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Feedback and Feedforward Auditory-Motor Processes for Voice and Articulation in Parkinson's Disease

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ABSTRACT

Purpose: Unexpected and sustained manipulations of auditory feedback during speech production result in "reflexive" and "adaptive" responses, which can shed light on feedback and feedforward auditory-motor control processes, respectively. Persons with Parkinson's disease (PwPD) have shown aberrant reflexive and adaptive responses, but responses appear to differ for control of vocal and articulatory features. However, these responses have not been examined for both voice and articulation in the same speakers and with respect to auditory acuity and functional speech outcomes (speech intelligibility and naturalness).
Method: Here, 28 PwPD on their typical dopaminergic medication schedule and 28 age-, sex-, and hearing-matched controls completed tasks yielding reflexive and adaptive responses as well as auditory acuity for both vocal and articulatory features.
Results: No group differences were found for any measures of auditory-motor control, conflicting with prior findings in PwPD while off medication. Auditory-motor measures were also compared with listener ratings of speech function: first formant frequency acuity was related to speech intelligibility, whereas adaptive responses to vocal fundamental frequency manipulations were related to speech naturalness.
Conclusions: These results support that auditory-motor processes for both voice and articulatory features are intact for PwPD receiving medication. This work is also the first to suggest associations between measures of auditory-motor control and speech intelligibility and naturalness.

Over 90% of persons with Parkinson's disease (PwPD) develop the motor speech disorder hypokinetic dysarthria, involving impairments in the respiratory, vocal, and articulatory features of speech (Broadfoot et al., 2019). Recent findings implicate disruptions to auditory-motor processing in PwPD, which may contribute to these speech deficits (Liu et al., 2012; Mollaei et al., 2013, 2019).

Auditory-motor processing involves the combination of feedback and feedforward control systems of speech and can be examined by creating an experimentally generated "error" in auditory feedback. Unexpected perturbations in feedback (yielding "reflexive"[1] responses) allow for assessment of the feedback control system, which detects errors and generates corrective motor plans (Tourville &

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[1]*Reflexive:* The term *reflexive* refers here to automatic responses to auditory manipulations and is adopted from the "pitch shift reflex" literature. It is not meant to imply that the responses are mediated subcortically.

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Guenther, 2011). When speech errors are sustained over time, the feedforward control system is responsible for updating the motor plan based on the corrective commands from the feedback system. Sustained perturbations in feedback (yielding "adaptive" responses) allow for assessment of these updates to the feedforward control system. Experimentally, reflexive responses are elicited by sudden changes in auditory feedback within an utterance, whereas adaptive responses are elicited by gradual increases in perturbation that are held over the course of several vocalizations (Jones & Keough, 2008; Lester-Smith et al., 2020; Wang et al., 2019). Both reflexive and adaptive modifications to auditory feedback yield robust responses in speakers with typical speech, in which they compensate by opposing the direction of the perturbation for both vocal and articulatory features of speech (Abur et al., 2018; Burnett et al., 1998; Cai et al., 2011; Villacorta et al., 2007). Furthermore, auditory acuity to speech may relate to error detection (Villacorta et al., 2007), and the relationship between auditory-motor impairments and listener perceptions of speech (functional speech outcomes) in PwPD is unclear. Although diverse deficits have been implicated in feedback and feedforward control of speech in PwPD, they have not been examined in the same speakers and with respect to acuity and functional speech outcomes.

The time course of speech symptoms in PwPD appears to be disparate for vocal and articulatory features of speech (Skodda et al., 2013), suggesting that their underlying auditory-motor bases may also differ (supported by Mollaei et al., 2016). For voice, perturbations of fundamental frequency (f_o; the acoustic correlate of vocal pitch) are often used to examine auditory-motor processes. For articulatory features of speech, perturbations are typically applied to the first formant frequency (F_1), altering the vowel identity. Relative to controls, PwPD demonstrate greater reflexive f_o responses while off medication (Liu et al., 2012) but no differences in magnitude when on medication (Kiran & Larson, 2001), reduced reflexive F_1 responses while off medication (Mollaei et al., 2016), reduced adaptive f_o responses while on medication (Abur et al., 2018), and reduced adaptive F_1 responses while off medication (Mollaei et al., 2013). However, variable methodology, sample sizes (groups of 9–16), and medication status across studies make it difficult to interpret differences between vocal and articulatory features of speech. Additionally, consideration of cognition, hearing ability, and musicality have been inconsistent, despite their known impacts on auditory-motor processes (Moore et al., 2006; Pekkonen et al., 2001; Zarate & Zatorre, 2005).

Assessing auditory acuity when examining auditory-motor control processes in PwPD may provide additional insight: The ability to detect errors in self-generated speech (reflected in acuity measures) could relate to auditory-motor function (Villacorta et al., 2007). When judging their own voice, PwPD off medication demonstrated worse passive (listening) F_1 acuity but comparable passive f_o acuity compared with controls (Mollaei et al., 2019). However, during "active" acuity tasks, involving judgments about perturbations while actively voicing, the same PwPD showed no differences in F_1 acuity and better f_o acuity compared with controls. Actively voicing during an acuity task is likely to influence results due to evidence that cortical activity differs for voicing compared with listening tasks involving auditory perturbations (Behroozmand et al., 2009; Chang et al., 2013), supporting the differing findings for active and passive acuity in PwPD. However, the results of Mollaei et al. (2019) also suggest differing trends for active and passive acuity by speech domain. Differences in acuity by speech domain were also found in a study in young adults by Lester-Smith et al. (2020): F_1 acuity was better for a passive compared with an active task, but f_o acuity was better in an active compared with a passive task. Thus, measurements of passive acuity and active acuity, for both voice f_o and vowel F_1, require investigation in PwPD to inform the specific nature of auditory sensory disruptions.

