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Kotaro Takeda, Genichi Tanino & Hiroyuki Miyasaka

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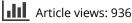


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#### REVIEW

# Review of devices used in neuromuscular electrical stimulation for stroke rehabilitation

## Kotaro Takeda<sup>1</sup> Genichi Tanino<sup>2</sup> Hiroyuki Miyasaka<sup>1,3</sup>

<sup>1</sup>Faculty of Rehabilitation, School of Health Sciences, <sup>2</sup>Joint Research Support Promotion Facility, Center for Research Promotion and Support, Fujita Health University, Toyoake, Aichi, <sup>3</sup>Department of Rehabilitation, Fujita Health University Nanakuri Memorial Hospital, Tsu, Mie, Japan

Correspondence: Kotaro Takeda Faculty of Rehabilitation, School of Health Sciences, Fujita Health University, 98-1 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan Tel +81 562 93 9000 Fax +81 562 93 6817 Email ktakeda@fujita-hu.ac.jp



**Abstract:** Neuromuscular electrical stimulation (NMES), specifically functional electrical stimulation (FES) that compensates for voluntary motion, and therapeutic electrical stimulation (TES) aimed at muscle strengthening and recovery from paralysis are widely used in stroke rehabilitation. The electrical stimulation of muscle contraction should be synchronized with intended motion to restore paralysis. Therefore, NMES devices, which monitor electromyogram (EMG) or electroencephalogram (EEG) changes with motor intention and use them as a trigger, have been developed. Devices that modify the current intensity of NMES, based on EMG or EEG, have also been proposed. Given the diversity in devices and stimulation methods of NMES, the aim of the current review was to introduce some commercial FES and TES devices and application methods, which depend on the condition of the patient with stroke, including the degree of paralysis.

**Keywords:** functional electrical stimulation, therapeutic electrical stimulation, EMG-triggered stimulation, brain–machine interface, brain–computer interface

## Introduction

The clinical application of electrical stimulation is historical, with live torpedo fish being used to deliver electric current for pain treatment ~2,000 years ago. In more recent years, several implanted and non-implanted electrical stimulation devices have been widely used in a clinical setting. Examples of implanted devices include the following: artificial cardiac pacemakers, which are placed under the skin in the chest or belly to electrically stimulate cardiac muscle to control heart rhythms;<sup>1</sup> cochlear implants placed in the inner ear, which electrically stimulate the auditory nerve corresponding to the frequency of the sound;<sup>2</sup> deep brain stimulation, which delivers electrical impulses to specific brain areas to reduce tremor in Parkinson's or other movement disorders;<sup>3,4</sup> spinal cord stimulators, which send a mild electric current to nerves in the spinal cord to mask a pain signal;<sup>5</sup> and non-implanted devices, including transcutaneous electrical nerve stimulation (TENS) and transcranial direct current stimulation (tDCS), which deliver electrical stimulation via electrode pads on the skin and scalp, respectively. For TENS, electrodes are often placed on the area of skin where the pain is present, and a low-voltage electrical current is delivered to treat a variety of painful conditions.<sup>6,7</sup> tDCS is a noninvasive brain stimulation technique in which a weak direct current (1-2 mA) is applied from electrodes to the scalp.<sup>8</sup> which excites or inhibits cortical excitability,9 depending on the polarity of electrode. In recent years, tDCS has been extensively studied in clinical neuropsychiatry and rehabilitation.<sup>10,11</sup>

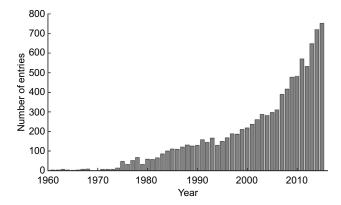
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Artificially controlling human muscles or muscle nerves by neuromuscular electrical stimulation (NMES) is widely used in clinical rehabilitation for spinal cord injury and stroke, which often impair upper motor neurons and/or their neuronal pathways to lower motor neurons, consequently leading to paralysis of upper and/or lower limbs. Unilateral paralysis (ie, hemiparesis or hemiplegia) is particularly seen in many patients who survive a stroke. Recovery from the motor impairments may occur over weeks and months. The poststroke motor recovery is complex due to genetic, pathophysiologic, sociodemographic, and clinical factors.<sup>12</sup> NMES is one of the therapeutic interventions that has been developed to try to induce the motor recovery.13 NMES can be used to stimulate the neuromuscular activity of the paretic limbs after stroke because normal electrical excitability often remains in lower motor neurons and their innervated muscles. Research on the use of NMES for rehabilitation has been increasing (Figure 1) since 1961, when Liberson et al<sup>14</sup> stimulated the tibialis anterior to dorsiflex the ankle joint of patients with hemiplegia.

