



Archived at the Flinders Academic Commons:

<http://dspace.flinders.edu.au/dspace/>

'This is the peer reviewed version of the following article: Doeltgen, S. H., & Huckabee, M.-L. (2012, February). Swallowing Neurorehabilitation: From the Research Laboratory to Routine Clinical Application. Archives of Physical Medicine and Rehabilitation. Elsevier BV. <http://dx.doi.org/10.1016/j.apmr.2011.08.030> ,

which has been published in final form at

DOI:

<http://dx.doi.org/10.1016/j.apmr.2011.08.030>

© <2012>. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <http://creativecommons.org/licenses/by-nc-nd/4.0/>

1 **Swallowing Neuro-rehabilitation: From the research laboratory to routine clinical** 2 **application**

3

4 **Abstract**

5 The recent application of neuro-stimulation techniques to enhance the understanding of
6 swallowing neural plasticity has expanded the focus of rehabilitation research from
7 manipulation of swallowing biomechanics to manipulation of underlying neural systems.
8 Neuromodulatory strategies that promote the brain's ability to reorganize its neural
9 connections have been shown to hold promising potential to aid the recovery of impaired
10 swallowing function. These techniques include those applied to the brain through the intact
11 skull, for example, transcranial magnetic stimulation or transcranial direct current
12 stimulation, or those applied to the sensorimotor system in the periphery, such as
13 neuromuscular electrical stimulation. Recent research has demonstrated that each of these
14 techniques, either by themselves or in combination with these and other treatments, can,
15 under certain circumstances, modify the excitability of motor representations of muscles
16 involved in swallowing. In some studies, experimentally induced plastic changes have been
17 shown to have functional relevance for swallowing biomechanics. However, the transition of
18 novel, neuromodulatory brain stimulation techniques from the research laboratory to routine
19 clinical practice is accompanied by a number of ethical, organizational and clinical
20 implications that impact professions concerned with the treatment of swallowing
21 rehabilitation. In this paper, we provide a brief overview of the neuromodulatory strategies
22 that may hold potential to aid the recovery of swallowing function, and raise a number of
23 issues which we believe the clinical professions involved in the rehabilitation of swallowing
24 disorders must confront as these novel brain stimulation techniques emerge into clinical
25 practice.

1

2 **Keywords**

3 Rehabilitation, neuroplasticity, deglutition, transcranial magnetic stimulation, electric

4 stimulation

5

6 **Abbreviations**

7 NMES: neuromuscular electrical stimulation; MEP: motor evoked potential; PAS: paired

8 associative stimulation; PES: pharyngeal electrical stimulation; TMS: transcranial magnetic

9 stimulation; rTMS: repetitive transcranial magnetic stimulation; tDCS: transcranial direct

10 current stimulation;

11

12

1 Traditionally, behavioral interventions for swallowing impairment, such as compensatory
2 swallowing maneuvers or active motor exercises, have focused on restoring safe and effective
3 swallowing through *functional* modification of swallowing biomechanics. Compensatory
4 maneuvers, including head positioning, food/fluid texture modifications and other techniques,
5 can have immediate beneficial effects by facilitating safer bolus transfer; however, these
6 effects are not considered to persist in the longer-term when the maneuver is not performed.
7 For longer-term, cumulative rehabilitation of swallowing function, active motor exercises are
8 available that are aimed primarily at strengthening the oropharyngeal musculature for
9 effective pharyngeal bolus clearance and optimal airway protection. The effortful swallow,
10 the tongue-hold swallow (1) and the headlift exercise (2) are all examples of this type of
11 rehabilitation approach. The immediate effects of these interventions on biomechanical
12 measures of swallowing function have been examined using a variety of functional
13 swallowing assessment tools, including clinical rating scales (3), videofluoroscopic
14 swallowing study (4), video-endoscopy (5), surface electromyography (eg, 6, 7) or
15 pharyngeal manometry (eg, 8, 9, 10, 11, 12). These exercises have been hypothesized to
16 engender long term rehabilitative change in a many patients through predominantly case
17 series reports or small trials, which reported on cumulative effects of a mix of treatment
18 approaches (eg, 13, 14, 15), as well as a small number of more recent, controlled trials on the
19 headlift exercise in particular (16). However, there is a paucity of research on the cumulative
20 rehabilitative effects of these approaches.

21

22 Perhaps in part as a response to this limited research base, recent advances in neuro-
23 stimulation techniques are expanding the focus from traditional, exercise-based swallowing
24 rehabilitation toward the development of novel swallowing rehabilitation approaches that
25 modulate the neuronal circuitries involved in swallowing motor control. Driven by increased

1 understanding of the neurophysiological underpinnings of swallowing sensorimotor control,
2 the changes induced in these networks by neurotrauma, and the functional improvements
3 brought about by swallowing rehabilitation interventions, speech pathologists increasingly
4 find themselves in the role of “neuropsychiatrists”, with the focus of treatment shifting
5 from manipulation of peripheral swallowing biomechanics to manipulation of underlying
6 neural systems.

7

8 **Neuro-modulatory techniques in swallowing rehabilitation**

9 The last decade in particular has seen the emergence of neuromuscular electrical stimulation
10 (NMES) protocols in rehabilitation medicine. In general, NMES employs the application of
11 pulsed electrical currents to muscles, nerves or neuromuscular junctions with the therapeutic
12 benefits thought to arise from improvements in muscle strength, stamina and reaction time
13 (17). Based on these general concepts, a number of differing protocols for applying NMES as
14 a swallowing rehabilitation intervention have been developed. In order to assist readability
15 and clarity, the term NMES will be used from here onwards as an umbrella term for any
16 technique employing an electrical stimulus to muscles involved in swallowing. The various
17 subtypes [Vitalstim, pharyngeal electrical stimulation (PES), and other forms of experimental
18 electrical stimulation] will be briefly outlined. However, for detailed information about the
19 existing research evaluating these NMES approaches in healthy research subjects and
20 swallowing impaired patients, the reader is referred to several comprehensive reviews (18,
21 19, 20, 21).

