Treatment of swallowing problems using compensatory and rehabilitation strategies: evidence from the literature

Tobias Warnecke

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Germany
## Symptoms of dysphagia in PD

<table>
<thead>
<tr>
<th>Phase of swallowing</th>
<th>Frequent findings</th>
</tr>
</thead>
</table>
| Oral                | Repetitive pump movements of the tongue  
|                     | Oral residue  
|                     | Premature spillage  
|                     | Piecemeal deglutition |
| Pharyngeal          | Residue in valleculae >>>  
|                     | pyriform sinuses  
|                     | Aspiration in 50% of dysphagic PD patients  
|                     | Somatosensory deficits  
|                     | Reduced rate of spontaneous swallows (48/h vs. 71/h) |
| Esophageal          | Hypomotility  
|                     | Spasms, multiple contractions |

*Suttrup and Warnecke. Dysphagia in Parkinson’s Disease. Dysphagia, 2016*
Symptoms of dysphagia in PD
Symptoms of dysphagia in PD

Table 7.2  PD-related oropharyngeal dysphagia symptoms and postulated pathomechanisms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pathomechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged oral transit time</td>
<td>Dopaminergic + non-dopaminergic (especially Lewy bodies in swallowing cortex?)</td>
</tr>
<tr>
<td>Premature spillage</td>
<td>Dopaminergic + non-dopaminergic (Lewy bodies in swallowing cortex?)</td>
</tr>
<tr>
<td>Delayed swallow reflex</td>
<td>Dopaminergic + decreased Substance P concentration</td>
</tr>
<tr>
<td>Prolonged pharyngeal transit time</td>
<td>Dopaminergic + non-dopaminergic (Lewy bodies in brainstem?)</td>
</tr>
<tr>
<td>Penetration</td>
<td>Dopaminergic + non-dopaminergic</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Dopaminergic + non-dopaminergic</td>
</tr>
<tr>
<td>Residue in valleculae</td>
<td>Primarily dopaminergic</td>
</tr>
<tr>
<td>Residue in piriform sinus</td>
<td>Dopaminergic + non-dopaminergic</td>
</tr>
<tr>
<td>Dysfunction of upper esophageal sphincter</td>
<td>Primarily non-dopaminergic (Lewy bodies in swallowing centers of medulla oblongata?)</td>
</tr>
<tr>
<td>Insufficient cough reflex</td>
<td>Decreased substance P concentration</td>
</tr>
</tbody>
</table>
Treatment of PD dysphagia

What do the guidelines recommend?

2.5.7 Dysphagie: Klinische Manifestationen, Diagnostik, Therapie (AHP5)

Empfehlung 58: 
IPS-Patienten mit Schluckstörungen sollten eine logopädische Schlucktherapie erhalten.

Hierbei sollten insbesondere folgende Aspekte berücksichtigt werden:

Empfehlung 59: 
Zur frühzeitigen Diagnostik IPS-bedingter Dysphagien können standardisierte Fragebögen und regelmäßige klinische Schluckuntersuchungen eingesetzt werden, welche die Effektivität des Schluckens sowie das Aspirationsrisiko beurteilen.

Empfehlung 60: 
Zur Schweregradbestimmung inklusive dem zuverlässigen Nachweis stiller Aspirationen sowie zur detaillierten Störungsmusteranalyse der IPS-bedingten Dysphagie können apparative Verfahren, wie die flexible endoskopische Evaluation des Schluckaktes (FEES) oder die Videofluoroskopie des Schluckens (VFSS) eingesetzt werden.

Empfehlung 61: 
Bei der logopädischen Schlucktherapie ist auf eine Störungsmuster-spezifische Auswahl der Therapieverfahren zu achten. Die Effektivität der jeweiligen Verfahren kann durch spezielle Diagnostik zu Therapiebeginn und im Verlauf mittels FEES oder VFSS beurteilt werden.

Empfehlung 62: 
Bei IPS-Patienten mit hypokinetischer Dysphagie kann auch eine Optimierung der dopaminergen Medikation eine Verbesserung des Schluckens bewirken.

German S3 Guideline „Parkinson’s Disease“ (German Neurological Society)
Treatment of PD dysphagia

What do the guidelines recommend?

2.5.7 Dysphagie: Klinische Manifestationen, Diagnostik, Therapie (AHP5)

Empfehlung 58:
IPS-Patienten mit Schluckstörungen sollten eine logopädische Schlucktherapie erhalten.

Basic principles:
Optimising dopaminergic medication
+
Swallowing therapy by trained speech and language therapist considering the specific dysphagia pattern of the individual PD patient
Dysphagia in Parkinson‘s disease

Optimising dopaminergic treatment

Non pharmacological treatment

Novel treatment strategies
Off and on state assessment of swallowing function in Parkinson's disease

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FEES showed premature spillage of liquid and semisolid consistencies to the piriform sinuses before the swallowing reflex was triggered predisposing the patient to pre- and intra- or glottal aspiration. Furthermore, when swallowing solids substantial residues were seen in the valleculae, and also, but less pronounced, in the piriform sinuses. Approximately 60 min later in the on state after receiving 300 mg of liquid levodopa, the motor score of the Unified Parkinson’s Disease Rating Scale (UPDRS) improved from 55 to 23 points. FEES now revealed a marked improvement in dysphagia. The swallowing reflex was triggered much sooner, i.e. at the base of tongue or valleculae. In addition, the amount of residue was significantly reduced. The video demonstrates the patient’s swallowing of two pieces of white bread in the off state compared to the degree and nature of improvement in the on state. We believe that visualizing the effect of levodopa on dysphagia is an important tool in patient management and a valuable addition to current dysphagia treatment protocols.

Finally, a decision was made for LCIG appropriate additional therapy. Arguments included the patient’s personal preference and the reversibility of dysphagia to levodopa treatment and the potential benefits of further decline in swallowing dysfunction.

Three months after starting LCIG treatment (1696 mg/16 h jejunal levodopa) in combination with physical therapy and swallowing treatment by a speech and language pathologist, motor fluctuations as well as dysphagia and associated quality of life had markedly improved (total sum score of the Swallowing Quality of Life Questionnaire: 201 points). The patient was now able to eat solid food again without any limitations. A weight gain of three kg was noted. These effects have been maintained for more than two years. Additional enteral feeding is currently not necessary.

This case illustrates that dysphagia at least in some PD patients...
Optimising dopaminergic treatment

Levodopa responsiveness of dysphagia in advanced Parkinson’s disease and reliability testing of the FEES-Levodopa-test

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Dear Editor

We read with interest the journal which proposed levodopa on dysphagia as the available literature suggests that levodopa individuals with PD [1]. A body of evidence suggests that levodopa in PD patients is crucial for the quality of life and dysphagia swallowing function is critical for rehabilitation states [3]. We believe that levodopa treatment could be an important factor in improving the quality of life of PD patients. Therefore, we present a flexible endoscopic swallowing evaluation (FEES) protocol developed to assess levodopa responsiveness of dysphagia. Measures were compared between the off- and on-state condition by using the Wilcoxon Test and marginal homogeneity test. Inter- and intrarater reliability was also investigated.

