Neuromuscular Electrical Stimulation for Motor Restoration in Hemiplegia

John Chae, Lynne Sheffler, and Jayme Knutson

Clinical applications of neuromuscular electrical stimulation (NMES) in stroke rehabilitation provide both therapeutic and functional benefits. Therapeutic applications include upper and lower limb motor relearning and reduction of poststroke shoulder pain. There is growing evidence that NMES, especially those approaches that incorporate task-specific strategies, is effective in facilitating upper and lower limb motor relearning. There is also strong evidence that NMES reduces poststroke shoulder subluxation and pain. Functional applications include upper and lower limb neuroprostheses. Lower limb neuroprostheses in the form of peroneal nerve stimulators is effective in enhancing the gait speed of stroke survivors with foot-drop. The development of hand neuroprostheses is in its infancy and must await additional fundamental and technical advances before reaching clinical viability. The limitations of available systems and future developments are discussed. **Key words:** *electrical stimulation, motor function, stroke*

Neuromuscular electrical stimulation (NMES) refers to the electrical stimulation of lower motor neurons to cause muscle contraction. Clinical applications of NMES in stroke rehabilitation provide both therapeutic and functional benefits. Therapeutic applications may lead to a specific effect that enhances function but does not directly provide function. An important example discussed in this article is motor relearning, defined as "the recovery of previously learned motor skills that have been lost following localized damage to the central nervous system."[1(p261)] The term functional electrical stimulation or FES refers to the use of NMES to directly accomplish functional tasks such as standing, ambulation, or activities of daily living (ADL).[2] Devices that provide FES are also referred to as neuroprostheses.

Specific therapeutic applications reviewed in this article include poststroke motor relearning and reduction of hemiplegic shoulder pain. Specific neuroprosthetic or "functional" applications include upper and lower limb motor movement for ADL and mobility, respectively. Perspectives on future developments and clinical applications of NMES will also be presented.

Motor Relearning

Basic science and theoretical considerations

Following experimental and clinical brain injury, goal-oriented, active repetitive movement training of a paretic limb enhances motor relearning. In nonhuman primate models, goal-oriented, active repetitive movement training of the paretic limb

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after local damage to the motor cortex shapes subsequent functional reorganization in the adjacent intact cortex, and the undamaged motor cortex plays an important role in motor relearning. Specific types of tasks that induce long-term plasticity in motor maps are repetitive movements that entail the development of motor skills. That is, the motor tasks are new and therefore "require" significant cognitive effort to learn and complete. For example, training to acquire new skills such as retrieving food pellets from a small well or a rotating well are associated with task-specific cortical reorganization. However, this is not the case with repetitive movement tasks that require minimal to no cognitive effort.[3] Clinical applications of these basic science findings include constraint-induced movement therapy,[4] robotic therapy,[5] and bilateral repetitive movement therapy.[6]

If goal-oriented repetitive movement therapy facilitates motor relearning, NMES-mediated goal-oriented repetitive movement therapy may also facilitate motor relearning. Accordingly, electrical stimulation of the peripheral nerve or motor points is associated with concomitant physiologic changes in the brain including activation of primary sensory and motor areas and the supplementary motor area, reduction of intracortical inhibition, and increased amplitude of motor-evoked potentials.[7–10]

NMES can be used by stroke survivors with hemiparesis who do not have sufficient residual movement to take part in volitional, active repetitive movement therapy. Regardless of cortical or spinal mechanisms, the experimental and theoretical considerations suggest that the necessary prerequisites for NMES-mediated motor relearning include high repetition, novelty of activity, concurrent volitional effort, and high functional content.[3]

Three forms of NMES are available for motor relearning: cyclic NMES, EMG-mediated NMES, and neuroprostheses. Cyclic NMES contracts paretic muscles at a set duty cycle for a preset time period. The NMES-mediated activity is novel in that the stroke survivor has difficulty performing the task. However, the user is a passive participant, no cognitive investment is required, and the task is not functionally relevant. EMG-mediated NMES couples cognitive intent to activate a muscle and the corresponding NMES-induced muscle contraction. This approach may be applied to patients who can partially activate a paretic muscle but are unable to generate sufficient muscle contraction for adequate exercise or functional purposes. Although this approach utilizes novel tasks and includes cognitive investment, the task itself is not functionally relevant. The third type of NMES includes neuroprosthetic applications that provide FES for completion of ADL and mobility tasks. Because repetitive movement training is performed in the context of meaningful, functional behavioral tasks that are novel, neuroprostheses have a theoretical advantage over both cyclic and EMG-mediated NMES for motor relearning. Neuroprosthesis applications are discussed in greater detail in a later section.

