

Research Note

Acuity to Changes in Self-Generated Vocal Pitch in Parkinson's Disease

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Purpose: Given the role of auditory perception in voice production, studies have investigated whether impairments in auditory perception may underlie the noted disruptions in speech in Parkinson's disease (PD). Studies of loudness perception in PD show impairments in the perception of self-generated speech, but not external tones. Studies of pitch perception in PD have only examined external tones, but these studies differed in terms of the interstimulus intervals (ISIs) that were used, did not examine the impact of cognition, and report conflicting results. To clarify pitch perception in PD, this work investigated perception of self-generated vocal pitch, controlling for cognition and ISI.

Method: A total of 30 individuals with and without PD completed (a) hearing threshold testing, (b) the Montreal Cognitive Assessment, and (c) an adaptive just-noticeable-difference paradigm under two separate ISIs (100 ms and 1,000 ms) to assess acuity to self-generated vocal pitch. **Results:** There was no significant difference in acuity between individuals with and without PD. Both groups demonstrated significantly worse acuity for longer compared to shorter ISIs. Montreal Cognitive Assessment scores were not a significant predictor of acuity. **Conclusions:** The results suggest that acuity to self-generated vocal pitch does not differ between individuals with and without PD.

Parkinson's disease (PD) is a progressive neurological condition that has an estimated lifetime risk of 1%–2% (Elbaz et al., 2002). In addition to the cardinal motor symptoms of PD (e.g., limb tremor and rigidity; Hoehn & Yahr, 1998), the majority of individuals with PD also develop *hypokinetic dysarthria*. Hypokinetic dysarthria is a motor speech disorder that commonly includes reduced fluctuation in pitch (Aronson & Brown, 1975; Canter, 1963), the perceptual correlate of voice fundamental frequency (f_0). These impairments in voice f_0 result in flat vocal prosody (i.e., intonation and stress patterns used during speech), which reduces the naturalness of speech (Anand & Stepp, 2015) and negatively impacts daily communication in PD (McNamara & Durso, 2003; Miller et al., 2006). The underlying physiological processes that are responsible for these disruptions to voice are unknown, and this poses a challenge to the development of long-term therapies

for voice symptoms in PD. Speech perception is known to interact with speech production (Houde & Nagarajan, 2011; Villacorta et al., 2007); thus, a possible explanation for the observed speech disturbances in PD may be disordered auditory perception. For features of voice production, this would manifest as an impairment in the perception of loudness and/or pitch.

Auditory perception in PD has been examined primarily in relation to loudness and pitch, since these features are commonly affected in hypokinetic dysarthria. In the loudness domain, individuals with PD do not differ from individuals without PD in their ability to make judgments about the loudness of externally generated tones (Abur et al., 2017; Dromey & Adams, 2000). In contrast, when asked to judge the loudness of a playback of their own voice (Ho et al., 2000), individuals with PD significantly overestimated loudness compared to individuals without PD. A separate study found worse performance on a loudness discrimination task, using an external voice as a stimulus, in individuals with PD compared to individuals without PD (Richardson & Sussman, 2019). Studies investigating loudness perception collectively suggest that, during passive listening, the recognition of the stimuli as a voice or a separate externally generated sound may affect perceptual accuracy in PD; therefore, it is possible that the same might be true in the pitch domain. Nonetheless, studies of pitch perception in PD have only employed paradigms using nonvoice

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stimuli (pure tones) and show inconsistent results. For instance, in examining perceptual acuity to the frequency (i.e., the acoustic correlate of pitch) of pure tones, one study reported a reduced ability to discriminate frequency in PD (Troche et al., 2012), whereas other work found no differences between individuals with and without PD (Abur et al., 2018). However, the interstimulus interval (ISI) that was used during stimulus presentation varied between the two studies and the latter study did not screen for typical cognition, which may account for the conflicting results.

