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ORIGINAL ARTICLE

Dual Tasking Influences Cough Reflex Outcomes in Adults with Parkinson's Disease: A Controlled Study

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Abstract

Coughing is an essential airway protective reflex. In healthy young adults, cough somatosensation changes when attention is divided (dual tasking). Whether the same is true in populations at risk of aspiration remains unknown. We present findings from a controlled study testing the effects of divided attention (via a dual-task paradigm) on measures of reflex cough in Parkinson's disease. Volunteers with Parkinson's disease ($n = 14$, age = 43–79 years) and 14 age-matched controls underwent five blocks of capsaicin-induced cough challenges. Within each block, capsaicin ranging from 0 to 200 µM was presented in a randomized order. Two blocks consisted of cough testing only (single task), and two blocks consisted of cough testing with simultaneous tone counting (dual task). Finally, participants completed a suppressed cough task. Measures of cough motor response, self-reported urge to cough, cough frequency, and cough airflow were collected. Historical data from healthy young adults was included for comparison. Between-group analyses revealed no differences between single- and dual-cough-task responses. However, *post hoc* analysis revealed a significant relationship between dual-task errors and cough frequency that was strongest in people with Parkinson's disease [$p = 0.004$, $r^2 = 0.52$]. Specifically, greater errors were associated with fewer reflexive coughs. Unlike healthy participants, participants with Parkinson's disease did not change the number of coughs between the single-, dual-, and suppressed-task conditions [$p > 0.05$]. When distracted, people with Parkinson's disease may prioritize coughing differently than healthy controls. Abnormal cortical resource allocation may be a mechanism involved in aspiration in this population.

Keywords Cough · Parkinson's disease · Dual task · Dystussia · Cough reflex

Introduction

Dysphagia (difficulty swallowing) and dystussia (a blunted coughing sensory/motor response) are serious disorders that can lead to the aspiration of oropharyngeal contents into the airway during eating and drinking. If aspirate is not removed with an effective cough, infection (aspiration pneumonia) may result. Aspiration pneumonia is a leading cause of death in people with neurodegenerative disease, such as Parkinson's disease [1, 2], and is associated with significant deteriorations in health and quality of life [2–4]. Despite this, there is an incomplete understanding of the mechanisms influencing airway protective dysfunction in people with Parkinson's disease (PWPD). For example, airway protective deficits appear to be exacerbated when Parkinson's disease is accompanied by cognitive decline [5, 6]. However, few studies have empirically explored the effects of cognition on swallowing function [7, 8] in this population, and none have explored the effects of cognition on cough.

Understanding the relationship between cognition and airway protection is important, considering how airway protection takes place in everyday contexts. Sipping coffee while driving, eating popcorn and watching a movie, or holding a conversation during a meal are all examples of the myriad ways in which airway protection occurs as a dual task in everyday life. Although reducing distractions during mealtimes is a common clinical recommendation

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given to PWPD, the rationale for this is poorly defined, and clinical evaluations of swallowing and coughing rarely involve distraction or competing attentional demands.

It has been well established in the limb literature that PWPD experience dual-task interference, whether the secondary task be motor (e.g., coin transference) or cognitive (e.g., digit subtraction) [9–11]. Current theory suggests that, during single tasking, PWPD compensate for faulty basal ganglia circuitry by engaging cortical regions to drive motor outputs [12, 13]. During dual tasking, the secondary task engages cortical resources and prevents these from being used for the primary task, leaving the defective basal ganglia to regulate performance of the primary task [10]. More recent work has also implicated the cerebellum, suggesting that PWPD may have a reduced capacity to access cerebellar resources to augment dual-task performance [14]. This usually results in observable errors such as gait variability, gait slowing, or falling. Whether or not these findings extend to airway protective behaviors remains largely unknown.

With Parkinson's disease progression, symptoms of dysphagia often emerge [15, 16]. Symptoms may include prolonged mastication, difficulty manipulating the bolus, difficulty initiating swallowing [17], reduced swallowing frequency (leading to sialorrhea [18]), and coughing or choking due to the aspiration of oropharyngeal contents [19, 20]. To date, only a single report by Troche et al. [8] has described the effects of dual-tasking on swallowing safety and timing in PWPD. The authors reported that measures of swallowing timing were significantly shorter during dual tasking. In terms of swallowing safety (penetration and aspiration), participants with the greatest impairments in the domains of cognitive flexibility and attention improved swallowing safety during dual tasking, while participants with mild cognitive impairments demonstrated worsening swallowing safety during the dual task.

Regarding cough, a small body of literature in healthy subjects supports a strong relationship between attentional focus and cough output. Janssens et al. [21] instructed participants to focus inwardly on cough sensations or outwardly on an auditory stimulus during cough reflex testing. The number of coughs and participants' self-reported urge to cough (UTC) were found to be greater during internal attentional focus, suggesting that the reflexive cough response can be modulated by manipulating attentional focus. Our research group recently demonstrated that participants coughed fewer times, required stronger cough-inducing stimuli to trigger a cough, and rated the UTC as lower when cough was elicited under a dual-task condition, compared to a single-task condition [22]. The combined findings of Janssens et al. [21] and Perry and Troche [22] add to the small body of literature emphasizing the role of cortical modulation of the cough reflex [21, 23, 24].

Despite the potential deleterious effects of dual tasking on cough execution, it is clear that healthy individuals can overcome the competing attentional demands and avoid constant airway invasion. For PWPD, the presence of concomitant cortical, subcortical, cerebellar, and brainstem changes, in addition to reduced respiratory function, mobility, and increased age, may make these same adaptions more difficult. Understanding the influence of dual tasking on cough behavior in PWPD is critical to informing the most valid methods for evaluating airway protection, and may reveal new avenues for the rehabilitation of cough dysfunction in PWPD by better defining the underlying mechanisms for dysfunction.

The goal of this study was to expand on our previous work [22] by investigating whether performing concurrent attention and coughing tasks (via a dual-task paradigm) would affect measures of reflex cough in adults with PD, compared to healthy controls. We had three main research questions: (1) what was the effect of age on dual-task cough response? (2) what was the effect of PD on dual-task cough response? (3) how would dual-task cough performance relate to volitional control of coughing? We hypothesized that performing concurrent attention and coughing tasks would change cough airflow patterns and the perception of cough-inducing stimuli compared to performing those tasks in isolation, with a greater effect on older participants compared to younger participants, as well as a greater effect in PWPD compared to healthy controls. Finally, given the unique involvement of cortical areas during cough suppression, we hypothesized that a suppressed coughing condition would show unique patterns of cough airflow and sensory response compared to a dual-task condition.

Methods

To answer our research questions, 14 people with idiopathic PD and 14 healthy adults were prospectively recruited. Historical data from 27 healthy young adults [22] were also included for age comparisons. All participants provided written consent prior to taking part in study procedures. Ethical approval was received by a local institutional review board (Teachers College, Columbia University Institutional Review Board #17-137). All testing procedures were completed by one examiner (S.P.). One HOA and one PWPD could not tolerate cough reflex testing; these participants discontinued the study and were replaced. One HOA discontinued the study due to unplanned surgery and was replaced.

