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ORIGINAL ARTICLE

Immediate Effects of Sensorimotor Training in Airway Protection (smTAP) on Cough Outcomes in Progressive Supranuclear Palsy: A Feasibility Study

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Abstract

Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized by a high prevalence of dysphagia, cough dysfunction, and resultant aspiration pneumonia. Sensorimotor cough function is important for airway clearance in people with dysphagia. Upregulation of cough has been demonstrated in healthy adults and Parkinson's disease; however, the feasibility of cough rehabilitation in PSP is unknown. We sought to assess feasibility by examining the immediate effects of a novel sensorimotor training in airway protection (smTAP) on upregulation of cough function in PSP. Fifteen individuals with PSP enrolled in this study. Baseline voluntary and reflex cough testing were completed. During smTAP, participants were presented with subthreshold capsaicin and instructed to cough with sufficient intensity to hit a target line (set 25% above baseline reflex peak cough flow) via cough airflow visual biofeedback. Twenty-five repetitions were targeted within a single session. Wilcoxon signed-rank tests compared cough airflow measures between baseline voluntary cough testing, the initial five trials of smTAP, and final five trials. Mean peak expiratory flow rate (PEFR) significantly increased from initial to final smTAP trials ($p < 0.001$). Fourteen participants increased PEFR, with gains of more than 10% in 11 participants. Variability of PEFR ($p = 0.01$) and cough expired volume ($p = 0.01$) significantly decreased across smTAP trials. This study is the first to demonstrate the ability of people with PSP to immediately upregulate cough function, providing preliminary support for the feasibility of cough rehabilitation in this population with this novel treatment approach. Future research examining the effects of multiple sessions of smTAP on cough outcomes is warranted.

Keywords Airway protection · Dystussia · Progressive supranuclear palsy · Rehabilitation · Deglutition · Deglutition disorders

Introduction

Progressive supranuclear palsy (PSP) is the most common neurodegenerative disease among Parkinsonian-plus syndromes. PSP is neuropathologically classified as a tauopathy, causing neural degeneration in the basal ganglia, diencephalon, brainstem, and cerebellum due to abnormal accumulation of phosphorylated tau proteins [1]. Clinically, PSP is characterized by symmetric parkinsonism, including bradykinesia, rigidity, tremor, and postural instability, as well as vertical supranuclear gaze palsy and behavioral disturbances [2]. Bulbar dysfunction is common and can occur early in the disease course [3], involving physiologic impairments of breathing [4], coughing [5], and swallowing [6–9].

Swallowing is a complex, life-sustaining sensorimotor behavior requiring precise coordination of more than twenty-five muscles innervated by six cranial nerves [10]. Swallowing dysfunction (dysphagia) is highly prevalent in individuals with PSP, characterized by oral, pharyngeal, and esophageal deficits resulting in impairments to both swallowing efficiency and safety [5–7, 9, 11]. Dysphagia is associated with a shorter length of survival [12] due to its role in the development of aspiration pneumonia, a leading cause of death in this population [13]. In the event of aspiration,

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a robust and consistent cough response is required to expel material from the trachea in order to maintain a homeostatic pulmonary environment. This cough response has been subjectively described as insufficient or absent in individuals with PSP [5], posing a large threat to airway protection and pulmonary health. The neurobiology of this airway protective behavior is mediated by peripheral afferents in the distal and proximal airways, as well as efferent control pathways via cortical, subcortical, and brainstem structures, including the nucleus tractus solitarius, paratrigeminal nucleus, basal ganglia, cerebellum, and prefrontal cortex [14]. Cough can be classified as either voluntary or reflexive in nature. Voluntary cough is initiated on command, whereas reflex cough occurs in response to sensory stimulation. Though traditional models have considered reflexive cough as a brainstem-mediated behavior which bypasses cortical control [15], recent research has suggested that various aspects of reflex cough are amenable to volitional modulation and upregulation (e.g., increased cough airflow, increased perception of cough stimuli) in both healthy adults and individuals with Parkinson's disease [16, 17]. In these studies, participants were able to increase cough airflow (i.e., upregulate their cough function) in the presence of a sensory stimulus with verbal cueing. Upregulation of cough function has been described several ways in the literature, most notably as the ability to increase cough airflow or increase one's perception of airway sensation during cough [16, 17]. For the purposes of this study, we were interested in the upregulation (i.e., increase) of cough expiratory airflow. Based on this growing body of literature, volitional cough modulation may be an effective strategy to improve cough strength in the presence of blunted reflex cough production. Thus, cough appears to be a feasible and clinically relevant therapeutic target for individuals with neurodegenerative disease at high risk for pulmonary compromise due to deficits in airway protection.