22 *Vitalstim*

23 Perhaps the most commercially recognized electrical stimulation protocol is that advocated
24 by Freed and colleagues, referred to as Vitalstim. This protocol was based on a randomized
25 controlled trial of 99 patients with dysphagia (22), in which electrical stimulation is provided

1 by means of surface electrodes applied overlying the floor of mouth and laryngeal
2 musculature. Research on this particular protocol reports contradictory functional outcomes
3 which have been widely discussed (for reviews, see 18, 19, 20, 21). It is noteworthy that the
4 emergence of this particular NMES modality has impacted the profession of speech
5 pathology beyond the rehabilitative potential of the intervention. Since its commercial
6 availability, significant controversy surrounding the clinical application of the Vitalstim
7 protocol for swallowing rehabilitation has highlighted a number of professional issues. One
8 of the main points of discussion relates to the wide-spread, routine clinical application of this
9 form of NMES prior to the establishment of a thorough, evidence-based research foundation.
10 In particular, the ramifications of providing a more invasive, non-behavioural treatment,
11 which is administered by the clinician, rather than being performed by the patient, are not yet
12 precisely understood. Further, provision of this form of NMES to patients presenting with a
13 vast variety of underlying impairments and issues surrounding the training of clinicians have
14 sparked extensive discussions within the profession (23). Although this technique may hold
15 rehabilitative potential for some patient groups under certain conditions, wide-spread use of
16 this technique does not imply that it is synonymous with a universally effective rehabilitation
17 approach for impaired swallowing.

18

19 *Pharyngeal electrical stimulation*

20 A very different electrical stimulation technique has been carefully investigated over the last
21 decade by Hamdy and colleagues (24). Pharyngeal electrical stimulation is applied to the
22 pharyngeal mucosa via surface electrodes mounted on an intraluminal catheter. In a number
23 of studies, these researchers have demonstrated that PES primarily affects swallowing
24 function through changes in the excitability of the pharyngeal representation in the primary
25 motor cortex (24, 25). For example, PES using certain stimulus parameters can increase

1 corticobulbar excitability in healthy research subjects and patients with dysphagia and,
2 importantly, improve dysphagic symptoms, including aspiration score and pharyngeal transit
3 times (24). Recently, this group demonstrated improvement in functional outcomes (the
4 severity of swallowing impairment, feeding status and duration of hospitalization) following
5 PES applied for three consecutive days in a placebo controlled trial involving 28 swallowing
6 impaired acute stroke patients (25).

7

8 *Experimental electrical stimulation paradigms*

9 Other experimental NMES paradigms targeting orofacial muscle groups have been tested in
10 the last decade. Power and colleagues demonstrated in healthy research subjects that NMES
11 applied to the muscles underlying the faucial pillar mucosa had frequency-specific effects on
12 corticobulbar motor excitability (26). Interestingly, inhibitory faucial pillar NMES resulted in
13 a lengthened swallow response time, whereas facilitatory faucial pillar NMES did not affect
14 swallowing function. Similarly, a subsequent sham controlled study of 16 acute stroke
15 patients showed no changes in swallowing function following facilitatory faucial pillar
16 NMES (27).

17

18 Doeltgen and colleagues systematically investigated the effects of swallowing-triggered
19 NMES applied to the floor of mouth musculature in healthy research subjects (28). Cortical
20 effects were frequency-specific, and were only observed following NMES triggered by
21 volitional swallowing, and not when applied at rest (28). Interestingly, although PES, faucial
22 pillar NMES and swallowing-triggered NMES all induced frequency-specific changes in
23 corticobulbar excitability, inhibitory and facilitatory frequencies differed across the different
24 modalities and stimulated muscle groups. This suggests that NMES-induced effects are not
25 only dependent on the stimulus frequency employed, but also depend on the stimulated

1 muscle group. In light of the apparent relationship between increased corticobulbar
2 excitability and enhanced swallowing function following facilitatory PES (24), and the
3 prolongation of swallowing response time following inhibitory faucial pillar NMES (26), the
4 results of these studies underscore the necessity and importance of carefully evaluating
5 optimal stimulus parameters for each NMES modality and target muscle group.

6
7 The clinical application of NMES marks the emergence of techniques that can be classified as
8 “neuro-modulatory”; this also includes techniques such as TMS and transcranial direct
9 current stimulation (tDCS). These techniques can, under certain circumstances, affect neural
10 mechanisms underlying motor function. A large body of research has investigated the effects
11 of neuro-modulatory techniques in the corticospinal motor system controlling the muscles of
12 the limbs and torso. Many of these studies have demonstrated that experimentally induced
13 changes in corticospinal excitability can be functionally relevant in health and disease (eg,
14 29, 30, 31). A small number of studies evaluating the effects in the head and neck
15 musculature controlled by the corticobulbar motor system have recently demonstrated a
16 similar functional relevance for swallowing. For example, changes in cortical synaptic
17 connectivity subserving the pharyngeal musculature affect peripheral swallowing
18 biomechanics (24, 32). This finding has significant clinical ramifications. If it were possible
19 to modify and interact with the brain’s capability of undergoing change, then induction of
20 neural plasticity might provide a very useful therapeutic tool for the recovery of impaired
21 swallowing function. Even if the application of neuromodulatory brain stimulation did not, in
22 the long term, prove to be an effective therapeutic approach *per se*, recent studies in the area
23 of physical rehabilitation medicine provide preliminary data to support the notion that a
24 combination of neuromodulatory brain stimulation and “traditional” behavioural exercise

1 may result in more beneficial therapeutic effects than either type of intervention alone (33,
2 34).