Keywords: Parkinson’s disease, Dysphagia, Swallowing, FEES, Levodopa responsiveness

ARTICLE INFO

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ABSTRACT

Background: It is still controversially discussed whether central dopaminergic stimulation improves swallowing ability in Parkinson’s disease (PD). We evaluated the effect of oral levodopa application on dysphagia in advanced PD patients with motor fluctuations.

Methods: In 15 PD patients (mean age 71.93 ± 8.29 years, mean disease duration 14.33 ± 5.94 years) with oropharyngeal dysphagia and motor fluctuations endoscopic swallowing evaluation was performed in the off state and on state condition following a specifically developed protocol (FEES-levodopa-test). The respective dysphagia score covered three salient parameters, i.e., premature spillage, penetration/aspiration events and residues, each tested with liquid as well as semisolid and solid food consistencies. An improvement of >30% in this score indicated levodopa responsiveness of dysphagia. Measures were compared between the off- and on-state condition by using the Wilcoxon Test and marginal homogeneity test. Inter- and intrarater reliability was also investigated.

Results: Severity of swallowing dysfunction in the off state varied widely. The lowest dysphagia score was 15 points (dysphagia without any aspiration risk). The highest dysphagia score was 84 points (dysphagia with aspiration of all consistencies). Seven patients showed a marked improvement of dysphagia in the on state condition. Eight PD patients did not respond. Inter- and intrarater reliability was excellent for all three subscales in the off state and on state conditions.

Conclusions: A significant proportion of advanced PD patients with motor fluctuations and mild to moderate oropharyngeal dysphagia may demonstrate a clinically relevant improvement of swallowing after levodopa challenge. The FEES-levodopa-test is a reliable and sensitive tool to differentiate these responders from non-responders.

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In advanced PD patients with (fluctuating) dysphagia an individual assessment of levodopa responsiveness of swallowing dysfunction may be useful: FEES-Levodopa-test

FEES-Levodopa-test
Treatment Options Developed to Bypass GI Dysfunction in Patients with PD

- Liquid levodopa formulations
- Rotigotine patch
- Subcutaneous apomorphine
- Deep brain stimulation
- Levodopa-carbidopa intestinal gel

**FEES-Apomorphine-test**

<table>
<thead>
<tr>
<th>Nahrungskonsistenzen</th>
<th>flüssig</th>
<th>halbfest</th>
<th>fest</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Leaking</td>
<td>1.  2.</td>
<td>1.  2.</td>
<td>1.  2.</td>
</tr>
<tr>
<td>0 = normal</td>
<td>1  = Valleculae</td>
<td>2  = seitlich der Epiglottis</td>
<td>3  = Sinus piriformis</td>
</tr>
<tr>
<td>II. Penetration/Aspiration</td>
<td>1  = normal</td>
<td>2  = Penetration mit Schutzreflex</td>
<td>3  = Penetration ohne Schutzreflex</td>
</tr>
<tr>
<td>III. Residuen</td>
<td>1  = Schlemhaut benetzt</td>
<td>2  = &lt; 50 % eines Spatiums</td>
<td>3  = &gt; 50 % eines Spatiums</td>
</tr>
</tbody>
</table>

IV. Gesamtpunktzahl: 108
Effects of apomorphine on esophageal motility?

45 years-old-female PD patient with delayed On" but normal Gastric scinitigrafy not showing any signs for gastroparesis
Rotigotine Transdermal Patch Improves Swallowing in Dysphagic Patients with Parkinson’s Disease

Makito Hirano¹ ² · Chiharu Isono¹ · Hikaru Sakamoto¹ · Shuichi Ueno¹ ² · Susumu Kusunoki² · Yusaku Nakamura¹

**Effects of the rotigotine transdermal patch versus oral levodopa on swallowing in patients with Parkinson's disease**

Makito Hirano¹, Chiharu Isono², Kanji Fukuda³, Shuichi Ueno⁴, Yusaku Nakamura⁵, Susumu Kusunoki⁶

Affiliations  + expand

PMID: 31323520  DOI: 10.1016/j.jns.2019.07.003
Are All Dopamine Agonists Essentially the Same?

Margherita Torti¹,² · Daniele Bravi¹,³ · Laura Vacca¹,⁴ · Fabrizio Stocchi¹,⁵

Published online: 9 April 2019
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Makito Hirano¹, Chihiro Isono², Kanji Fukuda³, Shuichi Ueno⁴, Yusaku Nakamura⁵, Susumu Kusunoki⁶

Affiliations + expand
PMID: 31323520 DOI: 10.1016/j.jns.2019.07.003
**Fig. 1** Algorithm for the choice of dopamine agonists in the treatment of non-motor symptoms

- Neuropsychiatric
  - Premorbid ICDs, impulsivity, altered executive functions, greater novelty seeking
    - Discourage the use of DA or prefer DA acting on D1
  - Cognitive decline
    - Discourage the use of DA
  - Apathy
    - Piribedil
  - Depression
    - Pramipexole
    - In depressed patients, attention to young, male patients: greater risk of developing ICDs

- Gastro-intestinal dysfunctions, drooling, dysphagia
  - Apomorphine
    - Rotigotine

- Nocturnal akinesia and early morning dystonia
  - Ropinirole
  - Rotigotine

- Orthostatic hypotension
  - Discourage the use of DA
Research Article

Effect of Intestinal Levodopa-Carbidopa Infusion on Pharyngeal Dysphagia: Results from a Retrospective Pilot Study in Patients with Parkinson’s Disease

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Background. Pharyngeal dysphagia is a common symptom of Parkinson’s disease (PD) leading to severe complications. PD-related pharyngeal dysphagia (PDpPD) may significantly improve in up to half of patients following acute oral levodopa challenge. Objective. The aim of this study was to investigate the effects of levodopa-carbidopa intestinal gel (LCIG) on PDpPD. Methods. Forty-five PD patients under LCIG treatment were available for retrospective analysis. In all patients with PDpPD who underwent flexible endoscopic evaluation of swallowing (FEES) in the clinical “on-state” both before and after implementation of LCIG treatment, FEES videos were systematically reassessed. PDpPD was characterized using a PD-specific FEES score evaluating premature bolus spillage, penetration/aspiration, and pharyngeal residue. Further, the duration of white-out was assessed, as a parameter for pharyngeal bradykinesia. Results. Eleven patients with PDpPD (mean age 74.6 ± 4.4 years, mean Hoehn and Yahr stage 3.8 ± 0.6) received FEES both before and after the onset of LCIG treatment. The mean swallowing score improved from 14.9 ± 7.3 to 13.0 ± 6.9 after implementation of LCIG; however, this difference was not significant (p = 0.312). Premature bolus spillage decreased significantly (p = 0.002) from 5.4 ± 1.1 to 3.6 ± 1.0, and white-out duration decreased significantly (p = 0.002) from 984 ± 228 ms to 699 ± 131 ms after implementation of LCIG. Conclusions. LCIG may affect PDpPD and reduce premature bolus spillage and pharyngeal bradykinesia. Future studies with larger sample sizes are required to follow up on these pilot results and identify which factors predict a good response of PDpPD to LCIG treatment.
Deep brain stimulation?