Despite the importance of cough as an airway protective behavior to promote pulmonary health and prevent adverse outcomes, behavioral treatment paradigms targeting cough dysfunction are limited. To date, no studies have examined cough rehabilitation for persons with PSP. Our research group developed a novel cough rehabilitation paradigm: sensorimotor training in airway protection (smTAP). The paradigm involves several key features to facilitate improved sensorimotor coordination and function. smTAP involves a cough sensory stimulus of subthreshold capsaicin (a tussigenic agent derived from chili peppers), a verbal cue to enhance cough airflow (e.g., "cough hard"), visual biofeedback of cough airflow via spirometry, and an increased awareness to the urge-to-cough [16]. A sensory stimulus below the participant's reflex cough threshold provides a salient context targeting enhanced sensory perception of capsaicin for execution of the sensorimotor behavior (coughing). Upregulation of cough airflow is facilitated with a verbal cue from an assisting clinician [16]. Visual biofeedback of airflow during the task provides immediate feedback regarding the effectiveness of the cough and whether it was above or below a target line, which is set 25% above maximal peak expiratory flow rate (PEFR) from baseline reflex cough testing [17]. Finally, the task also focuses on upregulation of the urge-to-cough, a respiratory sensation known to precede reflex cough [18–20]. The ultimate aim of this treatment approach is to target both sensory and motor components of cough, in order to promote generalization and transference of cough upregulation to situations involving airway invasion during swallowing. Collectively, the aforementioned parameters target upregulation of cough airflow. A single session of smTAP adheres to the neuroplasticity principles of specificity, salience, intensity, and repetition [21, 22]. More specifically, the task central to the smTAP treatment paradigm, which was tested in this study, requires completion of a cough-specific task within a salient context of a background cough stimulus and with sufficient intensity to meet a target line 25% above the participant's baseline reflex cough peak flow. This task is repeated 25 times within one session. When the task is completed over several weeks, the treatment paradigm capitalizes on additional principles of motor learning and neuroplasticity, including transference [21, 22].

There is evidence to suggest that healthy young adults, healthy older adults, and people with Parkinson's disease are able to modify their cough airflow with cueing in the presence of a cough inducing stimuli, a task central to smTAP [16, 17]. In order to determine whether smTAP would be a feasible cough rehabilitation approach in PSP and warrant further study, we examined the effects of smTAP on sensorimotor cough function over the course of a single session. We examined (a) the immediate effects of introducing a subthreshold sensory stimulus on cough airflow compared to baseline voluntary cough testing, and (b) assessed improvements in cough airflow across a single session of smTAP. We hypothesized that persons with PSP (a) would demonstrate no immediate changes in cough airflow after the introduction of a subthreshold sensory stimulus, and (b) that improvements in both the magnitude and variability of cough airflow would be evident after smTAP. The ability to complete the task and increase cough airflow within a single session would suggest that this approach is feasible in PSP and would indicate the need for future studies testing the effects of multiple sessions of smTAP on cough outcomes.

Methods

Participants

The Institutional Review Board at Teachers College, Columbia University approved study procedures (IRB #: 17-396) and informed consent was obtained from all participants prior to study enrollment. Participants with a diagnosis of PSP were prospectively recruited and enrolled in a larger two-phase study. The first phase involved characterizing airway protection and communication, and the second phase examined treatment feasibility. All participants were enrolled in both phases of the study. During the first phase, participants underwent a baseline flexible endoscopic evaluation of swallowing (FEES). The FEES protocol included three trials of 90 mL thin liquid (IDDSI level 0) with barium dye. All participants were diagnosed by a fellowship-trained movement disorders neurologist based on the Movement Disorder Society clinical diagnostic criteria for PSP [23] and were enrolled independent of disease or dysphagia severity. Exclusion criteria included a history of other neurological disorders (e.g., stroke, brain tumor), head and neck cancer, respiratory disease (e.g., chronic obstructive pulmonary disease, asthma), or smoking within five years.