3 The intent of this article is not to provide an in-depth review of studies that have documented
4 the potential of neuromodulatory brain stimulation techniques for the rehabilitation of
5 swallowing disorders. There are excellent recent reviews provided by Martin (35) and Barritt
6 and Smithard (36). Instead, we first provide a general overview of the currently available
7 brain stimulation techniques and the emerging evidence of their potential to enhance and
8 inhibit the recovery of lost swallowing function. Then we raise a number of relevant
9 questions, which we believe the clinical professions involved in the rehabilitation of
10 swallowing disorders must confront as these novel brain stimulation techniques emerge into
11 clinical swallowing neuro-rehabilitation.

12

13 **Experimental transcranial brain stimulation and swallowing rehabilitation**

14 TMS and tDCS are the most common transcranial brain stimulation techniques, which
15 stimulate neuronal networks within the brain through the intact skull with little or no
16 discomfort. Both techniques are currently only used in experimental and clinical dysphagia
17 research settings. TMS is based on concepts of electromagnetism, and can be applied either
18 as single magnetic pulses (single or paired pulse TMS) or trains of magnetic pulses (repetitive
19 TMS, rTMS). Single-pulse TMS is used diagnostically to assess the excitability of
20 corticobulbar or corticospinal motor projections, mapping cortical motor representations of
21 certain muscles or groups of muscles, or studying central motor conduction time.

22 Specifically, a short-lasting magnetic field is generated by a strong electric current that passes
23 through a coil of wires placed over the head. If a sufficiently strong magnetic pulse is
24 generated over the primary motor cortex, it passes through the scalp nearly unimpeded and
25 trans-synaptically activates interneurons that project onto descending motor output neurons.

1 The resulting descending current, known as the motor evoked potential (MEP), can be
2 measured in the target muscle using surface electromyography. The amplitude and latency of
3 the MEP provide important information about the excitability of the stimulated neural
4 pathway.

5 Paired-pulse TMS employs application of two magnetic stimuli, a sub-threshold conditioning
6 stimulus and a supra-threshold test stimulus, in close temporal sequence. This TMS paradigm
7 provides important information about the excitability of intracortical inhibitory or facilitatory
8 motor networks, by selectively activating facilitatory or inhibitory interneuronal networks.

9 Interestingly, some disease conditions are characterized by imbalances of intracortical
10 facilitation and inhibition (37).

11 In contrast to single-pulse and paired-pulse TMS, which only produce short lasting responses,
12 eg, momentary activation of motor output cells, repeated application of trains of magnetic
13 stimuli (rTMS) has longer lasting effects on the stimulated neuronal networks, often
14 outlasting the stimulation period by 30-60 minutes (eg, 38, 39). The nature of these effects is
15 highly dependent on the pattern of stimulation, including the overall number, frequency and
16 intensity of the train of stimuli applied. For example, research in the corticospinal system
17 identifies that low stimulation frequencies generally inhibit corticospinal excitability, whereas
18 high stimulation frequencies (> 1Hz) facilitate corticospinal excitability. Safety limits have
19 been established for rTMS parameters, as rTMS is thought to be associated with a number of
20 potential side effects; these include mild effects on hearing, local pain and discomfort and,
21 under certain circumstances, the induction of seizures (40).

22

23 A small number of studies have explored the potential of rTMS to modulate the excitability
24 of cortical motor representations of muscles involved in swallowing and have investigated the
25 functional relevance of motor plasticity induced by rTMS. For example, 1 Hz rTMS applied

1 to the cortical hemisphere with dominant pharyngeal motor representation of healthy research
2 subjects has been shown to induce a reduction of excitability of corticobulbar motor
3 projections to pharyngeal musculature, as reflected in smaller pharyngeal MEPs (32). This
4 effect was accompanied by a reduction in swallowing reaction time of normal and fast
5 swallows, as assessed by a swallowing reaction time task (32). This finding may be
6 particularly relevant for the rehabilitation of patients who present with dysphagia
7 characterized by delayed pharyngeal onset of swallowing. Clinical studies are warranted to
8 test this hypothesis. It is noteworthy that there may be differences in the corticobulbar
9 processing of swallowing onset between the swallowing reaction time task employed (based
10 on visual cue to trigger swallow) and the initiation of a swallow in a deglutitive context. The
11 findings of this study further raise questions regarding the role of pharyngeal cortical motor
12 circuits in the initiation of swallowing. One may hypothesize that pharyngeal cortical motor
13 circuits exert an inhibitory influence on swallowing pattern generators at least in the
14 pharyngeal phase of the mainly brainstem driven swallowing response, which is temporarily
15 released by rTMS induced inhibition of these motor networks. Interestingly, the inhibitory
16 effects induced by 1 Hz rTMS could be reversed by high-frequency (facilitatory) 5 Hz rTMS
17 applied to the contralateral, “non-lesioned” hemisphere, which was associated with a
18 restoration of swallowing function (41).

