Advances in neuromuscular electrical stimulation for the upper limb post-stroke

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Objectives: To review current and explore future applications of neuromuscular electrical stimulation (NMES) to restore or retrain upper limb (UL) recovery after stroke.

Methods: Short summaries of NMES applications that have been investigated and a discussion of future research directions are presented.

Results: Neuromuscular electrical stimulation applications that have been developed and investigated to restore or retrain UL recovery after stroke include: cyclic NMES; triggered NMES which includes electromyogram-triggered NMES (EMG-NMES), positional feedback NMES, contralateral-triggered NMES, outcome-triggered NMES and accelerometer-triggered NMES; iterative learning control mediated NMES; and neuroprostheses such as the Bioness H200. Overall, published studies of these applications indicate that NMES can improve UL function after stroke, with improvements at the impairment level more common than improvements at the activity level. While EMG-NMES has been researched most widely and has the highest level of evidence to support its use, newer applications (e.g. outcome-triggered NMES, accelerometer-triggered NMES) appear promising, on the basis that key requirements for motor learning are employed.

Discussion: There are several areas for further research of NMES to achieve greater functional gains at the activity level than are currently achieved post-stroke. These include the use of NMES to retrain multijoint movements; and exploration of single- versus multichannel stimulation, cortical changes that occur after NMES, and NMES with other technologies. Use of NMES to restore or retrain UL function after stroke has come a long way and presents exciting challenges for research and clinicians in the future.

Keywords: Neuromuscular electrical stimulation, Stroke, Upper limb, Rehabilitation, Motor learning

Introduction

Neuromuscular electrical stimulation (NMES) refers to the stimulation of intact lower motor neurons to activate paralysed or paretic muscles and has been used to augment movement in stroke rehabilitation since the 1960s.¹ Clinical applications of NMES in stroke rehabilitation are generally considered as either therapeutic NMES or functional NMES (FES). Therapeutic NMES refers to the use of stimulation to minimize impairments and is viewed as a method to restore or retrain function post-stroke.² This can include the use of NMES to improve strength, increase range, reduce pain or improve components of hand function such as grasping. In contrast, FES or the use of stimulation as a neuroprosthesis is the use of electrical stimulation to replace lost function. As such, FES improves functional performance but only while receiving stimulation and is therefore a means of compensation rather than a training modality to restore lost function.² Neuroprostheses were initially developed for people with spinal cord injuries, but have been applied to stroke survivors, to enable them to perform specific functions or tasks such as gross grasping and key grasping.²,³ Applications of NMES often include components of both, for example a neuroprosthesis may be developed to improve function, but by definition replaces lost function. The purpose of this article is to review current and explore future applications of NMES that aim to restore or retrain upper limb (UL) function after stroke. Both therapeutic and functional applications will be discussed.

Cyclic NMES

Cyclic NMES was an early form of NMES used to promote UL recovery after stroke. With cyclic NMES, contraction of the paretic muscle occurs at
prescribed on and off periods for a preset duration. During cyclical applications, the stroke survivor needs only to be a passive recipient, as no voluntary activation of the target muscle is required. In early studies, cyclic NMES was used to repeatedly contract the target muscle to create movement through full range, which led to increased wrist and finger range of movement (ROM), strength and an improvement in impairment as measured by the Fugl–Meyer Assessment (FMA) but no change in activity. A later study reported an improvement in arm activity (Action Research Arm Test – ARAT) following cyclic NMES, however the change was not clinically meaningful (Table 1). To date there is no evidence that cyclic NMES has an effect on use of the arm in everyday tasks. When considering other impairments that occur after stroke, cyclic NMES of the rotator cuff has been found to be beneficial for the prevention of subluxation of the shoulder. When requirements for motor learning are considered, it would seem that unless cyclic NMES can be used to assist stroke survivors to work actively to achieve a task, it is unlikely to have an impact on UL function at the activity or participation level.

**Triggered NMES**

As the understanding of motor learning has expanded, methods to trigger NMES have been developed. These technologies include positional feedback NMES (PF-NMES), electromyogram-triggered NMES (EMG-NMES), contralateral-triggered NMES (CT-NMES), outcome-triggered NMES (OT-NMES) and accelerometer triggered NMES (AT-NMES), which will each be discussed in turn.

