

## Research Article

# Motor Performance During Sensorimotor Training for Airway Protection in Parkinson's Disease

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## ABSTRACT

**Introduction:** Cough dysfunction is highly prevalent in Parkinson's disease (PD) and associated with pneumonia, a leading cause of death. Although research suggests that cough can be volitionally upregulated, patterns of improvements that occur during cough skill training and potential correlates remain unexamined. Therefore, we sought to characterize changes to peak flow during cough skill training, examine whether early variability predicted motor performance trajectories during treatment, and explore the relationship between peak flow during cough skill training and motor learning on a similar but untrained task (i.e., reflex cough testing).

**Method:** This secondary analysis of treatment data from a randomized controlled trial included 28 individuals with PD who participated in five sessions of sensorimotor training for airway protection (smTAP). During this novel cough skill training, participants completed 25 repetitions of coughs targeting peak flow 25% above their baseline. Reflex and voluntary cough testing was performed pre- and posttreatment. Bayesian multilevel growth curve models provided group and individual-level estimates of peak flow during training.

**Results:** The magnitude and consistency of peak flow increased during cough skill training. Variability in peak flow during the first treatment session was associated with greater improvements to peak flow in later sessions. There was no relationship between changes to peak flow during cough skill training and motor learning.

**Conclusions:** Individuals with PD improved the strength and variability of cough peak flow during cough skill training. These findings provide a clinically relevant characterization of motor performance during cough skill training and lend insight into potential correlates to guide future treatment paradigms.

Cough is a sensorimotor airway protective behavior that functions to remove foreign material and secretions from the airways by generating shearing forces during expulsive airflow (Foster, 2002). In Parkinson's disease (PD), voluntary and reflex cough dysfunction (dystussia) is highly prevalent, commonly co-occurring with impairments to swallowing safety (Pitts et al., 2008; Troche et al., 2016). An ineffective reflex cough impedes the timely clearance of penetrant or aspirate material but can be difficult to address in treatment. Voluntary cough, often prescribed as compensation in individuals with

dysphagia, may be a more feasible clinical target. Additionally, voluntary cough airflow outcomes, such as peak expiratory flow rate (i.e., PEF or peak flow), have been associated with cough effectiveness to clear aspiration from the subglottis—making it a clinically meaningful target (Borders & Troche, 2022). With that being said, it is important to recognize that along with their shared substrates, voluntary cough and reflex cough also exhibit important neurophysiological and mechanistic differences, indicating that the nature and severity of impairments may vary between them (Mills et al., 2017). Moreover, these cough types exist along a continuum, suggesting that there is not a clear demarcation between them (Troche et al., 2014). Therefore, it is important to avoid the assumption that observations from reflex cough will directly transfer to voluntary cough or vice versa.

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Although traditionally considered a purely reflexive behavior (Eccles, 2009), induced cough (i.e., nonvoluntary) can be volitionally modified and upregulated with cueing (Brandimore et al., 2017; Hegland et al., 2012). This finding has also been extended to multiple treatment sessions with improvements to both voluntary and reflex cough outcomes in a PD cohort after five sessions of a novel sensorimotor cough skill training (Troche et al., 2023). These studies demonstrate the safety and efficacy of cough skill training approaches, highlighting the clinical relevance of treating both cough and swallowing in individuals with airway protective dysfunction (Curtis et al., 2020; Sevitz et al., 2022).

An effective cough requires precise coordination across three phases, specifically inspiration, compression of laryngeal and airway structures (e.g., true vocal folds, laryngeal vestibule, and subglottis), and forceful expiration (Dicpinigaitis, 2009; Hillel, 2001; Kim et al., 2023), as well as flexibility to perform and manipulate this behavior in a variety of contexts with different degrees of motor output (e.g., throat clear, single, or sequential cough). Like walking, cough can be disrupted due to aging, injury, or disease, requiring the relearning of various cough-related skills, such as modifying respiratory or laryngeal subsystems (Turnbull & Wall, 1989; VanSwearingen & Studenski, 2014). In this sense, coughing can be viewed as a complex sensorimotor skilled behavior that necessitates the process of reacquisition via motor learning for rehabilitation.

Improving the accuracy and efficiency of performing a motor skill, such as voluntary or reflex cough, with continued practice is known as motor skill learning (Willingham, 1998) and is characterized by two distinct components: motor performance and motor learning. In the context of cough skill training, motor performance refers to the ability to execute a cough on a *trained* task during treatment (e.g., in the presence of a subthreshold sensory stimulus or with cueing from a clinician). In this context, motor performance can be measured by monitoring the pattern and rate of change that occurs during cough skill training on an outcome of clinical importance (e.g., peak flow). Improvements to cough on a similar, but *untrained* task (e.g., reflex cough testing), on the other hand, is indicative of motor learning (Magill & Anderson, 2017). Importantly, motor performance represents real-time changes in cough skill reacquisition, whereas motor learning may indicate the ability to execute a cough in a variety of environments or task demands.

Although inconsistent performance of a motor skill is often viewed as disadvantageous, recent research has posited that trial-by-trial variations in movements may provide valuable insight into one's capability to adapt (Sánchez et al., 2017). Thus, early variability during cough skill training may reflect one's exploration of different

motor control strategies, such as increasing lung volume, prolonging vocal fold closure, or modifying the strength or timing of the cough. This variability may then facilitate the acquisition of an optimal motor solution to achieve an effective cough (Davids et al., 2003; Wu et al., 2014). Although trialing different strategies presumably results in elevated initial variability in the desired outcome (i.e., high peak flow), consistency should improve in subsequent trials once a solution strategy has been refined. Therefore, baseline variability and changes to variability during cough skill training are important outcomes when monitoring motor performance and motor learning.

Despite its importance as a potential indicator of skill reacquisition, changes to peak flow during cough skill training (i.e., motor performance) remain unexamined. It is also unclear whether early variability during treatment, which might reflect task exploration, predicts motor performance trajectories during treatment. Finally, although previous studies have reported improvements in motor learning following cough skill training (Troche et al., 2023), the influence of motor performance trajectories during training on motor learning outcomes remains unexplored. We sought to address these questions through four aims; specifically, we aimed to (a) characterize the pattern and rates of change to peak flow during cough skill training, (b) quantify changes in the variability of peak flow during cough skill training, (c) determine whether variability in the first treatment session predicted changes to peak flow in later sessions, and (d) explore the relationship between peak flow changes during cough skill training and motor learning on a similar, but untrained task after treatment. These aims were accomplished through a secondary analysis of treatment data from a randomized controlled trial examining the safety and efficacy of a novel cough skill training paradigm—sensorimotor training for airway protection (smTAP; Troche et al., 2023). We hypothesized that the magnitude and variability of peak flow would improve during cough skill training, that initial variability in the first treatment session would predict changes to peak flow in later sessions, and that the rate of change to peak flow during cough skill training would be associated with motor learning.

