Relative fundamental frequency during vocal onset and offset in older speakers with and without Parkinson's disease[a)]

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The relative fundamental frequency (RFF) surrounding production of a voiceless consonant has previously been shown to be lower in speakers with hypokinetic dysarthria and Parkinson's disease (PD) relative to age/sex matched controls. Here RFF was calculated in 32 speakers with PD without overt hypokinetic dysarthria and 32 age and sex matched controls to better understand the relationships between RFF and PD progression, medication status, and sex. Results showed that RFF was statistically significantly lower in individuals with PD compared with healthy age-matched controls and was statistically significantly lower in individuals diagnosed at least 5 yrs prior to experimentation relative to individuals recorded less than 5 yrs past diagnosis. Contrary to previous trends, no effect of medication was found. However, a statistically significant effect of sex on offset RFF was shown, with lower values in males relative to females. Future work examining the physiological bases of RFF is warranted. © *2013 Acoustical Society of America*.
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I. INTRODUCTION

Speech symptoms are prevalent in Parkinson's disease (PD; Logemann *et al.*, 1978), with voice changes being the earliest and most common (Holmes *et al.*, 2000). These symptoms cause significant decreases in patient quality of life, often well before obvious changes in speech intelligibility (Miller *et al.*, 2006). However, the specific pattern of the development of speech symptoms with disease progression is still unknown. Recent work in the field has indicated that acoustic measures of speech production can be highly predictive of patient function (e.g., Little *et al.*, 2009; Tsanas *et al.*, 2010). Our long-term goal is to identify a set of acoustic parameters that can be used as a biomarker for PD progression. One potential acoustic measure of interest may be "relative fundamental frequency" (RFF), which is defined here as the fundamental frequency (*F*0) of the cycles immediately before (vowel offset) and after (vowel onset) production of a voiceless consonant, normalized by the more typical *F*0 values of the voicing before and after the consonant.

Several studies have confirmed characteristic patterns in RFF of healthy speakers. Ohde (1984) first reported that speakers had a higher *F*0 during the first few vocal cycles of vowel onset after voiceless stop consonant production but that this pattern was not found during production of *voiced* stop consonants. Watson (1998) followed up on this finding and compared RFF of 10 healthy younger speakers (23 to 27 yrs) to those of 10 healthy older speakers (68 to 85 yrs). He found (1) that while younger speakers had relatively stable (near zero) offset RFF values, older speakers showed lower (negative) offset RFF (Watson, 1998) and (2) that both younger and older speakers displayed large, positive values of RFF in the first vocal cycles of vowel onset.

The physiological bases of RFF production are currently uncertain but several potential mechanisms have been suggested. Laryngeal tension is thought to be increased preceding, during, and immediately after voiceless consonant production (Stevens, 1977; Löfqvist *et al.*, 1989), which could contribute to a higher offset (before the consonant) and onset (after the consonant) RFF. Peak and minimum airflow values are known to increase during vowel offset and onset surrounding a voiceless consonant (Lofqvist and McGowan, 1992; Lofqvist *et al.*, 1995), which could create a large Bernoulli force and cause rapid adduction of the vocal folds and thus a higher onset RFF (Ladefoged, 1967, p. 33). Finally, vocal fold abduction can occur during vowel offset prior to voiceless consonant production (Fukui and Hirose, 1983), which could potentially lead to lowered offset RFF. Watson (1998) proposed that the steady offset RFF in younger speakers could be a result of a combined increase of tension (increasing RFF) and vocal fold abduction (decreasing RFF), whereas older speakers could be using only vocal fold abduction prior to devoicing, resulting in the noted lowering of their offset RFF.