- No significant improvement or worsening of swallowing following deep brain stimulation, data mainly available for STN-stimulation [Troche et al. Parkinsonism Relat Disord 2013]

- Subclinical modulation of pharyngeal swallowing after deep brain stimulation, especially alterations in quantitative temporal parameters, oral phase remains unchanged [Lengerer et al. Parkinsonism Relat Disord 2012]

- No studies available directly comparing STN vs. GPi-stimulation, but retrospective analysis found worsening of PAS only patients with STN-stimulation [Troche et al. Dysphagia 2014]

- 60 Hz STN stimulation may improve swallowing function in the short term (lower aspiration rate), but this was not confirmed in the long term observation, simultaneous STN + SNr-stimulation has no additional beneficial effects [Xie et al. Neurology 2015, Xie et al. JNNP 2018, Pflug et al. 2020]

- STN stimulation may improve esophageal motility [Derrey et al. Neurogastroenterol Motil 2015]
The Effect of Deep Brain Stimulation on Swallowing Function in Parkinson’s Disease: A Narrative Review

Min Cheol Chang1 · Jin-Sung Park2 · Byung Joo Lee3 · Donghwi Park4

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Abstract
Unlike appendicular motor symptoms, such as bradykinesia and rigidity, in Parkinson’s disease (PD), which have already been reported to respond well to deep brain stimulation (DBS), there is limited literature on the effects of DBS on swallowing function in patients with PD. The field lacks consensus as there are conflicting reports among existing studies regarding whether swallowing function improves or declines following DBS implantation. This narrative review aims to summarize and analyze the studies published on the effect of DBS on swallowing function in patients with PD. We collated studies published up to February 2020 using a comprehensive electronic database search of PubMed, SCOPUS, EMBASE, and the Cochrane Library. Two reviewers independently assessed the studies using strict inclusion and exclusion criteria. The primary literature search yielded 529 relevant papers. After reading their titles and abstracts and assessing their eligibility based on the full-text, we finally included and reviewed 14 publications. Nine of these studies reported positive effects of DBS on swallowing function and four studies showed no significant positive results. The remaining study showed decreased swallowing function after unilateral subthalamic nucleus-DBS surgery. In conclusion, we found that DBS has the potential to improve swallowing function in patients with PD. However, high-quality evidence is lacking. To clearly elucidate the effect of DBS on swallowing function in patients with PD, high-quality randomized controlled trials should be conducted in the future.
Deep brain stimulation?

**CME** Should We Consider Deep Brain Stimulation Discontinuation in Late-Stage Parkinson’s Disease?

Margherita Fabbri, MD, PhD,1,2,3 Maurizio Zibetti, MD, PhD,1* Mario Giorgio Rizzone, MD,1 Giulia Giannini, MD,4,5
Linda Borellini, MD,6 Alessandro Stefani, MD, PhD,7 Francesco Bove, MD,8 Andrea Bruno, MD,9
Giovanna Calandra-Buonaura, MD, PhD,4,5 Nicola Modugno, MD, PhD,9 Carla Piano, MD, PhD,9
Antonella Peppe, MD,10 Gianluca Ardolino, MD,6 Alberto Romagnolo, MD,1 Carlo Alberto Artusi, MD,1
Paola Berchialla, MS,11 Elisa Montanaro,1 Pietro Cortelli, MD, PhD,4,5 Romito Luigi, MD, PhD,12
Roberto Eleopra, MD,12 Brigida Minafra, MD,13 Claudio Pacchetti, MD, PhD,13 Tommaso Tufo, MD, PhD,14
Filippo Cogiamanian, MD,6 and Leonardo Lopiano, MD, PhD1

**Conclusions:** The vast majority of late-stage PD patients (92%) show a meaningful response to STN-DBS. Effects of stimulation may take days to disappear after its discontinuation. We present a safe and effective decisional algorithm that could guide physicians and caregivers in making challenging therapeutic decisions in late-stage PD. © 2020 International Parkinson and Movement Disorder Society

**Key Words:** caregivers; deep brain stimulation; dementia; late stage; Parkinson’s disease
Deep brain stimulation?

HY ≥4
S&E < 50

Med On/Stim On

Stim Off

ΔStim ≥ 10%
PGI-I/CGI-I <4

Stim On

ΔStim < 10%
PGI-I/CGI-I > 4

Med Off

Double blinded assessment

Med On/Stim Off

Open label assessment

No change vs. T0

Worsening vs. T0 (based on clinical scales* and CGI-I/PGI-I)

Med On/Stim Off

Med On/Stim Off

Med On/Stim Off

Med On/Stim On

T0

T1

T2

1 month
Med On/Stim Off
(medication adjustment and regular phone calls)
### TABLE 3. Acute and long-term adverse effects (AEs) related to the stim off condition

<table>
<thead>
<tr>
<th>Acute AEs related to Stim Off$^a$</th>
<th>n (%) – 35 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonism (bradykinesia, tremor, rigidity)</td>
<td>15 (42%)</td>
</tr>
<tr>
<td>Blepharospasm, eyelid apraxia</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Gait worsening/FOG</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Sialorrhea</td>
<td>4 (11%)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Agitation/anxiety</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Pain</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Long-term AEs related to Stim Off$^b$</td>
<td>n (%) – 7 patients</td>
</tr>
<tr>
<td>Sialorrhea</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Parkinsonism (bradykinesia, tremor, rigidity)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Appearance delay (days) – mean (range)</td>
<td>6.7 (3–10)</td>
</tr>
</tbody>
</table>

$^a$3 patients reported a considerable speech worsening during the Stim On condition.

$^b$Long-term: if the delay of appearance was > 24 hours. The AEs have been listed if clinically relevant for physician or the patient/caregiver. FOG: freezing of gait.
Dysphagia in Parkinson‘s disease

Optimising dopaminergic treatment

Non pharmacological treatment

Novel treatment strategies
Dysphagia Causes Symptom Fluctuations after Oral L-DOPA Treatment in a Patient with Parkinson Disease

Hiromasa Sato\textsuperscript{a} Toshiyuki Yamamoto\textsuperscript{a} Masako Sato\textsuperscript{b} Yoshihiko Furusawa\textsuperscript{a} Miho Murata\textsuperscript{a}

\textsuperscript{a}Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan; \textsuperscript{b}Department of Rehabilitation Medicine, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan
Fig. 2. Videofluoroscopic examination of the swallowing process. a Four tablets covered with a watersoluble film were administered orally in 10 mL of jelly containing barium. Tablets remained in the epiglottic vallecula (white frame). b Enlarged view of the epiglottic vallecula. The tablets remaining in the epiglottic vallecula are seen as filling defects (asterisks).

*Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan; †Department of Rehabilitation Medicine, National Center Hospital, National Center of Neurology and Psychiatry, Tokyo, Japan
Fig. 3. Results of the L-DOPA test. One ground L-DOPA 100 mg/carbidopa 10 mg tablet was administered orally on an empty stomach after waking in the morning, and the L-DOPA blood concentration was measured seven times from before the tablet was administered to 240 min after ingestion. Prior to rehabilitative intervention, the tablet was ineffective (a “no-on” state), parkinsonian signs did not improve, and the maximum blood L-DOPA concentration was 0.78 nmol/mL (solid line). After dysphagia rehabilitation, the patient was able to swallow the tablets quickly, his parkinsonism symptoms improved within 30 min after administration, and his maximum blood L-DOPA concentration was 9.99 nmol/mL (dashed line).
Treatment by speech and language pathologists using compensatory and rehabilitation strategies?

1) The selection of definitive techniques depend on the specific pattern of dysphagia in the individual PD patient, no general recommendations can be made
- rehabilitation, such as thermal-tactile stimulation
- compensation, such as effortful swallow
Thickened liquids have been shown to be more effective in reducing amount of liquid aspiration compared to chin tuck maneuver [Logemann et al. J Speech Lang Hear Res 2008.]
FEES or VFSS control assessments at regular intervals

2) The Lee Silverman Voice Treatment (LSVT® LOUD) may improve PD dysphagia, but data is rather limited [El Sharkawi et al. JNNP 2002]

3) An expiratory muscle strength training (EMST) improved laryngeal elevation and reduced severity of aspiration events in a RCT [Troche et al. Neurology 2010] as well as pharyngeal swallowing efficiency [Claus et al. MDS Congress Nice, Late-Breaking Abstracts, 2019]
Treatment by speech and language pathologists using compensatory and rehabilitation strategies?

1) The selection of definitive **techniques** depend on the specific pattern of dysphagia in the individual PD patient, no general recommendations can be made

- rehabilitation, such as thermal-tactile stimulation
- compensation, such as effortful swallow

Thickened liquids have been shown to be more effective in reducing amount of liquid aspiration compared to chin tuck maneuver [Logemann et al. J Speech Lang Hear Res 2008.]

**FEES or VFSS control assessments at regular intervals**
Video-assisted effortful swallow

Video-assisted swallowing therapy (VAST)
• control (n =21): 6 sessions of 30 min for 6 weeks to learn to effortful swallow;
• intervention (n =21): similar plus real time visual feedback using FEES (VAST);

Results
• less pharyngeal residue and better swallowing-related QoL in both groups,
• but significantly more in favor of VAST.

Manor et al. Parkinsonism Relat Disord 2013
Biofeedback using sEMG

ORIGINAL ARTICLE

Skill Training for Swallowing Rehabilitation in Patients With Parkinson’s Disease

Ruvini P. Athukorala, MSc, a,b Richard D. Jones, PhD, a,b,c Oshrat Sella, PhD, a,b Maggie-Lee Huckabee, PhD a,b

From the aDepartment of Communication Disorders, University of Canterbury, Christchurch; bNew Zealand Brain Research Institute, Christchurch; and cDepartment of Medical Physics and Bioengineering, Christchurch Hospital, Christchurch, New Zealand.
BiSSkiT Biofeedback in Swallowing Skill Training

Fig 1  Durational parameters for 10-ml water bolus. First tag indicates the go stimulus, whereas the tag at the end depicts the type of swallow: (A) PMT; (B) preswallow time; and (C) duration of submental muscle contraction.

Fig 2  Skill training display (swallowing target) in the BiSSkiT software.
What are useful techniques for improving lengthy chewing and slow initiation of swallowing?

➢ The SLP can consider evaluating the result on the initiation of swallowing when activation exercises are performed prior to each meal.

➢ For PD patients who chew too long (hypokinesia) and/or keep food in their mouth without swallowing it (akinesia), it can be useful to see whether the patient can learn to perform the process in conscious steps and by using specific cues.

➢ When it proves difficult to improve lengthy chewing and the initiation of swallowing from a behavioral perspective, it is recommended to advise easier food consistencies.

# Oropharyngeal freezing and its relation to dysphagia – An analogy to freezing

## Table 3
Descriptive statistics, signs for oropharyngeal freezing and percentage in relation to the investigated groups: SD = standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Parkinson's disease</th>
<th>stroke</th>
<th>healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean age in years ± SD</td>
<td>67.5 ± 8.4</td>
<td>76.3 ± 11.7</td>
<td>44.0 ± 21.2</td>
</tr>
<tr>
<td>men, n (%)</td>
<td>41 (82%)</td>
<td>26 (52%)</td>
<td>22 (44%)</td>
</tr>
<tr>
<td>dysphagia severity score 0, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>50 (100%)</td>
</tr>
<tr>
<td>dysphagia severity score 1, n (%)</td>
<td>29 (58%)</td>
<td>23 (46%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>dysphagia severity score 2, n (%)</td>
<td>20 (40%)</td>
<td>19 (38%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>dysphagia severity score 3, n (%)</td>
<td>1 (2%)</td>
<td>9 (16%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>oropharyngeal freezing, n (%)</td>
<td>17 (34%)</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>festination</td>
<td>15 (30%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>trembling</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>akinesia</td>
<td>3 (6%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
Oropharyngeal freezing: akinesia of swallowing
Oropharyngeal freezing: festination of swallowing
Oropharyngeal freezing: trembling of swallowing
What are useful techniques for reducing choking on fluids?

➢ For PD patients who have a history of choking but who do not choke during a swallowing evaluation and provocation test, it is recommended: 1. to explain choking as a result of dual tasking, and 2. by means of practicing, make them aware of safe swallowing with attention. The SLP should only consider other interventions after this has not resulted in enough improvement.

➢ For a PD patient who easily chokes on fluid, it is recommended that the SLP evaluates whether a chin tuck is an adequate compensation and can be maintained.
➢ For a PD patient who easily chokes on fluids, it is recommended that the SLP tries out whether smaller volumes and/or thicker consistencies are sufficient for preventing choking on fluids.