The purpose of NMES can be broadly classified into the following categories in general: functional electrical stimulation (FES), which, in a narrow sense, compensates for voluntary motion, and therapeutic electrical stimulation<sup>15</sup> (TES), with the aim of muscle strengthening or recovery from paralysis. Although there are both implanted<sup>16–18</sup> and non-implanted<sup>19</sup> NMES devices, this review mainly focused on the non-implanted type that uses surface electrodes for stimulation and is often applied for stroke rehabilitation.



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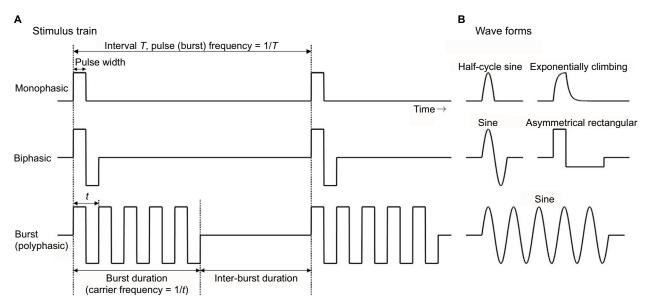
**Figure I** Results of a PubMed (service of the US National Library of Medicine [https://www.ncbi.nlm.nih.gov/pubmed/]) search for ("electrical stimulation" OR "electrical muscle stimulation" OR "electrical nerve stimulation" OR FES OR NMES) AND (stroke OR "cerebrovascular disease" OR hemiplegic OR hemiparetic OR hemiparesis OR paralysis OR rehabilitation).

Abbreviations: FES, functional electrical stimulation; NMES, neuromuscular electrical stimulation.

## Wave forms for NMES

In NMES therapy, various stimulation parameters are used in the devices. Generally, as shown in Figure 2A, the waveform of the stimulation pulse may be monophasic, biphasic, and burst (polyphasic) waves. The pulse width is usually  $150-300 \ \mu$ s, while the current intensity is dozens of milliampere. The pulse waveforms can be subdivided into rectangular waves, sine waves, etc. Biphasic waves, in contrast, can be further distinguished as symmetrical/asymmetrical or balanced/imbalanced (Figure 2B).

Muscle torque, fatigue, or pain induced by NMES depends on the wave parameters. Pain depends on the total amount of electrical charge delivered to the tissue.<sup>20</sup> Petrofsky



#### Figure 2 Parameters of NMES.

Notes: (A) Monophasic, biphasic, and polyphasic stimulus train. (B) Examples of wave forms. A specific stimulus, burst sine wave of carrier frequency of 2,500 Hz and burst and inter-burst duration of 10 ms is called a Russian current. Abbreviation: NMES, neuromuscular electrical stimulation.

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et al<sup>21</sup> showed that sine wave stimulation produced greater muscle strength, with less pain, in comparison with rectangular or polyphasic waves. Laufer et al<sup>22</sup> also reported that monophasic and biphasic waveforms are more advantageous than burst waveforms and argued that the electrically induced fatigue is affected by the number of cycles per second, rather than the number of bursts per second.<sup>23</sup> Therefore, monophasic or biphasic waveforms, rather than burst waveforms, may be more suitable for the clinical use of NMES. In fact, many NMES devices for stroke rehabilitation use the former.

