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FATORES ASSOCIADOS ÀS ALTERAÇÕES NA DINÂMICA DA DEGLUTIÇÃO OROFARÍNGEA NA DOENÇA DE PARKINSON: ACHADOS VIDEOFLUOROSCÓPICOS

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Para minha mãe, meus irmãos, meu marido e minha filha.

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"[...] devemos tomar realmente por um milagre o fato de que os métodos modernos de ensino não tenham sufocado ainda de todo a curiosidade investigadora, já que este gérmen delicado necessita não só de estímulo, mas acima de tudo liberdade."

Einstein

LISTA DE ILUSTRAÇÕES E TABELAS

LISTA DE SIGLAS E ABREVIATURAS

AEF – Ariepiglottic fold

CI – Confidence interval

DP – Doença de Parkinson

H&Y – Hoehn and Yahr

IMC – Índice de massa corporal

LP – Lingual pumping

ml – Mililitro

ms – Milissegundos

OR – Odds Ratio

OTT – Oral transit time

PAS – Penetration/Aspiration Scale

PD – Parkinson's disease

PET – Pharyngo-esophageal transition

PS – Pyriform sinus

PTT – Pharyngeal transit time

SLP – Speech-Language Pathologist

STD – Stage transition duration

TTF – Tempo de trânsito faríngeo

TTO – Tempo de trânsito oral

UES - upper esophageal sphincter

UFBA – Universidade Federal da Bahia

UKPDBB - United Kingdom Parkinson's Disease Brain Bank

UPDRS – Unified Parkinson's disease rating scale

VSS/VFSS – Videofluoroscopic Swallowing Study

SUMÁRIO

RESUMO

A disfagia é uma alteração frequente na doença de Parkinson (DP) e pode aumentar o risco de pneumonia e morte nesta população. Apesar disso, os mecanismos que levam à disfagia e os seus fatores associados ainda não são bem compreendidos dificultando a adoção de medidas preventivas. Desta forma, este estudo objetivou identificar a associação entre os eventos da dinâmica orofaríngea da deglutição e a aspiração de líquidos e alimentos na DP. Para isso, 69 pacientes com DP foram submetidos à videofluoroscopia da deglutição e avaliados com alimentos contrastados em volumes e consistências padronizadas. Em um primeiro estudo verificamos a associação entre os eventos da dinâmica da deglutição, consistências e volumes alimentares com a aspiração traqueal. A análise demonstrou que a retenção de alimentos em valécula e em transição faringo-esofágica, bem como a deglutição fracionada estiveram associadas à aspiração (odds ratio (OR) = 4.09, 2.87 e 3.83; P = 0.0040, 0.0071 e 0.0009, respectivamente). Além disso, a aspiração foi mais comum nas consistências líquida e semi-líquida e não houve diferença significativa entre o status de aspiração e os volumes alimentares. Em um segundo estudo, verificamos que a festinação lingual esteve associada à organização instável do bolo, pobre controle oral do bolo alimentar, retenção de alimento em transição faringo-esofágica e aspiração traqueal. Desta forma, conclui-se que alguns eventos da dinâmica da deglutição podem predizer aspiração em indivíduos com DP e os profissionais envolvidos no diagnóstico e tratamento da disfagia devem estar atentos à identificação destes achados durante o exame videofluoroscópico da deglutição. A festinação lingual é um evento que pode impactar negativamente a dinâmica da deglutição, associando-se a alterações tanto na fase oral quanto na fase faríngea da deglutição, incluindo aspiração. Além disso, maior prevalência de aspiração nas consistências alimentares mais fluidas alerta para a necessidade de implementação de medidas compensatórias visando a redução da entrada de alimentos em vias aéreas nesta população.

ABSTRACT

Dysphagia is a common disorder in Parkinson's disease (PD) and can increase the risk of pneumonia and death in this population. Nevertheless, the mechanisms that lead to dysphagia and its associated factors are not well understood hindering the adoption of preventive measures. Thus, this study aimed to identify the association between the events of oropharyngeal swallowing dynamics and the aspiration of food and liquids in individuals with PD. For this, 69 patients with PD underwent videofluoroscopic study of swallowing with standardized contrasting food volumes and consistencies. In a first study, we found the association between the events of the dynamics of swallowing, food consistencies and volumes with tracheal aspiration. The analysis showed that the retention of food in the vallecula and pharyngoesophageal transition, as well as the piecemeal deglutition were associated with tracheal aspiration (odds ratio (OR) = 4.09, 2.87 and 3.83, P = 0.0040, 0.0071 and 0.0009, respectively). Furthermore, the aspiration was more common in thin and thick fluids and there was no significant difference between the aspiration status and food volumes. In a second study, we found that the lingual pumping was associated with unstable organization of bolus, poor oral bolus control, retention of food in the pharyngoesophageal transition and tracheal aspiration. Thus, it is concluded that some events of the swallowing dynamics can predict aspiration in PD patients and clinicians should be alert to the identification of these findings during videofluoroscopy. The lingual pumping is an event that can negatively impact the dynamics of swallowing, which are associated with changes in both the oral and in the pharyngeal phase of swallowing, including aspiration. In addition, a higher prevalence of aspiration in more fluid food consistencies alert to the need for implementation of compensatory measures aimed at reducing food intake airway in this population.

1.0 Introdução

A disfagia é uma alteração bastante frequente na doença de Parkinson (DP) e sua prevalência, apesar de incerta, é relatada entre 70 e 100% dos pacientes, nesta população[1]. A maioria dos autores descreve tanto alterações na fase oral, caracterizadas por escape extra-oral do bolo, dificuldade mastigatória, redução na movimentação da língua e estase intra-oral após a deglutição quanto na fase faríngea tais como atraso no reflexo da deglutição, estase em recessos faríngeos, penetração laríngea e aspiração traqueal[2].

Estudos tentam correlacionar esses achados com a dificuldade motora na doença de Parkinson mas tem-se verificado que, além do aspecto motor, existem múltiplos fatores influenciando o distúrbio de deglutição na DP. Incoordenação respiratória[3] e alterações da sensibilidade laringo-faríngea[4] tem sido discutidas dentre as possíveis causas da disfagia na DP.

Apesar de tantos fatores influenciando a entrada de alimento em via aérea, o paciente com DP queixa-se pouco de sua dificuldade de deglutição e é relatada uma redução tanto da tosse reflexa como voluntária[5]. Estes aspectos, quando associados, podem comprometer a segurança alimentar destes pacientes e dificultar um diagnóstico precoce. A disfagia na DP torna-se ainda mais grave diante da presença de aspiração que aumenta o risco de pneumonia aspirativa, principal causa de morte nesta população[6].

Porém, quando a aspiração ocorre, uma série de outras alterações tanto na fase oral quanto na fase faríngea ocorreram e podem ter contribuído para a entrada de alimento em via aérea[7]. Verificamos na prática clínica e na realização dos exames videofluoroscópicos, que incoordenações na fase oral, redução na força lingual ou outras alterações que prejudiquem a adequada ejeção do alimento da cavidade oral para a faringe podem aumentar o risco de aspiração. Do mesmo modo, a presença de atraso no reflexo da deglutição ou estase em recessos faríngeos após a deglutição podem resultar em entrada de alimento em vias aéreas.

Desta forma, delineamos este estudo visando identificar como os eventos da deglutição se associam entre si, como a ocorrência de uma alteração pode influenciar a presença de outra, e tentar realizar uma análise patofisiológica sobre estas associações. Compreender o mecanismo subjacente à disfagia é crucial no estabelecimento de medidas preventivas e terapêuticas. Porém, poucos estudos têm investigado quais fatores clínicos e do exame instrumental de deglutição estão associados à entrada de alimento em via aérea nos pacientes com DP.

Portanto, este estudo se propõe a identificar a associação entre os eventos da dinâmica orofaríngea da deglutição e a aspiração de líquidos e alimentos na DP.

1 Kalf JG, de Swart BJM, Bloem BR, Munneke M. Prevalence of oropharyngeal dysphagia in Parkinson's disease: A meta-analysis. Parkinsonism Relat Disord. 2012;18(4):311–5.
2 Ali GN, Wallace KL, Schwartz R, DeCarle DJ, Zagami AS, Cook IJ. Mechanisms of oral-pharyngeal dysphagia in patients with Parkinson's disease. Gastroenterology. 1996;110(2):383–92.
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5 Pitts T. Using Voluntary Cough To Detect Penetration and Aspiration During Oropharyngeal Swallowing in Patients With Parkinson Disease. CHEST J. 2010;138(6):1426.
6 Nobrega A, Rodrigues B, Melo A. Is silent aspiration a risk factor for respiratory infection in Parkinson's disease patients? Parkinsonism Relat Disord. 2008;14(8):646–8.
7 Perlman AL, Booth BM, Grayhack JP. Videofluoroscopic predictors of aspiration in patients with oropharyngeal dysphagia. Dysphagia. 1994; 9(2):90–5.

2.0 Objetivos

GERAL:

- Identificar a associação entre os eventos da dinâmica orofaríngea da deglutição e a aspiração de líquidos e alimentos na DP;

ESPECÍFICOS:

- Determinar quais eventos da dinâmica orofaríngea da deglutição estão associados à aspiração de líquidos e alimentos em indivíduos com DP;
- Determinar se existe associação entre festinação lingual e as alterações na dinâmica da deglutição em indivíduos com DP;
- Avaliar como a consistência e o volume dos alimentos testados influencia a ocorrência de alterações de deglutição em indivíduos com DP;

3.0 Artigo de Revisão

A doença de Parkinson (DP) acomete o sistema nervoso central e é caracterizada por seu curso crônico e progressivo. Nos países industrializados, sua prevalência está em torno de 0-3% acomentendo mais de 1% da população mundial acima de 60 anos[1,2]. Apesar de descrita inicialmente em 1817 por James Parkinson, a DP permanece sem uma causa definida. Estudos apontam para a interação entre fatores genéticos, ambientais e comportamentais ativando eventos moleculares que levam à degeneração neuronal[3, 4].

