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Research report

Sensorimotor control of vocal pitch and formant frequencies in Parkinson's disease

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ABSTRACT

Background: Auditory feedback reflects information on multiple speech parameters including fundamental frequency (pitch) and formant properties. Inducing auditory errors in these acoustic parameters during speech production has been used to examine the manner in which auditory feedback is integrated with ongoing speech motor processes. This integration has been shown to be impaired in disorders such as Parkinson's disease (PD), in which individuals exhibit difficulty adjusting to altered sensory-motor relationships. The current investigation examines whether such sensorimotor impairments affect fundamental frequency and formant parameters of speech differentially.

Methods: We employed a sensorimotor compensation paradigm to investigate the mechanisms underlying the control of vocal pitch and formant parameters. Individuals with PD and age-matched controls prolonged a speech vowel in the context of a word while the fundamental or first formant frequency of their auditory feedback was altered unexpectedly on random trials, using two magnitudes of perturbation.

Results: Compared with age-matched controls, individuals with PD exhibited a larger compensatory response to fundamental frequency perturbations, in particular in response to the smaller magnitude alteration. In contrast, the group with PD showed reduced compensation to first formant frequency perturbations.

Conclusions: The results demonstrate that the neural processing impairment of PD differentially affects the processing of auditory feedback for the control of fundamental and formant frequency. The heightened modulation of fundamental frequency in response to auditory perturbations may reflect a change in sensory weighting due to somatosensory deficits associated with the larynx, while the reduced ability to modulate vowel formants may result from impaired activation of the oral articulatory musculature.

1. Introduction

Parkinson's disease (PD) is a multisystem disorder associated with a range of motor and sensory deficits. In PD, the speech motor symptoms of hypokinetic dysarthria include both laryngeal deficits and articulatory impairments (Ackermann et al., 1997; Caligiuri, 1989; Connor et al., 1989). Laryngeal deficits such as reduced F0 variability are among the clearest symptoms (Skodda et al., 2009). Articulatory abnormalities include a reduction in the vowel space, characterized by the lowering of high frequency formants and the elevation of low frequency formants (Skodda et al., 2012). It has been suggested that this acoustic restriction results from limited movements of the articulators, notably the tongue and jaw (Skodda et al., 2012). Sensory deficits for speech include impairments in auditory processing of voice and speech (Ho et al., 2000; Ackermann et al., 1997; Gräber et al., 2002).

PD also affects sensorimotor processing for speech with most studies focused on the ability of individuals with PD to integrate auditory feedback with speech motor control processes. Auditory feedback during speech production provides information on the control of multiple speech actions, including the principal vibratory characteristics of the larynx (fundamental frequency, or F0) and the shape of the vocal tract through the resonant (formant) properties. Changes in F0 primarily signal suprasegmental (i.e., intonational) properties (Möbius and Dogil, 2002) and are known to be sensitive to rapid, moment-to-moment auditory feedback modulations in healthy participants (Burnett et al., 1998;

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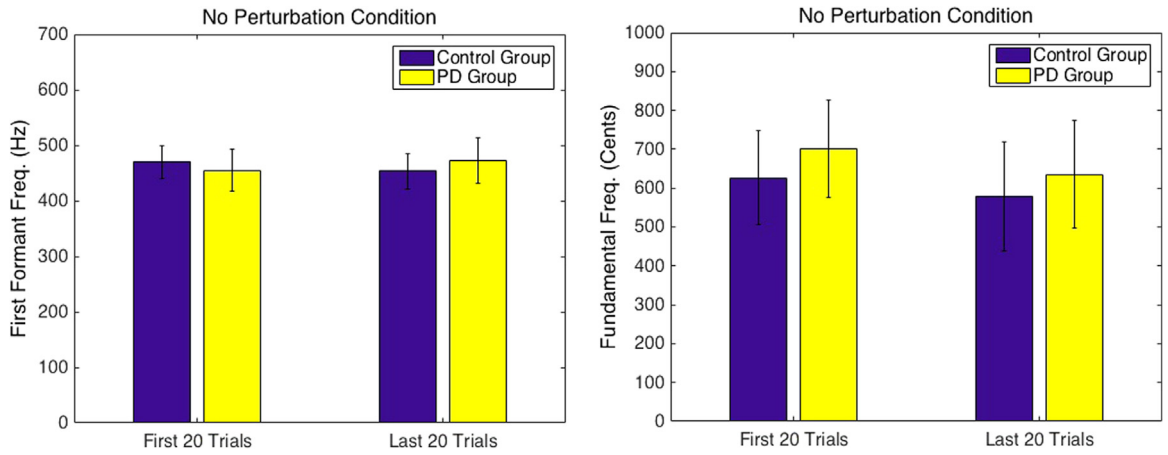

Fig. 1. No perturbation conditions: The mean first formant (F1) frequency (left) and the mean fundamental (F0) frequency (right) in Hertz for the first and last 20 trials productions of the target vowel /ɛ/ for the PD and Control subjects.

Larson et al., 2000), whereas formant properties are primarily associated with segmental (i.e., phonemic) distinctions, in particular for vowels and vowel-like consonants. The control of segmental parameters is typically less sensitive to sudden changes in auditory feedback, with compensatory changes occurring more slowly, and to a lesser degree, than for suprasegmental parameters (Perkell et al., 2000). Nonetheless, it has been demonstrated that during the course of a single production, talkers will compensate for an induced perturbation in pitch or formant structure by altering speech output in the direction opposite to the perturbation (Purcell and Munhall, 2006; Tourville et al., 2008; Burnett et al., 1998).