Effects of cognitive and motor dual-tasks on oropharyngeal swallowing assessed with FEES in healthy individuals

Paul Muhle, Inga Claus, Bendix Labeit, Mao Ogawa, Rainer Dziewas, Sonja Suntrup-Krueger & Tobias Warnecke

www.nature.com/scientificreports
Effect of cognitive and motor dual-task on oropharyngeal swallowing in Parkinson's disease

Bendix Labeit\textsuperscript{1,2} | Inga Claus\textsuperscript{1} | Paul Muhle\textsuperscript{1,2} | Liesa Regner\textsuperscript{1} | Sonja Suntrup-Krueger\textsuperscript{1,2} | Rainer Dziewas\textsuperscript{1} | Tobias Warnecke\textsuperscript{1}

\textsuperscript{1}Department of Neurology with Institute of Translational Neurology, University of Muenster, Muenster, Germany
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Funding Information
Else Kröner-Fresenius-Stiftung; Grant/Award Number: 2017,6XMS.03

Abstract

Background: Dysphagia frequently occurs in patients with Parkinson's disease (PD) and is associated with severe complications. However, the underlying pathology is poorly understood at present. This study investigated the effect of cognitive and motor dual-task interference on oropharyngeal swallowing in PD.

Methods: Thirty PD patients (23 men, mean age 65.90 ± 9.32 years, mean Hoehn and Yahr stage 2.62 ± 0.81, mean UPDRS 18.00 ± 7.18) were examined using flexible endoscopic evaluation of swallowing (FEES). FEES was performed during three paradigms: at baseline without interference, during a cognitive dual-task, and during a motor dual-task. Oropharyngeal swallowing function was rated using a score which was validated to detect changes in PD related dysphagia. The three paradigms were compared using a two-way-repetitive-measures-ANOVA and a post-hoc-analysis.

Results: Mean swallowing score in baseline FEES was 10.67 ± 5.89. It significantly increased (worsened) to 15.97 ± 7.62 (p < 0.001) in the motor dual-task and to 14.55 ± 7.49 (p < 0.001) in the cognitive dual-task. Premature bolus spillage and pharyngeal residue both significantly increased during both of the dual-task conditions whereas penetration/aspiration events did not change.

Conclusion: Oropharyngeal swallowing in patients with PD is not purely reflexive but requires mental capacity. Additional allocation of attentional resources in the central control of swallowing seems to be an effective compensatory mechanism in PD-related dysphagia. The proposed dual-task protocol may be useful to challenge swallowing functional reserve. Conversely, as a therapeutic strategy, it could be beneficial to focus attention on swallowing and to avoid dual-task situations.

KEYWORDS

attention, cognition, dual-task, dysphagia, Parkinson's disease
Cognitive dual-task
Cognitive task:
Repeating a six digit number in mind during FEES:
Semisolid:
• Swallow 1
• Swallow 2
• Swallow 3
Liquid:
• Swallow 1
• Swallow 2
• Swallow 3
Solid:
• Swallow 1
• Swallow 2
• Swallow 3

Motor dual-task
Motor task:
Clicking alternately left and right during FEES:
Semisolid:
• Swallow 1
• Swallow 2
• Swallow 3
Liquid:
• Swallow 1
• Swallow 2
• Swallow 3
Solid:
• Swallow 1
• Swallow 2
• Swallow 3

Assessment
Evaluation of
• Premature bolus spillage
• Penetration and aspiration
• Pharyngeal residue
Comparison between baseline, cognitive dual-task and motor dual-task

Baseline
FEES
Semisolid:
• Swallow 1
• Swallow 2
• Swallow 3
Liquid:
• Swallow 1
• Swallow 2
• Swallow 3
Solid:
• Swallow 1
• Swallow 2
• Swallow 3

Dual Task

What are useful techniques for reducing pharyngeal residue?

➢ It is recommended for the SLP to teach PD patients with reduced pharyngeal transport to swallow harder in a conscious and consistent manner.

➢ When it proves difficult to improve reduced pharyngeal transport from a behavioral perspective, it is recommended to advise easier food consistencies.

➢ When the SLP advises the patient to modify food consistencies, it is recommended to ask a dietitian to advise the patient on the best way to maintain a wholesome diet.

The FEESs demonstrated a significantly greater reduction in food residues in the pharynx in the VAST group compared to the conventional treatment group.

There were significant group improvement in some parameters of the quality of life, quality of care and pleasure of eating scales.
Aspiration and swallowing in Parkinson disease and rehabilitation with EMST: A randomized trial
M.S. Troche, M.S. Okun, J.C. Rosenbek, et al.
Neurology 2010;75:1912-1919
DOI 10.1212/WNL.0b013e3181fe1f15

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Demographic information by treatment group</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>EMST</td>
</tr>
<tr>
<td>Age, y</td>
<td>66.7 (8.9)</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>25/5</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr stage</td>
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</tr>
<tr>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>2.5</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>UPDRS III motor (total)</td>
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<tr>
<td>Pre</td>
<td>39.4 (9.2)</td>
</tr>
<tr>
<td>Post</td>
<td>38.9 (8.1)</td>
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</table>

Abbreviations: EMST – Expiratory Muscle Strength Training; UPDRS – Unified Parkinson’s Disease Rating Scale.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Mean (SD) values for the 2 groups for the significant outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EMST</td>
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<tr>
<td>Outcomes of swallowing</td>
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<tr>
<td>Duration of hyoid elevation, s</td>
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</tr>
<tr>
<td>1.91 (1.02)</td>
<td>1.88 (0.97)</td>
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<tr>
<td>Penetration-aspiration score</td>
<td></td>
</tr>
<tr>
<td>2.64 (1.87)</td>
<td>2.07 (1.28)</td>
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<tr>
<td>2.57 (1.76)</td>
<td>3.30 (1.75)</td>
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<tr>
<td>Swallowing phase</td>
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<tr>
<td>Hyoid displacement</td>
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<td>OB T</td>
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<tr>
<td>1.08 (0.19)</td>
<td>1.18 (0.10)</td>
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<tr>
<td>UES—opening</td>
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<tr>
<td>1.13 (0.20)</td>
<td>1.25 (0.08)</td>
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<tr>
<td>UES—widest</td>
<td></td>
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<tr>
<td>1.14 (0.21)</td>
<td>1.26 (0.09)</td>
</tr>
<tr>
<td>UES—closure</td>
<td></td>
</tr>
<tr>
<td>1.06 (0.17)</td>
<td>1.15 (0.08)</td>
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<tr>
<td>Laryngeal closure</td>
<td></td>
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<tr>
<td>1.09 (0.19)</td>
<td>1.18 (0.10)</td>
</tr>
<tr>
<td>Maximum laryngeal closure</td>
<td></td>
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<tr>
<td>1.13 (0.20)</td>
<td>1.21 (0.11)</td>
</tr>
<tr>
<td>Laryngeal opening</td>
<td></td>
</tr>
<tr>
<td>1.02 (0.17)</td>
<td>1.09 (0.08)</td>
</tr>
</tbody>
</table>

Abbreviations: EMST – Expiratory Muscle Strength Training; OBT – onset of bolus transit; UES – upper esophageal sphincter.
* Significant.
Expiratory Muscle Strength Training for Therapy of Pharyngeal Dysphagia in Parkinson’s Disease