Os sintomas motores característicos da DP são tremor de repouso, bradicinesia, rigidez e alteração postural e estão relacionados a alterações neurobiológicas na substância negra com a consequente perda da projeção dopaminérgica para o estriado[5]. No entanto, sinais pré-motores incluem depressão, alterações autonômicas como constipação intestinal e disfunção erétil, hiposmia e distúrbios do sono, os quais são observados em todas as fases da doença[3]. Braak *et al*. [6] relatam que a neurodegeneração tem início nos núcleos dos nervos glossofaríngeo, vago e olfatório e segue trajeto ascendente até o córtex.

Desta forma, centros envolvidos na deglutição como o núcleo motor dorsal do nervo glossofaríngeo e vago e o sistema reticular estão precocemente prejudicados na doença de Parkinson. Além disso, o núcleo pedunculopontino, que provê aferência para o trato solitário, também relacionado com a deglutição, estaria envolvido no processo degenerativo além de receber *input* patologicamente aumentado do globo pálido. O envolvimento precoce dos núcleos dos nervos glossofaríngeo e vago poderia estar relacionado ao início precoce de alterações de deglutição mesmo em indivíduos em fase inicial da doença[7]. Apesar da fisiopatologia da disfagia na doença de Parkinson ainda não estar bem estudada, alguns estudos tem indicado que além das alterações no tronco encefálico, algumas regiões corticais também estariam envolvidas na deglutição e teriam um papel na fisiopatologia da disfagia na DP[7].

Muitos indivíduos com DP apresentam disfagia orofaríngea[8], entretanto, apenas uma pequena parte destes indivíduos percebe e se queixa de suas alterações na deglutição[9, 10]. O reconhecimento deste sintoma torna-se ainda mais difícil pela dificuldade em estabelecer associações com a gravidade da doença. As alterações estão presentes em todas as fases da deglutição e os fatores envolvidos neste processo ainda não são completamente compreendidos[11].

A avaliação da deglutição através de exames dinâmicos de imagem permitiu a identificação de diversas alterações desta função em indivíduos com DP. Na fase oral são descritos: escoamento labial, escape intra-oral do alimento, deglutição múltipla, deglutição fracionada e resíduo em cavidade oral após a deglutição. Na fase faríngea são mais comuns o atraso no início da fase faríngea, resíduo em recessos faríngeos após a deglutição, elevação laríngea reduzida, penetração laríngea e aspiração[8, 10-13, 14].

Medidas temporais de trânsito oral e faríngeo do bolo alimentar também tem sido extraídos dos exames videofluoroscópicos. O tempo de trânsito oral, tempo de atraso faríngeo e tempo de trânsito faríngeo, dentre outros, são descritos como aumentados na doença de Parkinson[15].

A disfagia pode levar a aspiração de alimentos e resultar em pneumonia aspirativa, uma das principais causas de morte entre indivíduos com DP. Nóbrega *et al.*[16] relatam que a aspiração silente pode aumentar em quase dez vezes o risco de pneumonia aspirativa e em três vezes o risco de morte nesta população. A aspiração torna-se ainda mais perigosa entre os indivíduos com DP porque eles se queixam pouco de suas alterações de deglutição[17] e seus mecanismos de defesa, como a tosse reflexa e voluntária, estão comprometidos[18, 19].

O maior objetivo da avaliação de deglutição é identificar anormalidades fisiológicas que contribuam ou expliquem o risco do paciente para aspiração[20]. Sabe-se que, quando o paciente aspira, uma série de outras alterações orais e faríngeas ocorreram e podem ter contribuído para a entrada de alimento em via aérea. Este estudo visa realizar uma revisão da literatura sobre os eventos videofluoroscópicos associados à disfagia e/ou aspiração na DP.

Métodos

A busca foi realizada no Pubmed em outubro de 2014 e a estratégia de busca envolveu os seguintes termos: (“parkinson disease” [MeSH Terms] OR (“parkinson” [All Fields] AND “disease” [All Fields]) OR “parkinson disease” [All Fields] OR (“parkinson’s” [All Fields] AND “disease” [All Fields]) OR “parkinson’s disease” [All Fields]) AND (“deglutition disorders” [MeSH Terms] OR (“deglutition” [All Fields] AND “disorders” [All Fields]) OR

“deglutition disorders” [All Fields] OR “dysphagia” [All Fields]) AND (“associated fators”[All Fields] OR “risk factors[MeSH Terms] OR (“risk” [MeSH Terms] AND “factors”[MeSH Terms]) OR (“causality”[MeSH Terms]).

Os artigos foram considerados elegíveis se: a) fossem escritos em língua inglesa ou portuguesa; b) avaliassem a deglutição na doença de Parkinson analisando seus achados videofluoroscópicos; c) avaliassem apenas indivíduos com doença de Parkinson ou apresentasse os resultados relacionados à DP/disfagia de forma independente de outras doenças/alterações; d) estudassem seres humanos.

Resultados e discussão

A busca no pubmed resultou em 341 artigos. Após a análise do título e remoção dos artigos duplicados, 146 artigos foram excluídos e 195 seguiram para análise do *abstract*. Após a análise do *abstract* dos 195 artigos, foram excluídos 162 sendo:

- 24 em idioma diferente do português ou inglês;
- 75 não avaliaram achados videofluoroscópicos associados a disfagia/aspiração sendo 42 artigos sobre tratamento, 12 artigos sobre métodos diagnósticos, 16 revisões sobre outros temas, 5 comentários ou estudos de caso, 27 descritivos ou sobre questões neurofisiológicas e 18 sobre achados não-videofluoroscópicos associados à disfagia/aspiração;
- 24 não abordaram a disfagia ou não estudaram pacientes com DP;
- 4 por não separarem a análise entre DP e outras doenças ou entre disfagia e outras alterações;
- 3 não eram em humanos;
- 5 não tinham o *abstract* disponível;

Dentre os 15 artigos selecionados, poucos estudos foram desenhados para avaliar os fatores associados à disfagia ou aspiração na DP. Com relação aos eventos da dinâmica da deglutição relativos à fase oral, a festinação lingual é relatada como a produção de movimentos repetitivos da língua na tentativa de ejetar o bolo para a faringe. Este movimento involuntário

é frequentemente encontrado em exames videofluoroscópicos na DP e pode estar associado tanto à presença de disfagia[11] quanto à aspiração[12]. Essa associação é provavelmente relacionada à dificuldade na organização e ejeção oral do bolo resultante da incoordenação lingual. Sung *et al*.[9] encontraram que deglutição múltipla se associou a trânsito incompleto do bolo sugerindo que a deglutição múltipla seria uma estratégia para melhorar a limpeza de resíduos alimentares em recessos orofaríngeos e/ou compensar uma deglutição ineficiente.

Com relação aos eventos alterados na fase faríngea da deglutição na DP, os estudos incluem diminuição da mobilidade da parede faríngea e consequente estase em recessos faríngeos, principalmente em valécula e recessos piriformes[9].

Ali *et al*.[11] identificaram mais alterações de fase faríngea do que na fase oral em indivíduos com DP. Esses autores ressaltam o papel do esfíncter esofágico superior nas alterações de fase faríngea na DP. Relaxamento incompleto ou abertura reduzida deste músculo tem sido relatadas nesta população e associadas à redução da elevação laríngea, rigidez do músculo cricofaríngeo ou hipomobilidade faríngea resultando em maior estase nesta região após a deglutição[9, 11, 14]. A presença de estase faríngea nestes pacientes é ainda mais preocupante devido à incoordenação respiratória que estes pacientes apresentam

Com relação à influência das características dos alimentos sobre a deglutição dos pacientes com DP, os alimentos mais consistentes resultam em tempos de trânsito oral e faríngeo maiores nesta população[21]. Além disso, parece haver um consenso de que os líquidos finos são os mais prejudiciais a uma deglutição segura na DP. Vários estudos relatam que quanto mais espesso o alimento, menor a ocorrência de penetração/aspiração[8, 21, 22]. Os pacientes com DP também têm dificuldade para ingerir o alimento de uma vez apresentando, frequentemente, deglutição fracionada. Suntrup *et al*.[7] alertam para o fato de que pacientes com DP disfágicos ingerem volumes menores e Coriolano *et al*.[13] encontraram que estes pacientes precisam de mais tempo e de mais deglutições para deglutir o mesmo volume que controles saudáveis. Esta poderia ser uma medida compensatória visando reduzir o risco de aspiração na DP.

Conclusão

Apesar de encontrarmos muitos estudos sobre fatores associados à disfagia ou aspiração na DP, a maioria analisava aspectos clínicos como gravidade da doença, discinesia ou perda de peso e poucos tinham sido desenhados com o objetivo de identificar a associação entre os eventos da dinâmica da deglutição na DP. Observa-se que festinação lingual e estase em recessos faríngeos parecem estar associados à entrada de alimento em vias aéreas na DP. A ingestão de líquidos finos aumentaria os escores de aspiração nesta população. Estudos prospectivos, com amostras maiores e grupos controle, desenhados especificamente para identificação de preditores para aspiração na DP são necessários para possibilitar a identificação precoce do distúrbio de deglutição e a redução das suas consequências sobre a morbi-mortalidade nesta população.