Upper limb applications

Several randomized clinical trials evaluated the efficacy of surface cyclic NMES in enhancing upper limb motor relearning.[11–15] These studies demonstrated improved outcomes in motor impairment at end of treatment, with mild to moderately impaired subjects benefiting most. Enduring effects were seen among acute stroke survivors but not for chronic stroke survivors.[13,14] Only two of these studies demonstrated short-term benefit with respect to activity limitations.[14,15]

The strengths of these studies rest on their randomized designs. However, numerous methodological limitations such as inadequate blinding, unequal treatment intensity, limited follow-up, inadequate accounting of drop-outs, and failure to use intent-to-treat analysis render the results difficult to interpret. Nevertheless, even with these methodological limitations, these trials do suggest that cyclic NMES enhances the upper limb motor relearning of stroke survivors. The effect may be more clinically relevant for acute stroke survivors and for those with milder impairments. However, the effect of cyclic NMES on activity limitations is uncertain.

Several clinical trials evaluated EMG-mediated surface NMES for upper limb motor relearning.[16–21] In general, these studies demonstrated improved outcomes in motor impairment at end of treatment. In the few studies that evaluated activity

limitations, improved outcomes were noted.[18,21] Several studies demonstrated evidence of central mechanisms using neurophysiologic assays such as reaction time and fMRI.[19–21]

As with the cyclic NMES studies, numerous methodological deficiencies such as inadequate blinding, paucity of follow-up data, inability to assess equality between treatment groups, and small sample sizes limit the interpretation of results. Nevertheless, data suggest that EMG-mediated NMES reduces upper limb motor impairment and these changes, to at least some degree, translate into improvements in activity limitations.

Finally, hand neuroprostheses may facilitate motor relearning. One controlled trial using a hybrid brace-NMES device that incorporates surface electrodes into a brace for hand grasp and release (**Figure 1**) demonstrated improvements in a limited set of functional tasks.[22] Two additional studies using hand neuroprostheses, one using the above device and another using an electrical stimulator garment, resulted in significant improvement in upper limb motor function among acute stroke survivors.[23,24] Several novel neuroprosthesis approaches with encouraging preliminary results are presently under investigation including injectable microstimulators,[25] contralaterally controlled surface FES,[26,27] and the incorporation of work stations.[28]

Overall, the literature suggests that surface NMES is effective in reducing motor impairment. However, the effect on upper limb-related activities remains uncertain. This is consistent with the results of a systematic review of randomized clinical trials of NMES interventions for motor relearning.[29] The authors concluded that the literature "…suggests a positive effect of electrical stimulation on motor control. [However] no conclusion can be drawn with regard to the effect on functional ability [activity]."(p347) The authors further concluded that the effect appears to be more significant for those with milder impairments. A subsequent review by the same group concluded that EMG-mediated NMES may be more effective than cyclic NMES.[30] However, to date, there are no studies that directly compare these types of approaches. Although neuroprostheses may be most effective in facilitating motor relearning, and results to date are encouraging, additional studies are needed to demonstrate that the reported improvements in function are clinically important and cost-effective.

Figure 1. A hybrid brace-transcutaneous neuroprosthesis system (NESS H200) that is worn on the hand and forearm. The exoskeleton positions the wrist in a functional position and the five surface electrodes built into the exoskeleton stimulate specific muscles to provide coordinated hand opening and closing. (Courtesy of Bioness Inc., Santa Clarita, CA)

Lower limb applications

Lieberson and associates described the first single-channel surface peroneal nerve stimulator to provide ankle dorsiflexion during the swing phase of gait for stroke survivors.[31] However, they also commented, "On several occasions we observed, after training with the electrophysiologic brace [peroneal nerve stimulator]…patients acquire the ability of dorsiflexing the foot by themselves."(p103)

Since this early report, several controlled studies evaluated single- or dual-channel surface cyclic

NMES devices and confirmed the motor relearning effect in the lower limb. NMES combined with biofeedback is associated with improved knee and ankle joint angles, ambulation velocity, symmetry in stance, and knee extension torque.[32,33] Cyclical NMES alone also improves the strength of paretic ankle dorsiflexors.[34,35] In a recent double-blind randomized clinical trial, Yan and associates reported that cyclic NMES reduces spasticity, strengthens ankle dorsiflexors, improves mobility, and increases home discharge rate after acute inpatient stroke rehabilitation.[36]

Because gait deviation in hemiplegia is not limited to ankle dysfunction, several studies evaluated multichannel surface neuroprosthesis systems that additionally provide hip and knee control. Two case series demonstrated improvements in qualitative and quantitative measures of gait after training with a 6-channel surface neuroprosthesis system.[37,38] A follow-up controlled trial demonstrated significantly greater improvement in gait performance and motor function among participants treated with the neuroprosthesis compared to those treated with conventional therapy.[39]

As the number of electrodes increase, surface systems are difficult to implement and maintain clinically. The practicality of multichannel surface lower limb systems is further limited by reduced muscle selectivity, poor reliability of stimulation, and pain of sensory stimulation. Accordingly, Daly and associates developed and implemented a multichannel percutaneous system to facilitate lower limb motor relearning and mobility.[40] A single-blinded randomized clinical trial demonstrated that percutaneous NMES-mediated ambulation training improves gait components and knee flexion coordination relative to controls.[41]

As with upper limb applications, methodological limitations, including inadequate blinding in most studies, small sample sizes, limited follow-up data, and outcomes limited to impairment measures only limit the formulation of definitive conclusions. Nevertheless, the preponderance of evidence suggests that NMES in the form of cyclic stimulation, neuroprostheses, or in combination with biofeedback is effective in facilitating lower limb motor relearning. A recent meta-analysis concluded that "FES is effective at improving gait speed in subjects post-stroke."[42(p853)] However, it was still unclear whether NMES improved overall mobility function.