To better characterize auditory-motor deficits in PwPD, reflexive and adaptive responses must be examined in concert with auditory acuity, for both vocal and articulatory features of speech, while considering confounding factors and functional speech outcomes. Additionally, it is crucial to examine these auditory-motor processes in PwPD as they present typically in daily life; for the majority of PwPD, this means receiving medication for the treatment of motor symptoms (Karlsen et al., 2000). Prior work has almost exclusively characterized feedback and feedforward auditory-motor processes in PwPD while off medication (Chen et al., 2013; Liu et al., 2012; Mollaei et al., 2013, 2016, 2019), with the exception of two studies examining speakers receiving typical medication in modest cohorts (Abur et al., 2018; Kiran & Larson, 2001). There is substantial evidence from the literature that acoustic measures of speech and functional speech outcomes do not improve with dopaminergic medication for PwPD (De Letter et al., 2006; Goberman & Blomgren, 2003; Goberman et al., 2002; Ho et al., 2008; Plowman-Prine et al., 2009; Skodda et al., 2010, 2011; Spencer et al., 2009), supporting that speech symptoms in PwPD persist in the medicated state. However, auditory-motor control has not been clearly characterized in the medicated state, so it is necessary to examine the measures of auditory-motor processes in PwPD receiving medication to fully understand the implications for daily communication.

This work reports reflexive responses, adaptive responses, and acuity to f_o and F_1 in the same PwPD (on typical medication) and controls. On the basis of prior findings in PwPD reviewed earlier (Abur et al., 2018; Kiran & Larson, 2001; Mollaei et al., 2016, 2019), we hypothesized: *H1*: Reflexive f_o responses would not differ in PwPD, whereas the adaptive f_o responses would be reduced in PwPD compared with controls; *H2*: Relative to controls, both reflexive and adaptive F_1 responses would be reduced in PwPD; *H3*: Auditory acuity to F_1 would be worse in PwPD compared with controls, but there would be no group differences in f_o acuity. In both groups, we expected better f_o acuity for active (while speaking) compared with passive (listening) and worse F_1 acuity for active compared with passive (based on prior findings; Lester-Smith et al., 2020). Lastly, we investigated whether auditory-motor measures were related to functional speech outcomes: listener perception of speech intelligibility and naturalness. Given previous investigations of the relationships between listener perception and speech acoustics (Anand & Stepp, 2015; Yorkston et al., 1990), we hypothesized: *H4*: Measures involving voice features would be more strongly related to naturalness, whereas measures involving articulatory features would be more strongly related to intelligibility.

Method

Participants

Twenty-eight cisgender PwPD (11 women and 17 men) aged 45–73 years (M = 61.9 years, SD = 7.8 years) participated (see Table 1). Twenty-eight sex-, gender-, and hearing-matched individuals aged 48–81 years (M = 63.9 years, SD = 8.5 years) participated as controls (see Table 2). Groups were approximately matched for participants who reported musical training (formal training post–high school; n = 6 controls and n = 7 PwPD) since musicality has been found to influence adaptive responses (Jones & Keough, 2008), reflexive responses (Wang et al., 2019), and auditory acuity (Micheyl et al., 2006). Because of the possible impact of cognition and hearing on auditory processing (Pekkonen et al., 1994; Pichora-Fuller & Souza, 2003), participants completed the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) and underwent hearing threshold testing using a Grason-Stadler GSI 18 audiometer. MoCA scores are listed in Tables 1 and 2. In both groups, 24 participants had hearing thresholds within the normal range for older adults (using a 25-dB HL cutoff at 1000 Hz and below and a 40-dB HL cutoff above 1000 Hz; Schow, 1991). The remaining four participants had one frequency that did not meet the threshold criteria and were hearing matched across groups. No participants wore hearing aids. A blinded voice-specializing speech-language pathologist rated overall severity of dysphonia for each participant (via Consensus Auditory-Perceptual Evaluation of Voice; Kempster et al., 2009).

In the PwPD group, all participants included in the study were diagnosed with idiopathic Parkinson's disease by a neurologist. All PwPD were receiving medication and were not asked to change their typical medication cycle to maintain ecological validity and examine speech symptoms as they would present in daily life. PwPD completed Part I to Part III of the Movement Disorder Society–Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) to determine motor severity and classify motor phenotype (Stebbins et al., 2013). Control participants denied any neurological, speech, hearing, cognitive, or language disorders.

Five cisgender participants aged 18–29 years (four women and one man) and with no experience rating disordered speech completed listener ratings. All listeners denied a history of speech, language, hearing, or neurological conditions and passed a standard hearing screening (using a 25-dB HL cutoff at all tested frequencies; American Speech-Language-Hearing Association, 2005).

All study participants completed informed consent in compliance with the Boston University Institutional Review Board. All participants were native English speakers.

Data Collection

Data were collected in a sound-attenuated booth across two study sessions, each lasting 2–3 hr. Speech was recorded using a Shure omnidirectional MX153 microphone, and auditory feedback was administered via Etymotic ER-2 insert earphones. Experimental shifts in voice f_o were applied using the setup detailed in Heller Murray et al. (2019), with a processing delay ranging 10–30 ms (see Figure 1). Shifts in the vowel F_1 were achieved using Audapter 2.1 software (Cai et al., 2008) with a processing delay of approximately 20 ms. Before each experimental session, the earphone intensity output from the software and hardware systems was calibrated using a 2-cc coupler (Type 4946, Bruel and Kjaer Inc) and a sound level meter (Type 2250A with a Type 4947 ½″ Pressure Field Microphone, Bruel and Kjaer). For the active tasks (adaptive responses, reflexive responses, and active acuity to f_o and F_1), the earphone intensity was calibrated with an amplification of +5 dB relative to the microphone (see left panel of Figure 1). For the passive tasks (passive acuity to f_o and F_1), the same equipment was used to calibrate earphone output to be 75 dB SPL, regardless of the intensity of the speaker's voice recording (see right panel of Figure 1).

All participants completed the experimental tasks in the following order: speech adaptation, passive acuity, active acuity, sentence reading, and speech reflex. Reflex tasks were completed at the end of the study due to the clear presence of auditory perturbations. Speech feature (f_o or F_1) order for each task was counterbalanced across

Table 1. Participant information for persons with Parkinson's disease (PwPD).