## Method

### Study Design and Participants

This study is a secondary analysis of data from a randomized controlled trial of individuals with PD that were randomized to receive Expiratory Muscle Strength Training or smTAP and completed five sessions of this treatment across 5 weeks (Troche et al., 2023). Inclusion

criteria for the RCT were a diagnosis of PD based on the UK Brain Bank criteria (Daniel & Lees, 1993), a penetration–aspiration scale score > 2 at baseline (10 and 90 ml of thin liquid boluses; Rosenbek et al., 1996), maximal voluntary cough peak flow < 5 L/s at baseline, and not actively receiving swallowing therapy. Participants with other neurological disorders (e.g., multiple sclerosis and stroke), cognitive decline (i.e., a score of less than 23 on the Montreal Cognitive Assessment; Nasreddine et al., 2005), and a history of head and neck cancer, breathing disorders or diseases (e.g., chronic obstructive pulmonary disease), smoking in the past 5 years, or uncontrolled hypertension were excluded. For this secondary analysis, inclusion criteria included (a) randomly assigned to the smTAP group in the RCT and (b) completing both pre- and postassessments.

### **Reflex Cough Testing**

To assess motor learning, reflex cough testing was performed pre- and posttreatment. A face mask covering the nose and mouth was connected to a pneumotachograph, differential pressure transducer, and a side port with a one-way inspiratory valve that connected to a nebulizer (ADInstruments, Inc.). This nebulizer deVillbiss T-piece was connected to a dosimeter that delivered an aerosolized solution of saline or capsaicin. Prior to data collection, the pneumotachograph airflow signal was calibrated by injecting a known volume of air (3 L) with a calibration syringe (Vacumetrics, Inc.). Cough airflow data were then inputted into a Power Lab data acquisition system, digitized, low-pass filtered at 50 Hz via LabChart software (LabChart 8; ADInstruments, Inc.), and recorded to a computer. During reflex cough testing, participants were seated for an initial 45 s of quiet breathing; then presented with three randomized blocks of 0, 50, 100, and 200  $\mu$ M dissolved in a vehicle solution (80% physiological saline and 20% ethanol); and instructed to “cough if you need to” prior to delivery. Participants were provided with at least 1-min rest between each trial, asked to rate their urge-to-cough on a modified Borg scale, and provided water to drink between trials.

### **Voluntary Cough Testing**

Sequential voluntary cough testing was performed pre- and posttreatment with an identical spirometry setup as reflex cough testing, but without the presentation of any sensory stimulus. During voluntary cough testing, participants were instructed to “cough as if something went down the wrong pipe,” after which the clinician provided a model of a three-cough epoch. As described in the Statistical Analysis section below, baseline voluntary cough peak flow was included as a covariate in the third aim.

### **Cough Skill Training (smTAP)**

During cough skill training (smTAP), participants were seated at a computer with the same spirometry setup used for reflex cough testing and presented with a background dose of subthreshold capsaicin, defined as a concentration that was half that of their reflex cough threshold from baseline reflex cough testing. Following presentation of the subthreshold sensory stimulus, participants were instructed to direct their attention to 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 average peak expiratory flow rate based on the participant’s cough threshold (e.g., 200  $\mu$ M) from baseline reflex cough testing to promote improvements in reflex cough. Participants completed 25 repetitions (five sets of five repetitions) of sequential voluntary coughs during each smTAP session and were provided water after each trial. Feedback regarding both the knowledge of performance and results was provided from the clinician. Knowledge of results included feedback on whether peak flow was above the target line, whereas knowledge of performance included information related to the inspiratory phase (e.g., deeper breath in before coughing), compression phase (e.g., the phase was too long, too short, or required a Valsalva to increase vocal fold adduction), and expulsive phase (e.g., cough longer, harder, faster, or with more force). Feedback was provided on 100% of trials for the first half of each treatment session, with feedback decreasing to 50% for the second half of the session. Participants completed one session of smTAP weekly for 5 weeks with an additional 4 days of home practice each week. Home practice involved producing a single voluntary cough into a handheld peak flow meter 4 days per week with five sets of five repetitions daily. A home practice target was set 25% above baseline average voluntary cough peak flow and re-adjusted weekly to promote improvements in voluntary cough function and to support clinical translation and implementation.

### **Data Analysis**

The primary outcome was peak expiratory flow rate (i.e., PEFR or peak flow, L/s), defined as the peak airflow achieved during the expiratory phase of cough and measured from the first cough in each cough epoch. All aims used peak flow obtained from weekly smTAP treatment sessions as the outcome. The third aim included an additional covariate of peak flow from the baseline voluntary cough assessment and the fourth aim included a covariate of reflex cough peak flow at baseline and a fixed effect of reflex cough peak flow at postassessment (as described in more detail in the Statistical Analysis section below).

Home practice data were not included in these analyses. Measurement of peak flow for baseline, treatment, and postassessment time points was blindly completed by the first author. For inter- and intrarater reliability, 20% of coughs were re-analyzed by the primary rater and an additional trained research assistant. Both raters were blinded to participant and treatment session. The coefficient of variation was calculated for each set (i.e., every five trials) to examine changes to variability during cough skill training. To determine whether variability in the first session of cough skill training predicted later motor performance, the coefficient of variation was calculated from the first treatment session. Because most participants ( $n = 26$ ) demonstrated at least one 2-cough response to 200- $\mu\text{M}$  capsaicin at baseline, this suprathreshold presentation of capsaicin was used for reflex cough testing analyses. Motor performance was defined as changes to peak flow on the trained task during smTAP. Motor learning was defined as improvements from pre- to postassessment on a similar, but untrained task, specifically the presentation of 200  $\mu\text{M}$  during reflex cough testing.

## Statistical Analysis

In this study, we used Bayesian analyses to achieve our aims. Briefly, a Bayesian approach requires specification of uncertainty about each parameter in the model prior to analysis, also known as a prior distribution. The statistical model then combines the data with the prior to obtain a posterior distribution, which represents the distribution of plausible parameter values conditioned on the data and prior. These posterior distributions can then be summarized with a point estimate (i.e., median) and credible interval (CI; i.e., 95%), which represent the probability that a parameter falls within a given range or direction. In the context of this study, a Bayesian approach afforded three important benefits. First, it allowed us to determine the optimal pattern of change within our data by fitting different models with linear, quadratic, or cubic polynomials. Whereas a linear polynomial assumed that changes to peak flow during treatment increased in only one direction, quadratic and cubic polynomials assumed that patterns of peak flow during treatment changed direction either once (quadratic) or twice (cubic). Second, a Bayesian approach provided flexibility in accounting for a maximal random effect structure, which permitted unique intercepts and slopes for each participant in growth curve models. This provided each participant with a different starting point and rate of change during treatment—essential assumptions in a treatment design. Finally, this approach afforded a range of plausible values for our results, known as a CI. This CI provided the direction and degree of uncertainty in our model estimates (e.g., the rate of change during cough skill training).

For our first aim, our goal was to characterize patterns and rates of change to peak flow during cough skill training at both the group and individual level. We used a Bayesian linear multilevel growth curve model with fixed effects of trial, number of coughs during cough skill training, and their two-way interaction. Random effects included a unique slope and intercept for each participant. Separate nonlinear models with second (quadratic) and third order (cubic) polynomials were also performed. Models were compared with approximate leave-one-out cross-validation (Vehtari et al., 2017). Because the coefficient of variation ranges from 0 to 1, we used a Bayesian beta multilevel growth curve model to accomplish our second aim related to changes in peak flow variability during cough skill training. Fixed and random effects were identical to the model from the first aim, as described above.

