Examining the Links Among Motor Symptoms in Hyperfunctional Voice Disorders, Auditory Discrimination, and Auditory-Motor Function

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Abstract

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Voice disorders are experienced by nearly a third of people at some point in their lifetimes. Recent evidence suggests impaired auditory-motor function may be a factor in the development or evolution of hyperfunctional voice disorders (HVDs), the most common category. The series of studies outlined in this dissertation form a program of research that focused on further describing the role and nature of such auditory-motor (dys)function in HVDs. In chapter 1, we explored the reliability of common methods used to assess auditory-motor function for speech. Prior to this study, test-retest reliability had never been examined for these methods, which was important for interpretation of study findings across studies outlined in chapters 1 and 3. Results from the study outlined in chapter 1 showed different patterns of reliability of assays of speech auditory-motor control between the domains of voice and articulation, and supported the use of a categorical measure of fundamental frequency (f_o) adaptation employed in chapter 3. In chapter 2, we developed a protocol to assess volitional control of small changes in vocal f_o and intensity,

and tested for group differences between people with and without HVDs. Prior studies of auditory-motor impairment in HVDs found unusually large involuntary changes in vocal f_o during auditory-motor adaptive learning tasks. The study outlined in chapter 2 evaluated the possibility that people with HVDs simply are not able to make smaller changes, even when asked to do so volitionally. We found no significant differences in volitional control of f_o and intensity between people with and without HVDs. In chapter 3, we evaluated the specificity of vocal auditory-motor impairment in people with HVDs, by replicating studies of f_o discrimination and adaptive vocal learning, and extending findings to a second vocal parameter, intensity. In addition, we tested a novel hypothesis that manipulations of auditory feedback, particularly of f_o, may elicit a stabilization response in muscles around the larynx, as a form of vocal control. We posited that if this type of response exists, it may be dysregulated in people with HVDs. The results of these studies replicated and extended findings of prior work. Specifically, we found impaired auditory-motor adaptive learning for f_o that was similar to prior findings, and a trend for a significant difference from controls in adaptive learning for intensity that was qualitatively different. These findings occurred in the absence of differences in volitional control of small changes in f_o and intensity, as reported in chapter 2. Taken together, the results of this series of studies may suggest differences in the causal vs. compensatory nature of these impairments in people with HVDs, which should be explored in future studies. We also found preliminary evidence for laryngeal stabilization as a mechanism of control of vocal f_o, which was not present in measures of vocal intensity. Taken together with differences in vocal and articulatory auditory-motor control described in chapter 2, these findings reinforce the importance of refining theoretical models of speech sensorimotor control to account for differences across different parameters of speech. Future directions for research and clinical implications also are discussed.

Contents

LIST OF FIGURES

LIST OF TABLES

ORGANIZATION

This dissertation is organized as three self-contained manuscripts with a common goal of investigating auditory-motor control of voice in people with and without HVDs. Each manuscript was written in preparation for publication and can be read independently of the others. There is overlap in background information and references cited among all chapters, in particular chapters 2 and 3.

Chapter 1: Kapsner-Smith, M., Abur, D., Eadie, T., & Stepp, C. (2023). "Test-retest reliability of behavioral assays of feedforward and feedback auditory-motor control of voice and articulation," *Journal of Speech, Language, and Hearing Research*, 1-15. https://doi.org/10.1044/2023_JSLHR-23-00038

Chapter 2: Kapsner-Smith, M., Rosenzweig, J., Wilcox, H., Bhatt, N., Giliberto, J. P., Max, L., Eadie, T., & Stepp, C. "Volitional control of frequency and intensity in speakers with and without hyperfunctional voice disorders," to be submitted for publication.

Chapter 3: Kapsner-Smith, M., Díaz-Cádiz, M., Knutson, M., Eadie, T., & Stepp, C. "Relationships among auditory discrimination, adaptive vocal learning, and perilaryngeal muscle activation in people with and without hyperfunctional voice disorders," to be submitted for publication.

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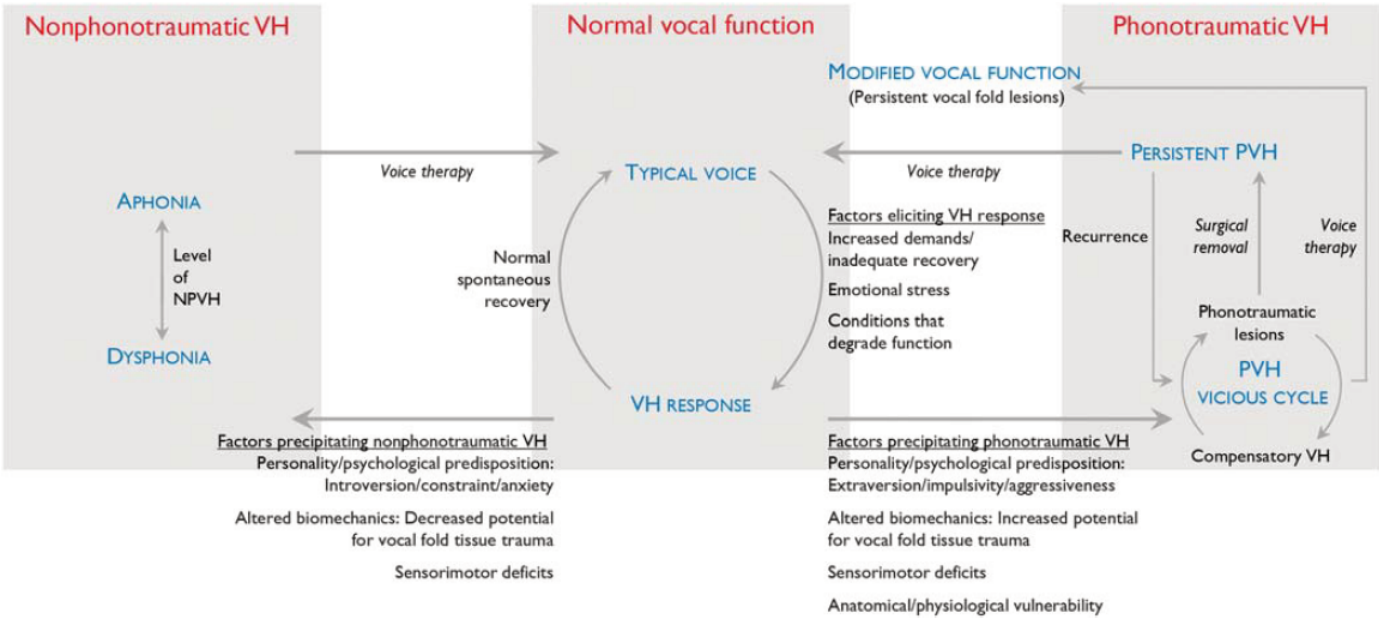
INTRODUCTION

Voice disorders affect 3–9% of the U.S. population at any one time (Ramig & Verdolini, 1998) and lead to significant individual and societal burdens including direct healthcare costs, reduced work productivity, and reduced quality of life (S. M. Cohen, Kim, Roy, Asche, & Courey, 2012a, 2012b; Smith et al., 1996). Patients with hyperfunctional voice disorders (HVDs) make up the majority of referrals to multidisciplinary voice clinics (Coyle, Weinrich, & Stemple, 2001; Van Houtte, Van Lierde, D'haeseleer, & Claeys, 2010), yet limited knowledge about the mechanisms that cause and sustain HVDs hampers effective management (Desjardins, Halstead, Cooke, & Bonilha, 2017; Hillman et al., 2020). Clinically, HVDs are characterized by vocal fatigue, dysphonia, and dysregulated muscle activation in and around the larynx during voicing (Oates & Winkworth, 2008). These disorders include those characterized by phonotraumatic vocal hyperfunction (PVH; e.g., vocal fold nodules and polyps), as well as non-phonotraumatic vocal hyperfunction (NPVH; e.g., primary muscle tension dysphonia) (Hillman et al., 2020). Although some progress has been made in understanding the contributing and sustaining factors underlying these disorders, a clear mechanistic framework remains elusive, particularly for NPVH. Such a framework is crucial to drive theoretically-motivated clinical research aimed at prevention, detection, and treatment of voice disorders. In particular, questions regarding dosage, intensity, and “active ingredients” of voice therapy, which are currently lacking in much of the evidence base (Roy, 2012; Van Stan, Roy, Awan, Stemple, & Hillman, 2015), would be facilitated by a clearer understanding of the causes of HVDs.

Vocal hyperfunction (VH) may be a common acute response to both internal and environmental factors that can impact vocal function, such as emotional stress, elevated vocal demands, inadequate vocal recovery, and conditions that degrade the vibratory capacity of the vocal folds (e.g., dehydration, laryngopharyngeal reflux). However, in some individuals, this acute VH response may become chronic, resulting in a voice disorder (see Figure 0-1; Hillman et al., 2020). In PVH, vocal fold tissue trauma caused by altered biomechanics during phonation interacts with compensatory hyperfunction to create and sustain phonotraumatic vocal fold lesions. In speakers with NPVH, however, chronic VH persists in the absence of peripherally observable neurogenic or structural impairments (Oates & Winkworth, 2008). This subtype of VH appears to be biomechanically distinct from PVH; although both groups demonstrate atypically elevated subglottal pressure during phonation, speakers with NPVH do not display aerodynamic characteristics consistent with increased amplitude of vocal fold vibration, closure velocity, and collision forces that are observed in speakers with PVH (Espinoza, Zanartu, Van

Figure 0-1. A theoretical framework for vocal hyperfunction (VH), including factors that may precipitate phonotraumatic and non-phonotraumatic VH (Hillman, Stepp, Van Stan, Zanartu, & Mehta, 2020, p. 2255).



Stan, Mehta, & Hillman, 2017). Rather, speakers with NPVH tend to have an increased open quotient (consistent with decreased vocal fold contact) leading to inefficient, and presumably fatiguing, phonation, which does not lead to the development of vocal fold lesions (Espinoza et al., 2017).

Understanding the mechanisms underlying HVDs is not only important for contributing to our understanding of the etiology and pathophysiology of HVDs, it also is crucial to developing theoretically-motivated interventions. To date, evidence points to underlying factors that may predispose certain individuals to HVDs, including psychobiological characteristics and sensorimotor deficits (Hillman et al., 2020). These also are described as precipitating factors in the model proposed by Hillman and colleagues (see Figure 0-1). The *trait theory* of voice disorders proposes that certain personality traits may predispose individuals to phonotraumatic vocal behaviors, whereas other traits may promote behavioral constraint and conflict in speaking out, manifesting in atypical and inefficient phonation patterns (Roy & Bless, 2000). Indeed, a number of studies have supported a relationship between personality traits and PVH or NPVH (McHugh-Munier, Scherer, Lehmann, & Scherer, 1997; Ng, Lo, Lim, Goh, & Kanagalingam, 2013; Roy, Bless, & Heisey, 2000a, 2000b; Toles, Roy, et al., 2021; Van Mersbergen, Patrick, & Glaze, 2008). Furthermore, emerging evidence suggests a relationship between autonomic nervous system dysfunction and NPVH (Demmink-Geertman & Dejonckere, 2002; Paes, Zambon, & Behlau, 2014; Park & Behlau, 2011), supporting the notion of an underlying psychobiological predisposition toward stress-reactivity that affects vocal function (Dietrich & Abbott, 2012; Dietrich, Andreatta, Jiang, Joshi, & Stemple, 2012; Dietrich & Verdolini Abbott, 2014; Helou, Rosen, Wang, & Verdolini Abbott, 2018; Helou, Wang, Ashmore, Rosen, & Abbott, 2013).

Finally, and most importantly for the present set of studies, although atypical sensorimotor function has been hypothesized to play a role in laryngeal hypersensitization and HVDs for over two decades (Morrison, Rammage, & Emami, 1999; Vertigan, Theodoros, Gibson, & Winkworth, 2006), until recently, few studies have examined the potential role of sensorimotor deficits in HVDs. Studies employing perturbations of auditory feedback have demonstrated that a subset of speakers with HVDs display atypical responses to these perturbations, suggesting a role for impaired auditory-motor control in the development and/or response to chronic VH (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017; Ziethe et al., 2019). In addition, speakers with HVDs may have underlying differences in auditory-perceptual discrimination (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Tam, Carding, Heard, & Madhill, 2018) and auditory-motor targets (McKenna, Hylkema, Tardif, & Stepp, 2020) compared to speakers without voice disorders, which may also impact auditory-motor control of voice.

Although emerging evidence supports a role for auditory-motor dysfunction in HVDs, many questions remain about the specificity of these impairments and their relationship to the core clinical features of HVDs, including dysregulated muscle activation in and around the larynx during voicing. To date, investigations of auditory-motor control of voice and auditory discrimination in speakers with HVDs have been limited to the parameter fundamental frequency (f_o), perceived as pitch (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Stepp et al., 2017; Tam et al., 2018; Ziethe et al., 2019). Thus, it is unknown whether atypical auditory discrimination and adaptive vocal learning seen in speakers with HVDs are specific to perception and integration of f_o, or if they are indicative of a broader impairment of perception and integration of vocal parameters that include, but go beyond f_o (e.g., f_o, intensity, quality, etc.).

Indeed, it is unknown whether auditory-motor integration of vocal parameters is achieved by a unified mechanism, or if impairment of individual parameters is dissociable. In addition, the reliability of behavioral assays used to examine auditory-motor control of speech has not previously been tested. Finally, no direct relationship has been identified between atypical adaptive vocal learning and auditory discrimination in speakers with HVDs and the dysregulated muscle activation that is characteristic of these disorders. Thus, the set of studies described in the chapters of this dissertation sought to address the following knowledge gaps:

1) What is the test-retest reliability of behavioral assays of auditory-motor control of articulation and voice (chapter 1)?
2) Can atypical adaptive vocal learning responses in people with HVDs be explained by a broader limitation of volitional control of vocal parameters (chapter 2)?
3) Are auditory-motor impairments in people with HVDs specific to f_0 or are they inclusive of other vocal parameters, such as intensity (chapter 3)?
4) Does auditory feedback perturbation elicit laryngeal stabilization, and is stabilization behavior different in people with and without HVDs (chapter 3)?

The findings of these studies are important to refine theoretical models, such as the one described in Hillman et al. (2020), that provide a framework for understanding causal and sustaining factors of HVDs and help to direct clinical research. The outcomes also have the potential to inform how perception of vocal parameters and their integration with vocal motor activities might become components of a viable and theoretically-motivated future program of treatment research.

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CHAPTER 1: TEST-RETEST RELIABILITY OF BEHAVIORAL ASSAYS OF FEEDFORWARD AND FEEDBACK AUDITORY-MOTOR CONTROL OF VOICE AND ARTICULATION

1.1 ABSTRACT

Purpose: Behavioral assays of feedforward and feedback auditory-motor control of voice and articulation frequently are used to make inferences about underlying neural mechanisms and to study speech development and disorders. However, no studies have examined the test-retest reliability of such measures, which is critical for rigorous study of auditory-motor control. Thus, the purpose of the present study was to assess the reliability of assays of feedforward and feedback control in voice vs. articulation domains.

Method: Twenty-eight participants (14 cisgender women, 12 cisgender men, 1 transgender man, 1 transmasculine/nonbinary) who denied any history of speech, hearing, or neurological impairment were measured for responses to predictable vs. unexpected auditory feedback perturbations of vocal (fundamental frequency, f_o) and articulatory (first formant, F_1) acoustic parameters twice, with three to six weeks between sessions. Reliability was measured with intraclass correlations.

Results: Opposite patterns of reliability were observed for f_o and F_1; f_o reflexive responses showed good reliability and f_o adaptive responses showed poor reliability, whereas F_1 reflexive responses showed poor reliability and F_1 adaptive responses showed moderate reliability. However, a criterion-referenced categorical measurement of f_o adaptive responses as typical vs. atypical showed substantial test-retest agreement.

Conclusions: Individual responses to some behavioral assays of auditory-motor control of speech should be interpreted with caution, which has implications for several fields of research. Additional research is needed to establish reliable criterion-referenced measures of F_1 adaptive responses as well as f_o and F_1 reflexive responses. Further, the opposite patterns of test-retest

reliability observed for voice vs. articulation add to growing evidence for differences in underlying neural control mechanisms.

1.2 INTRODUCTION

Humans learn and maintain movement patterns for intelligible speech by monitoring sensory feedback, especially in the auditory domain. By comparing auditory feedback of speech with internal predictions, speakers can detect errors and produce online corrections as well as updates to stored motor programs (Tourville & Guenther, 2011). In studies of sensorimotor control of voice and articulation, experimenters often measure behavioral responses to altered auditory feedback to assess auditory-motor control of speech (e.g., Burnett, Senner, & Larson, 1997; Cai, Ghosh, Guenther, & Perkell, 2011; Daliri, Chao, & Fitzgerald, 2020; Houde & Jordan, 1998; Jones & Munhall, 2000; Larson & Robin, 2016; Lester-Smith et al., 2020; Villacorta, Perkell, & Guenther, 2007). These behavioral assays provide experimental data that have been used to develop and test neurocomputational models of speech sensorimotor control and are used in combination with neurophysiological methods to investigate the neurobiology of speech (e.g., Houde & Chang, 2015; Tourville & Guenther, 2011). Studies of children and aging adults have contributed to our understanding of speech development across the lifespan (Caudrelier & Rochet-Capellan, 2019; H. Liu, Russo, & Larson, 2010; N Scheerer, Jacobson, & Jones, 2020). Recently, an increasing number of studies use these paradigms to examine impaired sensorimotor function in clinical populations (Caudrelier & Rochet-Capellan, 2019; Weerathunge, Tomassi, & Stepp, 2022). Such experiments can elucidate the pathophysiology of speech disorders as well as test hypotheses about sensorimotor control of speech using clinical populations as a model. However, to date, no studies have directly examined the reliability of behavioral assays of auditory-motor control of voice and articulation. This information is crucial to appropriately interpret differences between and within experimental groups in participants' responses to altered auditory feedback.

1.2.1 Behavioral Assays of Feedforward and Feedback Auditory-Motor Control

Sensorimotor control of speech is an incredibly complex task, requiring precise control of approximately 100 muscles to produce rapid movements and quickly changing acoustic features, on a scale of 50-300 ms (Parrell, Ramanarayanan, Nagarajan, & Houde, 2019). At the same time, a speaker must be able to adapt to changing environmental conditions, such as background noise, to maintain intelligibility. This is achieved through a combination of feedforward and feedback control mechanisms. Feedforward control involves execution of preprogrammed motor commands for speech movements that allow for fast and fluent production. At the same time, an internal prediction of the sensory outcomes of the movements is activated. Comparison of this prediction to the actual sensory feedback allows the speaker to detect errors and generate corrective, feedback-based motor commands. Persistent error signals may lead to changes to feedforward motor commands, i.e., sensorimotor learning.

An extensive body of literature has explored the role of auditory feedback in sensorimotor control of speech by applying near real-time perturbations to parameters of auditory feedback. These include parameters related to voice, such as fundamental frequency (fo; e.g., Burnett et al., 1997), and parameters related to articulation, such as formants (e.g., Houde & Jordan, 1998). When a speaker is exposed to persistent, predictable perturbations of their auditory feedback over many trials, they typically will adapt by progressively opposing the change across trials and will demonstrate a brief period of persistence of this change after the perturbation is removed (Daliri & Dittman, 2019; Houde & Jordan, 1998; Jones & Munhall, 2000; Purcell & Munhall, 2006a; Villacorta et al., 2007). This is interpreted as reflecting updates to underlying feedforward motor commands based on an error signal, often referred to as an adaptive response (Parrell & Houde, 2019; Tourville & Guenther, 2011). When a speaker is exposed to an unexpected, sudden

onset perturbation of their auditory feedback, they typically will respond with a rapid correction opposing the direction of the perturbation (Cai et al., 2011; Daliri et al., 2020; Larson & Robin, 2016; Niziolek & Guenther, 2013; Purcell & Munhall, 2006b). This is interpreted as a reflex-like correction produced by feedback control loops (Parrell & Houde, 2019; Tourville & Guenther, 2011). Measures such as the magnitude of the response to predictable or unexpected auditory feedback perturbations are thus used as behavioral assays of underlying feedforward and feedback control mechanisms, respectively, although both mechanisms are involved in these tasks.

1.2.2 Use of Assays to Study Neurophysiology of Speech

Behavioral assays of speech auditory-motor control have been combined with neurophysiological methods to elucidate underlying control mechanisms. Feedforward control assays combined with noninvasive neurostimulation methods including anodal transcranial direct stimulation and repetitive transcranial magnetic stimulation have provided information about the neurophysiological bases of speech sensorimotor learning. To date, these studies have focused on adaptive responses to predictable perturbations of the first formant (F_1), an acoustic parameter related to articulatory movements of the tongue and jaw. Changes in the magnitude and/or rate of adaptation in response to stimulation support the role of a sensorimotor cortico-cerebellar loop in integrating auditory feedback error signals into feedforward motor plans, i.e., adaptive auditory-motor learning for speech (Deroche, Nguyen, & Gracco, 2017; Lametti, Smith, Freidin, & Watkins, 2018; Scott et al., 2020; Shum, Shiller, Baum, & Gracco, 2011; Tang, McDaniel, & Watkins, 2021).

Feedback control assays combined with methods including positron-emission tomography, magnetoencephalography, electroencephalography, electrocorticography, and functional

magnetic resonance imaging (fMRI) have characterized the role of the auditory cortex in comparison of predicted and actual auditory feedback for voice and articulation. Responses of the auditory cortex are significantly smaller when speakers hear their own speech during speech production (i.e., auditory feedback) than when they listen passively to playback of the same speech signal, or when they hear auditory feedback that has been altered, a phenomenon known as speaking-induced suppression (Chang, Niziolek, Knight, Nagarajan, & Houde, 2013; Flinker et al., 2010; Greenlee et al., 2011; Hirano et al., 1997; Houde, Nagarajan, Sekihara, & Merzenich, 2002; Sato & Shiller, 2018). This evidence supports the hypothesis that auditory feedback is compared to an internal prediction to detect speech errors. Further evidence comes from studies of responses to altered auditory feedback, which reveal enhanced auditory cortical responses to altered auditory feedback during speech compared to passive listening to playback of the same altered signals, known as speech perturbation response enhancement (Behroozmand, Karvelis, Liu, & Larson, 2009; Chang et al., 2013; Greenlee et al., 2013; Kort, Nagarajan, & Houde, 2014; Parkinson et al., 2012). Furthermore, studies using fMRI during feedback control assays show increased activity in and connectivity between bilateral posterior superior temporal cortices, supporting their role in error detection, and right and/or bilateral motor cortices, suggesting a role in translating error signals into corrective motor output (Behroozmand et al., 2015; Floegel, Fuchs, & Kell, 2020; Niziolek & Guenther, 2013; Tourville, Reilly, & Guenther, 2008). Although such studies have contributed substantially to understanding the neurobiology of speech sensorimotor control, information about the test-retest reliability of the behavioral measures is crucial to understand whether these responses reflect state (temporary, situational) vs. trait (stable, long-lasting) characteristics of the speaker. Furthermore, information about

reliability could provide future directions for mechanistic studies to determine what causes the behavior of an individual to change.