Participant Demographics

Participants with PD were consecutively recruited from local neurology clinics and support groups. Healthy control

Table 1 Participant demographics

Participant number	Group						
	Parkinson's disease			Healthy older adults		Healthy young adults	
	Age	Sex	Disease duration (years)	Age	Sex	Age	Sex
1	60	F	8	65	M	24	F
2	79	M	9	60	F	23	F
3	69	M	4	77	F	23	F
4	75	M	8	67	M	29	F
5	68	M	14	40	F	25	F
6	59	M	15	77	F	23	F
7	71	M	8	73	M	23	F
8	43	F	9	60	F	23	F
9	61	M	3	68	F	35	F
10	70	M	11	70	M	24	F
11	71	F	3	77	M	26	F
12	71	M	17	70	M	29	M
13	64	F	18	69	M	23	F
14	74	F	5	65	M	23	F
15						33	F
16						24	F
17						22	F
18						21	F
19						22	F
20						25	F
21						25	F
22						30	F
23						23	F
24						23	F
25						23	F
26						31	F
27						30	F
Mean	66		9	66		25	
SD	9		5	10		4	
Total		M = 8 F = 6			M = 8 F = 6		M = 1 F = 26

SD standard deviation

subjects were recruited from a local research participation website, a local university, or were caregivers/relatives of participants with PD who volunteered to take part. Demographic information is listed in Table 1. Exclusionary criteria were (1) neurogenic disease (healthy controls) or neurogenic disease other than PD, (2) history of head and neck cancer, (3) respiratory disease, (4) smoking in the last 5 years, (5) uncontrolled hypertension, (6) neuropsychological dysfunction, i.e., severe depression (defined as a score ≥ 31 on Beck's Depression Inventory [25]) or dementia (defined as a score of > 20 on the Montreal Cognitive Assessment (MoCA [26, 27]), (7) hearing impairment (defined as inability to detect sounds of 40 dBA at 500 and 1000 Hz), (8) chest infection or common cold within the last 4 weeks, (9) chronic cough disorder, (10) use of cough medication or painkillers containing codeine in the previous 24 h, (11) central auditory processing disorder, and (12) learning disability per self-report.

Baseline Cognitive-Affective Screening

Participants underwent cognitive-emotional assessment to screen for exclusion criteria and to measure performance on various cognitive parameters important for dual tasking, including selective attention capacity, visual attention, task switching, and working memory. Assessments included the MoCA (general cognition) [26], Stroop color-word interference task (selective attention) [28], Adaptive Digit Ordering Test (working memory) [29], Trail Making Test (visual attention and task switching) [30], and the Beck Depression Inventory (depression/arousal) [25].

Procedures

Data collection took place on two separate days. Participants were counterbalanced to undergo either single tasking (attention task, cough task) on day one and dual tasking (concomitant attention + cough task) on day two, or dual tasking on day one, followed by single tasking on day two. The single and dual tasks are described below.

Attention Task

Audio clips containing repetitions of a 500 Hz tone with a 571.4 Hz distractor tone were selected from the Elevator Counting with Distraction subtest of the Test of Everyday Attention (Pearson International, London, UK; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996). Each clip contained between three and 14 repetitions. Participants were seated in a comfortable chair and fitted with headphones. Written instructions were provided on a computer monitor. Participants were presented with the tones and instructed to "count the number of low tones and ignore any high tones." Participants completed two practice trials. If 100% accuracy was not achieved on the practice trials, these trials were repeated until 100% accuracy was achieved. Participants then undertook ten tone-counting trials. The number of low tones during the counting trials was reported aloud and recorded for offline analysis.

Cough Single Task

Cough reflex testing was carried out using a DeVilbiss T-piece (DeVilbiss Healthcare, Port Washington, New York, USA) nebulizer connected to a dosimeter (Koko Dosimeter, nSpire Health, Longmont, CO, USA) that delivered aerolized capsaicin solution upon manual discharge, for two seconds. Participants were fitted with a facemask covering the nose and mouth. The facemask was coupled to a pneumotachograph (MLT 1000, ADInstruments, Inc.), differential pressure transducer (Validyne MP45), and side delivery port with a valve for nebulizer connection. Cough was induced during a single-breath inhalation of capsaicin solution. Capsaicin was dissolved in a vehicle solution consisting of 80% saline and 20% ethanol and prepared at five different concentrations: 0, 10, 25, 50, 100, and 200 µM that have been previously found to trigger a UTC and/or a reflexive cough in healthy adults [31–34]. Each capsaicin concentration was presented twice in a randomized block order, with a one-minute interval between presentations. Participants were instructed to "breathe through your mouth and cough if you need to." Following each presentation, participants rated their UTC and took a sip of water. Self-reported UTC was measured using a modified Borg scale labeled from 0 ("none at all") to 10 ("very, very, very severe") [35]. Cough airflow signals were digitized and recorded to a desktop computer via PowerLab Data Acquisition System (ADInstruments) for offline analysis. Prior to cough data collection, the integrated pneumotachograph signal was calibrated for volume and for flow by injecting a known volume (3 L) of air through the experimental set-up. Flow (F) was then calculated from the slope (rate of change) of the volume curve (V) using the formula:

$$F = \frac{\mathrm{d}V}{\mathrm{d}t}.$$

Dual Task: Cough + Attention Tasks

For the dual-task paradigm, participants were fitted with headphones and a facemask coupled to a pneumotachograph. Participants completed the tone-counting task and cough reflex test at the same time, with the instruction: "count the number of low tones and ignore any high tones. Cough if you need to." All other aspects of the cough test were identical to the single-cough task, including two presentations of each capsaicin concentration.

Suppressed Cough

In order to test the participants' ability to volitionally down-regulate the reflex cough outside of dual-task conditions, participants were presented with an additional block of six capsaicin concentrations and instructed to suppress their cough. Suppressed cough testing took place on the same day as the dual-task paradigm.

Data Extraction

In both the single- and dual-task conditions, only cough data from the second block of capsaicin presentations were analyzed, as participants' performance is considered to be more reliable following initial presentations [34]. Analysis of cough airflow patterns was conducted by two research assistants trained in spirometric analysis of cough, who were blinded to participant identity and testing condition, using LabChart 8.0 software (ADInstruments). From the sequential cough waveform, a cough (Cr1) was defined as an inspiratory period followed by a period of glottal closure (compression phase) and a sharp expiratory effort. Cough reaccelerations (Cr*N*) after the initial cough (Cr1) were characterized by a compression phase and sharp expiratory airflow but were not preceded by inspiration. A cough epoch was defined as a Cr1 and all subsequent cough reaccelerations associated with the same inspiratory event (Fig. 1). The total number of coughs per epoch was included as a dependent variable; however, specific analyses of cough airflow were only extracted from the first three coughs in an epoch associated with every presentation of capsaicin. These