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4.0 Resultados

Artigo 1 – **Videofluoroscopic predictors of aspiration status in Parkinson's disease patients.**

Situação: Re-submetido após solicitações dos revisores

Revista: *Dysphagia*

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Artigo 2 – **Swallowing disorders in Parkinson's disease: impact of lingual pumping**

Situação: Aceito para publicação

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4.1 Artigo 1

Title Page

1. **Title**

Videofluoroscopic predictors of aspiration status in Parkinson's disease patients.

2. **Running Head:** Predictors of aspiration in Parkinson's disease

3. **Key words:** Parkinson's disease, Deglutition disorders, Penetration/aspiration

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Abstract

Abstract

Parkinson's disease (PD) patients show a high prevalence of swallowing disorders and tracheal aspiration of food. The videofluoroscopic study of swallowing (VFSS) allows clinicians to visualize the visuoperceptual and temporal parameters associated with swallowing disorders in an attempt to predict aspiration risk. However, this subject remains understudied in PD populations. Our aim was to identify the predictors of aspiration in PD patients using the VFSS. Consecutive patients were evaluated using VFSS with different consistencies and volumes of food. A speech-language pathologist measured the type of intra-oral bolus organization, loss of bolus control, the start site of the pharyngeal phase, the presence of multiple swallows, piecemeal deglutition, bolus retention in the pharyngeal recesses and temporal measures. Scores ≥ 3 on the penetration-aspiration scale (PAS) indicated the presence of aspiration. Using logistic marginal regression, we found that retention in the vallecula, retention in the pharyngoesophageal transition (PET) and piecemeal deglutition were associated with aspiration status (odds ratio (OR) = 4.09, 2.87 and 3.83; P = 0.0040, 0.0071 and 0.0009, respectively). Aspiration occurred only with fluids (both of thin and thick consistency), and no significant differences were observed between fluid types. Food volumes were not associated with aspiration. The mechanisms underlying dysphagia and aspiration in PD patients and indications for further studies are discussed.

Key words: Parkinson's disease, Deglutition disorders, Penetration/aspiration

Introduction

Dysphagia is common in Parkinson's disease (PD) patients, and objective measurements have determined its prevalence to be approximately 72-87% [1]. Tracheal aspiration occurs in more than 50% of PD patients [2] and results in a high risk of aspiration pneumonia and death in this population [3, 4]. Despite the broad impact of dysphagia on morbidity, mortality and quality of life, the correlation with disease severity and its physiopathological mechanisms remains controversial [5-7]. Swallowing disorders appear to result from a combination of rigidity and bradykinesia associated with respiratory incoordination and the pharyngeal sensory deficits present in PD [8, 9].

The videofluoroscopic study of swallowing (VFSS) is the gold-standard method to evaluate swallowing dynamics. This assessment method allows clinicians to visualize the movements and alterations of deglutition. Moreover, the VFSS can be used to help determine the safety of continuing oral food intake and to better understand the pathophysiological mechanisms underlying dysphagia and aspiration. In PD patients, visuoperceptual alterations, such as piecemeal deglutition, lingual pumping, preswallow spill, oral and pharyngeal residue, laryngeal penetration and tracheal aspiration, have been reported [5, 6, 10]. A recent systematic review [11] reported that several kinematic measures of structural displacement can be extracted from VFSS videos and that hyoid movement is one of the most frequently assessed parameters. Temporal measures have also been extensively described, but there are several inconsistencies between the published definitions. Among one series of measures, the most widely used intervals are the stage transition duration, the pharyngeal transit time and the duration from laryngeal closure to upper esophageal sphincter (UES) opening.

Perlman *et al*. [12] reported that additional indicators of oropharyngeal dysphagia are usually present when food enters the airway. Thus, recognizing the risk factors associated with

aspiration may help clinicians make optimal choices regarding the best possible therapeutic plan. In stroke patients, vallecular stasis, reduced hyoid elevation, deviant epiglottic function, diffuse hypopharyngeal stasis, delayed initiation of the pharyngeal stage of swallowing [12] and several temporal measures [14] have been described as videofluoroscopic predictors of food aspiration.

In the dysphagic population as a whole, pharyngeal retention is cited as a predictor of aspiration on the subsequent swallow [13, 14]. In addition, a series of measures related to tongue strength, anatomically normalized hyoid movement, respiratory measures and the length of time the bolus remains in the pharynx with the airway open have also been associated with an increased risk of aspiration [15].

Because aspiration status has been associated with a number of swallowing measures, clinicians should understand how these associations occur in swallowing of PD patients. However, our literature search failed to identify studies addressing the videofluoroscopic predictors of tracheal food aspiration in PD populations. Some authors found that PD patients with severe sialorrhea [16], voluntary cough abnormalities [17] and respiratory incoordination [8] had more aspiration. Regarding food consistencies, swallowing thin liquids is associated with higher scores in penetration/aspiration scale (PAS) in the PD population [2, 18].

We hipothesized that temporal measures could be increased in individuals with PD and aspiration mainly because of bradykinesia of the oropharyngeal muscles found in this population. In addition, the retention of food and liquids in pharyngeal recesses may enhance the chance of aspiration because the respiratory incoordination in PD patients.

The process of swallowing is complex and integrated. Therefore, it is important to study the mechanisms that underlie dysphagia, especially in PD, as the causative agents of dysphagia are not well established in this population. Thus, the aim of this study was identify VFSS predictors of aspiration in PD patients.

Methods

Study Population

Consecutive idiopathic PD patients from the Ambulatory Care Center for Movement Disorders of the Federal University of Bahia were enrolled in this study. All patients had taken anti-PD medications. Disease severity was evaluated according to the Hoehn and Yahr scale. Exclusion criteria included diagnoses of other neurologic diseases, cognitive or psychiatric disorders, depression, head and neck cancer or severe dysphagia that precluded complete evaluations of swallowing. PD diagnoses were made by a certified neurologist in accordance with the United Kingdom Parkinson's Disease Brain Bank (UKPDBB) guidelines [16].

This study was approved by the local ethics committee of Bahia, Brazil and was conducted in accordance with the Helsinki declaration (1964). All patients signed an informed consent form before undergoing any procedures related to the study.

Swallowing Assessments

The VFSS was performed using a Flexavision HB/Package (Shimadzu®, Japan) with 70 Kv and 20 mAs of radiation and were digitalized with a resolution of 30 frames per second. The exam was conducted by a radiologist and a speech-language pathologist (SLP) and was performed using an edible barium sulfate radiopaque agent (Bariogel® 100%). Subjects completed the exam in a lateral position in a single phase. No instructions to hold the food or liquid in the mouth before swallowing were provided, so our study therefore examined uncued swallowing. To evaluate the patients' ability to swallow a thin fluid, each patient was asked to swallow barium mixed with water at a 1:1 ratio in 5, 10 and 20 ml portions. For thick fluids,

patients were asked to swallow 5, 10 and 20 ml of pure barium. Pasty barium was composed of 5, 10 and 15 ml of barium mixed with Nestlé® natural yogurt at a 2:1 ratio. For soft solid foods, half of a biscuit dipped in barium was used. Because the 20 ml bolus was fractionated in almost all patients, our analysis of this volume was limited. The 5, 10 and 15 ml portions were provided in a spoon, but the 20 ml volumes of thin and thick fluids were provided in a glass. Caregivers were trained to offer the food, except for the 20 ml trials, in which the participants drank by themselves.

The superior, inferior, anterior and posterior limits of the fluoroscopic image were the hard palate, the upper esophageal sphincter (UES), the lips and the posterior pharyngeal wall (C3-C5), respectively.

Measurements

The VFSS videos were analyzed by 3 trained SLPs in real time, frame by frame and in slow motion using Avidemux 2.5.3 open-source software. The following visuoperceptual parameters of VFSS were measured:

- The type of intra-oral bolus organization [17] was defined as *closed* (the bolus was positioned above the tongue dorsum), *open anterior-restricted* (the bolus was positioned anterior to the tongue), *open expanded* (the bolus was positioned anterior and above the tongue), *prolonged* (the bolus extended above the tongue from the tip to the soft palate) and *unstable* (the position of the bolus was oscillating with or without intra-oral food spill);
- A loss of bolus control was considered to have occurred when the bolus was observed to fall into the oral sulci before swallowing was initiated;

- The start site of the pharyngeal phase was defined as the location of the contrasted material when laryngeal elevation occurred;
- Multiple swallows were defined as the occurrence of more than three hard swallows after the posterior bolus propulsion;
- Piecemeal deglutition was considered to have occurred when the bolus was fractioned in many swallows. Piecemeal deglutition for volumes less than 20-ml is considered abnormal [19].
- Retention in the tongue and pharyngeal recesses was evaluated after the first swallow in the tongue, vallecula, pyriform sinuses, posterior pharyngeal wall and pharyngo-esophageal transition (PET), and was rated on a scale from 0 to 3. A score of 0 scores indicated that no residue was visible. A score of 1 was considered mild (up to 25% of the level of the height of the structure). Scores of 2 were considered moderate (the level of contrasted material constituted between 25% and 50% of the height of the structure). Scores equal to or greater than 3 indicated severe retention (*i.e.*, the barium level was higher than 50% of the height of the structure) [13]. In addition to this analysis, we also transformed this variable into a dichotomous variable, with no residue or mild residue in one group and moderate or severe residue in the other group.