**Positional feedback NMES**

Positional feedback electrical stimulation was developed in the late 1970s and combined the provision of feedback of limb position with cyclic NMES. When the stroke survivor achieved a preset degree of wrist extension a cycle of NMES would commence. This application was developed to enhance the benefits that had been reported with cyclic NMES, by inclusion of strategies known to promote motor learning, such as goal setting and provision of auditory and visual feedback. Furthermore, as the stroke survivor triggers delivery of stimulation by initiating the movement, there is greater cognitive investment in task performance than with passive cyclical NMES and thus, greater motor learning is likely to occur. There is one study that has investigated the effectiveness of PF-NMES. This randomized controlled trial (RCT) compared PF-NMES in addition to conventional therapy to conventional therapy alone. After 4 weeks of PF-NMES training, an improvement in wrist extension torque and selective ROM were found. However, the effect of PF-NMES on activity and participation is not yet known (Table 1).

**Electromyogram-triggered NMES**

The next NMES advance was EMG-NMES, which combines electromyographic (EMG) biofeedback of muscle activation with the delivery of NMES to the same target muscle. With electrodes placed over the target muscle, the stroke survivor attempts the task. When the EMG signal from the target muscle exceeds a preset threshold, electrical stimulation is delivered to the target muscle to augment movement through full range. Similar to earlier technologies, EMG-NMES provides visual and auditory feedback on achievement of a preset goal. A further development allows EMG-NMES units to vary the level of muscle activity required to trigger delivery of stimulation based on performance. That is, if a stroke survivor is repeatedly unable to reach the preset threshold to trigger delivery of stimulation, the threshold level automatically reduces. Similarly, if a stroke survivor repeatedly triggers delivery of stimulation, the threshold level automatically rises. With subsequent attempts the stroke survivor must then increase the level of muscle activation to trigger delivery of stimulation. It is important to note that to use EMG-NMES, the stroke survivor must be able to initiate a contraction of the target muscle to trigger stimulation. Furthermore, as the stroke survivor must be actively involved in achievement of the preset goal, there is cognitive investment in the activity. On that basis, use of EMG-NMES should ultimately lead to greater motor learning than cyclic NMES, which requires no cognitive investment.

To date, most studies that have investigated EMG-NMES have examined its use to improve isolated movements of the wrist and fingers as part of both unilateral and bilateral training protocols. Two meta-analyses have investigated the effect of EMG-NMES on impairment and activity after stroke. One meta-analysis reported a significant overall mean effect size (0.82) in favour of EMG-NMES to improve wrist extension motor capabilities, as measured on both impairment (e.g. FMA) and activity (e.g. Box and Block Test – BBT) scales. More recently, a second meta-analysis reported a trend towards an improvement in impairment (e.g. reaction time and sustained muscle contraction) and activity (e.g. dexterity as measured by BBT) in favour of EMG-NMES over conventional therapy. Across the studies included in the meta-analyses, training volume and duration ranged from as little as 6 hours over 2 weeks to as much as 96 hours over 16 weeks. Studies in these reviews predominantly investigate stroke survivors with mild to moderate paresis in the chronic stage of recovery, with notable exceptions that have investigated stroke survivors with moderate to severe paresis in the acute stage of recovery. Long-term benefits of this approach are not known as no studies included adequate follow-up.

