Relative Efficacy of Swallowing Versus Non-swallowing Tasks in Dysphagia Rehabilitation: Current Evidence and Future Directions

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Abstract Clinical trials published in 2012 and the first 6 months of 2013 were reviewed. These involved either traditional dysphagia therapy, indirect methods not involving dysphagia therapy, or a combination of direct and indirect methods. Of 27 studies, 7 were RCTs, 5 were controlled clinical trials, and the remainder were uncontrolled case series. Sixteen studies combined an indirect treatment with traditional dysphagia therapy; only one study examined one technique for direct swallowing therapy. Effect sizes were computed and contrasted for each trial. Traditional dysphagia therapy had small to moderate effect sizes (between 0.3 and 0.6), while spontaneous recovery in acute stroke had effect sizes of 1.2. Placebo effects on patient ratings of degree of improvement on swallowing were estimated as small to moderate. To improve effect sizes, adaptive research designs are needed to develop the optimal methods and dosages of therapy before future clinical trials.

Keywords Dysphagia therapy · Strengthening exercises · Electrical stimulation · Random controlled trials · Spontaneous recovery

Introduction

The purpose of this review was to examine the current trends and relative efficacy of different approaches to the rehabilitation of swallowing disorders. Dysphagia or swallowing

disorders are secondary to different diseases or disorders such as stroke, aging, neurodegenerative diseases such as Parkinson's disease, and following chemo-radiation for the treatment of head and neck cancer. Approaches include: (1) training a new approach for swallowing to improve airway protection; (2) treating the primary disorder in the expectation that the secondary swallowing disorder will improve; or (3) providing less direct approaches to dysphagia either by strengthening a muscle function or providing sensory stimulation. Here, we employed the classification approach used by Zhen et al. [1], that differentiates direct swallowing therapies from indirect swallowing therapy approaches. Direct therapies (DT) include: compensatory strategies while swallowing such as chin tuck or head turn to increase airway protection, augmentative swallowing maneuvers such as Mendelsohn [2] or supraglottic swallowing, or diet modification to reduce the risk of aspiration such as thickened liquids [3]. Indirect therapies (IDT) do not directly target swallowing retraining, but are aimed at treating the underlying disease through pharmacological means, surgery, or involving muscle strengthening, sensory stimulation, or cortical stimulation by transcranial magnetic stimulation or transcranial direct current stimulation [1].

Searches

To review the therapeutic trials on dysphagia over the 1.5-year period from January 2012 to June 2013, Scopus and Medline databases were searched for studies of dysphagia therapy using search terms of: (dysphagia or swallowing disorders) and (rehabilitation or therapy) and (treatment) and (2012 or 2013), and (human). Both Mesh and text terms were searched.

Initially, 1,546 articles were retrieved and were reviewed by the first author to select clinical trials providing treatment

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Fig. 1 The review and study classification process. Over 1,500 studies were identified for review from PUBMED and Scopus published between January 2012 and June 2013. After careful examination, 27 were selected as clinical trials involving treatment of dysphagia. Direct dysphagia therapy includes training patients on swallowing using compensatory techniques, swallowing maneuvers such as the Mendelsohn maneuver, consistency changes, and diet modification. Indirect therapy includes methods for modifying the

underlying disorder causing the swallowing deficits such as surgical and neuropharmacological treatment, and sensory or cortical stimulation of persons without coincident swallowing therapy. Combined direct and indirect therapy is when an indirect technique is applied during swallowing therapy such as neuromuscular stimulation while swallowing. *RCT* random controlled trials, *CCT* controlled clinical trials, *case series* are when no control group is employed

for patients with dysphagia. Of the initial group, 30 were selected as representing some aspect of treatment of swallowing disorders. Three studies were deleted. One only involved healthy volunteers and assessed the effects of effortful swallowing and Mendelsohn maneuver training on tongue pressure production and not swallowing [4]. Another was a study of surface electromyography measures of swallowing in a patient group with Parkinson's disease [5]. The third was a pilot study of the immediate effects of surface electrical stimulation on swallowing during videofluoroscopy in patients with Parkinson's disease and healthy volunteers [6]. After 3 deletions, 27 studies remained and are reported on here.

Classification of Evidence and Measures of Efficacy

Many clinical trials aimed at improving swallowing combined both direct and indirect approaches. Out of a total of 27 studies, we classified 1 study as involving direct swallowing retraining alone (DT), 10 studies involved non-swallowing indirect methods of treatment (IDT), and 16 examined a therapeutic regimen that combined IDT and DT methods (Fig. 1).

Random controlled trials (RCT) provided the highest level of evidence. These may involve multiple sites, include random assignment of patients to experimental and control groups, and conduct objective, blinded assessment of outcome measures. When the data on mean and standard deviations of both groups were available, we used G Power 3.1.7 [7] to estimate the effect size. Controlled studies that included a control group but did not qualify as RCTs either due to lack of random assignment to groups, unblinded assessment, or did not objectively assess outcomes were classified as controlled clinical trials (CCTs). The other studies that did not include a control group were classified as uncontrolled case series. Without an active sham or an untreated group for comparison with the treated group, the degree of benefit cannot be determined. In such studies, placebo effects or spontaneous recovery may have inflated reported treatment effects.

To measure treatment benefits Cohen's effect size [8] represents the amount of change due to the treatment relative to the amount of variance in patient scores between the two measurements. This measure can compare effects across clinical trials and does not depend on power differences as the number of patients can alter the statistical results [9]. When Cohen's *d* effect sizes were not provided

Table 1 Review of 1 study of direct swallowing therapy alone and 11 studies of indirect treatment effects on swallowing