Summary, clinical considerations, and future directions

Despite the numerous methodological limitations of controlled trials, the weight of evidence suggests that NMES-mediated repetitive movement therapy reduces motor impairment for persons with hemiplegia. The effect is likely to be more robust and enduring among acute stroke survivors relative to chronic stroke survivors. However, it remains uncertain whether the effect translates into clinically relevant improvements in ADLs and mobility. Although there are theoretical bases for expecting that EMG- or biofeedback-mediated NMES is more effective than cyclic NMES, there are no studies that compare these differing approaches.[30] At present, there are inadequate numbers of controlled trials to conclude that neuroprostheses facilitate motor relearning, although due to its high functional content, neuroprostheses may be most effective in facilitating motor relearning. Finally, the optimal dose and stimulation parameters remain to be elucidated.

In view of the methodological limitations of published controlled trials and the uncertain effect on ADLs and mobility, it is not possible to offer definitive clinical recommendations. Nevertheless, because the effect on motor impairment is consistent throughout the various studies and NMES does not appear to be harmful, a select group of stroke survivors may benefit from NMES therapy. Acute stroke survivors with no volitional finger extension may benefit from cyclic NMES of the finger extensor.[14,43] With emergence of volitionally activated muscle contraction or EMG activation, EMG-triggered NMES should be considered.[44] For those with good proximal control but minimal distal movement, the hybrid orthosis-NMES system may be offered.[45,46] With the emergence of additional volitional movement, other motor relearning strategies such as constraint-induced therapy may be implemented.[4] In the lower limb, acute stroke survivors with no volitional ankle dorsiflexion may benefit from cyclic peroneal

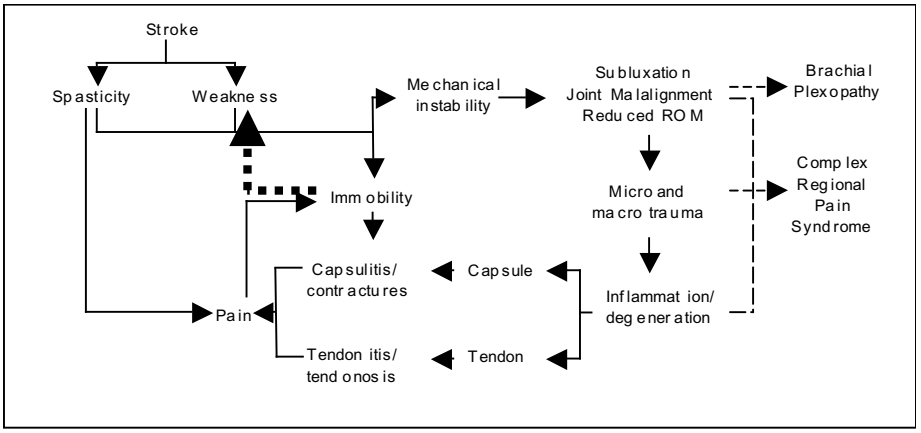

Figure 2. Theoretical framework describing the genesis and maintenance of hemiplegic shoulder pain. (Reproduced with permission, from Sheffler LR, Chae J. Neuromuscular electrical stimulation in neurorehabilitation. *Muscle Nerve.* 2007;35:562–590. Copyright © 2007 by Wiley Periodicals, Inc.)

nerve stimulation.[35,36] EMG-triggered NMES may be applied for those with evidence of volitional activation.[47] If the stroke survivor has some ability to ambulate, gait training with a peroneal nerve stimulator may facilitate lower limb motor relearning.[48–50] Similar principles could be applied to proximal muscles and multiple muscles. However, at this time, multichannel surface and percutaneous lower limb NMES systems are not as clinically accessible and are limited to research applications.

Future investigations on NMES for motor relearning should address the methodological limitations of prior studies and demonstrate the impact on clinical outcomes at the level of activity limitation and quality of life. Future studies should be large, multicenter, randomized clinical trials, which should be at least single-blinded. Studies should carefully define the subject populations, identify potential confounds, and evaluate long-term outcomes using valid and reliable measures of motor impairment, energy consumption, activity limitations, and quality of life. These trials should directly compare the various types of NMES to identify the most effective paradigm and the populations that will likely benefit from each approach. Future studies should determine the optimal dose and prescriptive parameters. Systems that utilize more natural proxies for cognitive intent, such as cortical control, should be developed.[51] Neuroprostheses that provide clear functional, cost-effective benefit to a broad range of stroke survivors should be developed to provide goal-oriented, repetitive movement therapy in the context of functional and meaningful tasks.[26,27] Finally, basic studies should further investigate mechanisms in order to optimize the treatment paradigm.