To accomplish our third aim, we used a Bayesian nonlinear multilevel growth curve model with a quadratic polynomial for the fixed effect of trial. This model included fixed effects of trial, number of coughs, variability in the first session, and the two-way interaction between trial and first session variability. We also fit an additional model with a covariate of baseline voluntary peak flow to ensure that inferences remained robust when holding this variable constant. We also ran a separate Bayesian beta regression to examine a potential relationship between variability in the first treatment session and baseline peak flow variability. If there was a relationship between these variables, then this would suggest that initial treatment variability is indistinguishable from baseline variability and may not be indicative of task exploration.

For our fourth aim, we performed a similar Bayesian nonlinear multilevel growth curve model, which included fixed effects of trial (quadratic polynomial), number of coughs, posttreatment reflex cough peak flow, and the two-way interaction between trial and posttreatment reflex cough peak flow. Baseline reflex cough peak flow was also included as a covariate to control for baseline performance.

Analyses were performed in R Version 4.0.1 (R Core Team, 2018) with the *brms* package (Bürkner, 2017). Apart from trial number, all fixed effects were mean centered to facilitate the interpretation of model estimates and reduce collinearity between two or more predictor variables. For trial number, 0 represented the first trial of cough skill training. Fixed effects were assigned weakly informative priors with a normal distribution centered at 0, which denoted that we assumed no a priori effects for parameters of interest, and a standard deviation of 1, which constrained physiologically unrealistic effects (i.e., improvements  $> 2$  L/s after each trial). Variance



parameters were assigned a Cauchy distribution with a mean of 0 and sigma of 0.20. Posterior distributions were sampled using Hamiltonian Monte Carlo with four chains and 2,500 post-warm-up samples per chain (Carpenter et al., 2017). All models demonstrated sufficient diagnostic statistics, including posterior predictive checks, the split-half potential scale reduction factor, no divergent transitions, and adequate effective sample size (Gelman et al., 2013). CIs that excluded 0 were considered statistically robust. The posterior probability (PP) for the presence of an effect (i.e., > 0) was also provided.

To understand the impact of prior distributions on the robustness of our inferences, we performed prior sensitivity checks for each model after completing data analysis. This was accomplished by fitting models with more informative (i.e., standard deviation of 0.10) and less informative (i.e., standard deviation of 5) prior distributions and determining whether inferences remained stable (see Appendix A). To estimate inter- and intrarater reliability of peak flow, two-way random effects (single measure and absolute agreement) intraclass correlation (ICC) coefficients were used.

## Results

### Participant Demographics

During cough skill training, 3,028 unique cough trials were included across 28 participants (22 men and six women) with an average of 108 trials ( $SD = 15$ ) per participant (see Appendix B). Participants had an average age of 69.64 years ( $SD = 7.05$ ) and disease duration since diagnosis of 6.88 years ( $SD = 4.56$ ). Most participants (64%) demonstrated a modified Hoehn and Yahr stage of two (see Table 1). Inter- and intrarater reliability showed perfect agreement for measurement of peak flow ( $ICC = 1.00$ ).

### Aim 1: Characterizing the Pattern and Rate of Change in Peak Flow During Cough Skill Training

To characterize peak flow during cough skill training, a quadratic polynomial provided optimal model fit, meaning that peak flow changed direction once during training (see Table 2). Average peak flow at the start of cough skill training was 2.68 L/s (95% CI [2.23, 3.14]), which increased by 0.38 L/s in the first treatment session, 0.29 L/s in the second session, 0.16 L/s in the third session, and 0.06 L/s in the fourth session (see Figure 1). The linear slope plateaued at the start of the fifth treatment session, with peak flow decreasing by 0.05 L/s by the end

**Table 1.** Group-level participant demographics.

Measure	<i>N</i> = 28
Age (years)	
<i>M</i> ± <i>SD</i>	69.64 (7.05)
Range	53–81
Sex	
Male	22
Female	6
Montreal Cognitive Assessment	
<i>M</i> ± <i>SD</i>	25.70 (3.45)
Range	16–29
Disease duration from diagnosis (years)	
<i>M</i> ± <i>SD</i>	6.88 (4.56)
Range	0.16–16.30
Disease duration from symptom onset (years)	
Mean ± <i>SD</i>	8.41 (4.86)
Range	0.57–18.50
Modified Hoehn & Yahr Stage	
1	2 (7%)
2	18 (64%)
2.5	1 (4%)
3	4 (14%)
4	3 (11%)

of this session. Number of coughs did not influence changes in peak flow during cough skill training, as evidenced by no statistically robust interaction between number of coughs and trial for linear ( $\beta = -0.0016$ , 95% CI [-0.004, 0.0009], PP = 89%) and quadratic ( $\beta = 0.00002$ , 95% CI [-0.000006, 0.00004], PP = 92%) slopes (see Appendix C). Participants' peak flow at the start of cough skill training did not have a large association with subsequent changes to peak flow during cough skill training (linear  $r = .30$ ; quadratic  $r = -.23$ ). At the individual level, 16 participants increased peak flow by  $\geq 0.25$  L/s after the first treatment session, whereas peak flow decreased for

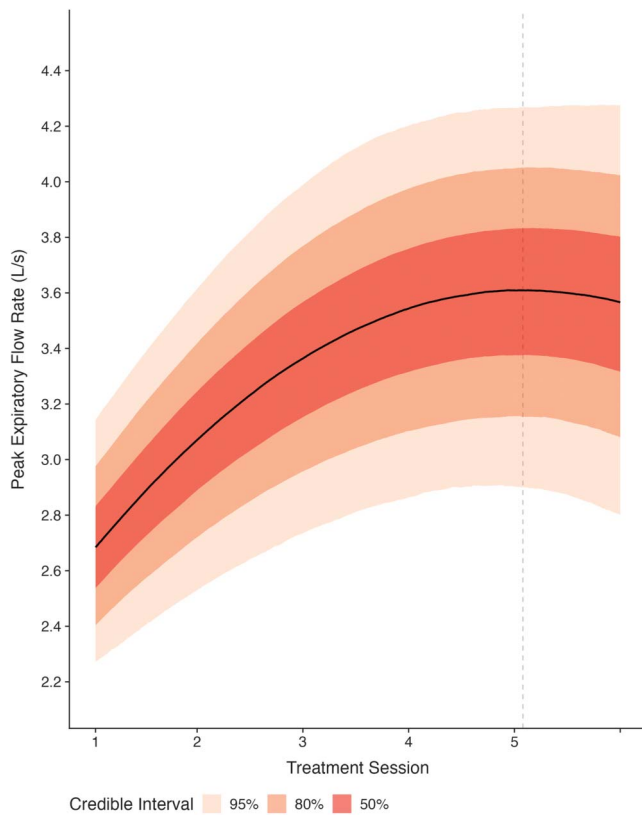
**Table 2.** Model comparisons to determine the pattern of motor performance during cough skill training.

Outcome	Polynomial	ELPD difference	SE difference
Peak flow	Quadratic <sup>a</sup>	0	0
	Linear	-159.20	31.40
	Cubic	-3,015.40	79.30
Peak flow variability	Cubic <sup>a</sup>	0	0
	Quadratic	-4.30	2.20
	Linear	-5.40	4.70

Note. ELPD = expected log pointwise predictive density; SE = standard error. Models are ordered by best fit as determined by leave-one-out cross-validation. ELPD difference is the difference in expected log pointwise predictive density for two models. SE difference is the standard error of the difference.