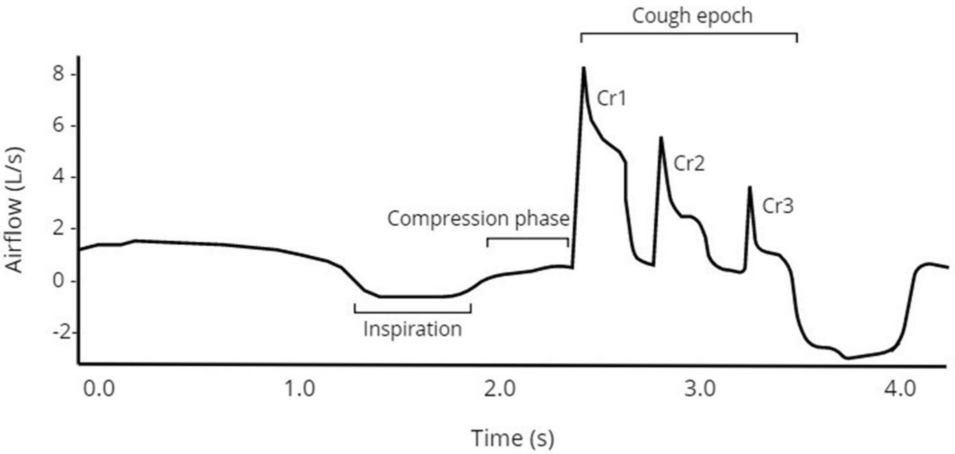

Fig. 1 Sequential cough airflow waveform within a cough epoch. Cr = cough re-acceleration. Original figure in "Dual tasking influences cough sensorimotor outcomes in healthy young adults", by S. Perry & M. Troche, 2019, *Journal of Speech, Language, and Hearing Research, 62*(9), p. 3600. Copyright 2019 by the American Speech-Language-Hearing Association. Reprinted with permission

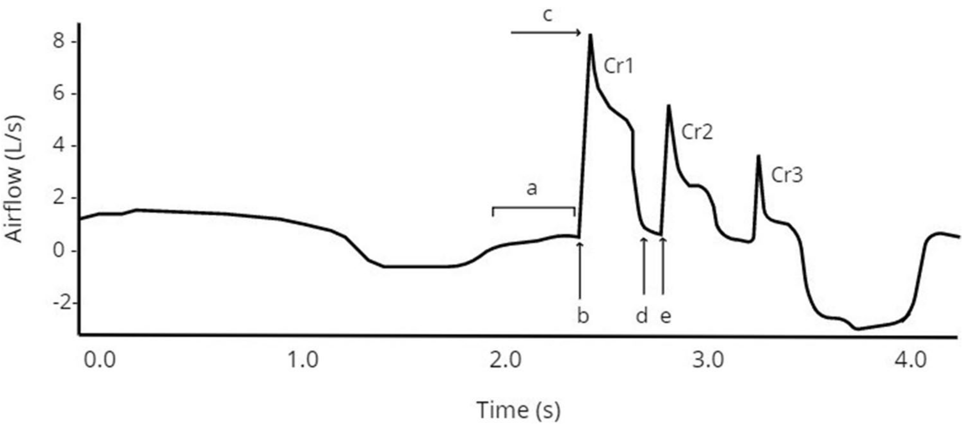

Fig. 2 Outcomes measured from the sequential cough airflow waveform. Cr(N) = number of coughs; a = compression phase duration (s); c = peak expiratory flow rate (L/s); c–b = peak expiratory flow rise time (s); c/(c–b) = cough volume acceleration (L/s/s); e–b = cough-expired volume (L); d–e = compression phase duration for Cr2. Original figure in "Dual tasking influences cough sensorimotor outcomes in healthy young adults", by S. Perry & M. Troche, 2019, *Journal of Speech, Language, and Hearing Research, 62*(9), p. 3600. Copyright 2019 by the American Speech-Language-Hearing Association. Reprinted with permission

analyses were partially automated using the LabChart software and its associated algorithms and were extracted into a spreadsheet (Microsoft Excel 2016). Specific measures were as follows (Fig. 2). The cough peak expiratory flow rate (PEFR) in liters per second was measured by selecting the area containing the peak airflow signal, which allowed for the automatic generation of the peak airflow signal. The compression phase duration (CPD) in seconds was measured by selecting the area immediately following the end of inspiration where the cough airflow signal was equal to zero and continuing the selection until an abrupt expiratory rise in the airflow signal, which represented the cough. The software automatically generated the duration of this selection. The peak expiratory flow rise time (PEFRT) in seconds was measured by selecting the area immediately after the CPD and terminating at the PEFR, from which the software automatically generated the duration.

Cough-expired volume (CEV) in liters was measured by selecting the area encompassing the entire cough from end of the CPD to the end of the cough expiratory effort where cough airflow is equal to zero. The LabChart software automatically generated the integral (CEV). The lowest concentration of capsaicin to elicit at least two consecutive coughs (C2 response) was considered to be the cough reflex threshold and was also recorded for analysis.

Tone counting accuracy was measured by comparing participants' responses to the correct number of tones. Relative tone error, as it relates to tone counting, was calculated using the formula:

$$\text{Relative error} = (\text{correct answer} - \text{participant's answer}) / \text{correct answer}$$

Average relative error within single tasking and dual tasking was used for statistical analysis.

Reliability

A random 20% sample of the data was extracted and re-analyzed in order to estimate intra- and inter-rater reliability. Raters were blinded to participant identity and task condition.

Statistical Analysis

IBM SPSS Statistics Version 26 (IBM Corporation, Armonk, New York, USA) was used to analyze the data. To answer our first question—what is the effect of age on dual-task cough response?—we compared data from HYAs with data from HOAs, using the statistical approaches outlined below. To answer our second question—what is the effect of PD on dual-task cough response?—we compared data from PWPD to age-matched HOAs using the same approaches. Finally, to answer our third question—how does dual-task cough performance relate to volitional control of coughing?—we compared data from the dual- and suppressed-task conditions within and across HYAs, HOAs, and PWPD using the approaches outlined below.

Paired samples *t* tests were used for within-group comparisons of differences in tone-counting accuracy and relative error in the single and dual tasks. Multivariate analyses of variance (MANOVAs) were used to compare between-group differences (HYA vs. HOA, HOA vs. PWPD) in tone counting accuracy and relative tone counting error.

Repeated measures ANOVAs (RM-ANOVAs) with Greenhouse–Geisser correction were used to evaluate within- and between-group differences (HYA vs. HOA, HOA vs. PWPD) in PEFR, CPD, PEFRT, and CEV. Because the majority of participants did not produce a Cr2 response to capsaicin trials below 200 µM, only coughs (Cr1–3) from trials of 200 µM were selected for analyses of cough airflow. Separate models were constructed for the single- vs. dual-task, and dual-task vs. suppressed-task conditions. Bonferroni adjustment for multiple comparisons was applied.

Paired samples *t* tests were used for within-group comparisons of differences in the total number of coughs, summed across all concentrations of capsaicin. Separate models were constructed for the single- vs. dual-task, and dual-task vs. suppressed-task conditions. RM-ANOVAs with Greenhouse–Geisser correction were used to evaluate between-group differences (HYA vs. HOA, HOA vs. PWPD) in the number of coughs. Because too few coughs were produced to lower concentrations of capsaicin, only trials of 100 and 200 µM were selected for analyses of number of coughs. Separate models were constructed for the single- vs. dual-task, and dual-task vs. suppressed-task conditions.