More recently, applications have been developed that use EMG-NMES to retrain multijoint movements.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Level</th>
<th>Method*</th>
<th>NMES and dosage</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ada et al. (2002)</td>
<td>I</td>
<td>n=5 RCTs</td>
<td>Cyclic NMES</td>
<td>There is strong evidence that electrical stimulation can prevent subluxation. There is strong evidence that electrical stimulation reduces subluxation. Significant overall effect size (0.82) in favour of EMG-NMES to improve wrist extension motor capabilities.</td>
</tr>
<tr>
<td>Bolton et al. (2004)</td>
<td>I</td>
<td>n=3 RCTs</td>
<td>EMG-NMES</td>
<td>There is limited evidence that EMG-NMES provides a large beneficial effect on impairment and activity. There is limited evidence that PF-NMES has any effect on impairments and no evidence that it has an effect on activity.</td>
</tr>
<tr>
<td>Hayward et al. (2010)</td>
<td>I</td>
<td>n=7 RCTs</td>
<td>EMG-NMES</td>
<td>There is insufficient evidence that electrical stimulation reduces subluxation.</td>
</tr>
<tr>
<td>Melink et al. (2009)</td>
<td>I</td>
<td>n=8 RCTs</td>
<td>EMG-NMES</td>
<td>There is insufficient evidence that EMG-NMES can improve muscle strength and dexterity.</td>
</tr>
<tr>
<td>Van Peppen et al. (2004)</td>
<td>I</td>
<td>EMG-NMES</td>
<td>Cyclic NMES</td>
<td>There is limited evidence that EMG-NMES reduces subluxation. There is insufficient evidence that EMG-NMES can improve muscle strength and dexterity.</td>
</tr>
<tr>
<td>Alon et al. (2007)</td>
<td>II</td>
<td>n=15</td>
<td>Exp: PFST</td>
<td>There was a significant between group difference in favour of the experimental group for impairment (motor control as measured by the FMA) and activity (BBT, JTLOT).</td>
</tr>
<tr>
<td>Barker et al. (2008)</td>
<td>II</td>
<td>n=33</td>
<td>Exp: SMART Arm</td>
<td>Both experimental groups displayed a reduction in impairment (strength, force) and an improvement in activity (distance reached, MAS upper arm function item).</td>
</tr>
<tr>
<td>Bowman et al. (1979)</td>
<td>II</td>
<td>n=30</td>
<td>Exp: CT alone</td>
<td>Both experimental groups displayed significantly greater improvements compared to the control. Gains were maintained at 2-month follow-up. Both experimental groups displayed an improvement in impairments of wrist extension torque and ROM. The experimental group displayed gains, which were significantly greater than the control group.</td>
</tr>
<tr>
<td>Cauraugh et al. (2003)</td>
<td>II</td>
<td>n=34</td>
<td>Exp: CT alone</td>
<td>The experimental group displayed greater improvements in impairment (reaction time, sustained muscular contraction) and activity (BBT) compared to the control group. Block and random practice protocols were found to be equally effective.</td>
</tr>
<tr>
<td>Cauraugh et al. (2002)</td>
<td>II</td>
<td>n=25</td>
<td>Exp: CT alone</td>
<td>The experimental groups displayed greater improvements in impairments (reaction time and sustained muscle contraction) compared to the unilateral protocol.</td>
</tr>
<tr>
<td>Chae et al. (1998)</td>
<td>II</td>
<td>n=28</td>
<td>Exp: CT alone</td>
<td>There was a significant between group difference for impairment (FMA) at post-intervention, and follow-up (4 and 12 weeks). There was no between group difference at any time-point for activity (FIM).</td>
</tr>
<tr>
<td>Chan et al. (2009)</td>
<td>II</td>
<td>n=20</td>
<td>Exp: CT alone</td>
<td>The experimental group displayed greater improvements in impairment (FMA, active ROM wrist extension) and activity (FTHUE) compared to the control group.</td>
</tr>
<tr>
<td>de Kroon et al. (2008)</td>
<td>II</td>
<td>n=22</td>
<td>Exp: CT alone</td>
<td>Both groups displayed improvements in impairment (FMA) and activity (ARAT), however these improvements did not reach clinical relevance and there were no between group differences.</td>
</tr>
</tbody>
</table>

Notes:
- **Table 1** Summary of the evidence. Levels are classified according to the Australian NHMRC Guidelines.
- **Method**: Cyclic NMES, EMG-NMES, PFST
- **Outcome**: There is strong evidence that electrical stimulation can prevent subluxation. There is strong evidence that electrical stimulation reduces subluxation. Significant overall effect size (0.82) in favour of EMG-NMES to improve wrist extension motor capabilities.
Table 1 Continued