Goberman and Blomgren (2008) studied the RFF of nine individuals with hypokinetic dysarthria and PD. They found that these individuals displayed significantly lowered offset and onset RFF while OFF medication when compared to eight age-matched controls. In addition they reported a trend for speakers with PD to have higher RFF values ON medication relative to OFF (Goberman and Blomgren, 2008). Potential explanations for these findings are varied. It is possible that individuals with PD initiate vocal fold abduction earlier in order to compensate for their difficulties with rapid termination of voicing (Gallena *et al.*, 2001), which would lower values of offset RFF but should not affect onset

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RFF. Individuals with PD have been shown to exhibit a high incidence of vocal fold bowing (Blumin *et al.*, 2004); although bowing has been shown to correlate with contact area of the vocal folds and breathiness (Mau *et al.*, 2011), the effects of bowing on *F*0 short-term modulation are not yet known. Increased bowing could potentially affect laryngeal kinematics, aerodynamics, and tension and could have myriad effects on RFF production. Finally, laryngeal rigidity is thought to be a symptom of PD and increased thyroarytenoid muscle activation has been correlated with perceptual measures of impairment in voice onset and offset in individuals with PD (Gallena *et al.*, 2001). Increased baseline laryngeal muscle tension in individuals with PD could impede their ability to use tension as a devoicing strategy, effectively lowering both offset and onset RFF values.

Although consistent RFF patterns have been found in healthy speakers, many factors that may affect RFF are still unknown. In this work, we sought to examine RFF in a larger population of older speakers, including individuals with PD without overt hypokinetic dysarthria to better understand the impact of PD (and PD medication status) as well as the potential effects of PD progression and sex. Given the previous findings by Goberman and Blomgren (2008), we hypothesized that both offset and onset RFF values would be significantly lower in individuals with PD relative to healthy controls. We hypothesized that use of a greater number of participants would show onset and offset RFF values to be significantly higher while ON medication relative to OFF medication, confirming the previously reported trend (Goberman and Blomgren, 2008). We further hypothesized that individuals with early PD would show higher RFF values relative to individuals with more progressed PD. Because no previous study has tested or reported an effect of sex on RFF, we did not hypothesize an effect of sex on the RFF in our study population.

II. METHODOLOGY

A. Participants

Participants were 32 individuals with PD (9 females) and 32 control speakers with no history of neurological or speech disorders (9 females), all of whom completed the study with informed consent. All participants were free of any other neurological, speech, or language disorders except that several individuals reported minor age-related hearing loss. The mean disease duration of participants with PD was 8.6 yrs for females [standard deviation (SD) = 7.3, range = 1 to 20] and 5.3 yrs for males (SD = 3.655, range = 0.5 to 16). For statistical analysis of the effects of disease duration, PD participants were grouped into individuals with disease durations of less than 5 yrs ($N = 15$; 3 female) and those with disease durations of 5 yrs or more ($N = 17$; 6 female). Full demographics for PD participants are shown in Table I.

TABLE I. Participant characteristics.

Participant	Sex	Age	Years post-Dx	UPDRS 2.1	UPDRS-III (OFF)	UPDRS-III (ON)
S2	M	75	0.5	0	20	10
S3	F	68	7.0	0	10	3
S4	M	60	5.0	1	26	22
S5	M	64	16.0	0	16	14
S6	F	48	6.0	1	54	40
S7	M	83	3.5	0	22	22
S8	M	67	1.0	0	22	17
S10	F	72	7.0	3	25	20
S11	M	89	4.5	0	24	19
S12	F	56	1.0	0	12	8
S13	F	64	2.5	0	8	8
S14	M	60	1.5	0	13	6
S15	M	63	6.0	2	33	25
S16	M	76	5.5	1	23	12
S17	M	71	3.0	1	14	13
S18	M	68	4.0	0	10	8
S19	M	73	3.0	2	20	16
S21	M	77	4.0	0	15	15
S22	M	66	7.0	1	22	13
S23	M	73	9.0	3	45	44
S24	F	59	18.0	1	22	20
S25	M	65	7.0	3	27	27
S26	M	81	3.0	2	24	24
S27	M	70	5.5	1	16	16
S28	M	51	12.0	3	25	16
S29	M	69	5.0	0	9	2
S30	F	70	1.0	0	4	4
S31	M	70	3.0	3	25	7
S32	M	61	10.0	1	4	4
S33	F	77	16.0	2	41	30
S35	F	79	20.0	3	43	29
S36	M	58	2.5	0	15	15

B. Experimental design

Participants with PD regularly used carbidopa/levadopa medication but each participant with PD was tested first OFF and then ON medication for this study. Individuals with PD did not take their regular morning medication on the day of testing such that their last dose was taken at least 9 h prior to testing. After the completion of OFF testing, participants took their medication at the regular dose. ON testing commenced after the medication took effect, which was usually within 45 min. For control participants, speech data were collected only at a single time point.