Poststroke Shoulder Pain

Theoretical considerations

Shoulder pain is a common complication following stroke.[52] **Figure 2** shows a theoretical framework describing the genesis and maintenance of poststroke shoulder pain.[53] The framework postulates that the initial spasticity and weakness lead to mechanical instability and immobility of the glenohumeral joint. These conditions cause pain directly or place the capsule and extracapsular soft tissue at risk for micro and macro trauma, subsequently leading to inflammation or degenerative changes, immobility, and pain. In view of the importance of repetitive and functional use of the limb for motor recovery, as reviewed earlier, the immobility exacerbates the state of the already paretic muscles (heavy dashed line in **Figure 2**). The cycle repeats with worsening of the condition. Numerous treatment approaches have

been reported, but with limited success.[54] However, the use of NMES to the muscles surrounding the shoulder to improve biomechanical integrity of shoulder complex may be an effective strategy for reducing poststroke shoulder pain.

Surface systems

Excluding the authors' randomized clinical trial of percutaneous NMES,[55,56] nine controlled trials of NMES for the treatment of poststroke shoulder pain have been reported.[57–65] One of these studied electroacupuncture using needle electrodes,[63] but the remaining eight used surface NMES. Radiographic glenohumeral subluxation was the most consistently evaluated outcome measure. Eight of nine studies[57,59–62,64,65] evaluated radiographic inferior glenohumeral subluxation and seven of these[57,59–65] reported improvements. The six of seven trials that demonstrated significant effect on subluxation included only acute stroke survivors[59–61,63,64] or a combination of acute and chronic stroke survivors.[57] Among these, only two reported sustained improvements beyond end of treatment.[59,60] One recent trial with chronic stroke survivors reported no significant effect on inferior subluxation.[64] However, another trial with chronic stroke survivors reported significant effect by stressing or loading the hemiparetic upper limb.[62]

Other commonly evaluated measures included pain-free passive external rotation range of motion (ROM), motor impairment using a standardized measure, and resting shoulder pain. Six of nine studies[58–61,65] evaluated pain-free passive ROM. Significant and sustained improvement in pain-free ROM in the treatment group compared to controls was reported in only one study.[60] Three studies reported no significant effect. Six of nine studies evaluated motor impairment using a standardized measure.[59–61,63,65] Two acute studies reported improvements at end of treatment and at follow-up.[60,65] One acute study demonstrated improvement at end of treatment but not at follow-up.[59] Three studies (two acute and one chronic) reported no improvements in motor impairment.[61,63,65] Two treatment studies and one prevention study evaluated shoulder pain at rest; the treatment studies reported improvements whereas the prevention study did not.

These studies all point to important therapeutic benefits of surface NMES, but small sample sizes limit formulation of definitive conclusions. Accordingly, meta-analyses may provide further insight. The Cochrane Review[66] included four studies[11,58,59,61] and concluded that NMES improves pain-free passive external rotation ROM and reduces subluxation but does not improve shoulder pain or motor impairment. Ada and Foongchomcheay[67] included seven studies[57,59,61,62,64,65] and concluded that surface NMES reduces or prevents subluxation and improves motor impairment in the subacute phase but not in the chronic phase.

Intramuscular systems

Despite the evidence for therapeutic benefit, the clinical implementation of surface NMES for shoulder subluxation and pain in hemiplegia is difficult for several reasons. First, stimulation of cutaneous pain receptors cannot be avoided, resulting in stimulation-induced pain that limits tolerance and compliance. Second, due to stimulation-induced pain and the rapid onset of fatigue, an escalating stimulation schedule is needed. Third, skilled personnel or intensive patient training is required to reliably place electrodes and adjust stimulation parameters to provide optimal and tolerable treatment with minimal muscle fatigue. Accordingly, Baker and Parker, the authors of the first clinical trial of surface NMES for poststroke shoulder dysfunction, concluded that "until implanted electrode systems become available… long-term use of surface electrical stimulation can be managed by only a few patients with hemiparesis and their families."[57(p1937)]

Two implanted NMES systems are under investigation: an injectable system with an external antenna, and a percutaneous system with an external stimulator. The injectable microstimulator[68–70] is presently under investigation for various applications, including poststroke shoulder dysfunction. Uncontrolled observational studies suggested feasibility and effectiveness in reducing glenohumeral subluxation and associated pain.[71,72] Preliminary controlled trials are in their early stages. The stimulators are permanently implanted and, if shoulder subluxation or pain recurs, additional treatments can be provided without

