Biofeedback as an Adjunctive Treatment for Post-stroke Dysphagia: A Pilot-Randomized Controlled Trial

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Running title: Biofeedback treatment in post-stroke dysphagia

ABSTRACT

Background and Purpose: Post-stroke dysphagia affects almost half of the survivors and severely influences quality of life, thus becoming swallowing rehabilitation of paramount importance. However, there is little adequate evidence on which the best rehabilitative strategy can be. Surface electromyography (sEMG) allows for recording swallowing muscles' activity and provides real time visual feedback, as a biofeedback adjunctive technique to improve treatment outcome. This study aimed to analyze the effectiveness of biofeedback rehabilitation of swallowing through sEMG compared to standard techniques, in post-stroke dysphagia.

Methods: A pilot randomized controlled trial included 17 patients diagnosed with post-stroke dysphagia. Nine underwent sEMG-biofeedback rehabilitation; seven controls were submitted to control treatment, one dropout. The primary outcome was the functional oral intake scale (FOIS), secondary outcomes was pharyngeal clearance and safe swallowing, assessed through fiberoptic endoscopic evaluation of swallowing (FEES).

Results: FOIS improved in all patients, regardless of treatment. sEMG-biofeedback rehabilitation led to improvements of the pharyngeal clearance and swallowing safety. The rehabilitative effects appeared stable at 2-months follow-up.

Conclusions: The application of biofeedback based on sEMG in post-stroke dysphagia patients resulted in an effective rehabilitative technique, in particular for pharyngeal clearance improvements and safe swallowing, thus reducing the risk of aspiration and malnutrition.

Keywords: Biofeedback, Dysphagia, Stroke, Rehabilitation, FEES

INTRODUCTION

Stroke is considered one of the main causes of oropharyngeal dysphagia. Approximately 50% of the stroke survivors show swallowing disorders [1] and for up to half of those, dysphagia is still present at three months, with a trend over one year [2]. Although the severity of dysphagia varies among individuals, it can be strictly associated with a high risk of malnutrition, dehydration, longer hospitalization and pulmonary complications such as aspiration pneumonia, which lead to an increase of mortality [3-5]. As a consequence, dysphagia impacts the quality of life as well as independence and social participation [6,7], and its rehabilitation is of paramount importance.

From the most recent Cochrane review, the primary recovery goal in post-stroke dysphagia is to directly train the swallowing pathologic mechanisms, aiming to provide a safe deglutition, adequate nutritional intake and hydration [8]. Most of the swallowing interventions include compensatory postural manoeuvres and adjustments of food characteristics (i.e., texture, viscosity, temperature, volume). Nevertheless, targeted motor exercises are fundamental for a rehabilitative approach [9]. Therefore, the rehabilitation programs should be based on the principles of motor learning and neuro-plasticity, as *use it or lose it*, *use it and improve it*, *specificity*, *transference*, and *intensity* [10].

Swallowing consists in a complex mechanism, involving both motor control and sensorial functions. Sensory input is essential for accurate motor control in planning, execution and evaluation of any phase of swallowing. Therefore, sensory feedback is necessary to set the right movements [11-13]. This principle is crucial for each swallowing phase, since constant sensory feedback about state, position and progression of the bolus allows activating and supporting the swallowing acts with proper timing and forcing [11]. Taking into account these concepts, the use of visual feedback of physiological mechanisms could provide significant additional input to improve motor control abilities of swallowing in patients with dysphagia.

Given the importance of feedback, the application of surface electromyography (sEMG) as an augmentative tool for recording the swallowing act has been recently investigated [14,15]. It can provide real time biofeedback on quantitative muscular electrical activity, which encourages patients awareness and control on muscle activation and relaxation, improving motor accuracy and coordination during the exercises [14-17].

A recent systematic review showed that the sEMG-biofeedback as an adjunctive treatment for swallowing problems might increase hyoid and laryngeal excursion and oral food transit time in several pathologies [15]. Only a few studies including stroke patients are presented, reporting, unfortunately, low to moderate methodological quality, and no randomized controlled studies evaluating sEMG's effectiveness are available so far [15].