Previous investigations have shown that individuals with PD exhibit complex speech production responses to such manipulations that depend on the specific feedback parameter being manipulated (Chen et al., 2013; Liu et al., 2012; Mollaei et al., 2013). When auditory feedback is altered, a motor response is typically observed in the direction opposite to the shift. The manipulation can be predictable, used to evaluate error-based learning, or unpredictable, used to assess online sensorimotor control. For unpredictable shifts in F0, individuals with PD have been shown to respond with a *larger* compensatory response than individuals without PD (Chen et al., 2013; Liu et al., 2012). In contrast, for predictable formant frequency changes, individuals with PD have been found to respond with a *reduced* adaptation response compared to healthy individuals (Mollaei et al., 2013). The contradictory findings suggest that auditory feedback control of F0 and formant properties may be differentially impaired in PD, giving rise to different compensatory patterns. However, it is difficult to directly compare the results of prior studies examining these different acoustic parameters, as they have been investigated under different speech motor control tasks (online control versus error-based sensorimotor learning).

Here, we investigated the compensatory responses in individuals with PD and healthy control participants to unpredictable, real-time perturbations in F0 and first formant frequency (F1) during vowel production. Participants were instructed to repeatedly produce and sustain the vowel [ɛ] in the embedded word “head”. Two blocks of auditory feedback perturbations, one with fundamental frequency perturbation condition and the other with first formant frequency perturbation condition, were used to alter participants' auditory feedback. Each manipulation condition consisted of two magnitudes and lasted for the whole duration of the trial (for more details see Section 4.3). To ensure that participants did not learn and adapt to the unpredictable auditory feedback manipulations, we compared the average of the first and the last 20 trials between and across the two groups. As noted above, it has been previously found that during the course of a single trial, healthy control participants compensate for an induced perturbation in F0 or F1 by altering speech output in the direction opposite to the perturbation (Purcell and Munhall, 2006; Tourville et al., 2008; Larson et al., 2000; Burnett et al., 1998).

Based on previous findings, we hypothesized that individuals with PD would display a different pattern of compensatory responses from control participants, and further, that different response patterns would emerge for F0 and F1 in individuals with PD. Based on previous research, we expect individuals with PD to show an increased response to F0 manipulations and a reduced response to F1 manipulations. If confirmed in the same group of subjects, these findings would suggest two different dissociable patterns in the manner in which acoustic parameters are processed and integrated during speech in individuals with PD.

2. Results

The average F0 and F1 between the first and last 20 non-perturbed trials in each of the two perturbation conditions (F0 and F1) was compared to ensure that no adaptation as a result of the intervening perturbation was present (see Fig. 1). No statistically reliable differences were observed between the first and last trials for either group (PD group F0: $t[28]=-0.32$, $p=0.28$; PD group F1: $t[28]=-0.37$, $p=0.26$, Control group F0: $t[28]=-0.24$, $p=0.31$; Control group F1: $t[28]=0.48$, $p=0.24$). In addition, we did not observe any differences between groups for the first and the last 20 trials of F0 or F1 (F0 first 20 trials: $t[28]=0.43$, $p=0.23$; F0 last 20 trials: $t[28]=0.33$, $p=0.29$; F1 first 20 trials: $t[28]=-0.27$, $p=0.36$; F1 last 20 trials: $t[28]=0.26$, $p=0.37$).

2.1. Fundamental frequency perturbation

For perturbations in F0, both the individuals with PD and control participants exhibited compensatory changes in production in the direction opposite to the feedback manipulation (Fig. 2). However, overall, the group with PD showed a greater degree of compensation compared to the control participants. A linear mixed-effects model was fitted to the averages of the compensatory responses with *time* (every 10 ms, totaling 40 time points over 400 ms) and *magnitude* (small vs. large perturbation) as the within-subject factors, and *group* (PD vs. control) as a between-subjects factor. Significant main effects of time ($F[39, 2160]=10.52$, $p<0.01$), magnitude ($F[1, 2160]=21.16$, $p<0.01$),

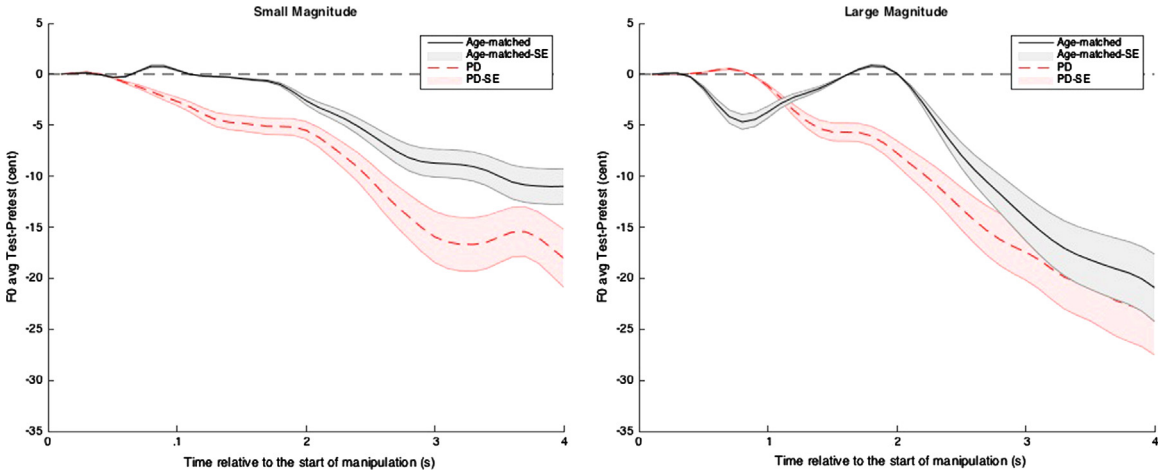

Fig. 2. F0 compensation: Change in the fundamental frequency of the vowel for the target word during the F0 upward perturbation condition. Shown are normalized F0 test minus pre-test for the small magnitude (right) and large magnitude (left) over 0.4 s of vowel production.

and group (F[1, 2160]=31.73.52, $p<0.01$) were found, with no reliable three-way (F[39, 2160]=0.19, $p=0.41$) or two-way interactions (group X time: F[39, 2160]=0.32, $p=0.29$; group X magnitude: F[1, 2160]=1.69, $p=0.19$; time X magnitude: F[39, 2160]=0.56, $p=0.24$).