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
McCullough et al. [10•, 11]	RCT	Direct therapy study with 2 crossover groups of different orders, 2 weeks treatment (AABB) versus 2 weeks no treatment (BBAA); dysphagia post-stroke between 6 weeks and 22 months post-onset	Mendelsohn maneuver with EMG (17)	No treatment same 17 patients	0.334 anterior hyoid motion, 0.470 hyoid vertical; 0.056 upper esophageal sphincter opening	No statistical differences in maximum hyoid vertical and anterior hyoid displacement or upper esophageal opening	Patients unblinded
Park et al. [14]	RCT	Comparison of treatment and control groups, 1 month post stroke	5 Hz transcranial magnetic stimulation for 10 min daily for 2 weeks to unaffected hemisphere (9)	Sham transcranial magnetic stimulation for 10 min daily for 2 weeks (9)	Videofluoroscopic dysphagia scale scores in the experimental group at 2 weeks post-therapy had an effect size of 0.746 and 0.146 in the control group. PAS scores had an effects size of 0.725 in the experimental group and 0.143 in the control group	Significant effects ($p = 0.05$) post-treatment on videofluoroscopic dysphagia in the pharyngeal phase and the PAS only in the experimental group	Possible regression towards the mean may account for some of the treatment effect as the experimental group was more impaired than the control at baseline
Striezel et al. [17•] and Alajbeg et al. [16]	Initial RCT cross-over with open label uncontrolled follow-up at 3, 5, 8, and 11 months	RCT includes sham ($n = 56$) and active patients ($n = 58$) with xerostomia of multiple etiologies; follow-up study of 94 patients in uncontrolled open label	In the RCT following device use, the active device was evaluated	An active sham device control group was studied in the RCT	In the RCT, the active device use had an effect of 0.178 and sham had 0.035. The uncontrolled effect sizes following 3 months device use was 0.140; and 0.214, 0.316, and 0.210 at 5, 8 and 11 months in the treatment group, respectively	In the uncontrolled follow-up after 5, 8, and 11 months of device use [16], statistical comparisons were significant at $p = 0.05$, 0.002, and 0.05, respectively	The sham device and experimental device groups in the initial double blind study differed at baseline ($p = 0.05$) with an effect size of 0.467
Wada et al. [18]	Case series	Pre-/post-treatment analysis ($n = 8$); all treated with jaw opening exercise for 4 weeks	Chronic dysphagia with decreased UES opening ($n = 8$)	No control	Effect sizes on videofluoroscopic swallowing study comparing baseline with 4-week follow-up were 0.89 for hyoid elevation, 0.69 for hyoid forward movement, and 0.74 for both UES opening and time for passage through the pharynx	Statistical comparisons on videofluoroscopic swallowing study comparing baseline with 4-week follow-up were $p = 0.012$ for hyoid elevation, $p = 0.05$ for hyoid forward movement, $p = 0.036$ for UES opening and $p = 0.043$ for time for passage to the pharynx	No mention of blinding to pre- or post-treatment conditions
Nakamura and Fujishima [19]	Case series	Cross-over design; dysphagia post-stroke ($n = 24$); 12 had ABAB and 12 had BABA order for the 4 trials administered	Trials with and without ice massage. Subdivided into swallow trigger on all 4 trials ($n = 14$) and <4 swallows triggered ($n = 10$)	No control	In the 14 patients who responded on every trial, the effects size for swallow latency reduction was 0.452; 10 patients who did not swallow on every trial with ice massage had an opposite effect. They took longer to swallow with ice massage and the effect size was 1.28	Both comparisons within each group were significant, with a significant reduction in swallowing latency at $p = 0.0366$ in the larger group of 14 patients and an increase in swallowing latency with treatment at $p = 0.0267$ in the smaller group	An acute pilot study and not a clinical trial

Table 1 continued

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
Sdravou et al. [20]	Case series	Cross-over design; acute study; Patients with neurogenic dysphagia (<i>n</i> = 17)	Patients administered 5, 10, and 25 ml liquids as tolerated both with and without carbonation	No control	Effect of carbonation on duration of 5 ml oral transit time effect size was 0.16, and 0.29 for 10 ml and 0.30 for 25 ml. For pharyngeal transit time, the effect sizes were 0.25, 0.25, and 0.19, and for stage transition duration were 0.30, 0.22, and 0.97. For the three PENASP rating scales, the effect sizes were <i>r</i> = 0.46, 0.51, and 0.20	No statistical effect of carbonation was found on any of the swallowing timing measures. Significant improvement in PEN ASP scores were found (<i>p</i> < 0.05) on one-tailed tests at 5 and 10 ml volumes	Multiple comparisons were conducted using a one-tailed <i>t</i> test without Bonferroni corrections noted
Theurer et al. [21]	Case series	Single acute cross-over study; dysphagia after hemispheric stroke (<i>n</i> = 8)	Baseline without device was compared with device with and without stimulation	Sham device was evaluated in 5 of the 8 patients	No group data were presented to evaluate effect size	Only 4 of the 8 patients showed an increase in swallowing that was greater than 2 standard deviations of baseline swallowing rate during bilateral stimulation	Small acute proof of principal pilot study
Tawadros et al. [22]	Controlled trial	Mixed design, cross-over. Patients compared without Levodopa and 1 h after levodopa with age-matched controls	Electromyographic measures of submental muscle activation burst amplitude and duration and swallow duration on accelerometry	Age-matched controls were compared with patients at baseline prior to Levodopa	Effect sizes could not be measured. Means and standard deviations before and after Levodopa not reported. Based on means and SD plotted in a graph, the effect size at 20 ml was 0.48	No statistical effects of levodopa in the patient group were found on the measures of EMG or the number of swallows required for bolus ingestion. Only inter-burst latency between submental and infrahyoid onsets was longer in PD and reduced with levodopa for boluses less than 25 ml (<i>p</i> < 0.01)	No numerical group data were provided; the surface laryngeal data most likely included the sternohyoid and thyrohyoid neck muscles and not laryngeal muscles which are too deep to be recorded with surface EMG
Silbergleit et al. [24]	Case series	Cross-over design; patients with advanced Parkinson's disease (<i>n</i> = 14) evaluated at baseline before implant and at 3 and 12 months post-implant	Baseline at pre-treatment with and without medication. Post-conditions were: stimulation on/off/medication off, stimulator off/medication on, and stimulator on/off/medication on	No control	Dysphagia handicap index comparing baseline with 12 months on function = 0.483, on emotion = 0.859, and total = 0.682	No significant objective improvement seen on any of the swallowing measures. Statistical significance (<i>p</i> < 0.01) was reported on patient dysphagia handicap scale measures at 12 months post-implant compared with baseline	
Kulneff et al. [24]	Case series	Cross-over design; patients with Parkinson's disease (<i>n</i> = 11) before and at 6 and 12 months post-implant	Baseline without medication and after a test dose of levodopa. After surgery measurements at 6 and 12 months in 4 conditions (stimulator on and off and medication on and off)	No control	Effect size for comparing patient judgment of percent deterioration in swallowing from normal between stimulator off and on at 6 months was 0.783 and 0.555 at 12 months. Medication effects prior to implant = 0.522	Swallowing function measures showed no statistical significance; only the patient subjective ratings showed benefit with stimulation (<i>p</i> = 0.01)	

Table 1 continued

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
Sundstedt et al. [23]	Case series	Cross-over design; Parkinson's patients evaluated at baseline and at 6 and 12 months post-stimulator insertion on fiberoptic endoscopic examination of swallowing	Comparisons were between medication and no medication at baseline and between stimulator on and off at 6 and 12 months	No control	Effect size 6 months post-implant for stimulation off was 0.459 and with stimulation 0.433. At 12 months, the effect of stimulation was an increase in spillage = 0.3	Pre-swallow spillage showed significant effects at $p = 0.01$ with stimulation on and off both better than L-dopa pre-operatively, but a worsening with stimulation over no stimulation at 6 and 12 months. No effects on patients' subjective ratings were found	

by the authors in the article, we used the data presented to compute effect sizes. For a repeated or cross-over design, the repeated effect size, dz , was computed comparing the pre and the post treatment measures. When there was an independent control group, d was computed comparing the outcomes in the treated and control groups. If the control group had traditional dysphagia therapy, then the effect size was computed for that type of therapy. Two tables present a summary of the results: Table 1 reports on the 1 study involving direct therapy (DT) and the 10 indirect therapy (IDT) studies. Table 2 reports on 14 studies examining a combination of direct and indirect treatments. Two case studies are not included in Table 2 as they do not contain group data. Based on Cohen [8], we considered effect sizes of 0.2–0.499 to be small, 0.5–0.799 to be moderate, and 0.8 or greater to be large effect sizes. Less than 0.2 was considered no effect.