During testing, all participants read the first paragraph of "The Rainbow Passage" (Fairbanks, 1960, p. 127) as well as three iterations of the sentence "At sea, Molly feeds Luke toffee too." This sentence was chosen to provide ample samples of RFF production within a relatively short stimulus. These tasks were part of an extended speech production protocol consisting of vowel productions, read speech, and spontaneous speech that took approximately 10 min to complete. Speech was recorded at 44.1 kHz in a quiet room using a portable digital audio recorder (Olympus Linear PCM recorder, LS-10, Olympus Corp., Tokyo) and a headset microphone (Shure WH20, Shure, Inc., Niles, IL) placed 10 cm from the lips (at a 45° angle from the midline). Participants were directed to speak in their normal, conversational voices.

During both the OFF and ON medication states, a licensed physical therapist and clinical researcher (S.P., see

Acknowledgments) administered and scored the UPDRS (Unified Parkinson's Disease Ratings Scale; Sec. I, II, and III) for participants with PD.

C. Data analysis

A total of 12 voiced-voiceless-voiced (VcV) productions were used for analysis (see Table II): Three from the Rainbow Passage and three from each of the three productions of the additional sentence, "At sea, Molly feeds Luke toffee too." A single investigator (author C.S.) performed acoustic analysis by displaying the time wave-forms of the samples in Praat acoustic analysis software (Boersma and Weenink, 2008) and measuring the ten periods of vibration prior to (vowel offset) and after (vowel onset) the voiceless consonant using the pulse function (see Fig. 1). Ten periods were used for analysis in order to be consistent with previous work (e.g., Goberman and Blomgren, 2008). The instantaneous *F*0 for the ten offset and ten onset cycles were calculated as the inverse of each period. All instantaneous frequencies were converted to semitones (STs) relative to a reference instantaneous frequency: For offset cycles the first cycle and for onset cycles the final (10th) cycle. These reference frequencies come from the two furthest cycles from the consonant production and are least likely to be affected by it. Conversion from instantaneous frequencies (f) to STs was accomplished via Eq. (1) using the appropriate reference frequency (f_{ref}),

$$\mathrm{ST} = 39.86 \times \log_{10}(f/f_{\mathrm{ref}}). \quad (1)$$

RFF for each sample was averaged across all 12 available VcV productions studied to provide a more stable estimate of RFF. The decision to include VcV productions from a variety of phonetic contexts is supported by previous work in healthy young adults (Stepp *et al.*, 2010), which did not find statistically significant differences among the RFF across three different voiceless consonant productions within individual participants. For some of the 12 productions, glottalization or a lack of periodicity prior or following the voiceless consonant production or inadequate length of voicing made it impossible to reliably determine RFF. In these cases RFF values from that production were excluded and only the remaining productions contributed to the average for that sample. An average of 7.4 [standard deviation (STD) = 2.4] productions were used for the RFF offset averages and 7.5 (STD = 2.6) productions for the RFF onset averages of each sample.

The author re-evaluated approximately 15% of the samples 9 months after the initial evaluation to assess intra-rater reliability (Pearson's $r = 0.96$); the average difference for all RFF values in this sample was 0.08 ST. A second trained researcher (M.C., see Acknowledgments) analyzed approximately 15% of the samples to assess inter-rater reliability (Pearson's $r = 0.96$); the average difference for all RFF values between the two raters was –0.04 ST. These results suggest high reliability of the acoustic analysis methodology employed.

TABLE II. RFF productions used for analysis.