19

20 The technique of paired-associative stimulation (PAS) consists of repeated applications of a
21 single electrical stimulus applied over a peripheral muscle paired with a single pulse of TMS
22 over the corresponding motor cortex (38). When this technique is applied over the pharyngeal
23 mucosa and the cortical region associated with the pharynx, an increase of the excitability of
24 pharyngeal motor representation was evident for two hours following stimulation. This
25 change was associated with a reduction in glutamate concentration in the stimulated

1 hemisphere, suggesting that mechanisms consistent with long-term potentiation underlie the
2 PAS-induced plastic changes in pharyngeal motor representation (42). The relevance of PAS-
3 induced increases in corticobulbar excitability for swallowing function are unknown;
4 however, emerging evidence in the corticospinal motor system suggests that PAS-induced
5 plasticity may have functional relevance and may, therefore, be therapeutically useful (43).
6
7 Transcranial direct current stimulation employs low-intensity electrical direct currents that
8 modify neuronal activation in the stimulated brain areas. The nature of effects induced by
9 tDCS is dependent on the direction of current flow. Anodal stimulation of the motor cortex
10 generally produces facilitation of motor cortical excitability, whereas cathodal stimulation
11 reduces it. Functionally, anodal tDCS of the primary motor cortex has been shown to improve
12 the performance of healthy research subjects in a choice reaction-time task (31). When
13 applied to the region of pharyngeal motor representation for 10 min with an intensity of
14 1.5mA and a cathodal current direction, tDCS has been shown to reduce corticobulbar
15 excitability. In contrast, 10 min of 1.5 mA and 20 min of 1mA anodal stimulation increased
16 corticobulbar excitability (44). The functional correlates of tDCS-induced plasticity in regard
17 to swallowing are currently being investigated. For example, it has been shown in the
18 corticospinal motor system that anodal tDCS facilitates the effects of unilateral motor training
19 following stroke (45) and enhances motor function in young (46) and older (47) healthy
20 research subjects. Furthermore, tDCS has been shown to facilitate motor learning when
21 applied over the human motor cortex (48) and has the potential to enhance the retention of
22 declarative memory (49). In a recent pilot study of 14 subacute stroke patients with
23 dysphagia, application of anodal tDCS over the unaffected hemisphere on five consecutive
24 days, in combination with an effortful swallowing exercise and lemon taste exposure, resulted
25 in greater improvement of swallowing function than sham tDCS paired with exercise (50).

1

2 As outlined above, the plastic effects induced by neuro-modulatory stimulation techniques
3 hold the potential for improving motor function in healthy individuals and aiding the
4 recovery of impaired motor function after damage to the central nervous system. Importantly,
5 the plastic changes induced in the motor cortex critically depend on the stimulus parameters
6 employed. For example, the stimulus frequency and stimulation pattern of rTMS determine
7 whether corticospinal excitability is facilitated or inhibited. Evidence is emerging that this is
8 also true for the corticobulbar motor system. Interestingly, for NMES of the corticobulbar
9 motor system, facilitatory and inhibitory parameters appear to depend also on the muscle
10 group stimulated, with high frequency NMES being facilitatory for the floor of mouth
11 muscle representation (28) and low frequency NMES facilitating the excitability of the
12 pharyngeal muscle representation (24).

13

14 In the context of optimal stimulation parameters and paradigms, the question arises whether
15 the combined administration of behavioural swallowing exercise and neuro-modulatory brain
16 stimulation may be the most promising approach. In fact, one might wonder whether the
17 duration of the after-effects induced by experimental brain stimulation, which generally
18 outlast the stimulation period by around 30-60 minutes, could on its own ever be sufficient to
19 be therapeutically beneficial. As Ridding and Rothwell have outlined in their review of the
20 therapeutic potential of TMS (51), if one assumes that experimental brain stimulation can
21 “repair” imbalanced brain function caused by insult or disease, then the relatively short-lived
22 nature of the effects induced by currently available paradigms would critically limit the
23 therapeutic potential of these interventions. In fact, if experimental brain stimulation induced
24 permanent changes in cortical circuits, it would ethically be highly problematic to explore the
25 effects of the techniques in healthy individuals. In contrast, perhaps the more effective

1 strategy to improve function may be to promote the brain's intrinsic neural repair
2 mechanisms by providing conventional rehabilitative training during a period of
3 experimentally enhanced cortical excitability. Therefore, providing a 1 hour "therapeutic
4 window" would be sufficient for most training protocols. Indeed, there is evidence in the
5 corticospinal motor system for the efficacy of this combined approach in both healthy
6 research subjects and stroke patients (34, 35). In addition, application of sensory stimulation
7 of peripheral nerves and muscles involved in swallowing, or performance of a motor task,
8 combined with transcranial brain stimulation may provide a promising approach that holds
9 greater effects than the sum of its parts. One such approach, PAS, has been shown to be
10 capable of bidirectionally modifying the excitability of corticospinal (38) and corticobulbar
11 motor projections (52). Similarly, short intervals of NMES triggered by volitional swallows
12 provide a promising approach toward optimizing the potential of this rehabilitative
13 intervention (28).

14
15 The observation that the spontaneous recovery of swallowing function following unilateral
16 stroke is associated with natural reorganization of cortical motor circuits in the contralateral
17 hemisphere (53) further underscores the notion that experimentally induced plasticity in
18 cortical muscle representations may have a promising potential to assist in the recovery of
19 swallowing function. Taken together, the above mentioned studies provide promising support
20 for the notion that experimental brain stimulation techniques may one day play an important
21 role in the rehabilitation of swallowing disorders. However, larger clinical trials are needed to
22 confirm these findings and provide a strong evidence base. In addition, a number of
23 experimental challenges will need to be overcome before these techniques can be applied
24 routinely in clinical practice. For example, optimal placement of the stimulation coil or
25 electrodes over the relevant oropharyngeal motor representations is arguably more difficult

1 than, for example, for the limb musculature and requires extensive expertise in the use of
2 these techniques. The risk for the induction of seizures following rTMS is recognized (40)
3 and in and of itself requires either formal medical training of the treating clinician, or
4 availability of an emergency response team. In addition, incorrect application of tDCS holds
5 the risk for burns of the scalp surface (54). Clinical professions concerned with the care of
6 those affected by swallowing disorders, in particular speech pathologists, will, therefore, face
7 a number of critical questions regarding the provision of these services. We raise a number of
8 questions, which we believe require consideration if experimental brain stimulation
9 techniques were to be established in routine clinical practice.

