法是通过意图、学习机制、运动计划预演、本体感觉反馈以及奖励系统的心理生理整合来训练神经调节的控制，达到远端肢体偏瘫患者运动意图的修复和协调。
- BCI holds great promise as a future cost-effective, in-home, adaptive, augmentative medical device platform for stroke survivors.
BCI是一种低成本、家用、有适应能力、辅助中风患者的医疗设备平台。
- BCI and its possible adjuvants provide a rich suite of personalizable rehabilitations capable of incorporating existing physiotherapies as well as future therapies.
BCI和辅助物提供了丰富的个性化康复治疗，可以结合现有的物理疗法或未来治疗方法。
- Several BCI methodological studies were conducted on healthy subjects, which posits the needs for more methodological studies conducted on individuals post-stroke for future clinical studies
一些对健康被试进行的BCI方法学研究表明，在未来的临床研究中对中风后患者进行更多方法学研究的需要。

Table 1

Reviewed studies of efficacy of BCI in stroke rehabilitation.

Study	Stroke chonicity	*N* (sex)	System and regimen	Did therapy result in noted improvements?	Are BCI therapy results statistically significant at exit?	Outcomes and behavioral outcome measures of interest
Ang et al. (2015)	Chronic	*N* = 19	10 sessions of tDCS or sham before 1 h of MI-BCI with robotic feedback for 2 weeks (sham-controlled, RCT)	No	No	UE FMMA
Ang et al. (2014)	Chronic	*N* = 21 M = 14 F = 7	3-arm RCT; MI-BCI with HK, HK, and standard therapy; 18 sessions of 1 h interventions	Yes, BCI-HK group	Yes, BCI-HK group	FMMA
Biasiucci et al. (2013)	Chronic	*N* = 4	At least 10 sessions of FES controlled by BCI over a period of 2 months	Yes	N/A	FMA
Broetz et al. (2010)	Chronic	*N* = 1 M = 1 F = 0	1 h physiotherapy with each BCI session	Yes	No	FMA, Wolf motor function test, modified Ashworth scale
Buch et al. (2008)	Chronic	*N* = 8	13–22 sessions MEG-BCI with hand orthosis over 3–8 weeks	Yes	No	In-house measure of success (>50% target 'hit')
Bundy et al. (2012)	Chronic	*N* = 4	Subjects performed between 85 and 246 control trials of BCI	Yes	Yes	ARAT
Caria et al. (2011)	Chronic	*N* = 1 M = 1 F = 0	After 2–4 weeks MEG-BCI, case study had EEG-BCI and 4-week periods of EEG-BCI 3 & 9 months later. 1 h physiotherapy w/each BCI session	Yes	Yes	FMA; Wolf motor function test; modified Ashworth scale, and goal attainment score
Daly et al. (2009)	Chronic	*N* = 1 M = 0 F = 1	Nine 45-min BCI-FES sessions over 3 weeks. Also weekly 1.6 h of non-BCI FES therapy	Yes	Yes	Isolated movement index finger extension
Liu et al. (2012)	Sub acute and chronic	*N* = 314	12–20 weekly or twice-weekly 1 h sessions using EEG-BCI triggering a hand orthosis for finger extension over 4–7 months	Yes	Yes, significance was found in FMA and ARAT, but no significance indicated in MAL	FMA, ARAT, and MAL-14
Mihara et al. (2013)	Chronic	*N* = 20	6 sessions of NIRS-guided BCI with mental practice with MI + standard rehabilitation	Yes	Yes	FMA and ARAT
Murlidharan et al. (2011)	Chronic	*N* = 4	1 session a week for 4 weeks of BCI	Yes	Yes	FMA
Ono et al. (2014)	Chronic	*N* = 12	Visual feedback and somatosensory feedback groups. Each group received 12–20 sessions of 1 h length	Yes, motor improvements in somatosensory group	N/A	SIAS for finger function
Prasad et al. (2010)	Chronic	*N* = 5 M = 4 F = 1	2 treatment sessions each week of BCI-MI + PP for a total of 6 week	Yes	Yes	Motricity index ARAT, 9-Hole Peg Test grip strength; fatigue and mood and qualitative feedback

Study	**Stroke chonicity**	***N* (sex)**	**System and regimen**	**Did therapy result in noted improvements?**	**Are BCI therapy results statistically significant at exit?**	**Outcomes and behavioral outcome measures of interest**
Ramos-Murguialday et al. (2013)	Chronic	$N = 32$	17.8 ± 1.4 days of training with BCI with an orthotic	Yes	Yes	FMA
Rayegani et al. (2013)	N/A	$N = 30$	10 sessions of conventional OT, in addition to either EMG-biofeedback therapy or neurofeedback therapy	Yes	Voluntary contraction of abductor pollicis brevis increased significantly after EMG-biofeedback therapy	Jebsen hand function test
Shin do et al. (2011)	Chronic	$N = 8$ M = 8 F = 0	12–20 weekly or twice-weekly 1 h sessions over 4–7 months using EEG-BCI triggering a hand orthosis for finger extension	Yes	Yes	SIAS; MAL amount of use; modified Ashworth scale; resting motor threshold
Young et al. (2014)	Chronic	$N = 11$ M = 8 F = 3	At least nine- and up to fifteen 2-h sessions of interventional BCI + FES + TS	Yes	Yes	Stroke impact scale; ARAT; 9-Hole Peg test; laterality index

N: Number; tDCS: transcranial direct current stimulation; MI: motor imagery; BCI: brain–computer interface; RCT: randomized control trial; UE: upper extremity; FMMA: Fugl-Meyer Motor Assessment; M: male; F: female; HK: Haptic-Knob robotic arm; FES: functional electrical stimulation; MEG: magnetoencephalograms; EEG: electroencephalogram; FMA Fugl-Meyer Assessment; ARAT: Action Research Arm Test; MAL: Motor Activity Log; NIRS: near-infrared spectroscopy; SIAS: Stroke Impairment Assessment Set; PP: physiotherapy; EMG: electromyography; TS: tongue stimulation.