Baseline Reflex and Voluntary Cough Evaluations

Baseline reflex cough testing was performed with a facemask coupled to a pneumotachograph with a side port and inspiratory valve connecting to a nebulizer. This connected to a dosimeter which provided single doses of capsaicin during inhalation for a duration of two seconds. Concentrations of 0, 50, 100, and 200 µM capsaicin were each presented randomly across three blocks. Participants were instructed to "cough if you need to" during each presentation of capsaicin and self-reported their urge-to-cough immediately following the stimulus presentation using a modified Borg scale, which ranged from 0 (no urge-to-cough) to 10 (maximal urge-to-cough). A 30 s interval separated each capsaicin presentation during which participants were provided with water. Participants also performed sequential voluntary coughs with an identical spirometric setup. They were instructed to "cough as if something went down the wrong tube" after which a model of a three-cough epoch was performed for the participant by the examiner. Airflow data were inputted into the PowerLab Data Acquisition system, digitized, and recorded on a computer at 2000 Hz. Participants' reflex cough threshold was determined by identifying the lowest dose of capsaicin at which they produced a reliable two-cough response on two out of three trials.

smTAP Procedure

smTAP was performed an average of six days (SD = 5) after baseline cough evaluations, with the majority of participants (87%) receiving smTAP less than seven days after their baseline evaluation. During smTAP, participants were seated at a computer with LabChart and the same spirometry setup used during reflex cough testing (Fig. 1). They were presented with a background dose of subthreshold capsaicin, which was defined as a concentration that was half that of their reflex cough threshold determined from baseline reflex cough testing. Capsaicin was chosen in light of prior research which has demonstrated a relationship between swallowing outcomes and sensorimotor cough responses (e.g., cough airflow, urge-to-cough, cough thresholds) elicited from capsaicin [16, 17, 19]. Furthermore, the short- and long-term reproducibility of capsaicin response ensured reliable cough outcomes across multiple trials [24]. Following presentation of the subthreshold sensory stimulus, participants were instructed to direct their attention to

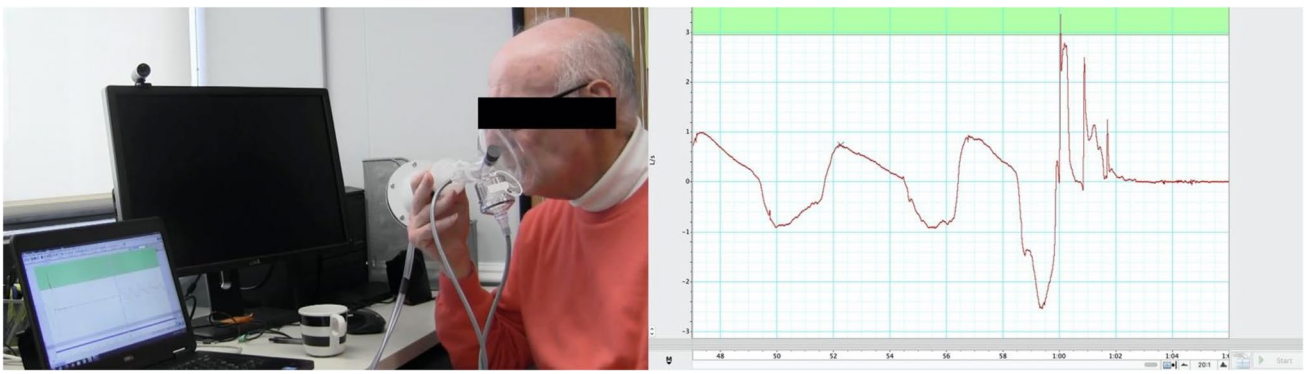

Fig. 1 smTAP experimental setup. Example of the experimental setup (left) with a facemask coupled to a pneumotachograph with a side port and inspiratory valve connected to a nebulizer for subthreshold capsaicin administration and real-time visual biofeedback of the spirometry waveform (right) with target line

their urge-to-cough and "cough hard" in order to elicit a cough with sufficient intensity to hit a target line provided via cough airflow visual biofeedback. The target line was set 25% above maximum peak expiratory flow rate (PEFR) based on baseline reflex cough testing [17]. Real-time visual biofeedback of the cough airflow waveform was available to the participant. Twenty-five repetitions were targeted within a single session. This number of repetitions was selected to remain consistent with prior airway protection rehabilitation paradigms and to provide ample opportunities for practice [25]. Feedback regarding both the knowledge of performance and results was provided from the clinician.