Speaker	Age	Sex	Years since dx	Motor phenotype	MDS-UPDRS PIII	MoCA	CAPE-V
PwPD01	60	F	6	TD	47	28	6.6
PwPD02	70	F	4	TD	37	21	6.8
PwPD03	72	M	7	TD	22	26	13.1
PwPD04	60	M	7	TD	54	24	18.5
PwPD05	49	M	7	TD	47	29	3.4
PwPD06	54	F	6	PIGD	36	24	7.4
PwPD07	63	F	14	PIGD	38	29	6.6
PwPD08	73	M	4	TD	63	29	10.3
PwPD09	66	F	9	PIGD	45	28	2.3
PwPD10	46	M	10	TD	75	27	8.8
PwPD11	69	M	2	PIGD	64	28	10.8
PwPD12	45	M	10	PIGD	51	21	10
PwPD13	67	M	13	TD	76	29	12
PwPD14	50	M	1	TD	17	28	5.7
PwPD15	65	F	1	PIGD	20	29	2.8
PwPD16	67	F	3	TD	52	26	8
PwPD17	68	F	3	PIGD	55	26	7.7
PwPD18	55	M	21	Ind	49	27	19.1
PwPD19	62	M	3	TD	50	26	21.4
PwPD20	55	M	2	TD	26	28	14.8
PwPD21	67	M	4	Ind	63	26	2.6
PwPD22	61	F	9	TD	34	27	9.7
PwPD23	59	M	2	PIGD	38	26	8
PwPD24	62	M	12	PIGD	47	28	33.6
PwPD25	72	M	2	TD	23	25	4.6
PwPD26	68	M	6	TD	38	28	4.6
PwPD27	65	F	10	PIGD	48	29	16.8
PwPD28	63	F	9	PIGD	60	29	34.5

Note. Age (in years), sex (F = female, M = male), years since diagnosis (dx), Movement Disorder Society–Sponsored Revision of the Unified Parkinson's disease rating scale (MDS-UPDRS) Part III motor scores (< 33 indicated mild impairment, and > 59 indicated severe impairment), motor phenotype (TD = tremor dominant, PIGD = postural-insufficiency gait dominant, Ind = indeterminate), Montreal Cognitive Assessment (MoCA) scores (score out of 30), and Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) ratings for percent overall severity (0 = no symptoms and 100 = maximum severity).

participants. The screening procedures, MDS-UPDRS assessment, adaptation tasks, and passive acuity tasks were collected in Session 1. The sentence reading, active acuity tasks, and reflex tasks were collected in Session 2. The sessions were completed at least 1 day apart and up to 41 days apart.

Adaptation and Reflex (Active Tasks)

For the speech adaptation and reflex tasks, speakers were instructed to produce either a sustained /ɑ/ (f_o tasks) or extended versions of the words "bid," "tid," and "hid" (F_1 tasks) for 2–3 s while receiving auditory feedback of their speech (see left panel of Figure 1). The words "bid," "tid," and "hid" were selected as target words for this study because they continued to be real words (i.e., "bed," "Ted," and "head") during upward perturbation of F_1 (Lester-Smith et al., 2020). The three words appeared equally across phases. The intertrial interval was randomly jittered between 1 and 3 s to prevent rhythmic cues. Each task was 108 trials.

Adaptation tasks consisted of four ordered phases: "baseline," 24 trials of unaltered feedback; "ramp," 30 trials with a gradual increase of +3.3 cents in f_o or +1% in F_1 of auditory feedback each trial; "hold," 30 trials with the perturbation maintained at +100 cents or +30% F_1; and "after-effect," 24 trials of unaltered feedback (Lester-Smith et al., 2020; Weerathunge et al., 2020). For voice f_o, speakers also completed additional 108 unperturbed trials ("control condition"; Abur et al., 2018).

For reflex tasks, 84 trials had no perturbations in auditory feedback and 24 trials had perturbations of +100 cents f_o or +30% F_1 applied. For f_o, the perturbation onset occurred randomly between 0.05 and 0.1 s after voicing began to allow the voice to stabilize before the perturbation (Burnett et al., 1997) and persisted until the end of the trial (Weerathunge et al., 2020). For F_1, the perturbations began at voicing onset and persisted until the end of the word (per Tourville et al., 2008). There were at least three unperturbed trials between each perturbed trial to limit habituation.

Auditory Acuity (Passive and Active Tasks)

Participants' acuity to their self-generated f_o and F_1 was assessed using four just-noticeable-difference (JND) experiments. Each JND experiment consisted of an adaptive one-up, two-down staircase procedure with an equal up–down step size to obtain a target threshold of 70.71% (Garcıa-Pérez, 1998).

Table 2. Participant information for speakers in the control group.

Speaker	Age	Sex	MoCA	CAPE-V
C01	68	M	26	9.4
C02	56	M	28	0
C03	77	M	30	11.7
C04	61	F	27	1.4
C05	66	F	28	5
C06	63	M	26	0
C07	80	F	28	12
C08	56	M	29	8.5
C09	81	M	24	13.1
C10	50	M	29	12.5
C11	67	M	24	4.3
C12	61	M	30	0
C13	62	M	29	0
C14	68	F	29	9.1
C15	61	F	29	6.8
C16	48	M	28	16.2
C17	54	F	27	2.8
C18	67	F	29	13.1
C19	59	F	30	4
C20	59	F	29	10
C21	61	F	29	3.4
C22	76	M	30	19.4
C23	68	F	28	7.4
C24	57	M	29	3.7
C25	77	M	23	10.3
C26	61	M	27	10
C27	64	M	23	7.7
C28	62	M	29	5.4

Note. Age (in years), sex (female = F, male = M), Montreal Cognitive Assessment (MoCA) scores (score out of 30), and Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) ratings for percent overall severity (0 = no symptoms and 100 = maximum severity).

Two participant-specific recordings were collected as stimuli for the passive f_o and F_1 acuity tasks, respectively (see right panel of Figure 1). For the passive f_o acuity task, participants were instructed to sustain the vowel /ɑ/ for 2–3 s and the middle 500 ms of the production was extracted for the listening task. For the passive F_1 acuity task, participants were instructed to produce sustained versions of the words "bid," "bed," and "bad" 3 times each. Multiple words were selected as production prompts to prevent participants from expecting to hear the word "bid" during the listening portion. The token with the median F_1 of the three "bid" productions was used as stimuli in the listening task.

