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Decreased Cough Sensitivity and Aspiration in Parkinson Disease

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BACKGROUND: Aspiration pneumonia is a leading cause of death in people with Parkinson disease (PD). The pathogenesis of these infections is largely attributed to the presence of dysphagia with silent aspiration or aspiration without an appropriate cough response. The goal of this study was to test reflex cough thresholds and associated urge-to-cough (UTC) ratings in participants with PD with and without dysphagia.

METHODS: Twenty participants with PD were recruited for this study. They completed a capsaicin challenge with three randomized blocks of 0, 50, 100, and 200 μM capsaicin and rated their UTC by modified Borg scale. The concentration of capsaicin that elicited a two-cough response, total number of coughs, and sensitivity of the participant to the cough stimulus (UTC) were measured. The dysphagia severity of participants with PD was identified with the penetration-aspiration scale.

RESULTS: Most participants with PD did not have a consistent two-cough response to 200 μM capsaicin. UTC ratings and total number of coughs produced at 200 μM capsaicin were significantly influenced by dysphagia severity but not by general PD severity, age, or disease duration. Increasing levels of dysphagia severity resulted in significantly blunted cough sensitivity (UTC).

CONCLUSIONS: UTC ratings may be important in understanding the mechanism underlying morbidity related to aspiration pneumonia in people with PD and dysphagia. Further understanding of decreased UTC in people with PD and dysphagia will be essential for the development of strategies and treatments to address airway protection deficits in this population.

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ABBREVIATIONS: Cr2 = two-cough response; Cr5 = five-cough response; CrTot = total number of coughs produced in response to 200 μM capsaicin; H&Y = Hoehn and Yahr; P-A = penetration-aspiration scale; PD = Parkinson disease; UTC = urge to cough

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Aspiration pneumonia is a leading cause of death in people with idiopathic Parkinson disease (PD).[1-3] Although the pathogenesis of these infections is largely attributed to the presence of silent aspiration (aspiration without a reflex cough response), we know relatively little about reflex cough in PD. One important aspect of reflex cough is the urge to cough (UTC), a respiratory sensation that precedes the reflex cough. The UTC for induced reflex cough increases in a log-log linear fashion with increasing magnitude of a cough (tussigenic) stimulus.[4-7] People with a history of aspiration pneumonia have comparable reflex cough thresholds to age-matched control subjects but demonstrate a blunted UTC at subthreshold levels of a tussigenic stimulus.[8]

Although the literature suggests that both dysphagia and dystussia coexist in PD,[9,10] few studies have tested reflex cough in PD,[11-13] and no studies have examined the relationship of reflex cough responses to swallowing ability. Leow and colleagues[13] observed that the cough sensory threshold was not different for people with PD vs age-matched control subjects; however, Fontana et al[11] found slightly higher thresholds for people with PD. Neither of these studies included a metric for UTC or account for the influence of swallowing function on reflex cough outcomes. The goal of the present study was to test reflex cough thresholds and UTC ratings in participants with PD with and without dysphagia. We hypothesized that worsening dysphagia severity would result in significantly higher cough thresholds and reduced UTC ratings.

Materials and Methods

This prospective study included 20 participants with mild to moderate PD. Participants were recruited from the University of Florida Center for Movement Disorders and Neurorestoration by consecutive referral to speech-language pathology over a 3-month period. Fellowship-trained movement disorders neurologists diagnosed PD using UK brain bank criteria.[14] This study received ethical approval by the University of Florida Institutional Review Board (188-2012). All participants provided written informed consent prior to the initiation of any study procedures. They were tested within the window of optimized medication function (ie, 1 h after taking anti-PD medications). Inclusion criteria were (1) diagnosis of idiopathic PD, (2) Hoehn and Yahr (H&Y) stages II to IV, and (3) age 45 to 85 years. Exclusion criteria were (1) history of other neurologic disorders; (2) history of head, neck, or lung cancer; (3) history of chronic respiratory disorders/diseases; (4) smoking in the past 5 years; (5) uncontrolled hypertension; (6) mini-mental status examination score of at least 24; and (7) failed pulmonary function screening test (ie, $FEV_1/FVC < 75\%$).

Cough Testing

Participants were outfitted with a face mask covering the nose and mouth. The face mask was coupled to a pneumotachograph and differential pressure transducer and had a side port with a one-way inspiratory valve for nebulizer connection. The nebulizer was a DeVilbiss T-piece (DeVilbiss Healthcare LLC) connected to a dosimeter that delivered an aerosolized solution during inspiration (delivery duration, 2 s). Participants completed a capsaicin challenge with three randomized blocks of 0, 50, 100, and 200 μM capsaicin. The capsaicin was dissolved in a vehicle solution of 80% physiologic saline and 20% ethanol. The maximum concentration of 200 μM has been identified as a suprathreshold concentration for eliciting the reflex cough in healthy participants.[15-17] The cough airflow signal was recorded by a laptop computer through the PowerLab data acquisition system (ADInstruments Pty Ltd).

Participants were seated comfortably for an initial 30 s of quiet breathing to acclimate to the face mask. They were given the instruction, "Cough if you need to," prior to capsaicin delivery. The solution was automatically administered upon detection of an inspired breath, with a minimum of 1 min between each presentation of capsaicin during which time participants were provided water.

Swallow Testing

Swallowing was assessed by a certified speech-language pathologist. Participants were positioned in the lateral viewing plane while sitting in a chair and self-administered a 3-oz thin-liquid challenge bolus of barium sulfate contrast solution. Images were acquired with a Siemens radiographic/fluoroscopic unit (Siemens Corporation) and recorded at 30 frames/s. The selected swallowing outcome measure was quantified with the penetration-aspiration scale (P-A),[18] a valid and ordinal eight-point assessment.

Outcome Measures

Cough Threshold: Total number of coughs produced in response to 200 μM capsaicin (CrTot) was counted from the first cough epoch (defined as an initial cough and the subsequent cough reaccelerations following one inspiration) with each presentation of capsaicin. These measures were made from the recorded cough airflow signals. The concentration of capsaicin that elicited the reliable two-cough response (Cr2) was recorded and identified as the cough threshold. A reliable Cr2 was defined as at least two coughs produced within 30 s following presentation of the stimulus in two of three trials of that concentration.

Urge to Cough: Following each capsaicin trial, participants rated their UTC on a modified Borg rating scale of 0 to 10, where 0 was no UTC and 10 was maximal UTC. The median UTC ratings were plotted against capsaicin concentration on a log-log scale, and a linear regression line was used to fit the data. The slope of the line was used as a measure of UTC sensitivity to capsaicin and was compared in participants with and without (P-A score ≤ 2) dysphagia.

Statistical Analysis

Descriptive statistics were used to summarize the data. Spearman ρ correlations and regression analyses were used to assess the influence of PD severity (H&Y score), age, sex, disease duration, and dysphagia severity (P-A score) on UTC and CrTot. Sex, H&Y score, disease duration, and age were entered into the first step of the stepwise hierarchical regression model, with UTC or CrTot as the dependent variables. P-A score was entered in the second step to assess its contribution to the dependent variables above and beyond other person- and PD-specific factors. Differences in age and disease severity between participants with and without dysphagia were compared by Mann-Whitney *U* tests. The significance criterion was set at $P < .05$.