The *gain* of the response in both F0 and F1 was also calculated as the magnitude of compensation divided by the magnitude of feedback shift. The effects of group (PD vs. control) and magnitude (small vs. large) on F0 *gain* were evaluated using a two-way analysis of variance. Mean F0 gain values for the last 100 ms of each vowel (of the 400 ms analysis window) at the two magnitudes are shown in Fig. 3. A reliable main effect of magnitude (F[1, 28]=6.96, $p<0.01$) was found with no reliable effect of group (F[1, 28]=0.57, $p=0.24$). The two-way interaction was significant (F[1, 28]=4.94, $p<0.05$). Post hoc simple effects analyses with Holm-Bonferroni correction were carried out to examine each magnitude and each group separately. There was a reliable difference between the two groups only for the small magnitude perturbation (F[1, 28]=4.67, $p<0.01$), showing that individuals with PD compensated with a higher gain for this condition. There was no difference between groups for the large magnitude perturbation (F[1, 28]=2.13, $p=0.11$). In addition, a reliable difference between small and large magnitudes was observed for the group with PD (F[1, 28]=7.86, $p<0.01$), but not for the control group (F[1, 28]=2.06, $p=0.13$).

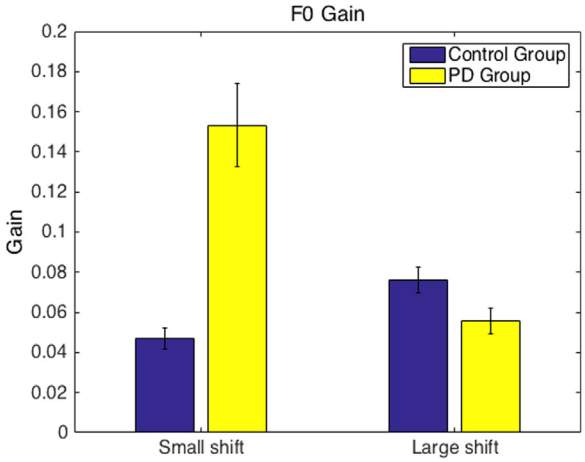

Fig. 3. F0 gain: The mean F0 compensatory gain as measured by the difference of the shifted and the pre-shifted baseline trials divided by the shift of the feedback system. The error bars show the standard error.

2.2. Formant frequency perturbation

For F1, the two groups responded to the auditory feedback perturbation (F1 increase) with a compensatory decrease in F1 output. Overall, however, the group with PD showed reduced compensation compared to the control participants (Fig. 4). A linear mixed-effects model was fit to the within-subject averages of each magnitude of the compensation responses with time (every 4 ms, totaling 100 time points) and magnitude (small vs. large perturbation) as the within-subject factors and group (PD vs. control) as a between-subjects factor. Significant main effects of time (F[99, 5000]=4.18, $p<0.01$) and group (F[1, 5000]=71.16, $p<0.01$) were found, with no reliable main effect of magnitude (F[1, 5000]=0.03, $p=0.81$). The two-way and the three-way interactions were not statistically significant (F[99, 5000]=0.08, $p=0.91$; group X time: F[99, 5000]=0.59, $p=0.23$; group X magnitude: F[1, 5000]=0.00, $p=0.98$; time X magnitude: F[99, 5000]=0.07, $p>0.01$; group X time X magnitude: F[99, 5000]=0.08, $p>0.01$).

To parallel the analyses for F0, the effects of group (PD vs. control) and magnitude (small vs. large) on F1 gain were evaluated using a two-way analysis of variance. Mean F1 gain values of the last 100 ms of each vowel (within the 400 ms analysis window) at the two magnitudes are shown in Fig. 5. A reliable main effect of magnitude (F[1, 28]=14.50, $p<0.01$) was found with no reliable effect of group (F[1, 28]=0.23, $p=0.75$); however, the two-way interaction was significant (F[1, 28]=4.98, $p<0.05$). Simple effects analyses with Holm-Bonferroni correction revealed a reliable effect of group for the small magnitude shift (F[1, 28]=−8.33, $p<0.01$), showing that individuals with PD compensated with a smaller gain than controls for the small magnitude shift. No difference in compensation was observed between groups for the large magnitude perturbation (F[1, 8]=0.87, $p=0.29$). For the group with PD, a reliable difference between small and large magnitudes was observed (F[1, 28]=4.19, $p<0.01$), whereas no such difference was found for the control group (F[1, 28]=1.14, $p=0.16$).