The PAS [18] was used to measure aspiration status. We considered aspiration to have occurred when the PAS score was ≥ 3, which is consistent with a previous study that reported PAS scores of 1 and 2 in a healthy population [20]. These analyses were made at the level of the swallow, rather than at the level of the participant; this approach enabled the determination of the precise factors that led to aspiration during each swallowing event.

The temporal parameters included oral transit time (OTT), which was measured from the first backward movement of the bolus until the head of the bolus passed the angle of the mandible. The pharyngeal transit time (PTT) was measured from the time the head of the bolus passed the angle of the mandible until the tail of the bolus left the cricopharyngeal region (the last frame in which material in the UES could be observed). The stage transition duration (STD) was measured from the time at which the bolus passed the angle of the mandible until the onset of laryngeal elevation [10].

When multiple swallows or piecemeal deglutition were observed, we evaluated only the first swallow in the series for each bolus.

Statistical Analysis

Data were analyzed using R software version 3.0.2. Descriptive statistics are presented as the mean ± standard deviation. The Shapiro test was used to assess the normality of the data. We used Cochran-Mantel-Haenszel tests in bivariate analyses to select the videofluoroscopic variables to use for logistic marginal regression analysis to control for food consistency and volume. In this selection, the variables for which $P < 0.15$ were chosen. The regressions were subsequently adjusted using the backward method. The final model was a logistic marginal regression stepwise model that combined forward and backward procedures. The logistic marginal regression was also performed separately between aspiration status and OTT, STD and PTT. The results from the logistic marginal regression analysis between aspiration status and food consistencies and volumes were corrected via multiple comparisons using the Holm-Bonferroni method.

Results

Of the 71 patients enrolled in the study, 69 completed the VFSS protocol. Two patients were excluded because they had severe dysphagia that precluded a complete evaluation of all food consistencies. A total of 690 swallowing events (10 per patient) were assessed in the current study. There were 44 men and 25 women in the study population, and the mean age of the participants was 63.36 ± 11.62 years. The mean disease duration was 7 ± 5.2 years, and the mean Hoehn and Yahr stage was 2.3 ± 0.9. Regarding aspiration, 11 (15.94%) patients had PAS scores ≥ 3, and 23 (3.33%) swallowing events exhibited aspiration.

Table 1 presents the associations that were identified using the bivariate analyses between aspiration and VFSS visuoperceptual factors. The results of the logistic marginal regression revealed that piecemeal deglutition, retention in the vallecula and retention in the PET were all significantly associated with aspiration (as shown in Table 2).

With respect to the temporal VFSS factors, the means, standard deviations and results of the logistic marginal regression analyses between OTT, STD and PTT and aspiration for each consistency/volume are shown in Table 3. A statistically significant difference was observed for patients swallowing 10 ml of thin fluid; specifically, patients with PAS scores ≥ 3 showed higher PTTs. A significant P-value was also obtained in trials using 5 ml of thick fluid for OTT, STD and PTT, but only one patient aspirated while swallowing this consistency/volume. For trials in which 10 ml of thick fluid was swallowed, the STD and PTT were significantly reduced in subjects who exhibited aspiration.

With respect to aspiration according to food consistencies, thin liquid was associated with a higher prevalence of aspiration (12 swallows) than thick fluid (11 swallows), but this difference was not statistically significant (as shown in Figure 1). Aspiration was only observed in patients swallowing thin and thick liquids. Clinically relevant, statistically significant

differences were observed for the comparisons between pasty vs. thin, pasty vs. thick, solid vs. thin and solid vs. thick, and all of the P-values were less than 0.0001. Regarding food volume, no significant associations were observed between aspiration prevalence and different food volumes.

Discussion

The videofluoroscopic findings of retention in the vallecula, retention in the PET and piecemeal deglutition were observed to be significant predictors of aspiration in PD patients.

In the studied group, rigidity and bradykinesia may lead to intra-oral abnormalities in the capture, organization and posterior propulsion of food and liquids to the pharynx. Slower and smaller tongue movements [21, 22], in combination with pharyngeal dysmotility [6], result in an increased difficulty associated with the safe transport of food. Concurrently, upward and forward laryngeal movements are also important because they promote the opening of the cricopharyngeal muscle, which permits the passage of the food bolus. When this movement is reduced, the food remains in the pharyngeal recesses, including in the region of the PET, which contributes to post-swallowing aspiration. The retention in PET may be also related with disorders in the cricopharyngeal muscle relaxation. Some studies [5] suggest PD patients show an incomplete UES relaxation and a reduced UES opening. However, there is still controversy about this topic [23].

At the same time, vallecular retention is also associated with reduced hyoid elevation, deviant epiglottic function and oral impairments [24], a fact that highlights the strong relationship between the oral and pharyngeal phases of swallowing. Steele *et al*. [15] previously reported a reduction in the tongue-palate pressures for bolus propulsion and reduced laryngeal elevation in dysphagic populations with aspiration.

It is important to emphasize that in the PD population, the occurrence of post-swallowing pharyngeal retention is even more troubling because patients with decreased swallowing safety, such as those with higher PAS scores, perform more inspiratory cycles after swallowing and have a shorter duration of swallowing apnea [8]. This respiratory incoordination can result in residue being retained in the pharyngeal recesses, where it can then transit down to the lungs with the inspiratory flow. This is especially serious because PD patients have a diminished cough reflex, impairments in voluntary coughing [25, 26] and a high prevalence of silent aspiration, which enhances the risk of aspiration pneumonia [4], the major cause of death in this population [3].

Regarding piecemeal deglutition, a majority of our patients fractioned the 20-ml content, which was also associated with a higher prevalence of aspiration. In the healthy population, including healthy elderly individuals, a typical bolus size is usually 21 ml [27], but higher aspiration scores have been observed with this volume [28]. We hypothesized that PD patients at risk of aspiration may fractionate bolus volumes of 20 ml as a protective measure to reduce the likelihood of aspiration.

Although retention in the pyriform sinus was shown to be statistically significant in the bivariate analyses, it was not verified as a significant predictor after the logistic marginal regression. Despite the fact that the prevalence of pyriform sinus retention in subjects with PAS scores ≥ 3 was fourfold higher than in subjects with PAS < 3, we believe that the low occurrence of this symptom in our population reduced the statistical impact. Nevertheless, we highlight the importance of examining this parameter during VFSS because it appears to be associated with a similar risk of post-swallowing aspiration as that observed for retention in the vallecula and retention in the PET. The study of Michou *et al.* [29] supported this recommendation because they found an association between the residue in pyriform sinuses and the PA scores in PD patients.

Similarly, the start site of the pharyngeal phase was also shown to be significant only in bivariate analyses. A previous study [30] reported that the bolus position at the initiation of the pharyngeal stage does not by itself differentiate between normal and dysphagic swallowing in healthy elderly individuals. The bolus location at the beginning of the laryngeal elevation can also vary between various swallows in the same individual [30], suggesting that multiple factors influence the initiation of the pharyngeal phase. Although most of our patients who aspirated performed laryngeal elevation only when the food had reached the very low regions of the airway, we emphasize that this factor should be evaluated along with other potential risk factors for aspiration.

Although some authors have reported that PD patients with a history of aspiration pneumonia have longer swallowing durations [31], there has been a great deal of variability in the timing measures reported in these studies, and no clear patterns have been established [11]. Some of the variability likely results from differences in bolus volume, age, sex, barium density and methodologies, including whether the swallow is cued or uncued [11]. Steele and Cichero [15] have reported that the STD is a good measure for aspiration risk; these authors concluded that if a bolus is sitting in the pharynx while the airway is open, this increases the risk of aspiration. However, our study revealed no patterns in temporal measure variations between swallowing with or without tracheal aspiration. This outcome is most likely related to the small number of cases of aspiration in which OTT, STD and PTT were measured. The highest prevalence of aspiration was observed for the 20-ml volume, and because most patients fractionated this volume, the corresponding time intervals were not measured. Thus, it is difficult to interpret the importance of this finding because of the fact that the observed differences could have occurred by chance. Fractionation of the content was likely also the reason that we observed no differences between the aspiration status and the bolus volume.

Another point to be stressed is that thin and thick barium liquids elicited a higher frequency of aspiration than the other food consistencies. As to be expected, thin liquids are more dangerous in patients who exhibit a delay in triggering the pharyngeal swallow, impaired oral control or reduced airway protection during swallowing [2]. PD patients usually show motor disturbances, such as rigidity and bradykinesia of the oral and pharyngeal muscles, which prevents them from properly and safely swallowing thin liquids [22]. We would like to highlight the fact that the thick fluid that we observed to be aspirated was composed of pure barium and was not diluted like the other materials, a fact that could enhance some rheological characteristics leading to greater swallowing difficulties. Other authors have stressed that patients with reduced tongue strength may have more problems with thickened liquids because more viscous material requires the generation of greater tongue pressure [2, 32]. However, Logemann *et al.* [2] observed reduced aspiration of a nectar-like barium solution compared to a thin liquid, reporting that the greatest improvements occurred with honey-like materials. One limitation of our study is the fact that we did not have an exact measure of the viscosity of the fluids used in the VFSS evaluations, which makes it difficult to compare our results with those reported in other studies. Furthermore, the presence of piecemeal deglutition prevented a reliable analysis of the differences between the tested volumes. Although we found no statistically significant differences between frequency of aspiration and food volumes, the professional involved in evaluation and treatment of swallowing should be aware of a possible increased risk of aspiration with the increased bolus volume [33]. The absence of a reliability measure in SLP analysis are another limitation of our study.