1.2.3 Use of Assays to Study Speech Development

Studies of the developmental trajectory of auditory feedback perturbation responses suggest that young children use auditory feedback to guide sensorimotor control and learning for both vocal and articulatory parameters. Children as young as 24 months have been shown to compensate for perturbations of auditory f_o feedback, suggesting that toddlers use auditory feedback to facilitate motor control of vocal parameters of speech (N Scheerer et al., 2020). It is possible that feedback-based control of vocal parameters matures earlier than articulatory control (MacDonald, Johnson, Forsythe, Plante, & Munhall, 2012; N Scheerer et al., 2020), but more research is needed to confirm these findings. Maturation decreases variability of both vocal and articulatory parameters, and decreases the latency of feedback responses to unpredictable f_o perturbations (H. Liu, N. M. Russo, et al., 2010; P. Liu, Chen, Larson, Huang, & Liu, 2010; MacDonald et al., 2012; N. Scheerer, Jacobson, & Jones, 2016; N Scheerer et al., 2020; N Scheerer, Liu, & Jones, 2013; van Brenk & Terband, 2020). This may be due to neurodevelopmental factors such as myelination that increase neural transmission speed and reduce processing and response times for auditory feedback responses.

Two studies have investigated the influence of aging on responses to auditory feedback perturbations of f_o. Aging appears to increase the magnitude of compensatory responses to unpredictable f_o perturbations, but it is unknown whether this reflects changes in feedback control mechanisms or physiological pitch control more generally (H. Liu, N. M. Russo, et al., 2010; P. Liu, Chen, Jones, Huang, & Liu, 2011). The influence of aging on responses to auditory

feedback perturbations of articulatory parameters and on adaptive responses to predictable perturbations remains unexplored.

1.2.4 Use of Assays to Study Speech Disorders

An increasing number of auditory feedback perturbation studies examine clinical populations. One purpose of such studies is to elucidate the pathophysiology of voice and articulation disorders that previously were poorly understood, such as developmental stuttering and hyperfunctional voice disorders. Numerous studies document a broad, likely developmental impairment of sensorimotor control and learning in individuals who stutter, including articulatory (Cai, Beal, Ghosh, Guenther, & Perkell, 2014; Cai et al., 2012; Daliri, Wieland, Cai, Guenther, & Chang, 2018; Kim, Daliri, Flanagan, & Max, 2020; Sengupta, Shah, Gore, Loucks, & Nasir, 2016), vocal (Bauer, Hubbard Seery, LaBonte, & Ruhnke, 2007; Loucks, Chon, & Han, 2012; Sares, Deroche, Shiller, & Gracco, 2018; Sares, Deroche, Ohashi, Shiller, & Gracco, 2020) and limb control (Kim, Daliri, et al., 2020). Recent evidence points to impaired adaptive auditory-motor learning for voice in some people with hyperfunctional voice disorders, with likely preserved feedback auditory-motor control (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017). Such studies may have substantial implications for diagnosis and treatment of speech disorders.

In contrast, patient populations with known neurogenic impairments can serve as models to understand underlying neural mechanisms of typical sensorimotor control. For example, in people with aphasia secondary to left hemisphere stroke, lesion-mapping combined with feedback control assays and neurophysiological methods has supported the role of fronto-temporal networks in error detection and correction (Behroozmand, Bonilha, Rorden, Hickok, & Fridriksson, 2022; Behroozmand et al., 2018). Behavioral and EEG data from people with

cerebellar disease suggest cerebellar function is important for feedforward auditory-motor adaptive learning, and may play a role in feedback auditory-motor control through interactions with cortical regions that modulate auditory-motor integration (Hilger, 2020; Houde et al., 2019; Li et al., 2019; Parrell, Agnew, Nagarajan, Houde, & Ivry, 2017). Finally, people with PD, a neurodegenerative disease associated with impaired dopamine production, have shown increased responses to feedback control assays for the vocal parameters f_o and intensity while off dopaminergic medications (X. Chen et al., 2013; H. Liu, Wang, Metman, & Larson, 2012; Mollaei, Shiller, Baum, & Gracco, 2016), but decreased responses for the articulatory parameter F_1 (Mollaei et al., 2016). This dissociation of impaired feedback auditory-motor control of voice vs. articulation suggests differences in underlying neural mechanisms. Although no studies to date have examined differences in medication state within the same individuals, studies of people with PD while on dopaminergic medications have shown typical feedback control responses for both vocal and articulatory parameters (Abur, Subaciute, Daliri, et al., 2021; Kiran & Larson, 2001), suggesting that dopaminergic signaling is involved in typical auditory-motor feedback control. Crucially, most of these studies of clinical populations have relied on group-level findings, despite substantial variability in behavior at the individual level (e.g., Abur, Subaciute, Daliri, et al., 2021). Information about the test-retest reliability of individual responses to behavioral assays of speech sensorimotor control will help determine whether they are rigorous measures capable of reliably detecting differences between groups or changes in individuals over time.

1.2.5 Reliability of Behavioral Assays of Auditory-Motor Control

Reliability refers to "the extent to which an experiment, test, or measuring procedure yields the same results on repeated trials" (Merriam-Webster, n.d.). Good test-retest reliability suggests that

a measure is an accurate representation of an individual's performance rather than artifact related to irrelevant aspects of the testing session or environment. Stability of a measure over time may also suggest that it is sensitive to trait, rather than state, characteristics of the individual being measured, e.g., a stable capacity of the speech sensorimotor control system vs. one that fluctuates in response to internal and/or external conditions. Despite the importance of reliability for interpretation of results, to date no studies have explicitly examined the test-retest reliability of behavioral assays of auditory-motor control of speech. One study examined adaptive auditory-motor learning for voice in response to two differently-sized perturbations of f_o, one standard perturbation and one that was personalized to the individual's f_o discrimination threshold (Alemi, Lehmann, & Deroche, 2020). Participants' responses were only weakly related across the two experiments, with substantial variability in the magnitude and the direction of f_o changes. Another study examined feedback control responses to perturbations of F_1 with and without the addition of noise (i.e., artificially increased variability) in participants' auditory feedback prior to the experiment (Niziolek & Parrell, 2021). The authors noted that interpretation of results in this study was limited by a high degree of intra-individual variability, potentially due to "limited stability of auditory feedback compensation measures...across sessions" (Niziolek & Parrell, 2021, p. 2169). In addition, it is unknown whether learning effects occur with repeated exposure to identical tasks. Although learning effects have been observed in studies of reaching movements, these studies often involve longer exposure to perturbations (e.g., Shadmehr & Holcomb, 1997), and important differences have been documented between learning in limb and speech systems, such as the presence (limb) and absence (speech) of explicit learning mechanisms (Kim & Max, 2021; Lametti, Quek, Prescott, Brittain, & Watkins, 2020). These

studies highlight the importance of directly investigating the test-retest reliability of measures of feedforward and feedback auditory-motor control of voice and articulation.

To interpret within- and between-group differences in auditory perturbation experiments, investigators must know how reliable responses to auditory perturbation are in individuals with typical speech. To date, no studies have examined the test-retest reliability of common assays of feedforward and feedback control of voice and articulation. Thus, the purpose of the present study was to measure the test-retest reliability of adaptive responses to predictable perturbations, and reflexive responses to unexpected perturbations, in both the voice (f_o) and articulation (F_1) domains. Given the variability of responses to auditory feedback perturbations between individuals and across similar experiments (Alemi et al., 2020; Niziolek & Parrell, 2021), we hypothesized that test-retest reliability of these assays may be only moderate. As a secondary analysis, we also examined whether systematic learning effects occurred with repeated exposure to typical experimental tasks measured several weeks apart.

1.3 METHODS

All procedures were approved by the Institutional Review Board of the University of Washington.

1.3.1 Participants

Twenty-eight adults reporting normal speech, language, and hearing function were recruited to participate in the study (14 cisgender women, 12 cisgender men, 1 transgender man, 1 transmasculine/nonbinary; 16 assigned female at birth, 12 assigned male at birth; M_{age} = 25 years, range = 18 – 35, SD = 4.5). The sample size provided 80% power to detect medium effect sizes (ICC ≥ 0.6). Individuals with a self-reported history of neurological disease, stroke, or any health conditions affecting communication or the ability to pay attention were excluded.

Individuals who were smokers were excluded due to potential effects on vocal function. Individuals who reported formal singing training or were active vocal performers were excluded. Speakers of tonal languages were excluded. All participants passed a hearing screening with thresholds at or below 25 dB HL at 125, 250, 500, 1000, 4000, and 8000 Hz (ASHA, 2018). All participants learned English in infancy.

Participants were screened for voice concerns via interview and administration of the Voice-Related Quality of Life (V-RQOL; Hogikyan & Sethuraman, 1999). Participants reported no voice overuse or upper respiratory symptoms for at least 48 hours prior to each recording session. Participants reporting illness or voice overuse were rescheduled to allow for vocal recovery (Hunter & Titze, 2009).

1.3.2 Procedures

Adaptive and reflexive responses to f_o and F_1 perturbations (Lester-Smith et al., 2020) were each measured twice, for all participants. Baseline measures of f_o and F_1 control occurred in separate sessions due to additional data collection for a different study, and were conducted within a span of two weeks (hereafter referred to as time one). Retest measures of f_o and F_1 control occurred in a single session, which was conducted three to six weeks after the second baseline session (hereafter referred to as time two). Each session lasted 1-2 hours. We chose a timeline that we expected was unlikely to induce learning and might occur in a longitudinal study design, while also avoiding changes in vocal function over time due to seasonal or other factors. The order of the first two sessions, and the order of f_o and F_1 tasks in the third session, were counterbalanced across participants to control for order effects.

Participants were seated comfortably in front of a monitor that presented visual stimuli. They were provided with water before and during the experiments. Participants wore a head-mounted

Shure Omni Mic MX153 7 cm from the center of the mouth at an approximately 45 degree angle and Etymotic ER-2 insert earphones. The microphone signal was amplified +5dB and played back to participants via the headphones with a total processing delay of <35 ms (Kim, Wang, & Max, 2020; Weerathunge, Abur, Enos, Brown, & Stepp, 2020). Both the microphone and headphone digitized signals were recorded at 16 kHz for F_1 experiments and 44.1 kHz for f_o experiments.

For f_o perturbation experiments, the microphone signal was amplified by an RME QuadMic II Microphone Preamp and digitized by an RME Fireface sound card. Manipulations of f_o were performed by an Eventide Eclipse V4. The manipulated signal was amplified by a Behringer Xenyx Q802USB amplifier and played back to the participant via headphones, as well as being digitized via the RME Fireface sound card. Initiation of trials and Eventide Eclipse manipulations was controlled by a custom MATLAB program (MathWorks, 2016).

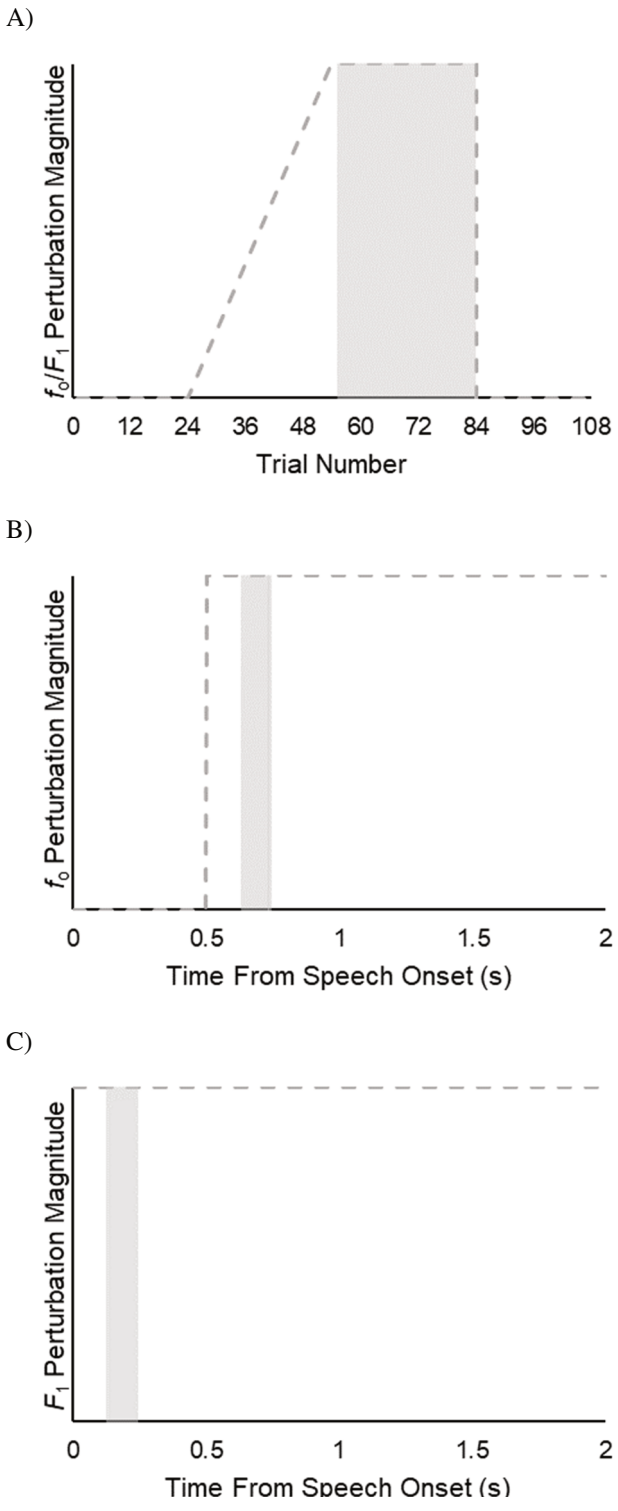
For F_1 perturbation experiments, the microphone signal was amplified and digitized by a MOTU MicroBook IIC microphone preamplifier, using MicroBook II CueMix software. F_1 manipulations were performed by Audapter (Cai, Boucek, Ghosh, Guenther, & Perkell, 2008), a MATLAB software package that performs real-time transformations of acoustic parameters. The signal was then sent to headphones via a Behringer Xenyx Q802USB amplifier. Initiation of trials and Audapter manipulations were controlled by a custom MATLAB program (MathWorks, 2016).

There were three f_o perturbation conditions: adaptation shift up, adaptation control, and reflex shift up (each 10 minutes; Lester-Smith et al., 2020). Adaptation conditions always occurred before the reflex condition. The order of the two adaptation conditions was counterbalanced across participants. Each condition consisted of 108 trials, during which participants produced a

2-s sustained /ɑ/. During the adaptation shift up condition, participants received unperturbed feedback during the first 24 trials (*baseline* phase), gradually upward-shifted feedback of +3.4 cents per trial relative to the participant's fundamental frequency during the next 30 trials (*ramp* phase), 30 trials at the maximum perturbation of +100 cents (*hold* phase), and 24 trials of unperturbed feedback (*after-effect* phase). Perturbations during the adaptation condition, when applicable, were applied for the duration of the trial. During the adaptation control condition, participants received unperturbed feedback for all 108 trials. During the reflex shift up condition, participants produced a 2-s sustained /ɑ/ for 12 blocks of 9 trials (total 108). Each block included two perturbed trials. Perturbations consisted of a sudden +100 cent shift of f_o. Onset of perturbations was jittered between 0.5 to 1-s after the onset of phonation. After onset, perturbations remained for the remainder of the trial.

There were two F_1 perturbation conditions: adaptation shift up and reflex shift up (each 10 minutes; Lester-Smith et al., 2020). The adaptation conditions always occurred before the reflex condition. Each condition consisted of 108 trials. Participants produced a prolonged word for approximately 2-s when presented with the word on the screen. During the adaptation shift up condition, a block consisted of one presentation of each of the stimuli "bid," "tid," and "hid," in random order (36 blocks x 3 trials = 108 trials). These stimuli were chosen so that they would be perceived as a real word when F_1 was perturbed upward (toward "bed", "Ted," and "head"). Participants received unperturbed feedback during the first 8 blocks (*baseline* phase), gradually upward-shifted F_1 feedback of +1.03% per trial relative to F_1 produced by the participant across the next 10 blocks (*ramp* phase), 10 blocks at the maximum perturbation of +30% of F_1 (*hold* phase), and 8 blocks of unperturbed feedback (*after-effect* phase). During the reflex shift up condition, a block consisted of 3 presentations of each of the stimuli "bid," "tid," and "hid," in

Figure 1-1. Schematics of A) adaptation conditions and of a single perturbed reflex trial for B) f_o and C) F_1. Dashed lines represent the perturbation magnitude, and shaded regions represent the analysis windows.



random order (12 blocks x 9 trials = 108 trials). Each block included two perturbed trials. Perturbations consisted of a +30% shift up of F_1. For both the adaptation and reflex conditions, perturbations were applied for the duration of the trial, beginning with the onset of speech. Schematics for adaptation and reflex experiments are provided in Figure 1.

1.3.3 Data Analysis

For adaptation measures, the mean value of f_o or F_1 was calculated during the window 40 – 120 ms after the onset of the vowel in each trial. This window was chosen to assess contributions of the feedforward sensorimotor control system after the voice stabilized but before auditory feedback responses are expected to occur (Burnett, Freedland, Larson, & Hain, 1998). For the f_o adaptation experiment, mean f_o of each trial was extracted using an autocorrelation method via Praat (Boersma & Weenink, 2016) and converted to cents, a relative

measure of f_o, by normalizing to the average of the 24 baseline trials. Trials with inadequate pitch tracking or duration were replaced with the average of the trial before and the trial after. For f_o, a total of 0.36% of all trials were replaced, averaging 0.4 trials per experimental condition (range = 0 – 9 trials per condition). The f_o shift-up condition was then normalized to the f_o control condition by subtracting the mean f_o in cents of the respective control trial from each shift-up trial. This normalization accounted for any change in f_o across trials that was not related to the auditory feedback perturbation. This procedure was used for f_o, and not F_1, because f_o tends to drift upward over many trials (Jones & Munhall, 2000). For the F_1 adaptation experiment, F_1 was extracted using linear predictive coding and converted to a percentage relative to the mean F_1 of the 24 baseline trials (Lester-Smith et al., 2020). For F_1, no trials needed to be replaced. For both experiments, the average of the 30 trials in the hold phase was used for statistical analyses of the adaptive responses. A second measure using the mean of last 15 trials (second half) of the hold phase was also calculated and compared to the primary measure. This was conducted as a post hoc analysis to assess whether responses were more stable in the later portion of the hold phase, for example if adaptation has plateaued.

For reflex measures, f_o or F_1 traces were extracted for all trials. Perturbed f_o trials were normalized in cents relative to the 100-ms period preceding the start of the perturbation. Perturbed F_1 trials were normalized as a percentage relative to the mean trajectory of unperturbed trials containing the same vowel (Lester-Smith et al., 2020). Perturbed trials with inadequate pitch tracking or duration were removed from the analysis. For f_o, there was an average of 22.89 usable reflex trials per participant (range = 17 – 24 out of 24 possible trials). For F_1, only two reflex trials were removed from the entire data set, resulting in an average of 23.99 usable F_1 reflex trials per participant (range = 23 – 24 out of 24 possible trials). The mean

normalized value of f_o or F_1 was calculated across all perturbed trials during the window 120 – 240 ms after the onset of the perturbation (Lester-Smith et al., 2020), consistent with timing of reflexive responses reported by Tourville et al. (2008) and Hain et al. (2000). This mean was used for statistical analyses of the reflexive responses.

1.3.4 Statistical Analyses

For f_o adaptation, F_1 adaptation, f_o reflex, and F_1 reflex, intraclass correlation coefficients (ICCs) were used to assess the reliability of the responses at time one and time two. ICCs and 95% confidence intervals were calculated using SPSS (Version 26, IBM, Inc.) based on single measures, absolute agreement, and two-way random effects (McGraw & Wong, 1996). Categories of poor (<.50), moderate (.50 – .75), good (.76 – .90) and excellent (>.90) reliability have been suggested for ICCs (Koo & Li, 2016). As a secondary analysis, two-tailed paired *t* tests were used to assess whether learning effects occurred from repeated exposure to the behavioral assays, with an alpha level of .05.

Prior studies of f_o adaptive responses in individuals with typical voice and speech have documented substantial variability, including both responses that oppose the perturbation, and responses that follow (i.e., change in the same direction as) the perturbation (e.g., Abur, Subaciute, Kapsner-Smith, et al., 2021; Lester-Smith et al., 2020). An additional categorical analysis of f_o adaptive responses using cutoff criteria from a prior study was therefore conducted to assess its reliability. This analysis was not conducted for the other behavioral assays (f_o reflex, F_1 adaptation, F_1 reflex) because similar criterion cutoff scores were not available. The mean f_o adaptive response was categorized as typical or atypical, based on 90th percentile *z*-score cutoffs taken from non-singing control participants in Abur, Subaciute, Kapsner-Smith, et al. (2021).

Cohen's kappa statistic was calculated to assess agreement of this categorical score between time one and time two.

1.4 RESULTS

Table 1-1. Descriptive statistics for the magnitude of adaptive and reflexive responses, and paired *t* tests. Note that negative values reflect opposing responses whereas positive values reflect following responses.

Experiment	**Time**	**Mean Response**	**Min**	**Max**	***SD***	***t*(27)**	***p***	***d***
f_o adaptation	1	-37.7 cents	-154.1	109.4	70.3	.70	.492	0.13
f_o adaptation	2	-51.3 cents	-233.5	95.2	72.3			
F_1 adaptation	1	-9.0%	-19.2	15.4	7.3	-2.04	.051	0.39
F_1 adaptation	2	-6.6%	-14.4	7.7	5.7			
f_o reflex	1	-8.9 cents	-36.4	5.3	8.7	1.85	.075	0.35
f_o reflex	2	-10.8 cents	-39.4	9.8	10.0			
F_1 reflex	1	-1.1%	-5.6	1.3	1.6	0.09	.932	0.02
F_1 reflex	2	-1.2%	-5.3	2.1	1.6			

Descriptive statistics for group results for each of the four experiments (f_o adaptation, F_1 adaptation, f_o reflex, F_1 reflex) are provided in Table 1. On average, participants opposed the f_o and F_1 auditory perturbations at both time points. The average magnitudes of f_o adaptive responses were -37.7 (SD = 70.3) and -51.3 (SD = 72.3) with a similar number of participants producing following responses at each time point. The average magnitudes of f_o reflexive responses were -8.9 (SD = 8.7) and -10.8 (SD = 10.0). The average magnitudes of F_1 adaptive responses were -9.0 (SD = 7.3) and -6.6 (SD = 5.7). The average magnitudes of F_1 reflexive responses were -1.1 (SD = 1.6) and -1.2 (SD = 1.6). Individual data are presented in Figures 2 – 5. As a secondary analysis, paired *t* tests were calculated for each of the four experiments to

determine if systematic learning effects occurred. There was no significant difference for any of the measures at the two time points (*t* statistics and *p* values are provided in Table 1).

Figure 1-2. Individual f_o adaptive responses at time one and time two. One participant produced a response in the atypical range at time one and in the typical range at time two (outlined in grey), and one produced responses in the atypical range at both times (outlined in black).