Finally, for individuals in the group with PD, we examined the relationship between the degree of compensation in F0 and F1 and the degree of severity of either UPDRS or the clinical dysarthria rating scores. No significant correlations were found for the severity of motor symptoms as indexed by UPDRS scores or the dysarthria score, as shown in Fig. 6 for the large magnitude (F0 and UPDRS: $r=-0.43$, $p=0.10$; F0 and total dysarthria score: $r=-0.27$, $p=0.32$; F1 and UPDRS: $r=-0.20$, $p=0.49$; F1 and total dysarthria score: $r=0.25$, $p=0.47$), and Fig. 7 for the small

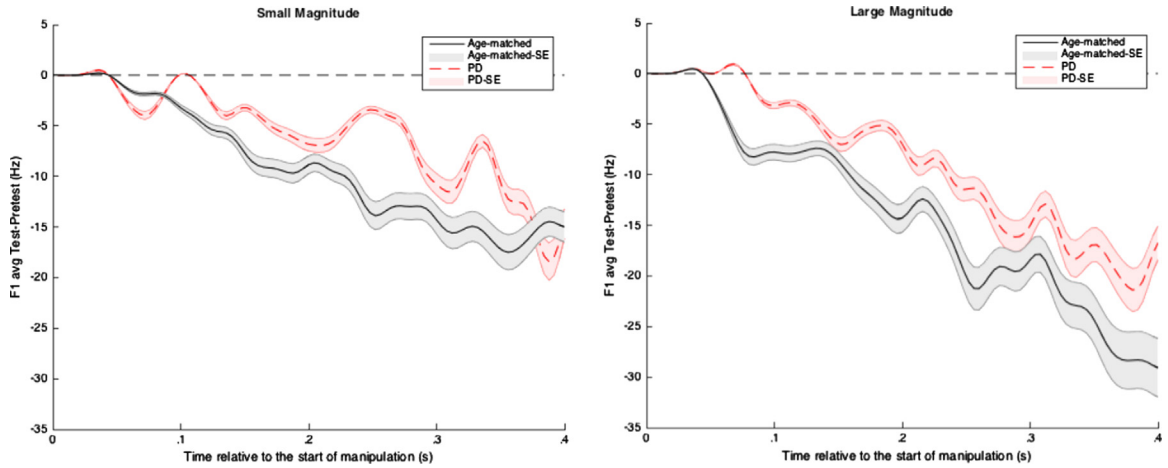

Fig. 4. F1 compensation: Change in the first formant frequency of the vowel for the target word during the F1 upward perturbation. Shown are normalized F1 test minus pre-test for the small magnitude (right) and large magnitude (left) over 0.4 s of vowel production.

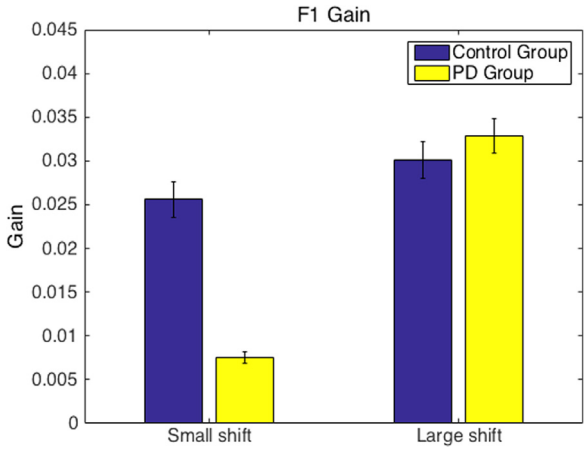

Fig. 5. F1 gain: The mean F1 compensatory gain as measured by the difference of the shifted and the pre-shifted baseline trials divided by the shift of the feedback system. The error bars show the standard error.

magnitude (F0 and UPDRS: $r=-0.01$, $p=0.96$; F0 and total dysarthria score: $r=0.20$, $p=0.46$; F1 and UPDRS: $r=-0.01$, $p=0.64$; F1 and total dysarthria score: $r=-0.02$, $p=0.92$). The lack of relationship between UPDRS or clinical dysarthria rating score with F0 or F1 compensation responses may be related to the fact that most of the individuals with PD were mild in their UPDRS rating and dysarthria rating score (2 participants moderate, 4 participants mild-to-moderate, 6 participants mild, 3 participants within the normal limit).

3. Discussion

During sustained vowel production, different acoustic properties of auditory feedback provide information on the control of multiple speech actions, including laryngeal vibration and articulation. Here we examined the manner in which PD, a disorder involving basal ganglia dysfunction, affected the online sensorimotor control of F0 and vowel formant frequencies. Overall, individuals with PD differed from non-PD controls in the manner and scale of their compensatory responses to auditory feedback alterations during vowel production. The response to F0 perturbations was enhanced relative to the control group, consistent with previous reports for F0 and loudness perturbations in PD (Chen et al., 2013; Liu et al., 2012). In contrast, the response to formant perturbations was less robust, consistent with a previous study of sensorimotor adaptation in PD (Mollaei et al., 2013). This is the first observation, in the same group of individuals with PD, of a differential effect of the disease on discrete auditory feedback parameters during speech motor control.

3.1. Sensorimotor control of vocal pitch

The control of pitch requires the integration of sensory signals (auditory and somatosensory) with the activation of laryngeal muscles. The heightened response to pitch manipulations in the group with PD (notably for the small magnitude perturbation) suggests increased auditory-motor gain for vocal control. One possible explanation for the enhanced gain in PD is that it reflects a compensation for reduced somatosensory sensitivity in the larynx. Previous research has shown reduced somatosensory sensitivity of the laryngeal mucosa to air pressure stimulation in individuals with PD (Hammer and Barlow, 2010), possibly contributing to reduced control of laryngeal-vibratory properties during phonation. Additionally, anesthetization of the vocal fold mucosa in healthy participants enhances the responses to F0 perturbations (Larson et al., 2008). These findings suggest that in healthy individuals, both somatosensory and auditory feedback contribute to the control of F0 during vocalization. However, when one of these feedback control subsystems is reduced or eliminated, the nervous system may place greater weight on the intact feedback subsystem. The increased gain for pitch shifts observed in the current study is consistent with such a re-weighting in response to reduced somatosensory sensitivity. Moreover, an increased auditory gain for phonation can be extended to loudness control and may explain the frequent observation that individuals with PD perceive their own speech as loud when in fact they produce speech with reduced loudness.