Direct Therapy Study

A multi-center RCT examining direct therapy effects using the Mendelsohn maneuver for dysphagia post-stroke [10•] was published in 2012 with further data analysis published in 2013 [11]. This was a prospective, cross-over study design with measures on 17 patients randomly assigned between 2 orders: (1) Mendelsohn training followed by 2 weeks of no therapy and (2) the opposite order. The Mendelsohn training used surface electromyography biofeedback and was intensive; participants trained twice daily for 45 min during each session with 30–40 swallows per session [11]. Videofluoroscopy swallowing studies at baseline and after 1 and 2 weeks of treatment included three measures. No significant differences were found between treatment versus non-treatment changes in either set of analyses [10•, 11]. Group means at 2 weeks post-treatment and 2 weeks post-control were compared to determine effect size based on data provided [11], deriving standard deviation from the standard errors scores ($SD = SE \times \sqrt{n}$) to compute effect sizes (dz). The effect sizes were small for maximum anterior and vertical hyoid motion and no effect was found on extent of upper esophageal sphincter opening (Table 1). Penetration–Aspiration Scale [12] and the Dysphagia Outcome and Severity Scale [13] showed no changes in dysphagia severity with treatment and data were not available for computing effects sizes [10•, 11]. This was a well-designed study with intensive therapy with small effect sizes.

Indirect Therapy Studies

These studies employed treatment that either examined the use of a device, surgical, or pharmacological treatment of

the disease underlying dysphagia, or used sensory or cortical stimulation in the absence of direct swallowing therapy. Two were controlled studies, eight were uncontrolled.

An RCT examined the effects of excitatory 5-Hz transcranial magnetic stimulation over the unaffected hemisphere that might assist with recovery of swallowing [14]. The effect sizes were moderate in the experimental group (>0.7) and demonstrated no effect in the control group (<0.2) on both the videofluoroscopic dysphagia scale [15] and the Penetration–Aspiration Scale [12]. However, the experimental group had a more severe videofluoroscopic dysphagia score at baseline of 33.6 while the baseline score of the control group was 23.4 which was similar to the post-treatment mean for the experimental group of 25.3. Although non-significant, the group differences at baseline represented a moderate effect size of 0.76, similar to the effect size for treatment effects within the experimental group. The group difference at baseline may have contributed to a regression towards the mean affecting the treatment results in the experimental group but not in the control group.

The other controlled trial, an application of an intraoral electrostimulation device for treatment of xerostomia, was a large multicenter open-label, clinical trial follow-up published in 2012 [16] from a RCT conducted in 2011 [17•]. The 2011 RCT was a multi-center prospective randomized controlled trial involving 2 stages, an initial 1-month double blind cross-over study comparing the experimental device with a sham device followed by a 3-month open-label study for the treatment of xerostomia. The electrical stimulation delivered current to the lingual nerve to enhance the salivary reflex. Swallowing difficulties were subjectively rated on a visual analogue scale (0–100) by patients on their difficulty swallowing due to dry mouth. The sham device and experimental device groups in the initial double-blind study differed at baseline ($p = 0.05$) with a small effect size; the stage 1 comparison between baseline and post-treatment in the experimental group showed no effect. Similarly, no effect was found following 3 months of device use in the treatment group alone [17•]. In the uncontrolled follow-up after 5, 8, and 11 months of device use [16], although statistical comparisons within the case series of 94 patients were significant at $p = 0.05$, 0.002, and 0.05, respectively, the effect sizes were all small (Table 1).

All of the remaining indirect therapy studies were uncontrolled case series. As no control group was included, placebo and spontaneous recovery effects may have contributed to the results. One study examined effects of jaw opening exercise on upper esophageal sphincter opening [18]. Effect sizes for 4 objective measures from the videofluoroscopy after 4 weeks of jaw opening exercise were moderate to large. Three studies evaluated the use of

sensory stimulation before swallowing or during swallowing. In an acute pilot study, 24 patients with dysphagia post-stroke were treated using ice massage to trigger swallowing, and the latency for triggering swallowing on trials with and without ice massage was measured [19]. In the 14 patients with a swallow on every trial, the effect size of the reduction in swallowing latency was moderate. However, for the 10 patients who did not swallow on every trial, the ice massage had an opposite effect: they took longer to swallow with ice massage than without and the effect size was large. In an acute study, the effects of carbonated liquids on oropharyngeal swallowing in patients with neurogenic dysphagia and pharyngeal delay were examined using a cross-over design [20] during a videofluoroscopic swallowing study. No significant effects were found on any swallowing timing measures. All but one of the effect sizes were small indicating limited benefits. Significant changes were found on the Penetration–Aspiration Scale ratings with a moderate effect at 10-ml volumes. A third study examined the acute effects of air pulse stimulation intra-orally on swallowing rates in 8 subjects with dysphagia post-stroke [21]. Only 4 of the 8 patients showed an increase in swallowing rates greater than 2 standard deviations of the baseline rates and no group data were provided for computing effect sizes on the 8 patients.

Four uncontrolled studies of indirect treatment in patients with Parkinson's disease have been published; one examined the effects of Levodopa on swallowing [22] in patients with Parkinson's disease and three studies examined the effects of deep brain stimulation on swallowing in Parkinson's disease [23–25]. The Levodopa study showed limited effects on submental and infrahyoid electromyographic measures; only the intra-burst onset latencies were reduced with Levodopa. Effect sizes based on the means and standard deviations plotted, were small.

Deep brain stimulation implant into the subthalamic nucleus was evaluated in 12 patients at 3 and 12 months post-implant in 4 conditions combining medication on and off and stimulator on and off [25]. Results revealed no significant changes in swallowing function on objective measures taken from the videofluorographic swallowing study; but some improvement was reported by patients on the Dysphagia Handicap Index [26] with small effects on swallowing function, high effects on emotion; and moderate effects on overall score compared with baseline at 3 and 12 months post-implant. The authors raised the point that some of these changes in patient perceptions in the absence of objective changes in swallowing may represent placebo effects.