With the purpose to verify the effects of sEMG-biofeedback on neurogenic dysphagia, hereby we propose a randomized controlled trial (RCT) on a sample of subacute stroke patients with spontaneous recovery. Both experimental and control groups were submitted to the same swallowing behavioural exercises, and sEMG-biofeedback was added only to the first group. According to the statistical recommendation for RCT, we examined how treatments influenced patients' swallowing by controlling for inter subject variability at baseline. The main aim of the study was to verify whether control treatment with biofeedback was more effective than control treatment alone in functional oral intake, pharyngeal clearance and swallowing safety, usually linked to pneumonia and malnutrition, and frequency of tracheostomy that affect patients' autonomy. Main outcomes were evaluated both directly at the end of the rehabilitation program, and at 2 months, to detect any long-term effects during recovery.

MATERIALS AND METHODS

This is a prospective, parallel group, single-blind RCT conducted at IRCCS San Camillo Hospital from December 2017 and February 2020 (registration ClinicalTrials.gov:

NCT03247374). The study was approved by the Ethics Committee of the hospital (Prot.2017.12–Bio_Dys) and carried out in accordance with the Declaration of Helsinki. All participants signed an informed consent for their inclusion.

Participants, randomization and masking

Seventeen participants were enrolled in the study following these inclusion/exclusion criteria: (1)first stroke, (2)onset from stroke >6 weeks to ensure deficit stability, (3)level of dysphagia at the Functional Oral Intake Scale (FOIS≤5) [18,19], (4)preserved comprehension (Token Test >53) [20], (5)absence of hearing or visual impairments, (6)absence of severe concomitant medical conditions (i.e., fever, infections, metabolic problems, serious cardiac insufficiency, serious dystonia or unintentional movements) or (7)other neurological diseases to not compromise the rehabilitation (such as neurodegenerative disorders). Details are provided in Table 1.

Patients were allocated in two groups through a simple randomization with parallel assignment. A random order (of 0s and 1s) was computer-generated using an excel file, to assign patients (without reallocation). The order was concealed to the enrolling speech pathologists until group assignment. Patients knew to take part in a rehabilitation program, but they were blinded to different types of treatment for a single-blind design, while the speech pathologists involved in the rehabilitation were not due to clear clinical reasons. The otorhinolaryngologist and the speech therapist in charge for the assessments of dysphagia did not know about patients' allocation, to contrast possible biases in data collection at best. No patients underwent previous rehabilitation. After recruitment, one patient dropped out (due to somnolence and consequent discontinuous collaboration) and the final sample of 16 patients included 9 patients in the experimental group and 7 in the control group (Figure 1).

Rehabilitation protocol

The two treatments consisted of one-to-one behavioural exercises with a speech pathologist, with equal method and timing of administration. It was a 5-week program, with 1 hour/day sessions (25 overall), including recovery periods.

Biofeedback treatment

sEMG-Biofeedback was applied though the ProComp5 Infiniti™ System (www.thoughttechnology.com). Its preparation took about 10 minutes for assembly and 5 minutes for removal. Two surface electrodes were secured over patient's submental muscles for registering larynx's raising (i.e., collectively covering mylohyoid, geniohyoid, anterior belly of digastric and genioglossus) and one at the shoulder as neutral reference [21]. The sEMG (filtered 10-370Hz) can detect muscular electrical signals (0.2-2000μV). They were rectified, digitized and sent to the computer via a fiber optic cable. The electromyographic signal was real time registered and depicted on a computer screen as a wave of muscular activity, which provided an on-line performance's feedback to the patient. During the first session, participants were instructed how to keep their own movements in a range between 5 and 30 μV, in accordance with the subjective clinical level.

During the rehabilitation, the patients were required to swallow at a given time and to perform manoeuvres for swallowing strength, coordination and efficacy, randomly including: 10 minutes of effortful swallow [22], 10 minutes of supraglottic swallow [23] and 10 minutes of Masako manoeuvre [24].Specifically, during effortful swallow the patient was asked to swallow and push hard with the tongue against the hard palate, to increase posterior tongue base movement and facilitate bolus clearance. For supraglottic swallow, the patient had to voluntarily hold breath just before swallowing, to close the vocal folds, and immediately to produce a volitional cough. This manoeuvre was designed to protect the airways before and

during swallowing. During Masako exercise, the patient held the tongue between the teeth while swallowing, with the intent to improve movements and strength of the base of the tongue and the posterior pharyngeal wall during swallowing.