Frequency discriminatory ability under longer ISIs may show greater decline for populations with cognitive impairments compared to individuals with typical cognition. The longer the time intervals in the stimuli presentation, the more the temporary auditory memory trace will decay; this makes perceptual judgments more difficult, since less information is available to the listener at the time they are asked to make a judgment. Additionally, this difficulty may be more pronounced if listeners have concurrent cognitive impairments, specifically in the prefrontal cortex, since this area mediates and facilitates auditory memory storage (Alain et al., 1998; Bodner et al., 1996). In line with this, one previous study reported that longer ISIs degraded frequency discriminatory ability, or acuity, in listeners with and without Alzheimer's disease and that discriminatory ability was *more* affected by longer ISIs in individuals with Alzheimer's disease compared to individuals without Alzheimer's disease (Pekkonen et al., 1994). Given that Alzheimer's disease and PD both affect cognition via the prefrontal cortex (DeKosky & Scheff, 1990; Gotham et al., 1988; Taylor et al., 1986), experimental ISIs could similarly have a greater effect on pitch perception measures in PD compared to individuals without PD. When examining loudness discrimination under increasing memory load conditions in individuals with and without PD, one study reported reduced discriminatory ability for both groups, but no significant interaction of group and task (Richardson & Sussman, 2019). However, across all participant groups, a significant correlation was found between performance on an auditory memory task and loudness discrimination (Richardson & Sussman, 2019). This suggests that a greater prevalence of prefrontal changes in PD might interact with auditory discriminatory tasks.

A negative effect of longer ISIs on pitch perception measures in PD is also supported by the experimental results of the two conflicting studies investigating pitch discrimination of externally generated pure tones. The study with a longer ISI (750 ms; Troche et al., 2012) found poorer pitch acuity in individuals with PD compared to individuals without PD, whereas the study with the shorter ISI (20 ms; Abur et al., 2018) found no group differences in pitch acuity. Auditory acuity measures are related to hearing, which was controlled for in both studies, and the central processing of auditory information; thus, if auditory memory is impacted in PD, it may confound the ability of experimental measures to accurately relay perceptual acuity.

Thus, the literature indicates a possible interaction of ISI duration with prefrontal changes in PD that might have confounded prior work, especially given the evidence of long ISIs negatively impacting a similar task in Alzheimer's disease. Previous work in loudness perception in PD also suggests that acuity may be different for externally generated compared to self-generated sounds in PD, which has not been investigated in relation to pitch. This project aimed to clarify pitch perception in PD by investigating acuity to changes in self-generated voice f_0 in individuals with and without PD using two different ISIs. This study is the first to quantify acuity to changes in voice f_0 of self-generated voice in PD and to examine cognition and the effect of ISI in a voice perception task in PD. Based on the literature in the loudness domain, we hypothesized that individuals with PD would show reduced acuity to self-generated vocal pitch compared to individuals without PD. Additionally, when the vocal pitch perception task contained longer ISIs, we expected differentially worse acuity for individuals with PD compared to individuals without PD due to cognitive interactions with auditory memory.

Method

Participants

Thirty-eight individuals diagnosed with idiopathic PD were recruited for the study. Nine individuals with PD were excluded from the study due to abnormal hearing for older adults at more than one frequency ($N = 4$; see Hearing Threshold Testing section), inability to complete tasks due to severity of PD symptoms ($N = 4$). Thus, a total of 30 individuals diagnosed with idiopathic PD by a neurologist (13 women, 17 men) participated in the study (see Table 1). Thirty-five individuals without PD were recruited for the study. Five individuals without PD were excluded from the study due to abnormal hearing for older adults at more than one frequency ($N = 5$; see Hearing Threshold Testing section). A total of 30 individuals without PD (15 women, 15 men) with no history of neurological disease and speech, language, or hearing disorders participated in the study (see Table 2). One individual with PD wore a unilateral deep brain stimulation device, which was turned off for the duration of the study. Speakers had no history of speech, language, or hearing impairments other than those associated with PD. Given that musicality benefits performance on pitch discrimination tasks (Kishon-Rabin et al., 2001; Micheyl et al., 2006), the participant groups had similar distributions of musical experience (quantified as the number of years of playing an instrument or singing post-high school via patient self-report; see Tables 1 and 2). All participants completed written consent in compliance with the Boston University Institutional Review Board.

Hearing Threshold Testing

All recruited individuals underwent pure-tone hearing threshold testing at 125, 250, 1000, 2000, and 4000 Hz

Table 1. Age, sex, Movement Disorder Society–sponsored revision of the Unified Parkinson’s disease Rating Scale PIII (UPDRS PIII) scores, and Montreal Cognitive Assessment (MoCA) scores for all individuals with Parkinson’s disease included in the study.