In conclusion, our data show that piecemeal deglutition, retention in the vallecula and retention in the PET are all significantly associated with aspiration status in PD patients. Recognizing the factors associated with the tracheal aspiration of food is necessary to implement preventive measures and to identify the most effective therapeutic strategies. We

suggest that further studies expanding the parameters of swallowing should be performed to better understand the risk factors associated with the tracheal aspiration of food in the PD population.

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Table 1: Videofluoroscopic findings according to aspiration status.

Swallowing Abnormalities		Aspiration		
		Absent (%)	Present (%)	P-value
Bolus positioning	Closed	45.8	34.8	0.1861
	Open anterior-restricted	11.5	8.7	
	Open expanded	11.9	26.1	
	Prolonged	12.0	13.0	
	Unstable	18.7	17.4	
Loss of bolus to anterior sulci	Absent	88.3	87.0	0.2036
	Present	11.7	13.0	
Loss of bolus to lateral sulci	Absent	95.05	95.65	0.2915
	Present	4.95	4.35	
Loss of bolus to mouth floor	Absent	78.3	60.9	0.9715
	Present	21.7	39.1	
Posterior loss of bolus	Absent	68.8	60.9	0.4404
	Present	31.2	39.1	
Start site of the pharyngeal phase	Tongue base/vallecula	78.6	43.5	0.0081*
	PS/ AEF/ PET	21.4	56.5	
Multiple swallows	Absent	44.4	43.5	0.6698
	Present	55.6	56.5	
Piecemeal deglutition	Absent	76.9	39.1	0.0064*
	Present	23.1	60.9	
Retention on tongue	Absent/mild	95.20	91.30	0.376
	Moderate/severe	4.80	8.70	
Retention in vallecula	Absent/mild	80.96	30.4	0.0120*
	Moderate/severe	19.04	69.6	
Retention in PS	Absent/mild	93.7	73.9	0.0621*
	Moderate/severe	6.3	26.1	
Retention in AEF	Absent/mild	98.65	91.3	0.8080
	Moderate/severe	1.35	8.7	
Retention in PET	Absent/mild	95.35	69.6	0.0271*
	Moderate/severe	4.65	30.4	

PS: pyriform sinus, AEF: aryepiglottic fold, PET: pharyngoesophageal transition; * $P < 0.15$.

Table 2: Logistic marginal regression data of VFSS predictors.

Coefficients:	OR	95% CI	P-value
Retention in the vallecula	4.09	1.56 – 10.7	0.0040
Retention in the PET	2.87	1.33 – 6.17	0.0071
Piecemeal deglutition	3.83	1.73 – 8.5	0.0009

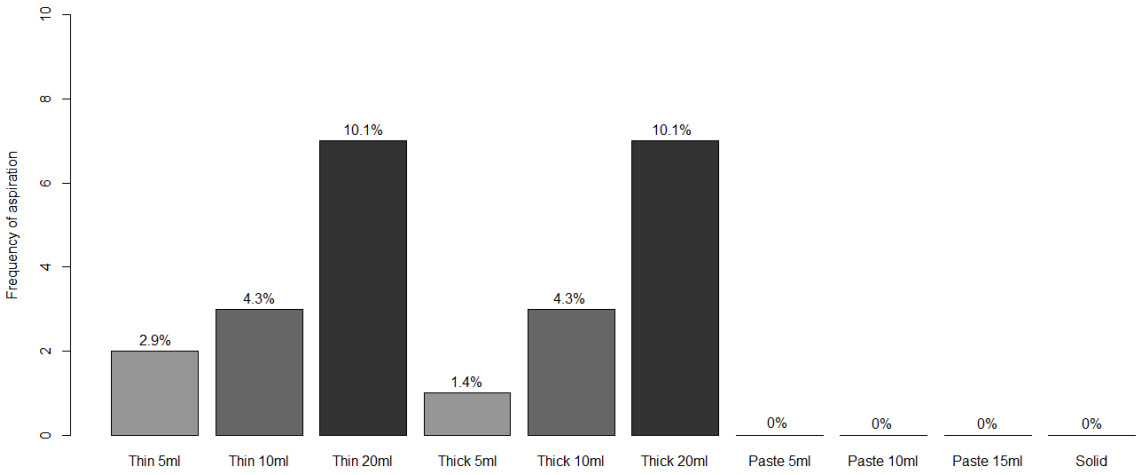
VSS: Videofluoroscopic swallowing study; PET: Pharyngo-esophageal transition; OR: Odds ratio; CI: Confidence interval

Table 3: Temporal measures according to consistency, volume and aspiration status analyzed by **log-linear and linear** marginal regression.

Cons/Vol	PAS≥ 3	N	OTT				STD				PTT			
			Mean	SD	**Exp(β)**	P-value	Mean	SD	**β**	P-value	Mean	SD	**Exp(β)**	P-value
Thin 5	No	67	1.706	1.428	1.19	0.660	0.754	1.627	-0.37	0.160	1.480	1.655	0.79	0.420
	Yes	2	2.025	1.525			0.384	0.354			1.170	0.614		
Thin 10	No	66	1.522	1.334	0.75	0.160	0.318	0.669	1.07	0.096	1.040	0.679	2.06	0.032*
	Yes	3	1.146	0.417			1.390	1.356			2.140	1.483		
Thick 5	No	68	2.166	1.698	0.43	<0.001*	0.900	1.433	0.50	0.004*	1.650	1.495	1.36	0.005*
	Yes	1	0.935	NA			1.401	NA			2.230	NA		
Thick 10	No	66	1.953	1.321	0.93	0.790	0.914	1.417	-0.60	0.010*	1.670	1.450	0.69	0.029*
	Yes	3	1.812	1.015			0.312	0.336			1.160	0.321		

Cons/Vol=Consistency/Volume; PAS=Penetration/aspiration scale; N=Number of individuals; OTT=Oral transit time; STD=Stage transition duration; PTT=Pharyngeal transit time.

Figure 1: Prevalence of aspiration according to food consistency and volume.



4.2 Artigo 2

Title Page

1. Title

Swallowing disorders in Parkinson's disease: impact of lingual pumping

2. **Running Head:** Lingual pumping in Parkinson's disease

3. **Key words:** Parkinson's disease, Deglutition disorders, Lingual pumping

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Abstract

Background: Lingual pumping (LP) is the repetitive movement of the tongue along the soft palate before the transfer or after the ejection of a food bolus. LP may be associated with rigidity and bradykinesia in patients with Parkinson's disease (PD). This phenomenon tends to be more prevalent in dysphagic PD patients, and its impact on swallowing dynamics remains poorly understood.

Objective: To evaluate how LP interferes with the oral and pharyngeal phases of the swallowing of foods of different consistencies and volumes.

Methods: We used videofluoroscopy to study the swallowing of 69 PD patients performing 10 deglutitions of barium mixed with foods of different consistencies and volumes.

Results: LP was associated with the unstable intra-oral organisation of the bolus, the loss of bolus control, the pharyngeal retention of food and food entering the airway. This abnormal movement was also associated with a shorter oral transit time and was found to be more prevalent with food of thicker consistencies.

Conclusion: LP is associated with uncoordinated swallowing and with food entering the airway. Preventive measures to minimise the pulmonary or nutritional consequences of this behaviour are necessary.

Introduction

Among the numerous motor and non-motor consequences of Parkinson's disease (PD), dysphagia is the primary cause of mortality in PD patients (Wang *et al.* 2002). Swallowing disorders associated with PD include anterior escape, premature loss of bolus, oral and pharyngeal retention, multiple swallows, laryngeal penetration and aspiration of food (Umemoto *et al.* 2010).

Lingual pumping (LP), also called festination of the tongue or lingual rocking, is a videofluoroscopic finding in approximately 75% of PD patients (Troche *et al.* 2007, Nóbrega *et al.* 2008). Ali *et al.* (1996) described LP as a repetitive, involuntary, anteroposterior movement of the tongue on the soft palate that is executed prior to transferring the food bolus to the pharynx, but we also observed LP when multiple swallows were taken (See video in the supplementary file online). This abnormal movement may be associated with rigidity and bradykinesia, but its underlying pathophysiological mechanisms remain unclear (Bushmann *et al.* 1989). Among PD patients, LP is most frequently observed in those with dysphagia and food aspiration (Ali *et al.* 1996, Nagaya *et al.* 1998). However, the effects of LP on swallowing dynamics remain poorly understood.

During the oral phase of normal swallowing, the tongue performs a series of stereotyped but not invariant movements in synergy with the jaw to move the food bolus posteriorly. During mastication, the tongue moves the bolus coordinately, placing the bolus on the teeth for chewing and lifting the bolus from the teeth as they close upon the bolus. The bolus is then mixed with saliva and replaced on the teeth using a repetitive rotary tongue movement until a manageable consistency is reached (Logemann 2007). In PD patients, the lingual movements are fewer and slower than normal, and several authors have described involuntary movements during swallowing in PD patients (Van Lieshout *et al.* 2011, Ali *et al.* 1996, Leopold and Kagel 1996).

We hypothesised that abnormal involuntary movements, such as LP, could alter the swallowing process and result in an uncoordinated intra-oral organisation of the bolus, which

could affect the pharyngeal phase of swallowing, resulting in post-swallowing residue and aspiration of food. Another hypothesis is that this incoordination could lead to increased oral and pharyngeal transit times due to the difficulty of initiating the swallow. In addition, food boluses of different consistencies and volumes that demand different lingual motor efforts to organise and eject could affect the occurrence of LP. Therefore, the aim of this study was to evaluate how LP interferes with the oral and pharyngeal phases of swallowing depending on the consistency and volume of food.