For the passive acuity tasks, participants were presented with pairs of /ɑ/ recordings with both 100- and 1000-ms interstimulus intervals (see Abur & Stepp, 2020) and pairs of the word "bid" with a 500-ms interstimulus interval. For each trial, one stimulus was a reference (using the original recording)[2] and the other had a perturbation in f_o or F_1 applied at the onset based on the adaptive procedure. Participants were asked to judge if the two stimuli sounded the "same" or "different." The initial perturbation applied was +50 cents f_o or +40% F_1, with a 4-cent f_o or a 3% F_1 change in direction following two correct responses (decreasing) or one incorrect response (increasing). The sizes of the initial perturbation and perturbation increments during the task were determined during the pilot testing. For 20% of trials ("catch trials"), the reference stimulus was played twice to ensure attention to the task; these trial responses were not used in the adaptive logic. For passive f_o acuity, the average catch trial accuracy was 87.5% (*SD* = 20.6%) for the PwPD group and 87.0% (*SD* = 17.7%) in the control group. For passive F_1 acuity, the average catch trial accuracy was 93.1% (*SD* = 11.7%) for the PwPD group and 95.6% (*SD* = 6.8%) in the control group. The full experiment included either 10 reversals (i.e., changes in the direction) or 60 trials, whichever occurred first.[3]

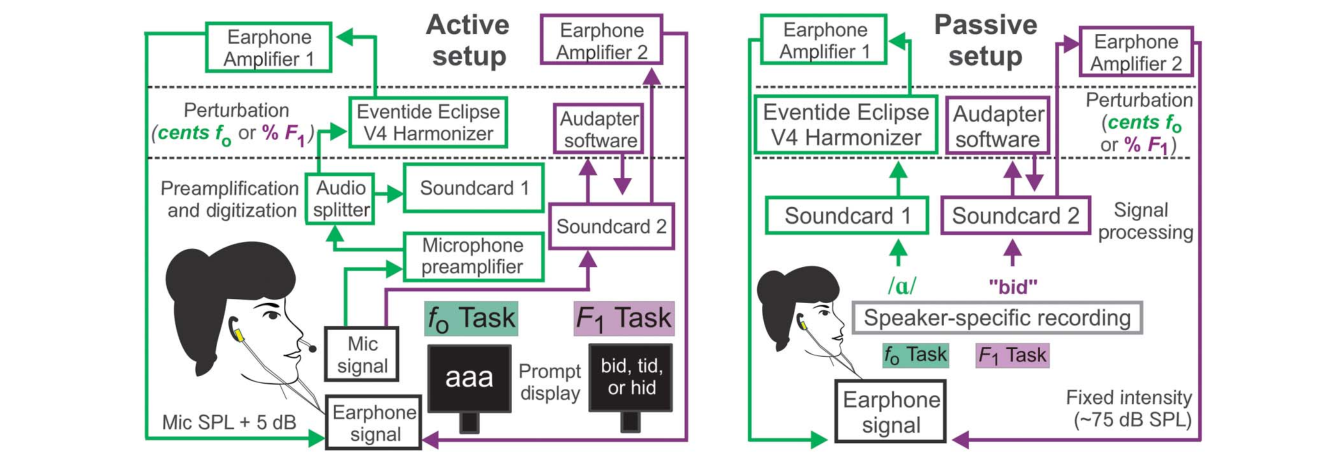
For the active acuity task, participants were instructed to produce the vowel /ɑ/ (for the f_o task) or a prolonged "bid" (for the F_1 task) while receiving real-time auditory feedback of their production (see left panel of Figure 1). Auditory feedback was adaptively perturbed (using the same logic as the passive task) starting at voicing onset and held for the duration of voicing. Participants were asked to judge whether the pitch or the vowel that they heard in their earphones sounded the "same" or "different" than the one they had produced. The initial perturbation was +75 cents f_o or +65% F_1, and the changes were in steps of 6 cents in f0 or 4% in F_1 (also determined during pilot testing). Catch trial frequency was 50% to prevent sensorimotor adaptation to the perturbation, as in prior work (Lester-Smith et al., 2020). For active f_o acuity, the average catch trial accuracy was 78.1% (*SD* = 18.4%) for the PwPD group and 75.3% (*SD* = 23.4%) in the control group. For active F_1 acuity, the average catch trial accuracy was 79.6% (*SD* = 22.3%) for the PwPD group and 81.9% (*SD* = 18.6%) in the control group. The experiment ended after either 10 reversals or 60 trials, whichever occurred first.[4]

[2] *Reference stimulus:* A 1% increase in F_1 was applied to the reference stimuli for the F_1 tasks, so that all signals were processed through Audapter, thus minimizing any perceptual differences other than the magnitude of F_1 perturbation.

[3] *Passive reversals:* For the passive f_o task, participants who reached 60 trials first had an average of 6.7 reversals in the PwPD group and nine reversals in the control group. For the passive F_1 task, participants who reached 60 trials first had an average of 7.5 reversals in the PwPD group and 6.5 reversals in the control group.

[4] *Active reversals:* For the active f_o task, participants who reached 60 trials first had an average of 5.3 reversals in the PwPD group and 5.3 reversals in the control group. For the active F_1 task, participants who reached 60 trials first had an average of 6.1 in the PwPD group and 6.7 reversals in the control group.

Figure 1. Separate hardware and software were used for shifts in voice fundamental frequency (f_o, in green) and vowel first formant (F_1, in purple) for the active (left) and passive (right) setups.