Surrounding text	RFF phonetic transcription
"no one ev***er fi***nds it"	/ər/ /f / /aɪ/
"is l***ooking*** for"	/ʊ/ /k/ /ɪŋ/
"look***ing for*** the"	/ɪŋ/ /f / /ɔr/
"Moll***y fee***ds Luke"	/i/ /f/ /i/
"Luke t***offee*** too"	/ɔ/ /f/ /i/, alternatively /ɑ/ /f/ /i/
"Luke toff***ee too***"	/i/ /t/ /u/

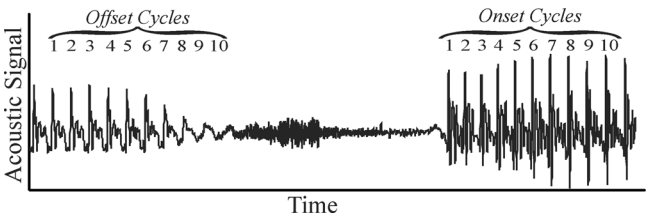

FIG. 1. Example of the acoustic waveform during voice offset and onset occurring during a healthy older speaker's production of /ifi/ in "Molly feeds."

D. Statistical analysis

All statistical analyses were completed using Minitab Statistical Software (Minitab Inc., State College, PA). A 3-factor general linear model was used on the full dataset (96 samples) to determine the effects of group (PD OFF, PD ON, and control), sex (male or female), and vocal cycle (offset cycles 1 to 10 and onset cycles 1 to 10) as well as the three interactions among these factors. A 4-factor general linear model was applied to only the PD data (64 samples) to determine the effects of disease duration (<5 yrs or ≥ 5 yrs), medication status (OFF or ON), sex, and vocal cycle as well as the 6 interactions among the factors. An alpha level of 0.05 or less was considered significant. *Post hoc* Tukey simultaneous tests were applied as appropriate. To determine the strength of linear relationships among measures, coefficients of determination (R^2) were calculated to predict the variance explained.

III. RESULTS

The mean UPDRS total scores in female participants with PD while OFF medication was 52.1 (SD = 35.8, range = 9 to 97). The mean UPDRS total scores in male participants with PD while OFF medication was 40.9 (SD = 19.8, range = 9 to 91). On average, UPDRS scores were reduced by 5.0 (SD = 5.0; range = 0 to 18) while ON medication relative to OFF medication. Disease duration and OFF medication UPDRS scores were statistically significantly ($p = 0.003$) but weakly ($R^2 = 0.25$) correlated. This finding is not surprising given the uncertainty associated with PD diagnosis due to its long preclinical period and the non-linear progression of the disease (Hilker *et al.*, 2005).

A 3-factor general linear model applied to the full dataset (see Table III) found a significant effect of group (PD OFF, PD ON, and control; $p = 0.008$), sex ($p < 0.001$), and vocal cycle ($p < 0.001$) as well as the interaction of cycle × sex ($p < 0.001$). The effects of group and sex were small (both $\eta_p^2 = 0.01$), whereas the effect of the cycle was large ($\eta_p^2 = 0.76$) and the interaction of cycle × sex was in the

TABLE III. Results of 3-factor general linear model on full dataset.

Effect	DF	η_p^2	F	p
Cycle	19	0.76	214.1	<0.001
Group (CTRL, PD ON, PD OFF)	2	0.01	4.9	0.008
Sex (M, F)	1	0.01	21.6	<0.001
Group × sex	2	<0.01		0.454
Cycle × group	38	0.01	0.7	0.944
Cycle × sex	19	0.08	9.0	<0.001

moderate range ($\eta_p^2 = 0.08$). The interactions of group × cycle and group × sex were not significant. *Post hoc* Tukey's tests indicated that RFF was significantly higher in controls compared to PD ON medication but did not show any significant differences between controls and PD OFF or between PD ON and PD OFF. A *post hoc* Tukey's test comparing male and female RFF found that RFF was statistically significantly higher in females compared with males. Figure 2 shows a plot of RFF as a function of cycle and group. Figure 3 shows RFF as a function of cycle and sex.