When possible, the first two tasks were performed with bolus administration, whose consistency depended on each patients' status, while Masako manoeuvre was performed without any food or liquid intake, to prevent coughing or choking.

This training lasted for 40 minutes (with additional two five-minute pauses between exercises) with the support of muscle activity's visualization on the screen though the sEMG-biofeedback and of verbal feedback about correct execution from the speech therapist. All the visual and verbal feedbacks were useful to improve the quality of performance at the specific exercise (i.e., speech therapist directs patient's attention to the height of the curve on the screen in effortful swallow, timing and coordination in supraglottic swallow, high and coordination in Masako manoeuvre). Additionally, the verbal feedback included positive reinforcement or encouragement to improve strength (in effortful swallow), coordination and timing of deglutition (in supraglottic swallow) or strength and coordination (in Masako manoeuvre).

Control treatment

The control treatment included the same random behavioural exercises of the experimental group (40 minutes, excluding pauses), without sEMG-biofeedback application. Patients received only verbal feedback.

Assessment of outcomes

A complete assessment of dysphagia was administered with functional and instrumental evaluations as primary and secondary outcome measures, respectively. Presence of tracheostomy and enteral nutrition were also considered as secondary outcomes. Each

measure was delivered at three time points: at baseline (T0), after the 5-week treatment (T1) and at 2-month follow-up (T2).

Primary outcome measure: Functional Oral Intake Scale (FOIS)

The Italian validated version of FOIS [19] is a reliable tool to document changes in the intake of food and liquid in stroke patients. It consists of a 7-point ordinal scale. Levels 1 to 3 relate to non-oral feeding; levels 4 to 7 to degrees of oral feeding without non-oral supplementation.

Secondary outcome measures: PAS, P-score, P-SCA, tracheal tube, enteral nutrition

The Fiberoptic Endoscopic Evaluation of Swallowing (FEES) was performed by an otorhinolaryngologist (D.C.), using a Storz endoscope. Water-soluble lubricant was used to minimize patient discomfort.

During FEES, three different instrumental outcomes were extracted: Penetration Aspiration Scale (PAS) [25], Pooling Score (P-Score) [26] and Pooling-Sensation Collaboration Age (P-SCA) [26] scores, to document the severity of swallowing impairments. PAS is an 8-point scale used to quantify the increasing severity of inhalation of bolus (1=Material does not enter the airway; 2-5=Penetration; 5-8=Aspiration). Instead, according to the Scale proposed by Farneti and colleagues, any pooling of materials in the containment cavities of the hypopharynx and larynx before and/or after the act of swallowing is evaluated for each ingested bolus. Two different parameters were assessed: the P-Score considers location (identified by anatomical landmarks), amount of pooling materials and management (ability of the patient to clear the residue); then, its subscale P-SCA assesses sensitivity of pharynx/larynx during the exam, patient collaboration and age. Both are continuous variables, with a minimum score corresponding to *no dysphagia*, and a high score to *severe dysphagia*. Scores ranged between 3 and 16 for the P-SCA and between 4 and 11 for the P-scores.

The FEES was completed with the following bolus: first, a cracker for solid food, then 5-mL yoghourt for pureed/semi-solid food, followed by 5-mL water for liquid food. Semi-solids and liquids were mixed with one drop of blue dye in each millilitre, to improve visualization during endoscopy and avoid confounding food with salivary secretion. All fluids were given at fridge temperature (at 3-5°C) to minimize the risk of aspiration. We avoided testing neither liquids in patients who had a compromised ability to swallow the saliva and/or present aspiration during pureed, nor solid if the masticatory system was significantly impaired, to minimize the possibility of aspiration. The entire clinical procedure was recorded on video, which was later analysed by an otorhinolaryngologist (D.C.) and a speech and language pathologist (I.K.).

Finally, the presence of tracheostomy through tracheal tube and/or tube feeding for enteral nutrition were documented at T0, T1 and T2 as additional secondary outcomes of respiration and eating autonomy, respectively.