Functional Speech Outcomes

Each participant read a unique, randomly generated Sentence Intelligibility Test[5] (SIT; Beukelman et al., 2007), which have been used in several prior investigations of listener ratings of dysarthric speech (Abur et al., 2019; Beverly et al., 2010; Cannito et al., 2012; Eadie et al., 2016; Hustad, 2007; Sheard et al., 1991; Stipancic et al., 2018; Yorkston & Beukelman, 1996). Each SIT consistent of 11 sentences increasing in word count from five to 15 words. Audio recordings were collected using the same microphone as the active tasks and SONAR Artist (Cakewalk Inc.). Each listener rated five sentences from each participant in the PwPD and control group (Sentences 2, 4, 6, 8, and 10), and 10% of sentences were repeated for intrarater reliability. The average intrarater and interrater reliabilities, via two-way mixed-effects intraclass correlations, were all above 0.6.

Prior to the perceptual task, listeners were given definitions of speech intelligibility and naturalness and oriented to the visual analog scale (VAS) that was used for ratings (Abur et al., 2019; Anand & Stepp, 2015). Intelligibility was defined as "the degree to which a speaker's message can be recovered by a listener" (Kent et al., 1989), and naturalness was defined as conforming to "the listener's standards of rate, rhythm, intonation, and stress patterning" and to "the syntactic structure of the utterance being produced" (Yorkston et al., 2010, p. 288). The definition for each percept remained presented on a nonexperimental computer screen throughout the task for reference.

[5]*Exception:* One participant in each group was unable to complete the SIT sentence task. For these two individuals, five sentences were extracted from other study tasks ranging from six to 14 words to match the word count of the SIT sentences.

If listeners had questions about terminology for the percept, dictionary definitions were provided.

For intelligibility ratings, the recordings were combined with multispeaker babble from four male and four female speakers who were not included in the data set. The multispeaker babble was combined with the speech at a 1-dB signal-to-noise ratio (determined via pilot testing) to increase ecological validity and reduce ceiling effects (Bunton, 2006; Tjaden et al., 2014). For naturalness ratings, the audio recordings had no noise added. For each speech sample, listeners first listened to the stimuli with multispeaker babble for the intelligibility ratings, and then they listened to the stimuli without noise added for the naturalness ratings. Listeners could play the stimuli up to 2 times prior to their rating for each percept on the VAS scale ranging from 0% to 100%.

All stimuli were presented to listeners over Sennheiser 280 Pro HD headphones. The headphone amplification was calibrated such that the output was between 60 and 70 dB SPL (Abur et al., 2019), reflecting the intensity range of conversational speech (Olsen, 1998).

Data Analysis

For adaptation tasks, a single mean value of f_o or F_1 was calculated across 40–120 ms of each trial in order to capture the initial feedforward response after the voice stabilized postonset (determined via sensitivity analysis with the current data set and two additional data sets in typical young speakers to occur approximately 40 ms into production). Voice f_o in Hz was extracted and converted into cents relative to the mean of the 24 baseline trials, and the control condition was subtracted from the shift up condition to account for vocal variability over time. For F_1, the formant values were extracted for each trial with linear predictive coding and the percent change relative to the mean of the 24 baseline trials was determined (Lester-Smith et al., 2020). The average across trials in the "hold" phase was termed the *mean adaptive response*.

For reflex tasks, f_o and F_1 traces were extracted for all trials. Perturbed f_o trials were normalized relative to the 100-ms baseline period, whereas for F_1, perturbed trials were normalized relative to unperturbed trials (Lester-Smith et al., 2020). All normalized responses were then averaged into one trace: the mean across the 120–240 ms following perturbation onset. This time segment was chosen since it reflects the beginning of the feedback portion of the vocal response (Tourville et al., 2008) prior to the second, voluntary vocal response observed during sudden perturbations (Hain et al., 2000). The averaged trace was termed the *mean reflexive response*.

For all acuity tasks, the JND threshold was estimated by calculating the average f_o and F_1 perturbation values across the last six reversals. Given that prior work did not find an effect of interstimulus interval on differences in group JND values in PwPD and controls (Abur & Stepp, 2020), JNDs of two f_o passive conditions (the 100- and 1000-ms interstimulus intervals) were averaged, yielding one JND value per participant. The listener ratings of speech intelligibility and naturalness were averaged across sentences for each speaker and then averaged across listeners.

Statistical Analysis

For adaptive responses, two-way analyses of variance (ANOVAs) were used to assess the effect of group (PwPD vs. control), phase (baseline, ramp, hold, and after-effect), and their interaction for both f_o and F_1. For reflex tasks, one-way ANOVAs were conducted to assess the effect of group (PwPD vs. control) on reflexive f_o and F_1 responses. Two additional two-way ANOVAs were used to determine the effect of group (PwPD vs. control) and task (active vs. passive) on acuity values. Factor effect sizes were quantified using the squared partial curvilinear correlation η_p^2. Post hoc Tukey tests were used to determine the direction of relationships. For acuity tasks, two-sample *t* tests were used to assess catch trial accuracy between groups (PwPD and control group), and linear regressions were used to determine if catch trial accuracy was predictive of JND values for each acuity task. Speech intelligibility and naturalness were modeled using two linear regressions with all auditory-motor control measures of f_o and F_1 (mean adaptive responses, mean reflexive responses, and passive and active acuity JNDs) and group as potential predictor variables. Standardized β coefficients were used to interpret effect sizes.

All statistical analyses were performed using Minitab 19 software. A significance level of $p < .05$ was set a priori.

Results

Adaptation and Reflex (Active Tasks)

There was no statistically significant effect of group on adaptive f_o responses (p = .99). The average adaptive f_o response was −45.3 cents with a standard deviation of 78.7 cents for PwPD and −42.2 cents with a standard deviation of 90.1 cents for controls (see upper panel of Figure 2). There was a statistically significant effect of phase on adaptive f_o responses (baseline vs. ramp vs. hold vs. after-effect, $df = 3$, $F = 10.3$, $\eta_p^2 = .32$, large effect size, $p < .001$) but no effect of the interaction between group and phase on adaptive f_o responses ($p = .96$). There was no significant effect of group on adaptive F_1 responses (p = .26). The average adaptive F_1 response was −4.6% with a standard deviation of 6.8% for PwPD and −7.2% with a standard deviation of 7.6% for controls (see lower panel of Figure 2). There was a significant effect of phase on adaptive F_1 responses ($df = 3$, $F = 18.73$, $\eta_p^2 = .26$, large-effect size, $p < .001$) but no significant effect of the interaction between group and phase ($p = .12$).