A 4-factor general linear model applied only to the PD data (see Table IV) found a significant effect of disease duration (<5 yrs or ≥5 yrs; $p < 0.001$), sex ($p < 0.001$), and vocal cycle ($p < 0.001$) as well as the interactions of disease duration × cycle ($p < 0.001$) and sex × cycle ($p < 0.001$). The effect size of the cycle was again large ($\eta_p^2 = 0.77$) and the interactions of sex × cycle and disease duration × cycle were both in the small-to-moderate range ($\eta_p^2 = 0.07$ and $\eta_p^2 = 0.05$, respectively). The effect sizes for sex and disease duration were both small ($\eta_p^2 = 0.01$ and $\eta_p^2 = 0.02$, respectively). No significant effect was found for medication status (OFF or ON) or the interactions disease duration × sex, medication status × cycle, medication status × duration, or medication status × sex. A *post hoc* Tukey's test showed that individuals with more progressed PD had statistically significantly lower RFF compared to the individuals in earlier stages of the disease. A *post hoc* Tukey's test on sex showed that as in the full dataset females had statistically significantly higher RFF than males. RFF as a function of cycle and disease status in participants with PD is shown in Fig. 4.

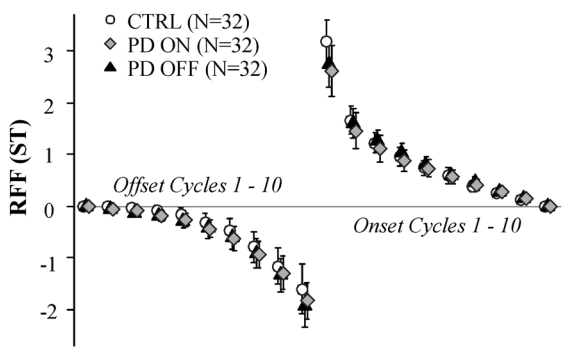

FIG. 2. Mean values of RFF as a function of group (control, ON medication speakers with PD, and OFF medication speakers with PD) and cycle (offset 1 to 10 and onset 1 to 10). Error bars indicate the 95% confidence intervals for the means.

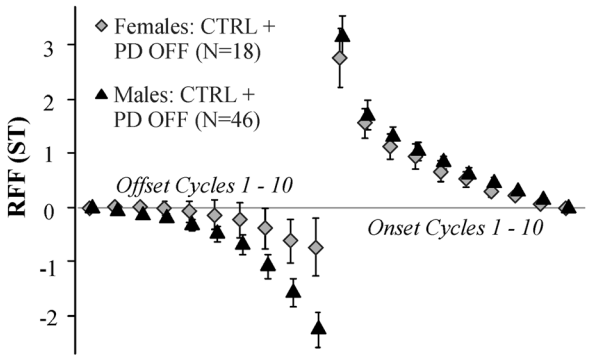

FIG. 3. Mean values of RFF as a function of sex and cycle (offset 1 to 10 and onset 1 to 10). Error bars indicate the 95% confidence intervals for the means.

The changes in RFF offset cycle 10 and onset cycle 1 with medication (ON medication—OFF medication) were determined for each participant with PD. These RFF changes with medication were compared with: (1) Each participant's change (ON medication—OFF medication) in motor function estimated by the change in the motor section of the UPDRS (UPDRS-III) and (2) each participant's self-reported score on UPDRS item 2.1 (UPDRS scale: Score = 0 [nonexistent symptoms], score = 1 [slight symptoms], score = 2 [mild symptoms], score = 3 [moderate symptoms], score = 4 [severe symptoms]. Change in UPDRS-III scores were not statistically significantly ($p > 0.05$) correlated with the change in RFF offset cycle 10 ($R^2 = 0.05$) or with the change in RFF onset cycle 1 ($R^2 = 0.02$). Likewise, UPDRS item 2.1 scores were not statistically significantly ($p > 0.05$) correlated with the change in RFF offset cycle 10 ($R^2 < 0.01$) or with the change in RFF onset cycle 1 ($R^2 < 0.01$). The relationships between RFF changes, changes in UPDRS-III, and UPDRS item 2.1 scores are shown in Fig. 5.

IV. DISCUSSION

The goal of this work was to characterize RFF in a large population of older speakers with and without PD to determine the impact of PD (including medication status and disease progression) and sex. Overall, our results indicate that RFF is statistically significantly lower in individuals with PD compared with healthy age-matched controls and individuals with PD with longer disease durations have a lower RFF

TABLE IV. Results of 4-factor general linear model on PD data only.