Statistical Analysis

Demographic (age, sex) and general clinical information (aetiology, time from onset, Token test, FIM scale and Barthel Index) are reported and compared in relation to Type of treatment (Biofeedback vs. Control) for descriptive purposes.

In statistical analysis, the rehabilitative effects of treatments were investigated on all primary and secondary outcome measures. Data were analyzed by mixed-effects multiple regression models [27], which provide several statistical advantages for our study's aims: they allow us to handle repeated measures in a regression design and to deal with missing data, without forcing us to discard the observations [28]. Importantly, by including baseline values as covariate, the inter-subjects variability is taken into account into the models, resulting in gold

standard analysis to compare two treatments in RCTs and to overcome biases related to treatment design, as the regression-to-the-mean and presence of small sample size [29]. Linear mixed-effect regression models were run separately for each outcome. Only for tracheal tube and enteral nutrition, generalized linear mixed models for binomial distribution were applied.

In all models computation, the random intercept was the subject, as recommended for the clinical population to take in consideration inter-individual variability [30]. With the aim to explore treatments and long lasting effects, each model was run on the post-treatment outcome as dependent variable, with Type of treatment (Biofeedback vs. Control) and Time (T1 vs T2), as independent variables and Baseline (values at T0) as covariate, including also the interaction between these variables. The models' fitting approach was the residual maximum likelihood estimation using Satterthwaite's estimation [31], which is reported to be adequate for slightly unbalanced small samples [32]. Results are reported only for models that satisfied the convergence during the fitting step (results' details in supplementary materials. Power-calculation and effect sizes' computation are reported in supplementary materials. Data are presented as means and 95% confidence interval (95%CI)[33]. Finally, non-parametric analysis was applied on the same data and reported as supplementary materials. All analyses were run with the software R (The R Core Team, 2018), using lme4 [34] and lmerTest packages [35].

RESULTS

Descriptive analysis showed the two groups of patients (biofeedback treatment vs. control treatment) matching for demographic and clinical data (Table 1).

Overall, two patients missed the evaluation at T2 and one patient had only FOIS evaluation at T1 and no other measures at T1 and T2 due to early hospital discharge, but they were all included in the analysis.

As primary outcome measure, the FOIS indicated significant results of the variable of Time ($F_{(1, 11.548)}$=18.49, p=0.001) and of the Baseline as covariate ($F_{(1, 13.461)}$=26.14, p=0.0001), with higher mean values at T2 (mean=6.08 [95%CI=5.27, 6.89]), than at T1 (mean=5.56 [95%CI=4.76, 6.36]) (Figure 2a).

As regards secondary outcomes, the PAS for semisolids showed significant effect of Type of treatment ($F_{(1, 12.493)}$=7.81, p=0.02), with Baseline as significant covariate ($F_{(1, 12.055)}$=49.87 p<0.0001), reporting lower scores (i.e. better results) in average for the group underwent biofeedback (mean=1.22 [95%CI=0.78, 1.66]), than for the control treatment group (mean=1.67 [95%CI=0.37, 2.97]) (Figure 2b).

The P-Scores for semisolids showed the significant effects of Type of treatment ($F_{(1, 12.043)}$=6.10, p=0.03) and of Baseline as covariate ($F_{(1, 12.153)}$=8.07, p=0.01), with lower scores in average for the group with biofeedback (mean=5 [95%CI=3.97, 6.03]), than with control treatment (mean=7 [95%CI=5.32, 8.68]). Similarly, P-score for liquids reported significant effects for Type of treatment ($F_{(1, 12.239)}$=8.22, p=0.02) and of Baseline as covariate ($F_{(1, 12.125)}$=50.34, p<0.001) with lower scores in average for the group with biofeedback (mean=5.22 [95%CI=4, 6.44]), than with control treatment (mean=6.33 [95%CI=4.2, 8.46]) (Figure 2c).