Subject	Age	Sex	UPDRS PIII	MoCA score (out of 30)	Musical experience (years)
PD01	61	F	47	28	30
PD02	70	F	36	21	—
PD03	72	M	22	26	—
PD04	60	M	54	23	—
PD05	49	M	47	29	—
PD06	73	F	57	24	—
PD07	54	F	36	24	—
PD08	63	F	38	29	—
PD09	66	F	45	28	20
PD10	46	M	75	27	—
PD11	69	M	64	28	—
PD12	70	F	77	22	50
PD13	70	M	61	25	49
PD14	67	M	76	29	—
PD15	50	M	17	28	10
PD16	65	F	20	29	—
PD17	67	F	50	25	34
PD18	68	F	52	26	—
PD19	55	M	49	24	—
PD20	58	F	7	27	—
PD21	62	M	50	25	—
PD22	55	M	26	28	—
PD23	67	M	63	25	49
PD24	61	F	34	27	—
PD25	59	M	23	26	—
PD26	62	M	47	28	—
PD27	63	F	39	27	—
PD28	72	M	23	25	—
PD29	68	M	38	28	—
PD30	68	M	66	23	—

Note. Musical experience is defined as the patient reported number of years of playing an instrument or singing post–high school. Em dashes indicate no musical experience. Bolded rows indicate individuals with MoCA scores indicative of mild cognitive impairment. F = female; M = male.

using 3M E-A-RTONE Gold 3A insert earphones and the Grason-Stadler GSI 18 Screening Audiometer. Individuals with hearing thresholds within normal range for older adults (under 25 dB HL for frequencies 1000 Hz and below, and under 40 dB HL above 1000 Hz; Schow, 1991) were included in the study ($N = 24/30$ in each group). Individuals who had abnormal hearing thresholds for older adults at more than one frequency were excluded from participation. Six participants with PD had one frequency with an abnormal threshold for older adults.¹ These participants with PD were included in the study with six hearing-matched (within 5 dB HL) participants without PD. None of the study participants had hearing aids.

¹Hearing thresholds for six participants with PD: Two participants had hearing thresholds of 35 dB HL at 250 Hz, two participants had hearing thresholds of 50 dB HL at 4000 Hz, and two participants had hearing thresholds of 60 dB HL at 4000 Hz.

Table 2. Age, sex, and Montreal Cognitive Assessment (MoCA) scores are listed for all individuals without Parkinson’s disease included in the study.

Subject	Age	Sex	MoCA score (out of 30)	Musical experience (years)
C01	68	M	26	9
C02	56	M	29	—
C03	77	F	26	47
C04	77	M	30	—
C05	46	M	28	—
C06	61	F	27	—
C07	66	F	28	48
C08	63	M	26	13
C09	64	F	27	—
C10	51	F	27	33
C11	80	F	28	—
C12	56	M	29	—
C13	81	M	24	—
C14	50	M	29	—
C15	61	M	30	—
C16	62	M	29	—
C17	68	F	28	50
C18	61	F	29	—
C19	48	M	28	—
C20	54	F	27	—
C21	67	F	29	—
C22	67	M	25	—
C23	59	F	30	—
C24	59	F	27	—
C25	61	F	29	—
C26	76	M	30	—
C27	68	F	28	—
C28	83	F	30	20
C29	57	M	29	—
C30	77	M	23	—

Note. Musical experience is defined as the number of years of playing an instrument or singing post–high school. Em dashes indicate no musical experience. Bolded rows indicate individuals with MoCA scores indicative of mild cognitive impairment. M = male; F = female.

Montreal Cognitive Assessment

All recruited individuals completed the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) to quantify impairments in global cognitive function. Scores $\geq 26/30$ were interpreted as normal cognition (Nasreddine et al., 2005).

Movement Disorder Society–Sponsored Revision of the Unified Parkinson’s Disease Rating Scale

All individuals with PD completed the Movement Disorder Society–sponsored revision of the Unified Parkinson’s Disease Rating Scale (Goetz et al., 2008) to assess motor function (see Table 1). The Movement Disorder Society–sponsored revision of the Unified Parkinson’s Disease Rating Scale examination was administered and scored per protocol by a certified researcher. Prior work suggests that a score of 32 or below indicates mild motor impairment, a score between 33 and 59 indicates moderate motor

impairment, and a score above 59 indicates severe motor impairment (Martínez-Martín et al., 2015).