## **Functional electrical stimulation**

Although FES is a method that compensates for voluntary motion in a narrow sense, it cannot strictly be distinguished from TES. Many studies have demonstrated that rehabilitation training with FES improves activity of patients with stroke.24 The WalkAide system (Innovative Neurotronics, Inc., Austin, TX, USA)25 and NESS L300 (Bioness Inc., Valencia, CA, USA)<sup>26</sup> are examples of typical commercial FES devices that are available for paralyzed lower limbs after stroke (Figures 3 and 4A, respectively). These devices are commonly used against forefoot dropping, which is a gait abnormality that occurs due to paralysis of the muscles of the lower leg (decreased ankle dorsiflexion). The drop foot during the swing phase (non-weight-bearing phase) of gait is one of the risk factors for a fall.<sup>27</sup> In these devices, surface electrodes for stimulation are fixed by a cuff to the leg below the knee. Electrical stimulation is delivered during the



#### Figure 3 WalkAide system.

**Notes:** Surface electrode pads (red arrows) are fixed by a cuff to the leg below the knee. The stimulator is also tied to the cuff. Initially, a clinician connects a hand switch device (black arrow head) to the stimulator to dorsiflex the ankle manually during the swing phase of the patient's gait. The specific stimulation timing is then programmed, so that the electrical stimulation can be accurately performed consequently with the stimulator alone. A heel sensor under the insole of shoe or a tilt sensor built in the stimulator is used as a measure of the patient's gait. Image courtesy of Innovative Neurotronics, Inc., Austin, TX, USA.



Figure 4 Commercial FES devices. Notes: (A) NESS L300 and wireless foot switch for gait and (B) NESS H200, which is worn over the paralyzed arm and hand. Image courtesy of Bioness Inc., Valencia, CA, USA.

Abbreviation: FES, functional electrical stimulation.

swing phase of gait, producing ankle dorsiflexion to keep leg clearance. The heel contact and off (stance and swing phases) are detected by a tilt sensor placed with the knee cuff (WalkAide) or by a pressure sensor placed under the insole of shoe to determine stimulation periods (WalkAide and NESS L300).

Since NESS H200 (Bioness Inc.)<sup>28,29</sup> is the only commercially available FES device for the upper limb and hand (Figure 4B), more robust and versatile devices are required for a wider group of people.<sup>30</sup> Since hand or upper limb motion is more diverse in comparison to lower limb motion, the electrical stimulation system associated with stimulating the former is also complicated. The NESS H200 has five electrodes, which stimulate the five muscle groups of forearm and hand (ie, the extensor digitorum, extensor pollicis brevis, flexor digitorum superficialis, flexor pollicis longus, and thenar muscles) and implement both key gripping and palmar grasping.

## Therapeutic electrical stimulation

Although some parameters of electrical stimulation (ie, stimulus position, stimulus intensity, pulse width, etc.) are adjusted according to the motion or condition of patient during FES, the stimulation methods for TES are even more varied.

Patients who have survived a stroke sometimes undergo electrical stimulation for muscle strengthening, although its use is not particular to stroke rehabilitation. In general, NMES often stimulates specific muscles, but in the case of muscle strengthening in stroke rehabilitation, multiple muscles, including those on the non-paralyzed side, are stimulated to enhance muscle strength. The reason for muscle strengthening in the non-paralyzed limb is to improve muscle weakness due to hospitalization (for example, knee extension force of the unaffected side decreases by ~30% on the seventh day after the onset of stroke)<sup>31</sup> or to acquire the compensatory strategies using the non-paralyzed limb. The belt electrode skeletal muscle electrical stimulation (B-SES) was also recently developed (Auto Tens Pro; Hormer Ion Co. Ltd., Tokyo, Japan) for muscle strengthening (Figure 5). For the B-SES, belt-like electrodes are wrapped around the waist, both knees, and both ankles to contract all lower limb skeletal muscles simultaneously.<sup>32</sup> Since it is desirable to induce stronger muscle contraction to obtain sufficient muscle strengthening effect, the stimulus intensity is set to the limit that patients can endure. Therefore, B-SES adopts the exponentially climbing wave form shown in Figure 2B, which can produce greater muscle strength with less pain.33