Another study examined deep brain stimulation in Parkinson's disease in the subthalamic nucleus [24]. No benefits were found on measures of swallowing function from videofluoroscopy ratings, but patients reported a moderate

Table 2 Review of 16 studies combining direct swallowing therapy with indirect treatment effects on swallowing

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
Carnaby-Mann et al. [27•]	RCT	Random assignment to 3 patient groups: usual care, sham therapy, pharyngocise exercise	Pharyngocise exercise (<i>n</i> = 20)	Usual care <i>n</i> = 20, sham therapy <i>n</i> = 18	Pharyngocise and sham effect size = 0.291; Pharyngocise and usual care effect size = 0.422	Mann Assessment of Swallowing Ability (MASA) comparison between the three groups was ≤ 0.006	Outcome measures were administered after 6 weeks of therapy during chemoradiation
Manor et al. [28•]	RCT	Random assignment of patients with Parkinson's disease with dysphagia (<i>n</i> = 42)	21 patients received video assisted dysphagia therapy	21 patients received usual dysphagia therapy	Effect size for residue on the FEES for the VAST group was 1.60 and 0.55 for conventional therapy group. Dysphagia symptoms on the SDQ for VAST group were 0.279 and 0.072 in the control group. SWAL-QOL measures showed VAST ES at 4 weeks of 0.759 and the control group of 0.087 on Burden. Symptom Freq in SWAL-QOL ES for VAST group was 0.756 and 0.2 in control group	Statistical reductions in residue on the FEES for the VAST and for the dysphagia therapy group was $p = 0.05$. Dysphagia symptoms on the SDQ showed greater improvement in the VAST group than in the control group ($p = 0.005$). SWAL-QOL measures for VAST at 4 weeks showed greater improvement than the control group $p = 0.05$ on Burden. and Symptom Freq showed a greater improvement in the VAST group than in the control group ($p = 0.002$)	Only 6 interventions were given. Provides measures of effect sizes for conventional dysphagia therapy
Yang et al. [31]	RCT	Post-stroke patients with dysphagia (<i>n</i> = 16); randomly assigned to 2 groups	tDCS treatment (<i>n</i> = 9); anodal stimulation combined with dysphagia therapy for 10 sessions over 2 weeks	Sham stimulation (<i>n</i> = 7) combined with dysphagia therapy for 10 sessions over 2 weeks	Evaluation immediately after therapy effect size for tDCS group was 0.630 and 1.18 for sham group. At 3 months, effect size for the tDCS group was 1.10 and 1.28 in the sham group	No significant differences between the baseline and measures immediately after treatment. Significant differences were found between baseline and 3 months post only on the FDS score ($p = 0.041$)	As patients entered the study in the first month post-stroke, spontaneous recovery likely accounted for the 3 months effect sizes in both groups
Shigematsu et al. [32••]	RCT	Post-stroke patients with dysphagia (<i>n</i> = 20) randomly assigned to 2 groups	10 patients had anodal tDCS for 10 sessions with stimulation and conventional dysphagia therapy	10 patients had sham tDCS for 10 sessions with stimulation and conventional dysphagia therapy	For evaluation immediately after therapy effect size for the tDCS group was 1.24 and 0.5 for the sham group. Immediately after treatment. At 1 month post-treatment, the effect size for the tDCS group was 3.42 and 1.258 in the sham group		

Table 2 continued

Study	Trial type	Design and patient group	Experimental group type (n)	Control group type (n)	Effects sizes	Statistical results	Comments
Nam et al. [33]	RCT	Random assignment to suprahyoid electrical stimulation or suprahyoid and infrahyoid electrical stimulation	10–15 sessions over 1–2 weeks of suprahyoid stimulation along with traditional therapy (n = 25)	10–15 sessions over 1–2 weeks of suprahyoid and infrahyoid stimulation along with traditional therapy (n = 25)	Suprahyoid stim anterior hyoid displacement $d = 0.512$; supra and infrahyoid stimulation anterior hyoid displacement $d = 0.3022$; effect size for difference between supra and supra + infrahyoid tx groups was $d = 0.291$. Suprahyoid stim group max anterior hyoid excursion velocity, $d = 0.513$; supra and infra stim group superior laryngeal elevation, $d = 0.282$ and maximal absolute laryngeal excursion distance, $d = 0.294$	Significance in the suprahyoid stim group was found with maximal anterior hyoid excursion distance ($p = 0.008$) and anterior hyoid excursion velocity ($p = 0.017$). In the suprahyoid and infrahyoid stim group, superior excursion distance ($p = 0.013$) and maximal absolute excursion distance ($p = 0.013$) showed significance	
Park et al. [34]	RCT	Random assignment to levels of infrahyoid electrical stimulation that induced motor output (7 mA) or that only induced sensory responses (2 mA)	Motor levels of stimulation (n = 10); 3 sets of 20 min of stimulation exercise per week for 4 weeks of infrahyoid stimulation paired with effortful swallowing every 10 s during stimulation	Sensory levels of stimulation (n = 10) with 3 sets of 20 min of stimulation exercise per week for 4 weeks of infrahyoid stimulation paired with swallowing every 10 s during stimulation	Change in extent of laryngeal vertical movement in the motor stimulation group was 0.933, and 0.051 in the sensory stimulation group. Hyoid vertical movement had an effect size of 0.715 in motor stimulation group and 0.059 in sensory group	Significant increases in the extent of laryngeal vertical movement occurred in the motor stimulation group ($p = 0.029$); no significance in the sensory group	The sensory stimulation group shows no effect of spontaneous recovery affecting their swallowing movement over the 4 weeks of treatment
Baijens et al. [35]	Controlled trial	Quasi-randomized dysphagic Parkinson's patients (n = 90) allocation between 3 groups: dysphagia therapy alone, submental motor stimulation, and submental sensory stimulation	15 days dysphagia therapy with submental motor stimulation (n = 30) or with submental sensory stimulation (n = 30)	15 days dysphagia therapy (n = 30)	No data were provided for computing effect sizes	No group differences were found although there was an overall treatment effect	