Effect	DF	η_p^2	F	p
Cycle	19	0.77	143.3	<0.001
Disease duration (<5 yr, ≥5 yr)	1	0.02	21.1	<0.001
Sex (M, F)	1	0.01	21.4	<0.001
Medication status (OFF, ON)	1	<0.01	1.9	0.171
Disease duration × sex	1	<0.01	0.5	0.490
Disease duration × cycle	19	0.05	3.1	<0.001
Cycle × sex	19	0.07	5.4	<0.001
Medication status × cycle	19	<0.01	0.2	1.000
Medication status × disease duration	1	<0.01	0.0	0.976
Medication status × sex	1	<0.01	1.6	0.211

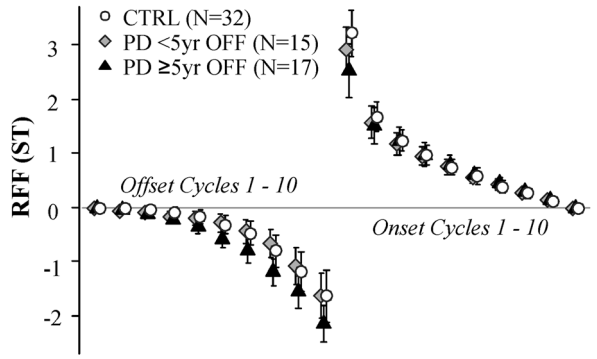

FIG. 4. Mean values of RFF as a function of disease progression and cycle (offset 1 to 10 and onset 1 to 10). Participants with PD were separated into two groups: Those with disease durations of less than 5 yrs ($N = 15$) and those with disease durations of 5 yrs or more ($N = 17$). Error bars indicate the 95% confidence intervals for the means.

compared to individuals with PD who have been more recently diagnosed. However, these effects were overshadowed by a strong effect of sex and strong interaction between sex and cycle in which females (both PD and control speakers) showed a higher offset RFF compared with males.

A. Effects of PD on RFF

Consistent with our initial hypothesis, our results show that RFF is statistically significantly reduced in individuals with PD (ON medication) relative to healthy controls, although no significant difference was seen between individuals with PD while OFF medication and control speakers. Although significant, the effect size as a function of group was small ($\eta_p^2 = 0.01$), indicating that whether data were obtained from healthy speakers or individuals with PD did not explain a large proportion of the variance in the RFF data. Samples from speakers with PD ($N = 32$) while OFF medication were found to have an average offset RFF value of –1.9 ST (SD = 1.2 ST) at cycle 10 and an average onset RFF value of 2.7 ST (SD = 1.2 ST) at cycle 1. Goberman and Blomgren (2008) reported an average offset RFF value in OFF medication speakers with PD ($N = 9$) of roughly –2.2 ST at cycle 10, and an average onset RFF value of roughly 1.75 ST at cycle 1. These offset values are similar but our speakers with PD showed a larger onset RFF relative to those studied by Goberman and Blomgren (2008).