The P-SCA scores for semisolids had significant effects of Type of treatment ($F_{(1, 12.759)}$=12.76, p=0.004) and of Baseline as covariate ($F_{(1, 12107)}$=6.32, p=0.03), providing lower average scores for the biofeedback group (mean=4.78 [95%CI=3.76, 5.8]) in comparison with controls (mean=8.5 [95%CI=6.43, 10.60]). Analogously, P-SCA scores for liquids reported significant effects of Type of treatment ($F_{(1, 12.016)}$=9.44, p=0.01) and of Baseline as covariate ($F_{(1, 12.002)}$=13.79, p=0.003), with lower average scores for when biofeedback was in adjunct (mean=4.94 [95%CI=3.78, 6.1]), than for controls (mean=8.33 [95%CI=5.07, 11.6]) (Figure 2d). No other models reached convergence, indicating not to appropriately estimate the data. Additional information on models is reported in supplementary materials.

DISCUSSION

Post-stroke dysphagia represents a demanding and challenging condition firstly for the patient itself [3-5], and for clinicians employed in rehabilitation, as well. Swallowing training is of utmost importance, as stated in a recent Cochrane systematic review, and several rehabilitation programs are proposed. Visual feedback and sEMG-biofeedback applied during the rehabilitative phases in adjunction to the behavioural care provided encouraging results [15], however they are based on studies not reaching high levels of evidence.

To the best of our knowledge, this is probably the first RCT study to investigate the efficacy of sEMG-biofeedback in adjunction to standard treatment for swallowing rehabilitation in post-stroke dysphagia. Overall, in the present study swallowing behavioural exercises positively influenced patients' oral intake. Moreover, the application of sEMG-biofeedback significantly reduced pharyngeal residue and increased swallowing safety, the effects being long lasting over time.

Treatments efficacy

In the mixed effect models, a significant role of the type of treatment was reported for semisolid consistencies with PAS, P-Score, and P-SCA, and for liquids with P-SCORE and P-SCA. Patients in the sEMG-biofeedback group showed better pharyngeal clearance and lower risk of aspiration than for the controls. In literature, it is well known that pharyngeal residue is caused by a deficit of oral-pharyngo-laryngeal motor coordination and hyolaryngeal excursion during swallowing in stroke patients. The sEMG-biofeedback improved maximal elevation and anteriorization of hyoid excursion in these patients [14]. Considering such aspects together, it could be supposed that the sEMG-biofeedback may have effect on the oral-pharyngeal coordination pattern during swallowing, with a reduction of pharyngeal residue, as

well as a decrease of penetration and aspiration events after treatment in the present study sample.

Accordingly, evidences in rehabilitative literature suggest that behavioural task-specific swallowing treatments generally increase the recovery, with increasing functional outcomes as at the FOIS scale [36]. Furthermore, the use of biofeedback may support those exercises' specificity and contribute thus to the acquisition of swallowing skills [37].

The application of sEMG for swallowing biofeedback has already been described for different pathologies [14,15,17]. In particular, a recent systematic review confirmed its benefits in swallowing recovery, with half of studies including stroke patients. However, only the FOIS was adopted as outcome measure, and almost only case series were included, so that a cautious interpretation of results is recommended due to poor description of designs and methodology [15].

Differently, in the present RCT, FOIS improvement over time was registered, which may relate instead to both treatments and, probably, to their underlying behavioural exercises. However, we showed statistically significant improvements in terms of airways safety and management of pharyngeal residues, specifically for the experimental group with sEMG-biofeedback, and not in the control treatment group. Moreover, by qualitatively checking the results for secondary outcomes, the experimental group showed smaller 95%CI ranges, with less variability and, at times, lower values than baseline (i.e., particularly in P-score and PSCA) (Figure 2). These could be explained with low intra-patients' variability along with precise and steady improvements after the biofeedback treatment. Thus, these results of treatment might be supposed as an additional and specific effect of applying the sEMG-biofeedback.

Interestingly, no statistical effects were observed for solid consistencies, which was somehow expected, as solids are hardly managed by dysphagic patients. The sample of the present study included patients with moderate to severe dysphagia, and only few were able to eat solid food

during protocol treatment. Moreover, we did not report any results for tracheal tube and enteral nutrition, needed only for a few patients at baseline. We might not exclude this little subgroup of sample impact to reveal statistical differences. Probably we cannot completely decline possible effects on both solids and frequency of tracheostomy and enteral nutrition with moderate or mild dysphagia, which may execute these evaluations.