10

11 **Provision of experimental brain stimulation services in clinical dysphagia rehabilitation**

12 Although rTMS is already being tested in large-scale clinical trials as a treatment for other
13 health conditions (eg, treatment-resistant depression and tinnitus), brain stimulation for the
14 purpose of swallowing rehabilitation is currently only used by trained researchers conducting
15 carefully monitored experimental protocols in a few research centres across the world. As
16 more data are collected and if outcomes support the viability of neuro-stimulation protocols,
17 the natural progression will be a transfer of these techniques to clinical practice. Given that
18 speech pathologists traditionally have provided swallowing rehabilitation services in most
19 countries, can it be assumed that the eventual provision of interventional brain stimulation
20 will also fall to that profession? If speech pathologists were indeed the most likely providers
21 of these novel rehabilitation techniques, how can our profession prepare for these impending
22 new challenges? What qualifications would be necessary to ensure that experimental brain
23 stimulation is applied in a safe and effective manner? Given that these techniques are
24 powerful enough to temporarily alter the synaptic connections in the stimulated tissues of the
25 human brain, and have successfully been used to alter the psychological state of patients (eg,

1 those with depression), appropriate training of how to apply which kind of intervention to
2 which area of the brain is critical. This is particularly vital as various dysphagic presentations
3 can result from a variety of underlying pathophysiologies (eg, flaccidity, spasticity,
4 dyscoordination), each of which may respond differentially to specific stimulation protocols.
5

6 A consensus group of international experts comments on issues of professional responsibility
7 in the most recently updated TMS safety guidelines (40). The authors list a number of
8 potential research settings in which TMS/rTMS may be applied on clinical populations. Most
9 relevant for the application of rTMS in swallowing rehabilitation are the categories referred
10 to as Class 3 (“indirect benefit, low risk”) and Class 2 (“indirect benefit, moderate risk”)
11 research studies on “normal subjects and patients with stable medical conditions (p. 2033)
12 and Class 1 studies (“direct benefit, potential high risk”) as “treatment for any medical
13 condition” (p.2033). For Class 3 and Class 2 studies, the authors recommend that any form of
14 TMS may be carried out by “trained professionals”, who may include “MDs, Technicians,
15 Psychologists, Physicists, Physiotherapists, Engineers”. In this scenario, speech pathologists
16 may likely be considered qualified to perform rTMS in studies of stable, dysphagic patients
17 and healthy control subjects, if adequately trained. For Class 1 studies, the consensus group
18 states that “it is advisable that a licensed physician...closely supervises the rTMS
19 application” (p. 2033), with medical staff trained in the diagnosis and emergency
20 management of seizures available at all times (40). These guidelines were issued in relation
21 to research studies employing rTMS in healthy research subjects and clinical populations. It
22 appears likely that similar recommendations would apply for the eventual routine use of
23 rTMS in clinical rehabilitation settings. Although probably most of the dysphagic patients
24 treated in in- and outpatient clinics are medically stable, and may therefore not present with a
25 directly increased medical risk for rTMS/tDCS-induced side effects, the consensus statement

1 raises several important questions. Which patients can safely receive rTMS/tDCS and who
2 will decide whether or not these interventions will be administered? Will neuro-modulatory
3 interventions be prescribed by a physician and administered by a speech pathologist, or will
4 the speech pathologist decide who does and does not receive rTMS (-assisted) therapy? As
5 importantly, what constitutes “adequate training” of rTMS/tDCS operators, which ensures
6 safe and effective application of neuro-modulatory techniques in a variety of clinical
7 populations? Consideration of these questions is imperative and will require consultation and
8 consensus of various professional groups involved in the care of patients with dysphagia
9 before neuro-modulatory stimulation techniques can be safely and effectively implemented in
10 routine clinical practice. It is noteworthy that these questions not only pertain to novel
11 transcranial brain stimulation techniques, but should also have been carefully considered for
12 NMES techniques that are already commonly used in dysphagia rehabilitation settings.
13 Research is further warranted to evaluate optimal treatment frequencies and intensities and to
14 develop standardized outcome measures for the assessment of clinical effects of all of these
15 interventions.

16

17 **Professional training – Guidelines for ensuring optimal patient care**

18 The development of reliable and standardized brain stimulation protocols for routine clinical
19 use should be accompanied by the development of guidelines for the training and application
20 of these paradigms in clinical practice. To date, no international or national guidelines have
21 been established that outline the training requirements for experimental brain stimulation.

22 The International Federation of Clinical Neurophysiology is currently in the process of
23 developing such guidelines (40). Although (Neuro)-physiology and (Neuro)-anatomy courses
24 form part of the majority of speech pathology undergraduate training programmes, a
25 multifaceted curriculum does not always allow in-depth coverage of these topics. However, a

1 thorough understanding of the neurophysiological underpinnings of neural plasticity, and the
2 induction thereof, should be a critical objective of competency training. Neuro-rehabilitation
3 training for swallowing (and probably also speech and language) should include basic
4 information about the physics of electromagnetism and its interaction with human neural
5 systems, as well as an introduction to the various stimulation paradigms and their
6 mechanisms of action. In addition, academic preparation in the rationales underlying
7 selection of paradigms for application to specific clinical presentations would be necessary,
8 as well as an introduction to current safety recommendations. It would appear sensible that
9 basic first aid training should also form part of training for the application of neuro-
10 modulatory techniques. Given the complexity of these requirements, the question arises
11 whether undergraduate or graduate clinical speech pathology programmes can provide such
12 specialized training. Alternatively, it may be that postgraduate professional development
13 courses could provide the necessary training, for example in the form postgraduate training
14 courses offered by academic institutions. National legal regulations may vary across
15 countries, and may provide a legal framework for such training. Whatever the optimal or
16 most practical format, the objective of specialized training programs should be to convey a
17 thorough understanding of the precise neural mechanisms by which neuro-modulatory
18 techniques interact with the human nervous system, and ultimately motor function. Providing
19 simplified treatment protocols without provision of in-depth neurophysiological education is
20 undesirable and may pose a risk to both clinicians and patients.