Data Analysis

Measurement of cough airflow for baseline voluntary cough and smTAP trials were completed for the first cough produced in a cough epoch by a blinded, trained research assistant. Twenty percent of coughs were re-analyzed by the primary rater and an additional blinded research assistant for inter- and intra-rater reliability. Coughs were defined as a distinct waveform with a compression phase and explosive airflow event with a turbulent peak above tidal breathing which returned to zero airflow at the end of expiratory phase [26]. Coughs with a turbulent airflow peak that did not exceed tidal breathing were defined as "cough attempts". The spirometry waveform was time-locked with audio–video recordings. Additionally, all coughs were tagged in real-time by a separate researcher on the computer for offline analysis. Only PEFR from "cough attempts" were included in statistical analyses; other airflow outcomes from these "coughs attempts" were not included. The primary outcome for this study was PEFR (L/s). Secondary outcomes included inspiratory volume (CIV; Liters), cough expiratory volume (CEV; Liters), compression phase duration (CPD; seconds), PEFRT (seconds), total coughs produced (CrTot), and cough volume acceleration (CVA; L/s/s), which was derived by dividing PEFR by PEFRT. Cough airflow measures were compared among three different periods: (1) baseline voluntary cough trials (before smTAP trials), (2) across the initial (defined as the first five) smTAP trials, and (3) across the final (defined as the last five) smTAP trials. In order to capture potential changes in performance across several trials, the mean value was compared. In order to capture the participants' best performance on a single trial, maximum PEFR was also examined. Finally, changes in variability between initial and final smTAP trials were examined with the coefficient of variation (CoV), which was calculated for each cough airflow outcome by dividing the standard deviation by the mean of five trials. Airway safety was rated with the penetration-aspiration scale (PAS) during FEES as a descriptive variable. The PAS is an eight-point scale describing the depth and sensory response to airway invasion [27]. The maximum PAS score from 90 mL thin liquid barium trials was reported.

Statistical Analysis

Intra-class correlation coefficients were used to assess inter- and intra-rater reliability for continuous variables. ICC values ≥ 0.90 were considered 'excellent', 0.75–0.90 were 'good', 0.50–0.75 were 'moderate', and < 0.50 were 'poor' [28]. Cohen's unweighted and weighted kappa (κ) were used to assess inter- and intra-rater reliability for nominal (CrTot) and ordinal (PAS) variables and were interpreted as follows: values ≤ 0 indicating no agreement, 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement [29]. Wilcoxon signed-rank tests were performed to compare differences in cough airflow outcomes between voluntary and initial smTAP trials, and initial and final smTAP trials. A Wilcoxon signed-rank test was also used to examine differences in CoVs between initial and final smTAP trials across cough airflow outcomes. A Holm–Bonferroni adjustment corrected for multiple comparisons to adjust the familywise error rate. Alpha was set at $p < 0.05$ and adjusted p values are reported. Pearson correlation coefficients were used as a metric of effect size [30]. Statistical analyses were completed using SPSS v26.0.

Results

Nineteen participants with PSP were enrolled in the study. Three participants (two with PSP-Richardson's Syndrome, one with PSP-Predominant Parkinsonism) did not meet inclusion criteria due to an inability to perform three trials of voluntary coughs, resulting in insufficient baseline voluntary cough data. One participant with PSP-Richardson's Syndrome was excluded due to hypersensitivity to low levels of capsaicin, resulting in insufficient smTAP data. Thus, fifteen participants with PSP (9 males, 6 females) met study inclusion criteria. Participant demographics including information regarding PSP subtype, disease duration, and swallowing severity are included in Table 1. Participants had an average age of 72 years (SD = 5.92) and median disease duration of 4 years (SD = 2.53) since symptom onset and 3 years (SD = 1.64) since date of diagnosis. PSP subtypes included Richardson's syndrome ($n = 10$), PSP with predominant Parkinsonism ($n = 4$), and PSP with predominant frontal presentation ($n = 1$). The majority of participants had some degree of airway invasion with penetration (40%) or aspiration (47%). Maximum penetration-aspiration scale scores ranged from 1 to 8 with a median of 5 (IQR 4–7) and mode of 8. Urge-to-cough ratings during baseline reflex

Table 1 Participant demographics

ID	Age (years)	Sex	PSP subtype	Disease duration since symptom onset (years)	Disease duration since diagnosis (years)	Maximum PAS Score	Median urge-to-cough
1	70	F	Probable PSP-RS	10.88	1.54	7	5
2	71	M	Probable PSP-RS	9.92	4.92	8	5
3	69	F	Probable PSP-RS	5.52	4.28	7	6
4	70	M	Probable PSP-RS	5.41	3.41	3	6
5	76	M	Probable PSP-RS	4.18	1.01	8	8
6	80	F	Probable PSP-RS	4.13	1.10	5	3
7	77	M	Probable PSP-RS	4.03	2.02	5	4
8	67	F	Probable PSP-RS	2.36	2.36	1	4
9	69	F	Probable PSP-RS	2.14	3.28	5	3
10	66	M	Suggestive PSP-RS	3.26	0.42	8	5
11	84	M	Probable PSP-P	4.10	4.02	3	7
12	71	M	Suggestive PSP-P	6.49	3.48	8	8
13	62	F	Suggestive PSP-P	6.01	5.01	1	7
14	70	M	Suggestive PSP-P	3.06	2.14	8	1
15	79	M	Probable PSP-F	6.62	5.87	5	5

PSP-RS PSP with Richardson's syndrome, *PSP-P* PSP with predominant Parkinsonism, *PSP-P* PSP with predominant frontal presentation, *PAS* penetration-aspiration scale, Median urge-to-cough ratings obtained from 200 µM

cough testing at 200 µM ranged from 1 to 8 with a median of 5 (IQR 4–7).