Table 2 continued

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
Kushner et al. [36]	Controlled trial	Feeding tube-dependent in patients with dysphagia after acute stroke; assignment was dependent upon the referring physician order	Neuromuscular electrical stimulation plus dysphagia therapy and resistance (<i>n</i> = 65); initiated on average 15 days post-stroke	Dysphagia therapy and resistance (<i>n</i> = 27)	Grossly different <i>n</i> between NMES and control (trad. Dysphagia tx). Calculated effect size in G-power which assumes <i>n</i> ₁ = <i>n</i> ₂ for comparison between NMES tx + trad tx and control of only trad tx, <i>d</i> = 0.8955. Using www.campbellcollaboration.org (George Mason Univ.) calculator and entering specific <i>n</i> , the <i>d</i> = 0.9355	Treating speech pathologist assigned the pre- and post-FIOS score. Recovery was greater in the NMES group but this could have been because of assignment bias and the FIOS scores being assigned by the treating therapist	NMES group started with significantly lower initial FIOS scores and group assignment was not randomized (group assignment bias). Regression towards the mean could account from greater improvement in the NMES group
Zhen et al. [1]	Controlled trial if patients post-tongue resection for cancer	Patients post-tongue resection (<i>n</i> = 46). Group assignment determined by hospital ward	30 min of swallowing therapy 6 days a week for 2 weeks (<i>n</i> = 23)	No therapy (<i>n</i> = 23)	Authors reported means/SD dependent upon degree of tongue resection. For less than 50 % resection: <i>d</i> = 1.29 when comparing experimental and control MDADI global scores; <i>d</i> = 0.891 for ≥50 % tongue resection		
Kang et al. [37]	Controlled trial	Subacute patients post-stroke (<i>n</i> = 50); evaluated after 2 months of therapy. Conventional therapy in both groups for 30 min per day, 5 days a week.	Additional hour of bedside laryngeal, oral, pharyngeal and respiratory exercises paired with conventional swallowing therapy (<i>n</i> = 25)	Conventional swallowing therapy (<i>n</i> = 25)	For oral phase: experimental group pre/post <i>d</i> = 2.01 while control <i>d</i> = 0.733. Comparing post-test experimental and control for oral phase yielded <i>d</i> = 0.708. For pharyngeal phase: experimental group pre/post, effect size was 0.897 while control <i>d</i> = 0.846. Comparing post-test for 2 groups yielded <i>d</i> = 0	Significant increase in oral phase ratings post-treatment in New VFSS Scale for the experimental bedside exercise program group over the control. Differences in pharyngeal at post-test between groups were not significant. Experimental group had less depressive mood (BDI) and higher QOL (SS-QOL) in energy, family role, and mood. Experimental group had significant change in FIOS	The types of therapies are not well defined. The assignment to group is not described. No Bonferroni correction made for 32 comparisons at <i>p</i> < 0.05

Table 2 continued

Study	Trial type	Design and patient group	Experimental group type (<i>n</i>)	Control group type (<i>n</i>)	Effects sizes	Statistical results	Comments
Crary et al. [39]	Case series	McNeill Dysphagia Therapy Program administered to chronic dysphagia patients (<i>n</i> = 9)	Intensive therapy for 3 weeks = 15 sessions (<i>n</i> = 9)	No control	Reported Hedge's <i>g</i> comparing baseline to post-MDTP as follows: MASA <i>g</i> = 0.94, FOIS <i>g</i> = 1.42, VFE score <i>g</i> = 0.177, VAS <i>g</i> = 1.26. Effect sizes comparing post-test with 3 months follow-up (looking for detraining) were negligible	Functional outcomes included increases in MASA (by 17 points), FOIS scores and functional oral intake were maintained at 3 months. VFSS measures improved post-treatment but not significant. Significant secondary outcome measures included: increased laryngeal and hyoid elevation for thin and 5 ml (but not pudding) and lingual-palatal pressure increased for pudding with no evident detraining at 3 months post-treatment	
Lan et al. [37]	Case series	McNeill Dysphagia Therapy Program administered to chronic dysphagia patients (<i>n</i> = 8)	Intensive therapy for 3 weeks = 15 sessions (<i>n</i> = 8)	Healthy	No data available for computing effect sizes	Baseline measurements of timing significantly lower than healthy. post-MDTP, experimental group participants did not exhibit significantly different timing data. Thin liquid data had the greatest magnitude of change	
Moon et al. [40]	Uncontrolled case series	Healthy adults over 70 years of age and younger adults less than 30; examination of improvements after NMES	Older adults (<i>n</i> = 18) received NMES therapy for 60 min a day, 5 days a week for 2 weeks	Younger adults did not receive therapy: no active control	Effect size of e-stim on functional dysphagia scale scores was 0.641	The FDS values were significantly lower after the NMES treatment for the older healthy adults than prior to the treatment	
Sun et al. [41]	Uncontrolled case series	Cross-over design; patients were greater than 3 weeks post-stroke with moderate to severe dysphagia (<i>n</i> = 29)	12 sessions of electrical stimulation 1 h per day, 5 days per week for 2–3 weeks; then each patient received 12 sessions of traditional swallowing therapy	No control	Means and standard deviations were not available	On follow-up 6 months and 2 years later, significant improvements in degree of dysphagia and visual analogue scale of the patients' subjective assessment of their dysphagia were found	

effect size of stimulation benefit on their swallowing at 6 and 12 months which may include a placebo effect. A third study of the effects of deep brain stimulation on swallowing in Parkinson's disease determined if there were deficits with stimulation in the Zona Incerta [23]. No effects were found except for a small worsening in pre-swallow spillage with stimulation on at 12 months post-implant; no subjective effects were found on patient ratings.

Overall, the two controlled studies of indirect treatment approaches had small or moderate treatment effects while the 8 uncontrolled studies varied with large effects only seen in patients performing jaw opening exercises; however, as this study was uncontrolled, the results cannot be distinguished from potential placebo effects. The two studies of the effects of subthalamic nucleus stimulation on swallowing in Parkinson's disease showed no benefits on objective measures of swallowing. The only benefits were in patient subjective ratings which are particularly susceptible to placebo effects after implantation and were small to moderate effects.

Combined Direct and Indirect Therapy Studies

Sixteen studies combined indirect therapy with direct swallowing therapy. Some included controls with direct therapy or a sham with direct therapy. Of these studies, five were RCTs, four were CCTs, and the remaining seven were uncontrolled case series. The combined approach was the most frequent approach in research on dysphagia treatment in recent years. This may be based on the assumption that if direct therapy shows small to moderate effect sizes then adding further therapeutic approaches will augment the results.

An RCT on a therapy described as “pharyngocise” evaluated whether active exercise combined with usual care for patients with head and neck cancer undergoing chemoradiation therapy (CRT) is beneficial [27•]. Strengthening exercise combined with swallowing therapy was compared with a sham therapy group (active controls) and a usual care group which included supervision and precautions for safe swallowing with positioning and slowed rate of feeding by the hospital speech pathology service. Both active treatment groups were seen twice daily for 45 min of exercise for 6 weeks. The sham treatment received a buccal extension maneuver while the pharyngocise group received jaw resistance/strengthening using the Therabite Jaw Motion Rehabilitation System. As all patients consumed a normal diet at baseline, effect size differences on the Mann Assessment of Swallowing Ability (MASA) between the three independent groups were determined at 6 weeks. The effect sizes were small between pharyngocise and sham therapy and between pharyngocise and usual care.

Another RCT compared patients with Parkinson disease and swallowing difficulties who were randomly assigned to two groups: usual dysphagia therapy ($n = 21$) and video-assisted dysphagia therapy ($n = 21$) showing videos of the typical swallowing process and patients' own swallowing as part of regular therapy during all six interventions [28•]. A large effect size for residue reduction on FEES examination in the video-assisted group compared with a moderate effect size in the usual dysphagia therapy group. Patient responses on the SDQ questionnaire [29] only showed a small effect improvement and no effect in the controls. Difference in effect size occurred on scores in the video and conventional therapy group at 4 weeks and 8 months; at least moderate effect sizes occurred in the video group compared with no or small effects in the conventional therapy group on the SWAL_QOL [30]. This study is notable as the effect size of the experimental therapy was large (1.6) when compared with the moderate effect size (0.55) of conventional dysphagia therapy on residue after a swallow.