A possible mechanism for the increased response to F0 perturbations in PD may be found in the role of the basal ganglia (BG) in processing auditory information. Previous studies have reported that the BG play a role in filtering relevant from non-relevant auditory sensory information (Schneider et al., 1987; Teo et al., 1997). This function may be impaired in PD, resulting in a failure to filter and modulate the sensory input to cortical and subcortical areas (Haslinger et al., 2001; Liotti et al., 2003). The present results suggest a reduction in inhibition, yielding heightened sensory input to motor areas for F0 consistent with the observation of increased activity in the left superior parietal area reported in PD associated with prosodic pitch modulations (Arnold et al., 2014).

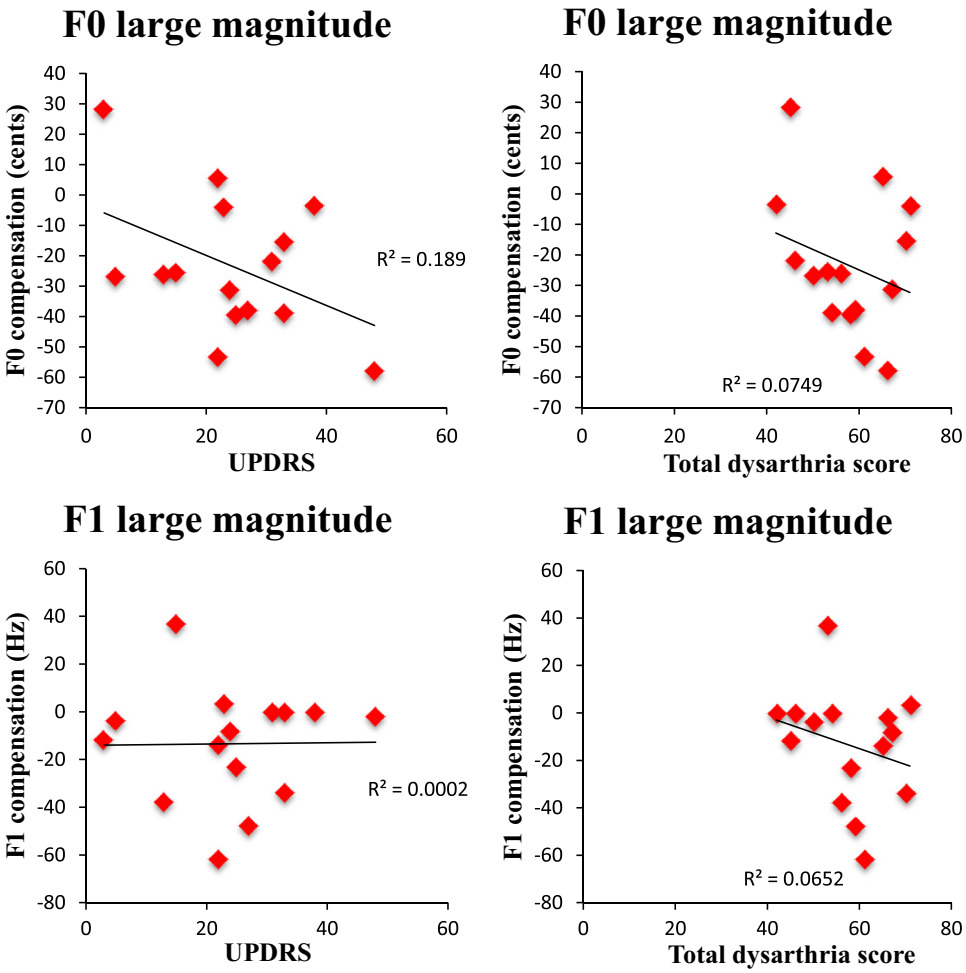

Fig. 6. Large magnitude correlations: The two upper scatterplots show the relationship between the F0 compensation in the large magnitude and the UPDRS and the total dysarthria rating score. The two lower scatterplots show the relationship between the F1 compensation in the large magnitude and the UPDRS and the total dysarthria rating score.

Overall, these findings at the cortical level are consistent with our findings of increased compensatory responses to pitch perturbations.

Interestingly, the largest increase observed in the gain of the compensatory response in the PD group was associated with the smaller F0 shift. The higher response gain of individuals with PD to small magnitude perturbations may reflect a greater sensitivity in English-speaking individuals with PD to smaller shift magnitudes compared to larger shift magnitudes (50 vs. 100 cents). These patterns of response contrast with a recent study using comparable magnitudes of F0 shifts in which Cantonese-speaking participants with PD exhibited larger compensatory responses as a function of shift magnitude without any response latency differences (Chen et al., 2013). A possible explanation for the conflicting findings is that fundamental frequency has a different function in Cantonese compared to English, given that Cantonese is a tonal language in which variations in F0 alone may signal phonemic (between speech-sound categories) distinctions, and hence lexical distinctions. It has been argued that mechanisms underlying the sensorimotor control of pitch are language-specific (Chen et al., 2007, 2012).