Descriptive statistics for cough airflow parameters are included in Table 2. On average, participants completed 24 trials of smTAP (SD = 7.77). There were no statistically significant differences between baseline voluntary coughs and initial smTAP trials across all mean and maximum cough airflow measures ($p > 0.05$). During smTAP, the total number of coughs produced did not differ between initial and final smTAP trials ($p = 0.31$). Five participants' PEFR exceeded the target line on at least one trial during smTAP with an average success rate of 48% (SD = 31%). Mean PEFR significantly increased from initial ($M = 1.69$ L/s, $SD = 0.69$) to final ($M = 2.05$ L/s, $SD = 0.71$) smTAP trials ($Z = -3.18$, $p < 0.001$, $r = 0.25$; Fig. 2). The majority (93%) of participants demonstrated increased mean PEFR airflow, with 11 showing gains of more than 10%. Though maximum PEFR descriptively increased from initial ($M = 2.16$ L/s) to final ($M = 2.34$ L/s) smTAP trials, this finding was statistically nonsignificant after adjusting for multiple comparisons ($p = 0.060$). Mean IV ($Z = -3.24$, $p < 0.001$, $r = 0.22$) and CPD ($Z = -2.56$, $p = 0.016$, $r = 0.27$) significantly increased across smTAP trials. Mean CEV also improved from initial to final smTAP trials; however, this finding was statistically nonsignificant after multiple comparison adjustments ($p = 0.071$). No other significant differences in the remaining mean cough airflow measures were evident ($p > 0.05$).

Variability of PEFR ($Z = -2.44$, $p = 0.01$, $r = 0.38$) and CEV ($Z = -2.50$, $p = 0.01$, $r = 0.38$; Fig. 3), significantly decreased between initial and final smTAP trials. Eleven participants showed decreased PEFR variability and 12 participants demonstrated decreased variability of CEV. The

Table 2 Cough airflow descriptive statistics across time points

	Voluntary cough trials	Initial smTAP trials	Final smTAP trials
PEFR (L/s), mean (SD)	1.93 (0.99)	1.69 (0.69)	2.05 (0.71)
CEV (L), mean (SD)	0.38 (0.37)	0.43 (0.39)	0.52 (0.35)
IV (L), mean (SD)	0.72 (0.49)	0.52 (0.43)	0.70 (0.54)
CPD (seconds), mean (SD)	0.38 (0.36)	0.51 (0.63)	0.64 (0.67)
PEFRT (seconds), mean (SD)	0.12 (0.14)	0.11 (0.15)	0.12 (0.12)
CVA (L/s/s), mean (SD)	31.45 (23.86)	27.84 (14.86)	31.34 (17.51)
Cough Attempts, freq (%)	1 (6.7%)	0 (0%)	0 (0%)

CrTot number of coughs in a cough epoch, *PEFR* peak expiratory flow rate, *CEV* cough expired volume, *IV* inspiratory volume, *CPD* compression phase duration, *PEFRT* peak expiratory flow rise time, *CVA* cough volume acceleration, Cough attempts defined as coughs with a turbulent airflow peak that did not exceed tidal breathing