<table>
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</tr>
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<tbody>
<tr>
<td>Fransisco et al. (1998)22</td>
<td>II</td>
<td>n=9</td>
<td>Exp: EMG-NMES to extensor carpi radialis + CT</td>
<td>The EMG-NMES group displayed a significant reduction in impairment (B-FMA) and an increase in activity (FIM) compared to the control group.</td>
</tr>
<tr>
<td>Gabr et al. (2005)23</td>
<td>II</td>
<td>n=27</td>
<td>Exp: EMG-stim 80%</td>
<td>After EMG-stim, there was a reduction in impairment (FMA) but no change in activity (ARAT). Gains were lost at follow-up. After a home exercise program, there were no changes in impairment (FMA) or activity (ARAT).</td>
</tr>
<tr>
<td>Hayward et al. (2008)24</td>
<td>II</td>
<td>n=5</td>
<td>Exp: SMART Arm + CT-NMES to triceps brachii + CT</td>
<td>Both groups displayed improvements in impairment (triceps strength, shoulder external rotation ROM) and activity (MAS upper arm function), however, there was no difference between those trained with compared to without OT-NMES. No gains were made in impairment or activity in either group.</td>
</tr>
<tr>
<td>Hemmen and Seelen (2007)25</td>
<td>II</td>
<td>n=27</td>
<td>Exp: EMG-NMES with movement imagery + CT</td>
<td>Hydrotherapy group displayed improvements in muscle strength (H200), activity (H200), and quality of life (H200) compared to the control group.</td>
</tr>
<tr>
<td>Kimberley et al. (2004)26</td>
<td>II</td>
<td>n=16</td>
<td>Exp: EMG-NMES + cyclic NMES to wrist and finger extensors</td>
<td>Hydrotherapy group displayed improvements in muscle strength (H200), activity (H200), and quality of life (H200) compared to the control group.</td>
</tr>
<tr>
<td>Powell et al. (1999)6</td>
<td>II</td>
<td>n=60</td>
<td>Exp: cyclic NMES to wrist extensors + CT</td>
<td>The cyclic NMES group displayed a significant reduction in impairment (strength) and improvement in activity (ARAT) compared to CT alone. There were no differences between the two groups at 24-week follow-up.</td>
</tr>
<tr>
<td>Shin et al. (2008)27</td>
<td>II</td>
<td>n=14</td>
<td>Exp: stimulation to wrist extensors</td>
<td>The EMG-NMES group displayed significant improvements in impairment (strength) activity (BBT), and corticospinal activation (as seen on fMRI) compared to the control group.</td>
</tr>
<tr>
<td>Mann et al. (2008)28</td>
<td>III</td>
<td>n=15</td>
<td>Exp: AT-NMES to wrist, finger and thumb extensors and triceps</td>
<td>At post-intervention a reduction in spasticity and improvement in activity (ARAT) was reported. Gains were maintained at 12-week follow-up.</td>
</tr>
<tr>
<td>Pandyan et al. (1997)5</td>
<td>III</td>
<td>n=11</td>
<td>Exp: cyclic NMES to wrist extensors</td>
<td>Cyclic NMES facilitated temporary improvements in impairments of wrist posture and passive range of extension. There were no significant gains for resistance to passive movement. Gains were mostly lost at 2-week follow-up.</td>
</tr>
<tr>
<td>Ring and Rosenthal (2005)30</td>
<td>III</td>
<td>n=22</td>
<td>Exp: neuroprosthesis (H200) wrist/thumb extension and flexors + CT</td>
<td>The experimental group (H200) displayed significantly greater improvements in impairments (spasticity, active ROM for the shoulder and wrist) and activity (hand test scores of JTHFT and BBT) than the control group.</td>
</tr>
<tr>
<td>Alon et al. (2003)2</td>
<td>IV</td>
<td>n=77</td>
<td>Exp: neuroprosthesis (H200) wrist/thumb extension and flexors</td>
<td>At post-intervention a reduction in impairment (pain and spasticity of shoulder, elbow, wrist, finger and thumb) and improvement in activity (JTHFT, JTHOLT, BBT, 9-HPT) was reported.</td>
</tr>
<tr>
<td>Alon et al. (1998)30</td>
<td>IV</td>
<td>n=21</td>
<td>Exp: neuroprosthesis (H200) wrist/thumb extension and flexors</td>
<td>Training was performed for 20 hours per day for 6 weeks. The experimental group (H200) improved impairments of active ROM of elbow flexion, wrist flexion, wrist extension, and UL spasticity.</td>
</tr>
<tr>
<td>Dunning et al. (2008)31</td>
<td>IV</td>
<td>n=1</td>
<td>Exp: neuroprosthesis (H200) wrist/thumb extension and flexors</td>
<td>At post-intervention a reduction in impairment (FMA) and improvement in activity (ARAT, AMAT), participation (SIS, MAL) and quality of life was reported.</td>
</tr>
<tr>
<td>Hedman et al. (2007)32</td>
<td>IV</td>
<td>n=1</td>
<td>Exp: CT-NMES (hand switch) to deltoid and triceps brachii</td>
<td>At post-intervention an increase in activity (ARAT) and quality of life were reported. No improvement in impairment (FMA) was demonstrated.</td>
</tr>
</tbody>
</table>