Two studies examined the combination of transcranial direct current stimulation (tDCS) combined with swallowing training post-stroke [31, 32••]. Both compared anodal tDCS with sham stimulation during ten trials of dysphagia therapy. One study used the DOSS [13, 32••] for pre- and post-measures of dysphagia while the other used the Functional Dysphagia Scale (FDS) [15, 30]. In the first study [31], the effect size immediately after treatment in the tDCS group was moderate and high in the sham group. At 3 months post-therapy, both groups had a high effect size. Mean days post-stroke was 25.9 days ($SD = 10.2$) so most patients were within the first month post-stroke on entering the study and spontaneous recovery could account for partial improvement in both groups, particularly 3 months after therapy. In the second study [32••], patients were at least 1 month post-stroke. After 10 sessions of therapy, the tDCS group had a large effect size while the sham group had a moderate effect size, similar to the effect of usual dysphagia therapy reported for traditional therapy. Thus, after 10 sessions of traditional dysphagia therapy along with tDCS in patients seen within 1 month post-stroke, both studies had an immediate effect size of 0.6 or greater. However, the post-therapy follow-up on 3 months in one study and 1 month in the second both showed a high effect size in the sham group suggesting that spontaneous recovery can contribute an effect size of 1.2 or greater.

Two other RCTs evaluated a combination of transcutaneous electrical stimulation [33, 34]. In the first study, 50 subacute stroke or brain injury patients were randomly assigned; 25 to suprahyoid stimulation only and the other 25 to suprahyoid and infrahyoid stimulation for 10–15 sessions over 2–3 weeks. Electrical stimulation was combined with traditional dysphagia therapy including chin

tuck, multiple swallowing, effortful swallowing, supra-glottic swallowing, Shaker's exercise and the Mendelsohn maneuver. All of the effect sizes evaluating objective measures of movement excursion of the hyoid and larynx in each of the two groups between before and after therapy were less than 0.52. No differences in the treatment effects were found between the suprahyoid and infrahyoid groups. When objective movement changes were measured after therapy in subacute patients, the effect sizes were more modest (0.5) than when patients were studied in the first month post-stroke or -brain injury. The second study [34] using electrical stimulation tested the effect of effortful swallow therapy combined with either motor levels of infrahyoid stimulation or sensory levels of infrahyoid stimulation. Twenty patients were randomly assigned, 10 to each treatment group. Here, the patients were required to be more than 1 month post-stroke and three sets of exercise for 20 min each week were provided for 4 weeks. Using data provided in the paper, a high effect size occurred with motor stimulation on the extent laryngeal vertical movement and a moderate effect size for hyoid extent of vertical movement in the motor group. No effects occurred in the sensory group indicating that spontaneous recovery was not contributing significantly to the results.

Four studies were controlled without random assignment between the experimental and control groups, not qualifying as RCTs. A study combining surface electrical stimulation in three groups of Parkinson's disease with dysphagia used quasi-random allocation to three groups [35]. All received daily treatment for 15 days of dysphagia therapy with two groups also receiving surface submental electrical stimulation; one at a motor level and the other at a sensory level. No data were provided to compute effect sizes as odds ratio were provided. The statistical analysis showed no differences between treatment groups, although there was an overall treatment benefit indicating that differences in electrical stimulation did not alter the treatment outcome. Another study added electrical stimulation to traditional dysphagia therapy along with progressive resistance therapy ($n = 65$) for comparison with dysphagia therapy along with progressive resistance therapy without electrical stimulation ($n = 27$) [36]. Physician referral assigned patients to either treatment group; the NMES group was more impaired at baseline suggesting assignment bias, and regression towards the mean may have affected recovery in that group. Further FIOS scores were assigned by the treating speech therapist pre and post-treatment, also a likely source of bias.

A controlled trial compared inter-disciplinary swallowing therapy exercises in 23 patients post-tongue resection with a control group ($n = 23$) receiving no training [1]. Assignment was based on patient ward assignment with two floors of eight wards each assigned to the experimental

and control groups. Therapy consisted of 30 min of swallowing therapy 6 days a week for 2 weeks. High effect sizes were reported when outcomes were compared between the treatment and control groups with similar degrees of tongue resection.

The addition of a bedside exercise program to conventional swallowing therapy in subacute patients <6 months post-stroke was evaluated in a controlled trial [37]. The addition of bedside laryngeal, oral, pharyngeal, and respiratory exercises to conventional therapy was evaluated after 2 months of conventional swallowing therapy in both groups. A high effect size was found on oral phase improvements in the exercise group while the conventional therapy group had a moderate effect size. In the pharyngeal phase, both groups had a high effect size and there were no group differences in benefit.

Six uncontrolled studies were published in the 2012–2013 period examining treatment effects of a combined regimen. Some examined proprietary treatment programs and are difficult to evaluate as the intensive therapy program is not clearly described. It may include home therapy and professional therapy with exercises, direct dysphagia therapy and NMES [38, 39]. The patients had chronic dysphagia, however, placebo effects cannot be determined and both studies include multiple comparisons with no Bonferroni corrections. Subjective measures show large effect sizes while objective measures from videofluoroscopy show no significant improvement [38]. A case series evaluated the use of electrical stimulation in normal adults over 70 years of age on a functional dysphagia scale with significant improvement and moderate effect sizes [40]. Another study assessed swallowing after 12 sessions of electrical stimulation with dysphagia therapy followed by 12 sessions of traditional swallowing therapy [41]. Finally, two case studies were reported, one reporting using electrical stimulation for dysphagia in Wilson's disease [42] and another using manual facilitation with deep massage of the submental and infrahyoid regions to help initiate swallowing [43], along with oral sensory stimulation and Mendelsohn maneuver in 3 severely impaired dysphagia patients unresponsive to verbal commands post-stroke. All increased their ability to initiate a swallow. As there were no group data to be analyzed, these case studies are not reported in Table 2.

Discussion

The number of studies evaluating therapy for dysphagia in a 1.5-year period was impressive. Most studies were aimed at augmenting traditional dysphagia therapy by adding therapy components such as electrical stimulation to traditional therapy. Few, if any, RCTs have evaluated the

effects of traditional dysphagia therapy alone in particular patient populations. Traditional dysphagia therapy usually combines compensatory approaches such as chin tuck and head turn, effortful swallowing, Mendelsohn maneuver, thickened liquids, and supraglottic swallowing [3]. We could not find previous RCTs in the literature comparing a non-treatment control with traditional dysphagia therapy to determine the effect size to expect for traditional therapy alone. In this review, some studies used a traditional therapy group as a control and reported effect sizes ranging from 0.3 to 0.7, which are small to moderate. Except for studies carried out in the early spontaneous recovery period post-stroke, most effect sizes for dysphagia therapy alone are small to moderate. That may be the basis for many clinical studies combining many therapy approaches in order to augment effect sizes.