Acuity to Self-Generated Vocal Pitch

All participants in the study completed a frequency discrimination listening task to determine acuity to playback of self-generated voice f_o under two conditions. Acuity was quantified using a just-noticeable-difference (JND) paradigm with an adaptive two-forced choice-procedure (Levitt, 1971), obtaining a discrimination threshold (García-Pérez, 1998). Prior to the listening tasks, all participants were asked to produce the vowel /a/ for 2–3 s. Speech was recorded using a Shure omnidirectional MX153 eartset microphone positioned at approximately 45° from the midline and 7 cm from the corner of the mouth. A custom-written MATLAB (Mathworks, 2013, Version 8.1.0.604 [R2013b]) script was used to extract the middle 500-ms segment of each recorded utterance. The extracted segment was used as the stimulus for both conditions of the JND paradigm, wherein participants heard their voice recording playback through Etymotic ER-2 insert earphones in a listening task. The Etymotic ER-2 insert earphone output was calibrated to ensure a comfortable listening intensity (regardless of the intensity of the participant's recording) of approximately 75 dB SPL (Raz et al., 1989) prior to each experimental session using a Brüel & Kjær 2cc Coupler Type 4946, a Brüel & Kjær Type 2250 Sound Pressure Level Meter, and a 1000-Hz pure tone played with an Olympus Linear PCM Recorder LS-10 as sound input.

The listening task involved a comparison of one stimulus (a reference) to another stimulus that was either the reference repeated (a “catch trial”) or a perturbed version of the stimulus with an increase in voice f_o in semitones (ST)². The time difference between the first and second stimulus (the interstimulus interval or ISI) was set based on the task condition. In one condition, the duration of the ISI was 100 ms. In the other condition, the duration of the ISI was 1,000 ms. All participants completed the JND paradigm under both conditions in a counterbalanced order.

During the task, voice f_o was shifted adaptively based on the participant responses. A custom-written MATLAB (Mathworks, 2013, Version 8.1.0.604 [R2013b]) script interfacing with Eclipse V4 Harmonizer (Eventide) hardware was used to adaptively modify the voice f_o in ST. The initial difference in voice f_o between the two stimuli was set to be half of an ST. Each trial, participants were asked to identify whether the two stimuli they heard were the same or different in terms of their pitch. Participants could only listen to each trial once. A correct answer for two consecutive trials *decreased* the ST difference between the stimuli, making the task more difficult. One incorrect answer *increased* the ST difference between the stimuli, making the task less difficult. Therefore, the task adapted

²Changes in voice f_o were made in ST, a logarithmic measure equal to 1/12 of a musical octave, since auditory perception is roughly logarithmic.

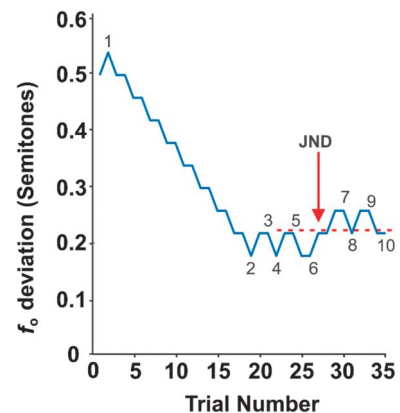
according to each participant's responses, allowing for an efficient estimate of acuity for each participant. Any change in the direction of the paradigm (i.e., when the ST difference was lowered after being increased, or vice versa) was considered a “reversal.” The paradigm completed after 10 “reversals” occurred (set a priori by pilot testing).

The threshold of vocal pitch discrimination (JND) was quantified as the average of the last six “reversals” (shown in Figure 1). Thus, two JND values (in ST) were determined for each participant (one for the 100-ms ISI and one for the 1,000-ms ISI). All participants had a greater than chance (> 50%) average catch trial accuracy, which is a gross indicator of attention to the task. The catch trial accuracy for individuals with PD ($M = 92.3\%$, $SD = 8.6\%$) was similar to that of individuals without PD ($M = 90.9\%$, $SD = 10.8\%$).

Statistical Analysis

A two-way mixed model analysis of variance (ANOVA) was used to examine the effect of group (between-participant; participants with and without PD), ISI condition (within-participant; 100 ms and 1,000 ms), and their interaction. A two sample *t* test was used to compare the MoCA scores between individuals with and without PD. The ANOVA did not reveal a significant interaction between group and ISI, so average JND values (the average of the 100-ms and 1,000-ms JND scores for each participant) were used in a linear regression analysis to determine the relationship between MoCA scores (independent variable) and average JND values (dependent variable). An alpha of .05 was set to be statistically significant.

Figure 1. The just-noticeable-difference (JND) paradigm is shown for a participant with Parkinson's disease (PD28) during the 1,000-ms interstimulus interval condition with “reversals” (changes in direction of the adaptive paradigm) numbered from 1 to 10. The difference in voice fundamental frequency (f_o) in semitones between the two stimuli played is plotted as a function of trial number. The JND (discrimination threshold; red dashed line) was determined for each participant as the average of the last six reversals.