* Reference Level Method: NMES and dosage Outcome

**Table Note:**
- Exp: Experimental
- Con: Control
- CT: Control
- HEP: High-intensity exercise program
- SMART Arm: Self-management and rehabilitation arm training
- OT-NMES: Otis-NMES
- AT-NMES: Adaptive-TNMES
- H200: Hydrotherapy group
- JTHFT: Joints-hand finger test
- BBT: Box-and-block test
- JTLOLT: Joint test of lower limb
- SIS: Stroke impact scale
- MAL: Modified arm limitation
<table>
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<th>NMES and dosage</th>
<th>Level Method*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hill Hermann et al. (2008)</td>
<td>Exp: neuroprosthesis (H200) wrist/finger extensors and adductors during ADL retaining flexors, thumb flippers and abductors during ADL retaining flexors</td>
<td>Chronic</td>
<td>At post-intervention a reduction in impairment (FMA) and improvement in activity (ARAT, AMAT) was reported.</td>
</tr>
<tr>
<td>Hughes et al. (2009)</td>
<td>Exp: ILC mediated NMES to triceps brachii at robot workstation 18 one-hour sessions 56 hours over 12 weeks</td>
<td>Chronic</td>
<td>At post-intervention an improvement in activity (BBT) was reported.</td>
</tr>
<tr>
<td>Knutson et al. (2009)</td>
<td>Exp: CT-NMES via hand glove to wrist and finger extensors 3 months</td>
<td>Chronic</td>
<td>An increase in intervention duration from 6 to 12 weeks led to greater improvements in impairment (finger motor control, finger extension ROM, finger strength) and activity (BBT). Gains were mostly lost at follow-up.</td>
</tr>
<tr>
<td>Knutson et al. (2007)</td>
<td>Exp: CT-NMES via hand glove to wrist and finger extensors 90 hours over 6 weeks</td>
<td>Chronic</td>
<td>At post-intervention an improvement in impairment (FMA, hand) but not activity was reported, however, subjects were then able to participate in modified constraint induced movement therapy.</td>
</tr>
<tr>
<td>Merletti et al. (1975)</td>
<td>Exp: neuroprosthesis with stimulation to finger, wrist and elbow extensors</td>
<td>Chronic</td>
<td>After use of the neuroprosthesis, 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.</td>
</tr>
<tr>
<td>Page et al. (2009)</td>
<td>Exp: neuroprosthesis (H200) wrist/finger extensors and adductors 168 hours over 12 weeks</td>
<td>Chronic</td>
<td>At post-intervention an improvement in impairment (finger motor control, finger extension ROM, finger strength) and activity (BBT) was reported. Gains were mostly lost at follow-up.</td>
</tr>
<tr>
<td>Page et al. (2010)</td>
<td>Exp: neuroprosthesis with stimulation to finger, wrist and finger extensors and adductors 3 months</td>
<td>Chronic</td>
<td>Exp: EMG-NMES to wrist extensors 46.5 hours over 8 weeks</td>
</tr>
<tr>
<td>Vodovnik et al. (1973)</td>
<td>Exp: neuroprosthesis with stimulation to wrist and finger extensors 20 minutes per day</td>
<td>Chronic</td>
<td>Arm activity increased in a subset of patients who had greater motor activity at the beginning of training (BBT &gt; 4). Functional improvement was paralleled by an increase in ipsilesional sensorimotor cortical activation.</td>
</tr>
</tbody>
</table>

Notes: *Stage of chronicity is based on each articles classification.
9-HPT, 9 Hole Peg Test; ARAT, Action Research Arm Test; AT, Action Timing Test; AT-NMES, accelerometer-triggered neuromuscular electrical stimulation; BBT, Box and Block Test; B-FMA, Brunnstroem Fugl-Meyer Assessment - finger; CCT, clinical controlled trial; con, control; CT, conventional therapy; CT-NMES, contralateral-triggered neuromuscular electrical stimulation; EMG-NMES, electromyogram-triggered neuromuscular electrical stimulation; FMA, Fugl–Meyer Assessment; fMRI, functional magnetic resonance imaging; FTHUE, Functional Test for the Hemiplegic Upper Extremity; ILC, iterative learning control; JTHFT, Jebsen–Taylor Hand Function Test; JTLOLT, Jebsen–Taylor Light Object Lift Task; JTHOLT, Jebsen–Taylor Heavy Object Lift Task; MAL, Motor Activity Log; MAS, Motor Assessment Scale; NMES, neuromuscular electrical stimulation; OT-NMES, outcome-triggered neuromuscular electrical stimulation; PF-NMES, positional feedback neuromuscular electrical stimulation; PMT, physiotherapy control trial; RCT, randomized control trial; ROM, range of movement; SIS, Stroke Impact Scale; stim, stimulation; UL, upper limb.
of the UL via multichannel stimulation or by combining it with an ancillary device to guide the movement (Table 1). Von Lewinski and colleagues used multichannel EMG-NMES to retrain UL tasks (e.g., grasp and release, reaching) in a group of nine stroke survivors (Table 1). At the completion of 8 weeks of training a significant gain in activity measures (ARAT and BBT) was only evident in those stroke survivors who displayed higher levels of activity at baseline (BBT score >4). Similarly, Barker and colleagues found that 4 weeks of training with EMG-NMES in conjunction with an ancillary device, the SensoriMotor Active Rehabilitation Training (SMART) Arm, led to an improvement in impairment (strength and force) and activity (upper arm function and reach distance) at post-intervention and at 2-month follow-up assessments. However, these improvements were not significantly different to those who received SMART Arm training alone. Stroke survivors included in both these studies had severe paresis and were in the chronic stage of recovery. As minimal muscle activation is required to trigger the delivery of EMG-NMES, it is reasonable to assume that EMG-NMES would be most suitable for stroke survivors with severe paresis rather than stroke survivors with mild or moderate paresis, who have a greater capacity to actively perform training. However, anecdotal findings within the SMART Arm study suggested that EMG-NMES may not be the optimal method for triggering stimulation for stroke survivors with severe paresis as in some cases, ‘trick’ methods were used to trigger delivery of stimulation (e.g., co-contraction) that were not consistent with the desired movement outcome.