<sup>a</sup>The optimal model fit.

**Figure 1.** Group-level model-based estimates of peak flow motor performance during cough skill training. The dotted line represents the point where the linear slope plateaus and the quadratic slopes take effect. Credible intervals represent ranges containing a given percentage of probable group-level values of peak flow motor performance. Group-level slopes are shown when holding average number of coughs constant across trials.



three participants (see Figure 2). Most participants demonstrated more than a 0.25 L/s increase in peak flow by the end of the second ( $n = 20$ ) and third ( $n = 24$ ) sessions. Across in-person treatment sessions for the entire cohort, peak flow was above the treatment target for 35.90% of trials for the first session, 53.20% for the second session, 56.40% for the third session, 55.80% for the fourth session, and 52.40% for the fifth session (see Appendix D).

### **Aim 2: Quantifying Changes in Peak Flow Variability During Cough Skill Training**

A cubic polynomial provided the best overall model fit to characterize peak flow variability during cough skill training, meaning that peak flow variability changed direction twice during training (see Table 2). On average, peak flow variability was 18.30% (95% CI [15%, 21%]) on the first set of cough skill training, which then decreased by 4.80% in the first treatment session (to 13.50% variability) and 2.10% in the second session (to 11.40%

variability). Variability then slightly increased by 0.10% from the middle of the third treatment session throughout the fourth session (to 11.50% variability), with a final decrease of 1.05% in the fifth session (to 10.45% variability; see Figure 3). Number of coughs did not influence changes in peak flow variability during cough skill training, as evidenced by no statistically robust interaction between number of coughs and trial for linear ( $\beta = 0.018$ , 95% CI [-0.05, 0.08], PP = 71%), quadratic ( $\beta = -0.002$ , 95% CI [-0.009, 0.004], PP = 76%), or cubic polynomials ( $\beta = 0.00006$ , 95% CI [-0.0001, 0.0003], PP = 74%). At the individual level, all participants decreased peak flow variability from pre- to posttreatment with 24 participants demonstrating more than a 5% reduction (see Appendix E).

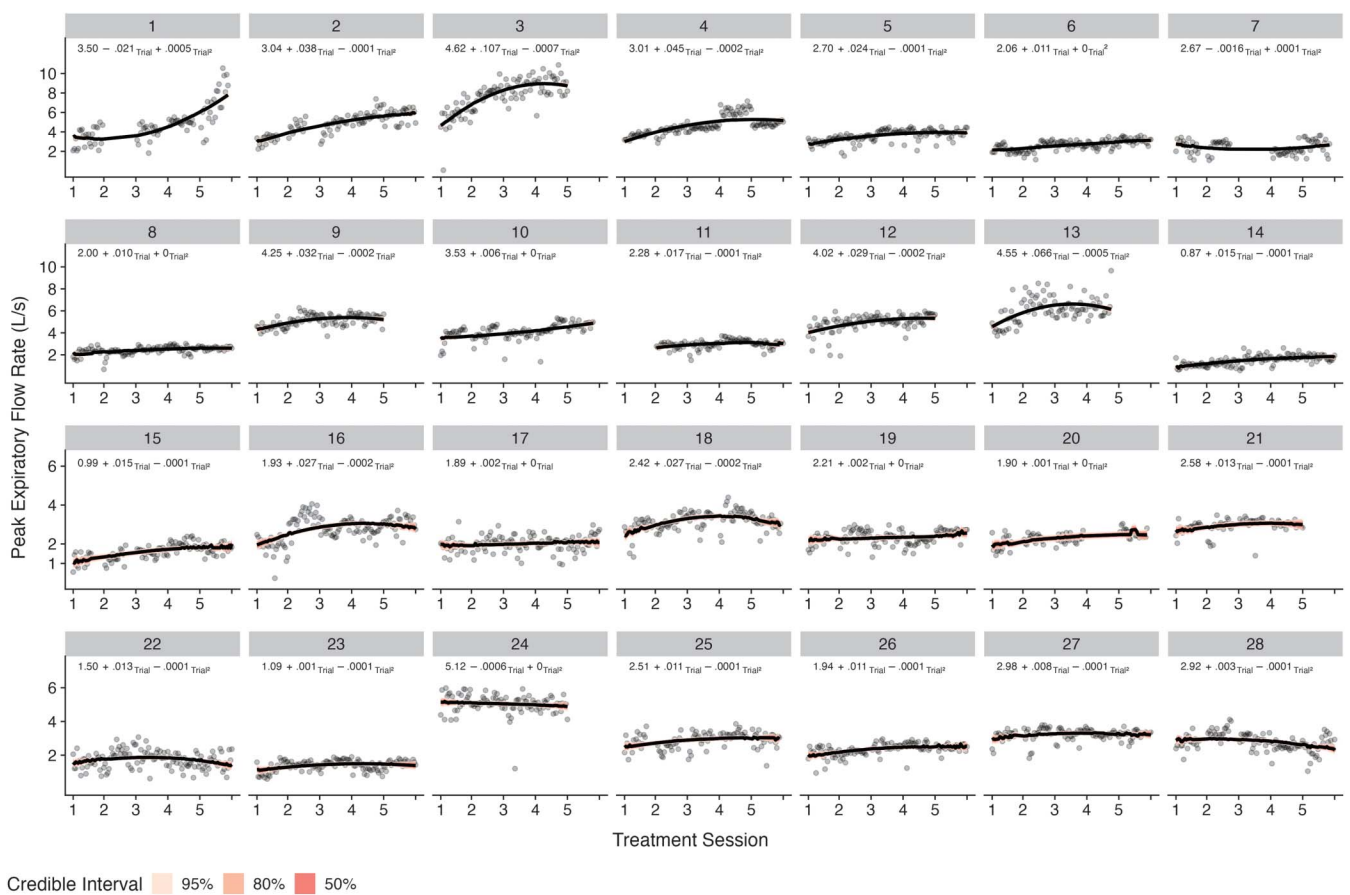
### **Aim 3: Examining Whether Variability in the First Treatment Session Predicts Peak Flow Changes in Later Cough Skill Training Sessions**

Participants with higher variability in the first treatment session demonstrated increased peak flow in later treatment sessions (linear  $\beta = -0.117$ , 95% CI [-0.199, -0.041], PP = 99.70%; quadratic  $\beta = 0.0015$ , 95% CI [0.0006, 0.0024], PP = 99.80%). Specifically, participants with higher variability in the first treatment session initially demonstrated lower rates of change to peak flow; however, this slope became steeper during the fourth treatment session, resulting in higher peak flow for these participants by the end of the treatment (see Figure 4). This interaction remained statistically robust (linear  $\beta = -0.114$ , 95% CI [-0.19, -0.04], PP = 99.88%; quadratic  $\beta = 0.014$ , 95% CI [0.0005, 0.002], PP = 99.90%) when baseline voluntary peak flow was included as an additional covariate in this model. Additionally, we found no statistically robust relationship between variability in the first treatment session and baseline voluntary peak flow variability ( $\beta = 0.37$ , 95% CI [-0.53, 1.25], PP = 80%).