UTC ratings were plotted against capsaicin concentration to determine the minimum capsaicin concentration that elicited an UTC ≥ 1. This was considered the UTC threshold. Then, UTC ratings were plotted against capsaicin concentration on a log–log scale, and a linear regression was used to fit the data. The slope of the line was considered to represent UTC sensitivity. For analyses of cough and UTC thresholds, if a participant did not cough to 200 µM capsaicin, they were automatically assigned a threshold of 500 µM (known to be a suprathreshold concentration in healthy adults [31–34] and adults with Parkinson's disease (unpublished laboratory data)). Cough reflex thresholds were log transformed for statistical analyses.

RM-ANOVAs with simple main effects analyses were used to evaluate within- and between-group comparisons of differences in log-transformed cough reflex threshold, log-transformed UTC threshold, and UTC sensitivity slope. Separate models were constructed for the single- vs. dual-task, and dual-task vs. suppressed-cough-task comparisons. Tukey's Honestly Significant Difference was applied for post hoc comparisons.

Statistical significance was set at $p \leq 0.05$ (two-tailed). Inter- and intra-rater reliability assessment was completed using the intraclass correlation coefficient (ICC) using an absolute agreement definition. Post hoc analysis involved linear regression to evaluate the relationship between relative error in dual-task tone counting and the change in number of coughs between single and dual tasking.

Results

No participants were excluded based on cognitive-affective screening. Four HOAs and seven HYAs did not cough to any concentration of capsaicin and were excluded from analyses of cough airflow. As a large number of participants did not cough in response to capsaicin concentrations below 200 μM, only data from 200 μM trials were considered for analyses of cough airflow.

Performance in Single- vs. Dual-Task Conditions: Attention Task

Age Effects

In the single task, HOAs counted tones with an average accuracy of 74.29% and average relative error of 6.36%. This was not significantly different from HYAs, $F(2, 38)=0.47$, $p=0.63$, Wilks' $\Lambda=0.88$, partial $\eta^2=0.12$. In the dual task, accuracy dropped significantly in HOAs: the average accuracy decreased to 50.45% [32% decrease relative to single tasking; $t(13)=3.37$, $p=0.01$], and relative error was 16.21% [155% increase relative to single tasking, $t(13)=-3.80$, $p=0.01$] (Fig. 3). Differences in dual-task tone-counting accuracy were not significant between HOA vs. HYA, $F(2, 38)=2.09$, $p=0.14$, Wilks' $\Lambda=0.90$, partial $\eta^2=0.10$.

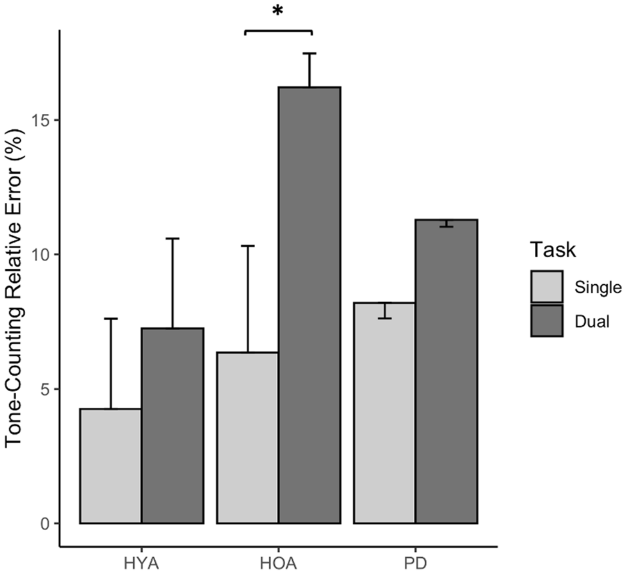

Fig. 3 Dual-task tone-counting performance expressed as % relative error in healthy young adults (HYA), healthy older adults (HOA), and adults with Parkinson's disease (PD). *$p<0.05$

Disease Effects

PWPD were less accurate at counting tones [60.71%] and had higher relative error [8.20%]. However, this was not significantly different from HOAs, $F(2, 25)=1.69$, $p=0.21$, Wilks' $\Lambda=0.88$, partial $\eta^2=0.12$. In the dual task, average accuracy for PWPD significantly decreased to 44.64% [26% decrease relative to single tasking, $t(13)=2.21$, $p=0.046$]. Although there was a 38% increase in relative error [11.29%] compared to the single task, this was not statistically significant, $t(13)=-1.45$, $p=0.17$ (Fig. 3). Differences in dual-task tone counting were not significant between PWPD vs. HOA, $F(2, 25)=1.91$, $p=0.17$, Wilks' $\Lambda=0.87$, partial $\eta^2=0.13$.

Performance in Single- vs. Dual-Task Conditions: Cough Task

Cough Airflow Measures

Age Effects

Between single and dual tasking, the average number of coughs dropped significantly for HYAs, from six to four coughs [$p=0.01$, $d=0.43$]. The change in average number of coughs was non-significant for HOAs [from three coughs to two coughs; $p=0.19$] (Fig. 4). RM-ANOVA revealed no significant task x capsaicin concentration x group interaction effects [$F(3.04, 113.45)=2.53$, $p=0.06$]. In terms of cough airflow, when coughs from trials of 200 μM capsaicin were analyzed, no within- or between-group differences in PEFR, PEFRT, CEV, or CPD between the single- and dual-task conditions were found for HYAs and HOAs [$p>0.05$].

Disease Effects

In the dual task, the average number of coughs reduced for PWPD, from five coughs to three coughs; however, this was not statistically significant [$p=0.14$] (Fig. 4). When comparing HOAs and PWPD, RM-ANOVA revealed a three-way task x capsaicin concentration × group interaction effect that approached statistical significance [$F(2.28, 1.55)=3.00$, $p=0.05$]. Simple two-way interaction analyses revealed that the single-task response to 100 μM capsaicin was significantly higher in PWPD [$\bar{x}=2$ coughs] compared to HOA [$\bar{x}=1$ cough, $F(1, 26)=6.16$, $p=0.02$, $\omega^2=0.16$] and the dual-task response to 200 μM capsaicin was significantly