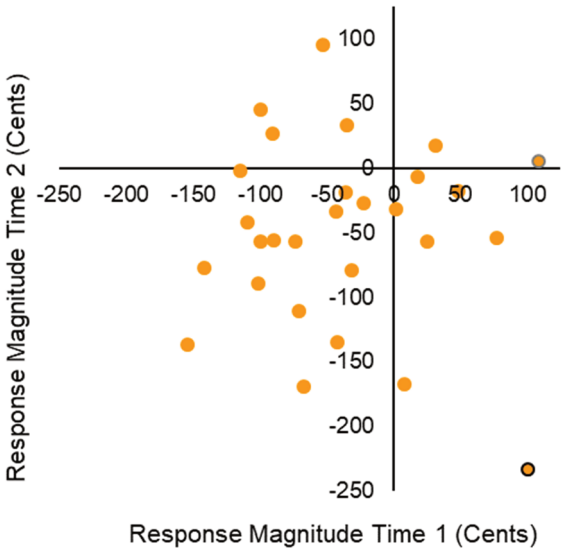
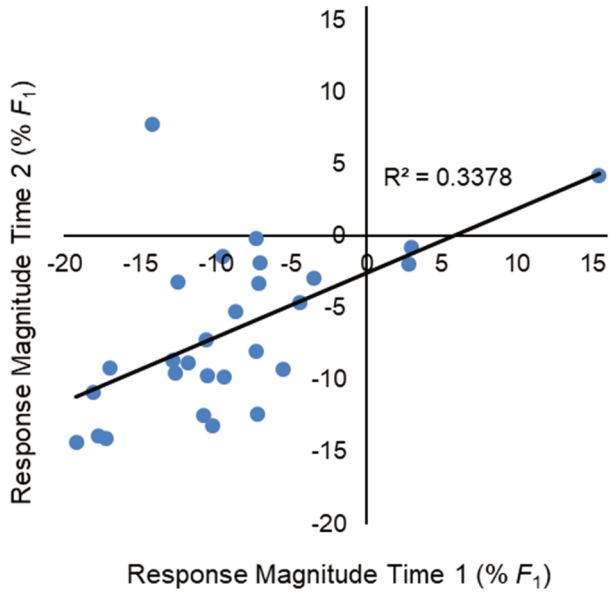


Figure 1-3. Individual F_1 adaptive responses at time one and time two.



For the f_o reflex task, at time one participants responded to an average of 54.7% of perturbed trials in a compensatory direction (SD = 17.8%), 20.0% of trials in a following direction (SD = 12.0%), and did not respond to 25.3% (SD = 11.8%). Similarly, at time two participants responded to an average of 55.4% of perturbed trials in a compensatory direction (SD = 18.6%), 19.7% in a following direction (SD = 14.3%), and did not respond to 25.0% (SD = 11.8%).

ICCs were calculated for each of the four experiments. For f_o adaptive responses, ICC(2,1) = -.052 [-.422, .326], p = .604, consistent with poor test-retest reliability. For F_1 adaptive responses, ICC(2,1) = .536 [.219, .753], p = .001, consistent with moderate test-retest reliability. For f_o reflexive responses, ICC(2,1) = .833 [.663,

.919], $p < .001$, consistent with good test-retest reliability. For F_1 reflexive responses, ICC(2,1) = .474 [.122, .718], $p = .005$, consistent with poor test-retest reliability.

Figure 1-4. Individual f_o reflexive responses at time one and time two.

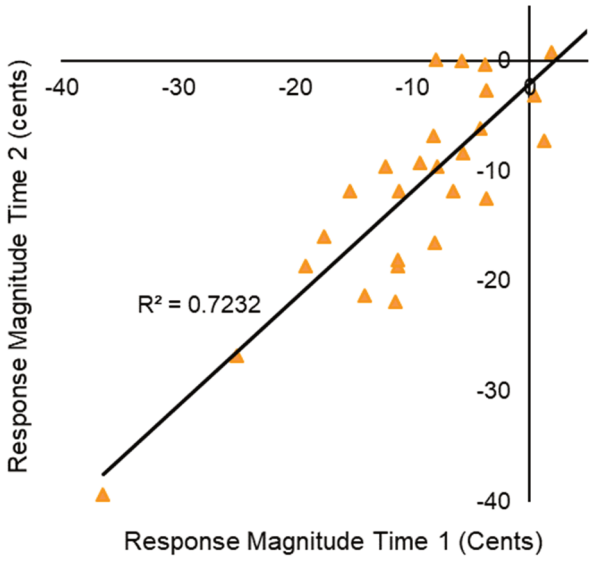
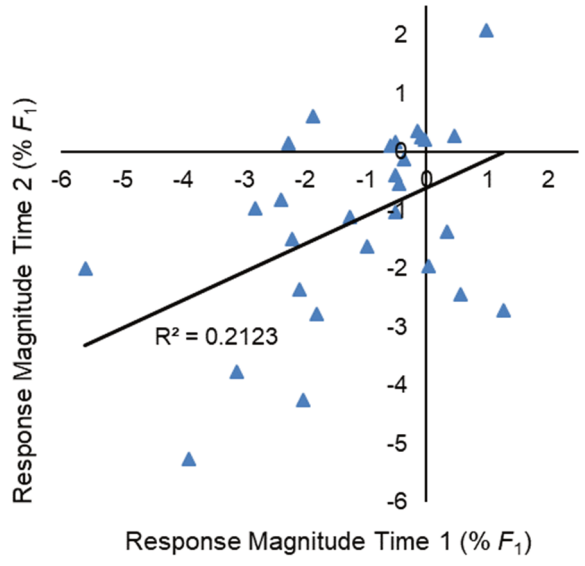


Figure 1-5. Individual F_1 reflexive responses at time one and time two.



ICCs were also calculated for the two adaptation experiments using the mean of the last 15 trials (second half) of the hold phase. For f_o adaptive responses, ICC(2,1) = -.115 [-.475, .270], $p = .719$, consistent with poor test-retest reliability. For F_1 adaptive responses, ICC(2,1) = .525 [.206, .745], $p = .001$, consistent with moderate test-retest reliability. These results were slightly less reliable than ICCs calculated using the mean of the entire hold phase.

Criterion-referenced assessments are a common way to categorize responses into typical or atypical categories based on normative data. This type of approach was used by Abur, Subaciute, Kapsner-Smith, et al. (2021) to identify atypical f_o adaptive responses in a subgroup of people with vocal hyperfunction. To assess the stability of f_o adaptive responses within a typical range in the present study, participants'

responses were categorized into typical vs. atypical using 90th percentile z-scores from data collected by Abur, Subaciute, Kapsner-Smith, et al. (2021). Cutoff scores were calculated based on non-singers with typical voices (n = 33). f_o adaptive responses were categorized as typical if they were greater than -199.5 cents or less than 97.8 cents. Based on these cutoffs, 26 participants in the present study were categorized as typical responders at both time one and time two, one participant was categorized as an atypical responder at both time one and time two, and one participant was categorized as an atypical responder at time one and a typical responder at time two. This results in 96.4% agreement with k = .65 reflecting substantial agreement.

1.5 DISCUSSION

Test-retest reliability was assessed for common behavioral assays of feedforward and feedback auditory-motor control of voice and articulation in people with typical speech. These included adaptive learning responses and reflexive responses to predictable vs. unexpected perturbation of voice (f_o) and articulation (F_1) parameters of auditory feedback. The magnitudes of F_1 adaptive and reflexive responses were similar to those reported in Lester-Smith et al. (2020) which used the same methods. Consistent with our hypothesis, test-retest reliability for the magnitude of F_1 adaptive responses was moderate, and reliability for F_1 reflexive responses was poor. However, test-retest reliability for the magnitude of f_o adaptive and reflexive responses followed an opposite pattern, with good reliability for reflexive responses and poor reliability for adaptive responses. Notably, when f_o adaptive responses were categorized into typical vs. atypical scores based on the distribution of scores among control participants in a prior study (Abur, Subaciute, Kapsner-Smith, et al., 2021), there was substantial agreement between scores at the two time points.

Secondary testing revealed no significant changes from time one to time two suggestive of systematic learning effects in any of the auditory-motor control assays. Although results were borderline for two of the assays (F_1 adaptation and f_o reflex), effect sizes were small. This suggests that these assays may be used for repeated testing in study designs with exposure duration and spacing similar to the present study, without substantial concern for systematic changes such as learning effects due to the measurement task itself. However, reliability of these measures should be taken into account when interpreting repeated measures. Concerns regarding reliability may be particularly relevant for studies examining individual responses as well as individual changes in longitudinal and interventional designs. Such studies are crucial for characterization of causal mechanisms and for clinical applications in people with communication disorders.

The opposite patterns in reliability we observed for behavioral assays of auditory-motor control of voice vs. articulation suggest differences in underlying neurophysiological mechanisms. For voice, reflexive responses to unpredictable f_o perturbations were highly reliable, whereas the magnitude of adaptive responses to predictable f_o perturbations showed no relationship between time points. It has been suggested that online feedback-based control of parameters related to voice, such as f_o and intensity, may be important for maintaining intelligibility in response to changing environmental or other conditions (Perkell et al., 1997). Vocal parameters may be controlled at multiple time scales, with a phrase component extending across numerous phoneme and word boundaries (Ladd, 2008). Fast and slow components of f_o control may be modeled separately (Fujisaki, 2004) and there is evidence for distinct neural control mechanisms (Dichter, Breshears, Leonard, & Chang, 2018). The slower components of vocal parameters thus may be amenable to feedback-based control. In contrast, acoustic parameters associated with speech

articulation, such as formants, change more rapidly than the time that is required for online feedback-based responses. Thus, to produce fluent and intelligible speech, a speaker must rely on an internal model for feedforward control of articulation. Theories of speech motor control include auditory feedback as crucial for both learning and maintaining such models (Parrell et al., 2019; Perkell et al., 1997; Tourville & Guenther, 2011). These views are consistent with our findings of more reliable reflexive responses to f_o perturbations than F_1, and the reverse finding for adaptive responses.

The present study adds to growing evidence for differences in sensorimotor control mechanisms underlying voice vs. articulation. Studies that have compared adaptive and reflexive responses to perturbations of f_o and formants suggest that there is no significant relationship between responses to f_o and formant feedback perturbations in the same speakers (MacDonald & Munhall, 2012; Weerathunge, Voon, Tardif, Cilento, & Stepp, 2022). Average compensation for unexpected perturbations of f_o (e.g., Burnett et al., 1998; Chen, Liu, Xu, & Larson, 2007) tends to be larger as a percentage of the shift than compensation for perturbations of formants (e.g., Purcell & Munhall, 2006b; Tourville et al., 2008), including when responses are measured within the same speakers (Lester-Smith et al., 2020). The same pattern occurred in the present study. Computational models of speech motor control such as the Directions into Velocities of Articulators (DIVA) model suggest that that magnitude of adaptive and reflexive responses will be related to the speaker's discrimination threshold for the perturbed parameter, with the latter closely related to the speaker's feedforward speech target (Tourville & Guenther, 2011). Indeed, some studies have found significant relationships between F_1 discrimination and F_1 reflexive responses (Lester-Smith et al., 2020), and F_1 discrimination and F_1 adaptive responses (Nault & Munhall, 2020; Villacorta et al., 2007), in people with typical speech, although others have failed

to find a relationship (Daliri et al., 2020). Specifically, individuals with better discrimination thresholds produced larger responses in both paradigms. However, studies of f_o discrimination and perturbation responses have failed to find significant relationships for reflexive or adaptive responses in people with typical speech (Abur et al., 2018; Abur, Subaciute, Kapsner-Smith, et al., 2021; Alemi et al., 2020; Lester-Smith et al., 2020). Furthermore, a study of people with congenital amusia, characterized by impaired f_o discrimination, revealed preserved reflexive responses to unpredictable f_o perturbations (Hutchins & Peretz, 2013). These findings suggest that, whereas auditory discrimination thresholds for articulatory parameters may indeed reflect characteristics of underlying control mechanisms such as the size of articulatory targets, auditory discrimination and auditory-motor control of voice appear to be independent for people with typical speech. Notably, a relationship between poor f_o discrimination and atypical f_o adaptive responses was found for some individuals with hyperfunctional voice disorders (Abur, Subaciute, Kapsner-Smith, et al., 2021), suggesting that these functions share some underlying mechanism and/or have a causal relationship when auditory-motor control of voice is atypical. Finally, additional evidence for mechanistic differences between auditory-motor control of articulation and voice comes from studies of people with PD, a neurodegenerative disease associated with hypokinetic dysarthria which impacts both articulation and voice. Studies of speakers with PD while off anti-parkinsonian medication have shown larger reflexive responses to f_o and intensity perturbations (X. Chen et al., 2013; H. Liu et al., 2012; Mollaei et al., 2016; Mollaei, Shiller, Baum, & Gracco, 2019) but decreased reflexive responses to F_1 perturbations (Mollaei et al., 2016). This dissociation of impaired auditory-motor control of voice vs. articulation supports mechanistic differences between the two domains.

The magnitude of adaptive responses to persistent f_o perturbations had poor test-retest reliability in the present study. This may reflect susceptibility of the adaptive auditory-motor learning system for voice to factors that were not controlled. People with typical speech display a wide range of f_o adaptive responses, including large compensatory responses as well as following responses, i.e., changes in f_o in the same direction as the feedback perturbation (e.g., Abur, Subaciute, Kapsner-Smith, et al., 2021; Lester-Smith et al., 2020). Researchers have suggested that the f_o auditory-motor control mechanism may respond flexibly to auditory feedback errors depending on whether they are perceived as internally- vs. externally-generated (Burnett et al., 1998), and that there may be separate compensatory vs. imitative modes resulting from different underlying neural processes (Korzyukov, Sattler, Behroozmand, & Larson, 2012; Li et al., 2013; S. Patel et al., 2019; S. Patel et al., 2014). However, to date these studies have focused on reflexive responses to unpredictable f_o perturbations. When averaged across trials, these responses were highly reliable in the present study. It is possible that f_o adaptive responses may have similar flexibility and may vary depending on uncontrolled factors such as internal states of the participant during an individual testing session.

Although the magnitude of f_o adaptive responses was not reliable across testing sessions, categorical scoring of f_o adaptive responses as typical vs. atypical showed substantial test-retest agreement. This scoring method was implemented by Abur, Subaciute, Kapsner-Smith, et al. (2021) to detect differences in people with and without hyperfunctional voice disorders that were masked in comparisons of group means due to the presence of atypical responses at both ends of the distribution (i.e., compensating vs. following). Because there is substantial variability in f_o adaptive responses in people with typical speech, scores that fall significantly outside of that distribution are remarkable. This scoring method has relevance for studying impaired auditory-

motor control of speech in people with communication disorders. Studies with larger normative samples and/or meta-analysis of existing f_o adaptation studies are needed to establish more precise cutoff scores for typical f_o adaptive responses. Furthermore, normative data for F_1 reflexive responses could be used to assess the reliability of categorical measurement of articulatory feedback control using a similar approach.

One limitation of the present study is the difference in tasks (sustained phonation vs. words) for the f_o vs. F_1 experiments. This approach was used because most current studies of f_o adaptive responses use sustained phonation, and most current studies of F_1 adaptive responses use speech or speech-like tasks. It is possible that participants' f_o feedforward targets may be less well-defined for sustained phonation than their F_1 feedforward targets are for prolonged words. This could lead to more variability in f_o responses than F_1 responses. However, the opposite pattern of reliability results observed for reflexive vs. adaptive responses to f_o and F_1 perturbations is not easily explained by task differences alone. Prior studies suggest differences in task may affect the magnitude of f_o reflexive responses, with larger responses observed for singing than for speech (Natke, Donath, & Kalveram, 2003), and for speech than for sustained phonation (Chen et al., 2007). These studies suggest f_o feedback control is more active when the feedforward target is more defined. In addition, responses to f_o perturbations may vary depending on linguistic and musical experience, for example singers (Zarate & Zatorre, 2008) and speakers of tonal languages (H. Liu, E. Q. Wang, et al., 2010) in whom the f_o auditory-motor control system is likely more developed. Future studies should examine the reliability of f_o adaptation during different tasks and in participants with different linguistic and musical experience to see if responses are more stable depending on task and experience.

Reliability of assays of auditory-motor control of speech may be impacted by noise. F_1 and f_o production are highly variable from trial to trial, and this variability may mask the stability of feedback and feedforward control mechanisms. It is possible that reliability may be improved by increasing the number of trials or other methodological changes that decrease the noisiness of the measures. Furthermore, the sample size in this study was relatively small, with 80% power to detect medium (ICC ≥ .6) effect sizes. A larger sample size could lead to different results.

In studies of auditory-motor control of speech, numerous methodological options exist for parameters including task and perturbation type, size and timing. For example, the use of extended words in the F_1 tasks in this study means participants' exposure to the perturbation was greater than in a natural word duration, which could have impacted the adaptive response. Outcomes such as the magnitude of responses may vary systematically with changes to task parameters, and it is conceivable that test-retest reliability could also be different depending on methodological choices. Future studies should examine the effects of such parameters on test-retest reliability.

1.6 CONCLUSIONS

Opposite patterns of reliability were observed for behavioral assays of feedforward and feedback control of voice (f_o) vs. articulation (F_1). f_o reflexive responses showed good reliability and f_o adaptive responses showed poor reliability, whereas F_1 reflexive responses showed poor reliability and F_1 adaptive responses showed moderate reliability. However, a criterion-referenced categorical measurement of f_o adaptive responses as typical vs. atypical showed substantial test-retest agreement. Individual responses to some behavioral assays of auditory-motor control of speech should be interpreted with caution, especially when analyzing individual performance and/or change over time. Future studies should examine the reliability of criterion-

referenced measures of F_1 adaptive responses as well as f_o and F_1 reflexive responses. Further, the opposite patterns of test-retest reliability observed for voice vs. articulation add to growing evidence for differences in underlying neural control mechanisms.

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CHAPTER 2: VOLITIONAL CONTROL OF FUNDAMENTAL FREQUENCY AND INTENSITY IN SPEAKERS WITH AND WITHOUT HYPERFUNCTIONAL VOICE DISORDERS

2.1 ABSTRACT

Purpose: Prior studies of vocal auditory-motor control in people with hyperfunctional voice disorders (HVDs) have found evidence of unusually large responses to auditory feedback perturbations of fundamental frequency (f_o) and more variable voice onset times. However, it is unknown whether people with HVDs perform similarly to people with typical voices when asked to make small changes in vocal parameters in volitional tasks. The purpose of this study was to compare performance on minimal movement tasks for f_o and intensity in people with and without HVDs.

Method: Twenty-six people with HVDs and 26 matched controls participated in tasks to assess the smallest volitional increases and decreases they could make in vocal f_o and intensity. Measures included the mean smallest change, variability of change, and accuracy of the direction of change. Group differences were tested with general linear models.

Results: No significant differences were found between people with and without HVDs on any of the measures. Singers produced significantly smaller mean smallest changes of both f_o and intensity than non-singers.

Conclusions: Our findings support the interpretation of prior studies of auditory-motor control in people with HVDs. Specifically, unusually large responses to perturbations of vocal auditory feedback cannot be explained by a broader impairment of the ability to make small changes in the vocal parameters f_o or intensity. The method devised to assess minimal movements for voice is sensitive to relevant group differences, such as singing experience.

2.2 INTRODUCTION

Hyperfunctional voice disorders (HVDs) are characterized by dysregulated laryngeal muscle activation, sensations of increased effort and vocal fatigue, and varying degrees of disrupted voice quality, with or without trauma to vocal fold tissues from phonation (Hillman et al., 2020). Recent evidence from multiple sources points to underlying auditory-motor impairment in at least some people with HVDs, including impaired f_o discrimination and atypical adaptive responses to altered auditory feedback for f_o (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Stepp et al., 2017; Tam et al., 2018). Specifically, people with HVDs were more likely to produce extreme adaptive responses to altered f_o feedback than people with typical voices (Abur, Subaciute, Kapsner-Smith, et al., 2021). However, it is unknown whether this represents a specific impairment of sensorimotor learning, or if people with HVDs were unable to make smaller f_o changes due to other limitations of the motor control system or the effector, i.e., the peripheral vocal mechanism.

Speech motor control relies on learned, feedforward motor programs for fluent, accurate speech (Parrell et al., 2019; Tourville & Guenther, 2011). When a speaker produces an utterance, preprogrammed motor commands are executed, and at the same time, the sensorimotor control system predicts the sensory outcomes of the actions, including auditory feedback. If a mismatch between actual and predicted auditory feedback occurs, this provides an error signal that can elicit involuntary, reflex-like corrections (Hain et al., 2000). Error signals also may be integrated into the feedforward motor program by way of adjustments that affect future productions, i.e., adaptive sensorimotor learning. Adaptive sensorimotor learning for speech has been shown to be an implicit process, that is, it does not appear to be driven by explicit strategies or volitional mechanisms (Kim & Max, 2021; Lametti et al., 2020). In fact, even when participants were

instructed to ignore auditory feedback that had been shifted in f_o, thus producing a feedback mismatch, they produced adaptive responses that were not significantly different to when they were instructed to compensate for the f_o shift (Keough, Hawco, & Jones, 2013).

Auditory-motor impairment may be one underlying factor in HVDs (Hillman et al., 2020). On average, people with HVDs have worse auditory discrimination for f_o, both for pure tones (Nguyen et al., 2022; Tam et al., 2018) and for their own voices (Abur, Subaciute, Kapsner-Smith, et al., 2021). This may suggest that people with HVDs have less well-defined (i.e., larger) auditory targets for vocal f_o. People with HVDs also are more likely to produce atypical adaptive responses to f_o-shifted auditory feedback. On average, typical responses oppose the f_o shift (often referred to as compensation), however the distribution of typical responses spans both opposing responses and responses in the same direction as the perturbation (often referred to as following; Miller et al., 2023). However, people with HVDs are more likely to have responses that fall outside a typical distribution, in either direction. Furthermore, these atypical adaptive responses were associated with worse auditory discrimination for f_o (Abur, Subaciute, Kapsner-Smith, et al., 2021).

Evidence regarding reflexive feedback control in people with HVDs is mixed. In one study, participants with HVDs produced significantly larger reflex-like responses to f_o shifts than people with typical voices (n = 61 controls, n = 22 participants with HVDs; Ziethe et al., 2019). However, in a larger study, no significant differences were found (n = 62 controls, n = 62 participants with HVDs; Abur, Subaciute, Kapsner-Smith, et al., 2021). In addition to sample size, an important methodological difference between these two studies was the size of the f_o shift, which was very large in Ziethe et al. (2019; 700 cents) and elicited larger reflexive responses (control group M = 43.6 cents, SD = 24.0 cents; HVD group M = 69.8 cents, SD =

33.1 cents), and relatively small in Abur, Subaciute, Kapsner-Smith, et al. (2021; 100 cents) and elicited smaller responses (control group M = 13 cents, SD = 13 cents; HVD group M = 16 cents, SD = 14 cents). One interpretation of the results of these studies is that larger reflexive responses in people with HVDs may occur due to underlying auditory-motor impairment. Further, when the results from discrimination, adaptive, and reflexive experiments are considered together, they suggest that people with HVDs may have impaired auditory discrimination and impaired involuntary auditory-motor processes for vocal control and learning. However, the current body of evidence is not yet sufficient to rule out a second possible interpretation: that is, larger responses to f_o-shifted auditory feedback in people with HVDs might occur because of impairments of the peripheral vocal mechanism or of volitional control, rather than a specific impairment of sensorimotor learning.