### **Aim 4: Exploring the Relationship Between Changes to Peak Flow During Cough Skill Training and Motor Learning**

Participants with steeper linear improvements in peak flow during cough skill training demonstrated higher reflex cough peak flow at postassessment (i.e., increased motor learning) when controlling for number of coughs and baseline reflex cough peak flow (linear  $\beta = 0.009$ , 95% CI [-0.0003, 0.019], PP = 97.21%). Based on our a priori definition, this interaction was not statistically robust since the CI included 0; however, there was a 97.21% probability for the presence of a positive effect

**Figure 2.** Individual-level model-based estimates of peak flow motor performance during cough skill training. Credible intervals represent ranges containing a given percentage of probable group-level values of peak flow motor performance. Individual-level slopes are shown when holding the average number of coughs constant across trials.



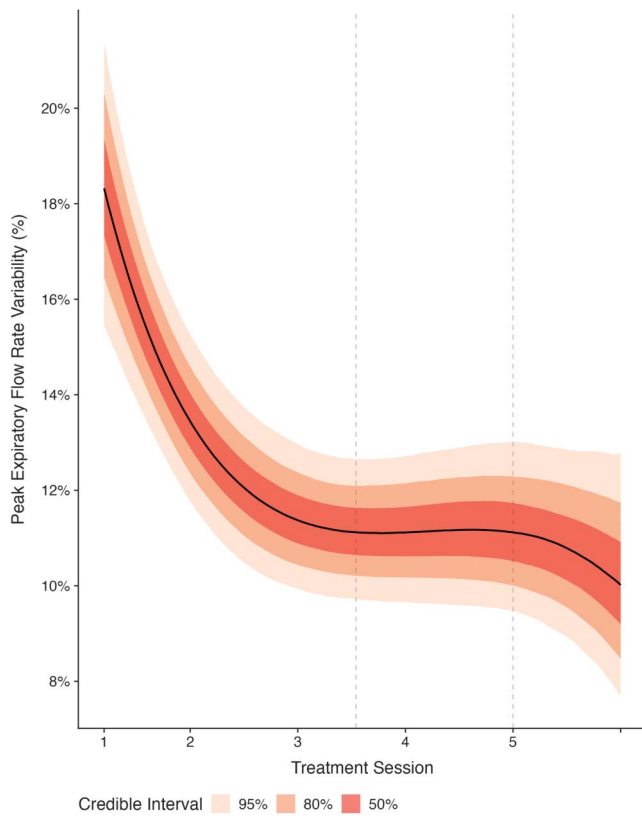
(see Figure 5). Additionally, there was no statistically robust interaction with the quadratic polynomial (quadratic  $\beta = 0.00004$ , 95% CI  $[-0.0001, 0.00005]$ , PP = 82%).

## Discussion

Acquisition of a skilled motor behavior, like coughing, requires repetition and practice. During cough skill training, understanding the pattern and rate of changes to peak flow can provide valuable insight into the acquisition, refinement, and eventual generalization of the motor skill of cough. However, this remains unexamined in the cough literature, limiting our understanding of how individuals with cough dysfunction adapt and respond during cough skill training. Addressing this gap is critical for the ongoing refinement of cough skill training paradigms and is a necessary step toward eventual clinical implementation. Therefore, this study sought to characterize changes in the pattern, rate, and variability of peak flow during five

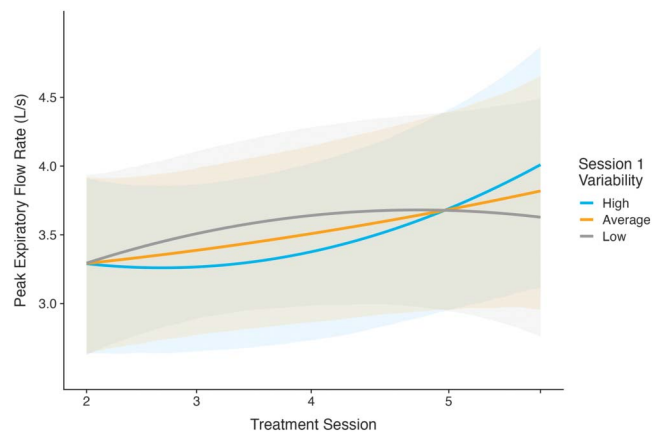
sessions of a weekly cough skill training in individuals with PD. Secondly, we examined whether elevated variability in the first treatment session, which might reflect task exploration, predicted changes to peak flow in later sessions, and whether changes to peak flow during cough skill training were associated with improvements on an untrained reflex cough task (i.e., motor learning). Our results suggest that participants demonstrated improvements in both the strength and consistency of peak flow during cough skill training, and that early variability may be associated with changes to peak flow in later treatment sessions. However, we found no statistically robust relationship between rates of change to peak flow during cough skill training and motor learning (i.e., PEFR improvements on the similar but untrained task of reflex cough testing). Collectively, these findings provide a clinically relevant characterization of patterns and rates of change in peak flow during cough skill training, as well as preliminary evidence that early variability during treatment may correlate with later treatment changes to peak flow.

**Figure 3.** Group-level model-based estimates of peak flow variability during cough skill training. Variability was calculated with the coefficient of variation every five trials; therefore, each session included five variability trials. The dotted line represents shifts in the polynomial. Credible intervals represent ranges containing a given percentage of probable group-level values of peak flow motor performance.



A comprehensive characterization of changes to the strength and consistency of peak flow during cough skill training may advance our understanding of the acquisition and refinement of this skilled motor behavior. Our findings suggest that individuals with PD who participated in 5 weeks of a cough skill training demonstrated an initial increase in peak flow throughout the fourth session, followed by a slight decrease in the final fifth session. Trial-by-trial variability of peak flow, on the other hand, rapidly decreased after two treatment sessions, followed by a period of minimal change in the third and fourth sessions, and an eventual slight decrease in variability in the final fifth session. Together, these findings suggest that motor adaptations occur rapidly during cough skill training, with the largest improvements appreciated at the beginning of treatment. As participants converge on a motor solution to achieve an effective cough in the middle of treatment, peak flow becomes more consistent with small, incremental increases in its strength. It is important to highlight, however, that there were a wide range of

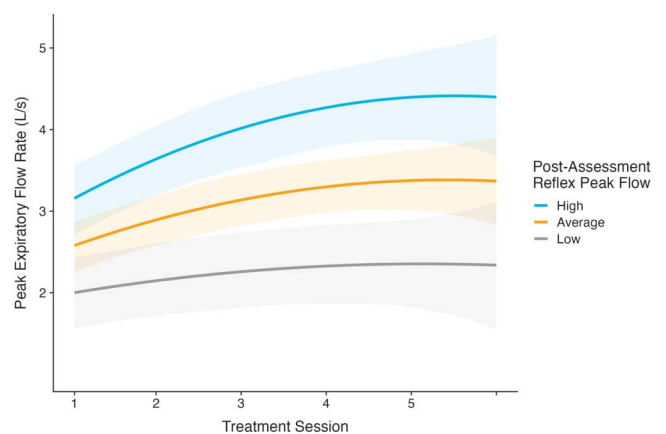
**Figure 4.** The relationship between early task exploration and later changes to peak flow during cough skill training. Session 1 variability was treated as continuous in multilevel growth curve models but is categorized here for visualization purposes. “High” and “low” variability represents 1 SD above and below average variability in the first session, respectively. Model-based slopes shown hold number of coughs constant at its mean. 95% credible intervals surround each categorization.



peak flow patterns and rates of change across participants. Future research should investigate demographic and disease-specific correlates of this between-subject variability during cough skill training.