There was no statistically significant effect of group on reflexive f_o responses ($p = .70$) or reflexive F_1 responses (p = .54). The average reflexive f_o response was −11.6 cents with a standard deviation of 7.9 cents in PwPD and −12.5 cents with a standard deviation of 8.3 cents for the control group (see upper panel of Figure 2). The average reflexive F_1 responses was −0.6% with a standard deviation of 1.7% in PwPD and −0.9% with a standard deviation of 1.2% for controls (see lower panel of Figure 2).

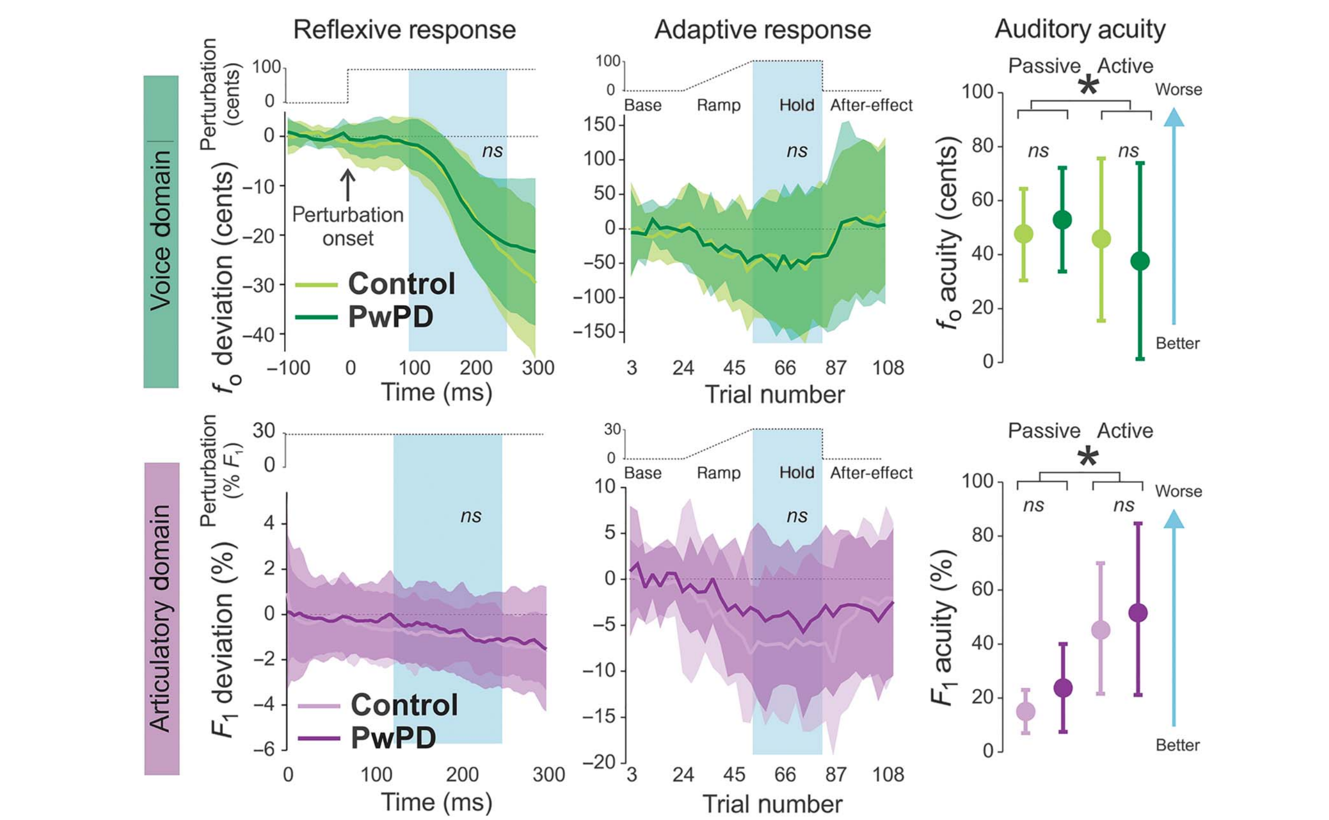
Auditory Acuity (Passive and Active Tasks)

For f_o acuity measures, there was no statistically significant main effect of group on f_o acuity (p = .99) but there was a statistically significant effect of task (passive vs. active; $df = 1$, $F_1 = 5.11$, $\eta_p^2 = .09$, medium effect size, $p = .02$). Post hoc tests showed that both the PwPD and control group demonstrated better acuity to f_o (smaller JND values) in the active compared with passive acuity task (see upper panel of Figure 2). There was no statistically significant effect of the interaction between group and task for f_o acuity ($p = .21$).

For F_1 acuity measures, there was no statistically significant main effect of group on passive F_1 acuity (p = .06). There was a statistically significant effect of task (passive vs. active; $df = 1$, $F = 53.56$, $\eta_p^2 = 0.50$, large effect size, $p < .001$) on F_1 acuity but no effect of the interaction between group and task (p = .85). Post hoc tests showed that PwPD demonstrated worse acuity to F_1 compared with controls across acuity tasks, and both participant groups demonstrated worse acuity in the active compared with passive task (see lower panel of Figure 2).

There were no statistical group differences in catch trial accuracy for the passive F_1 acuity (p = .23), active F_1 acuity (p = .66), passive f_o acuity (p = .65), or active f_o

Figure 2. Auditory-motor measures for persons with Parkinson's disease (PwPD; dark colors) and controls (light colors). Group means are plotted as solid lines for reflexive and adaptive responses and solid circles for auditory acuity. Group standard deviations are shown as shaded regions for reflexive and adaptive responses and interval bars for auditory acuity. JND = just-noticeable difference. *Indicates statistical significance at p < .05 level. *ns* indicates not statistically significant.



acuity (p = .67) tasks. Catch trial accuracy was also not a significant predictor of JND value for passive F_1 acuity (p = .63), active F_1 acuity (p = .63), passive f0 acuity (p = .89), or active f_o acuity (p = .47).