21

22 **Access to stimulation equipment – practical considerations**

23 Unlike NMES devices, which are relatively inexpensive, and can be operated by a patient or
24 carer using clinician defined protocols, experimental brain stimulation tools, especially
25 rTMS, are expensive (in excess of ten thousand U.S. dollars) and cannot be patient-operated.

1 Therefore, patients will be required to attend the swallowing rehabilitation service providers'
2 clinics to receive treatment. This may be clinically optimal, since paired application of brain
3 stimulation with conventional swallowing rehabilitation exercises may prove an ideal
4 combination of treatments (as outlined above). For example, patients may attend a brain
5 stimulation session, which is followed by a “conventional” swallowing rehabilitation session,
6 although basic research is yet to establish optimal treatment protocols. In the planning of
7 individual rehabilitation programmes, consideration will need to be given to the fact that
8 having to attend a clinic for treatment, possibly on a daily basis, would be more demanding of
9 patients and carers than, for example, home-based exercises programmes that are monitored
10 by less frequent therapy sessions. One could argue that home-based programmes are not
11 optimal for any rehabilitative approach, but for brain stimulation techniques, they would be
12 impossible.

13

14 **Conclusion**

15 We conclude that the currently available research evidence suggests that experimental brain
16 stimulation holds the potential for (i) inducing changes in the motor cortical areas that are
17 involved in swallowing, which outlast the stimulation period, and importantly, (ii) that such
18 experimentally induced plastic changes can under certain circumstances be relevant for
19 swallowing function. Given the promising potential that these novel rehabilitation techniques
20 hold for improving the health, safety and quality of life of patients living with dysphagia,
21 further research and development of safe and effective treatment paradigms is warranted.
22 Before tested treatment paradigms can be applied in routine clinical practice, it will be
23 necessary to develop a strategic plan that will allow the profession of speech pathology, as
24 well as others, to move forward to meet the academic, clinical and ethical challenges that
25 accompany the advent of these novel interventions. Large scale clinical trials will be needed

1 to confirm the safety and efficacy of brain stimulation protocols that are often developed in
2 healthy populations, or small patient subgroups. Trials of this nature should evaluate (i) the
3 functional benefits of novel modulatory interventions, and, as importantly, (ii) determine
4 changes in the impact of the disability perceived by the patient (55). A coordinated
5 international effort would likely speed up the development of a thorough clinical evidence
6 base. Consensus groups involving experts from a variety of medical and therapeutic
7 backgrounds may provide answers to some of the questions raised in this article and facilitate
8 the transfer of these emerging techniques from the research laboratory to clinical practice. In
9 light of the recent discussion around the efficacy of rTMS in the treatment of depression (eg,
10 51), or the by some perceived premature use of NMES in swallowing rehabilitation, which
11 overshadows the theoretical potential of this technique to improve swallowing function,
12 patience will be necessary before widespread clinical use of neuro-modulatory brain
13 stimulation techniques can be implemented in routine clinical swallowing rehabilitation
14 practice.

15

16

1 References

- 2 1. Fujii M, Logemann JA. Increased Postoperative Posterior Pharyngeal Wall Movement in
3 Patients with Anterior Oral Cancer: Preliminary Findings and Possible Implications for
4 Treatment. *Am J Speech-Lang Pat* 1995;4(2):24-30.
- 5
- 6 2. Shaker R, Kern M, Bardan E, Taylor A, Stewart ET, Hoffmann RG, Arndorfer RC,
7 Hofmann C, Bonnevier J. Augmentation of deglutitive upper esophageal sphincter opening in
8 the elderly by exercise. *Am J Physiol-Gastr L* 1997;35(6):G1518-G1522.
- 9
- 10 3. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration
11 scale. *Dysphagia* 1996;11(2):93-98.
- 12
- 13 4. Logemann JA. 1997. Evaluation and treatment of swallowing disorders (2nd ed).
14 Austin, TX: Pro-Ed.
- 15
- 16 5. Langmore SE, Schatz K. Fiberoptic endoscopic examination of swallowing safety: a new
17 procedure. *Dysphagia* 1988;2(4):216-219.
- 18
- 19 6. Huckabee ML, Butler SG, Barclay M, Jit S. Submental surface electromyographic
20 measurement and pharyngeal pressures during normal and effortful swallowing. *Arch Phys*
21 *Med Rehab* 2005;86(11):2144-9.
- 22
- 23 7. Doeltgen SH, Hofmayer A, Gumbley F, Witte U, Moran C, Carroll G, Huckabee ML.
24 Clinical measurement of pharyngeal surface electromyography: Exploratory research.
25 *Neurorehab Neural Re* 2007;21(3):250-62.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24

8. Hiss, SG, Huckabee ML. Timing of pharyngeal and upper esophageal sphincter pressures as a function of normal and effortful swallowing in young healthy adults. *Dysphagia* 2005;20(2):149-56.