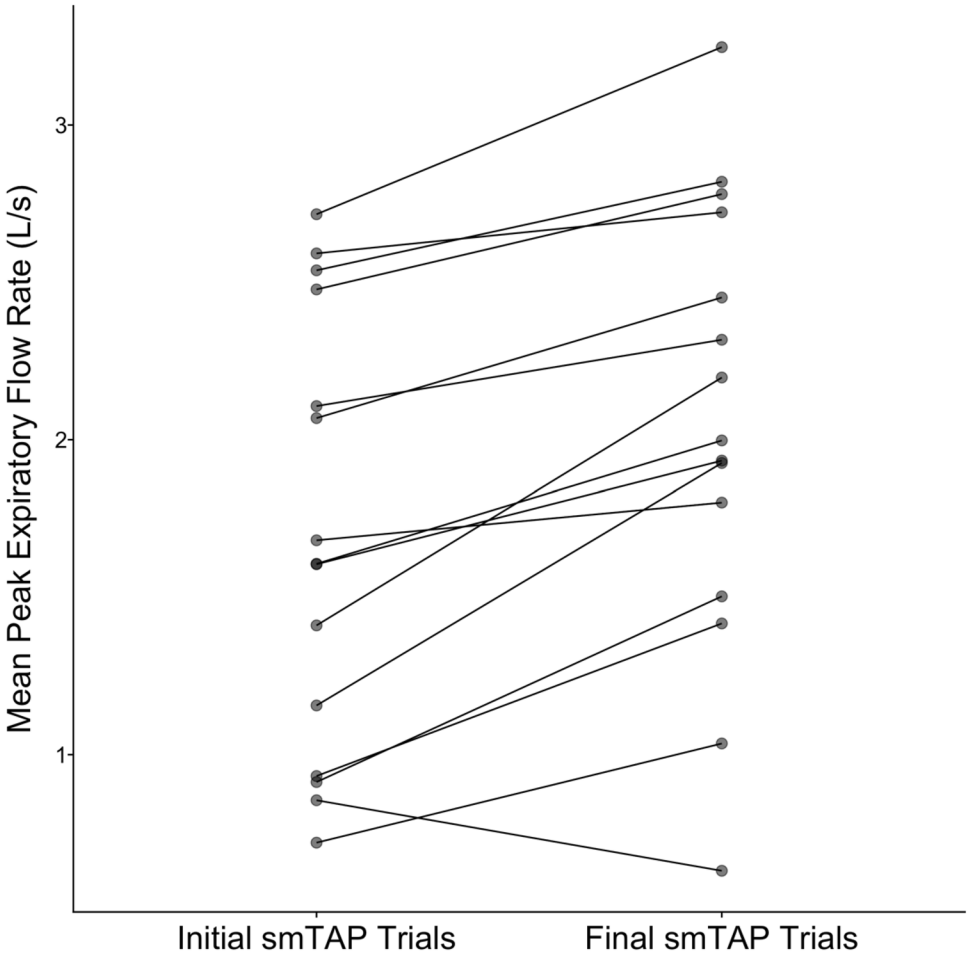

Fig. 2 Peak expiratory flow rate across initial and final smTAP trials. Note: Data points represent individual participants

majority of participants demonstrated improvements in the magnitude and consistency of cough airflow. Specifically, 11 (73%) participants demonstrated improvements in both mean PEFR airflow and variability, while mean CEV airflow and variability improved in 12 (80%) participants.

Inter-rater reliability was 'excellent' for measures of PEFR, CVA, CIV, and CEV (ICCs = 0.99, 0.95, 0.93, and 0.90, respectively), 'good' for PEFRT (ICC = 0.87), and 'moderate' for CPD (ICC = 0.68). Intra-rater reliability was 'excellent' for all airflow measures (ICC > 0.95). CrTot inter-rater reliability was 'substantial' ($\kappa = 0.62$) and intra-rater reliability was 'almost perfect' ($\kappa = 0.97$). PAS inter-rater reliability was 'substantial' ($\kappa = 0.78$, 77% absolute agreement) and intra-rater reliability was 'almost perfect' ($\kappa = 0.87$, 89% absolute agreement).

Discussion

Aspiration pneumonia is a leading cause of death in PSP due to a high prevalence of cough and swallowing dysfunction [13]. A robust and consistent cough response is important to expel aspirate material from the airways to maintain pulmonary health [26]. There is evidence to suggest that healthy young adults, healthy older adults, and people with Parkinson's disease are able to modify cough airflow with cueing in the presence of a cough inducing stimuli [16, 17]. However, there had been no studies examining whether people with PSP could upregulate their cough. The present study demonstrated that individuals with PSP were able to complete the upregulation task central to smTAP, supporting the feasibility of this treatment approach in this patient population. Specifically, increased peak expiratory flow rate (PEFR), inspiratory volume (IV), and compression phase duration (CPD), as well as reduced variability of PEFR and cough expired volume (CEV) were evident after a single session of smTAP. These findings contribute to a growing body of literature suggesting that many individuals with dystussia due to neurodegenerative disease have the potential to upregulate cough function via supramedullary control.

The treatment paradigm, smTAP, was designed to incorporate multiple components that are thought to facilitate upregulation of cough function. These components targeted both sensory and motor aspects of cough, including a