Inga Claus, MD,1,2* Paul Muhle, MD,1,2† Judith Czechowski, PhD,1 Sigrid Ahring, BSc,1 Bendix Labeit, MD,1,2
Sonja Suntrup-Krueger, MD,1,2 Heinz Wiendl, MD,1 Rainer Dziewas, MD,1 and Tobias Warnecke, MD1

1Department of Neurology with Institute of Translational Neurology, University Hospital of Muenster, Muenster, Germany
2Institute for Biomagnetics and Biosignal Analysis, University Hospital Muenster, Muenster, Germany

ABSTRACT: Background: Pharyngeal dysphagia in Parkinson’s disease (PD) is a common and clinically relevant symptom associated with poor nutrition intake, reduced quality of life, and aspiration pneumonia. Despite this, effective behavioral treatment approaches are rare. Objective: The objective of this study was to verify if 4 week of expiratory muscle strength training can improve pharyngeal dysphagia in the short and long term and is able to induce neuroplastic changes in cortical swallowing processing. Methods: In this double-blind, randomized, controlled trial, 50 patients with hypokinetic pharyngeal dysphagia, as confirmed by flexible endoscopic evaluation of swallowing, performed a 4-week expiratory muscle strength training. Twenty-five participants used a calibrated (“active”) device, 25 used a sham handheld device. Swallowing function was evaluated directly before and after the training period, as well as after a period of 3 month using flexible endoscopic evaluation of swallowing. Swallowing-related cortical activation was measured in 22 participants (active: sham: 11:11) using whole-head magnetoencephalography. Results: The active group showed significant improvement in the flexible endoscopic evaluation of swallowing-based dysphagia score after 4 weeks and after 3 months, whereas in the sham group no significant changes from baseline were observed. Especially, clear reduction in pharyngeal residues was found. Regarding the cortical swallowing network before and after training, no statistically significant differences were found by magnetencephalography examination. Conclusions: Four-week expiratory muscle strength training significantly reduces overall dysphagia severity in PD patients, with a sustained effect after 3 months compared with sham training. This was mainly achieved by improving swallowing efficiency. The treatment effect is probably caused by peripheral mechanisms, as no changes in the cortical swallowing network were identified. © 2021 The Authors. Movement Disorders published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society

Key Words: Parkinson’s disease; FEES; oropharyngeal dysphagia; swallowing therapy; rehabilitation
EMST

Claus et al. Mov Disord. 2021
EMST:
Effect on pharyngeal residues in PD?

Before EMST

After 4 weeks EMST training
Intensive voice treatment: indirect effects without any specific swallowing training

The impact of intensive voice treatment on swallowing in Parkinson disease

D. McFarland, L. Ramig, B. Martin-Harris, K. Humphries, J. Logemann, K. Freeman, A. Halpern, J. Spielman (Montréal, QC, Canada)

Meeting: 2017 International Congress

ABSTRACT NUMBER: 130

Keywords: Dysphagia, Motor control, Rehabilitation

Session Information

Date: Monday, June 5, 2017
Session Title: Parkinson's Disease: Non-Motor Symptoms

Session Time: 1:45pm-3:15pm
Location: Exhibit Hall C

➢ For PD patient with dysphagia and hypokinetic dysarthria, the SLP can consider to give only the necessary advice and to reevaluate the chewing and swallowing after treatment with PLVT/LSVT.
Dysphagia in Parkinson’s disease

Optimising dopaminergic treatment

Non pharmacological treatment

Novel treatment strategies
What do you see?

Upper esophageal spasms

What is the best treatment?
## Symptoms of dysphagia in PD and feasible treatment approaches

*Suttrup and Warnecke. Dysphagia in Parkinson’s Disease. Dysphagia, 2016*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pharmacotherapy</th>
<th>Swallowing therapy by SLTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetitive pump movements of tongue</td>
<td>• Increase dose of L-dopa before mealtimes</td>
<td>• Triggering of swallowing reflex</td>
</tr>
<tr>
<td></td>
<td>• Amantadine?</td>
<td>• External triggers?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premature spillage</td>
<td></td>
<td>• Oral bolus control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Avoid dual tasks</td>
</tr>
<tr>
<td>Silent aspiration</td>
<td>• Non oral delivery: patch or pump?</td>
<td>• Protective reflexes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sensory stimulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PEG?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Supraglottic swallow maneuver</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Safe food consistencies?</td>
</tr>
<tr>
<td>Pharyngeal residues without motor fluctuations</td>
<td>Individual assessment of L-dopa responsiveness, if positive:</td>
<td>• Effortful swallow exercise</td>
</tr>
<tr>
<td></td>
<td>• Increase dose of L-dopa before meals</td>
<td></td>
</tr>
<tr>
<td>Pharyngeal residues without motor fluctuations</td>
<td>Individual assessment of L-dopa responsiveness, if positive:</td>
<td>• Meal times during <em>on</em> state condition</td>
</tr>
<tr>
<td></td>
<td>• Optimize oral treatment</td>
<td>• Effortful swallow exercise in <em>off</em> state condition</td>
</tr>
<tr>
<td></td>
<td>• Non oral delivery: patch or pump?</td>
<td></td>
</tr>
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<td></td>
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<tr>
<td>Esophageal spasms</td>
<td>• Non oral delivery: patch or pump?</td>
<td>• Protective reflexes</td>
</tr>
<tr>
<td></td>
<td>• Botulinum toxin injections into upper esophageal sphincter?</td>
<td>• Safe food consistencies?</td>
</tr>
<tr>
<td></td>
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<td>• Mendelsohn swallow exercise</td>
</tr>
</tbody>
</table>

Pilot cohort study of endoscopic botulinum neurotoxin injection in Parkinson’s disease

George Triadafilopoulos a, *, Rita Gandhy b, Carrolee Barlow b

* Stanford Multidimensional Program for Innovation and Research in the Esophagus (S-MPIRE), Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA, 94305, USA
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Keywords:
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Gastrointestinal dysfunction
Dysphagia
Gastroparesis
Constipation

ABSTRACT

Background: Gastrointestinal symptoms, such as dysphagia, postprandial bloating, and defecatory straining are common in Parkinson’s Disease (PD) and they impact quality of life. Endoscopic botulinum neurotoxin (BoNT) injection has been used in the treatment of dysphagia, gastroparesis and chronic anismus.

Aims: To examine the feasibility, safety and efficacy of endoscopically delivered BoNT injection to distal esophagus, pylorus or anal canal aiming at relieving regional gastrointestinal symptoms in patients with PD.

Methods: This is a retrospective open cohort pilot study to assess the clinical response to endoscopic BoNT injection on selected PD patients with symptoms and identifiable abnormalities on high-resolution manometry and wireless motility capsule, to generate early uncontrolled data on feasibility, tolerability, safety and efficacy. Baseline symptoms and response to therapy were assessed by questionnaires.