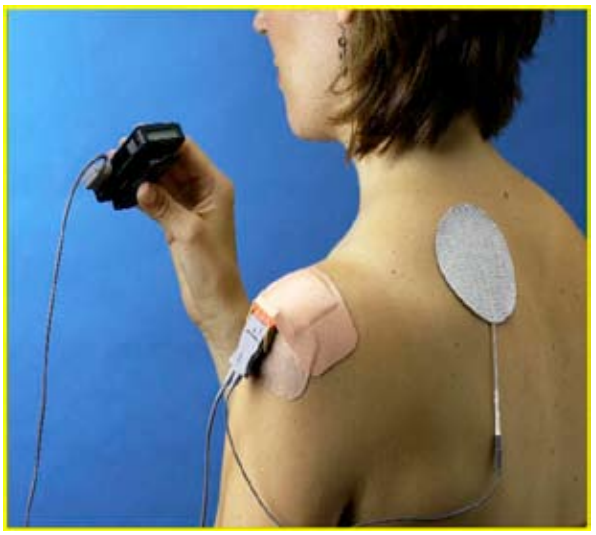

Figure 3. A percutaneous intramuscular electrical stimulation system (RestoreStIM) for treatment of hemiplegic shoulder pain. The pager size stimulator is connected to the implanted electrodes via a connector that can be disconnected when not in use. (Courtesy of NeuroControl Corporation, North Ridgeville, OH)

an additional invasive procedure. However, the system also requires a large antenna that must be worn, which may interfere with daily activities and compromise clinical acceptance.

The percutaneous system includes helical intramuscular electrodes, a "pager" size stimulator, and a connector (**Figure 3**). Electrodes are placed in a minimally invasive procedure under local anesthesia. Electrodes traverse the skin and remain across the skin for the duration of treatment. After completion of treatment, the electrodes are removed by gentle traction. A series of preliminary studies in the United States and the Netherlands demonstrated the feasibility of the system in reducing poststroke shoulder pain.[73–77] A multicenter clinical trial confirmed the results of these initial findings with pain reduction maintained up to 12 months after completion of treatment (**Figure 4**).[55,56] Post hoc analysis revealed that stroke survivors treated within 18 months of stroke are most likely to experience treatment success.[78] Although percutaneous NMES is effective in reducing poststroke shoulder pain, the use of percutaneous wire electrodes poses the risk of electrode-related infections.

Summary, clinical considerations, and future directions

In spite of the methodological limitations, the preponderance of evidence suggests that surface NMES is effective in reducing poststroke shoulder subluxation, increasing pain-free lateral rotation ROM, and facilitating motor recovery, especially for those in the acute phase of stroke. Thus, a

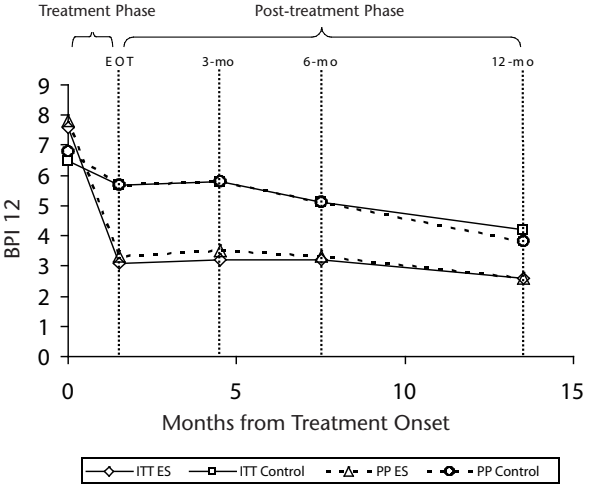

Figure 4. Results of a multicenter randomized clinical trial of percutaneous intramuscular electrical stimulation (ES) for the treatment of hemiplegic shoulder pain. Per-protocol (PP; dashed lines) and intent-to-treat (ITT; solid lines) approaches showed that percutaneous intramuscular ES significantly reduces hemiplegic shoulder pain (Brief Pain Inventory Question 12) for up to 12 months after completion of treatment compared to controls who were treated with a cuffed hemisling. (Reproduced with permission, from Chae J, Yu DT, Walker ME, et al. Intramuscular electrical stimulation for hemiplegic shoulder pain: A 12-month follow-up of a multiple-center, randomized clinical trial. *Am J Phys Med Rehabil.* 2005;84(11):832–842. Copyright © 2005 by Lippincott Williams & Wilkins.)

trial of surface NMES to the supraspinatus and posterior deltoid should be considered for those with flaccid hemiplegia and subluxation during the acute phase of stroke to prevent the development of poststroke shoulder pain. Surface NMES should also be considered for those who already developed glenohumeral subluxation and pain. At present, it is unclear whether NMES renders any therapeutic benefit for those with poststroke shoulder pain in the absence of glenohumeral subluxation. Patients and family members should be trained by an experienced therapist to continue and complete the treatments at home. Although optimal dose and duration are not known, most studies with positive effects provided treatment for 6 hours a day for a minimum of 6 weeks.

Additional studies are needed to address the various methodological limitations in order to more definitively address the question of clinical efficacy. A large, multicenter, single-blinded randomized clinical trial is needed that clearly defines the subject population, identifies potential confounds, and evaluates long-term outcomes. The trial should be clinically relevant and focus on pain as the primary outcome with activity limitations, societal participation, and quality of life as secondary outcomes. Motor impairment and biomechanical and physiological measures may be included for elucidation of mechanisms. Finally, optimal timing, dose, and duration of treatment need to be determined.

Although surface NMES systems may ultimately prove effective for the treatment of poststroke shoulder pain, clinical implementation may be difficult due to issues of pain of stimulation, compliance, reliability of stimulation, and need for skilled personnel. Intramuscular systems, which are presently under investigation, may address these barriers to clinical implementation.