In contrast, weak current NMES, which is approximately at sensory threshold or below motor threshold, has also been proposed as a possible supplemental therapy to facilitate motor function in patients with stroke.<sup>34</sup> This is based on reports that somatosensory input enhances corticomotoneuronal excitability to the stimulated body parts.<sup>35,36</sup> In this approach, rather than being used in isolation, NMES is applied in combination with rehabilitation training. The advantages of this approach are high safety, low pain, and high usability for various types of rehabilitation, including robot training (Figure 6).<sup>37</sup>

In the abovementioned TES approaches, the electrical stimulation is applied continuously and passively. However,

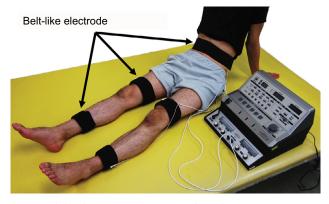


Figure 5 B-SES by Auto Tens Pro (Hormer Ion Co. Ltd.). Notes: Using the belt-like electrodes, B-SES can be used to stimulate all the

muscles in the lower extremities, including the quadriceps femoris, hamstring, tibialis anterior, and triceps surae muscles. This device is currently used in Fujita Health University Nanakuri Memorial Hospital.

Abbreviation: B-SES, belt electrode skeletal muscle electrical stimulation.



**Figure 6** Robotic training for affected upper limb using MIT-Manus/InMotion2 system (Interactive Motion Technologies, Inc., Cambridge, MA, USA) (**A**) combined with NMES at sub-motor threshold intensity.<sup>37</sup> NMES was delivered to the anterior deltoid and triceps muscles (**B**) using the Trio300 system (Ito Co. Ltd., Tokyo, Japan). (**C**) These devices are currently used in Fujita Health University Nanakuri Memorial Hospital.

Abbreviation: NMES, neuromuscular electrical stimulation.

for the motor recovery of paretic limbs after stroke, it is more common to perform NMES to encourage muscle contraction for an intended motion or to perform reciprocal NMES with agonists and antagonists. Rosewilliam et al<sup>38</sup> recruited patients with stroke with no upper limb function and demonstrated that repetitive NMES for 30 minutes (on and off periods = 15 s), which was applied twice in a working day for 6 weeks, to produce repetitive wrist extension, improved the wrist function of patients. Wu et al<sup>39</sup> developed bilateral arm training combined with NMES for the triceps brachii muscle and anterior deltoid muscle in the affected arm. During the training, patients were required to move both their paralyzed and non-paralyzed arms simultaneously in the same way, and the NMES was triggered by the difference in movement of both arms to assist the motion. Osu et al<sup>40</sup> used a surface electromyogram (EMG) of the unaffected hand as a clue for electrical stimulation of the paralyzed hand in a bilateral simultaneous motion. The EMG recorded by surface electrodes on the skin above skeletal muscle tissue is a common noninvasive method to assess the electrical activity that initiates muscle contraction and produces a physical force.<sup>41,42</sup> For reciprocal NMES, alternate stimulation of dorsiflexors and plantarflexors according to the timing of gait improved the walking ability of patients with stroke.43,44 This therapeutic approach is similar to that of FES described earlier, which is triggered depending on the phase of gait. Essentially, there is little distinction between "TES" and "FES" in stroke rehabilitation.

Since adjusting the NMES to the timing of motion means synchronizing it to motor intention, EMG-triggered NMES has been developed.<sup>45-47</sup> In this system, electrical stimulation is voluntarily triggered by EMG in the affected limb (the residual muscle activity of the paralyzed muscle). In recent years, EMG-triggered NMES has been combined with robot-aided rehabilitation, which has demonstrated improved motor function in patients with stroke.48,49 Furthermore, EMG-modulated NMES devices have also been developed,<sup>50–52</sup> which controls not only the timing but also the intensity of electrical stimulation in direct proportion to the amount of residual voluntary EMG. Since Muraoka<sup>53</sup> developed the device, where a pair of surface electrodes simultaneously records EMG from a muscle and stimulates the same muscle, EMG-modulated NMES can be applied even to a small muscle, in which it can be challenging to apply separate stimulating and recording electrodes. This NMES device, which is known as the integrated volitional control electrical stimulator (IVES), has been manufactured in Japan since 2008.54 The commercial IVES devices (PAS System and IVES+ System, OG Wellness Technologies Co., Ltd., Okayama, Japan) have two modes, ie, EMG-triggered NMES and EMG-modulated NMES (Figure 7).