Results: Fourteen PD patients (10 M:4 F), mean age 73 (range: 62-93) were treated. Three patients had esophageal Botox for ineffective esophageal motility (IEM) (n = 1), esophago-gastric junction outlet obstruction (EGJOO) & IEM (n = 1), and diffuse esophageal spasm (DES) (n = 1). Nine patients were treated with pyloric BoNT injection for gastroparesis with mean gastric transit time of 21.2 h, range 5.2–44.2 h. Two patients received anal Botox for defecatory dyssynergia ((Type 1) (n = 1) and overlap (slow-transit and dyssynergic) constipation (n = 1). Endoscopic BoNT injection (100-200 units) was well tolerated and there were no significant adverse events.

Conclusions: Endoscopic BoNT injection to esophagus, pylorus or anal canal is safe, well-tolerated and leads to symptomatic improvement that lasts up to several months. The procedure can be repeated as needed and combined with other therapies.
Symptoms of dysphagia in PD and feasible treatment approaches


Pilot cohort study of endoscopic botulinum neurotoxin injection in Parkinson's disease

George Triacca

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ARTICLE

28 July 2017

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Keywords:

Parkinson's disease
Botulinum neurotoxin
Gastrointestinal dysmotility
Dysphagia
Gastroparesis
Constipation

Esophagus

Pylorus

Esophageal symptoms, including dysphagia (n = 5), esophageal motor disorders (n = 3), dysphagia–gastroesophageal reflux disease (n = 7), obstructions (EGJOO & IEM (n = 1), and diffuse esophageal spasm (DES) (n = 1). Nine patients were treated with pyloric BoNT injection for gastroparesis with mean gastric transit time of 21.2 h, range 5.2–44.2 h. Two patients received anal Botox for defecatory dyssynergia (Type I) (n = 1) and overlap (slow-transit and dyssynergic) constipation (n = 1). Endoscopic BoNT injection (100–200 units) was well tolerated and there were no significant adverse events.

Conclusions: Endoscopic BoNT injection to esophagus, pylorus or anal canal is safe, well-tolerated and leads to symptomatic improvement that lasts up to several months. The procedure can be repeated as needed and combined with other therapies.

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TABLE 1 | Subject characteristics and clinical features.

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Dysphagia +</th>
<th>Dysphagia -</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Number of patients (M/F)</td>
<td>20 (12/8)</td>
<td>10 (6/2)</td>
<td>10 (4/6)</td>
<td>0.068</td>
</tr>
<tr>
<td>Mean age (year)</td>
<td>69.5 ± 12.5</td>
<td>71.7 ± 11.8</td>
<td>67.2 ± 13.3</td>
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</tr>
<tr>
<td>Disease duration (year)</td>
<td>9.35 ± 5.8</td>
<td>10.9 ± 6.5</td>
<td>5.8 ± 3.7</td>
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<tr>
<td>Hoehn and Yahr stagea</td>
<td>2.4 ± 0.8</td>
<td>2.8 ± 0.6</td>
<td>2.0 ± 0.7</td>
<td>0.698</td>
</tr>
<tr>
<td>UPDRS III, pointsb</td>
<td>16.5 ± 4.7</td>
<td>18.2 ± 4.8</td>
<td>14.8 ± 4.1</td>
<td>0.120</td>
</tr>
<tr>
<td>L-Dopa Dose Equiv, mg</td>
<td>768.9 ± 276.4</td>
<td>640.2 ± 264.7</td>
<td>698.3 ± 277.1</td>
<td>0.199</td>
</tr>
<tr>
<td>Saliva quantity, microliters</td>
<td>702.9 ± 122.5</td>
<td>702.1 ± 108.1</td>
<td>833.8 ± 127.5</td>
<td>0.287</td>
</tr>
<tr>
<td>PPI intake (g)</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>0.180</td>
</tr>
</tbody>
</table>

UPDRS, Unified Parkinson Disease Rating Scale.
aAt clinical “On” stage.
bAt clinical “Off” stage.

FIGURE 1 | Levels of Substance P in saliva of dysphagic and not dysphagic PD patients.
Effects of Capsaicin on Older Patients with Oropharyngeal Dysphagia: A Double-Blind, Placebo-Controlled, Crossover Study

Nakato R.\textsuperscript{a} · Manabe N.\textsuperscript{b} · Shimizu S.\textsuperscript{c} · Hanayama K.\textsuperscript{c} · Shiotani A.\textsuperscript{a} · Hata J.\textsuperscript{b} · Haruma K.\textsuperscript{d}

\textsuperscript{a}Author affiliations

Keywords: Capsaicin · Oropharyngeal dysphagia · Ultrasonographic tissue Doppler imaging · Substance P · Saliva

Digestion 2017;95:210-220
https://doi.org/10.1159/000463382
Abstract

*Background/Aims:* The standard of care for older patients with oropharyngeal dysphagia (OD) is poor. Stimulation of transient receptor potential vanilloid 1 might become a pharmacological strategy for these patients. This study aimed to compare the therapeutic effect of film food containing 0.75 µg of capsaicin in these patients. *Methods:* In a crossover, randomized trial, 49 patients with OD were provided capsaicin or identical placebo at least 7 days apart. Patients' reported symptoms during repeated swallowing, the volume, pH and substance P (SP) concentrations in saliva, and cervical esophageal wall motion evaluated by ultrasonographic tissue Doppler imaging were obtained before and after capsaicin or placebo administration.

*Results:* Significantly more patients with OD who took capsaicin experienced improvement in symptoms than those who took placebo. Salivary SP levels were significantly increased after capsaicin administration compared with placebo in the effective group. The duration of cervical esophageal wall opening was significantly shorter in capsaicin administration in the effective group. Furthermore, a significant negative correlation was found between the duration of cervical esophageal wall opening and salivary SP levels. *Conclusion:* Elevated salivary SP concentrations stimulated by capsaicin greatly improve the safety and efficacy of swallowing, and shorten the swallow response in older patients with OD.
TRPV1-, TRPA1-, TRPM8-Agonists

Capsaicin  
Piperine  
Menthol
A comparative study on the therapeutic effect of TRPV1, TRPA1, and TRPM8 agonists on swallowing dysfunction associated with aging and neurological diseases

D. Alvarez-Berdugo1,2 | L. Rofes1,2 | V. Arreola1 | A. Martin1 | L. Molina3 | P. Clavé1,2,4

1) GI Physiology Lab, Hospital de Mataró, Barcelona, Spain
2) Centre de Investigación Biomédica en Red de enfermedades hepáticas y digestivas (CIBERhdb), Institute of Salud Carlos III, Madrid, Spain
3) Escola Superior de Ciències de la Salud Tecnocampus, Barcelona, Spain
4) Fundación Instituto de Investigación en Ciencias de la Salud Germans Trias i Pujol (IGTP), Barcelona, Spain

Abstract

Background: Oropharyngeal sensory impairment is a potential target to treat swallowing dysfunction in patients with oropharyngeal dysphagia (OD).