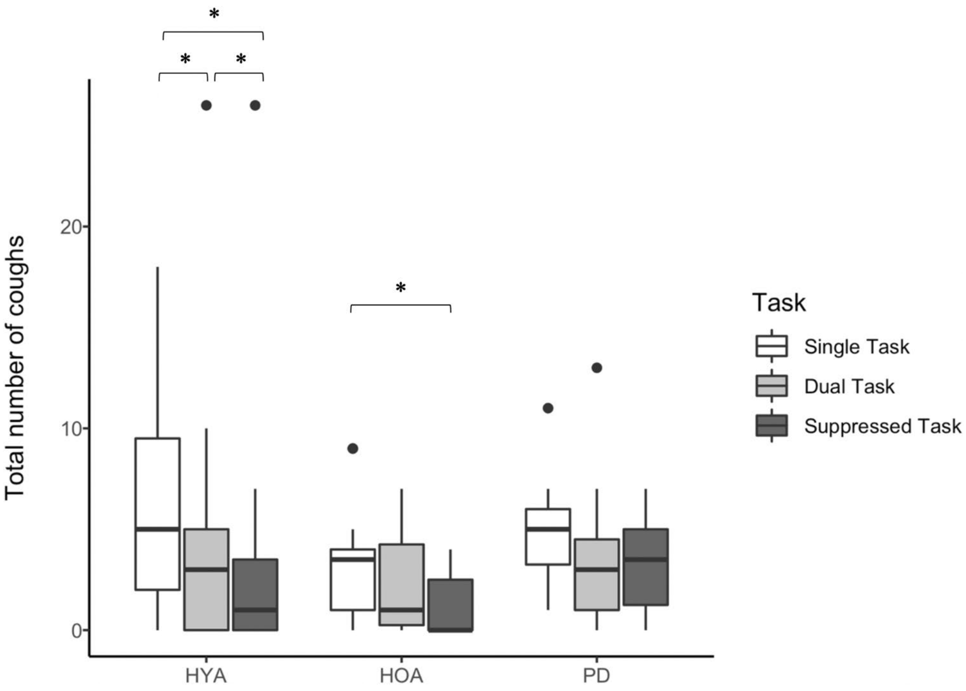

Fig. 4 Total number of coughs produced during the single, dual, and suppressed cough tasks among healthy young adults (HYA), healthy older adults (HOA), and people with Parkinson's disease (PD). $*p < 0.05$; ● = outlier

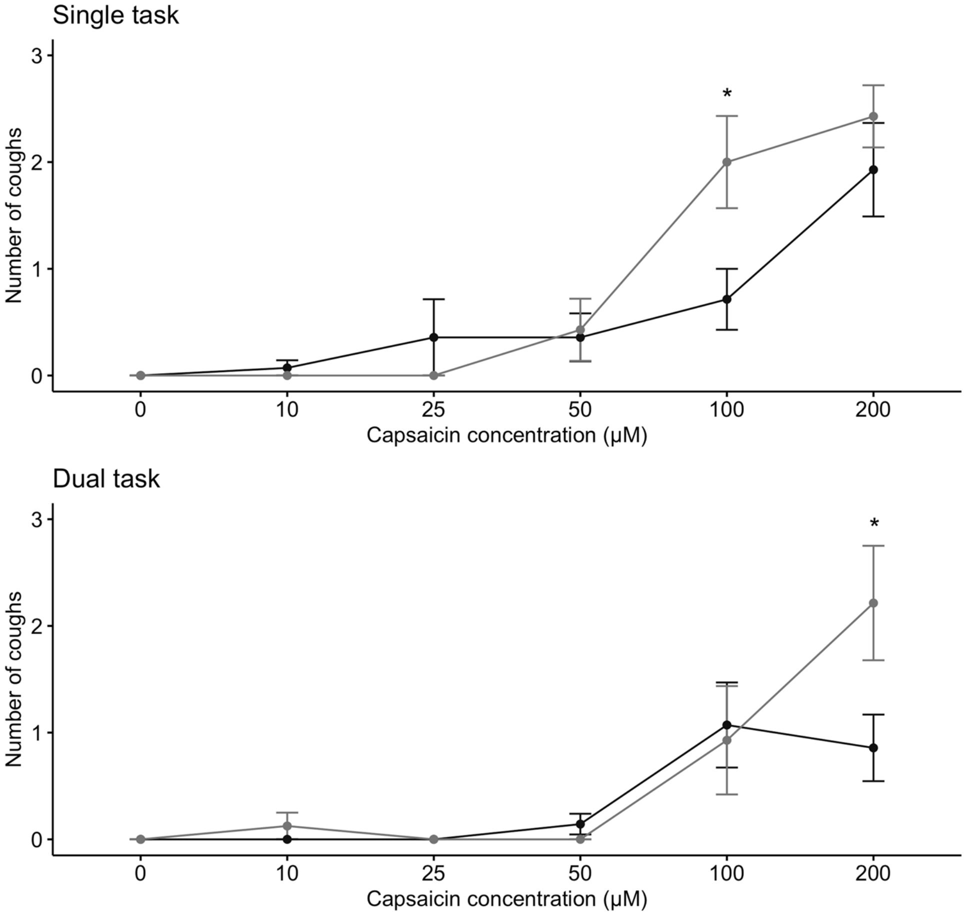

Fig. 5 Average number of coughs produced during the single (top) and dual (bottom) tasks among healthy older adults (black), and people with Parkinson's disease (gray). $*p < 0.05$, standard error bars shown

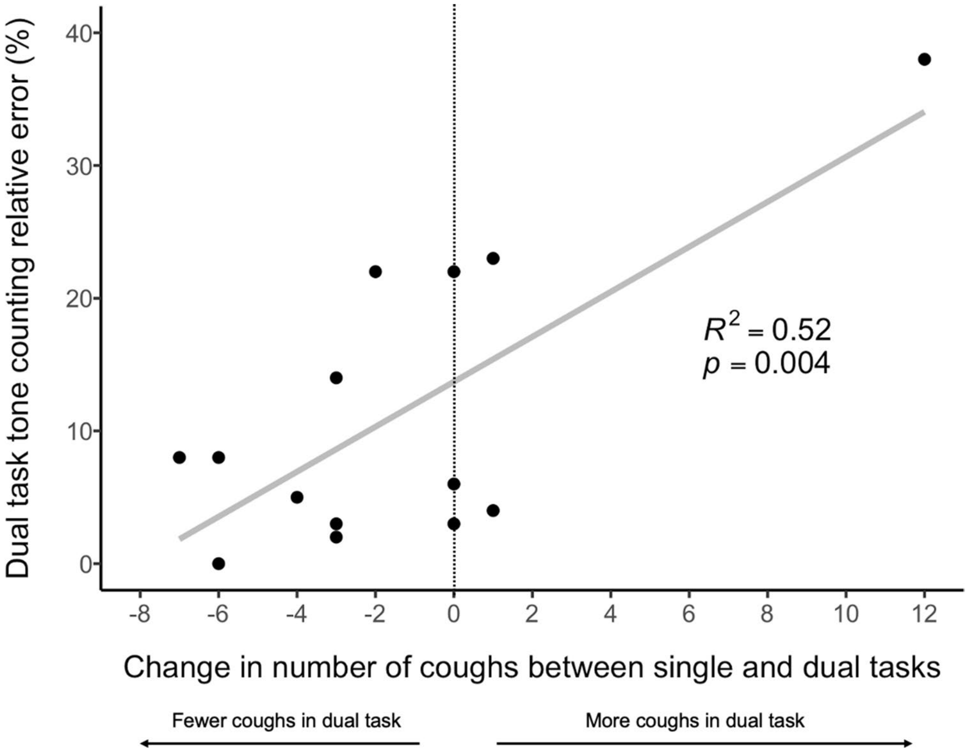

Fig. 6 Relationship between the change in number of coughs between single and dual tasks and percent relative error in dual-task tone counting in people with Parkinson's disease. The dashed line indicates no change in number of coughs. Points to the left of this line represent participants who coughed fewer times in the dual task compared to the single task. Points to the right of this line represent participants who coughed more times in the dual task compared to the single task. The solid gray line represents the line of best fit

higher in PWPD [$\bar{x} = 2$ coughs] compared to HOA [$\bar{x} = 1$ cough, $F(1, 26) = 4.78$, $p = 0.04$, $\omega^2 = 0.12$] (Fig. 5).