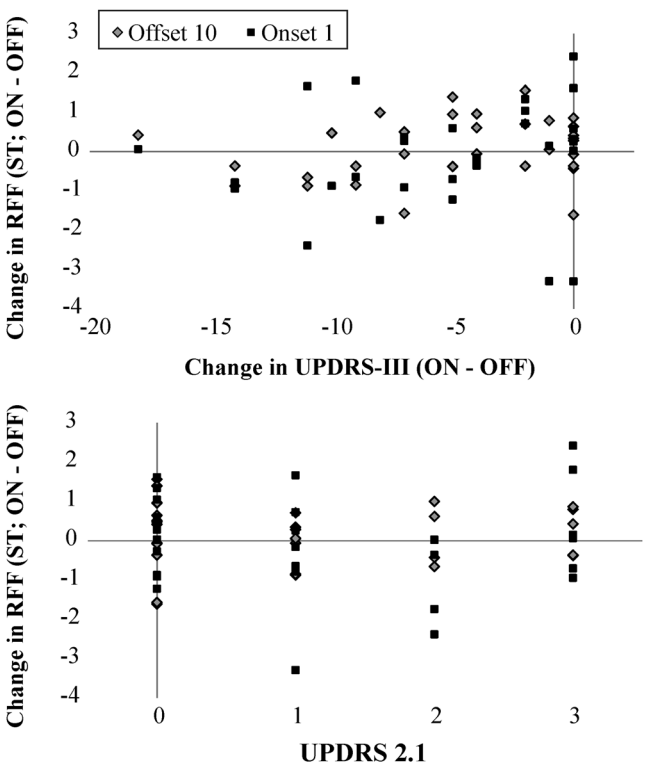

FIG. 5. Upper panel: Change in offset cycle 10 and onset cycle 1 RFF values (ON medication—OFF medication) of speakers with PD ($N = 32$) as a function of their change in UPDRS-III (motor section) scores (ON medication—OFF medication). Lower panel: Change in offset cycle 10 and onset cycle 1 RFF values (ON medication—OFF medication) of speakers with PD ($N = 32$) as a function of speaker report of speech symptoms using the UPDRS item 2.1. Scores of 0 indicate no speech symptoms and scores of 3 indicate moderate speech symptoms.

Control speakers ($N = 32$) in this study were found to have an average offset RFF value of –1.6 ST (SD = 1.3 ST) and an average onset RFF value of 3.2 ST (SD = 1.2 ST). These values are fairly consistent with those found by Watson (1998), who found an average offset RFF value of –1.7 ST at cycle 10 and an average onset RFF value of 2.8 ST at cycle 1 in $N = 10$ healthy elderly speakers. Our control data match less well with the previous data ($N = 8$) of Goberman and Blomgren (2008). They reported an average offset RFF value of roughly –1.1 ST at cycle 10, and an average onset RFF value of 5.5 ST at cycle 1.

In short, the mitigation of the effect of PD on RFF in our data compared with the previous work by Goberman and Blomgren (2008) seems to be largely a result of a difference in our control speaker data: The healthy speakers in their study seem to show a higher RFF during both offset and onset compared with the healthy speakers in the current study. Our belief is that these differences are likely a result of the differences in the acoustic methodology and sample size ($N = 8$ vs $N = 32$). In the previous study, an estimate of RFF was calculated for each speaker based on a single instance in running speech. Here we have estimated RFF for each speaker based on the mean of up to 12 instances in running speech, which we believe may provide a more accurate estimate of the behavior.

We originally hypothesized that individuals with early PD would show higher RFF values relative to individuals with more progressed PD, which was confirmed by our results. Individuals with disease durations of less than 5 yrs ($N = 15$) had statistically significantly higher RFF compared to the individuals with disease durations of 5 yrs or more ($N = 17$). However, this significant result has an associated effect size that is in the low range ($\eta_p^2 = 0.01$).

B. Effects of medication in speakers with PD

Contrary to our initial hypothesis, in our sample of 32 speakers with PD, we did not find a significant effect of medication on RFF values. The previous work in this area by Goberman and Blomgren (2008) did see a clear trend for higher offset and onset RFF during ON medication. We did not see such a trend. Potential differences for this

discrepancy include (1) differences in characteristics of the study populations, (2) a general lack of medication effect in our participants, or (3) differences in study methodology.

The participants in this study were similar to those studied by Goberman and Blomgren (2008). The majority of participants in both studies were male speakers (23/32 = 72% versus 6/9 = 69%) and comprised a similar age group [mean 68 yrs here and mean 69 yrs in Goberman and Blomgren (2008)]. However, here we studied a large population of individuals with PD, irrespective of whether the individuals had voice and speech issues associated with their PD with an average time since diagnosis of 6.3 yrs. In contrast, Goberman and Blomgren (2008) specifically studied individuals who had been diagnosed with hypokinetic dysarthria with an average time since diagnosis of 11.4 yrs. Another potential factor is the general medical response of participants. Our participants showed an average reduction in UPDRS of 5 (0 to 18 range) during ON medication compared with OFF medication. The participants in Goberman and Blomgren (2008) were all known to have motor fluctuations in response to medication, and of the nine individuals with PD studied eight showed an improvement in their UPDRS-III scores while ON medication relative to OFF. If differences in speech involvement and response to medication were primary causes for a lack of medication effect on RFF in our sample, we would expect a strong correlation between changes in RFF with medication and both general changes in motor function with medication (change in UPDRS-III scores) and speech involvement (UPDRS item 2.1 scores). However, relationships were not strong, as shown in Fig. 5. It may be more likely that differences in sample size and individual estimation methodology (using one VcV instance versus an average of 12) are responsible for the differences in results.