Although inconsistent performance of a motor skill is often viewed as disadvantageous, recent motor learning frameworks, such as the dynamical systems theory, have posited that variability may instead represent one’s

**Figure 5.** Relationship between changes to peak flow during cough training and motor learning. Reflex cough peak flow at postassessment was treated as continuous in the multilevel growth curve model but is categorized here for visualization purposes. “High” and “low” variability represents 1 SD above and below average reflex cough peak flow at postassessment, respectively. Model-based slopes shown hold number of coughs and baseline reflex cough peak flow constant at their means. Reflex cough peak flow was obtained from 200- $\mu$ M trials. 95% credible intervals are shown around each categorization.





capacity to adapt (Davids et al., 2003; Hossner et al., 2015). In this respect, variability may indicate that a participant is exploring various motor control strategies to upregulate cough during skill training. This task exploration can be driven by the learner, practice conditions in a treatment, or both. Interestingly, our findings suggest that participants exhibiting higher trial-by-trial variability in the first treatment session demonstrated greater changes to peak flow in subsequent sessions. This relationship was not linear; instead, participants with elevated variability in the first treatment session showed an initial decrease in peak flow in the second and third sessions but eventually showed greater improvements in peak flow in the fourth and fifth sessions. However, the specific motor control strategies or adaptations, which participants made over time to facilitate these improvements in peak flow, are unknown. Therefore, future research will be necessary to characterize the contribution of respiratory and laryngeal subsystems to cough upregulation during cough skill training, as well as examine the effects of treatment paradigms that explicitly manipulate practice conditions to facilitate task exploration (Magill & Hall, 1990). Overall, these findings provide preliminary support for the concept that variability is not necessarily unfavorable during cough skill training and may be a key component to rehabilitate cough dysfunction.

One of the primary goals of rehabilitation is the retention and generalization of a motor skill to untrained tasks. From the perspective of cough skill training, motor learning for reflex cough ensures that an effective cough can be performed under a variety of conditions and environments including airway invasion, thereby successfully integrating the behavior into daily life. Although improvements to motor learning have been recently established after cough skill training (Troche et al., 2023), whether changes to peak flow *during* training can lend insight into motor learning outcomes remains unexplored. Although the CI for this result included 0, it is promising that we found such a high probability (97.21%) for the presence of a positive relationship between motor performance during training and motor learning. This high probability suggests that there is preliminary evidence for a relationship between performance and learning, such that improved motor performance during training may confer greater improvements in motor learning. Because reflex cough is often diminished in PD and necessary to promote airway clearance (Troche et al., 2016), identifying predictors of improvements to both sensory and motor components of cough in the context of a similar but untrained task (i.e., reflex cough testing) is of high-clinical importance. Future research will be necessary to determine the presence and magnitude of this relationship, as well as identify additional treatment predictors of motor learning, such as demographic, task-specific, or mechanistic variables,

which may demonstrate a stronger association with generalization and carryover effects after cough skill training.

This study is not without limitations. Because cough is a skill embedded within a sensorimotor behavior, we are unable to fully disentangle the influence of sensory input versus motor coordination. Cough skill training has the potential to influence a wide range of similar but untrained tasks, which we did not measure in this study. The operationalization of motor learning as improvements on reflex cough testing may have influenced our results; however, we believe that reflex cough fits the criteria of a “similar but untrained task” in relation to the trained task during smTAP, because it involves a different magnitude of the same type of sensory stimulus. The cough skill training paradigm in this study (i.e., smTAP) incorporated both sensory and motor components, and it remains unclear how each component contributed to observed changes in peak flow during training. Future research designed to determine the impact of specific sensory or motor practice conditions on skill reacquisition and cough upregulation is necessary. Repeated exposure to capsaicin and frequent coughing may pose risks to patients. However, no adverse events, such as phonotraumatic vocal fold lesions or bowing, were reported after smTAP across all participants (Doruk et al., 2023; Troche et al., 2023). Implementing practices such as regular breaks and offering water between trials may help mitigate these potential risks (Chung et al., 2009). Although the present investigation focused on changes to peak flow across five smTAP sessions, variability in adherence to the home practice regimen may have influenced cough outcomes. However, adequate adherence was reported in the larger randomized controlled trial (Troche et al., 2023). Finally, it is possible that variability during the first treatment session may have been unrelated to task exploration, instead merely representing inconsistency in one’s ability to perform an effective and coordinated cough, although we found no relationship between baseline variability and variability in the first treatment session. Treatment paradigms that explicitly incorporate variable practice will require future investigation to adequately describe relationships between task exploration, skill reacquisition, and learning. Although the frequency of feedback was standardized, the type of cueing provided by the clinician during smTAP was not standardized and may have impacted early variability. Future research on the effects of different amounts and types of cues is clearly warranted.

## Conclusions

The ability to execute a trained task during treatment (i.e., motor performance) and generalize this

performance to similar but untrained tasks (i.e., motor learning) is an important component of rehabilitation. However, patterns and rates of change to peak flow during cough skill training, as well as potential correlates of motor performance and learning, remain unexamined among individuals with cough dysfunction. Findings from this study suggest that individuals with PD increased the strength and consistency of cough peak flow across five sessions of a novel sensorimotor cough skill training. Additionally, elevated variability in the first treatment session may have contributed to peak flow improvements in later sessions, potentially due to early exploration of various motor control strategies to upregulate cough. These findings suggest that important, rapid adaptations occur during cough skill training among individuals with PD, which may be increased by promoting task exploration during treatment.

## Author Contributions

**James C. Borders:** Conceptualization, Data curation, Formal analysis, Software, Visualization, Writing – original draft, Writing – review & editing. **Karen W. Hegland:** Funding acquisition, Investigation, Methodology, Resources, Writing – review & editing. **Nora Vanegas-Arroyave:** Investigation, Writing – review & editing. **Michelle S. Troche:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Compliance With Ethical Standards