Results

Individuals without PD showed worse scores for the 1,000-ms ISI condition ($M = 0.49$ ST, $SD = 0.17$ ST) compared to the 100-ms ISI condition ($M = 0.44$ ST, $SD = 0.19$ ST). Similarly, individuals with PD showed worse scores for the 1,000-ms ISI condition ($M = 0.60$ ST, $SD = 0.33$ ST) compared to the 100-ms ISI condition ($M = 0.55$ ST, $SD = 0.33$ ST). The ANOVA revealed a significant effect of ISI, $F(1, 58) = 9.94$, $p = .003$, but no effects of group, $F(1, 1) = 2.34$, $p = .13$, or the interaction of ISI and group, $F(1, 1) = 0$, $p = .96$, on JND values (see Figure 2). The ISI factor had a large effect size ($\eta_p^2 = .15$). Descriptively, no differences were seen in the number of trials needed to yield a JND between participant groups for both the 100-ms ($M = 37.13$, $SD = 7.93$ for PD; $M = 36.45$, $SD = 8.87$ for controls) and 1,000-ms ($M = 34.93$, $SD = 6.01$ for PD; $M = 36.76$, $SD = 6.10$ for controls) conditions. The MoCA scores were significantly lower ($p = .002$) in individuals with PD ($M = 0.87$, $SD = 0.07$) compared to individuals without PD ($M = 0.93$, $SD = 0.06$). The linear regression did not show a significant relationship between MoCA scores and average JND values, $F(1, 1) = 0.64$, $p = .43$ (see Figure 3).

Discussion

To our knowledge, this is the first work to examine acuity to changes in self-generated vocal pitch in PD. The goal of this study was to examine pitch perception in PD, specific to self-generated voice, and to clarify discrepancies in prior auditory acuity studies in PD. Considering prior work in the loudness domain, we hypothesized that individuals with PD would show reduced acuity to self-generated vocal pitch compared to individuals without PD. The acuity task was examined using two ISIs to clarify how stimuli timing affected perception. We hypothesized that longer ISIs would result in worse acuity compared to shorter ISIs.

Figure 2. The just-noticeable-difference (JND) values are shown by interstimulus interval condition of 100 ms (circles) or 1,000 ms (squares) for individuals with Parkinson's disease (PD group; dark blue) and individuals without Parkinson's disease (control group; light blue). The error bars indicate 95% confidence intervals. The asterisks display significant differences and "ns" displays a nonsignificant difference.

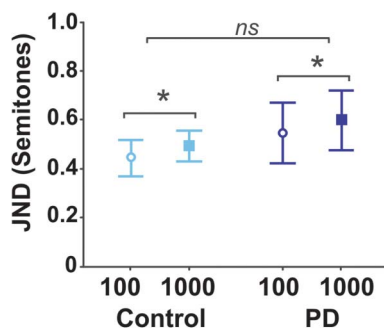
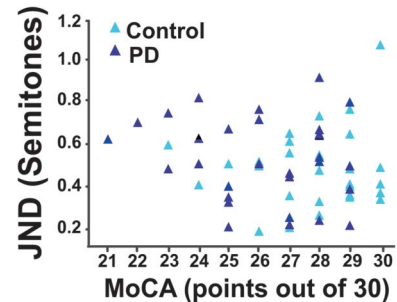


Figure 3. The average just-noticeable-difference (JND) values across the 100-ms and 1,000-ms conditions are shown by Montreal Cognitive Assessment (MoCA) score for individuals with Parkinson's disease (PD group, dark blue) and individuals without Parkinson's disease (control group, light blue).



In line with prior work in Alzheimer's disease (Pekkonen et al., 1994), we expected that this decline in acuity would be more pronounced in PD. Furthermore, we hypothesized that worse performance on the MoCA would be associated with worse performance on the acuity task due to cognitive interactions with pitch perception.

In contrast with our hypothesis, no significant differences were found in acuity to self-generated voice between individuals with and without PD, but individuals with PD showed a trend for slightly worse acuity ($p = .132$; see Figure 2). This study found no impairments to self-generated voice perception in PD, but we cannot rule out the possibility that a small group difference exists that could not be captured by the current work. The current study was designed to detect medium-to-large effect sizes with 80% power; thus, increased power through use of a larger sample size would be necessary to detect a group difference with a small effect size. It is also important to consider whether there was an effect of the distance between the initial pitch difference and the JND threshold (i.e., if a listener has a JND that lies further away from the initial pitch difference, it will take more time to reach their threshold and result in a facilitating effect on the task over time). However, the total amount of JND trials in each task did not clearly differ by group or condition (see Results section), which suggests that it did not impact the results of this work.