9. Gumbley F, Huckabee ML, Doeltgen SH, Witte U, Moran C. Effects of Bolus Volume on Pharyngeal Contact Pressure during Normal Swallowing. *Dysphagia* 2008;23:280-85.

10. Witte U, Huckabee ML, et al. The Effect of Effortful Swallow on Pharyngeal Manometric Measurements During Saliva and Water Swallowing in Healthy Participants. *Arch Phys Med Rehab* 2008;89(5):822-8.

11. Omari TI. Apnea-Associated Reduction in Lower Esophageal Sphincter Tone in Premature Infants. *J Pediatr* 2009;154(3):374-8.

12. Doeltgen SH, Witte U, Gumbley F, Huckabee ML. Evaluation of manometric measures during tongue-hold swallows. *Am J Speech-Lang Pat* 2009;18(1):65-73.

13. Crary MA. A direct intervention program for chronic neurogenic dysphagia secondary to brainstem stroke. *Dysphagia* 1995;10(1):6-18.

14. Huckabee ML, Cannito MP. Outcomes of swallowing rehabilitation in chronic brainstem dysphagia: A retrospective evaluation. *Dysphagia* 1999;14(2):93-109.

- 1 15. Crary MA, Carnaby Mann GD, Groher ME, Helseth E. Functional benefits of dysphagia
2 therapy using adjunctive sEMG biofeedback. *Dysphagia* 2004;19(3):160-64.
3
- 4 16. Shaker R, Easterling C, Kern M, Nitschke T, Massey B, Daniels S, Grande B, Kazandjian
5 M, Dikeman K. Rehabilitation of swallowing by exercise in tube-fed patients with pharyngeal
6 dysphagia secondary to abnormal UES opening. *Gastroenterology* 2002;122(5):1314-21.
7
- 8 17. Alon G. Principles of electrical stimulation. In: Nelson RM, Currier DP (eds). *Clinical*
9 *Electrotherapy*. 2nd Edition. Norwalk, CT: Appleton & Lange; 1991, p35–101.
10
- 11 18. Carnaby-Mann GD, Crary MA. Examining the evidence on neuromuscular electrical
12 stimulation for swallowing. *Arch Otolaryngol* 2007;133:564-71.
13
- 14 19. Huckabee ML, Doeltgen SH. Emerging Modalities in Dysphagia Rehabilitation:
15 Neuromuscular Electrical Stimulation. *The New Zealand Medical Journal* 2007;120:1-9.
16
- 17 20. Steele CM, Thrasher AT, Popovic MR. Electric stimulation approaches to the restoration
18 and rehabilitation of swallowing: a review. *Neurol Res*, 2007;29:9-14.
19
- 20 21. Burns MI, Miller RM. The effectiveness of neuromuscular electrical stimulation (NMES)
21 in the treatment of pharyngeal dysphagia: a systematic review. *J Med Speech-Lang Pa*
22 2011;19(1):13-24.
23
- 24 22. Freed ML, Freed L, Chatburn RL, Christian M. Electrical stimulation for swallowing
25 disorders caused by stroke. *Respiratory care* 2001;46:466-474.

- 1 23. Logemann JA. The Effects of VitalStim on Clinical and Research Thinking in Dysphagia.
2 Dysphagia 2007;22(1):11-12.
3
- 4 24. Fraser C, Power M, Hamdy S, Rothwell J, Hobday D, Hollander I, Tyrell P, Hobson A,
5 Williams S, Thompson D. Driving plasticity in the human adult motor cortex is associated
6 with improved motor function after brain injury. *Neuron* 2002;34:831-40.
7
- 8 25. Jayasekeran V, Singh S, Tyrrell P, Michou E, Jefferson S, Mistry S, Gamble E, Rothwell
9 J, Thompson D, Hamdy S. Adjunctive functional pharyngeal electrical stimulation reverses
10 swallowing disability after brain lesions. *Gastroenterol* 2010;138(5):1737-46.
11
- 12 26. Power M, Fraser C, Hobson A, Rothwell JC, Mistry S, Nicholson DA, Thompson DG,
13 Hamdy S. Changes in pharyngeal corticobulbar excitability and swallowing behavior after
14 oral stimulation. *Am J Physiol-Gastr L* 2004;286(1):G45-G50.
15
- 16 27. Power ML, Fraser CH, Hobson A, Singh S, Tyrrell P, Nicholson DA, Turnbull I,
17 Thompson DG, Hamdy S. Evaluating oral stimulation as a treatment for dysphagia after
18 stroke. *Dysphagia*. 2006;21(1):49-55.
19
- 20 28. Doeltgen SH, Dalrymple-Alford J, Ridding MC, Huckabe ML. Differential effects of
21 neuromuscular electrical stimulation parameters on submental motor-evoked potentials.
22 *Neurorehab Neural Re* 2010;24(6):519-27.
23
- 24 29. McDonnell MN, Ridding MC. Afferent stimulation facilitates performance on a novel
25 motor task. *Exp Brain Res* 2006;170(1):109-115.