Aim: To assess the therapeutic effect of stimulating oropharyngeal sensory afferents with TRPV1, TRPA1, or TRPM8 agonists vs increasing bolus viscosity in older and neurologic patients with OD by comparing four studies of similar experimental design.

Methods: Swallow function of 142 older patients with impaired safety of swallow at nectar (50-350 mPa-s) viscosity was evaluated with videofluoroscopy (VFS) while treated with TRPV1 (150 μmol/L), TRPV1/A1 (150 μmol/L and 1 mmol/L), or TRPM8 (1 mmol/L or 10 mmol/L) agonists or modified starch (MS) at spoon thick viscosity (>1750 mPa-s).

Results: TRPV1 stimulation with capsaicinoids reduced penetrations by 50%, pharyngeal residue by 80%, and LVC time by 24.38% and increased bolus velocity by 36.51%. TRPV1/A1 stimulation with piperine reduced penetrations by 56.52%, LVC time by 25.55% and increased bolus velocity by 23.63%. TRPM8 stimulation with menthol reduced penetrations by 37.5% while 10 mmol/L reduced LVC time by 18.44%. Thickener reduced penetrations by 77.11%, but increased pharyngeal residue by 19.89%, delayed LVC by 41.73%, and reduced bolus velocity by 13.44%.

Conclusion: Natural capsaicinoids have a stronger therapeutic effect on VFS signs and swallow response by stimulating TRPV1 than TRPV1/A1 or TRPM8 agonists. While TRP stimulants increased bolus velocity and reduced swallow response times, thickeners reduced bolus velocity and further delayed the swallow response. This study sets the bases to develop new pharmacologic strategies for older patients with OD, moving away from compensation toward the recovery of swallow function.

Keywords:
capsaicin, dysphagia, menthol, piperine, thickeners
A comparative study on the therapeutic effect of TRPV1, TRPA1, and TRPM8 agonists on swallowing dysfunction associated with aging and neurological diseases

D. Alvarez-Berdugo1,2 | L. Rofes1,2 | V. Arreola1 | A. Martin1 | L. Molina3 | P. Clave1,2,4

**TABLE 1** Demographic and oropharyngeal dysphagia-related data. *P*-value for categorical variables corresponds to chi-squared test; *P*-value for continuous variables corresponds to Kruskal–Wallis test. Neurodeg = neurodegenerative disease

<table>
<thead>
<tr>
<th></th>
<th>Capsaicinoids study (N = 33)</th>
<th>Piperine study (N = 40)</th>
<th>Menthol study (N = 36)</th>
<th>Starch based thickener (N = 33)</th>
<th><em>P</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>75.94 ± 1.88</td>
<td>75.8 ± 2</td>
<td>77.14 ± 1.37</td>
<td>73.94 ± 2.23</td>
<td>.614</td>
</tr>
<tr>
<td>Gender (men)</td>
<td>20 (60.61%)</td>
<td>17 (42.50%)</td>
<td>16 (44.44%)</td>
<td>16 (48.48%)</td>
<td>.432</td>
</tr>
<tr>
<td>SSQ</td>
<td>315.15 ± 47.97</td>
<td>529.6 ± 44.9</td>
<td>843 ± 61.84</td>
<td>432.9 ± 73.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.021</td>
</tr>
<tr>
<td>Aging</td>
<td>10 (30.3%)</td>
<td>23 (57.5%)</td>
<td>22 (61.1%)</td>
<td>10 (30.3%)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>8 (24.2%)</td>
<td>4 (10%)</td>
<td>8 (22.2%)</td>
<td>8 (24.2%)</td>
<td></td>
</tr>
<tr>
<td>Neurodeg</td>
<td>15 (45.5%)</td>
<td>13 (32.5%)</td>
<td>6 (16.7%)</td>
<td>15 (45.5%)</td>
<td></td>
</tr>
</tbody>
</table>

1 mmol/L reduced penetrations by 37.3% while 10 mmol/L reduced LVC time by 18.44%. Thickener reduced penetrations by 77.11%, but increased pharyngeal residue by 19.89%, delayed LVC by 41.73%, and reduced bolus velocity by 13.44%.

**Conclusion:** Natural capsaicinoids have a stronger therapeutic effect on VFS signs and swallow response by stimulating TRPV1 than TRPV1/A1 or TRPM8 agonists. While TRP stimulants increased bolus velocity and reduced swallow response times, thickeners reduced bolus velocity and further delayed the swallow response. This study sets the bases to develop new pharmacologic strategies for older patients with OD, moving away from compensation toward the recovery of swallow function.

**Keywords**
capsaicin, dysphagia, menthol, piperine, thickeners
**Figure 2** Normalized effect on the prevalence of laryngeal vestibule penetrations of each treatment compared with its control (#P<.05, ##P<.01, ###P<.001) and between treatments (*not overlapping confidence intervals of the odds ratio from the McNemar's test). CAPS = capsaicinoids; PIPE = piperine; MENT = menthol; ST MS = spoon thick viscosity achieved with modified starch.

**Figure 3** Normalized effect on the swallow response and final bolus velocity of each treatment compared with its control (#P<.05, ##P<.01, ###P<.001) and between treatments (*P<.05, **P<.01, ***P<.001). CAPS = capsaicinoids; PIPE = piperine; MENT = menthol; ST MS = spoon thick viscosity achieved with modified starch; LVC, laryngeal vestibule closure; UESO, upper esophageal sphincter opening.
Quickcard-Based Approach to Guiding Specific Nonpharmacological Treatments in a German Parkinson’s Network

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**Figure 2.** Quickcard Dysphagia. Notes: "Individual assessment of levodopa responsiveness of dysphagia, if positive: consider permanent treatment. Abbreviations: EMST = Expiratory Muscle Strength Training, FEES = fiberoptic endoscopic evaluation of swallowing, PEG = percutaneous endoscopic gastrostomy."
Online-Tool (Nuromedia)
Figure 1. Schematic representation of an interdisciplinary treatment process using Quickcards.
Conclusions

The basic principles of dysphagia treatment in PD are optimizing dopaminergic medication in combination with swallowing therapy by trained speech and language therapist considering the specific dysphagia pattern of the individual PD patient

• Levodopa, apomorphine, and rotigotine may have beneficial effects on pharyngeal motility and swallowing efficiency in individual PD patients

• Improving lengthy chewing and slow initiation of swallowing: amantadine, learn to swallow in conscious steps, specific cues, easier food consistencies

• Reducing choking on fluids: explain influence of dual task situations, learn safe swallowing with attention, chin tuck?, smaller volumes and/or thicker consistencies

• Reducing pharyngeal/tablet residue: effortful swallowing with biofeedback, EMST training, easier food consistencies, ask a dietitian to advise the patient on the best way to maintain a wholesome diet

• Intensive voice treatment: unspecific indirect effects

• Novel treatment strategies: Substance P stimulation, botulinum neurotoxin, and telemedicine-supported network approaches