Functional Speech Outcomes

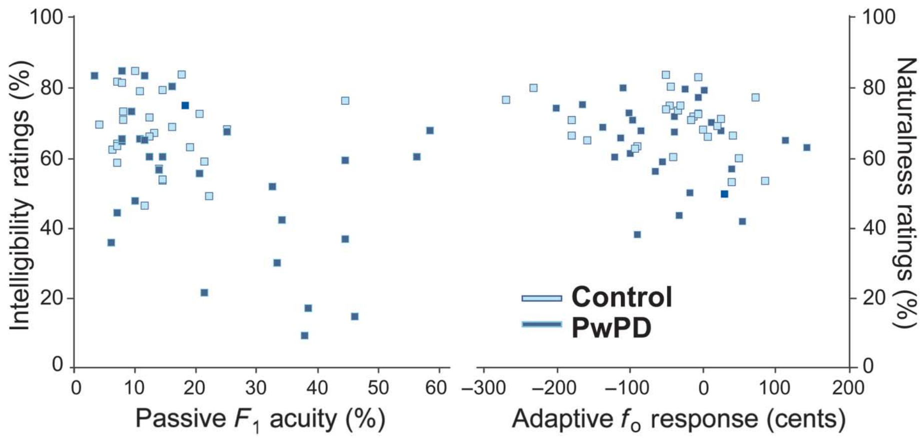
A linear regression revealed that for speech intelligibility, passive F_1 acuity ($\beta = -6.53$, p = .02) and group ($\beta = -9.44$, p = .05) were statistically significant predictor: Higher speech intelligibility was associated with better (reduced) passive F_1 acuity. For speech naturalness, mean adaptive f_o response ($\beta = -4.27$, p < .01) was the only statistically significant predictors: Higher speech naturalness was associated with more negative adaptive f_o responses (i.e., larger compensatory responses; see Figure 3).

Discussion

Vocal Features of Speech

In agreement with our first study hypothesis, *H1*, and prior work in a small cohort of PwPD receiving medication (N = 10; Kiran & Larson, 2001), f_o reflexive responses did not differ by group. Multiple studies have observed greater reflexive f_o response magnitudes in PwPD off medication (Chen et al., 2013; Liu et al., 2012; Mollaei et al., 2016), and both our work and the earlier study in PwPD receiving medication (Kiran & Larson, 2001) found no group differences in reflexive f_o responses. For both groups, the average reflexive f_o response magnitudes in the analysis window (M = −11.6 cents, SD = 7.9 cents in PwPD and M = −12.5 cents, SD = 8.3 cents in controls) were descriptively larger compared with prior findings in young adults (M = −7.1 cents and SD = 6 cents; Lester-Smith et al., 2020). Future work should examine this measure within the same PwPD on and off medication (with medication dosage as a factor) to directly assess possible interactions of medication status and auditory-motor processes in PwPD. Work by Mollaei et al. (2019) found that perturbation magnitude differentially impacted the degree of compensations to altered auditory f_o feedback in PwPD compared with controls, so this is another consideration to explore in future work. The average adaptive f_o responses did not differ between groups (M = −45.3 cents, SD = 78.7 cents in PwPD and M = −42.2 cents, SD = 90.1 cents in controls), and both groups demonstrated average adaptive f_o magnitudes that

Figure 3. Speech intelligibility ratings (left) are shown as a function of passive F_1 acuity (%), and speech naturalness ratings (right) are shown as a function of mean adaptive f_o responses (cents) for persons with Parkinson's disease (PwPD; dark blue markers) and controls (light blue markers).



were descriptively smaller than prior findings in young adults (M = −61.2 cents and SD = 79 cents; Lester-Smith et al., 2020). This is unsurprising because auditory-motor control appears to be impacted by the aging process (Liu et al., 2010). The lack of group differences in adaptive f_o responses contrasts with prior work reporting reduced mean adaptive f_o responses in PwPD on medication compared with a control group (Abur et al., 2018). The experimental delay (45 ms compared with 20–30 ms), sample size (15 compared with 28 speakers per group), or medication dosage (not collected in either study) could explain the contrasting results. Previous work suggests that speakers have sensory preferences (auditory or somatosensory) when using feedback control during speech (Lametti et al., 2012), which could have also influenced adaptive f_o response results based on sensory preferences of the specific participants.

As predicted by our study hypothesis, *H3,* no group differences were found for acuity to voice f_o and both groups showed better acuity in the active compared with the passive task. These results are in alignment with active and passive f_o acuity findings in young adults (Lester-Smith et al., 2020). This finding is also supported by event-related potential findings (Behroozmand et al., 2009), as well as evidence from electrocortographic monitoring (Chang et al., 2013), which reported larger cortical activity to voice f_o perturbations during voicing compared with passive listening. In the passive f_o acuity task, the results of two tasks with differing interstimulus intervals were averaged based on findings from a prior study, which could have impacted our findings. However, an ANOVA with factors of group (PwPD or control), condition (100- or 1000-ms interval), and their interaction, was used to confirm that there was no interaction between group and condition (p = .83) in this work. Regarding the lack of group differences, this is in line with a prior study reporting no group differences in passive f_o acuity in PwPD off medication (Mollaei et al., 2019), suggesting that f_o acuity is not impaired in PwPD regardless of medication status.

In sum, our findings and the literature support that auditory f_o acuity (a sensory component of speech) is not impaired in PwPD (both on and off medication) and that motor components of auditory-motor control of f_o (which show deficits in PwPD off medication; Chen et al., 2013; Liu et al., 2012; Mollaei et al., 2016) are not impaired in PwPD receiving medication (observed in the this work and in Kiran & Larson, 2001).