Many studies showed no benefits on objective measures of swallowing, while patient subjective ratings showed small to moderate effects, which may contain placebo effects. Patients often assume that if they are undergoing treatment they are improving. Therefore, a well-defined control group is needed when using patient ratings, as both groups may show gains that are small to moderate reflecting placebo effects [25].

Another notable finding in patients seen early post-stroke is that therapy effects are usually moderate when measured immediately after a few weeks of therapy. However, on follow-up 1 month later in one study and 3 months in another, both showed a similar high effect size in the sham group suggesting that spontaneous recovery can contribute a high effect size of 1.2 or greater. The large effect size for spontaneous recovery relative to treatment effect sizes present a significant difficulty when designing studies of treatment effects in acute stroke.

The vast majority of the treatment studies used 1 session of 30–60 min daily for 2 weeks for a total of 10 sessions of therapy in the experimental group. However, no studies have examined the optimal session duration, number of sessions, and time period of therapy necessary for effecting change in swallowing behavior. Many of these treatment studies may not have an adequate duration or intensity to effect change. This needs to be determined before embarking on expensive and time-consuming RCTs. Continual reassessment designs can be used to determine the optimal treatment parameters, require fewer participants, and are relatively short in duration to determine the optimal treatment parameters before embarking on a large multicenter RCT.

O'Quigley et al. [44] and associates introduced the concept of the continual reassessment method when designing clinical trials for cancer treatment. In such studies, small reiterative studies are sequenced so that ongoing data analysis “learns” from the results of

particular therapy regimens in a small number of patients and adjusts the next phase treatment to be more effective and less adverse. Such trials can be blinded, with only the statistician able to analyze the results in a continuous fashion to make treatment decisions. The study proceeds with small numbers of patients at a time (3–5 participants), and the treatment parameters are readjusted in a reiterative fashion based on the data learned after each patient, and the dose response curve is remodeled [45]. This method of adjusting to find the optimal treatment dosage at the highest maximal tolerated dose can provide an effective treatment regimen with the least number of adverse events. Some of these designs might be very useful for determining the optimal dosage and intensity of a therapy before embarking on a controlled trial.

Conclusions

To date, the treatment effects in dysphagia are small to moderate in contrast to the much larger effects of spontaneous recovery in acute stroke. Objective measures of swallowing kinematics generally show limited change, while patient ratings are often confounded by placebo effects. Usually, dysphagia therapy has small to moderate effect sizes; thus, the field is actively pursuing combined treatment approaches to improve outcomes. To date, some of the highest effect sizes reported in RCTs are for cortical stimulation combined with dysphagia therapy in acute stroke. However, spontaneous recovery may be contributing to a greater degree than therapy to dysphagia recovery post-stroke.

Compliance with Ethics Guidelines

Conflict of Interest T.C. Drulia declares no conflicts of interest. C.L. Ludlow works for an institution that has received NIH grants; and consulting fees, travel expenses, patent income, and fees for developing educational presentations from Passy Muir, Inc.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Zhen Y, Wang JG, Tao D, Wang HJ, Chen WL. Efficacy survey of swallowing function and quality of life in response to therapeutic intervention following rehabilitation treatment in dysphagic tongue cancer patients. *Eur J Oncol Nurs*. 2012;16(1):54–8.