To explore participants' prioritization during dual tasking, post hoc analysis of the magnitude of errors made during dual-task tone counting was completed. A linear regression comparing relative error in dual-task tone counting and the change in number of coughs between single and dual tasking revealed a strong, positive relationship between these variables for PWPD [$p = 0.004$, $r^2 = 0.52$]. In other words, as participants made greater tone-counting errors, the difference in cough response (number of coughs) between single and dual tasking was also greater. This relationship was not apparent for HOAs [$p = 0.38$, $r^2 = 0.38$] (Fig. 6).

A second RM-ANOVA was conducted to determine the effect of cognition on the change in number of coughs between single and dual tasking in PWPD. The final model including relative error in dual-tasking tone counting, MoCA score, and digits-ordering score accounted for 60% of the variance in the change in number of coughs [$F(3, 13) = 7.41$, $p = 0.01$, adjusted $R^2 = 0.60$]. However, only relative errors in dual-task tone counting emerged as significantly related to the number of coughs [$p = 0.01$], with increased magnitude of errors associated with increased dual-task coughing.

In terms of cough airflow, when coughs from trials of 200 µM capsaicin were analyzed, no within- or between-group differences in PEFR, PEFRT, CEV, or CPD between the single- and dual-task conditions were found for HOAs and PWPD [$p > 0.05$].

Self-reported UTC

Age Effects

Between single and dual tasking, HYAs showed no significant differences in the log UTC threshold [$F(1, 24) = 0.03$, $p = 0.86$; Fig. 7] or UTC sensitivity slope [$F(1, 24) = 0.49$, $p = 0.49$]. Similarly, there were no differences in the log UTC threshold [$F(1, 13) = 0.79$, $p = 0.39$] or UTC sensitivity slope [$F(1, 13) = 1.21$, $p = 0.31$] for HOAs.

Comparing HOAs to HYAs revealed no significant task x group interaction effects on the log UTC threshold [$F(1, 37) = 0.76$, $p = 0.39$] or UTC sensitivity slope [$F(1, 37) = 0.99$, $p = 0.33$].

Disease Effects

There were no differences in the log UTC threshold [$F(1, 13) = 3.06$, $p = 0.10$; Fig. 7] or UTC sensitivity slope [$F(1, 13) = 3.06$, $p = 0.33$] for PWPD between the single and dual tasks. Comparing HOAs to PWPD, RM-ANOVA revealed no significant task x group interaction effects on the log UTC threshold [$F(1, 26) = 3.38$, $p = 0.08$] or UTC sensitivity slope [$F(1, 26) = 0.41$, $p = 0.53$].

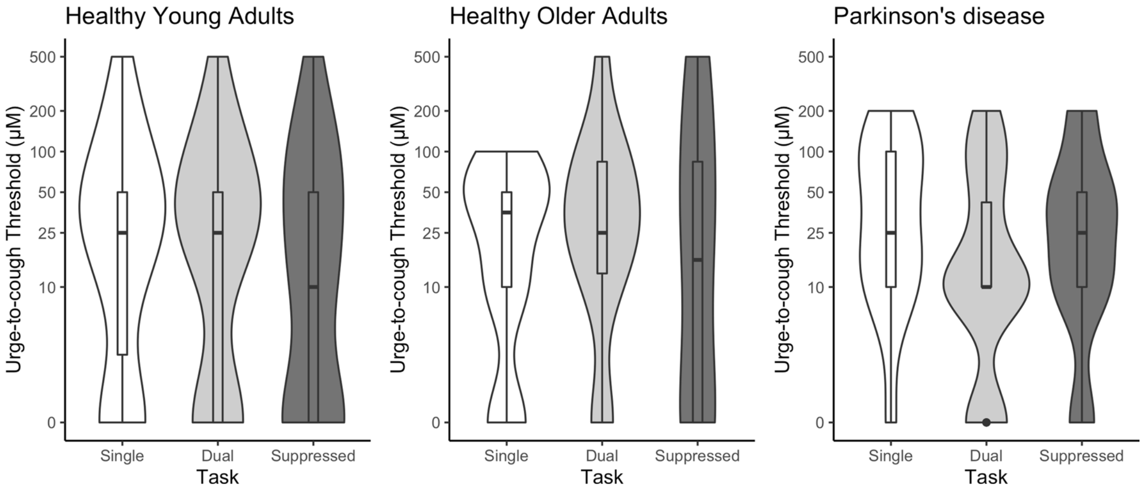

Fig. 7 Violin plots including median, interquartile range and probability density for urge-to-cough (UTC) thresholds for healthy young adults, healthy older adults, and people with Parkinson's disease across the single-, dual-, and suppressed-task conditions. The *y*-axis has been adjusted to a non-log-transformed scale for ease of interpretation. Note that, if a participant did not report any UTC, they were assigned a UTC threshold of 500 μM capsaicin. ● = outlier

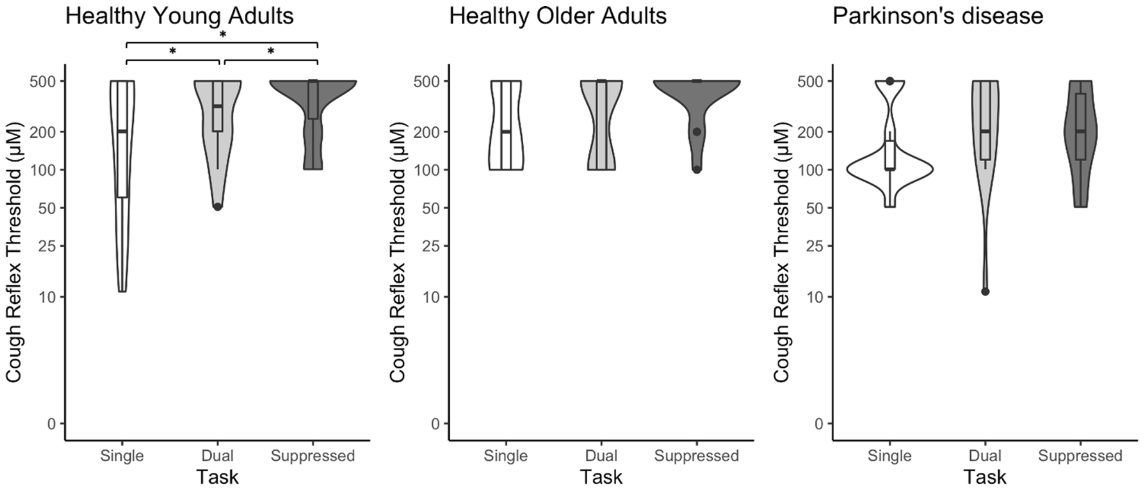

Fig. 8 Violin plots including median, interquartile range ,and probability density for cough reflex thresholds for healthy young adults, healthy older adults, and people with Parkinson's disease across the single-, dual-, and suppressed-task conditions. The *y*-axis has been adjusted to a non-log-transformed scale for ease of interpretation. Note that, if a participant did not cough to 200 μM capsaicin, they were assigned a cough reflex threshold of 500 μM. *$p < 0.05$; ● = outlier

Cough Reflex Thresholds

Age Effects

HYAs' cough reflex thresholds were significantly higher in the single task compared to the dual task [$p = 0.01$, partial $\eta^2 = 0.36$] (Fig. 8); this difference did not reach statistical significance in the HOA group [$p = 0.43$]. Between HOAs and HYAs, RM-ANOVA revealed no significant task x group interaction effects on the log cough reflex threshold, $F(1, 39) = 1.89$, $p = 0.18$.