- 1 30. Uy J, Ridding MC, Hillier S, Thompson PD, Miles TS. Does induction of plastic change
2 in motor cortex improve leg function after stroke? *Neurology* 2003;61(7):982-4.
3
- 4 31. Elbert T, Lutzenberger W, Rockstroh B, Birnbaumar N. The influence of low-level
5 transcortical DC-currents on response speed in humans. *Int J Neurosci* 1981;14:101-14.
6
- 7 32. Mistry S, Verin E, Singh S, Jefferson S, Rothwell JC, Thompson DG, Hamdy S.
8 Unilateral suppression of pharyngeal motor cortex to repetitive transcranial magnetic
9 stimulation reveals functional asymmetry in the hemispheric projections to human
10 swallowing. *J Physiol* 2007;585(2):525-538.
11
- 12 33. McDonnell MN, Hillier SL, Miles T, Thompson PD, Ridding MC. Influence of combined
13 afferent stimulation and task-specific training following stroke: A pilot randomized
14 controlled trial." *Neurorehab Neural Rep* 2007;21(5):435-43.
15
- 16 34. Bastos Conforto A, Nocelo Ferreiro K, Tomasi C, Laurenti dos Santos R, Moreira V,
17 Marie SK, Baltieri SC, Scaff M, Cohen LG. Effects of somatosensory stimulation on motor
18 function after subacute stroke. *Neurorehab Neural Re* 2010;24(3):263-272.
19
- 20 35. Martin RE. Neuroplasticity and Swallowing. *Dysphagia* 2009;24:218-229.
21
- 22 36. Barrit AW, Smithard DG. Role of cerebral cortex plasticity in the recovery of swallowing
23 function following dysphagic stroke. *Dysphagia* 2009;24:83-90.
24
- 25 37. Ridding MC, Inzelberg R, Rothwell JC. Changes in excitability of motor cortical

- 1 circuitry in patients with Parkinson's disease. *Ann Neurol* 1995a;37(2):181-188.
- 2
- 3 38. Stefan K, Kunesch E, Cohen LG, Benecke R, Classen J. Induction of plasticity in the
4 human motor cortex by paired associative stimulation. *Brain* 2000;123(3):572-84.
- 5
- 6 39. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of
7 the human motor cortex. *Neuron* 2005;45(2):201-6.
- 8
- 9 40. Rossi S, Hallett M, et al. Safety, ethical considerations, and application guidelines for the
10 use of transcranial magnetic stimulation in clinical practice and research. *Clin Neurophysiol*
11 2009;120(12):2008-9.
- 12
- 13 41. Jefferson S, Mistry S, Michou E, Singh S, Rothwell JC, Hamdy S. Reversal of a Virtual
14 Lesion in Human Pharyngeal Motor Cortex by High Frequency Contralesional Brain
15 Stimulation. *Gastroenterology* 2009;137(3):841-9.
- 16
- 17 42. Singh S, Mistry S, Jefferson S, Davies K, Rothwell J, Williams S, Hamdy S. A Magnetic
18 Resonance Spectroscopy Study of Brain Glutamate in a Model of Plasticity in Human
19 Pharyngeal Motor Cortex. *Gastroenterology* 2009;136(2):417-24.
- 20
- 21 43. Classen J, Wolters A, Stefan K, Wycislo M, Sandbrink F, Schmidt A, Kunesch E. Paired
22 Associative Stimulation. *Suppl Clin Neurophysiol* 2004;57:563-69.
- 23

- 1 44. Jefferson S, Mistry S, Singh S, Rothwell J, Hamdy S. Characterizing the application of
2 transcranial direct current stimulation in human pharyngeal motor cortex. *Am J Physiol-Gastr*
3 *L* 2009;297(6):G1035-G1040.
- 4
- 5 45. Williams JA, Pascual-Leone A, Fregni F. Interhemispheric modulation induced by
6 cortical stimulation and motor training. *Phys Therap* 2010;90(3):398-410.
- 7
- 8 46. Vines BW, Nair DG, Schlaug G. Contralateral and ipsilateral motor effects after
9 transcranial direct current stimulation. *Neuroreport* 2006;17;671-4.
- 10
- 11 47. Hummel FC, Heise K, Celnik P, Floel A, Gerloff C, Cohen LG. Facilitating skilled right
12 hand motor function in older subjects by anodal polarization over the left primary motor
13 cortex. *Neurobiol Aging* 2010;31:2160-8.
- 14
- 15 48. Nitsche MA, Schaunburg A, Lang N, Liebetanz D, Exner C, Paulus W, Tergau F.
16 Facilitation of implicit motor learning by weak transcranial direct current stimulation of the
17 primary motor cortex in the human. *J Cog Neurosci* 2003;15(4):619-626.
- 18
- 19 49. Marshall L, Helgadottir H, Moelle M, Born J. Boosting slow oscillations during sleep
20 potentiates memory. *Nature* 2006;444(7119):610-613.
- 21
- 22 50. Kumar S, Wagner CW, Frayne C, Zhu L, Selim M, Feng W, Schlaug G. Noninvasive
23 brain stimulation may improve stroke-related dysphagia: a pilot study. *Stroke*
24 2011;42(4):1035-40.
- 25

- 1 51. Ridding MC, Rothwell JC. Is there a future for therapeutic use of transcranial magnetic
2 stimulation? *Nature Rev Neurosci* 2007;8(7):559-567.
3
- 4 52. Gow D, Hobson AR, Furlong P, Hamdy S. Characterising the central mechanisms of
5 sensory modulation in human swallowing motor cortex. *Clin Neurophysiol*
6 2004;115(10):2382-2390.
7
- 8 53. Hamdy S, Aziz Q, Rothwell JC, Power M, Singh KD, Nicholson DA, Tallis RC,
9 Thompson DG. Recovery of swallowing after dysphagic stroke relates to functional
10 reorganization in the intact motor cortex. *Gastroenterology* 1998;115(5):1104-12.
11
- 12 54. Nitsche MA, Liebetanz D, Lang N, Antal A, terGau F, Paulus W, Priori A. Safety criteria
13 for transcranial direct current stimulation (tDCS) in humans. *Clin Neurophysiol*,
14 2003;114:2220-2223.
15
- 16 55. Burkhead LM, Sapienza CM, Rosenbek JC. Strength-training exercise in dysphagia
17 rehabilitation: Principles, procedures, and directions for future research. *Dysphagia*,
18 2007;22:251-65.
19
20
21
22