For example, people with HVDs often demonstrate peripheral impairment of vocal production, such as vibratory impairment due to phonotrauma, which subsequently affects f_o and intensity (Bastian, Keidar, & Verdolini-Marston, 1990; Carroll et al., 2006; Toles, Ortiz, et al., 2021). Furthermore, increased laryngeal tension during vocal production may also be present in people with HVDs, not specific to auditory-motor integration tasks (Stepp, Hillman, & Heaton, 2010), which may also affect vocal parameters such as f_o even in the absence of phonotrauma (Van Stan et al., 2021). Thus, atypically large vocal responses to f_o-shifted auditory feedback in the Ziethe et al. (2019) and Abur, Subaciute, Kapsner-Smith, et al. (2021) studies in people with HVDs could simply have been due to an inability to make smaller vocal changes. However, the difference between findings for reflexive feedback control in people with HVDs in these two studies does not support this interpretation. Specifically, no group differences were found when participants made small responses to small auditory feedback perturbations in Abur, Subaciute,

Kapsner-Smith, et al. (2021), whereas people with HVDs produced larger responses than people with typical voices when the auditory feedback perturbations were large in the study by Ziethe et al. (2019).

To clarify the interpretation of the above findings, evidence regarding volitional control of small changes in vocal parameters in people with HVDs is needed. If previous findings of atypically large adaptive responses to f_o-shifted feedback in people with HVDs were driven by impairments such as phonotrauma or laryngeal tension affecting all vocalizations, we would expect to see larger mean volitional changes in vocal parameters in people with HVDs than people with typical voices. On the other hand, if the previous findings were driven by impaired sensorimotor learning, which is an implicit, involuntary process, we would expect to see no difference in mean volitional changes in vocal parameters between people with HVDs and people with typical voices. However, in this study, it was important not only to include measures of mean volitional changes in vocal parameters, but also measures of accuracy and variability. Because there is evidence of increased variability of voice onset times during volitional speech in people with HVDs (McKenna et al., 2020), it also was possible that increased variability would be observed in volitional control of f_o and intensity, reflected in larger standard deviations for the volitional control tasks. This finding would be consistent with the suggestion that people with HVDs have larger auditory targets for vocal parameters.

The purpose of this study was to assess volitional vocal sensorimotor control in individuals with and without HVDs. To study sensory and motor aspects of jaw control in people who stutter, De Nil and Abbs (1991) and Daliri, Prokopenko, and Max (2013) used a task to assess participants' volitional control of small jaw displacements relevant for speech, referred to as a minimal movement task. In the present study, we devised an adaptation of this task to assess participants'

abilities to make small changes in vocal f_o and intensity, specifically by examining differences between two utterances, as occurs in adaptive auditory-motor learning paradigms. We assessed the smallest volitional changes participants were able to make, task accuracy (the percentage of trials with f_o or intensity changes in the correct direction), and variability. Thus, this study addressed the following questions: 1) Do people with HVDs perform worse (i.e., produce larger mean changes) than people with typical voices in tasks assessing smallest producible voluntary changes for vocal f_o and intensity, i.e. minimal movement?; and 2) Are people with HVDs less accurate or more variable in these same minimal movement tasks? We hypothesized that people with and without HVDs would not differ significantly on mean minimal movements for f_o and intensity, reflecting grossly preserved volitional movement capacity for voice in people with HVDs. However, we hypothesized that people with HVDs would be less accurate and more variable in their performance of minimal movement tasks, consistent with prior findings of more variable voice onset times in people with HVDs (McKenna et al., 2020).

2.3 METHODS

All procedures were approved by the University of Washington Institutional Review Board.

2.3.1 Participants

Twenty-six individuals with HVDs and 26 participants with typical voices were matched pairwise for relevant variables including age (+/- 5 years), voice f_o range (typically masculine vs. typically feminine), and singing experience. Participant characteristics are included in Table 2-1. The participant age range was limited to 18 – 65 years to eliminate two potential confounding factors: 1) ongoing auditory-motor and laryngeal development in pediatric speakers (Kent, 1976; N. Scheerer et al., 2016); and 2) compensation for glottal insufficiency (Belafsky, Postma, & Koufman, 2002) in presbyphonia. Both participant groups included more individuals who were

assigned female at birth. HVDs are more prevalent in female speakers, justifying skewed enrollment with respect to sex (Roy, Merrill, Gray, & Smith, 2005). In this study, musician was defined as an individual with musical training beyond secondary school. Non-singer musicians were excluded due to confounding effects on f_o perception (Micheyl, Delhommeau, Perrot, & Oxenham, 2006). An exception was made to include musicians who were singers due to the high prevalence of HVDs in this population (Pestana, Vaz-Freitas, & Manso, 2017). Singer was defined as an individual with post-secondary singing training and/or performing experience. Speakers of tonal languages were excluded due to confounding effects on auditory-motor control of vocal f_o (H. Liu, E. Q. Wang, et al., 2010). Participants taking hormone treatments that affect vocal f_o were only included if they reported no changes in hormone treatment for at least 12 months (n = 2 control participants, n = 2 participants with HVDs).

Table 2-1. Participant characteristics.

Group	Age	Sex assigned at birth	Gender	Singers
Control	M = 39.35 (22 – 65, SD = 14.09)	21 AFAB, 5 AMAB	19 cis women, 4 cis men, 2 non-binary, 1 trans man	13 singers, 13 non-singers
HVD	M = 39.42 (20 – 64, SD = 12.68)	21 AFAB, 5 AMAB	18 cis women, 5 cis men, 2 non-binary, 1 trans man	13 singers, 13 non-singers

AFAB = assigned female at birth; AMAB = assigned male at birth

Participants with HVDs were recruited from the Laryngology Clinic at the University of Washington Medical Center and from the University of Washington Speech and Hearing Clinic in the Department of Speech and Hearing Sciences. Participants with HVDs had a confirmed diagnosis of an HVD, with or without phonotrauma (e.g., benign vocal fold lesions, muscle tension dysphonia), provided by a board certified otolaryngologist (see Table 2-2). Individuals with voice diagnoses related to neoplasm, neurological conditions, and/or presbyphonia were

excluded. Control participants reported no history of voice disorders and completed an auditory-perceptual and vocal health history screening by the author (MKS, a certified speech-language pathologist with experience assessing and treating individuals with voice disorders). All participants reported no other known neurological, speech, language, or hearing disorders. Participants were screened to ensure typical hearing using pure tone air conduction at octave frequencies: 125–8000 Hz, pass criterion of 25 dB HL at all frequencies <50 years of age (ASHA, 2018), or 25 dB HL at 125–1000 Hz and 40 dB HL at 2000–8000 Hz age 50+ (Schow, 1991). Overall severity of dysphonia (OS) was rated on a visual analog scale (0 – 100, where 0 = typical voice for age/gender/culture; 100 = severe) by an experienced speech-language pathologist who was blinded to group assignment. The mean OS rating for control participants was 4.0 (SD = 3.1, range = 0.6 – 10.5). The mean OS rating for participants with HVDs was 7.7 (SD = 8.7, range = 0.9 – 35). Intrarater reliability was tested by randomly repeating 20% of samples, and was good (r = .87).

Table 2-2. Diagnoses in the hyperfunctional voice disorder group (n = 26).

Diagnosis	**Number of Participants**
Primary muscle tension dysphonia	13
Bilateral benign vocal fold lesions and vocal hyperfunction	9
Unilateral benign vocal fold lesion and vocal hyperfunction	2
Bilateral vocal fold edema and vocal hyperfunction	1
Unilateral sulcus vocalis status post excision of benign vocal fold lesion and vocal hyperfunction	1

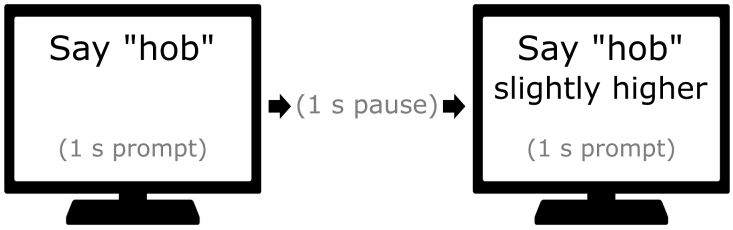
Procedures

2.3.1.1 Setup

All participants underwent the same procedures. They were seated in a sound-attenuated booth in front of a computer monitor used to display stimulus prompts. These data were collected as part of a larger study that included measures of auditory discrimination and adaptive auditory-motor vocal learning. Voice signals were captured with an omni-directional ear-set microphone (Shure MX153), 7 cm from center of mouth, at a 45 degree angle. Auditory feedback was presented to the participant through insert earphones (Etymotic ER-2). Microphone gain was adjusted with a preamplifier (RME Quadmic II) and digitized at 44.1 kHz by a soundcard (RME Fireface UCX). Microphone intensity was calibrated based on a monotone electrolarynx (TruTone, Griffin Labs) tone recorded during the experiment. Sound pressure level of the reference tone (Bruel and Kjaer Type 2250 SLM) was recorded to enable calibration of recordings to SPL in post processing as needed. Participants heard near real-time auditory feedback of their own voice (10 to 30 ms delay; Weerathunge et al., 2020). Earphone levels were adjusted with an amplifier (Behringer Xenyx Q802) to provide 0 dB amplification relative to the microphone signal. Software and hardware systems were calibrated using a 2 cc coupler (Type 4946, Bruel and Kjaer) connected to a sound level meter (Type 2250A with a Type 4947 ½" Pressure Field Microphone, Bruel and Kjaer).

2.3.1.2 Task

Figure 2-1. Structure of a single trial in the minimal movement task (example shown for f_o up condition).



The minimal movement task, adapted from Daliri et al. (2013), assessed the least producible change in vocal frequency (f_o; Brennan, 1926; Seashore & Jenner, 1910) and intensity (Jacobsen, 1936) that each participant was able to voluntarily produce in both directions, comprising four experimental conditions: higher (f_o up), lower (f_o down), louder (intensity up), and softer (intensity down). During this task, participants produced a series of pairs of syllables with a 1-s inter-stimulus interval (Seashore & Jenner, 1910) in response to prompts on a computer monitor (see Figure 1). The syllable "hob" was chosen to elicit a vowel similar to the sustained /ɑ/ used in prior studies of auditory-motor control in this population, but in a speech task. The initial /h/ discouraged creaky onsets and the final voiced consonant encouraged a long enough vowel for analysis. Participants were given verbal instructions explaining the task and the condition before each block of trials. They were instructed to produce the first token at a comfortable pitch and loudness, followed by a second production that was slightly higher in pitch, slightly lower in pitch, slightly louder, or slightly softer than their first production within the syllable pair. They were instructed to produce the smallest change possible. Before each new condition (higher, lower, louder, softer), a single presentation of a prerecorded model was played to the participant via the headphones. Models differed by 3 dB or 1 ST. Participants were then verbally instructed to produce smaller changes than the model if possible. Auditory targets other than the initial

model were not provided to avoid confounding influences of f_o and intensity discrimination and matching abilities. After five practice trials, two sets of 10 trials were performed in each of the four conditions, with direction (up/down) of sets interleaved within f_o and intensity blocks. The order of f_o and intensity experiments and direction (up/down) was counterbalanced across participants. The entire experiment took approximately 15 minutes.

2.3.2 Data Analysis

Onsets and offsets of vowels produced by the participants were selected manually for each trial and f_o and intensity were extracted using *Praat* (Boersma & Weenink, 2016) scripts. Mean f_o was calculated using an autocorrelation method and mean intensity using a root-mean-square (RMS) method. To isolate the response of the feedforward motor control system during steady-state phonation, the 40 – 120 ms portion of each vowel within each paired syllable trial was analyzed. The difference in f_o of the second vowel relative to the first was measured in semitones (ST) for the f_o experiment in both the high/lower conditions. The difference in intensity of the second vowel relative to the first was measured in decibels (dB) for the intensity experiment in both the louder/softer conditions. Because averaging all trials could cause trials that are produced in the wrong direction (e.g., a decrease in f_o when instructed to increase pitch) to "improve" a participant's score, only the 10 best trials (i.e., smallest change in ST or dB in the correct direction) were averaged for each condition, resulting in a measure that was called *mean smallest change* (Brennan, 1926; Jacobsen, 1936; Seashore & Jenner, 1910). The standard deviation of all trials also was calculated as a measure of *variability*. Prior work shows increased variability in voice onset times in people with HVDs (McKenna et al., 2020), suggesting this was a dependent measure of interest. Finally, to account for accuracy in the direction of change, a third measure was calculated: the percentage of trials with change produced in the correct direction (i.e.,

percent correct). This accuracy measure was included because atypical auditory-motor integration in response to f_o perturbation has been observed in individuals with HVDs both in terms of degree and direction of adaptation (Abur, Subaciute, Kapsner-Smith, et al., 2021). All three measures (mean smallest change, variability, and percent correct) were calculated for each of the four conditions for each participant.

2.3.3 Statistical Analysis

Statistical analyses were conducted using SPSS Statistics, Version 26 (IBM, 2019). For the purposes of statistical analysis, the mean smallest change scores for the minimal movement tasks were converted to absolute values. To examine the relationship between voice disorder status and voluntary control of vocal f_o and intensity, repeated measures general linear models were conducted (function GLM) to examine mean smallest change and variability with between-subjects factors of HVD status (HVD vs. control) and singing experience (non-singer vs. singer), and the within-subjects factor direction of change (up vs. down), and all two- and three-way interactions. Effect sizes were measured using the squared partial curvilinear correlation η^2. These analyses were conducted for the vocal parameters f_o and intensity (two outcome variables × two vocal parameters = four GLMs). Because percent correct data were not normally distributed due to ceiling effects, a categorical analysis was employed, motivated by the findings of Abur, Subaciute, Kapsner-Smith, et al. (2021). The 10^{th} percentile was calculated for the control group, and this was used as a criterion to categorize accuracy for each participant and each condition into typical (≥10%ile) and atypical (<10%ile). A chi-squared test for association was used to assess whether there was a difference in the number of participants with atypical accuracy scores between groups. Effect size w was measured for chi-squared tests. These

analyses were conducted for the vocal parameters f_o and intensity (one outcome variable × two vocal parameters × two directions = four chi-square tests).

2.4 RESULTS

Descriptive statistics for HVD and control group results for the three variables (mean smallest change, variability, and percent correct) and the two vocal parameters (f_o and intensity) are provided in Tables 2-3 and 2-4.

Table 2-3. Mean results for HVD and control groups for f_o tasks.

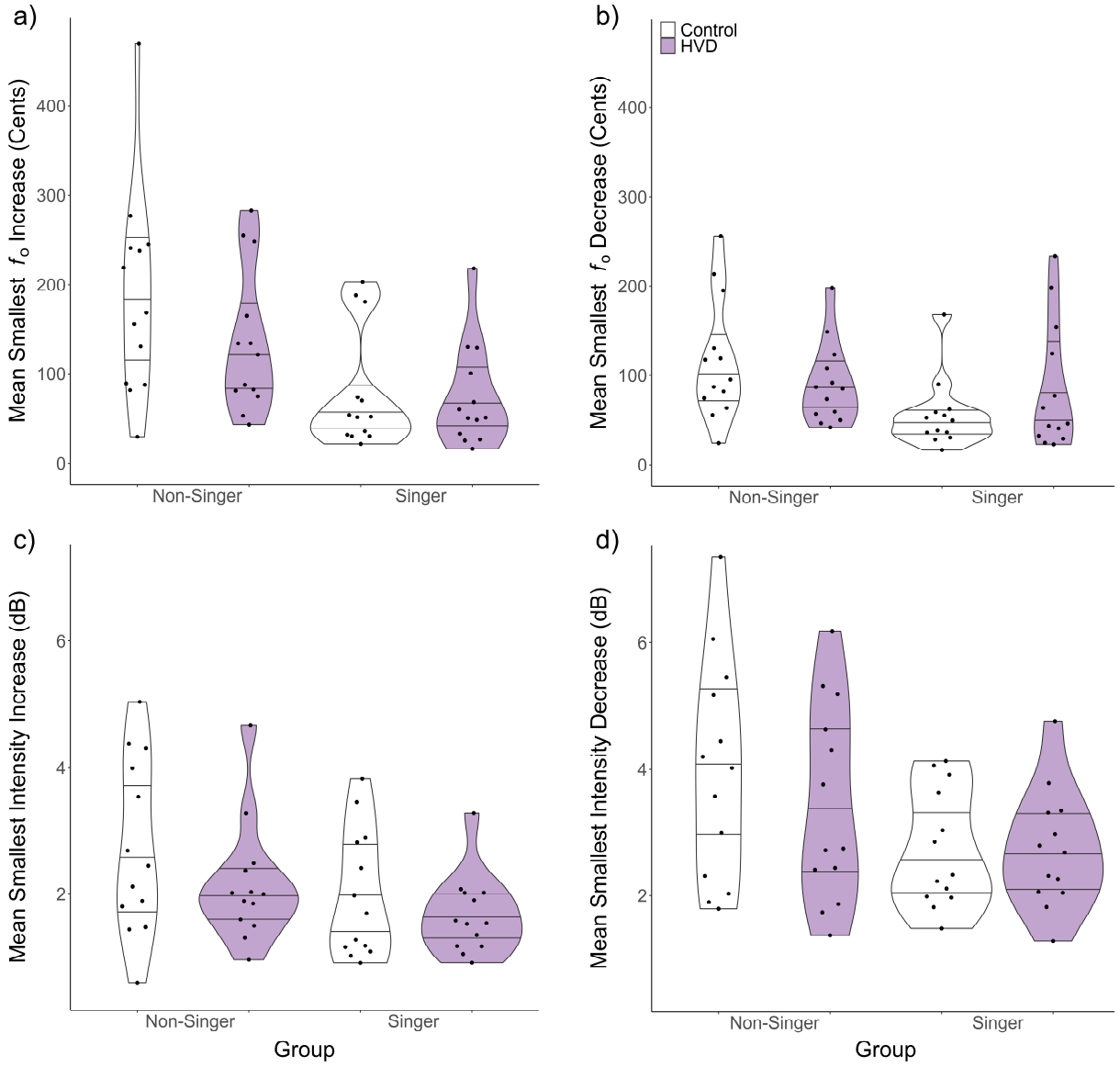
Group	Smallest Increase	Smallest Decrease	Increase Variability	Decrease Variability	Increase Accuracy	Decrease Accuracy
Control	*M* = 133 cents, *SD* = 107	*M* = 86 cents, *SD* =45	*M* = 92 cents, *SD* = 59	*M* = 77 cents, *SD* = 44	*M* = 90%, *SD* = 14	*M* = 89%, *SD* = 12
HVD	*M* = 105 cents, *SD* = 75	*M* = 87 cents, *SD* = 59	*M* = 94 cents, *SD* = 68	*M* = 76 cents, *SD* = 41	*M* = 88%, *SD* = 14	*M* = 88%, *SD* = 13

Table 2-4. Mean results for HVD and control groups for intensity tasks.

Group	Smallest Increase	Smallest Decrease	Increase Variability	Decrease Variability	Increase Accuracy	Decrease Accuracy
Control	*M* = 2.36 dB, *SD* = 1.24	*M* = 3.34 dB, *SD* = 1.50	*M* = 2.12 dB, *SD* = 0.63	*M* = 2.20 dB, *SD* = 0.62	*M* = 89%, *SD* = 10	*M* = 96%, *SD* = 8
HVD	*M* = 1.91 dB, *SD* = 0.83	*M* = 3.08 dB, *SD* = 1.30	*M* = 2.17 dB, *SD* = 0.65	*M* = 2.33 dB, *SD* = 0.64	*M* = 86%, *SD* = 13	*M* = 96%, *SD* = 7

2.4.1 Mean Smallest Change

Figure 2-2. Mean smallest changes by HVD status and singing experience for a) f_o increase, b) f_o decrease, c) intensity increase, and d) intensity decrease.



Group data are shown in Figure 2-2. Repeated measures GLMs were conducted to examine mean smallest change with between-subjects factors of HVD status (HVD vs. control) and singing experience (non-singer vs. singer) and the within-subjects factor direction of change (up vs. down), and their interactions (see Tables 2-5 and 2-6).

There was no significant main effect of HVD status (control/HVD) for mean smallest f_o change. There were significant main effects of singing experience (p = .001) and direction (p = .002), both with large effect sizes. Singers produced significantly smaller f_o changes than non-singers. Changes in f_o were significantly smaller when decreasing f_o than when increasing f_o There was a significant interaction of direction and singing experience (p = .014), with a medium effect size. The difference between singers and non-singers was greater for f_o increases than f_o decreases. There were no other significant interactions.

Table 2-5. Statistical results for mean smallest f_o changes.

Effect	***df***	η_p^2	***F***	***p***
HVD status (control, HVD)	1	.01	0.65	.423
Singing experience (singer, non-singer)	1	.21	12.38	.001*
Direction (up, down)	1	.18	10.20	.002*
Direction * Singing experience	1	.12	6.57	.014*

*Significant at $p < .05$

Table 2-6. Statistical results for mean smallest intensity changes.