Equivocal findings regarding the effect of medication on voice and speech in PD are not an entirely unexpected result. Although dopamine agonists have been noted to improve tremor, bradykinesia, rigidity, and postural abnormalities in patients (Rascol *et al.*, 2002), it is still unclear to what extent medication improves PD voice and speech. Medication has been reported to improve subjective rating and intelligibility scores of PD speech (Nakano *et al.*, 1973; Solomon and Hixon, 1993; De Letter *et al.*, 2005) but there is not yet evidence that medication leads to consistent changes in *F*0. Two previous studies on the effects of medication on mean *F*0 have found no difference between ON and OFF medication (Jiang *et al.*, 1999; Goberman *et al.*, 2002). Sanabria *et al.* (2001) found that *F*0 in sustained vowels was higher when patients were ON medication relative to OFF, an unanticipated finding given that speakers with PD have been shown to have significantly higher mean *F*0 relative to control speakers (Goberman *et al.*, 2002). In addition, no significant effect of medication has yet been found for the variability (SD) of *F*0 (Goberman *et al.*, 2005; Skodda *et al.*, 2011).

C. Sex effects

Contrary to our initial hypothesis, we did find a significant effect of sex on RFF. RFF was significantly higher in females compared with males but with a low ($\eta_p^2 = 0.01$) effect size. More interestingly, a significant interaction between cycle and sex was found with a moderate effect size ($\eta_p^2 = 0.08$). Examining Fig. 3 it is clear that males and females differed most substantially on offset RFF rather than onset RFF. No interaction was found between group and sex; thus, this sex difference is not dominated by either the control group or the speakers with PD but occurs in both groups.

Although the previous work examining RFF in healthy elderly speakers and individuals with PD included both male and female participants (i.e., Watson, 1998; Goberman and Blomgren, 2008), neither differentially studied the effects of sex on RFF. However, a supplementary analysis performed in a larger study by Robb and Smith (2002) found a trend for higher offset RFF in $N = 5$ 21-yr old women (mean offset cycle 10 value of 1.2 ST) compared with $N = 5$ 21-yr old men (mean offset cycle 10 value of 0.5 ST). Their discussion of this trend suggested a potential relationship to sex-mediated differences in voice onset time, which have been postulated to be driven by both physiological and also sociophonetic factors such as female use of over-articulated speech (Swartz, 1992; Ryalls *et al.*, 1997). Future work to test the role of speaking style and rate on RFF in a population of male and female speakers using variants of both clear and conversational speech could further elucidate these factors.

Potential physiological explanations for differences in RFF in men and women stem from any of the proposed mechanisms for RFF: Vocal fold tension, vocal fold kinematics, and glottal airflow. To our knowledge no study has yet studied vocal fold tension or kinematics during voiceless consonant production in males versus females. However, anatomical differences in laryngeal geometry in males and females have been shown to be responsible for differences in mean *F*0 as well as glottal characteristics during voicing, with females showing a higher mean *F*0 and a greater steady state glottal airflow (Titze, 1989). If the vocal folds are placed in a partially abducted state during phonation (i.e., a glottal chink), this could potentially reduce the possible effects of early abduction on offset RFF and may explain the difference we found as a function of sex. Future simultaneous study of both vocal fold kinematics and RFF may elucidate this subject.

V. CONCLUSIONS

We have estimated the RFF in a large sample of older speakers including individuals with PD both ON and OFF medication. We found statistically significantly lower RFF in individuals with PD while ON medication compared with healthy age-matched controls. We found that RFF was statistically significantly lower in individuals diagnosed 5 yrs or more prior to experimentation relative to individuals diagnosed less than 5 yrs prior to experimentation but we did not find an effect of medication on RFF. Unexpectedly, we found a substantial effect of sex on offset RFF, with lower values in males relative to females. Future work examining the physiological bases of RFF is necessary to fully interpret this finding.

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