Methods

Patients

Consecutive idiopathic PD patients who presented at the Ambulatory Movement Disorders Clinic of the Federal University of Bahia were enrolled and subjected to a videofluoroscopic study of swallowing (VSS). PD diagnoses were made by a certified neurologist in accordance with the United Kingdom Parkinson's Disease Brain Bank (UKPDBB) guidelines (Gibb and Lees 1988). The exclusion criteria were as follows: the existence of other neurological diseases, psychiatric or cognitive disorders; head and neck cancer; and severe dysphagia (that prevents the completion of the exam with food samples of all consistencies and volumes). The majority of the patients included in this study took levodopa and were evaluated during the *"on"* state of medication.

This study was approved by the local ethics committee of Bahia, Brazil and was conducted according to the guidelines of the Helsinki declaration (1964). All patients signed an informed consent form before any procedure was conducted.

Assessments

For the VSS evaluations, the subjects were seated in a lateral position and instructed to eat 5, 10 and 20 ml of a suspension of thin fluid (barium mixed with water at a 1:1 ratio) and thick fluids (pure barium); 5, 10 and 15 ml of barium paste composed of barium mixed with Nestlé® natural yoghurt at a 2:1 ratio; and half of a biscuit dipped in barium (solid). These evaluations were performed using an edible radiopaque barium sulphate agent (Bariogel® 100%).

The following visuo-perceptual parameters of the VSS analyses were examined:

- The type of intra-oral bolus organisation, which was divided into closed (i.e., the bolus is positioned above the tongue dorsum), open anterior-restricted (i.e., the bolus is positioned anterior to the tongue), open expanded (i.e., the bolus is positioned anterior to and above the tongue), prolonged (i.e., the bolus is spread above the tongue from its tip to the soft palate) and unstable (i.e., the bolus exhibits an oscillating positioning with or without intra-oral food spill) (Yamada *et al.* 2004).
- The loss of bolus control, as determined by the occurrence of premature loss of bolus into the oral sulci or the pharynx before the onset of swallowing (Ali *et al.* 2006).
- Start site of the pharyngeal phase, defined as the location of the contrasted material when laryngeal elevation occurred (tongue base, valleculae, ariepiglotic fold, pyriform sinuses or pharyngo-oesophageal transition).
- Multiple swallows, defined as more than three hard swallows after posterior bolus propulsion.
- Piecemeal deglutition, in which the bolus was fractionated into many swallowing units.
- Retention on the tongue or in the pharyngeal recesses, in which the contrasted material remained in the valleculae or the pyriform sinuses, on the posterior

pharyngeal wall or in the pharyngo-oesophageal transition zone after the first swallow was performed.

- Food entering the airway, which was defined as the laryngeal penetration and/or aspiration of the contrasted material.

During the examination, when multiple swallows or piecemeal deglutition were observed, only the first swallow in the series was analysed for each bolus.

The temporal parameters included the oral transit time (OTT), which was defined as the period from the first anteroposterior movement of the tongue until the head of the bolus passed through the mandibular angle, and the pharyngeal transit time (PTT), which was defined as the period from when the bolus tail passed the mandibular angle until it passed through the cricopharyngeal region (Troche *et al.* 2007). OTTs of up to two seconds were considered to be normal, except in the case of solids, when OTTs as long as 18 seconds were considered normal to account for the mastication period. In all cases, a PTT longer than 1 second was considered to be abnormal (Logemann 2007).

Statistical Analyses

The data were analysed using R software, version 3.0.2 (R Core Team, Vienna, Austria). Descriptive values are presented as the mean ± standard deviation. Cochran-Mantel-Haenszel tests were used to evaluate the association between LP and the qualitative data for swallowing while controlling for food consistency and volume. Marginal logistic regression was performed for the following two analyses: the LP and food consistency and the LP and food volume. Subsequently, the results of the latter analysis were corrected via multiple comparisons using the Holm-Bonferroni method. The analysis between LP and OTT and PTT was performed using marginal log-linear regression.

Results

Of the 71 patients enrolled in this study, 69 completed the VSS protocol. Prior to the examinations, all patients had a history of ingesting food of all consistencies through their mouths without any restrictions or having to use an alternative pathway. During the VSS studies, two patients experienced severe aspiration of food of one or more consistencies, which prevented them from completing the examination with all of the food consistencies and volumes investigated in this study. These two patients were excluded from the study and were referred for speech therapy. The study population included 44 men and 25 women, and the mean age of the study participants was 63.36 ± 11.62 years. The mean disease duration was 7 ± 5.2 years, and the mean Hoehn & Yahr stage was 2.3 ± 0.9. Thirteen patients (18.84%) exhibited LP. The swallowing assessments of 69 patients resulted in 690 swallowing events (ten per patient), 52 (7.54%) of which involved LP.

Table 1 presents the associations between LP and swallowing abnormalities. The occurrence of LP was associated with the unstable positioning of the food bolus, the loss of bolus control with food spillage into the anterior sulci and the floor of the mouth, retention in the pharyngo-oesophageal transition zone and food entering the airway.

No association was observed between LP and lingual tremor ($P = 0.7151$).

With respect to the duration of deglutition, LP was associated with a shorter OTT (a mean value of 4.22 ± 6.85 milliseconds in PD patients without LP vs. a mean value of 2.47 ± 2.64 milliseconds in those with LP; $\text{Exp}(\beta) = 0.58$; $P = 0.0031$). However, no significant association between LP and PTT was detected (a mean value of 0.857 ± 0.911 milliseconds in PD patients without LP vs. a mean value of 1.005 ± 1.007 in patients with LP; $P = 0.545$).

When we investigated the occurrence of LP with respect to food consistency, we noted that the likelihood of LP increased with increases in food consistency. The thick fluid was associated with a 2.89-fold increase in LP when compared to the thin fluid ($P = 0.0297$), and

barium paste increased the incidence of LP 3.57-fold compared to the thin fluid, (P = 0.0088) (Figure 1). No significant differences in LP were observed between the paste material and the thick fluid, the solid food and the thin fluid, the solid food and the thick fluid and the solid and the paste material (P = 0.7483, 0.6789, 0.2491, and 0.2616, respectively).

Using marginal logistic regression analysis, no association was detected between the occurrence of LP and food volume. For thin fluids, the comparisons of LP between 5 and 10 ml, 5 and 20 ml and 10 and 20 ml yielded P - values of 1, 0.57 and 0.57, respectively. For thick fluids, these P - values were 1, 0.16 and 0.16, respectively. For food paste, the comparisons of LP between 5 and 10 ml, 5 and 15 ml and 10 and 15 ml yielded P - values of 0.71, 0.48 and 0.32, respectively. We did not perform this analysis with solid foods because only one volume using this consistency was tested.

Discussion

Our data reveal that LP is associated with swallowing incoordination during the oral phase, pharyngeal retention of food and food entering the airway. Our results also demonstrate that LP was more frequent with food of thicker consistencies.

According to our findings, LP increased the occurrence of unstable positioning of the bolus above the tongue prior to its propulsion to the pharynx. As a result, mostly intraoral leaks occurred, and food was ejected into the pharynx in an uncoordinated manner. Because LP interferes with the coordination of tongue movements for the correct propulsion of the bolus LP also increases bolus retention in the pharyngeal recesses after swallowing and can contribute to laryngeal penetration and/or aspiration of food in PD patients. Nagaya *et al*. (1998) performed VSS studies in PD patients and reported repetitive tongue pumping only in the group exhibiting aspiration. Our results thus confirm that LP can interfere with both the oral and

pharyngeal phases of swallowing, including the organisation of the bolus within the oral cavity, bolus ejection, and the mechanisms of airway protection.

Concerning the impact of LP on the duration of swallowing, the occurrence of LP was associated with lower OTTs in our study. This result may be explained by the accelerated motion of the tongue during this activity, which can result in more rapid but less coordinated deglutition. Troche *et al*. (2007) reported a positive correlation between the number of lingual pumps and OTT. In our study, we did not quantify the number of lingual pumps; our analysis consisted only of identifying whether each individual exhibited LP.

With respect to the relationship between LP and food consistency, Troche *et al*. (2007) observed a higher number of lingual pumps with thicker foods in PD patients, which is consistent with our results. The lack of resistance to the flow of thin liquids may reduce the extent of oral manipulation required, whereas more tongue movement may be required to move thicker liquids within the oral cavity, which could thus demand a larger amount of motor energy (Van Lieshout *et al.* 2008). Moreover, bradykinesia can cause a loss of motor energy and can predispose PD patients to the onset of LP when eating food of thicker consistencies (Hallett 2011).

Logemann *et al*. (2008) reported that reductions in the aspiration of thin liquids occurred most frequently with honey thick liquids followed by nectar thick liquids and highlighted the importance of managing the consistency of food to reduce the chance of aspiration in dysphagic patients. In our study, the occurrence of aspiration was also observed to be greater with thin liquids than with thick liquids and pastes. In contrast, the occurrence of LP exhibited the opposite trend, increasing in frequency as the consistency thickened. The strongest association between LP and aspiration occurred with the thick liquid consistency. However, it is important to emphasise the fact that the thick fluid material we used consisted of pure barium that was not diluted with water (as was the thin liquid) or mixed with yoghurt (as was the material of the

paste consistency), which could have led to more pronounced rheological characteristics, such as adhesion, and increased the difficulty of ejecting this substance.