Articulatory Features of Speech

Further study hypotheses, *H2* and *H3*, predicted that reflexive and adaptive F_1 responses would be reduced in PwPD compared with controls and that acuity to vowel F_1 would be worse in PwPD relative to controls for both passive and active acuity. In contrast to *H2* and prior work in speakers with PD while off medication, adaptive F_1 responses did not differ in PwPD compared with controls. This result differs from prior evidence of reduced adaptive F_1 responses in PwPD off medication (Mollaei et al., 2013). Instead, groups demonstrated no statistical differences in adaptive F_1 responses in this work. Compared with adaptive F_1 responses reported in a prior study in young adults (M = −8.6%, SD = 6.2%; Lester-Smith et al., 2020), both the PwPD and control groups demonstrated descriptively smaller F_1 adaptive response magnitudes (M = −4.6%, SD = 6.8% for PwPD and M = −7.25% and SD = 7.6% for controls). There were also no statistically significant group differences for reflexive F_1 responses, which conflicts with findings that PwPD off medication show reduced reflexive F_1 responses relative to controls (Mollaei et al., 2016). Descriptively, the average reflexive F_1 response magnitudes in the analysis window (M = −0.6%, SD = 1.7% in PwPD and M = −0.9%, SD = 1.2% in controls) were comparable to prior findings reported in young adults (M = −0.6% and SD = 1.3%; Lester-Smith et al., 2020). The lack of group differences in reflexive and adaptive F_1 responses here supports that components of feedback and feedforward auditory-motor processes in PwPD receiving typical medication are intact for articulatory features of speech as well. For acuity to vowel F_1, the current results conflict with our hypotheses *H3* and prior findings in PwPD while off medication (Mollaei et al., 2019): PwPD demonstrated no differences in acuity to F_1 compared with controls. However, in line with prior work (Lester-Smith et al., 2020), both groups demonstrated worse F_1 acuity for the active compared with passive task. Together, these studies suggest that medication status may influence measures of sensory acuity in PwPD.

Functional Speech Outcomes

To examine whether auditory-motor measures were related to speech function, a linear regression was used to assess the relationship between auditory-motor measures for vocal and articulatory features of speech and perceptual ratings of speech intelligibility and naturalness ratings. The fourth study hypothesis, *H4*, predicted that vocal auditory-motor measures would be more strongly associated with speech naturalness, whereas articulatory auditory-motor measures would be more strongly associated with speech intelligibility. In line with our hypotheses, mean adaptive f_o responses were related to speech naturalness (for both groups), and acuity to F_1 was related to speech intelligibility ratings. Although speaker group was related to speech intelligibility, there was no association between speaker group and naturalness ratings. This suggests that naturalness was not clearly disrupted in the PwPD group. Together with the overall voice severity ratings (ranging 2.3%–34.5% in the PwPD group and 0%–19.4% in the control group; see Table 1), these results suggest that the PwPD in this study did not have severe speech symptoms. However, these findings strengthen evidence that speech features related to voice and articulation may best predict speech naturalness and speech intelligibility, respectively (Anand & Stepp, 2015; Yorkston et al., 1990). Importantly, these results are also the first to confirm a relationship between measures of auditory-motor function and functional speech outcomes, suggesting that some auditory-motor measures are reflective of speech function. The characterization of specific relationships between measures of auditory-motor control and functional speech outcomes are vital to understand which components of auditory-motor control have meaningful effects on daily communication.

Limitations

This work provides a comprehensive assessment of auditory-motor processes, but there are limitations. These results provide ecologically valid information for PwPD receiving their typical medication, but the impact of Parkinson's disease, alone, on auditory-motor processes was not assessed. Additionally, having speech complaints was not an inclusion criterion for the study, which resulted in speakers with more mild to moderate speech symptoms; hence, these findings may not be reflective of PwPD with more severe speech symptoms. When examining functional speech outcomes, this study was designed to collect intelligibility and naturalness on the same stimuli to control for semantic, syntactic, and phonetic features of sentence stimuli that could differentially impact one of the two percepts; yet a reading task, which is not a naturally elicited speech task, could have also impacted the naturalness ratings for both groups.

Finally, although prior work has utilized the same experimental methods as this study and reported typical, compensatory responses (Lester-Smith et al., 2020; Weerathunge et al., 2020), studies of speech motor control that yield typical responses can still vary considerably in their experimental design (e.g., feedback amplification, time delay, number of trials, and perturbation sizes; Abur et al., 2018; Burnett et al., 1997; Chen et al., 2013; Jones & Keough, 2008; Kearney et al., 2020; Liu et al., 2012; Mollaei et al., 2013; Stepp et al., 2017; Weerathunge et al., 2020). Prior work has examined accuracy of auditory judgments of one single stimuli difference in PwPD compared with controls (Mollaei et al., 2019), whereas this work employed an acuity measure that adaptively modified differences to find a threshold of discrimination for each speaker. An accuracy measure is better suited to minimize response bias for a specific auditory error, but an adaptive measure can determine a specific threshold for auditory error by speaker. Future work could explore a combination of these methods to optimize a measure of acuity in PwPD. Additionally, for the auditory-motor responses, different time windows for analysis could impact the degree of feedback or feedforward control responses contained within the reported auditory-motor response. Therefore, it is not clear to what degree methodological factors in experimental design may have influenced the current investigation and comparisons to prior work.

Conclusions

In order to interpret how auditory-motor findings relate to the ability to communicate effectively in daily life, it is critical to understand auditory-motor function in PwPD while on their typical medication cycle and whether auditory-motor measures are associated with speech function. Although prior studies have employed auditory-motor measures to examine disparate aspects of speech motor control in PwPD, they have primarily investigated PwPD off medication and did not include measures of speech function. This work is the first to comprehensively characterize how auditory-motor processes in PwPD typically present (on medication) across vocal and articulatory features of speech and confirm their relationship to measures of speech function, which provides important insight for the interpretation of these measures in the literature.

Our results revealed no group differences for any components of auditory-motor control across both vocal and articulatory speech features. When taken together with separate studies of auditory-motor measures in PwPD on and off medication, this work adds to the evidence that medication for PwPD benefits sensory and motor components of both feedback and feedforward auditory-motor processes for voice and articulation. These findings also suggest that, although PwPD receiving medication do not have disrupted auditory-motor control, they still demonstrate reduced speech intelligibility. Therefore, although auditory-motor measures were associated with functional speech outcomes, it appears that benefits to auditory-motor control with medication do not necessarily improve speech symptoms in PwPD.

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