Effect	***df***	η_p^2	***F***	***p***
HVD status (control, HVD)	1	.03	1.51	.225
Singing experience (singer, non-singer)	1	.14	7.48	.009*
Direction (up, down)	1	.49	48.89	<.001*

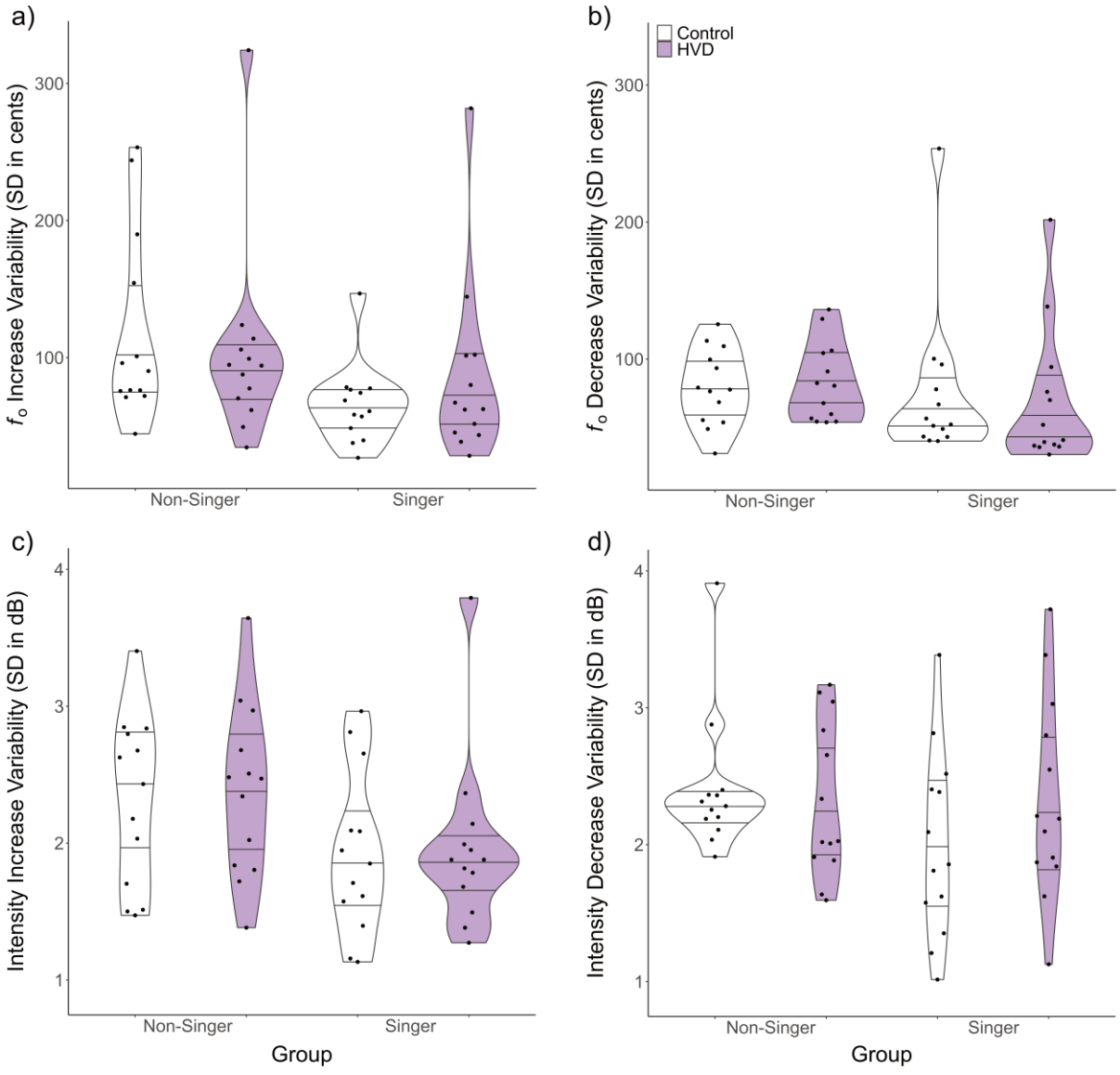
*Significant at $p < .05$

There was no significant main effect of HVD status (control/HVD) for mean smallest intensity change. There were significant main effects of singing experience (p = .009) and direction ($p <$ .001), again both with large effect sizes. Singers produced significantly smaller changes in

intensity than non-singers. Intensity changes were significantly smaller when increasing intensity than when decreasing intensity. There were no significant interactions.

2.4.2 Variability

Figure 2-3. Variability by HVD status and singing experience for a) f_o increase, b) f_o decrease, c) intensity increase, and d) intensity decrease.



Group data for variability of f_o and intensity changes are shown in Figure 2-3. Repeated measures GLMs were conducted to examine variability with between-subjects factors of HVD

status (HVD vs. control) and singing experience (non-singer vs. singer) and the within-subjects factor direction of change (up vs. down), and their interactions (see Tables 2-7 and 2-8).

Table 2-7. Statistical results for f_o change variability.

Effect	***df***	η_p^2	***F***	***p***
Group (control, HVD)	1	.00	.00	.985
Singing experience (singer, non-singer)	1	.06	3.18	.081
Direction (up, down)	1	.09	4.73	.035*

*Significant at $p < .05$

There were no significant main effects of HVD status (control/HVD) or singing experience for f_o change variability. There was a significant main effect of direction ($p = .035$) with a medium effect size. Change variability was significantly less when decreasing f_o than when increasing f_o. There were no significant interactions.

There were no significant main effects of HVD status (control/HVD) or direction for intensity change variability. There was a significant main effect of singing experience ($p = .048$) with a medium effect size. Singers were significantly less variable when changing intensity than non-singers. There were no significant interactions.

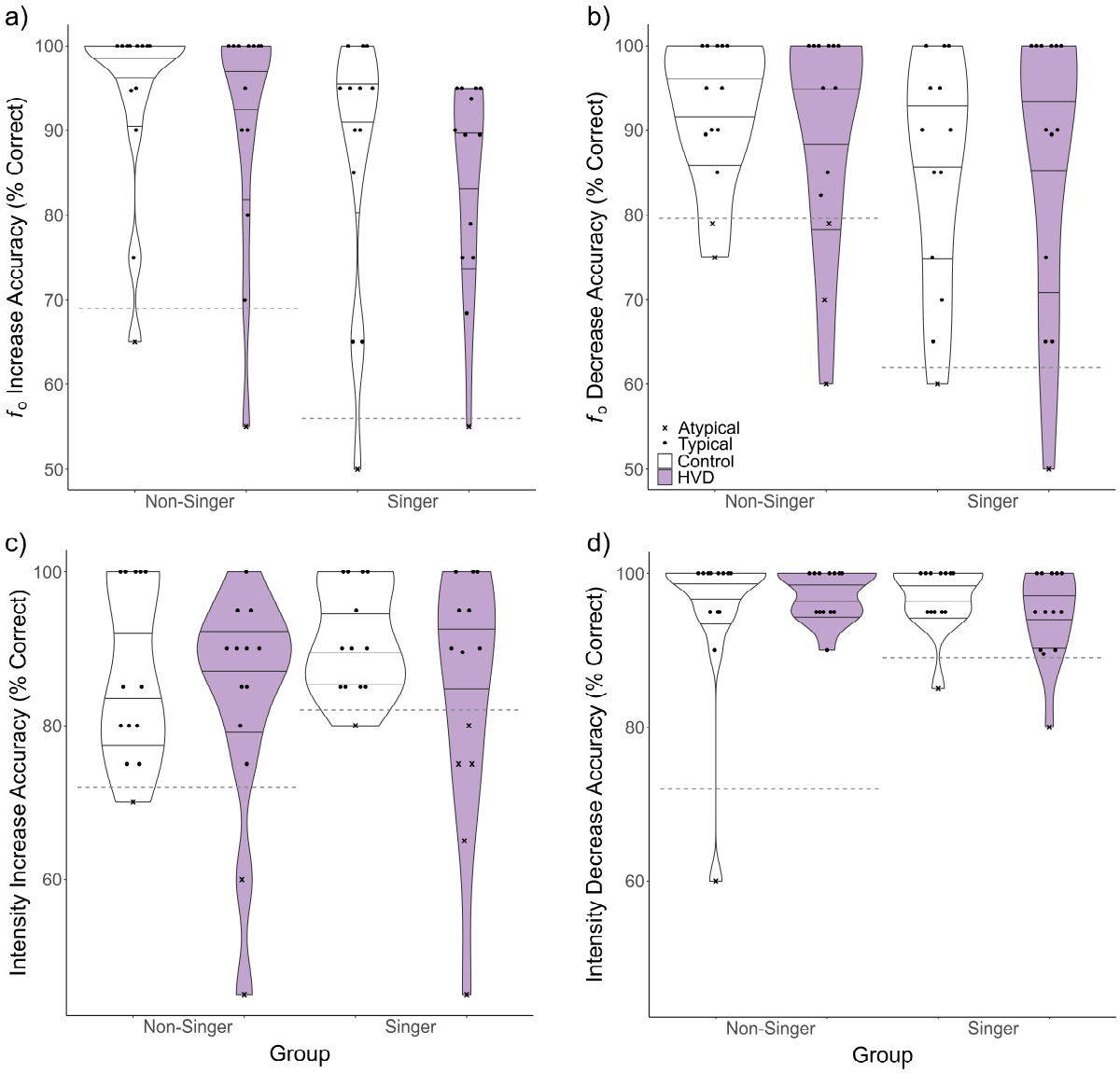
Table 2-8. Statistical results for intensity change variability.

Effect	***df***	η_p^2	***F***	***p***
HVD status (control, HVD)	1	.01	0.37	.547
Singing experience (singer, non-singer)	1	.08	4.13	.048*
Direction (up, down)	1	.04	1.90	.175

*Significant at $p < .05$

2.4.3 Percent Correct

Figure 2-4. Accuracy of change direction for a) f_o increase, b) f_o decrease, c) intensity increase, and d) intensity decrease.



For statistical analyses, percent correct cutoff scores were derived from the 10th percentile of scores in the control group. Because significant effects of singing experience were observed in the mean smallest change and variability results, separate cutoffs were calculated for singers and non-singers. Scores were categorized as atypical if they fell below the following thresholds: f_o increase, 56.00% singer / 69.00% non-singer; f_o decrease, 62.00% singer / 79.58% non-singer;

intensity increase, 82.00% singer / 72.00% non-singer; intensity decrease, 89.00% singer / 72.00% non-singer (see Figure 2-4).

A chi-square test of association was performed on the categorical accuracy scores for the two vocal parameters and two directions. Results are shown in Table 2-9. There were no significant effects of HVD status (control/HVD) on accuracy in any of the four tasks.

Table 2-9. Statistical results for change accuracy (typical vs. atypical).

Task	***df***	**w**	χ^2	***p***
f_o Increase	1	<0.01	<0.01	1.000
f_o Decrease	1	0.06	0.17	.685
Intensity Increase	1	0.25	3.36	.067
Intensity Decrease	1	0.08	0.35	.552

*Significant at $p < .05$

2.5 DISCUSSION

The purpose of this study was to determine whether differences exist between people with and without HVDs in volitional control of small changes in vocal f_o (perceived as pitch) and intensity (perceived as loudness). We developed a protocol to elicit these changes modeled after Daliri et al. (2013), with some key alterations to increase the similarity to speech tasks found in studies of vocal auditory-motor integration. We found no significant differences related to voice disorder status in the magnitude, variability, or accuracy of changes when individuals were instructed to make the smallest possible changes in these parameters during a speech task. However, we did find significant effects of singing experience and of the direction of the task (increase vs. decrease), which suggests this protocol is able to capture differences between speakers with different characteristics.

Consistent with our first hypothesis, we found no evidence of differences in volitional production of minimal differences in f_o and intensity between people with and without HVDs. This suggests volitional control of these parameters is preserved in this population. It also lends support to interpretation of prior findings of unusually large adaptive responses to f_o feedback alteration in people with HVDs as reflecting underlying impairment in auditory-motor integration (Abur, Subaciute, Kapsner-Smith, et al., 2021), rather than an inability to make smaller changes. This is also consistent with findings in the same study of preserved reflex-like responses to unexpected f_o feedback alterations, which are small in magnitude.

In contrast with our second hypothesis, we did not find significant differences in the variability or accuracy of volitional production of minimal differences in f_o and intensity between people with and without HVDs. In a prior study, McKenna et al. (2020) found that although mean voice onset times did not vary between people with and without HVDs, voice onset times were more variable in people with HVDs. This finding suggests subtle underlying sensorimotor impairment in control of voicing for speech. We did not find differences in variability or accuracy in the present study. There are key differences between the tasks that were produced in the present study vs. McKenna et al. (2020). Whereas voice onset time requires fine coordination of the timing of phonation onset, the task in the present study involves control of the spectro-temporal parameters f_o and intensity through small adjustments in vocal fold length, tension, adduction, and subglottal pressure. Furthermore, voice onset time is a linguistic parameter, whereas changes in f_o and intensity are paralinguistic parameters in English. It is noteworthy that the result for intensity increase accuracy was substantially closer to significance than any of the other findings (p = .067), with a small effect size (w = 0.50). It is possible that the study was underpowered for this parameter, and that a larger sample size might detect a significant effect. Of the seven

participants with HVDs who had atypical intensity increase accuracy scores, six (86%) had diagnoses of phonotraumatic vocal hyperfunction (vs. 54% of the entire HVD sample). Phonotrauma can cause increased stiffness of the vocal folds and create difficulty increasing intensity. It is possible that vibratory impairment affected these participants' accuracy in the intensity increase task. However, these results should be interpreted with caution, given the lack of statistical significance.

We found a significant effect of singing experience on smallest changes in f_o and intensity and the variability of intensity changes. It is not surprising that singers would perform better than non-singers in these tasks, likely due to the effects of prior training in volitional control of vocal f_o and intensity, two parameters that are of substantial importance in musical dynamics. Trained musicians are also better at auditory discrimination of parameters such as f_o (Micheyl et al., 2006), which could play a role in auditory-motor control (Tourville & Guenther, 2011).

This study has some limitations. We did not control the f_o or intensity range produced by participants, for example by requiring them to match a target for their first production. We chose instead to ask participants to begin with a comfortable pitch and loudness. This was done to avoid the confound of auditory discrimination ability, which is affected in this population (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Tam et al., 2018), and demands on f_o matching abilities. Our sample size was relatively small, and it is possible that the result for intensity increase accuracy in particular was underpowered. However, performance between the control and HVD groups was remarkably similar on all other variables. In addition, the average rating of overall severity of dysphonia in our sample was low (mean = 7.7, SD = 8.7, range = 0.9 – 35). It is possible that participants with more severe dysphonia would perform differently.

2.6 CONCLUSIONS

This study provides preliminary evidence for preserved volitional sensorimotor control of f_o and intensity in individuals with hyperfunctional voice disorders. Our results lend support to the interpretation of prior findings of impaired auditory-motor integration for vocal learning in this population (Abur, Subaciute, Kapsner-Smith, et al., 2021). Furthermore, we present a protocol for assessment of volitional control of f_o and intensity that is sensitive to differences in participant characteristics such as singing experience. Further characterization of vocal sensorimotor control in people with HVDs is necessary to elucidate their pathophysiology and to facilitate improved diagnosis and treatment.

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CHAPTER 3: EXAMINING RELATIONSHIPS AMONG AUDITORY DISCRIMINATION, ADAPTIVE VOCAL LEARNING, AND PERILARYNGEAL MUSCLE ACTIVATION IN PEOPLE WITH AND WITHOUT HYPERFUNCTIONAL VOICE DISORDERS

3.1 ABSTRACT

Purpose: Recent studies have identified deficits in auditory discrimination and auditory-motor integration of vocal f_o feedback in people with hyperfunctional disorders (HVDs). The purpose of this study was to investigate the specificity of these impairments by examining both vocal intensity and f_o. In addition, we examined possible relationships with dysregulated perilaryngeal muscle activation during voicing by measuring muscle activity during these adaptive vocal learning tasks.

Method: Twenty-six participants with HVDs and 26 matched controls with typical voices participated in auditory discrimination and adaptive vocal learning tasks for the vocal parameters intensity (perceived as loudness) and f_o (perceived as pitch). Surface electromyographic measures were collected from suprahyoid and infrahyoid muscles during adaptive vocal learning tasks. Analyses were conducted to examine the effects of HVD status and singing experience on discrimination thresholds and adaptation responses, including atypically large adaptation responses which follow the direction of the perturbation (i.e., following responses). Repeated measures GLMs were conducted to examine the effects of HVD status, singing experience, and vocal parameter on the co-contraction index (CCI), a measure of co-activation of agonist/antagonist muscles, during adaptive vocal learning tasks. Finally, relationships among discrimination thresholds, adaptation responses, and muscle activations were examined using regression and a mediation model.

Results: People with HVDs adapted more to intensity perturbations than matched controls (p = .050), whereas singers adapted significantly less than non-singers (p = .018). For f_o adaptation, significantly more participants with HVDs produced large following responses than controls (p = .017). There were no significant effects of time, vocal parameter, or HVD status on CCI

measured during adaptive vocal learning tasks. However, during unperturbed control conditions, suprahyoid activation increased over time in all participants ($p < .001$), with a trend for greater increases overall in people with HVDs ($p = .063$). For f_o, significant moderate relationships were found between discrimination threshold, CCI during the early hold phase of adaptation, and adaptation responses. Participants with better discrimination compensated less or followed the perturbation, in contrast with prior work in the articulatory domain, and co-contracted more. Participants who co-contracted more also compensated less or followed the perturbation. No significant relationships were found for vocal intensity.

Conclusions: This study replicates and extends findings of previous studies of auditory-motor impairment in people with HVDs. We found differences between people with HVDs and controls in integration of f_o and intensity feedback, however these were qualitatively different; whereas we found more frequent large following responses to f_o perturbation in people with HVDs, we found a greater degree of compensation for intensity perturbations. This dissociation of impaired f_o and intensity integration in HVDs suggests an independence of the underlying mechanisms. We also found preliminary evidence of a laryngeal stabilization response to altered auditory feedback for f_o. This effect was stronger in people who adapted less and who had better auditory discrimination, which may indicate stabilization occurs when the speaker perceives an auditory feedback mismatch to be externally generated. Implications for research and interventions for people with HVDs are discussed.

3.2 INTRODUCTION

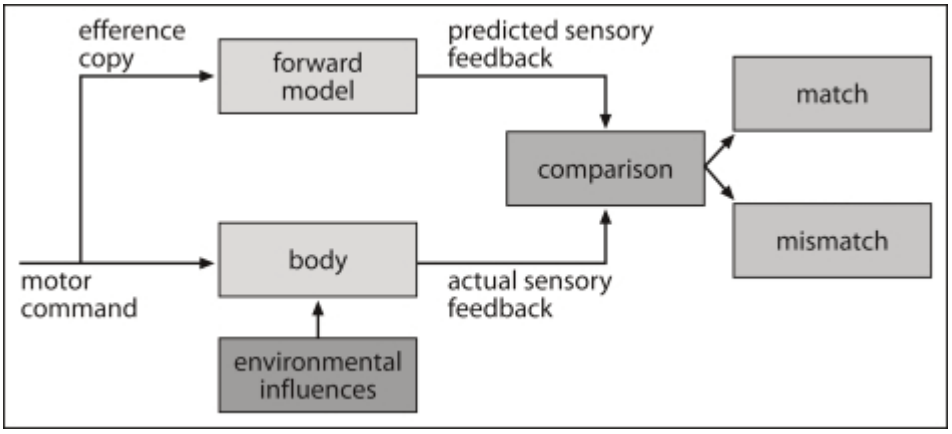
3.2.1 Auditory discrimination and adaptive vocal learning in people with and without hyperfunctional voice disorders

Sensorimotor control and learning require integration of sensory information to develop and maintain motor plans and to detect and correct for errors. In the case of speech, several models of speech sensorimotor control posit that auditory-perceptual goals are the control variables that govern movements to produce speech (Perkell, 2012). In these models, audition is a primary source of sensory information that facilitates the development and maintenance of internal models for speech production, along with somatosensation. These internal models allow for smooth and fluent feedforward control of speech. Deficits in auditory-motor integration for speech may cause or contribute to some types of voice disorders, including hyperfunctional voice disorders (HVDs; Hillman et al., 2020; Weerathunge, Tomassi, et al., 2022).

A large body of literature has explored the role of auditory feedback in sensorimotor control of voice and articulation through the application of perturbations to parameters of auditory feedback such as fundamental frequency (f_o; e.g., Burnett et al., 1997) and formants (e.g., Houde & Jordan, 1998). In summary, when an individual produces a motor act such as speech, it is hypothesized that the brain produces a model of the predicted sensory consequences of the action (forward model) through what is called an efference copy of the motor command (Miall & Wolpert, 1996). As the motor command is executed, reafferent sensory information (feedback) is compared to the predicted sensory consequences (see Figure 3-1). When a mismatch occurs, this information may be used to make immediate corrections and/or to update feedforward motor plans. In the case of speech, the speaker hears their own production, including multiple acoustic parameters such as f_o, intensity, and formants. If a speaker is exposed to an unexpected

perturbation of their auditory feedback, they typically will respond with a rapid correction opposing the direction of the perturbation (e.g., Larson & Robin, 2016; Purcell & Munhall, 2006b; Tourville et al., 2008). This is interpreted as a reflex-like correction produced by feedback control loops. If a speaker is exposed to persistent, predictable perturbations of their auditory feedback over many trials, they typically will adapt by progressively opposing the change across trials, and will demonstrate a brief period of persistence of this change after the perturbation is removed (e.g., Houde & Jordan, 1998; Jones & Munhall, 2000; Villacorta et al., 2007). This is interpreted as reflecting updates to underlying feedforward motor commands based on an error signal, i.e., adaptive sensorimotor learning. Speech-specific models of sensorimotor control account for these responses in control of voice and articulation (Parrell et al., 2019; Tourville & Guenther, 2011; Weerathunge, Alzamendi, et al., 2022).

Figure 3-1. A model of a feedback comparator for sensorimotor control (Bubic, Von Cramon, & Schubotz, 2010, p. 9).



HVDs are characterized by dysregulated laryngeal muscle activation for voicing, vocal fatigue, and varying degrees of dysphonia, with or without vocal fold tissue changes related to trauma (phonotrauma; Hillman et al., 2020). Prior studies of sensorimotor function in people with HVDs have suggested possible impairments of auditory discrimination (Abur, Subaciute, Kapsner-

Smith, et al., 2021; Nagy, Elshafei, & Mahmoud, 2020; Nguyen et al., 2022), auditory feedback control (Ziethe et al., 2019), and adaptive vocal learning (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017), compared to controls. One study found that 33% of a prospective cohort of 36 patients with HVDs had undiagnosed hearing impairment (Nagy et al., 2020), which is higher than the national prevalence of hearing loss of 23% (Goman & Lin, 2016); however, it should be noted that the study lacked a control group or statistical analyses related to prevalence. In a study of pure tone f_o discrimination, individuals with HVDs (n = 24) showed significantly worse discrimination thresholds than individuals without HVDs (n = 63; Tam et al., 2018). However, hearing status and singing experience were not controlled or reported, and may impact f_o discrimination (Micheyl et al., 2006). One study of reflex-like responses to unpredictable f_o perturbations of auditory feedback showed larger compensatory responses in individuals with HVDs (n = 22) compared to individuals without HVDs (n = 61; Ziethe et al., 2019). Singers were excluded from this study, despite being at increased risk of HVDs (Roy et al., 2005). A preliminary study of adaptive vocal learning also reported a larger proportion of atypical adaptation responses (i.e.., following the direction of the perturbation) in response to predictable f_o perturbations in a small sample of individuals with HVDs (n = 9) compared to individuals without HVDs (n = 9; Stepp et al., 2017).