One interesting finding of our study was the observed reduction in the occurrence of LP with solid foods. This result may be explained by the high levels of oral manipulation that mastication requires. In addition, the masticatory movements may require different types of motor control that may reduce the appearance of this abnormality. Hiiemae and Palmer (1999) have described the technique of food movement within the oral cavity during its processing as a "push-pull" system in which food is pushed backward using a "squeeze-back" mechanism and is intermittently pulled forward by the bodily movement of the tongue. This food-movement process, when associated with the constant contact between the tongue and hard palate, is likely to promote constant sensory input that affects motor performance.

Dantas *et al*. (1990) analysed the effects of bolus variables on the oral and pharyngeal phases of swallowing and reported that the magnitude of the anterior movement of the tongue base during swallowing increased linearly with increasing bolus volume. Although movements of larger amplitude can increase the extent of kinaesthetic feedback and larger food volumes can result in better sensory input, we hypothesised that increasing food volume would reduce the occurrence of LP (Van Lieshout *et al.* 2011). However, in our study, the 20-ml volume was offered in a cup, and most of the patients did not consume the entire 20 ml at once. Thus, we cannot determine the exact volume ingested, making such an analysis unfeasible.

It is interesting to note that most of our patients had PD with low Hoehn & Yahr staging, and it is possible that changes in the ability of patients to move their tongue may begin in the early stages of PD. Van Lieshout *et al*. (2011) also reported changes in the lingual movement abilities of PD patients during the early stages of disease, but further studies should be conducted to clarify the relationship between the severity of dysphagia and the severity of PD.

We also must stress that we observed lingual tremors in some patients, but the tremors were not associated with LP. Moreau *et al*. (2007) studied oral festination during orofacial diadochokinetic tasks and reported an association between oral festination and the festination of gait, but not with the freezing of gait or peripheral tremors. The authors concluded that oral festination shares the same pathophysiology as disorders of gait and that tremors and festination may arise through different mechanisms.

With respect to the management of LP, we did not find any studies that evaluated the effect of treatments on reducing LP. Furthermore, the effect of drugs or deep-brain stimulation (DBS) on LP remains poorly studied. Cantiniaux *et al*. (2014) reported that levodopa and DBS did not improve the velocity or the rhythm of speech. The reported effects of levodopa on swallowing are also inconsistent (Menezes and Melo 2009). Although there is a strong association between festination of gait and festination of speech, the relationships of these variables with LP during swallowing have not been established, and it is difficult to predict whether these interventions might alleviate LP in PD patients.

Understanding the neurophysiological mechanisms underlying LP is necessary to define the optimal therapeutic interventions to reduce this symptom. More studies investigating the effects of levodopa and DBS on LP are necessary to clarify the mechanisms involved in the neurological control of the tongue and swallowing in PD patients. In addition, studies of preventive measures, such as changing the consistency and/or volume of food or the adoption of tools that facilitate better organisation of the bolus, should also be conducted.

Because LP is associated with swallowing incoordination and food entering the airway, it may increase morbidity and mortality in PD patients. However, more studies are necessary to clarify the role of this repetitive tongue movement in swallowing and the mechanisms associated with its occurrence. Recognition of this alteration and its potential effects on the

morbidity of PD patients may lead to the elucidation of optimal treatments for LP in this population.

What this paper adds:

What is already known on this subject: Lingual pumping (LP) is a common finding in patients with Parkinson's disease, and it may be associated with dysphagia and aspiration. However, the impact of LP on swallowing dynamics remains poorly understood.

What this study adds: Our data demonstrate that LP is associated with swallowing incoordination during the oral phase, the pharyngeal retention of food and the occurrence of food entering the airway and that LP occurs more frequently with foods of thicker consistencies. The adoption of preventive measures, such as changing the consistency of food, may decrease the negative impact of LP, but additional studies of the management of LP in patients with Parkinson's disease should be performed.

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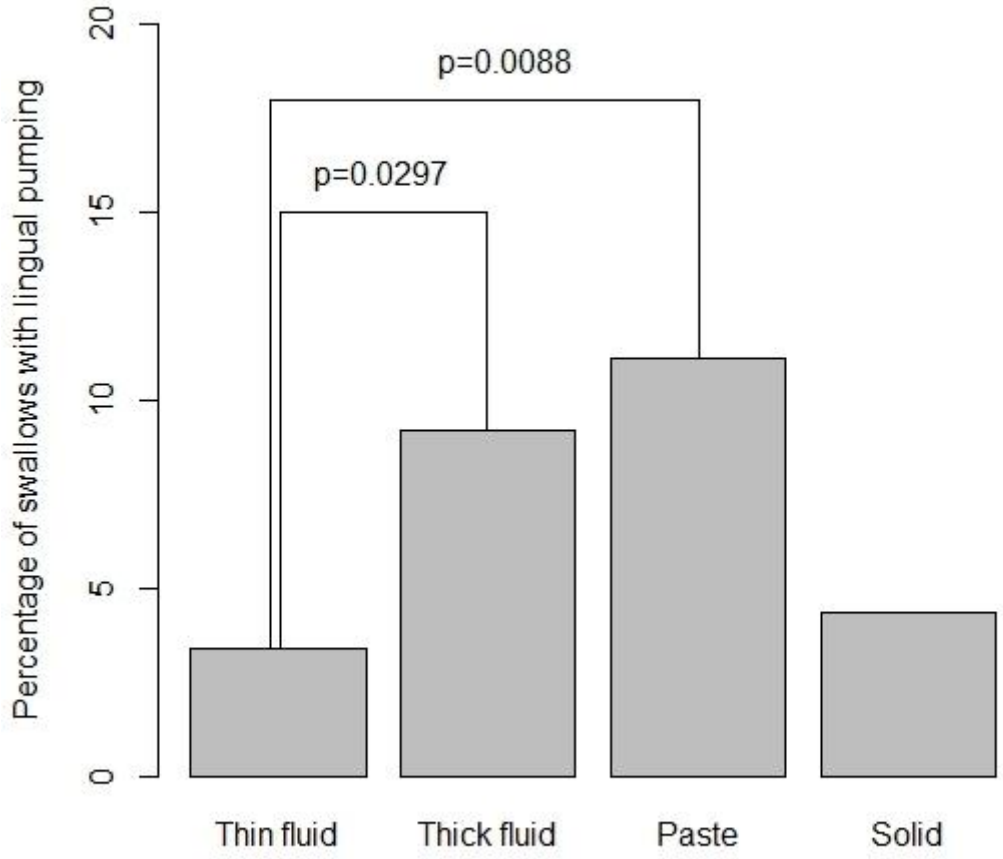
Table 1: Associations between lingual pumping and swallowing abnormalities.

Swallowing Abnormality		Lingual Pumping		
		Absent (%)	Present (%)	*P* - value
Type of intra-oral bolus organisation	Closed	47.20	24.49	0.0161*
	Open Anterior Restricted	11.71	8.16	
	Open Anterior Expanded	12.24	14.29	
	Prolonged	12.06	12.24	
	Unstable	16.78	40.82	
Loss of bolus to anterior sulci	Absent	89.50	73.08	0.0017*
	Present	10.50	26.92	
Loss of bolus to lateral sulci	Absent	95.45	90.38	0.1473
	Present	4.54	9.62	
Loss of bolus to mouth floor	Absent	79.00	61.54	0.0053*
	Present	21.00	38.43	
Posterior loss of bolus	Absent	69.94	57.69	0.0936
	Present	30.56	42.30	
Start site of the pharyngeal phase	Tongue Base/Valleculae	77.90	71.15	0.2186
	AEF/ PS/ PET	22.10	28.85	
Multiple swallows	Absent	44.98	36.54	0.4378
	Present	55.02	63.46	
Piecemeal deglutition	Absent	76.18	69.23	0.2188
	Present	23.82	30.77	
Retention on tongue	Absent	95.14	94.23	0.8608
	Present	04.86	05.77	
Retention in vallecula	Absent	79.62	75.00	0.8958
	Present	20.38	25.00	
Retention in PS	Absent	93.57	86.54	0.2043
	Present	06.43	13.46	
Retention in AEF	Absent	98.59	96.15	0.5268
	Present	01.41	03.85	
Retention in PET	Absent	95.61	80.77	0.0001*
	Present	04.39	19.23	
Food entering the airway	Absent	95.14	88.46	0.0287*
	Present	4.86	11.54	

AEF: aryepiglottic fold, PS: pyriform sinus, PET: pharyngo-oesophageal transition; * significant statistical difference ($P < 0.05$).

Figure 1: Percentage of swallows involving lingual pumping according to the consistency of the food analysed by logistic marginal regression correted by Holm-Bonferroni method.



5.0 Conclusões

- Os eventos da dinâmica orofaríngea da deglutição relativos a retenção de alimento em valécula e em transição faringo-esofágica, além de deglutição fracionada estão associados à aspiração na DP. O reconhecimento desses fatores faz-se necessário para implementar medidas preventivas e auxiliar na escolha da melhor conduta terapêutica nestes pacientes.

- A presença de festinação lingual na DP está associada à incoordenação durante a fase oral, retenção em recessos faríngeos e entrada de alimento em via aérea. Devido ao impacto sobre a aspiração de alimento, fazem-se necessários estudos sobre o manejo da festinação nos indivíduos com DP.

- Com relação ao papel da consistência alimentar, verificamos que a festinação lingual é mais frequente em consistências alimentares mais espessas como a pastosa, enquanto a aspiração traqueal é mais comum nas consistências mais fluidas, como líquida e semilíquida. Quanto ao volume, provavelmente devido ao fato de a maioria dos pacientes ter fracionado o volume de 20ml, não foi possível verificar associação entre aspiração traqueal e os volumes testados. A maior prevalência de aspiração nas consistências mais fluidas alerta para a necessidade na implementação de medidas preventivas e compensatórias como a modificação da consistência dos alimentos da dieta dos indivíduos com DP.