Finally, s-EMG-biofeedback treatment also monitors a good adherence of the participants to intervention, which is crucial to ensure safety and efficacy of a treatment. The positive results obtained for patients in a sub-acute phase after stroke may confirm a manageable administration and encouraging application of sEMG-biofeedback therapy with neurological patients.

Two months maintenance

One of the main results of the present RCT was the maintenance of effects at follow-up. Only the FOIS changed significantly over time in both control and study samples. This important result confirmed that the behavioural treatments delivered provided some benefits to swallowing function in post-stroke dysphagic patients. Furthermore, by means of instrumental assessment (FEES), significant effects were observed for the type of treatment, but all these outcomes were consistent at the follow-up assessments, probably reporting a stability of gain abilities over time. These results were confirmed through non-parametric direct comparisons that showed improvements after biofeedback treatment within baseline and post treatment (T1) and follow-up (T2). Instead, no changes were observed between T1 and T2 (Table 2S, supplementary materials).

Taken together, results over time may indicate a possible maintenance of treatment effects at follow-up (Figure 2b-d), which can be considered as possible signs of post-rehabilitative acquired and boosted neuroplasticity.

Considering that deficits of post-stroke dysphagia are common at three months since the causative event, with lasting and persisting disabilities, the improvement of functional abilities

on FOIS and the maintenance of instrumental outcome measures at follow-up might be thought as an indication of lasting treatment effects and of sEMG efficacy over time.

Limits and strengths of the study

The main weaknesses of the present study relate to the difficulty of including a large sample size, thus impeding stratification according to demographic and clinical data. We originally intended to recruit 40 patients in two years (NCT03247374) based on an estimate of the attendance of dysphagic patients to the hospital. Only 17 patients met all the inclusion/exclusion criteria, archiving a small-scale preliminary study. The limited sample size is due to the monocentric nature of the study, and possibly to the strict inclusion/exclusion criteria adopted by the investigators, which on the contrary might be considered a main strength for a systematic first inquiry of both feasibility and effectiveness of sEMG in dysphagia's rehabilitation. Accordingly, appropriate statistical analyses' methods (i.e mixed regressions, confirmed by non-parametric results) were applied in order to overcome this limit by considering inter-individual variability. RCT studies represent a strong design for the assessment of treatment efficacy. In the present series, a single-blind randomization was possible, due to the difficulty of a double-blind design in rehabilitation. As regards the patients' evaluation protocol, the third assessment was performed after a 2-month follow-up. Although not easy to conduct with neurological patients in a hospital setting, studies with longer follow-up are encouraged, as to determine the persistence of positive rehabilitative results over time. Finally, specific patient-reported outcome measures during or after treatment were not applied. However, patient's opinions indicated an impact of the treatment on well-being: patients generally report an increase of food selection and choice of food to eat. The achieved improvements are felt to enhance also the social activities related to food, active participation in conversations and social activities, as patients reported.

CONCLUSIONS

sEMG-biofeedback in adjunction to standard swallowing rehabilitation for patients diagnosed with sub-acute post-stroke dysphagia demonstrated to be an effective measure. With sEMG-biofeedback, patients showed prompt improvements of PAS, P-scores and P-SCA score, highlighting the simplicity of this technique for rehabilitative support, as well.

These results encourage an intensive behavioural program of swallowing intervention with the support of sEMG-biofeedback, for the management of these patients.

Author's contribution

All authors contributed to the study conception and design.

Material preparation, data collection and analysis were performed by Sara Nordio, Irene Battel, Daniela D'Imperio, Giulia Berta, Isabella Koch, Camilla Brisotto, Angela Dellai, Marta Aspidistria, Laura Ventura. The first draft of the manuscript was written by Sara Nordio and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

DECLARATIONS

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Conflicts of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

COMPLIANCE WITH ETHICAL STANDARDS

The study was approved by the Ethics Committee of the hospital (Prot.2017.12–Bio_Dys) and carried out in accordance with the Declaration of Helsinki. All participants signed an informed consent for their inclusion.

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TABLES

Table 1. Demographic, clinical data and allocated treatment for each patient.

FIGURES

Figure 1. CONSORT figure of complete patients' enrollment

Figure 2. Mean values for a) FOIS assessment over time in the whole sample and for b) PAS, c) P-Score and d) PSCA assessments in the two groups. Bars represent 95% confidence intervals.