**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. Approval was obtained from the institutional review board.

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

## Acknowledgments

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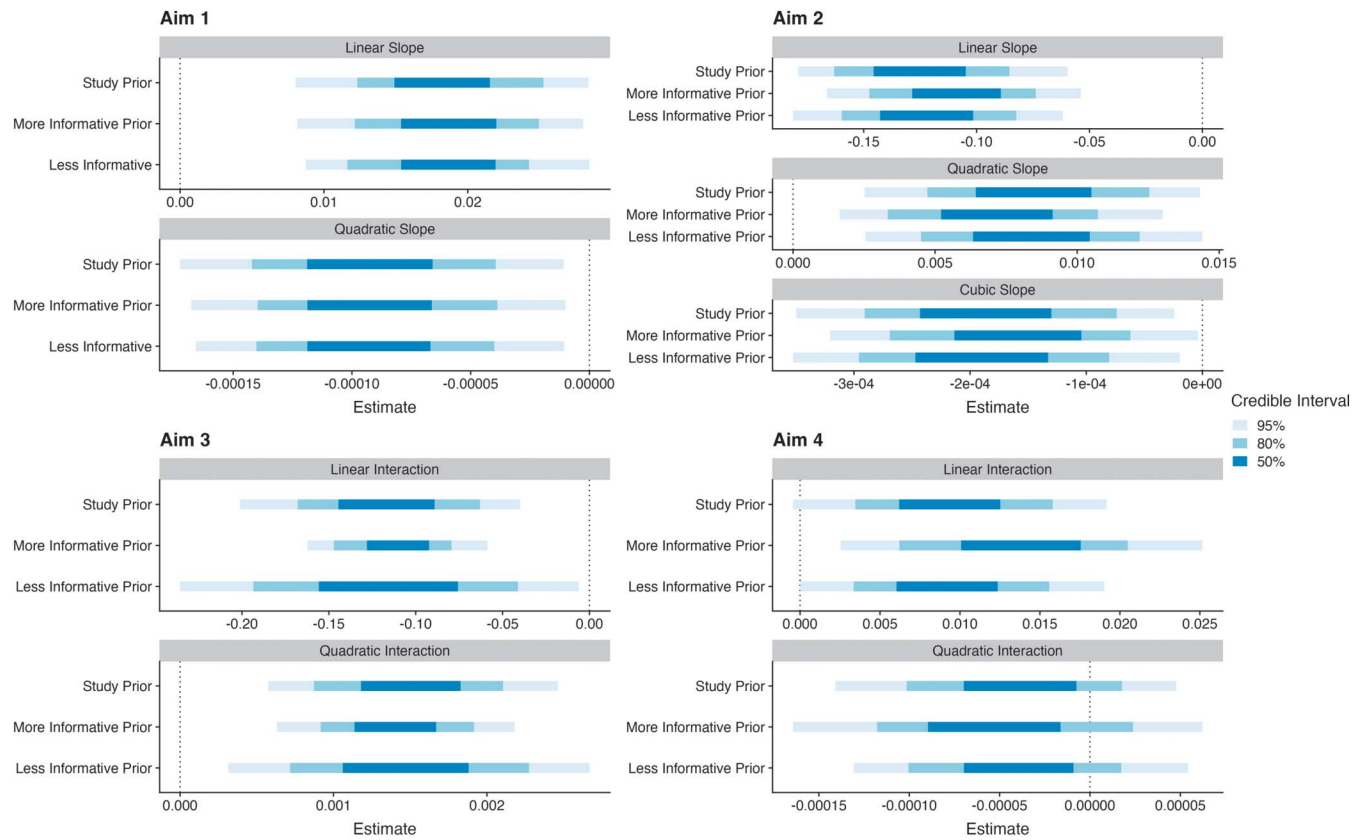
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## Appendix A

### Bayesian Prior Sensitivity Analysis



Note. "Study prior" denotes a Gaussian (i.e., normal) distribution with a mean of 0 and standard deviation of 1. "More informative prior" denotes a Gaussian distribution with a mean of 0 and standard deviation of 0.10. "Less informative prior" denotes a Gaussian distribution with a mean of 0 and standard deviation of 5. Note that all alternative prior distributions demonstrated similar inferences (i.e., excluded 0 in the 95% credible interval) compared with the prior distribution used in this study apart from the linear interaction in the fourth aim.



## Appendix B

### Participant Trial Frequencies Across Cough Skill Training Treatment Sessions

ID	Session number				
	1	2	3	4	5
1	24	0	19	20	22
2	17	14	22	25	25
3	25	25	25	25	0
4	20	25	25	25	25
5	25	25	25	25	25
6	25	25	25	25	25
7	19	18	0	25	21
8	25	25	25	24	25
9	25	25	25	25	0
10	20	20	22	23	20
11	0	23	25	24	25
12	25	25	25	25	0
13	24	25	24	19	0
14	25	25	25	25	25
15	15	17	25	25	25
16	25	25	25	25	25
17	20	25	24	25	25
18	23	25	20	25	23
19	19	25	25	24	25
20	16	16	22	0	22
21	20	21	20	25	0
22	25	25	25	25	25
23	25	25	25	25	25
24	25	25	25	25	0
25	18	20	20	21	22
26	25	21	25	21	25
27	19	22	25	25	25
28	19	19	25	25	25

Note. Missing data for ID 11, Session 1 was due to researcher data loss. All other instances of missing data were due to participants not completing trials.

## Appendix C

### Bayesian Multilevel Model Results

Aim 1						
Fixed effects	Estimate	95% CI	Random effects (SD)	Estimate	Random effects (correlation)	Estimate
Intercept	2.68	[2.23, 3.14]	Intercept	1.16	Intercept & Trial	0.30
Trial	0.018	[0.007, 0.028]	Trial	0.026	Intercept & Trial <sup>2</sup>	-0.23
Trial <sup>2</sup>	-0.00009	[-0.00017, -0.00001]	Trial <sup>2</sup>	0.0002	Trial & Trial <sup>2</sup>	-0.91
CrTot	0.052	[-0.012, 0.115]				
Trial × CrTot	-0.0017	[-0.004, 0.0009]				
Trial <sup>2</sup> × CrTot	0.00001	[-0.00001, 0.00004]				
Aim 2						
Fixed effects	Estimate	95% CI	Random effects (SD)	Estimate	Random effects (correlation)	Estimate
Intercept	-1.50	[-1.70, -1.31]	Intercept	0.34	Intercept & Trial	-0.17
Trial	-0.12	[-0.18, -0.06]	Trial	0.009	Intercept & Trial <sup>2</sup>	0.09
Trial <sup>2</sup>	0.008	[0.002, 0.014]	Trial <sup>2</sup>	0.0005	Intercept & Trial <sup>3</sup>	0.26
Trial <sup>3</sup>	-0.0001	[-0.0004, -0.00002]	Trial <sup>3</sup>	0.00002	Trial & Trial <sup>2</sup>	-0.15
CrTot	0.005	[-0.16, 0.17]			Trial & Trial <sup>3</sup>	-0.12
Trial × CrTot	0.018	[-0.05, 0.08]			Trial <sup>2</sup> & Trial <sup>3</sup>	-0.17
Trial <sup>2</sup> × CrTot	-0.002	[-0.009, 0.004]				
Trial <sup>3</sup> × CrTot	0.00006	[-0.0001, 0.0003]				
Aim 3						
Fixed effects	Estimate	95% CI	Random effects (SD)	Estimate	Random effects (correlation)	Estimate
Intercept	3.29	[2.64, 3.92]	Intercept	1.69	Intercept & Trial	-0.29
Trial	0.004	[-0.009, 0.015]	Trial	0.03	Intercept & Trial <sup>2</sup>	0.39
Trial <sup>2</sup>	0.00002	[-0.0001, 0.0002]	Trial <sup>2</sup>	0.0003	Trial & Trial <sup>2</sup>	-0.95
Session 1 Variability	-0.034	[-1.56, 1.60]				
CrTot	0.17	[-0.009, 0.04]				
Trial × Session 1 Variability	-0.118	[-0.20, -0.04]				
Trial <sup>2</sup> × Session 1 Variability	0.0015	[0.0006, 0.002]				
Aim 4						
Fixed effects	Estimate	95% CI	Random effects (SD)	Estimate	Random effects (correlation)	Estimate
Intercept	2.54	[2.24, 2.83]	Intercept	0.69	Intercept & Trial	-0.18
Trial	0.014	[0.006, 0.023]	Trial	0.018	Intercept & Trial <sup>2</sup>	0.04
Trial <sup>2</sup>	-0.00007	[-0.0001, 0.00001]	Trial <sup>2</sup>	0.0002	Trial & Trial <sup>2</sup>	-0.89
Pre-Assessment Reflex Peak Flow	0.30	[-0.05, 0.63]				
Post-Assessment Reflex Peak Flow	0.71	[0.32, 1.07]				
CrTot	0.026	[0.01, 0.05]				
Trial × Post-Assessment Reflex Peak Flow	0.009	[-0.0003, 0.019]				
Trial <sup>2</sup> × Post-Assessment Reflex Peak Flow	-0.00004	[-0.0001, 0.00005]				