The first RCT to compare cyclic NMES and EMG-NMES was published recently. This study reported improvements in impairment (FMA) and activity (ARAT) following both cyclical and EMG-NMES, but there were no significant differences between the two groups. As the intervention involved single-joint movements that required little cognitive engagement in the task, it is perhaps not surprising that no differences were found between groups.

There are a growing number of studies that have investigated cortical changes in response to EMG-NMES using functional magnetic resonance imaging (fMRI) (Table 1). An earlier study found that a combined protocol of 60 hours of EMG-NMES and cyclic NMES over 3 weeks did not increase cortical activation in the area of the somatosensory cortex. The authors suggested that the cortical area activated did not increase due to a lack of active engagement in cortical problem solving. In contrast, a study by Shin and colleagues, who provided 50 hours of EMG-NMES training over 10 weeks, reported a shift in activation from the ipsilateral sensorimotor cortex to the contralateral sensorimotor cortex for the hand. Shin and colleagues suggested that longer duration of EMG-NMES therapy and greater task complexity during fMRI scanning were possible reasons for the improved cortical activation, compared with the findings of Kimberley and colleagues. In support of this argument, a more recent study found an increase in ipsilateral cortical activation of the sensorimotor cortex, in only those who displayed improvement at the activity level of function, after participation in 27 hours of therapy over 8 weeks. Therefore, whilst it appears that EMG-NMES has the potential to increase cortical activation, further controlled studies are required to accurately define the location and pattern of these changes.

Contralateral-triggered NMES

More recently, a number of case studies have investigated use of a ‘contralateral trigger’ to control delivery of stimulation. One application uses a hand-switch operated by the less affected hand, to allow stroke survivors to trigger delivery of stimulation during reaching and manipulation tasks at the point in task performance where they perceive it is required. A single case study reported an improvement in activity (ARAT) and participation (Motor Activity Log Quality of Movement), but no change in impairment (FMA) after 6 weeks of training and gains were maintained at follow-up (Table 1). More recently, Knutson and colleagues experimented with a contralateral hand glove (Fig. 1), which controls the intensity of stimulation of finger and wrist extension and thus the degree of impaired hand opening. When the glove on the unaffected hand is opened and closed, proportional impedance changes in the sensors in the glove that detect finger movement, modulate the stimulus intensity delivered to the affected hand. In a series of three case studies, a training protocol of 90 hours over 6 weeks was found to reduce impairments (finger extension ROM, strength) and improve activity (BBT) (Table 1). When the treatment duration was increased to...
12 weeks, greater gains were reported. However, both studies reported a decline in performance at follow-up. In these examples of CT-NMES, the unimpaired hand is engaged, which could be considered a disadvantage, as the less affected hand is unavailable for use. In another RCT, which used a motion sensor on the unaffected index finger to trigger hand opening, bilateral tasks were trained. This study reported improvements in both impairment (active ROM, FMA) and activity (Functional Test for the Hemiplegic Upper Extremity), however no follow-up was performed. Thus, this study demonstrated positive benefits of CT-NMES when used during bilateral task training.

**Outcome-triggered NMES**

Due to the difficulties in achieving outcomes at the activity level of function when using EMG-NMES and the continual development of technology, other methods of triggering stimulation have been recently developed. One such method is OT-NMES, which refers to the delivery of stimulation when the stroke survivor reaches a preset distance in the direction of the goal. The distance to be reached to trigger delivery of a cycle of stimulation increases if the stroke survivor is repeatedly successful and reduces if unsuccessful. The key advantages of OT-NMES over EMG-NMES are that the requirements for delivery of stimulation are consistent with the desired movement outcome and only movements in the direction of the goal are rewarded. As such, this method of stimulation could lead to retraining of more normal patterns of movement than previous methods of stimulation.