3.2. *Sensorimotor control of formant trajectories*

In contrast to F0, which involves laryngeal vibration, formant modification requires changes to the shape of the vocal tract through movement of the oral articulators. The less robust response to unpredictable and intermittent formant shifts in the present study is consistent with a previous study of sensorimotor adaptation (Mollaei et al., 2013) in which the auditory feedback perturbations were predictable and maintained throughout a period of practice (100 trials). While all subjects demonstrated a clear adaptive change in the formant structure of the vowels they produced, individuals with PD showed a reduced adaptive response compared to control participants. In the present study, we used unpredictable perturbation to assess the contribution of real-time control to the reduced adaptive response. The lack of pre- and post-vowel changes indicated that no learning had taken place and that the observed responses reflected real-time sensorimotor control. The results from our previous (Mollaei et al., 2013) and present studies indicate that the sensorimotor control of speech production is disrupted in PD. A reduction in the capacity of sensory-based motor adaptation may reduce the effectiveness of traditional behavioral therapies for dysarthria that rely heavily on sensory feedback to drive changes in motor behaviour (Fox et al., 2002).

If PD affects the processing of auditory information similarly across subsystems, we would have expected similar response profile for F1 and F0 perturbations. However, the reduced response to formant perturbations, in contrast to the increased response to F0 perturbations, points to a differential impact of PD on these two feedback parameters. The reduced response to F1 manipulation may reflect a motor deficit yielding decreased auditory-motor gain or an auditory processing deficit resulting in reduced sensitivity to

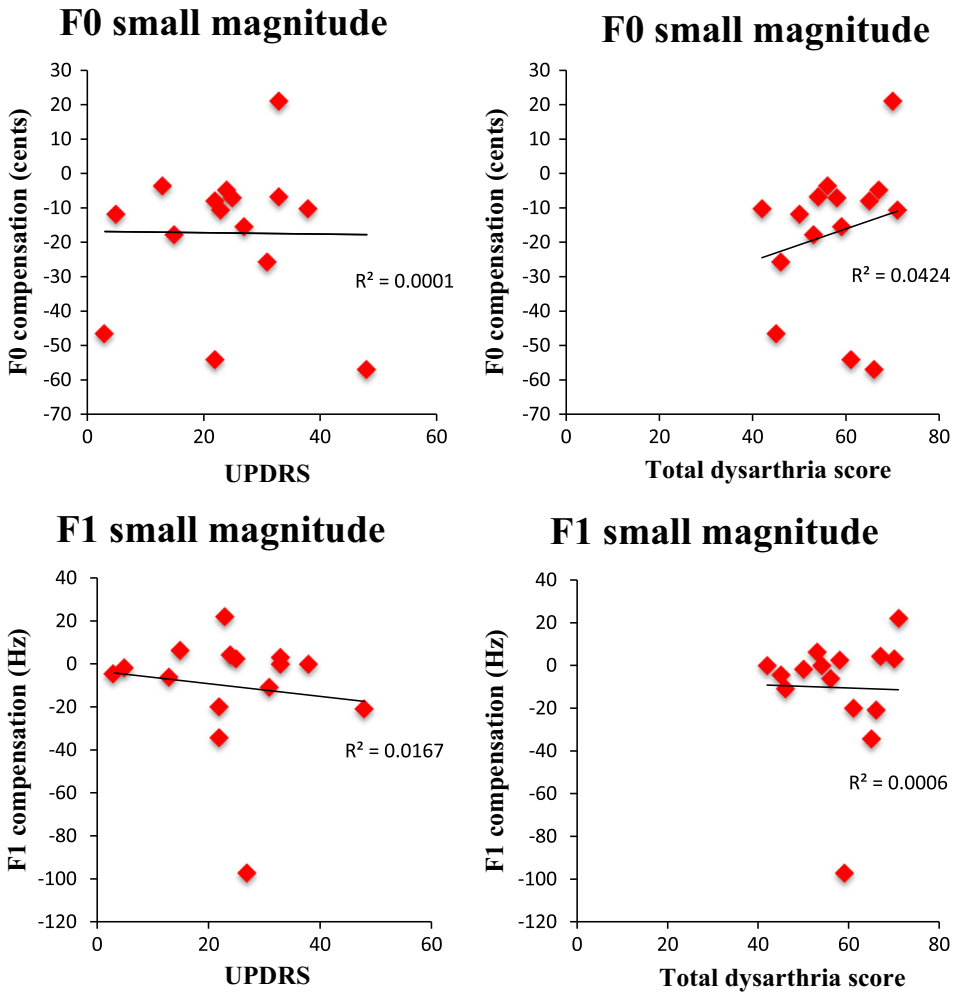

Fig. 7. Small magnitude correlations: The two upper scatterplots show the relationship between the F0 compensation in the small magnitude and the UPDRS and the total dysarthria rating score. The two lower scatterplots show the relationship between the F1 compensation in the small magnitude and the UPDRS and the total dysarthria rating score.

the formant manipulation. Although we cannot rule out reduced auditory feedback sensitivity in response to F1 manipulations, we can rule out any reduced hearing sensitivity within the F1 frequency range for subjects in this study (who all passed a hearing screening). Without additional information on the auditory processing of formant manipulations, we suggest that a reduced compensatory response to formant manipulation results from the motor deficit associated with PD. One possible neural source of the reduced compensation is from known impaired nigrostriatal dopaminergic projections to frontal tongue motor regions in individuals with PD (Ridding et al., 1995; Sabatini et al., 2000). The BG appear to contribute to the fluent execution and performance of such movements (Weiss et al., 1997). At the cortical level, reduced connectivity between auditory and dorsal premotor cortices has been found during speech production in PD (Arnold et al., 2014). Thus, it appears that a reduced modulation of the motor system underlies the limited response to F1 auditory feedback perturbations in individuals with PD.