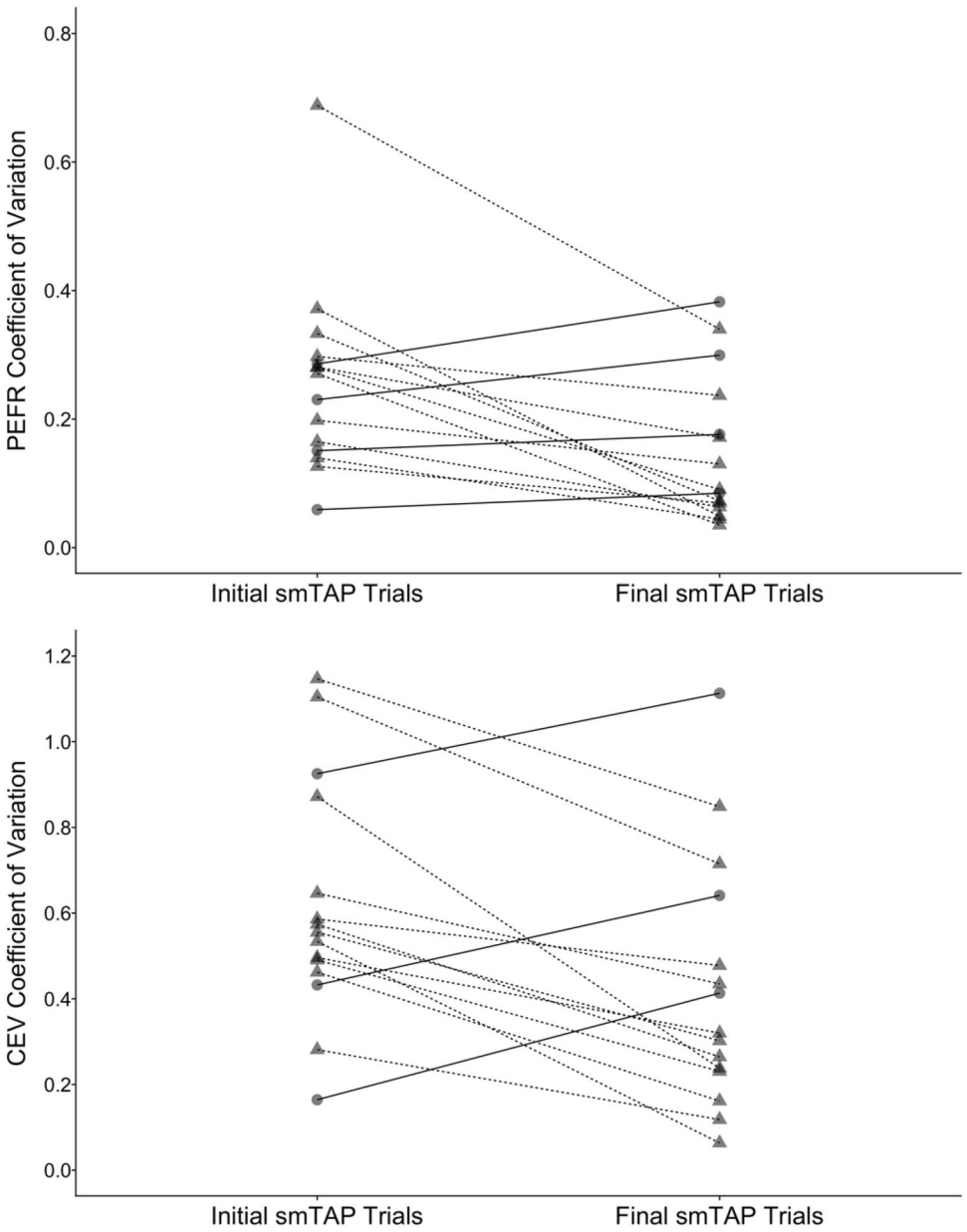

Fig. 3 Variability of peak expiratory flow (PEFR) and cough expired volume (CEV) across initial and final smTAP trials. Note: Dashed lines indicate reduced variability; triangles indicate improvements in both cough effectiveness and variability. Data points represent individual participants

salient sensory stimulus, visual biofeedback, verbal cueing, and awareness of the urge-to-cough [16, 17]. Our results showed that a background subthreshold sensory stimulus alone did not result in immediate changes to cough airflow in this patient population. Persons with PSP benefitted from a combination of a sensory stimulus with repeated trials and ongoing sensory and motor feedback via visual biofeedback and emphasis on the awareness of the urge-to-cough. Treatment paradigms that involve a salient sensory context for cough execution to rehabilitate neuromotor control and coordination via a skill-based approach appear to have utility for cough rehabilitation in PSP.