Disease Effects

Within PWPD, log cough reflex thresholds were higher in the dual task compared to the single task (Fig. 8); however this difference did not reach statistical significance [$p = 0.37$]. Comparing HOAs to PWPD, RM-ANOVA revealed no significant task x group interaction effects on the log cough reflex threshold, $F(1, 26) = 0.15$, $p = 0.71$.

Performance in Dual- vs. Suppressed-Task Conditions

Cough Airflow Measures

Age Effects

HYAs responded to the suppressed cough task with significantly fewer coughs compared to the dual task, $p = 0.01$ (Fig. 4). By contrast, the number of coughs from HOAs was similar in both the suppressed task and the dual task, $p = 0.25$. Between-group analysis suggested that the number of coughs produced in the suppressed task was not significantly different between HYAs and HOAs, $p = 0.47$. The majority of HOAs were able to completely suppress coughing; therefore, within- and between-subjects analysis of suppressed cough airflow patterns was not possible.

Disease Effects

PWPD responded with a similar number of coughs for both the suppressed task and dual task, $p = 0.99$ (Fig. 4). Between-group analysis revealed no significant differences between the number of suppressed coughs produced by HOAs compared to PWPD, $p = 0.30$. The majority of HOAs were able to completely suppress coughing; therefore, between-subjects analysis of suppressed cough airflow patterns was not possible.

Self-reported UTC

Age Effects

Between dual tasking and suppressed cough tasking, HOAs showed no significant differences in the log UTC threshold [$F(1, 11) = 3.12$, $p = 0.11$] or log UTC sensitivity slope [$F(1, 11) = 1.63$, $p = 0.23$]. Overall, no difference in log UTC thresholds in the suppressed cough condition between HOAs and HYAs was found, $F(1, 35) = 0.95$, $p = 0.34$. Similarly, no difference in the UTC sensitivity slope in the suppressed cough condition was found between HOAs and HYAs, $F(1, 35) = 0.69$, $p = 0.41$.

Disease Effects

Between dual tasking and suppressed cough tasking, PWPD showed no significant differences in the log UTC threshold [$F(1, 13) = 0.75$, $p = 0.40$] or UTC sensitivity slope [$F(1, 13) = 1.27$, $p = 0.28$]. Log UTC thresholds in the suppressed cough condition were higher in PWPD compared to HOAs; however, this did not reach statistical significance, $F(1, 24) = 3.46$, $p = 0.08$. Similarly, the UTC sensitivity slope in the suppressed cough condition was higher in PWPD compared to HOAs; however, this did not reach statistical significance, $F(1, 24) = 2.99$, $p = 0.10$.

Cough Reflex Thresholds

Age Effects

Within HYAs, cough reflex thresholds were significantly higher in the suppressed task compared to the dual task [$p = 0.02$] (Fig. 8). Although cough reflex thresholds were also higher within HOAs, this difference did not reach statistical significance [$p = 0.23$]. No significant task x group interaction effects on the log cough motor threshold were apparent, $F(1, 39) = 0.06$, $p = 0.81$.

Disease Effects

Within PWPD, there were no differences in cough reflex thresholds between dual and suppressed tasking [$p = 0.99$]. No significant task × group interaction effects on the log cough motor threshold were apparent, $F(1, 26) = 0.70$, $p = 0.41$.

Reliability

Inter-rater reliability was perfect for measures of PEFR (ICC = 1.00), excellent for measures of PEFRT and CEV (ICC = 0.94 and 0.95, respectively), and moderate for measures of CPD (ICC = 0.72) [36]. Intra-rater reliability was perfect for measures of PEFR (ICC = 1.00), good for measures of CPD (ICC = 0.83), and moderate for measures of CEV and PEFRT (ICC = 0.67 and 0.71, respectively).

Discussion

We set out to investigate whether performing concurrent attention and coughing tasks (via a dual-task paradigm) would affect cough sensorimotor function in adults with PD, compared to healthy controls. The ability to successfully protect the airway when dual tasking may be critical for PWPD, given their elevated risk of airway invasion during swallowing. In general, results supported that dual tasking elicited an overall blunting of the cough sensorimotor response in healthy controls, as well as a relationship between dual-task performance and cough frequency that appeared to be amplified in the PD group. However, the hypothesis that dual tasking would influence cough airflow measures was not supported.

Age Effects on Dual-Task Cough Function

Although age effects on reflexive cough function have been previously reported [37]; to our knowledge, this is the first report of dual-task effects on cough in HOAs. Based on our previous findings in HYAs [22], we expected to observe fewer coughs during dual tasking, particularly in HOAs. However, the number of coughs was unchanged between single and dual tasking in HOAs. This finding can be interpreted in several ways. First, it is possible that there was no dual-task effect on cough frequency in HOAs, although, given the strong body of literature supporting dual-task effects on other motor behaviors in HOAs [38], this explanation may not be entirely compelling. Alternatively, during dual tasking, HOAs in the present study may have prioritized cough function over tone counting, explaining the similar number of coughs between the single and dual tasks. However, this theory is not supported by the tone-counting data, which revealed relatively large errors in the dual-task condition. Another possible explanation is that the already low baseline (i.e., single task) number of coughs may have created a flooring effect, limiting the extent to which a difference in the number of coughs during dual tasking could be observed. Finally, it is possible that reduced statistical power limited the ability to detect a dual-task effect in HOAs (i.e., a Type II error occurred).

Disease Effects on Dual Task Cough Function

Contrary to our hypothesis, when we compared single- vs. dual-task performance, we found no evidence of a dual-task effect on cough frequency in PWPD. However, ANOVA may not have been sensitive to the different strategies that individuals used when dual tasking. That is, if some participants prioritized coughing while others prioritized tone counting, the overall dual-task effect may have been washed out. To investigate this, we compared relative tone-counting errors to reflexive cough frequency in the dual-task condition and found a strong relationship between these variables in PWPD. Specifically, as the magnitude of errors increased, PWPD coughed more times. This finding may also explain why PWPD appeared to cough more times during dual tasking as compared to HOAs—as the high number of coughs was likely being driven by the PWPD who had high tone-counting errors. This finding is novel, given that very few reports of dual-task sensorimotor performance in PWPD exist in the corticobulbar literature.

We did not find a significant correlation between relative tone-counting errors and cough frequency in HOAs. However, it is interesting to note that in our prior study [22] which included a larger sample, we observed a moderate correlation between these variables in HYAs (i.e., statistical power was increased). Taken together, it seems likely that this dual-task effect on cough frequency exists in all healthy individuals but may be amplified in the context of neurological disease. No differences in measures of cough aerodynamics were found in HYAs, HOAs, or PWPD, suggesting that dual tasking had a greater impact on the sensory processing of cough stimuli than the motor execution of cough.