3.3. Sensorimotor control and PD

Taken together, these findings have important implications for understanding the influence of auditory feedback on speech motor control and on the effects of PD on different sensorimotor control parameters in speech. It appears that auditory feedback manipulations of fundamental and formant frequencies tap into aspects of the sensorimotor control process that are differentially affected in PD. On the surface, the notion of different sensorimotor influences on speech production is consistent with observations of speech following adult-onset hearing loss. Suprasegmental parameters of speech, including pitch and loudness, tend to change rapidly with a change in hearing status (Svirsky et al., 1992; Perkell et al., 1997; Lane et al., 1997) but the phonemic parameters, including vowel formants, are less sensitive to auditory feedback changes and more stable and resistant to change (Perkell et al., 1992; Cowie and Douglas-Cowie, 1992). It appears that the speech motor control system is tuned to the pitch and articulatory properties of auditory feedback, and that the different acoustic properties encode information associated with different speech motor subsystems. Future work with individuals with PD is needed to clarify the source(s) of the differences to determine the impact on the sensory and motor components on the disorder. In addition, the current study suggests that other speech disorders secondary to basal ganglia involvement may also be differentially impaired in sensorimotor control similar to individuals with PD.

4. Experimental procedure

4.1. Ethics statement

This study was approved by the McGill Faculty of Medicine Institutional Review Board in accordance with principles

expressed in the Declaration of Helsinki. Informed written consent was obtained from participants prior to their involvement in the project.

4.2. Participants

Fifteen individuals with Parkinson's disease (6 female, 9 male; mean age: 65.87) and 15 age- and gender-matched control participants (6 female, 9 male; mean age: 63.13) were recruited for this study. The severity of PD motor symptoms, assessed using the Unified Parkinson's Disease Rating Scale (UPDRS), ranged from mild (a score of 13) to moderate (a score of 48; mean ±standard deviation [SD] score, 24.79±9.19). Cognitive functioning, assessed using the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), was in the normal range for all participants with PD (scores > 26). All participants with PD were taking L-dopa, but were tested off medication (12 h). Here, we were interested in investigating the effects of basal ganglia dysfunction associated with Parkinson's disease on the sensorimotor control of speech and thus tested PD participants without the effects of medication in order to maximize any measured effects. Only two participants had a history of speech therapy; they both mentioned that the treatment focused on increasing speech loudness and intelligibility.

A standard speech passage assessment (Rainbow Passage) was used to rate 43 perceptual characteristics related to phonatory (e.g., loudness and pitch), articulatory, resonatory, prosodic and respiratory properties. A licensed Speech-Language Pathologist listened to the speech samples of each participant and rated the speech on each characteristic using a 7-point scale (1 representing normal speech and 7 representing severe). A clinical "dysarthria severity score" was obtained for each participant, ranging from within normal limits to moderate (Duffy, 2005). The perceptual and UPDRS scores (presented in Table 1) were used to assess the relationship between speech and motor symptoms and the magnitude of compensation to the F0 and F1 manipulations.

Participants in the control group had no history of neurological impairment. All participants passed an audiometric screening with binaural pure tone hearing thresholds of 40 dB HL or less at 250, 500, 1000, 2000 and 4000 Hz; none wore hearing aids. All participants were native speakers of North American English.

4.3. Stimuli and experimental design

The study involved the repeated production of the word "head", containing the target vowel [ɛ]. The mid-front lax vowel is less constrained in its articulation compared to the tense vowels, giving the tongue more freedom to move higher and lower to compensate for the auditory perturbation. Numerous prior studies of sensorimotor adaptation of speech used the same vowel [ɛ] both in healthy control populations and in individuals with PD (Houde and Jordan, 1998; 2002; Shum et al., 2011; Lametti et al., 2012; Mollaei et al., 2013). A block of 200 trials was acquired for each perturbation condition (F0 or F1), yielding 400 trials in total. In 20% of the trials, the vowel F0 or F1 frequency was manipulated at one of two different magnitudes (small and large – see below). Altogether, 40 formant perturbations trials and 40 F0 perturbation trials were acquired with half of the trials at each of two shift magnitudes (20 small, 20 large), yielding 80 perturbation trials in total for each participant. A 10-min rest period was provided between the two conditions. The order of the manipulations was counterbalanced among participants. In order to more clearly assess the compensation associated with the F0 or F1 manipulations, participants were instructed to sustain the vocalic portion of the utterance for 2.5 s.[1] Fundamental frequency was manipulated upward because it has been shown that the upward direction of pitch perturbation elicits a significantly larger response magnitude than downward perturbations (Chen et al., 2013). The manipulation of F1 involved an increase in frequency (i.e., altering the vowel closer to [æ]) in line with our previous study of speech adaptation (Mollaei et al., 2013). The order of the trials was quasi-randomized with the constraint that two shifted trials would not occur consecutively, and the order of the two magnitudes was fully randomized.