Cough effectiveness is essential for airway clearance of aspirate and dysfunction in cough effectiveness is related to adverse health outcomes. Specifically, reduced peak expiratory airflow (PEFR) is a strong predictor of airway invasion in neurodegenerative populations [31–34], and has been associated with pulmonary complications and morbidity in individuals with dysphagia [35], making it a clear and important treatment target to improve health outcomes. At baseline, the individuals with PSP in this study demonstrated reduced cough strength (i.e., PEFR) as compared to prior studies with healthy younger and older adults [36–38]. Furthermore, our findings suggest that PEFR subsequently increased during a single session of smTAP among individuals with PSP. Participants were able to quickly modulate and upregulate their cough motor output across relatively few repetitions during a novel task, with the majority showing

improvements of more than 10% in PEFR. Given that healthy adults show relatively consistent PEFR across repetitions [39, 40], this increase could be attributed to motor learning and not merely variability across the task. However, this requires further study. Results also showed that individuals with PSP significantly increased the volume of inspired air (IV) and duration of glottic closure (CPD) across smTAP trials. In this manner, participants not only showed improvements in cough effectiveness, but also the underlying airflow components which facilitate expiratory airflow. However, it should be noted that effect sizes were small to moderate, potentially due to the limitation of a single session. Overall, results suggest that individuals with PSP have the ability to complete the upregulation task central to this treatment paradigm, similar to healthy young adults, healthy older adults, and people with Parkinson's disease [16, 17].

Variability is an important aspect of motor learning, reflecting changes in the central organization of motor systems to produce voluntary movements [41]. As a skill is acquired, variability in achieving the target goal gradually decreases with practice [42]. Clinically, consistently performing an effective cough (i.e., reduced variability) may be advantageous to repeatedly expel aspirate and promote airway clearance. Persons with PSP demonstrated elevated variability of cough airflow, specifically PEFR and CEV variability, during the initial trials of smTAP. This is likely due to both the novelty of smTAP, as well as characteristic neurodegenerative changes to structures implicated in sensory integration and neuromotor control, such as the basal ganglia, cerebellum, and brainstem [1]. Variability significantly decreased across smTAP trials, suggesting that participants improved the consistency of motor output. Moreover, the majority of participants improved *both* the consistency and effectiveness of their cough. Given that a robust and consistent cough response is required to expel material from the airways, it is promising that persons with PSP were able to consistently upregulate cough motor output with training. Future cough rehabilitation paradigms should continue to examine variability to better understand motor control strategies underlying learning and task generalization.

There are several limitations that warrant discussion. A post-mortem neuropathological examination is required for a definitive diagnosis of PSP; however, our diagnoses were performed based on the most recent clinical diagnostic criteria from the Movement Disorders Society [23]. Additionally, our sample was predominantly comprised of the Richardson's syndrome subtype of PSP, so the immediate effects of the treatment paradigm might not be generalizable across all subtypes of PSP. However, participants with predominant Parkinsonism and frontal presentation, in addition to Richardson's syndrome, also showed improvements, suggesting that this treatment is feasible with these subtypes. Though smTAP may not be appropriate for all patients, the treatment can potentially be modified for individuals who are unable to cough on command or exhibit hypersensitivity to capsaicin. For example, an increased dosage of capsaicin may be used in cases where individuals have difficulty initiating a voluntary cough. Notably, the participants in the present study who were unable to perform a voluntary cough were able to execute a cough when the background capsaicin stimuli were provided during smTAP. In cases where individuals exhibit hypersensitivity to capsaicin, the background capsaicin stimulus can be eliminated and potentially voluntary cough skill training with biofeedback can be used to target cough upregulation [43]. Additionally, the length of time between participants' baseline evaluation and smTAP was not standardized and could have impacted our findings. It is also plausible that repeated exposure to capsaicin may have introduced a habituation effect in our cohort. However, capsaicin has demonstrated adequate reproducibility within one doubling concentration for reflex cough sensitivity [24] and consistent responses have been observed across multiple patient populations (e.g., [19, 38, 44]). Notably, it is also promising that the present study's results showed improvements despite this potential confound, though future research will be necessary to determine whether a habituation effect exists and to better understand the relative effects of sensory and motor components of this treatment paradigm. Finally, the present study was limited to one smTAP session, did not include a control group, and did not examine potential effects on swallowing function or individual predictors of treatment success. Given that this study was designed to assess feasibility and ability to complete the smTAP task over a single session, changes in swallowing were not examined nor expected. Future studies will be needed to test the impact of multiple sessions and a longer duration of smTAP on cough, swallowing, and associated health outcomes, as well as individual predictors of patient success within this treatment paradigm.

Conclusion

Cough has been identified as an important and clinically relevant therapeutic target in multiple patient populations who are at elevated risk for pulmonary compromise due to deficits in airway protection [19, 31–34, 44]. This prospective study demonstrated reduced voluntary cough function and improvements in cough effectiveness and consistency in a cohort of individuals with PSP after a single session of smTAP. These findings are promising in that they highlight the feasibility of people with PSP to participate in smTAP and highlight their potential to improve sensorimotor cough function in a short period of time.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00455-021-10251-1.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all participants prior to enrollment in this research study.

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