We propose that PWPD prioritized the cognitive task at the expense of cortical resources for coughing, as evidenced by low overall relative tone-counting errors. The allocation of cortical resources to one task over another is multifactorial, involving factors such as baseline cognition, nature, and/or difficulty of the cognitive task [39, 40]; stimuli intensity, novelty, salience, and suddenness [21]; or prior expectations [41]. The cognitive-affective variables measured in this study did not improve the ability to differentiate participants who prioritized coughing versus tone counting, but it is possible that distinctive patterns may emerge in a larger sample. Of note, at two points during testing, participants were instructed to temporarily stop dual tasking ("don't count tones, just cough if you need to"). Under these conditions, there was increased responsiveness in terms of higher UTC, confirming that PWPD were able to switch cortical resource allocation temporarily back to cough sensation when required.

Evidence from functional magnetic resonance imaging (fMRI) studies can provide some insight into the relationship between attention and coughing. Once considered a purely reflexive behavior, imaging has revealed substantial supramedullary influence on cough, involving areas such as the primary motor cortex, prefrontal cortex, supplementary motor cortex, somatosensory cortices, cingulate cortex, inferior frontal gyrus, posterior parietal cortex, insula, thalamus, and cerebellum [42–49]. Several of these same areas are involved in attention [44], in monitoring the intensity and salience of cough stimuli [44], and in swallowing [46]. More recently, the striatum has been implicated as a site of increased activity during dual-task interference in PWPD [50], although the exact nature of the striatum's role in cough is not yet well understood. It has been hypothesized that when additional cortical load is added, cognitive-motor interference results and a breakdown in both cognitive and motor (in this case, coughing) performance ensues [8, 51]. Known as the capacity sharing model of dual-task interference [51], this theory may help to explain the finding of reduced coughing among participants with low relative errors in dual-task tone counting.

As far as the authors are aware, this is the first report to directly compare suppressed cough function with single- and dual-task coughing in PWPD. We found that, unlike HYAs or HOAs, PWPD showed no change in cough frequency between single-, dual-, and suppressed-task coughing. Furthermore, PWPD consistently reported a UTC during cough suppression, unlike some HYAs or HOAs. These findings can be interpreted in several ways. First, it is possible that in PWPD, volitionally modulating (i.e., suppressing) coughing required a high cortical load, much like the dual-task condition. This could explain why attempts to suppress coughing appeared very similar to dual-task coughing in PWPD and is in line with what we observed in terms of cough frequency, cough reflex thresholds, and UTC thresholds in PWPD. The present study was not designed to quantify cognitive load during different cough conditions, but this is a suggested direction for future work. One popular measure of cognitive load is the Paas scale [52]: a simple Likert scale used by participants to measure perceived invested mental effort. Quantifying cognitive load in this way would allow definitive comparisons to be made between suppressed coughing and dual-task coughing. Another explanation is that PWPD may have used cough suppression as a *strategy* when faced with the competing demands for cortical resources in the dual-task condition. Given that differences in reflexive cough frequency, cough reflex thresholds, and UTC thresholds were observed in healthy participants, it seems that this strategy may have been specific to PWPD. Although the present study was not designed to investigate strategy use during dual tasking, this could be incorporated into future research by asking participants questions about strategy use immediately following testing.

Although it is clear that the effects of dual tasking on reflexive cough do not uniquely affect PWPD, the implications of reduced cough function may be particularly serious for this population. Aspiration pneumonia is directly attributed to events of uncompensated aspiration [53]. PWPD are at high risk of dysphagia and airway invasion, increasing the importance of effective cough function as a means of avoiding pulmonary infection. One possible way to address the current high rates of aspiration pneumonia in PWPD could be to address dual tasking therapeutically. For example, Janssens et al. [21] showed that cough frequency increases when participants are directed to draw their attention towards coughing, as opposed to attending to an external stimulus. Another direction worthy of consideration is increasing the availability of cortical resources through cognitive rehabilitation. Given that swallowing and coughing share many neural and anatomical substrates [23], it is possible that rehabilitation in one area (e.g., cough) may have cross-over benefits for swallowing.

This study was not without limitations. First, the PWPD in this study all had mild-stage disease; thus, the likelihood of detecting group differences may have been reduced. Ebihara et al. [54] noted that cough reflex sensitivity is similar between early-stage PD and controls, while people with advanced PD show significantly reduced cough reflex sensitivity. We observed a similar pattern in our data, where PWPD either coughed the same number of times, or more times, to various concentrations of capsaicin compared to HOAs (as can be observed in Fig. 5).

Second, a large number of participants did not cough in response to capsaicin concentrations below 200 μM, limiting the available data for which to conduct analyses of cough airflow, UTC, and cough reflex thresholds. This most likely represents a flooring effect, as opposed to an adverse response to capsaicin. Although evidence from in vitro and animal studies suggests that direct exposure to capsaicin can damage or destroy respiratory epithelial cells [55, 56], the exposure is typically continuous, lasting from 30 min to 4 h. In contrast, participants in the present study received two seconds of non-continuous exposure, for up to 14 trials (28 non-continuous seconds of exposure) at each session. Furthermore, in line with published guidelines on cough assessment by the European Respiratory Society [57], testing sessions were separated by at least 24 h, to prevent tachyphylaxis (blunting of the cough response). To avoid a flooring effect in future research, stimuli should include higher concentrations of capsaicin.

Third, our hypothesis that PWPD allocated cortical resources to tone counting at the expense of coughing was based on the objective finding of low relative tone-counting errors, as well as an observable change in UTC when participants were asked to briefly ignore the tones, but this hypothesis requires further confirmation. One possibility is to simply ask participants which task they prioritized/paid more attention to and compare this to objective measures of task performance.

Fourth, although we attempted to control for the confounding variables of hearing acuity and noise on tone-counting accuracy by screening hearing, presenting tones via headphones, and, during the single-task tone-counting condition, leaving the compressor nebulizer on to control for background noise, it is possible that hearing acuity in older adults (both HOAs and PWPD) limited their ability to count tones accurately during the dual task.

Finally, given the nature of attention, direct measurement of attentional resource allocation can only be estimated via the use of self-report (e.g., The Attentional Resource Allocation Scale [58]) or behavioral observations, such as error-making patterns. The tone-counting task used in the present study was designed to measure selective attention [59] and has previously been found to be an effective measure of attentional focus in a study of reflex cough [21]; therefore, we considered it to be an appropriate estimate of attentional resource allocation in the present study.

Results of this study suggest that, in PWPD, cough frequency was sensitive to situations where attention was divided. Future research may explore whether this effect translates to ‘real world’ scenarios, such as coughing while attending to television or conversation. To further understand how dual tasking affects corticobulbar function, future work is planned to compare populations with predominately cognitive disturbance, predominately motor disturbance, and a combination of both. Understanding how coughing might be altered in models of cognitive/motor disease is important, due to the high prevalence of concomitant dysphagia and dystussia in these populations who may also have limited cognitive resources. Although more research is needed to understand the cognitive-motor interactions associated with coughing, this study highlights the potential for increasing prioritization towards respiratory/laryngeal sensations in order to facilitate optimum (i.e., upregulated) cough responses in dysphagic populations.

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Compliance with Ethical Standards

Conflict of interest S. Perry and M. Troche confirm that they have no relevant conflicts of interest to disclose.

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