In the largest and most comprehensive study of auditory discrimination and auditory-motor function in people with HVDs to date, auditory f_o discrimination, reflexive vocal motor control, and adaptive vocal learning were tested in 62 individuals with HVDs and 62 matched controls (Abur, Subaciute, Kapsner-Smith, et al., 2021). Results were threefold. First, as a group, individuals with HVDs displayed significantly worse auditory discrimination of vocal f_o compared to individuals without HVDs, when controlling for singing experience. This suggests

impaired vocal f_o discrimination may occur in individuals with HVDs as either a cause or a result of having the disorder. Second, individuals with HVDs did not show any differences from matched controls when they were presented with sudden auditory feedback f_o perturbations, suggesting preserved reflexive f_o control, in contrast with prior work (Ziethe et al., 2019). The authors postulated that the contrasting findings from Ziethe et al. (2019) may have been due to methodological differences, including the size of the f_o perturbation (700 cents in Ziethe et al. vs. 100 cents in Abur, Subaciute, Kapsner-Smith et al.), or the greater age range in the HVD group compared to controls in Ziethe et al., as previous work has shown that reflexive f_o responses increase with age (H. Liu, N. M. Russo, et al., 2010; P. Liu et al., 2011). Finally, individuals with HVDs were significantly more likely to display atypical adaptive vocal learning compared to individuals without HVDs (Abur, Subaciute, Kapsner-Smith, et al., 2021). Atypical adaptive learning included both following responses, in which the speaker's vocal f_o moved in the same direction as the perturbation, thus exacerbating the perceived error, and unusually large compensatory responses, in which the speaker's change in vocal f_o opposed the perturbation to a greater degree than is typical, overcorrecting for the perturbation. Notably, individuals who demonstrated atypical adaptive vocal learning in response to f_o perturbations also had worse vocal f_o discrimination. This result suggests impaired auditory discrimination and atypical adaptive vocal learning could share a mechanistic relationship in HVDs, despite evidence that auditory discrimination ability and adaptive vocal learning for f_o are not related in typical speakers (Lester-Smith et al., 2020). In summary, findings from Abur, Subaciute, Kapsner-Smith, et al. (2021) provide strong evidence for impaired auditory-motor function for at least one dimension of voice (f_o) in a subset of speakers with HVDs.

Although recent studies have demonstrated poor vocal f_o discrimination and atypical adaptive vocal learning in a subset of people with HVDs, individuals with HVDs also display atypical voice use patterns related to other parameters, such as voice quality (Kumar, Bhat, & Prasad, 2010; Mahalingam, Boominathan, Arunachalam, Venkatesh, & Srinivas, 2021; Van Stan et al., 2021) and intensity, perceived as loudness (Toles, Ortiz, et al., 2021; Van Stan et al., 2021). The most salient atypical vocal characteristics of many patients with HVDs relate to voice quality. It is possible to alter speech signals acoustically to approximate changes in voice quality. However, voice quality is a multi-dimensional percept, with many degrees of freedom in its production among the respiratory, phonatory, and resonatory systems. Because of this, responses to voice quality perturbations likely would not vary along a predictable acoustic axis, rendering voice quality adaptation experiments impractical if not impossible. On the other hand, f_o and intensity vary along a unidimensional acoustic axis that is easily measured in auditory feedback perturbation experiments. Furthermore, perception and control of vocal f_o and intensity have substantial ecological validity in dealing with environmental influences (see Figure 3-1) such as speaking over background noise, in addition to being implicated in HVDs.

There is mixed evidence regarding whether different vocal parameters (e.g., f_o and intensity) share underlying control mechanisms. In one study, perturbation of f_o during connected speech elicited adaptation in both f_o and intensity, suggesting these parameters may be controlled in an integrated manner (R. Patel, Niziolek, Reilly, & Guenther, 2011). However, the reverse was not found with perturbations of intensity in a separate study (R. Patel, Reilly, Archibald, Cai, & Guenther, 2015). A more recent study employed methods to isolate adaptive responses and to account for the physiological coupling of f_o and intensity and found a strong relationship between f_o and intensity adaptation during production of emphasized words, suggesting these prosodic

cues are controlled in a coordinated manner (Dahl, Cádiz, Zuk, Guenther, & Stepp, 2024). To date, there have been no other studies examining auditory-motor control of multiple vocal parameters in people with typical voices, or the specificity of impairments related to vocal parameters in patient populations, such as individuals with HVDs. For these reasons, this investigation focused on the vocal parameters f_0 and intensity.

3.2.2 Laryngeal stabilization during adaptive vocal learning in people with and without hyperfunctional voice disorders

Although recent studies have demonstrated poor vocal f_0 discrimination and atypical adaptive vocal learning in a subset of people with HVDs, a direct relationship between impaired auditory-motor function and the dysregulated muscle activation during voicing that is thought to be characteristic of HVDs has not been identified. Clinical descriptions of dysregulated muscle activation in HVDs include co-contraction of agonist and antagonist laryngeal and perilaryngeal muscles, which is thought to increase tension and vocal effort (Morrison & Rammage, 1993). Specifically, elevated activity in extrinsic laryngeal musculature often is reported clinically, and typically is measured subjectively via neck palpation by clinicians (Khoddami, Ansari, & Jalaie, 2015). However, to date, rigorous studies using surface electromyography (sEMG) have failed to confirm group differences in the amount of perilaryngeal muscle activation between people with HVDs and without HVDs (e.g., Khoddami, Talebian, Izadi, & Ansari, 2017; Stepp et al., 2011; Van Houtte, Claeys, D'haeseleer, Wuyts, & Van Lierde, 2013).

Interestingly, increased co-contraction of suprahyoid and infrahyoid extrinsic laryngeal musculature (measured using sEMG) has been observed in speakers with typical voices when purposefully increasing vocal effort (Groll, McKenna, Hablani, & Stepp, 2020; McKenna, Diaz-Cadiz, Shembel, Enos, & Stepp, 2018). Co-contraction of opposing (agonist/antagonist) muscles

provides mechanical stabilization for movements in the context of errors or external disturbances, referred to as impedance control (Franklin, Osu, Burdet, Kawato, & Milner, 2003). Such co-contraction has been documented in response to both physical and visuospatial perturbations of limb movements (Franklin et al., 2008; Huang & Ahmed, 2014). Adaptation to predictable perturbations may be achieved in limb movements through a combination of impedance control and sensorimotor mapping of the altered movement dynamics. This co-contraction has been observed to decrease as adaptive learning progresses in individuals without sensorimotor impairment, and therefore has been proposed to reflect a stabilization process early in learning when sensory feedback errors are large (Franklin et al., 2003; Franklin, So, Kawato, & Milner, 2004). In the speech domain, impedance control has been implicated in a study of adaptation to a lateral jaw perturbation affecting somatosensory, but not auditory feedback, with some important differences compared to the limb literature (Nasir & Ostry, 2006). Crucially, participants adapted to the perturbation but did not show after-effects when the perturbation was removed, which would be expected if adaptation occurred due to sensorimotor remapping. Participants also performed equally well when the direction of the perturbation was unexpectedly reversed after training. Furthermore, jaw impedance increased with learning, rather than decreasing, and those with greater impedance at the end of the experiment showed greater adaptation, suggesting participants were achieving adaptation by increasing impedance. Impedance has not been studied in sensorimotor control of the voice. Some studies of f_0 adaptation have found evidence of after-effects (e.g., Behroozmand & Sangtian, 2018; Jones & Munhall, 2000), whereas others have found limited or no after-effects, particularly in non-singers and speakers of non-tonal languages (e.g., Alemi et al., 2020; Jones & Keough, 2008). In a mega-analysis of f_0 adaptation experiments, evidence for adaptation was found across studies of

young adults (Miller et al., 2023). The variability in methods and findings across studies suggests that remapping occurs quickly such that after-effects are difficult to detect. It is also possible that mechanisms in addition to sensorimotor remapping play a role in f_o changes in response to auditory feedback perturbation, leading to variability. It is unclear whether impedance control is relevant in the context of voicing, as there typically is no interaction between the laryngeal system and the external environment. However, aspects of laryngeal dynamics, such as changes in laryngeal height, could be altered via co-contraction of opposing perilaryngeal musculature.

Although differences in sensorimotor control and learning exist between speech and limb effector systems (e.g., Lametti et al., 2020), theoretical models of learning in these systems rely on similar principles (e.g., Tourville & Guenther, 2011; Wolpert, Diedrichsen, & Flanagan, 2011), often leading to similar empirical results (e.g., Goodbody & Wolpert, 1999; Houde & Jordan, 1998). In the laryngeal system, suprahyoid and infrahyoid musculature can elevate or depress the larynx, respectively, when activated independently (Titze, 1994). In addition to altering effective vocal tract length, these actions also indirectly alter the length and tension of the vocal folds, thereby changing f_o (Kakita & Hiki, 1976; Maeda, 1976; Sokolowsky, 1943; Sonninen, 1968). Indeed, there is evidence that laryngeal elevation typically accompanies the production of vowels with high f_o and voiceless consonants (Ewan & Krones, 1974; Hudgins & Stetson, 1935; Kakita & Hiki, 1972; Ohala, 1973; Perkell, 1969), possibly to facilitate increased vocal fold tension either to raise f_o or to inhibit phonation entirely (Stevens, 1977). However, when suprahyoid and infrahyoid muscles are co-contracted, their opposing actions would neither elevate nor depress the larynx but rather stabilize its vertical position. Thus, it is possible that co-contraction of extrinsic laryngeal muscles could provide mechanical stabilization of the larynx, for example in response to auditory feedback perturbation. This may be particularly relevant for

responses to perturbations of f_o, for which laryngeal elevation may be an important control parameter. It is possible that mechanical stabilization of the larynx and sensorimotor remapping could interact to achieve adaptation, as has been observed in limb studies, with increased co-contraction in early trials during auditory perturbation that decreases as sensorimotor remapping progresses. Alternatively, laryngeal stabilization could be a primary driver of adaptation, reflected in increasing co-contraction as adaptation progresses. Whether laryngeal stabilization occurs and its potential role in adaptive vocal learning has yet to be studied.

3.2.3 Purpose of the Study

3.2.3.1 Research question 1

Several studies of vocal sensorimotor control and learning support the presence of auditory-motor impairment in a subset of individuals with HVDs (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017; Ziethe et al., 2019). Taken together, these studies suggest that some people with HVDs have atypical adaptive vocal learning in the absence of impaired reflexive vocal control. These impairments may be either a cause or a result of having the disorder. However, to date these studies have focused exclusively on production of vocal f_o. Determining the extent of auditory-motor impairment in this population is necessary for understanding the pathophysiology of HVDs. This motivates the first research question addressed in this investigation:

1. Is atypical adaptive vocal learning in individuals with HVDs specific to production of vocal f_o, or does it occur in response to perturbation of other vocal parameters, such as intensity?

We hypothesized that more people with HVDs would exhibit atypical adaptive vocal learning (i.e., different in extent or direction of vocal response) for both f_o and intensity compared to

people with typical voices. Understanding the specificity of auditory-motor impairment in this population will facilitate identification of potential targets for future treatment research.

3.2.3.2 Research question 2

Based on previous findings in limb and articulatory sensorimotor control (Franklin et al., 2008; Huang & Ahmed, 2014; Nasir & Ostry, 2006), we hypothesized that co-contraction of extrinsic laryngeal muscles may occur as a laryngeal stabilization response in both people with and without HVDs in response to large sensory errors. Consistent with patterns observed repeatedly in limb adaptive learning, we hypothesized that co-contraction would increase early in adaptive vocal learning, and decrease as adaptive vocal learning progresses. Although it is possible that all individuals may show similar co-contraction responses to large sensory errors early in adaptive vocal learning, studies of limb sensorimotor control suggest that poor sensory discrimination reduces adaptive learning (He et al., 2016). Given prior findings of poor vocal f_o discrimination and atypical adaptive vocal learning in some people with HVDs (Abur, Subaciute, Kapsner-Smith, et al., 2021), it is also possible that these auditory-motor impairments could interact with the hypothesized laryngeal stabilization response during adaptive vocal learning, thus eliciting atypical vocal motor behavior that is similar to clinical descriptions of dysregulated muscle activation in HVDs. Thus, the second research question addressed in this investigation was:

> 2. Does co-contraction of extrinsic laryngeal muscles occur in response to auditory feedback perturbation? Is there any difference between individuals with and without HVDs in the presence, extent, or timing of co-contraction of extrinsic laryngeal muscles in response to auditory feedback perturbation during adaptive vocal learning?

Perilaryngeal muscle activation was measured during adaptive vocal learning tasks. We hypothesized that co-contraction of extrinsic laryngeal muscles would increase in response to

auditory feedback perturbation, and decrease late in adaptation. We also hypothesized that this effect would be stronger in response to f_o perturbation than intensity perturbation due to the relationship between laryngeal height and vocal f_o. If co-contraction occurs as a laryngeal stabilization response, it has implications for models of sensorimotor control of speech as an additional error reduction mechanism that is not represented in current theoretical or computational models. We also hypothesized that people with HVDs would exhibit larger co-contraction that persisted for more trials compared to controls, in the context of atypical adaptive vocal learning. This would suggest a mechanistic connection between known auditory-motor impairment in HVDs and dysregulated muscle activation. Alternatively, because limb studies show more co-contraction when sensory errors are large (Franklin et al., 2003; Franklin et al., 2004), and people with HVDs may perceive perturbations as smaller due to worse auditory discrimination (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022), it is possible that people with HVDs may demonstrate less co-contraction, which would not support a clear link with clinical features of HVDs.

3.2.3.3 Research question 3

Studies of auditory discrimination in people with HVDs using tones (Nguyen et al., 2022) and voice stimuli (Abur, Subaciute, Kapsner-Smith, et al., 2021) provide evidence that these individuals have worse f_o discrimination than people with typical voices. This impairment may be either a cause or a result of having the disorder. However, to date, these studies have focused exclusively on f_o perception. Determining the extent of auditory-perceptual impairment in this population is crucial to understanding the pathophysiology of HVDs. This motivates the third research question addressed in this investigation.

3. Is impaired auditory discrimination in individuals with HVDs specific to perception of vocal f_o, or does it impact perception of other vocal parameters, such as intensity?

Based on the results of prior studies of f_o discrimination (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022), and the presence of atypical voice use patterns across multiple acoustic parameters including intensity (Toles, Ortiz, et al., 2021; Van Stan et al., 2021), we hypothesized that people with HVDs would demonstrate worse auditory discrimination of both f_o and intensity compared to people with typical voices.

3.2.3.4 Research question 4

In a prior study, individuals with HVDs who displayed atypical adaptive vocal learning in response to f_o feedback perturbations had worse auditory discrimination for vocal f_o (Abur, Subaciute, Kapsner-Smith, et al., 2021). In studies of limb sensorimotor control, worse sensory discrimination was associated with decreased adaptive learning (He et al., 2016). Because the hypothesized laryngeal stabilization response examined in question 2 was expected to be driven by auditory feedback errors during adaptive vocal learning, we hypothesized that auditory discrimination and perilaryngeal co-contraction would also be related. Therefore, it was important to examine relationships between auditory discrimination measured in question 3 and the variables measured in questions 1 and 2, adaptive vocal learning and perilaryngeal co-contraction. These hypothesized relationships motivated the fourth research question addressed in this investigation:

4. What are the relationships between auditory discrimination and adaptive vocal learning, and between auditory discrimination and perilaryngeal co-contraction during adaptation?

To address this question, relationships were examined among the variables from questions 1, 2, and 3 of this investigation. Specifically, the relationships between auditory discrimination and adaptive vocal learning, and auditory discrimination and perilaryngeal co-contraction were measured. Based on prior findings for f_o (Abur, Subaciute, Kapsner-Smith, et al., 2021), we hypothesized that poor auditory discrimination for both f_o and intensity would be associated with atypical adaptive vocal learning. Furthermore, we hypothesized that poor auditory discrimination would be associated with increases in perilaryngeal muscle co-contraction that were larger and persisted for more trials during adaptation. Although poor discrimination should theoretically cause less sensitivity to sensory errors, this relationship was hypothesized to be driven by atypical adaptive responses to sensory error in people with HVDs. Specifically, in limb literature co-contraction has been observed to decrease as adaptation progresses (Franklin et al., 2003). In people who demonstrate atypical adaptive responses, we hypothesized that co-contraction would persist for longer because of impaired adaptation behavior. Alternatively, it is possible that people with worse discrimination would demonstrate smaller increases in co-contraction due to reduced sensitivity to auditory errors.

3.3 METHODS

All procedures were approved by the University of Washington Institutional Review Board.

3.3.1 Participants

Twenty-six individuals with HVDs and 26 participants with typical voices were matched pairwise for relevant variables including age (+/- 5 years), voice f_o range (typically masculine vs. typically feminine), and singing experience. Participant characteristics are included in Table 3-1. The participant age range was limited to 18 – 65 years to eliminate two potential confounding factors: 1) ongoing auditory-motor and laryngeal development in pediatric speakers (Kent, 1976;

N. Scheerer et al., 2016) and 2) compensation for glottal insufficiency (Belafsky et al., 2002) in presbyphonia. Both participant groups included more individuals who were assigned female at birth. HVDs are more prevalent in female speakers, justifying skewed enrollment with respect to sex (Roy et al., 2005). Because auditory-motor impairment has been observed in both phonotraumatic (e.g., benign vocal fold lesions) and non-phonotraumatic (e.g., primary muscle tension dysphonia) HVDs (Abur, Subaciute, Kapsner-Smith, et al., 2021), both types of diagnoses were included in a single group. For the purposes of this study, musicians were defined as individuals with musical training beyond secondary school. Non-singer musicians were excluded due to confounding effects on f_o perception (Micheyl et al., 2006). An exception was made to include singers due to the high prevalence of HVDs in this population (Pestana et al., 2017). Singer was defined as an individual with post-secondary singing training and/or performing experience. Speakers of tonal languages were excluded due to confounding effects on responses to auditory feedback perturbations and f_o discrimination thresholds (Giuliano, Pfordresher, Stanley, Narayana, & Wicha, 2011; H. Liu, E. Q. Wang, et al., 2010). To be included in this study, participants taking hormone treatments that affected vocal f_o reported no changes in hormone treatment for at least 12 months (n = 2 control participants, n = 2 participants with HVDs).

Table 3-1. Participant characteristics.

Group	Age	Sex assigned at birth	Gender	Singers
Control	M = 39.35 (22 – 65, SD = 14.09)	21 AFAB, 5 AMAB	19 cis women, 4 cis men, 2 non-binary, 1 trans man	13 singers, 13 non-singers
HVD	M = 39.42 (20 – 64, SD = 12.68)	21 AFAB, 5 AMAB	18 cis women, 5 cis men, 2 non-binary, 1 trans man	13 singers, 13 non-singers

AFAB = assigned female at birth; AMAB = assigned male at birth

Table 3-2. Diagnoses in the hyperfunctional voice disorder (HVD) group (n = 26).

Diagnosis	Number of Participants
Primary muscle tension dysphonia	13
Bilateral benign vocal fold lesions and vocal hyperfunction	9
Unilateral benign vocal fold lesion and vocal hyperfunction	2
Bilateral vocal fold edema and vocal hyperfunction	1
Unilateral sulcus vocalis status post excision of benign vocal fold lesion and vocal hyperfunction	1

Participants with HVDs were recruited from the University of Washington Speech and Hearing Clinic in the Department of Speech and Hearing Sciences and the Laryngology Clinic at the University of Washington Medical Center. Participants with HVDs had a confirmed diagnosis of an HVD, with or without phonotrauma (e.g., benign vocal fold lesions, muscle tension dysphonia), provided by a board certified otolaryngologist. Individuals with voice diagnoses related to neoplasm, neurological conditions, and/or presbyphonia were excluded. Voice diagnoses of the participants in the HVD group are included in Table 3-2. Control participants reported no history of voice disorder and completed an auditory-perceptual and vocal health history screening by the investigator, an experienced speech-language pathologist (MKS). All participants reported no other known neurological, cognitive, speech, language, or hearing disorder. Participants were screened to ensure typical hearing (pure tone air conduction at octave frequencies: 125–8000 Hz, pass criterion of 25 dB HL at all frequencies <50 years of age (ASHA, 2018), or 25 dB HL at 125–1000 Hz and 40 dB HL at 2000–8000 Hz age 50+ (Schow, 1991). Overall severity of dysphonia (OS) was rated on a visual analog scale (0 – 100, where 0 = typical voice for age/gender/culture; 100 = severe) by an experienced speech-language pathologist who was blinded to group assignment. The mean OS rating for control participants

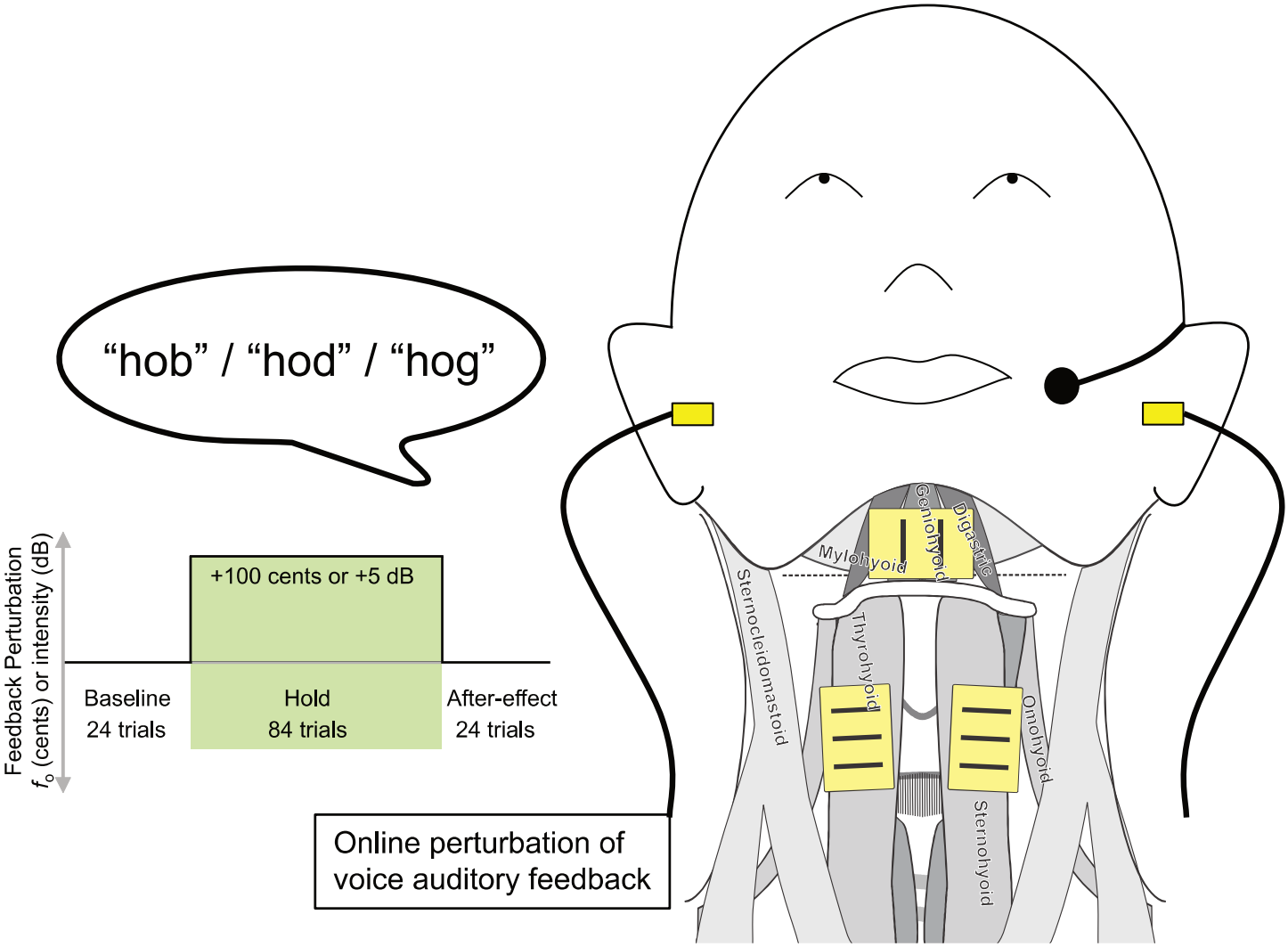
was 4.0 (SD = 3.1, range = 0.6 – 10.5). The mean OS rating for participants with HVDs was 7.7 (SD = 8.7, range = 0.9 – 35). Intrarater reliability was tested by randomly repeating 20% of samples, and was good (r = .87).