Outcome-triggered NMES was developed for use with the SMART Arm (Fig. 2), a non-robotic device, designed to retrain reaching in stroke survivors with severe paresis. The SMART Arm was developed with motor learning principles in mind and thus includes strategies to reduce the degrees of freedom to control, feedback on performance that is consistent with the movement outcome and incremental increases in load and distance to be reached. Preliminary findings from a pilot study have found that SMART Arm training with OT-NMES reduces impairments (triceps strength, shoulder external rotation ROM) and improves activity [upper arm function (Motor Assessment Scale)] (Table 1). However, these changes were similar to those found for stroke survivors who received SMART Arm training alone. No comparison was made to dose-matched conventional therapy. Thus, larger RCTs are required to investigate use of the SMART Arm with compared to without OT-NMES and to dose-matched conventional therapy.

**Accelerometer-triggered NMES**

Another method developed to trigger NMES to enable task training is AT-NMES. In this application, movement of the arm in the direction of the goal triggers delivery of stimulation. As the stroke survivor attempts the task, a tilt sensor detects the volitionally initiated active movement. When this movement reaches a preset threshold, stimulation is delivered to augment unavailable movements, e.g. shoulder flexion is used to trigger elbow, wrist and finger extension. An advantage of this method of stimulation is that it can stimulate several muscles of the UL (wrist, finger and thumb extensors and elbow extensors), to enable reach to grasp and release activation patterns. This method of stimulation has been developed for use with the Odstock two-channel programmable stimulator unit (Fig. 3). Preliminary findings suggest that...
AT-NMES can reduce impairment (spasticity) and improve activity (ARAT) in the chronic stage of recovery and that gains are largely maintained at 12-week follow-up (Table 1). The authors suggest that the ‘on demand’ nature of the stimulation during task practice was a key factor in participant satisfaction and use of the stimulation to perform everyday tasks in everyday environments. However, large RCTs are required which compare AT-NMES to conventional therapy at all stages of recovery.

Iterative Learning Control-Mediated NMES (ILC-NMES)

Most recently, ILC-NMES has been developed to enable stroke survivors to perform reaching tasks at a robot workstation, while providing feedback on performance. During each reaching attempt, information on the accuracy of tracking and force exerted during tracking are used by the ILC to alter the amount of stimulation delivered. As a result, progression of practice occurs automatically ensuring the stroke survivor is always working at the upper limit of their ability. To date, a case series demonstrated that ILC-NMES reduced impairment (FMA), but did not improve activity (ARAT), thus studies with larger numbers and of higher quality are required (Table 1). Perhaps the major limitation for this method of stimulation will be the cost associated with use of a robotic device.

Neuroprostheses

In the early 1970s the first neuroprostheses for the UL were developed to enable grasping and reaching. Variable improvements in grasp and release were reported after participation in training using these neuroprostheses. The key limitation of this early research was that investigations were small case series, which did not use rigorous design methods. Since this time, the main neuroprosthesis developed for stroke survivors has been the Bioness H200, which is a hybrid NMES system (Fig. 4). This device has various training modes, such as cyclic NMES for hand opening and closing and contralateral-triggered cyclic NMES to augment grasp and release to enable stroke survivors to perform activities of daily living. As such, it is being used primarily to restore function and is one of the few recent developments, which is available commercially. The H200 has been used with stroke survivors with mild, moderate and severe paresis to undertake repetitive task-specific practice. When considering mild to moderate paresis, both impairment (spasticity, active ROM) and hand activity (BBT, JTHFT). Similarly, in a number of single case studies of stroke survivors with no active extension of the wrist or fingers, reduced impairment (FMA), increased activity (ARAT, Arm Motor Ability Test) and participation (Stroke Impact Scale and Motor Activity Log) was demonstrated. More recently, it has been found that repetitive task-specific training for 20 hours over 8 weeks can lead to an increase in cortical activation, which the authors believe was associated with an increased use of the arm. Based on these findings the authors suggest that the H200 could be used as a ‘gateway’ or ‘bridge’ to participation in therapy regimes that demand greater volitional activity than is available to the stroke survivor with severe paresis, in particular constraint induced movement therapy. This indicates that neuroprostheses can be used to not only replace, but also retrain UL function.

Future Directions

While advances have been made in the field of NMES, there are several areas that require further development to ensure that long-term changes in UL function occur following use of NMES after stroke. Firstly, many studies investigate the efficacy of NMES when applied to isolated muscles, to perform single-joint movements. When the principle of task-specificity is considered, it would seem unlikely that an improvement at the activity level would occur unless NMES is used to achieve multijoint movements directed at a functional goal. As such, future NMES investigations should consider use of goal-directed training protocols.