2. Mendelsohn MS, McConnel FM. Function in the pharyngoesophageal segment. *Laryngoscope*. 1987;97(4):483–9.
3. Logemann JA. Evaluation and treatment of swallowing disorders. 2nd ed. Austin: Pro-Ed; 1998.
4. Fukuoka T, Ono T, Hori K, et al. Effect of the effortful swallow and the Mendelsohn maneuver on tongue pressure production against the hard palate. *Dysphagia*. 2013. doi:10.1007/s00455-013-9464-y.
5. Ws Coriolano MDG, R Belo L, Carneiro D, et al. Swallowing in patients with Parkinson's disease: a surface electromyography study. *Dysphagia*. 2012;27(4):550–5.
6. Baijens LWJ, Speyer R, Passos VL, Pilz W, Roodenburg N, Clavé P. The effect of surface electrical stimulation on swallowing in dysphagic Parkinson patients. *Dysphagia*. 2012;27(4):528–37.
7. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41(4):1149–60.
8. Cohen J. Statistical power for the behavioral sciences. 2nd ed. Hillsdale: Erlbaum; 1988.
9. Fleiss JL. The design and analysis of clinical experiments. New York: Wiley; 1999.
10. • McCullough GH, Kamarunas E, Mann GC, Schmidley JW, Robbins JA, Crary MA. Effects of Mendelsohn maneuver on measures of swallowing duration post stroke. *Top Stroke Rehabil*. 2012;19(3):234–243. *An RCT design using a randomized cross-over method comparing the Mendelsohn maneuver (a direct therapy treatment) with no treatment in 2 different orders. Physiological measurements of anterior and vertical hyoid movement during swallowing showed a small treatment effect and statistical significance was not reached.*
11. McCullough GH, Kim Y. Effects of the Mendelsohn maneuver on extent of hyoid movement and UES opening post-stroke. *Dysphagia*. 2013. doi:10.1007/s00455-013-9461-1.
12. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration–aspiration scale. *Dysphagia*. 1996;11(2):93–8.
13. O'Neil KH, Purdy M, Falk J, Gallo L. The Dysphagia Outcome and Severity Scale. *Dysphagia*. 1999;14(3):139–45.
14. Park JW, Oh JC, Lee JW, Yeo JS, Ryu KH. The effect of 5 Hz high-frequency rTMS over contralesional pharyngeal motor cortex in post-stroke oropharyngeal dysphagia: a randomized controlled study. *Neurogastroenterol Motil*. 2013;25(4):324–30.
15. Han TR, Paik NJ, Park JW, Kwon BS. The prediction of persistent dysphagia beyond six months after stroke. *Dysphagia*. 2008;23(1):59–64.
16. Alajbeg I, Falcão DP, Tran SD, et al. Intraoral electrostimulator for xerostomia relief: a long-term, multicenter, open-label, uncontrolled, clinical trial. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;113(6):773–81.
17. • Strietzel FP, Lafaurie GI, Mendoza GR, et al. Efficacy and safety of an intraoral electrostimulation device for xerostomia relief: a multicenter, randomized trial. *Arthritis Rheum*. 2011;63(1):180–190. *A large multi-center RCT compared an intraoral electrical stimulation to a sham in a cross-over design; xerostomia patients' perception of swallowing difficulty was evaluated. No treatment effects were evident at 1 month in the controlled study; however, an open-label follow-up reported small treatment effects at 5, 8, and 11 months post-treatment.*
18. Wada S, Tohara H, Iida T, Inoue M, Sato M, Ueda K. Jaw-opening exercise for insufficient opening of upper esophageal sphincter. *Arch Phys Med Rehabil*. 2012;93(11):1995–9.
19. Nakamura T, Fujishima I. Usefulness of ice massage in triggering the swallow reflex. *J Stroke Cerebrovasc Dis*. 2013;22(4):378–82.
20. Sdravou K, Walshe M, Dagdilelis L. Effects of carbonated liquids on oropharyngeal swallowing measures in people with neurogenic dysphagia. *Dysphagia*. 2012;27(2):240–50.
21. Theurer JA, Johnston JL, Fisher J, et al. Proof-of-principle pilot study of oropharyngeal air-pulse application in individuals with dysphagia after hemispheric stroke. *Arch Phys Med Rehabil*. 2013;94(6):1088–94.
22. Tawadros PB, Cordato D, Cathers I, Burne JA. An electromyographic study of parkinsonian swallowing and its response to levodopa. *Mov Disord*. 2012;27(14):1811–5.
23. Sundstedt S, Olofsson K, van Doorn J, Linder J, Nordh E, Blomstedt P. Swallowing function in Parkinson's patients following Zona Incerta deep brain stimulation. *Acta Neurol Scand*. 2012;126(5):350–6.
24. Kulneff L, Sundstedt S, Olofsson K, et al. Deep brain stimulation—effects on swallowing function in Parkinson's disease. *Acta Neurol Scand*. 2013;127(5):329–36.
25. Silbergleit AK, Lewitt P, Junn F, et al. Comparison of dysphagia before and after deep brain stimulation in Parkinson's disease. *Mov Disord*. 2012;27(14):1763–8.
26. Silbergleit AK, Schultz L, Jacobson BH, Beardsley T, Johnson AF. The Dysphagia handicap index: development and validation. *Dysphagia*. 2012;27(1):46–52.
27. • Carnaby-Mann G, Crary MA, Schmalfuss I, Amdur R. “Pharyngocise”: randomized controlled trial of preventative exercises to maintain muscle structure and swallowing function during head-and-neck chemoradiotherapy. *Int J Radiat Oncol Biol Phys*. 2012;83(1):210–219. *A RCT compared “Pharyngocise” and usual dysphagia care with sham therapy and usual care in patients undergoing chemoradiation treatment for head and neck cancer. In secondary outcome measures of swallowing maintenance, there was a small benefit of “pharyngocise” over sham therapy.*
28. • Manor Y, Mootanah R, Freud D, Giladi N, Cohen JT. Video-assisted swallowing therapy for patients with Parkinson's disease. *Parkinsonism Relat Disord*. 2013;19(2):207–211. *An RCT compared conventional dysphagia therapy with and without video-feedback. This study uniquely provided effect sizes on conventional therapy alone. Video-feedback had a large effect size while conventional therapy alone yielded small effects on physiological measures of residue. Improvements in patients' perceptions of swallowing difficulty were moderate in the video-feedback group with no effects in the conventional group.*
29. Manor Y, Giladi N, Cohen A, Fliss DM, Cohen JT. Validation of a swallowing disturbance questionnaire for detecting dysphagia in patients with Parkinson's disease. *Mov Disord*. 2007;22(13):1917–21.
30. McHorney CA, Martin-Harris B, Robbins J, Rosenbek J. Clinical validity of the SWAL-QOL and SWAL-CARE outcome tools with respect to bolus flow measures. *Dysphagia*. 2006;21(3):141–8.
31. Yang EJ, Baek SR, Shin J, et al. Effects of transcranial direct current stimulation (tDCS) on post-stroke dysphagia. *Restor Neurol Neurosci*. 2012;30(4):303–11.
32. • Shigematsu T, Fujishima I, Ohno K. Transcranial direct current stimulation improves swallowing function in stroke patients. *Neurorehabil Neural Repair*. 2013;27(4):363–369. *An RCT compared effects of tDCS paired with conventional dysphagia therapy with sham tDCS paired with conventional dysphagia therapy at a mean of 3 months post-onset. Evaluation post-tDCS immediately following therapy had a large effect size while sham therapy had a small effect. One month post-treatment follow-up indicated that spontaneous recovery added further gains that were large in both groups.*
33. Nam HS, Beom J, Oh BM, Han TR. Kinematic effects of hyolaryngeal electrical stimulation therapy on hyoid excursion and laryngeal elevation. *Dysphagia*. 2013. doi:10.1007/s00455-013-9465-x.
34. Park JW, Kim Y, Oh JC, Lee HJ. Effortful swallowing training combined with electrical stimulation in post-stroke dysphagia: a randomized controlled study. *Dysphagia*. 2012;27(4):521–7.

35. Baijens LWJ, Speyer R, Passos VL, et al. Surface electrical stimulation in dysphagic Parkinson patients: a randomized clinical trial. *Laryngoscope*. 2013. doi:[10.1002/lary.24119](https://doi.org/10.1002/lary.24119).
36. Kushner DS, Peters K, Eroglu ST, Perless-Carroll M, Johnson-Greene D. Neuromuscular electrical stimulation efficacy in acute stroke feeding tube-dependent dysphagia during inpatient rehabilitation. *Am J Phys Med Rehabil*. 2013;92(6):486–95.
37. Kang JH, Park RY, Lee SJ, Kim JY, Yoon SR, Jung KI. The effect of bedside exercise program on stroke patients with dysphagia. *Ann Rehabil Med*. 2012;36(4):512–20.
38. Lan Y, Ohkubo M, Berretin-Felix G, Sia I, Carnaby-Mann GD, Crary MA. Normalization of temporal aspects of swallowing physiology after the McNeill dysphagia therapy program. *Ann Otol Rhinol Laryngol*. 2012;121(8):525–32.
39. Crary MA, Carnaby GD, Lagorio LA, Carvajal PJ. Functional and physiological outcomes from an exercise-based dysphagia therapy: a pilot investigation of the McNeill dysphagia therapy program. *Arch Phys Med Rehabil*. 2012;93(7):1173–8.
40. Moon TY, Kwon KH, Kim JW, et al. A study of functional dysphagia scale improvements after neuromuscular electrical stimulation. *J Phys Ther Sci*. 2013;25(1):61–4.
41. Sun SF, Hsu CW, Lin HS, et al. Combined neuromuscular electrical stimulation (NMES) with fiberoptic endoscopic evaluation of swallowing (FEES) and traditional swallowing rehabilitation in the treatment of stroke-related dysphagia. *Dysphagia*. 2013. doi:[10.1007/s00455-013-9466-9](https://doi.org/10.1007/s00455-013-9466-9).
42. Lee SY, Yang HE, Yang HS, Lee SH, Jeung HW, Park YO. Neuromuscular electrical stimulation therapy for dysphagia caused by Wilson's disease. *Ann Rehabil Med*. 2012;36(3):409–13.
43. Won YS. Influence of manual facilitation technique on swallowing disorder and aspiration pneumonia caused by severe dysphagia with stroke. *J Phys Ther Sci*. 2012;24(9):909–13.
44. O'Quigley J, Pepe M, Fisher L. Continual reassessment method: a practical design for phase I clinical trials in cancer. *Biometrics*. 1990;46(1):33–48.
45. Garrett-Mayer E. The continual reassessment method for dose-finding studies: a tutorial. *Clin Trials*. 2006;3(1):57–71.