3.3.2 Experimental Setup

Participants sat in a sound-attenuated booth in front of a computer monitor used to display stimulus utterances. Voice signals were captured with an omni-directional ear-set microphone (Shure MX153), 7 cm from center of mouth, at a 45-degree angle. Microphone signals were amplified using an RME Quadmic II Microphone Preamplifier. Microphone and headphone signals were digitally recorded using an RME Fireface UCX Audio Interface at 44.1 kHz and 16 bits. Microphone intensity was calibrated based on a monotone electrolarynx (TruTone, Griffin Labs) tone recorded during the experiment. Sound pressure level of the reference tone (Bruel and Kjaer Type 2250 SLM) was recorded to enable calibration of recordings to SPL in post processing as needed. Auditory feedback manipulations were generated using custom MATLAB (MathWorks, 2021) scripts to control an Eventide Eclipse V4 Harmonizer. The processing delay for near real-time auditory feedback between speech data acquisition and playback was <35 ms, less than the 100 ms cut-off at which delays alter adaptive f_o responses (Weerathunge et al., 2020). Stimuli were amplified with a Xenyx Q802USB amplifier and presented to the participant through Etymotic ER-2 insert earphones, which provided approximately 30 dB of attenuation of air-conducted sound. Earphone levels were calibrated using a 1 kHz tone (SLM attached to a 2-cc insert earphone coupler).

During auditory feedback experiments, perilaryngeal muscle activation was measured using the same methodology and set-up as previous work that demonstrated sensitivity to modulations in vocal effort (McKenna et al., 2018). Three Delsys Bagnoli differential sEMG sensors were placed on the anterior neck to measure suprahyoid and infrahyoid extrinsic laryngeal muscle activation (see Figure 3-2). Unlike intramuscular EMG, sEMG is non-invasive, can be calibrated, and detects signals from a large, more representative number of motor units (Stepp, 2012).

Figure 3-2. Adaptive vocal learning and perilaryngeal muscle activation setup and task structure.



Extrinsic laryngeal muscles were of specific interest as they are frequently implicated in increased muscle tension in HVDs (Angsuwarangsee & Morrison, 2002; Oates & Winkworth, 2008), and are likely to be involved in laryngeal stabilization (Groll et al., 2020). Differential electrodes reduce noise by excluding signals that are common across all electrodes (Rutkove, 2007).

The skin surface was abraded and exfoliated to improve electrode contact and reduce noise and artifacts (Stepp, 2012). Sensor placement was determined via palpation by the investigator. One single-differential sensor was placed in the submandibular region at midline, posterior to the mandible, to capture bilateral suprahyoid muscle activation (mylohyoid, geniohyoid, anterior belly of digastric). A single midline sensor was used to intentionally sample a larger, bilateral volume that comprises multiple muscles involved in laryngeal elevation (McKenna et al., 2018; Stepp, 2012). Two double-differential sensors were placed approximately 1 cm on either side of the thyroid prominence, to capture activation of the left and right infrahyoid muscles (thyrohyoids, omohyoids, sternohyoids) while avoiding activity from the sternocleidomastoids (McKenna et al., 2018; Stepp, 2012). Double-differential sensors enhance spatial selectivity compared to single-differential sensors (Merletti & Hermens, 2004). Finally, a ground electrode was placed on the forehead, and was subtracted from the experimental signals to account for environmental noise and extraneous physiological signals such as heartbeat. After sensor placement, participants completed a series of maximum voluntary contraction maneuvers engaging the target muscles (McKenna et al., 2018), which were used to confirm sensor placement. sEMG signals were captured using custom MATLAB (MathWorks, 2021) scripts and digitally recorded using an RME Fireface UCX Audio Interface at 44.1 kHz and 16 bits.

3.3.3 Adaptation task

Participants completed four adaptation blocks (see Figure 3-2): f_o control, f_o shift up (Stepp et al., 2017), intensity control, and intensity shift up (Lane, Catania, & Stevens, 1961). Shift down blocks were not conducted to limit the study to a single recording session, and because shifting intensity down is confounded by bone-conducted sound. During f_o experiments, auditory feedback was amplified by +5 dB relative to the sound level at the microphone to provide masking of conflicting bone-conducted auditory feedback (Weerathunge et al., 2020). During intensity experiments, no amplification occurred during unperturbed trials. The order of f_o and intensity conditions, and of control and shift up blocks, was counterbalanced across participants. Each block consisted of 132 trials, approx. 3.5-s each (8.5 min per block). During each trial, a prompt appeared on the screen for 2 s, during which the participant produced a syllable, followed by a rest period jittered between 1–2 s. The syllables were "hob," "hod," and "hog," with four repetitions of each syllable pseudorandomly distributed in epochs of 12 trials. Each block included 3 phases: baseline (two epochs = 24 trials), adaptation (seven epochs = 84 trials), and after-effect (two epochs = 24 trials). Based on prior studies, it was anticipated that 24 trials in the after-effect phase would permit a complete return to baseline (i.e., washout) after adaptation (Abur, Subaciute, Kapsner-Smith, et al., 2021; Jones & Munhall, 2000; Stepp et al., 2017). Although a gradual introduction of perturbations (i.e., ramp phase) often is used in adaptation experiments, a sudden onset of the full perturbation may also be used (e.g., Kim, Daliri, et al., 2020). Because one purpose of this experiment was to simulate large feedback errors that may elicit co-contraction early in adaptation (see question 2), we did not include a ramp phase. During baseline, after-effect, and all control trials, no perturbations occurred. During adaptation trials, auditory feedback was shifted by +100 cents during the f_o condition, using a whole-

spectrum shift (Abur, Subaciute, Kapsner-Smith, et al., 2021), or by +5 dB during the intensity condition (Lane et al., 1961; Siegel & Pick Jr, 1974). Perturbations were applied for the entire duration of the trial.

3.3.4 Adaptation and co-contraction analyses

Adaptive responses to f_o and intensity feedback perturbation were measured over the 40–120 ms portion of voicing (i.e., the vowel) to isolate the response of the feedforward motor control system during steady-state phonation (Lester-Smith et al., 2020). The f_o responses were analyzed offline by calculating the mean f_o using an autocorrelation method, and intensity responses by calculating mean intensity using a root-mean-square (RMS) method, via *Praat* (Boersma & Weenink, 2016) scripts. Each trial was normalized to the mean of the baseline phase and measured in cents (f_o) or dB (intensity). To account for drift in f_o and intensity over many trials (Jones & Munhall, 2000), each trial during the control blocks was subtracted from the corresponding trial in the shift-up blocks. The mean of the hold phase was used in statistical analyses of adaptation responses (Kapsner-Smith, Abur, Eadie, & Stepp, 2024).

Perilaryngeal muscle activation was measured during the four adaptation blocks: f_o control, f_o shift up, intensity control, and intensity shift up. Raw sEMG signals were zero-meaned and band-pass filtered (25–450 Hz, 3rd order butterworth filter) to remove movement artifacts and high-frequency noise (De Luca, Gilmore, Kuznetsov, & Roy, 2010; Merletti & Hermens, 2004). During each trial, the RMS amplitude was calculated for the window from -200 ms to +120 ms relative to phonation onset for the suprahyoid and left and right infrahyoid sEMG signals. This window was selected based on inspection of recorded signals and on prior studies of laryngeal muscle activation for phonation (Buchthal & Faaborg-Andersen, 1964; Hillel, 2001) to capture speech-related perilaryngeal muscle activation, which predominantly precedes the acoustic

output of phonation, and to include the analysis window that was used to measure adaptive vocal learning responses. This window also excluded activation of suprahyoid muscles related to jaw lowering that occurred prior to production of the speech target in many participants. Left and right infrahyoid signals were averaged to obtain a single infrahyoid measurement (McKenna et al., 2018). The mean RMS of the 24 baseline trials was calculated for suprahyoid and infrahyoid muscles. Each trial was then normalized to the mean of the baseline trials as a ratio measure. For trials during the shift up blocks, the corresponding control trial was then subtracted to account for fatigue or other effects not related to the auditory feedback perturbations, and this was converted to a % change from baseline (suprahyoid change, infrahyoid change). Mean normalized change in activation of the suprahyoids and infrahyoids was calculated for the last epoch of the baseline phase (early baseline), the first epoch of the adaptation phase (early adaptation), the middle epoch of the adaptation phase (middle adaptation), the last epoch of the adaptation phase (late adaptation), and the first epoch of the after-effect phase (early after-effect). These five time points were selected to track changes in muscle activation as adaptation to auditory feedback perturbation progressed.

A co-contraction index (CCI) was adapted from reaching experiments to assess simultaneous activation of the opposing suprahyoid and infrahyoid musculature (Babadi, Vahdat, & Milner, 2021; Gribble, Mullin, Cothros, & Mattar, 2003; Thoroughman & Shadmehr, 1999). For each trial, the minimum of the suprahyoid change and the infrahyoid change was calculated as the CCI (% change from baseline). This measure was designed to capture activation that is matched between the agonist-antagonist pair, also termed “wasted contraction” (Thoroughman & Shadmehr, 1999). This mean CCI was calculated for the five epochs designated above as late baseline, early adaptation, middle adaptation, late adaptation, and early after-effect.

3.3.5 Auditory discrimination task and analysis

Because sensorimotor adaptation can lead to changes in sensory perception (Nasir & Ostry, 2009), auditory discrimination threshold tasks were conducted before the adaptation tasks. The order of f_o and intensity discrimination experiments was counterbalanced across participants. Participants were recorded saying the syllable "hob" extended for approximately 2 s. A steady 500-ms segment was selected from the middle of the vowel using *Praat* software (Boersma & Weenink, 2016). Stimuli were generated from this sample using the Eventide Eclipse V4 Harmonizer and presented in an AXB task (Hautus & Meng, 2002) using a 2-down, 1-up adaptive staircase procedure resulting in a 70.7% threshold estimate (Levitt, 1971). All f_o stimuli and reference intensity stimuli were presented at 75 dB SPL. The target stimulus (X) was identical to the first (A) or last (B) stimulus (500-ms ISI). The listener judged whether X was the same as A or B in terms of pitch (f_o) or loudness (intensity). Consistent with prior work in this population, the f_o interval between A and B on the first trial was +50 cents (Abur, Subaciute, Kapsner-Smith, et al., 2021). The step size was 20 cents until two reversals occurred, then 10 cents until two additional reversals occurred, then 4 cents until six additional reversals occurred. Intensity followed the same pattern with an initial interval of +6 dB, and large, medium, and small step sizes of 1.4, 0.8, and 0.2 dB, respectively (Marvit, Florentine, & Buus, 2003; Sinnott & Aslin, 1985). The participant's just noticeable difference (JND) score was the mean of the intervals in the last six reversals in cents (f_o) or dB (intensity; Garcıa-Pérez, 1998).

3.3.6 Statistical analyses

Statistical analyses were conducted using SPSS Statistics, Version 26 (IBM, 2019). In question 1, we hypothesized that more people with HVDs would exhibit atypical adaptive vocal learning (i.e., different in extent or direction of change in f_o or intensity) compared to controls, reflecting a

subset of this population with auditory-motor impairment. Because atypical adaptive vocal learning responses can occur in a direction that either opposes or follows the feedback perturbation, a non-parametric test was planned (Abur, Subaciute, Kapsner-Smith, et al., 2021). However, because a group mean effect was apparent when inspecting the distributions of the data for intensity adaptation, a univariate ANOVA was used instead to examine the effects of HVD status (control vs. HVD) and singing experience on intensity adaption responses. For f_o adaptation, post hoc visual inspection of the distributions of the data revealed greater variability in the HVD group, similar to Abur, Subaciute, Kapsner-Smith, et al. (2021), except with an apparent positive skew (i.e., more large following responses). This is consistent with findings from Stepp et al. (2017) of significantly more following during f_o adaptation in people with HVDs than people with typical voices. Therefore, the following non-parametric analysis was conducted for f_o adaptation responses: the 90th and 10th percentiles were calculated for the control group and used to categorize responses into typical ($\leq$90th and $\geq$10th percentiles) vs. atypical (>90th or <10th percentile) adaptation. A chi-square test was used to determine whether atypical (>90th percentile) following responses were more frequent in one of the groups (HVD vs. control). To account for the possibility that any group effects were driven by dysphonia rather than differences in auditory-motor integration, simple linear regressions were run to examine the effect of OS on f_o and intensity adaptation responses.

In question 2, we hypothesized that all participants would exhibit increased co-contraction of perilaryngeal musculature early in adaptive vocal learning compared to late baseline and to late adaptation (i.e., main effect of time). We expected this effect to be larger for f_o than for intensity (i.e., main effect of parameter). Additionally, we expected that people with HVDs would exhibit co-contraction that was larger and persisted for more trials compared to controls (interaction

effect of between-subjects variable of group and within-subjects variable of time). To test these hypotheses regarding perilaryngeal muscle activation, a repeated measures general linear model (function GLM) was conducted, with HVD status (+/-) as a between-subjects factor and parameter (intensity, f_o) and epoch (late baseline, early adaptation, middle adaptation, late adaptation, early after-effect) as within-subjects factors, for the dependent variable co-contraction index.

As a post hoc analysis, to assess whether changes in perilaryngeal muscle activation during demanding/tedious speech tasks differed between people with and without HVDs, three repeated measures GLMs were conducted to assess the effects of the factors HVD status, parameter, and epoch on measures collected during the control (no perturbation) conditions. As this was an exploratory analysis, it was conducted for all three sEMG measures: changes in suprahyoid activation, infrahyoid activation, and CCI.

In question 3, we hypothesized that people with HVDs would demonstrate worse auditory discrimination (higher JNDs) of both vocal f_o and intensity than controls, resulting in atypically large JNDs. Because musical training is known to improve auditory discrimination (e.g., Micheyl et al., 2006), singing experience was also included in statistical models. Two univariate ANOVAs were conducted with the between subjects variables HVD status (HVD, control) and singing experience (singer, non-singer), for the parameters f_o and intensity.

To address question 4, analyses of relationships among auditory discrimination, adaptive vocal learning, and perilaryngeal co-contraction were conducted. We hypothesized that poor discrimination of vocal f_o and intensity would be associated with atypical adaptive vocal learning and with perilaryngeal muscle co-contraction that was larger and persisted for more trials during adaptation. Originally, to test the relationship between auditory discrimination and adaptive

vocal learning, two logistic regressions (f_o, intensity) were planned with JND as the predictor variable and typical vs. atypical adaptation as the outcome variable. However, because a parametric analysis was used for intensity adaptation, logistic regression was only performed for the f_o parameter. A simple linear regression was performed instead for the intensity parameter, with intensity JND as the predictor variable and intensity adaptation as the outcome variable. To test the relationship between auditory discrimination and the magnitude and persistence of co-contraction, four *a priori* simple linear regressions were conducted with JND (f_o, intensity) as the predictor variable and CCI during adaptation (early, late) as the outcome variable.

As a post hoc analysis to further explain the nature of the relationships among auditory discrimination, adaptation, and co-contraction for the parameter f_o, a correlation matrix was calculated between f_o JND, f_o adaptation responses, and CCI at all time points during the f_o adaptation experiment. A mediation model was tested with CCI during early adaptation as a mediator of the relationship between JND and adaptation response by comparing a multiple linear regression with JND and CCI as predictors of adaptation to a simple linear regression with JND as a predictor of adaptation (Baron & Kenny, 1986). Significance of the mediation effect was tested with the function mediate in the R package 'mediation' and a bootstrapping test for significance with 1000 simulations (Tingley, Yamamoto, Hirose, Keele, & Imai, 2014).

3.4 RESULTS

3.4.1 Adaptation

The mean of the hold phase was calculated as an adaptation response and used for statistical analyses. Control participants had a mean intensity adaptation response of -0.86 dB (SD = 1.62) and a mean f_o adaptation response of -52 cents (SD = 74). HVD participants had a mean intensity adaptation response of -1.76 dB (SD = 1.73) and a mean f_o adaptation response of -25 cents (SD = 89). Baseline- and control-normalized time series data for intensity and f_o shift conditions are presented in Figures 3-3 and 3-4. Results of the univariate ANOVA testing the effects of group and singing experience on intensity adaptation are provided in Table 3-3. The main effect of

Figure 3-3. Group time series data for intensity adaptation (mean and 95% CIs).

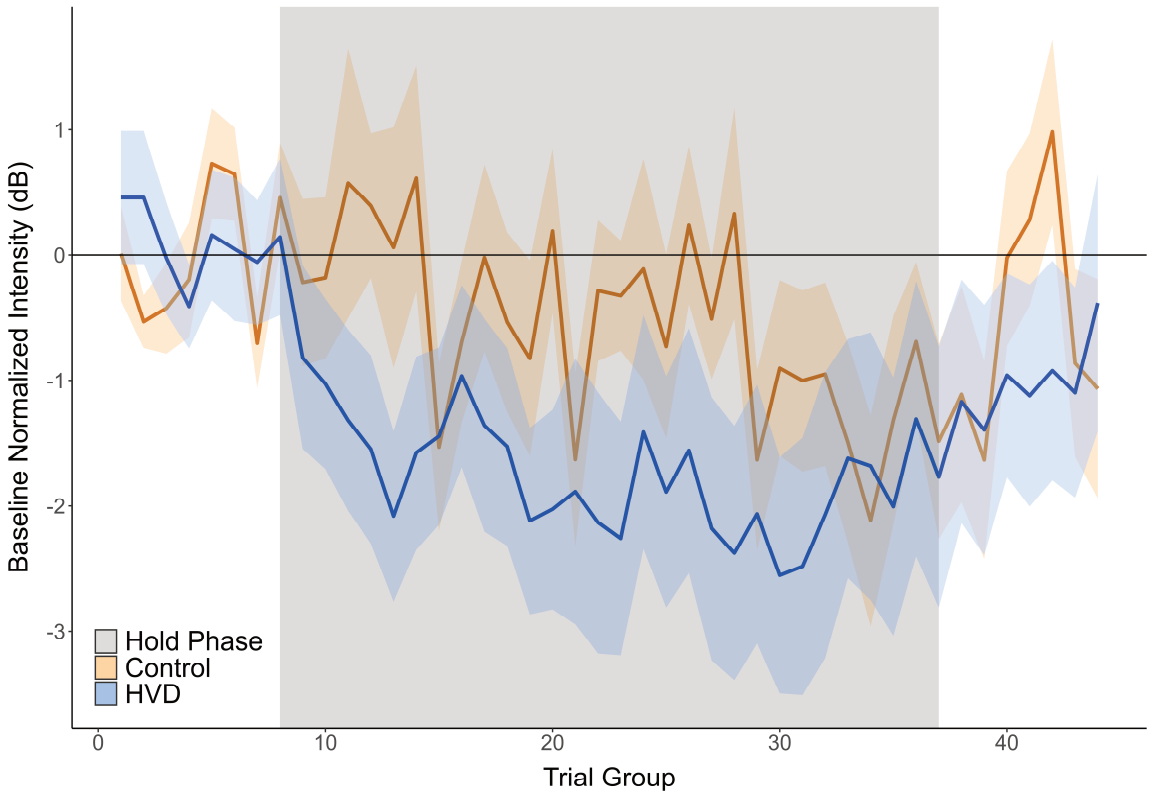
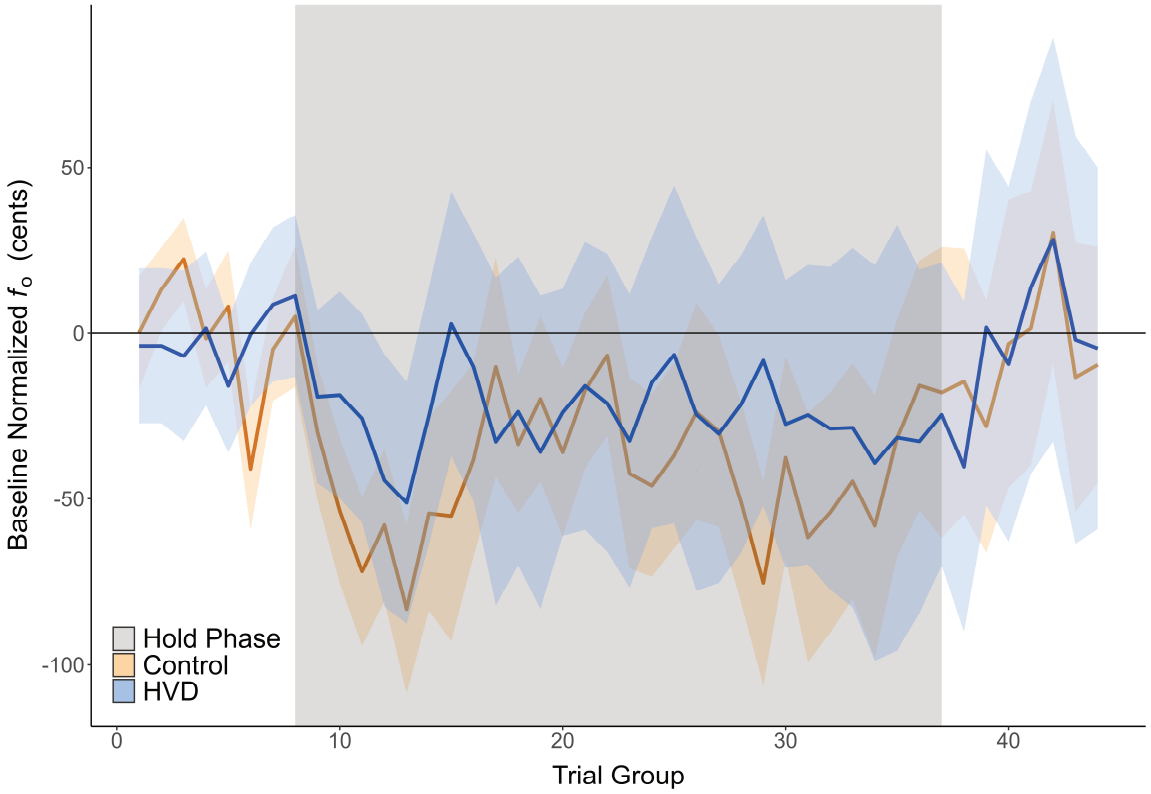


Figure 3-4. Group time series data for f_o adaptation (mean and 95% CIs).



HVD status on intensity adaptation responses was close to significance (p = .050) with a medium effect size: participants with HVDs tended toward larger (more negative) intensity adaptation responses than control participants. There was a significant main effect of singing experience (p = .018) with a medium effect size: singers had significantly smaller (less negative) intensity adaptation responses than non-singers. There was no significant interaction.