Neuroprotheses

The objective of a neuroprosthesis is the safe and efficient completion of functional tasks for those with more severe paralysis where motor relearning strategies are not amenable. Historically, neuroprostheses development focused on application to the spinal cord injury (SCI), including grasp and release function for persons with tetraplegia[79] and transfer and limited ambulation function for persons with paraplegia.[80,81] Given the initial success of neuroprostheses in the SCI population, it is reasonable to explore their feasibility in the stroke population.

Upper limb applications

There are four full-length publications in English language peer-review journals that evaluated the effectiveness of a hand neuroprosthesis for enhancing the upper limb function of stroke survivors.[45,82–84] All studies used limited sample sizes and open-label designs with performance evaluated with and without the neuroprosthesis.

In 1973, Rebersek and Vodovnik published the first paper on the use of a hand neuroprosthesis in hemiplegia.[84] Surface NMES opened the hand while closing was mediated by termination of the stimulation and subject's own volitional ability. A subset of subjects demonstrated progressive improvements in the number of plugs and baskets they could manipulate with the device. In 1975, Merletti and associates evaluated a similar device.[83] All subjects were able to move small baskets or bottles from one defined area to another with the device, albeit with varying degrees of success. The authors noted that the functional tasks required considerable amount of mental concentration and in several cases increased voluntary effort was associated with tremors, spasticity, and erratic shoulder movement. Alon and associates tested the previously described hybrid NMES-orthosis neuroprosthesis (**Figure 1**) and reported significant improvements in the percent of successful trials completing prespecified ADL tasks.[45]

Due to the limitations of surface NMES, Merletti and associates suggested that an implanted system would best meet the clinical needs of persons with hemiplegia.[83] Accordingly, Chae and Hart evaluated four chronic stroke survivors implanted with percutaneous intramuscular electrodes.[82] The percutaneous hand neuroprosthesis was able to open a spastic hemiparetic hand as long as the limb was in a resting position and subjects did not try to assist the stimulation. However, when subjects tried to assist the stimulation, especially during functional tasks, hand opening was significantly reduced due to increased finger flexor hypertonia.

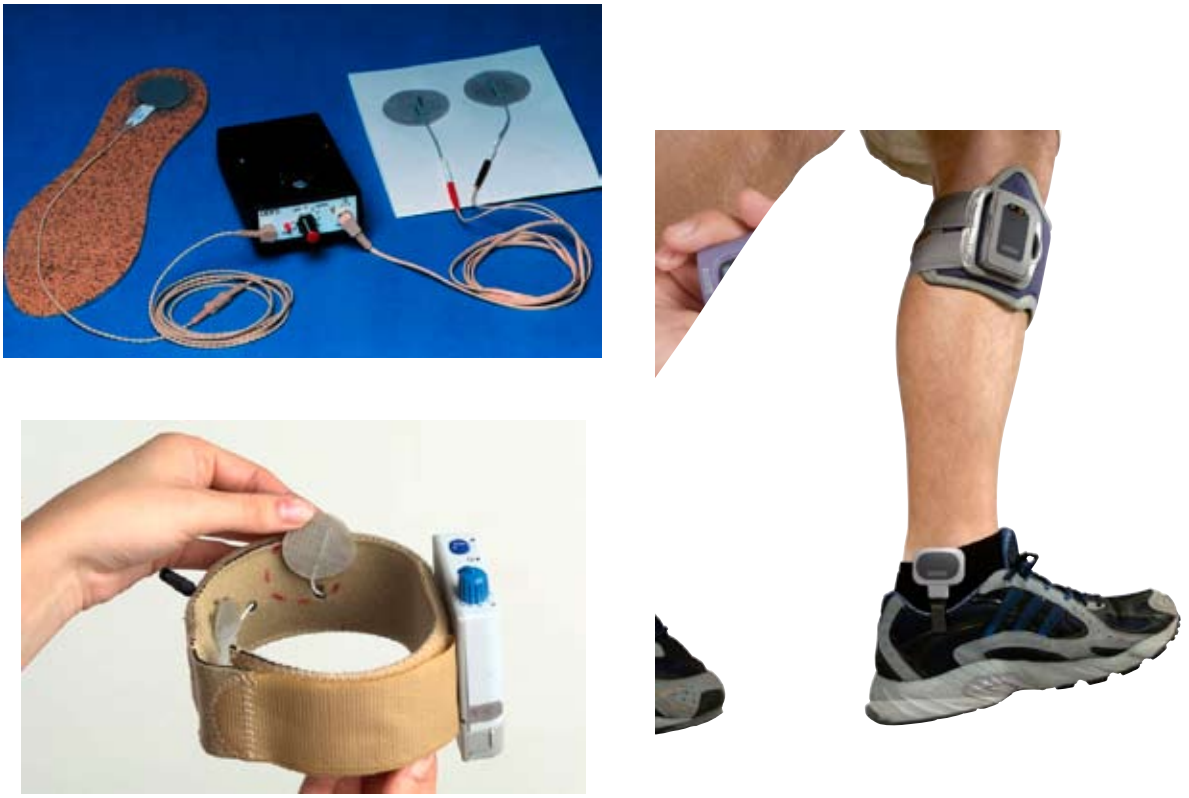

Figure 5. Three FDA-approved transcutaneous peroneal nerve stimulators. The Odstock Dropped Foot Stimulator (left-top; courtesy of the Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, UK, and NDI Medical, Cleveland, OH) and the wireless L300 (left-bottom; courtesy of Bioness Inc., Santa Clarita, CA) both use a heel switch to trigger ankle dorsiflexion. The WalkAide (right; courtesy of Hanger Orthopedic Group/Innovative Neurotronics, Bethesda, MD) uses a tilt sensor to trigger ankle dorsiflexion.