6.0 Considerações Finais

O estudo realizado deu origem a dois artigos que relatam como as alterações da dinâmica da deglutição visualizadas através videofluoroscopia da deglutição podem estar associadas à aspiração de alimentos nas diferentes consistências e volumes testados na DP. Estas associações são importantes para a análise dos mecanismos que levam à disfagia na DP e permitem aos fonoaudiólogos uma identificação precoce da aspiração nestes pacientes.

Frente ao impacto da aspiração sobre a morbi-mortalidade nesta população e ao conhecimento de que o indivíduo com DP queixa-se pouco do seu distúrbio de deglutição, a identificação de preditores para a aspiração reveste-se de especial interesse. Além disso, a identificação da festinação lingual e suas associações com os eventos da dinâmica orofaríngea possibilita o direcionamento de estudos sobre o adequado manejo desta alteração.

No que diz respeito à relação entre os eventos da dinâmica da deglutição e as consistências e volumes testados, o principal achado diz respeito à maior prevalência de aspiração nas consistências mais fluidas possibilitando a adoção de medidas compensatórias. Entretanto, a limitação quanto à falta da medida de viscosidade dos alimentos utilizados na videofluoroscopia de deglutição dificulta a comparação dos nossos achados com os relatos prévios na literatura. Outra limitação diz respeito à dificuldade em ofertar os volumes alimentares de uma vez, ocorrendo o fracionamento do conteúdo testado. Este fracionamento dificultou a comparação adequada entre os volumes alimentares e os eventos da dinâmica da deglutição orofaríngea. Outros métodos para oferta do alimento visando maior controle do volume ofertado estão sendo estudados visando reduzir esta limitação.

7.0 Perspectivas de Estudos

Dentro da linha de pesquisa relacionada aos fatores associados à disfagia orofaríngea na doença de Parkinson realizaremos um estudo descritivo comparando os eventos da dinâmica da deglutição entre indivíduos com DP e controles saudáveis.

Após essa análise, verificaremos a associação da consistência e volume alimentar com as outras alterações da dinâmica da deglutição, não abordadas nesta tese.

Além disso, dados clínicos e demográficos serão analisados quanto à sua associação com a disfagia orofaríngea. Para isso, a ampliação do banco de dados da videofluoroscopia de deglutição está sendo realizada visando um maior número de pacientes com um espectro mais amplo de gravidade da DP e gravidade da disfagia, possibilitando a identificação de diferenças entre os grupos com e sem disfagia/aspiração.

8.0 Anexos

8.1 Anexo 1 – Parecer do Comitê de Ética em Pesquisa

8.2 Anexo 2 – Penetration/aspiration Scale

8.3 Anexo 3 – Artigo publicado em formato de “Carta ao Editor” a respeito da relação entre disfagia e gênero na doença de Parkinson

8.1 Anexo 1 – Parecer do Comitê de Ética em Pesquisa

SECRETARIA DA SAÚDE DO ESTADO DA BAHIA - SESAB

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Fatores associados à disfagia orofaríngea na doença de Parkinson
Pesquisador: NATALIE ARGOLO PEREIRA PONTE
Área Temática:
Versão: 1
CAAE: 01534312.5.0000.0052
Instituição Proponente:

DADOS DO PARECER

Número do Parecer: 122.450
Data da Relatoria: 13/09/2012

Apresentação do Projeto:
Trata-se de uma pesquisa acerca fatores associados a alterações de deglutição na doença de Parkinson (DP). Esta doença foi descrita em 1817 como uma desordem motora caracterizada por bradicinesia, tremor de repouso e rigidez. Na sua descrição, James Parkinson já incluia a disfagia relatando dificuldade em iniciar a deglutição, em manter saliva e comida na cavidade oral e diminuição na mobilidade de língua1. Atualmente, sintomas não motores também têm sido descritos como depressão, demência e problemas olfatórios.Na doença de parkinson, a disfagia orofaríngea é bastante prevalente, podendo chegar a 100% dos indivíduos. Entretanto, apenas uma pequena parte destes indivíduos percebe suas alterações na deglutição. O reconhecimento deste sintoma torna-se ainda mais difícil pois a literatura é controversa quanto à relação entre presença da disfagia e gravidade da doença de Parkinson. As alterações estão presentes em todas
as fases da deglutição e os fatores envolvidos neste processo ainda não são completamente compreendidos.

Objetivo da Pesquisa:
Objetivo primário:
- Identificar os fatores associados à disfagia orofaríngea na doença de Parkinson.

Objetivo Secundário:
- Caracterizar as alterações de deglutição nos indivíduos com doença de Parkinson comparado

Endereço: R. Conselheiro Pedro Luiz, 171
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UF: BA **Município:** SALVADOR
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com controles sadios;

Avaliação dos Riscos e Benefícios:

Riscos:

Trata-se de estudo com dados secundários. Não trará riscos aos pacientes.

Benefícios:

Trata-se de um estudo com dados secundários. O estudo poderá responder quais fatores estão associados à presença de disfagia orofaríngea na
doença de Parkinson e sinalizar possíveis meios de minimizar estes fatores.

Comentários e Considerações sobre a Pesquisa:

Não há duvida quanto à relevância deste estudo, principalmente considerando a possibilidade de incentivo ao diagnóstico precoce da doença de Parkinson.

Considerações sobre os Termos de apresentação obrigatória:

Todos os termos de apresentação foram anexados

Recomendações:

Nada digno de nota

Conclusões ou Pendências e Lista de Inadequações:

Por tratar-se de um estudo desenvolvido a partir de dados secundários, este não representa riscos para os sujeitos. Assim, este estudo utilizará os dados demográficos e os resultados dos exames de deglutição de pacientes de dois estudos primários. Um deles avaliou pacientes com doença de Parkinson: Validação de dois instrumentos de avaliação da deglutição para indivíduos com doença de Parkinson, foi aprovado pelo Comitê de Ética em Pesquisa da Maternidade Climério de Oliveira da Universidade Federal da Bahia sob o número 113/2008. O outro avaliou indivíduos saudáveis para um estudo sobre Preditores clínicos para a doença de Parkinson, também já aprovado pelo comitê de ética e em fase de coleta de dados. Todos os dados demográficos e de deglutição já estão em banco de dados.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

SECRETARIA DA SAÚDE DO
ESTADO DA BAHIA - SESAB

SALVADOR, 16 de Outubro de 2012

Assinador por:
CARLOS ALBERTO LIMA DA SILVA
(Coordenador)

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8.2 Anexo 2 – Penetration/Aspiration Scale

8-Point Penetration-Aspiration Scale

Score	Description of Events
1.	Material does not enter airway
2.	Material enters the airway, remains above the vocal folds, and is ejected from the airway.
3.	Material enters the airway, remains above the vocal folds, and is not ejected from the airway.
4	Material enters the airway, contacts the vocal folds, and is ejected from the airway.
5.	Material enters the airway, contacts the vocal folds, and is not ejected from the airway.
6.	Material enters the ariway, passes below the vocal folds, and is ejected into the larynx or out of the airway.
7.	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort.
8.	Material enters the airway, passes below the vocal folds, and no effort is made to eject.

Fonte: Rosenbek, JC, Robbins, J, Roecker EV, Coyle, JL, & Woods, JL. A Penetration-Aspiration Scale. Dysphagia 11:93-98, 1996

8.3 Anexo 3 – Artigo publicado "Dysphagia complaint and gender in Parkinson's disease"

European Journal of Neurology 2013, 20: e42 doi:10.1111/ene.12029

LETTER TO THE EDITOR

Dysphagia complaint and gender in Parkinson's disease

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Keywords: dysphagia, gender, Parkinson's disease

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In issue 1 of the current volume, Perez-Lloret *et al.* [1] report the prevalence of oral-bucal symptoms in patients with Parkinson's disease (PD) from a French cohort (COPARK). These symptoms were defined as UPDRS items 5, 6 and 7 ≥ 1. The results showed presence of dysarthria, sialorrhea and dysphagia in 51%, 37% and 18% of the 419 participants, respectively.

They recognize the fragility of UPDRS as a measurement tool of oral-buccal symptoms. This is a subjective scale that is not validated for these symptoms. Nevertheless, we would like to stress the difficulty of patients with PD patients in perceiving their symptoms, particularly those related to swallowing disorders.

Although dysphagia is present in most patients with PD, only a few complain about it [2]. Rodrigues *et al.* [3] have found decreased sensitivity in the larynx and pharynx in this population, with silent episodes of laryngeal penetration an aspiration of saliva, which may be related with the reduction in perceiving swallowing disorders. Therefore, it is likely that the prevalence of dysphagia of the COPARK study has been underestimated.

Perez-Lloret *et al.* also found that dysphagia was associated to female gender, depressive symptoms and motor fluctuations, but they have no plausible explanation of this result. Previous study reports a higher prevalence of depressive symptoms in women with PD [4]. Women usually also tend to report poorer general health status and more chronic limitations of activity than men [5]. Thus, this group of patients may be more able to perceive and report about their emotional and physical disorders.

Despite these hypotheses, much still needs to be studied both about the influence of gender on perceptions of the disease and a higher prevalence of depressive symptoms, especially in PD, to determine how they may affect the ability of the patient to complain about their swallowing disorders. In the same way, it is necessary to investigate the role of decreased sensitivity in the reduction of swallowing complaints. The accurate identification of swallowing disorders in these patients could help to prevent episodes of tracheal aspiration, a risk factor for respiratory infection and death in PD [6].

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