4.4. Manipulation of auditory feedback

Auditory feedback was manipulated using a custom-configured digital signal processor specialized for altering speech acoustic signals (VoiceOne, TC Helicon) to modify in near-real time (11 ms delay) the fundamental or first formant frequency of the sustained vowel [ɛ]. This system has been used in a number of prior studies of sensorimotor adaptation during vowel production (Bourguignon et al., 2014; Mollaei et al., 2013; Shiller and Rochon, 2014; Shum et al., 2011). For F0, the large perturbation corresponded to an increase of 100 cents (1 semitone), and the small perturbation corresponded to an increase of 50 cents (0.5 semitone). For F1, the large perturbation corresponded to an increase of 30% (averaging 135.1 Hz) and the small perturbation corresponded to an increase of 15% (averaging 47.5 Hz). In previous studies of pitch perturbations (Chen et al. (2013) in individuals with PD; Liu and Larson (2007) and Zarate et al. (2010) in healthy controls) different magnitudes of F0 modulation were used. In healthy controls, it has been found that the behavioral and neural processing of auditory feedback is related to the size of the auditory error. With respect to PD, it has been demonstrated that the response characteristics to the perturbations are not linear. Therefore, based on pilot work we determined two magnitudes of perturbation for both F0 and F1. The large magnitude of F1 perturbation corresponded to that used in previous studies (Bourguignon et al., 2014; Mollaei et al., 2013; Shum et al., 2011).

All manipulations started at the beginning of each perturbation trial and lasted for the duration of the trial. The altered speech signal was amplified and presented to participants at a volume of approximately 70 dB (e.g., Mollaei et al., 2013). In order to reduce subjects' perception of their unmodified air- and bone-conducted speech signal, the subject's feedback signal was mixed with approximately 60 dB of pink masking noise.

4.5. Procedure

Participants sat in front of a computer monitor and spoke into a head-mounted microphone (C520, AKG, Germany). The microphone signal was digitized at 22,050 Hz/16-bit (Fast-Track Pro, M-Audio, Irwindale, CA), recorded on a PC using Matlab (The MathWorks, Inc., Natick, MA), and presented back to the participants through circumaural headphones (880 Pro, Beyerdynamic, Germany). Speaking was cued by the target word presentation on a computer screen for 2.5 s followed by a 1.5 s interval. Participants produced the target word at a comfortable volume immediately after visual presentation of the word and sustained the target vowel [ɛ] for the duration of the visual cue. Speaking volume was maintained at a consistent level by providing visual feedback to the subject throughout the course of testing in the form of a digital VU meter presented on the computer display.

[1] Whereas prolongation of the vowel may be somewhat unnatural, our primary interest was in a comparison across the participant groups, both of whom produced prolonged vowels.

Table 1
Individuals scores of participants with PD on UPDRS and dysarthria perceptual rating.

	UPDRS	Respiration	Phonation	Resonance	Articulation	Prosody	Total speech score
PD01	15	4	26	3	7	13	53
PD02	25	4	23	3	7	21	58
PD03	31	2	16	4	9	15	46
PD04	24	2	29	3	11	22	67
PD05	33	3	32	3	11	21	70
PD06	5	3	22	3	9	13	50
PD07	23	3	29	3	14	22	71
PD08	48	3	25	3	13	22	66
PD09	27	2	23	4	14	16	59
PD10	13	3	22	3	10	18	56
PD11	22	3	25	5	12	20	65
PD12	3	2	16	4	8	15	45
PD13	22	2	28	3	10	18	61
PD14	33	3	20	3	10	18	54
PD15	38	2	16	3	7	14	42

4.6. Data analysis

The first 400 ms of each vowel production was extracted for analysis. For pitch-perturbed trials, an auto-correlation method (Zahorian and Hu, 2008) was used to estimate F0 (in Hz) over a series of overlapping 25 ms windows (increments of 10 ms). The F0 contour was converted to the cent scale using the formula: $\text{cents} = 100 \times (39.86 \times \log_{10}(\text{F0/reference}))$, where reference = 195.997 Hz (the note G-4; Chen et al., 2007). For the formant-perturbed trials, the first formant was estimated using linear predictive coding (LPC) analysis in a series of overlapping 20 ms windows (increments of 4 ms). The LPC order was chosen manually for each participant based on the smoothest error. For each subject, all F0 and F1 contours were time-aligned at the onset of the vowel and then averaged across trials within each condition. The onset of the vowel was picked automatically, and then it was checked manually for any errors. Both F0 and F1 extraction were checked for outliers and measurement errors, and any erroneous extraction was deleted from further analysis.

F0 compensation in each perturbed trial was measured as the difference in F0 (at each 10 ms increment in time) between the perturbed trial and the immediately preceding, non-perturbed (baseline) trial. F1 compensation in each perturbation trial was similarly measured as the difference in F1 (at each 4 ms increment in time) between the perturbed trial and the immediately preceding, non-perturbed trial. The mean F0 and F1 compensation traces for each subject (representing the mean change from baseline) was then averaged across subjects in each group. The *gain* of the response in both F0 and F1 was also calculated as the magnitude of compensation divided by the magnitude of feedback shift.

A linear mixed-effects model was used to assess the between-group (PD vs. Control) differences in compensation for each type of auditory feedback perturbation (fundamental and formant frequency) and each magnitude (small vs. large) as a function of time. For the group with PD, a correlation analysis was carried out to assess the relationship between the degree of compensation (in F0 and F1) and measures of clinical severity (UPDRS and dysarthria rating scores).

Author's role

F. Mollaei – study conception, wrote the first draft, executed of the study including design; D. Shiller – major contribution to the design and statistical analysis, major contribution to the writing of the manuscript; S. Baum – study conception, review and critique of statistics, major contribution to the writing of the manuscript; V. Gracco – study conception, review and critique of statistics, major contribution to the writing of the manuscript. All authors have read and have approved the final manuscript.

Conflict of interest/financial disclosures

Nothing to report.

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