This work intentionally utilized self-generated vocalization as stimuli in a pitch discrimination task to determine how the recognition of stimuli as *self-generated* influences pitch perception; however, playback of voice involves only air-conducted sound perception whereas real-time auditory feedback of voice also encompasses bone-conducted sound. Thus, this study should be considered as only an approximation of real-time voice perception. Additionally, this study focused on examining vocal pitch perception during an isolated vowel and the findings may differ for other types of speech production tasks.

This study was designed to address confounding results in prior work (Abur et al., 2018; Troche et al., 2012) by utilizing two ISIs (100 ms and 1,000 ms), having an equal

distribution of musical experience in participant groups, and examining the role of cognition on task performance. As hypothesized, acuity was reduced for the longer ISI task. Yet, in contrast with our hypothesis, ISI did not differentially degrade acuity in individuals with PD compared to those without PD. Thus, ISI differences alone cannot explain the differing results of the two prior studies of pitch perception of pure tones in PD (Abur et al., 2018; Troche et al., 2012). It is important to consider the variability in sample size across these studies: this work ($N = 30$ in each group), the study of pure-tone perception with an ISI of 20 ms ($N = 15$ in each group; Abur et al., 2018), and the study of pure-tone perception with an ISI of 750 ms ($N = 12$ with PD and $N = 15$ without PD; Troche et al., 2012). When compared with prior work, the current study has a larger sample size and statistical power. Therefore, this work is less likely to result in a Type II statistical error (i.e., finding a difference in voice f_0 acuity between individuals with and without PD when there is no true group difference) than the previous studies. Additionally, neither of the prior studies controlled for musical experience, which is known to influence pitch discrimination (Kishon-Rabin et al., 2001). This work also had participant groups that were balanced for musical experience to control for musicality as a possible confound.

The relationship between cognitive status and acuity to self-generated vocal pitch was also examined in the current work as a possible reason for the differing results in previous studies; the study by Troche et al. (2012) screened for typical cognition, whereas Abur et al. (2018) did not. Given the role of the prefrontal cortex in auditory memory, we hypothesized that cognitive status quantified using the MoCA would be related to performance on the acuity task. The results here did not demonstrate an effect of cognition measured via the MoCA and do not support the notion that cognition affected prior results; however, this study included only participants with typical cognition and mild cognitive impairment. Future work should explore more robust and comprehensive measures of cognitive status, across a group of participants with a larger range of cognitive status, as a factor in perceptual sound discrimination task performance in PD. The study by Pekkonen et al. (1994), which reported nine individuals with Alzheimer's disease (involving cognitive changes to the prefrontal cortex) were more affected by longer ISIs than 10 individuals without Alzheimer's disease in a frequency discrimination task, employed 3,000- and 1,000-ms ISIs. The statistical power of the investigation by Pekkonen et al. (1994) is limited due to a small sample size, but it suggests a possibility that the ISIs used in the current work were too short to clarify interactions with cognition and perceptual discriminatory ability in PD.

The current findings suggest that impaired acuity to voice f_0 is not likely to be driving the disruptions in voice f_0 variability (i.e., reduced vocal prosody) commonly observed in PD. Although it is possible that there is an impairment in acuity to voice f_0 in PD with a small effect size that could not be detected in this work, prior work has

reported a large effect size ($\eta_p^2 = .35$) for reductions in voice f_0 variability during speech production tasks in PD compared to individuals without PD (Bowen et al., 2013). Given the large effect size and high occurrence of speech production disruptions related to voice f_0 variability in PD, it is unlikely that the underlying cause would have a small effect size.

Conclusions

Acuity to self-generated vocal pitch was not found to differ between individuals with and without PD. One study of acuity to externally generated pitch in individuals with and without PD similarly found no group differences (Abur et al., 2018), but another study reported worse acuity in individuals with PD compared to individuals without PD (Troche et al., 2012). Future work is needed to elucidate whether pitch perception in PD is different for externally generated compared to self-generated sounds. The current work also found that, for both individuals with and without PD, acuity to self-generated vocal pitch was significantly worse under longer ISIs compared to shorter ISIs. This finding suggests that ISI is an important experimental factor to consider when examining results of perceptual paradigms. The acuity task results also did not show significant linear relationships with cognitive status (quantified via the MoCA).

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