Note. All models are Bayesian linear models, except for Aim 2 (Bayesian beta regression). In the beta regression model, estimates are presented on the logit scale. Superscript numbers represent quadratic (<sup>2</sup>) or cubic (<sup>3</sup>) polynomials for the fixed effect of trial. CI = credible interval; CrTot = number of coughs.

## Appendix D

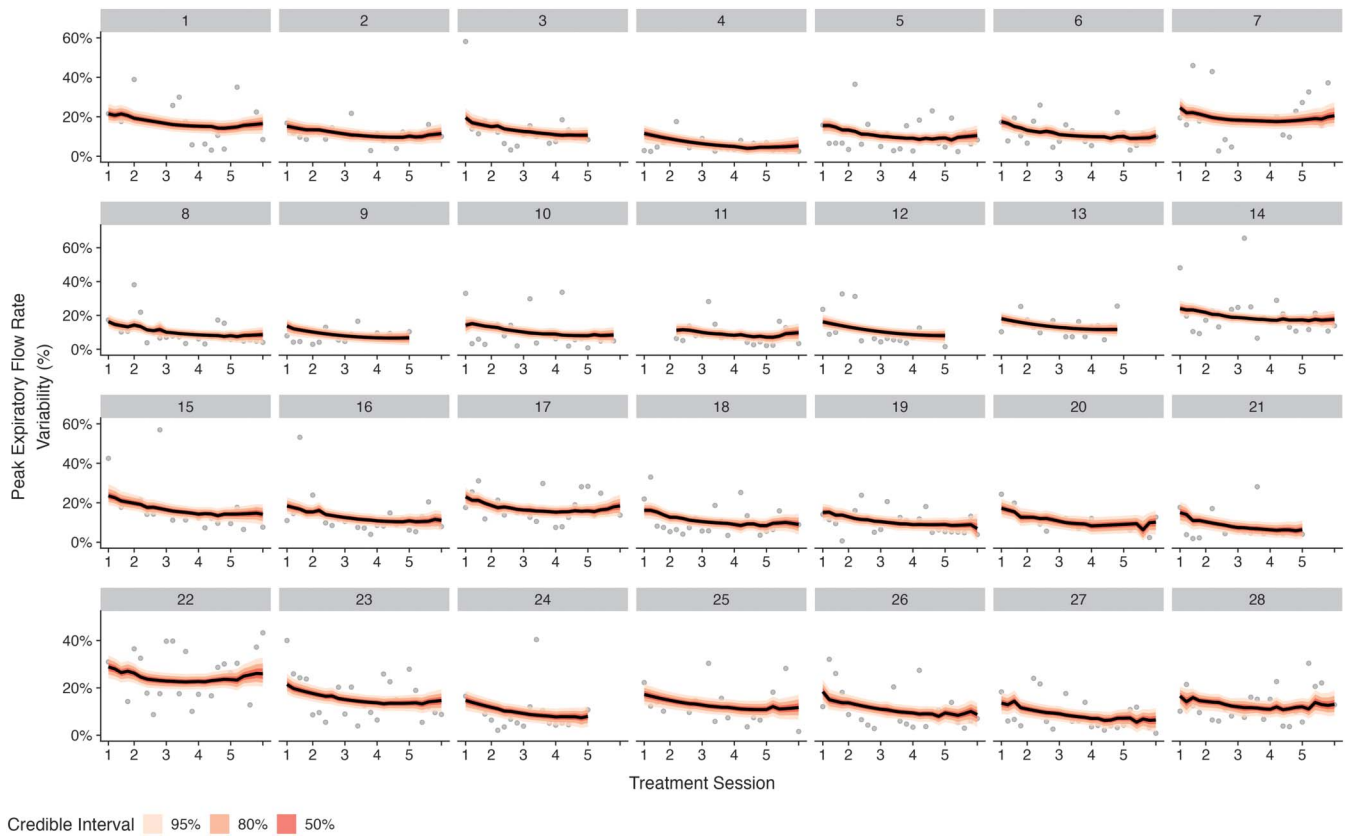
### Percentage of Trials Above Treatment Target During Cough Skill Training

ID	Target (L/s)	Session number				
		1	2	3	4	5
1	4.40	20.80%	N/A	36.80%	95%	90.90%
2	3.77	5.88%	92.90%	81.80%	100%	100%
3	5.63	60%	100%	100%	100%	N/A
4	3.00	100%	96%	100%	100%	100%
5	3.00	60%	80%	96%	92%	92%
6	2.50	24%	56%	80%	72%	100%
7	2.60	52.60%	66.70%	N/A	4.00%	71.40%
8	2.00	76%	80%	100%	91.70%	100%
9	5.73	0%	24%	16%	18%	N/A
10	4.00	45%	45%	31.80%	78.30%	100%
11	3.50	N/A	0%	0%	25%	0%
12	5.76	4%	0%	8%	8%	N/A
13	6.24	8.33%	76%	33.30%	52.60%	N/A
14	1.50	4%	20%	76%	92%	88%
15	1.90	0%	5.88%	4%	60%	24%
16	2.61	0%	96%	72%	76%	92%
17	2.00	40%	68%	54.20%	64%	52%
18	3.80	0%	0%	0%	28%	0%
19	2.39	15.80%	72%	36%	4.17%	96%
20	2.50	12.50%	12.50%	18.20%	N/A	54.60%
21	2.94	25%	52.40%	95%	72%	N/A
22	2.55	0%	20%	8%	0%	0%
23	1.84	4%	0%	8%	0%	0%
24	4.94	72%	88%	52%	60%	N/A
25	3.30	11.10%	5%	20%	28.60%	9.09%
26	3.00	0%	0%	0%	0%	0%
27	3.04	73.70%	77.30%	80%	96%	80%
28	3.70	0%	15.80%	0%	0%	0%

Note. N/A indicates missing data. L/s = liters per second.

## Appendix E

### Individual-Level Estimates of Peak Flow Variability During Cough Skill Training



Note. Credible intervals represent ranges containing a given percentage of probable group-level values of peak flow motor performance. Individual-level slopes are shown when holding the average number of coughs constant across trials.