Similarly, electrically stimulated hand opening was significantly reduced following voluntary hand closure. Due to these limitations, a formal ADL evaluation was not pursued.

Lower limb applications

The initial application of neuroprostheses in hemiplegia focused on surface peroneal nerve stimulation to treat ankle dorsiflexion weakness. In 1961, Lieberson and associates described a surface peroneal nerve stimulator that dorsiflexed the ankle during the swing phase of gait.[31] A systematic review of seven case series and one randomized clinical trial since this initial study reported a 38% pooled improvement in walking speed with the device relative to no device.[85] The authors concluded that the "…review suggests a positive orthotic effect of functional electrical stimulation on walking speed."[85(p577)]

Despite demonstrated effectiveness, surface peroneal nerve stimulation is not routinely prescribed in the United States. Likely reasons include difficulty with electrode placement, discomfort and inconsistent reliability of surface stimulation, insufficient medial-lateral control during stance phase, lack of technical support, and perhaps most important, the availability of custom-molded ankle-foot-orthoses. Recent US Food and Drug Administration approval of three surface peroneal nerve stimulators (**Figure 5**) and demonstrated comparability of the peroneal nerve

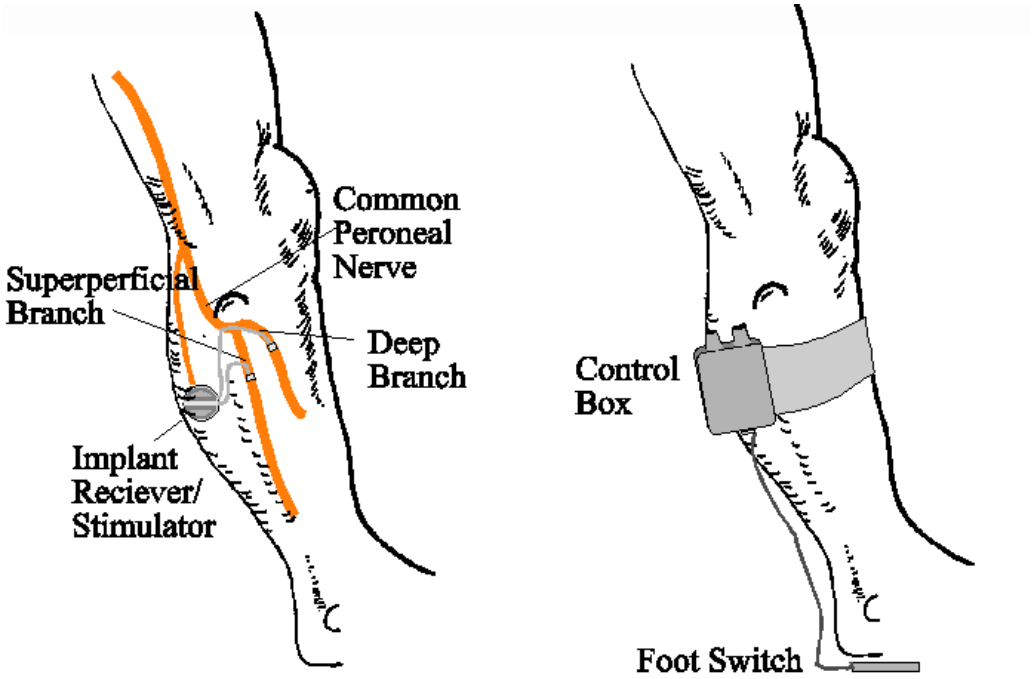

Figure 6. A two-channel implantable peroneal nerve stimulator (STIMuSTEP) allows individual stimulation of the deep and superficial branches of the common peroneal nerve for ankle dorsiflexion and eversion-inversion balance. (Courtesy of the Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, UK)

stimulator to an ankle-foot-orthosis in improving hemiplegic gait may facilitate broader clinical prescription and usage of these devices.[48,86]

Some of the inherent limitations of surface peroneal nerve stimulation might be addressed by implantable systems. Earlier implantable devices were plagued with electrode and stimulator displacement and/or failures requiring removal and reimplantation.[87,88] At present, two multichannel implantable peroneal nerve stimulators are available. A dual-channel device developed by the University of Twente and Roessingh Research and Development (The Netherlands) stimulates the deep and superficial peroneal nerves for ankle dorsiflexion and balanced eversion and inversion (**Figure 6**).[89] A four-channel device, developed at Aalborg University (Denmark), utilizes a nerve cuff with four tri-polar electrodes, oriented to activate different nerve fibers within the common peroneal nerve.[90] Both devices have the CE mark in Europe but are not yet available in the United States. Finally, an injectable microstimulator, which is percutaneously placed via a minimally invasive procedure, is also under investigation for the correction of foot drop.[70]

To address gait deviations due to deficits proximal to the ankle, several studies evaluated multichannel surface systems.[37–39] Although these systems were implemented as neuroprostheses, neuroprosthetic outcomes were not assessed. Instead, these studies focused on therapeutic or motor relearning effects and therefore were presented earlier.