When considering goal-directed training protocols it is important to compare the benefits of single-channel
stimulation with multichannel stimulation to determine if more channels lead to greater functional outcomes. While a multichannel stimulation set-up would seem most appropriate for goal-directed tasks that require the use of multiple muscles in a multijoint movement, it does present greater challenges, such as: (i) development of appropriate timing of stimulation onset for each muscle, which is consistent with the normal pattern of movement; and (ii) development of appropriate methods of triggering delivery of stimulation which does not cause an adverse reaction e.g. co-contraction. In addition, when more stimulation is provided is the stroke survivor more likely to be a passive rather than an active participant and at what point does NMES shift from being a modality that restores lost function to a modality that replaces lost function. One could assume there is a threshold level at which sensory input becomes non-specific and therefore cannot be interpreted at a higher level. Thus, there is a need to determine the critical number of muscles to be stimulated for UL tasks, which maximizes both active participation and achievement of functional tasks.

There are several areas for further research that will add to the evidence base for the effect of NMES on motor learning. More research is required to understand the influence of the various types of NMES on cortical activity. To further demonstrate motor learning, longer follow-up periods are also required. But, perhaps most importantly, there is a need to investigate use of the arm in everyday tasks. Once this occurs, practice will be undertaken as part of the stroke survivors’ everyday routine, thus increasing task-specificity as well as volume of training, both of which are required to experience any lasting effect on function.

It is yet to be determined which stroke survivors will benefit most from use of NMES. As more people are surviving stroke with more severe disabilities, the role of NMES in recovery of the UL for stroke survivors with severe paresis, needs to be explored. As NMES can be used to supplement available muscle activity to achieve movement through full range, NMES may be most beneficial to those stroke survivors who ‘do not have enough movement to work with.’49 This also highlights the need to further investigate the role of NMES as a ‘bridge’ to participation in repetitive task-specific training that demands greater volitional activity than is available to the stroke survivor with severe paresis.38 This may offer the opportunity for this group of stroke survivors to make changes not only in impairment but also in activity and participation. Furthermore, the majority of investigations to date have included stroke survivors in the chronic stage of recovery. As the acute stage of recovery is the ‘optimal’ time window for recovery, it is possible that the benefits may be greater for stroke survivors in the acute rather than the chronic stage of recovery when there are fewer physical limitations to be overcome and greater potential for brain plasticity.50 Thus, further high quality clinical trials and clinical prediction studies are required to identify which stroke survivors will benefit most from NMES-mediated rehabilitation.

There is also scope for further development of UL NMES devices. Wireless technology, which is currently used in lower limb NMES applications, could provide a more versatile, smaller and cosmetically appealing UL device. In addition, if devices are to be used independently by stroke survivors, consideration must be given to performance-based automatic progression of practice that occurs in a timely and appropriate manner. There is also scope for use of NMES in conjunction with other technologies and devices such as robotics, the SMART Arm and virtual reality, or with techniques to prime cortical excitability such as repetitive transcranial magnetic stimulation or transcranial direct current stimulation.51 If NMES is to be used with an ancillary technology or intervention, there is a need to confirm that functional improvements are above and beyond those achieved with conventional therapy alone, use of NMES alone or with use of the ancillary technology alone.

Several NMES applications are currently in the research phase (e.g. OT-NMES, AT-NMES) of development. Applications that are currently in clinical use include cycle-NMES, EMG-NMES and the H200 neuroprostheses. The uptake of these applications in the clinical setting is likely to be dependent on several factors, which are yet to be thoroughly explored. Barriers to clinical use of NMES may include negative perceptions regarding the application and effectiveness of NMES by staff, patients and their families, cost of purchasing new equipment, training requirements for use of NMES and limited evidence to support the use of NMES. A major facilitator for use of NMES may be the potential to reduce hands on therapy time11 and as such its potential as a cost-effective method for promoting UL recovery after stroke. The assumption is made that as NMES enables stroke survivors to practise independently, they require minimal assistance from a therapist to achieve the volume of practice required to promote a permanent change in UL function. However, as there are currently no cost-effectiveness studies to confirm this assumption, these cost analyses are required before therapists can advocate for funding for purchase of NMES devices to be used alone or in conjunction with other UL technologies.

**Conclusion**

Over the last two decades there has been a rapid expansion of NMES devices developed to restore or retrain UL function after stroke. While outcomes have been largely restricted to impairments, more recently there have been promising findings with...
regards to activity. As yet, increased use of the arm in everyday tasks in response to training using NMES has not been demonstrated. Ultimately, the widespread utilization of NMES will be more likely if cost-effectiveness studies are undertaken, which demonstrate how NMES can reduce the burden on the health care system.

References
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