In more recent years, there has also been an attempt to detect the motor intention using an electroencephalogram (EEG) instead of an EMG. Event-related desynchronization (ERD) and event-related synchronization (ERS), which respectively decrease and increase EEG frequency band power, are used to interpret the dynamics of brain oscillations<sup>55</sup> and are well known to be associated with

motor attempt, motor imagery, or voluntary movement.<sup>56</sup> A brain-computer interface (BCI) or brain-machine interface (BMI), a direct technological interface between the brain and a computer, based on the ERD and/or the ERS has recently been found to be a new tool to facilitate motor recovery after stroke.<sup>57</sup> Clinical reports of stroke rehabilitation using a BCI system to trigger NMES (EEG-triggered NMES) for finger function,<sup>58</sup> upper<sup>59</sup> and lower<sup>60</sup> limb training, and gait rehabilitation<sup>61</sup> have been published. Similar to the EMG-modulated NMES described earlier, an EEGmodulated NMES system has also been reported, which controls the current intensity of the NMES in a stepwise manner according to the appearance or disappearance of ERD.62 Although some of these BCI-NMES studies showed an improvement in paretic limbs of patients with stroke, currently, almost all are case reports or feasibility/safety studies. Thus, larger, controlled studies are warranted to validate the manufacture of commercial devices of EEGmodified NMES.

## Conclusion

In stroke rehabilitation, NMES is used not only for muscle strengthening and motor recovery of paralyzed limbs as introduced in this review but also for reducing spasticity<sup>63</sup> and improving swallowing function.<sup>64</sup> With the development of electronic engineering and clinical neuroscience, the devices and stimulation methods of NMES are diversifying. The application method of NMES differs depending on the condition of the patient with stroke, including the degree of paralysis. For patients with mild paralysis, weak NMES at sensory threshold or below motor threshold, combined with rehabilitation, may promote functional improvement. For moderate paralysis, EMG-triggered/modulated NMES may be a potential rehabilitative treatment option to restore

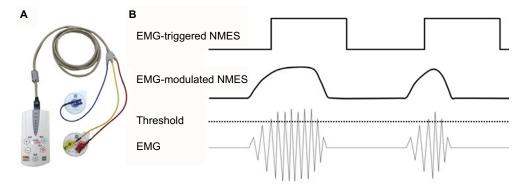


Figure 7 (A) The IVES+ system (OG Wellness Technologies Co., Ltd.) that is currently used in Fujita Health University Nanakuri Memorial Hospital. (B) EMG-triggered and EMG-modulated modes can be used for this device. In the former mode, NMES is applied with a constant current intensity for a fixed time when an EMG that exceeds a predefined threshold is detected. In the latter mode, the intensity of the stimulation current is proportional to the amplitude of EMG. Abbreviations: IVES, integrated volitional control electrical stimulator; EMG, electromyogram; NMES, neuromuscular electrical stimulation.

motor function and improve recovery. For severely affected patients in whom surface EMG is not detectable, EEGtriggered NMES may have therapeutic efficacy. Alternatively, in case of patients with severe paresis, in whom there is no motor intent, NMES aimed at muscle strengthening may be required to acquire compensatory movement in the non-paralyzed side.

Although the present review introduced some NMES devices and their clinical application, this was not a systematic review or a meta-analysis. The evidence of the applications of NMES in rehabilitation is still limited.<sup>65</sup> In particular, further research on recent new techniques, such as EEGtriggered/modulated NMES, using a controlled design is warranted.<sup>66</sup> From the viewpoint of device development, there are many devices in which various stimulation parameters can be set with one device; however, there are few commercial devices that correspond to complicated operations such as hand movements. Further development and evidence-based commercial manufacture of EMG/EEG-triggered/modulated NMES devices are expected in the future.

## Disclosure

The authors report no conflicts of interest in this work.

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