Summary, clinical considerations, and future directions

At present, a hand neuroprosthesis may allow stroke survivors to complete a limited number of selected functional tasks. However, a clinically viable system that provides broad functional benefit is not yet available. The requirements for a

clinically viable hand neuroprosthesis for persons with hemiplegia are significant. The system must allow stroke survivors to perform bilateral tasks or provide significant assistance to the unaffected upper limb to facilitate completion of additional tasks. Because many stroke survivors have both proximal and distal weakness, the system must provide both proximal and distal function. The stroke survivor must be able to use the device with minimal effort to avoid triggering generalized hypertonia or "associated reactions." Thus, control paradigms that produce effortless movement of the impaired upper limb without compromising the function of the intact limb should be incorporated into the system.[91] Finally, the system must "turn off" overactive muscles to address the problems of spasticity, associated reactions, co-activations, co-contractions, and delay in termination of muscle contractions.[82]

In contrast to upper limb neuroprostheses, lower limb neuroprostheses are closer to clinical viability. Data suggest that surface peroneal nerve stimulators are superior to no device in improving overall mobility, may be equivalent to an ankle-foot-orthosis, and are ready for clinical implementation.[48,86,92] Implanted peroneal nerve stimulation devices are available in Europe and are likely to be equivalent to the surface devices with respect to function. They may be appropriate for those who experience significant improvement in mobility with the surface system but have difficulty with electrode placement, skin irritation, painful sensation of stimulation, or donning and doffing of the device. However, in view of limited data, more definitive recommendations must await the emergence of additional clinical experience. At present, multichannel, multijoint systems are clinically less accessible and are limited to investigative purposes.

Although the development of lower limb neuroprostheses for hemiplegia is further along than upper limb systems, several issues remain to be further elucidated. First, surface systems can be limited by discomfort and difficulty with electrode placement for reliable muscle contraction. Percutaneous and implanted systems may address these issues, but potential benefits must be tempered with the risks and costs associated with an invasive procedure. Second, the indications for the level of complexity required for a specific individual remain undefined. Some individuals will require complex multichannel systems, whereas simple dorsiflexion assist devices will suffice for others. Finally, clinical relevance must be established by evaluating the effects of the intervention on mobility and quality of life and by comparing the neuroprosthetic system to a comparable standard of care such as the ankle-foot orthosis.

Conclusions

The principal goal of rehabilitation management of persons with hemiparesis is to maximize quality of life. NMES systems bypass the injured central circuitry to activate neural tissue and contract muscles to provide function to what is otherwise a nonfunctioning limb or structure. Recent advances in clinical medicine and biomedical engineering make the clinical implementation of NMES systems to enhance the ADL and mobility function of persons with hemiparesis more feasible.

NMES for motor relearning in hemiplegia is a promising application of goal-oriented repetitive movement therapy. Although rigorous multicenter clinical trials to confirm effectiveness and fundamental studies to elucidate mechanisms are still needed, the approach is ready for clinical implementation in a limited scale for a select group of stroke survivors. Similarly, NMES for the treatment of shoulder subluxation and pain in hemiplegia has yielded encouraging results. The community is ready for confirmatory large-scale multicenter clinical trials and more invasive approaches are being investigated, but surface NMES may be clinically implemented in a select group of patients. The development of the hand neuroprosthesis for stroke survivors is in its infancy and must await further technical and scientific developments. Similarly, multichannel, multijoint lower limb neuroprostheses need further development. However, surface peroneal stimulators appear to be effective in improving hemiplegic gait and should be included in the clinical armamentarium.

Although this article focused on NMES, clinical practice is rarely limited to a single intervention. Thus, with the development of pharmacological interventions, neuronal regeneration, and other

innovations such as robotic therapy, mental imagery, virtual reality, and constraint-induced therapy, the future will likely embrace combination therapies to treat the myriad of motor dysfunction for persons with central nervous system paralysis.[4,93–99]

After decades of development, the clinical utility of NMES systems is becoming realized. By necessity, scientists and clinicians must continue to explore new ideas and improve upon the present systems. Future developments will likely be directed by consumers. In the present health care environment where cost is an overwhelming factor in the development and implementation of new technology, the consumer will become one of technology's greatest advocates. Finally, the usual drive toward greater complexity will be tempered by the practical issues of clinical implementation where patient and clinician acceptances are often a function of a tenuous balance between the "burden and cost" associated with using a system and the system's impact on the user's quality of life.

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