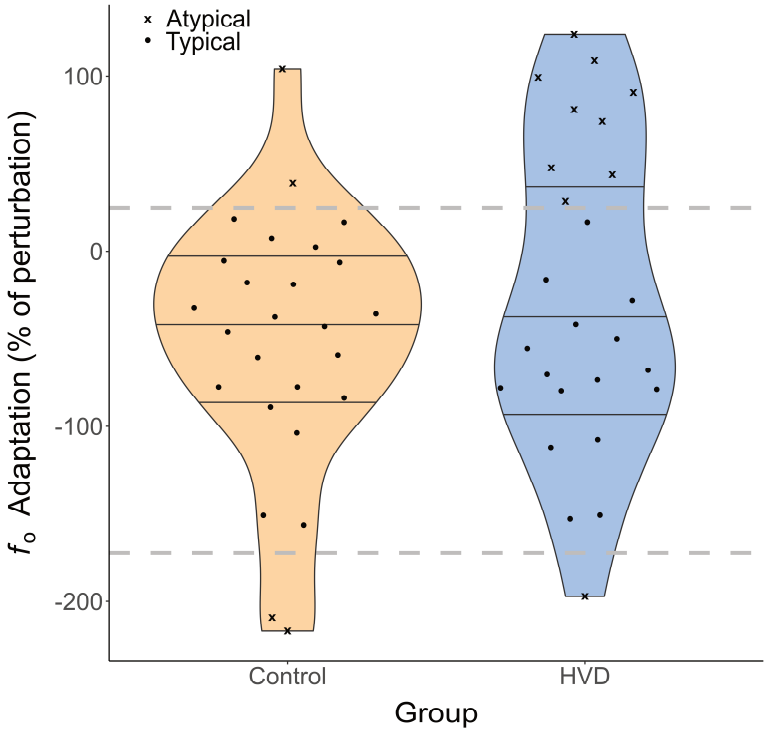
Table 3-3. Univariate ANOVA for intensity adaptation.

Effect	***df***	η_p^2	***F***	***p***
HVD status (control, HVD)	1	.08	4.06	.050
Singing experience (singer, non-singer)	1	.11	5.99	.018*
HVD status * Singing experience	1	.01	0.37	.546

*Significant at $p < .05$

Results of the categorical analysis of f_o adaptation are shown in Figure 3-5. For f_o adaptation, 4/26 control participants and 10/26 HVD participants were categorized as atypical. For following responses (>90th percentile), 2/26 control participants and 9/26 HVD participants were categorized as atypical. A chi-square test for atypical following responses was significant with a medium effect size (χ^2 = 5.65, p = .017, w = 0.33): significantly more people with HVDs demonstrated atypical following responses than controls. Of the participants with HVDs who demonstrated atypical following responses, 5 (56%) had NPVH and 4 (44%) had PVH. OS ratings were not significantly related to intensity adaptation responses (F = 1.56, p = .218, R^2 = .01) or f_o adaptation responses (F = 0.80, p = .376, R^2 = .02).

Figure 3-5. Categorical analysis of f_o adaptation.



3.4.2 Extrinsic laryngeal muscle activation during adaptive vocal learning

sEMG measures taken during intensity and f_o adaptation experiments are shown in Figure 3-6. One participant in the HVD group did not have usable sEMG data due to poor electrode contact

caused by facial hair, resulting in electrical noise contamination. Data for that participant and their matched control were excluded, resulting in a sample of $n = 50$ participants for sEMG measures. The CCI was used for statistical analyses, however the constituent measures of changes in suprahyoid and infrahyoid activation are also shown for descriptive purposes.

The results of the repeated measures GLM are given in Table 3-4. There were no significant main effects and no significant interactions. Qualitatively, the trends for intensity and f_o appear different (i.e., main effect of parameter), with a tendency for the change in CCI to be lower during intensity adaptation and higher during f_o adaptation, however the difference was not significant ($p = .110$).

Table 3-4. Results of a repeated measures GLM testing effects on the co-contraction index (CCI) during adaptation experiments.

Effect	***df***	η_p^2	***F***	***p***
Epoch	4	.10	1.26	.300
Parameter	1	.05	2.66	.110
HVD status (control, HVD)	1	<.01	.06	.815

*Significant at $p < .05$

Table 3-5. Results of a repeated measures GLM testing effects on changes in suprahyoid activation during adaptation control conditions (no perturbations).

Effect	***df***	η_p^2	***F***	***p***
Epoch	4	.12	6.69	<.001*
Parameter	1	.01	.63	.431
HVD status (control, HVD)	1	.07	3.63	.063

*Significant at $p < .05$

Data from exploratory analyses of sEMG measures during adaptation control conditions are shown in Figure 3-7. There were no significant effects for changes in infrahyoid activation or

CCI. However, there was a significant main effect of epoch on changes in suprahyoid activation ($p < .001$) with a medium effect size (see Table 3-5). See Table 3-6 for post hoc pairwise comparisons of epochs. Suprahyoid activation was significantly higher at the fourth epoch (late adaptation) and remained high at the fifth epoch (early after-effects; NB there were no auditory feedback perturbations during this task). There was also a trend for greater increases overall in

Table 3-6. Post hoc pairwise comparisons of change in suprahyoid activation during control conditions at each epoch.

Epoch		Mean Difference	Std. Error	p^b	95% Confidence Interval[b] Lower Bound	Upper Bound
1	2	0.00	0.01	>.999	-0.03	0.04
	3	-0.04	0.02	.413	-0.10	0.02
	4	-.071*	0.02	.007	-0.13	-0.01
	5	-0.06	0.02	.056	-0.13	0.00
2	1	0.00	0.01	>.999	-0.04	0.03
	3	-0.04	0.02	.147	-0.09	0.01
	4	-.073*	0.02	.002	-0.13	-0.02
	5	-0.06	0.02	.057	-0.13	0.00
3	1	0.04	0.02	.413	-0.02	0.10
	2	0.04	0.02	.147	-0.01	0.09
	4	-0.03	0.02	.994	-0.08	0.02
	5	-0.02	0.02	>.999	-0.08	0.04
4	1	.071*	0.02	.007	0.01	0.13
	2	.073*	0.02	.002	0.02	0.13
	3	0.03	0.02	.994	-0.02	0.08
	5	0.01	0.02	>.999	-0.04	0.05
5	1	0.06	0.02	.056	0.00	0.13
	2	0.06	0.02	.057	0.00	0.13
	3	0.02	0.02	>.999	-0.04	0.08
	4	-0.01	0.02	>.999	-0.05	0.04

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

suprahyoid activation in participants with HVDs than controls, although it was not statistically significant (p = .063). There was no main effect of parameter, and no significant interactions.

Figure 3-6. Surface electromyography measures from shift conditions, normalized to control conditions; means and 95% CIs. B = baseline, H = hold, AE = after effects.

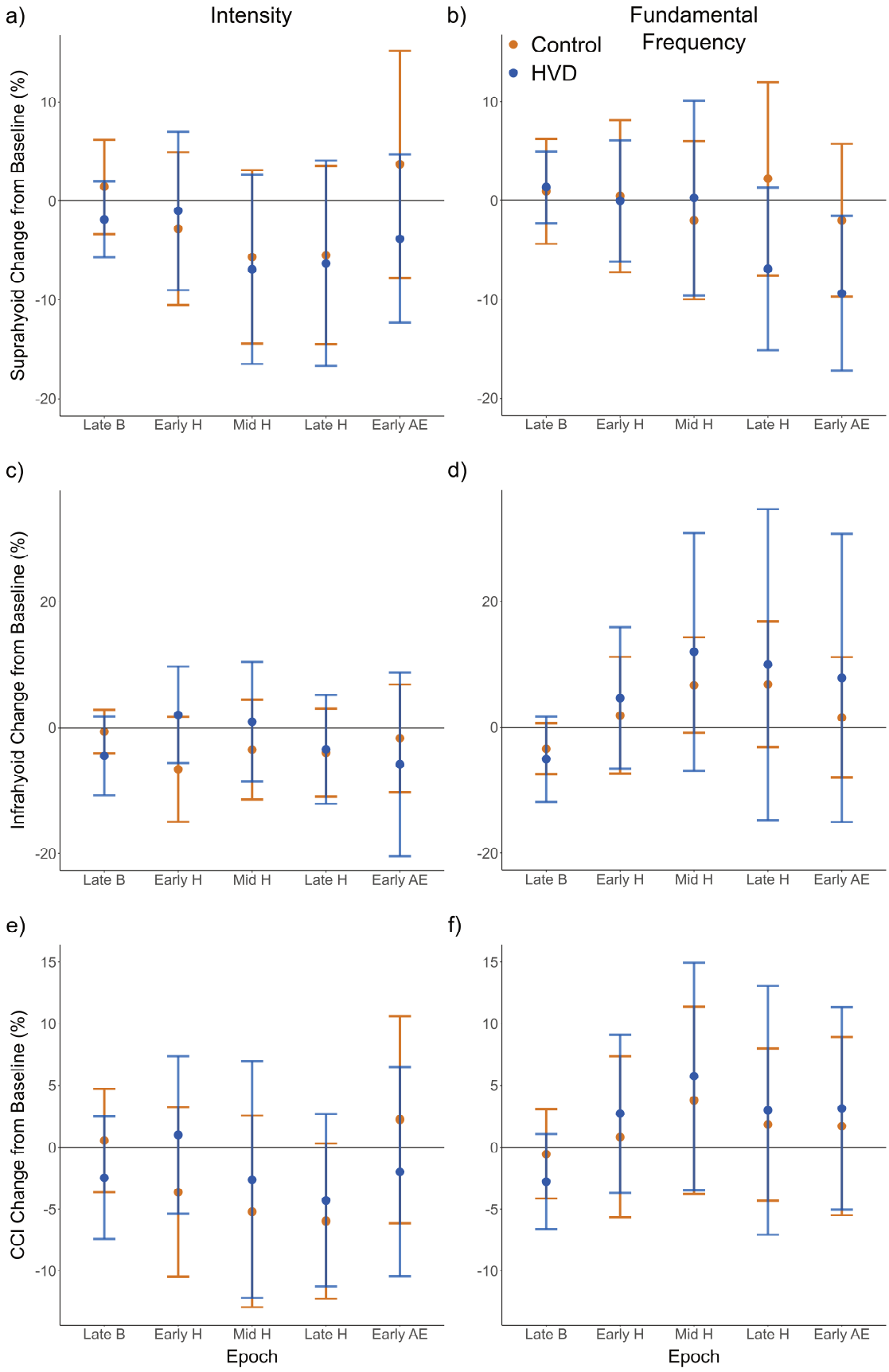
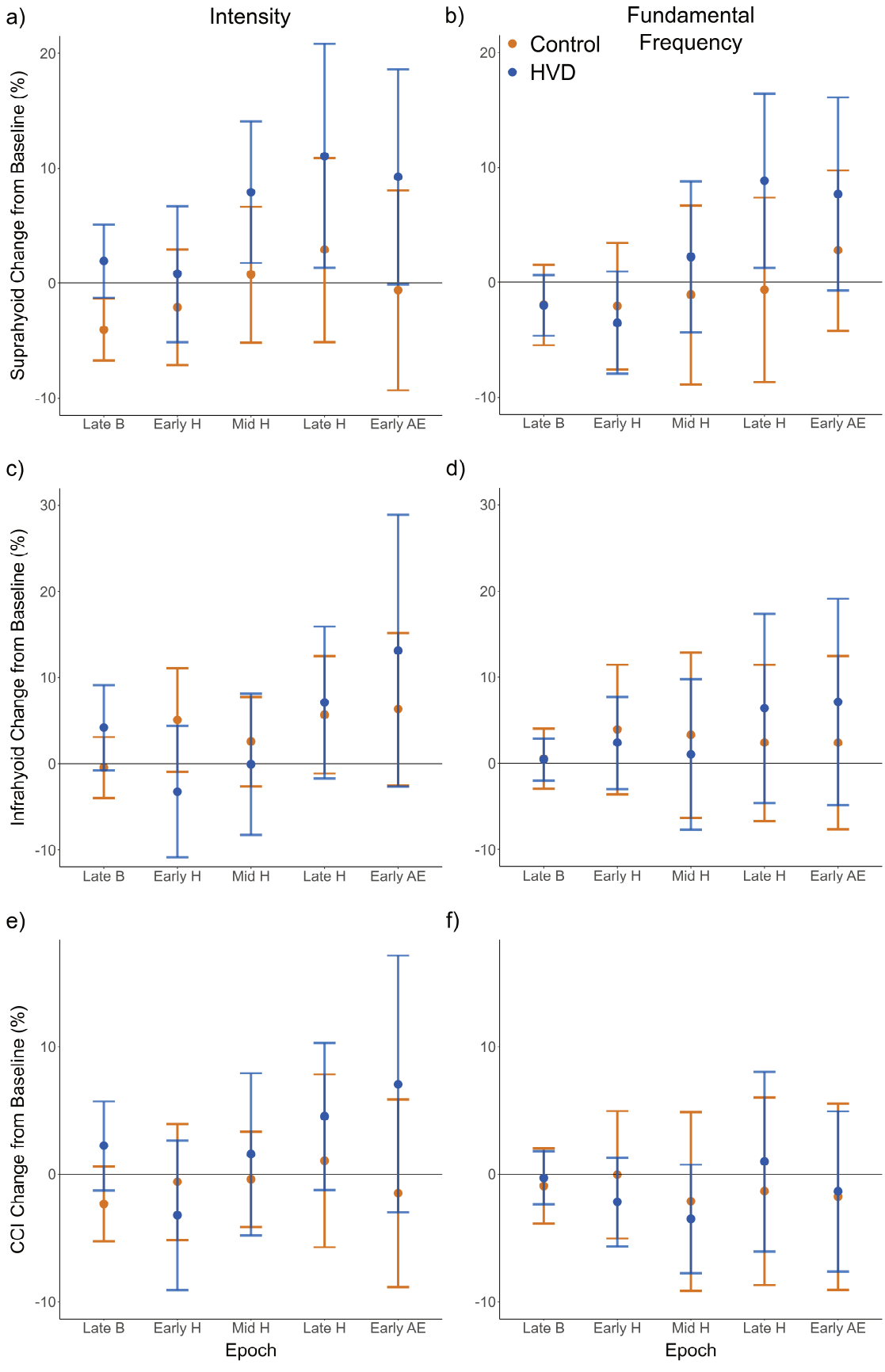


Figure 3-7. Surface electromyography measures from control conditions (no feedback perturbations applied), means and 95% CIs. NB auditory feedback was unamplified during loudness control (a, d, e) and amplified by +5 dB during pitch control (b, d, f). B = baseline, H = hold, AE = after effects.



3.4.3 Auditory discrimination thresholds

Figure 3-8. Distributions for intensity and f_o discrimination thresholds by HVD status and singing experience.

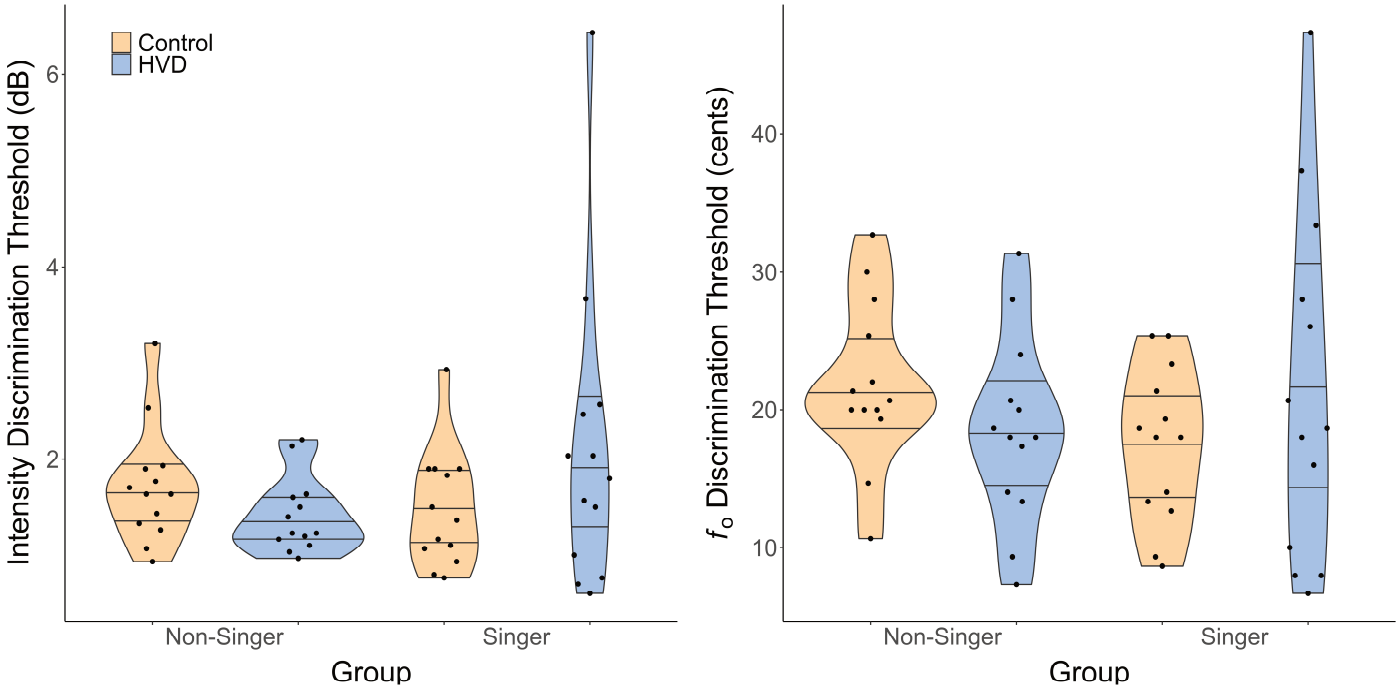


Table 3-7. Univariate ANOVAs for intensity and f_o discrimination.

Effect (Intensity)	***df***	**η_p^2**	***F***	***p***
HVD status (control, HVD)	1	.01	0.37	.544
Singing experience (singer, non-singer)	1	.02	0.71	.403
HVD status * Singing experience	1	.06	3.25	.078

*Significant at $p < .05$

Effect (f_o)	***df***	**η_p^2**	***F***	***p***
HVD status (control, HVD)	1	<.01	0.01	.920
Singing experience (singer, non-singer)	1	<.01	0.12	.746
HVD status * Singing experience	1	.05	2.59	.114

*Significant at $p < .05$

For control participants, the mean discrimination threshold for intensity was 1.60 dB (SD = 0.61), and for f_o was 20 cents (SD = 6.1). For participants with HVDs, the mean threshold for intensity was 1.75 dB (SD = 1.17) and for f_o was 20 cents (SD = 10.0). Distributions are shown by group and singing experience in Figure 3-8. Results of univariate ANOVAs are given in Table 3-7. There were no statistically significant effects of group, singing, or their interaction on discrimination thresholds for intensity or f_o. However, there was a non-significant trend for an interaction effect for both parameters, such that control singers had better discrimination thresholds than control non-singers, whereas singers with HVDs had worse discrimination than non-singers with HVDs.

3.4.4 Relationships among measures

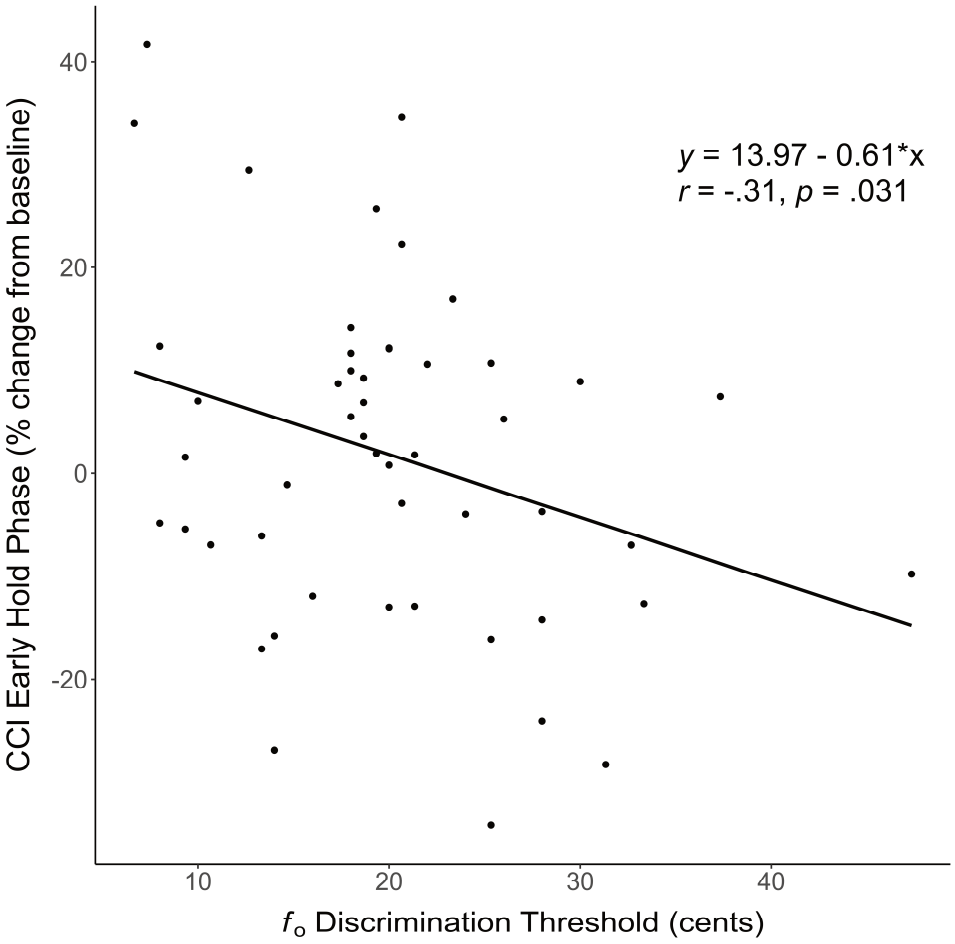
One *a priori* simple logistic regression was conducted to assess the relationship between f_o discrimination thresholds and atypical f_o adaptation responses for $n = 52$ participants. Discrimination threshold was not a significant predictor of atypical f_o adaptation ($\chi^2 = 2.78$, $df = 1$, $p = .095$, Nagelkerke pseudo $R^2 = .08$). A simple linear regression was conducted for the parameter intensity to test the relationship between discrimination threshold and adaptation, which also was not significant ($F = 0.10$, $p = .753$, $R^2 < .01$).

Table 3-8. Results of *a priori* simple linear regressions for discrimination thresholds and co-contraction index (CCI).

Relationship	***df***	***R*²**	**F**	***p***
Intensity Discrimination Threshold / Early Hold CCI	1	.01	0.31	.581
Intensity Discrimination Threshold / Late Hold CCI	1	.01	0.47	.498
f_o Discrimination Threshold / Early Hold CCI	1	.09	4.93	.031*
f_o Discrimination Threshold / Late Hold CCI	1	.04	1.87	.178

*Significant at $p < .05$

Figure 3-9. Simple linear regression with pitch discrimination threshold as a predictor of CCI in the first epoch of the pitch adaptation hold phase.



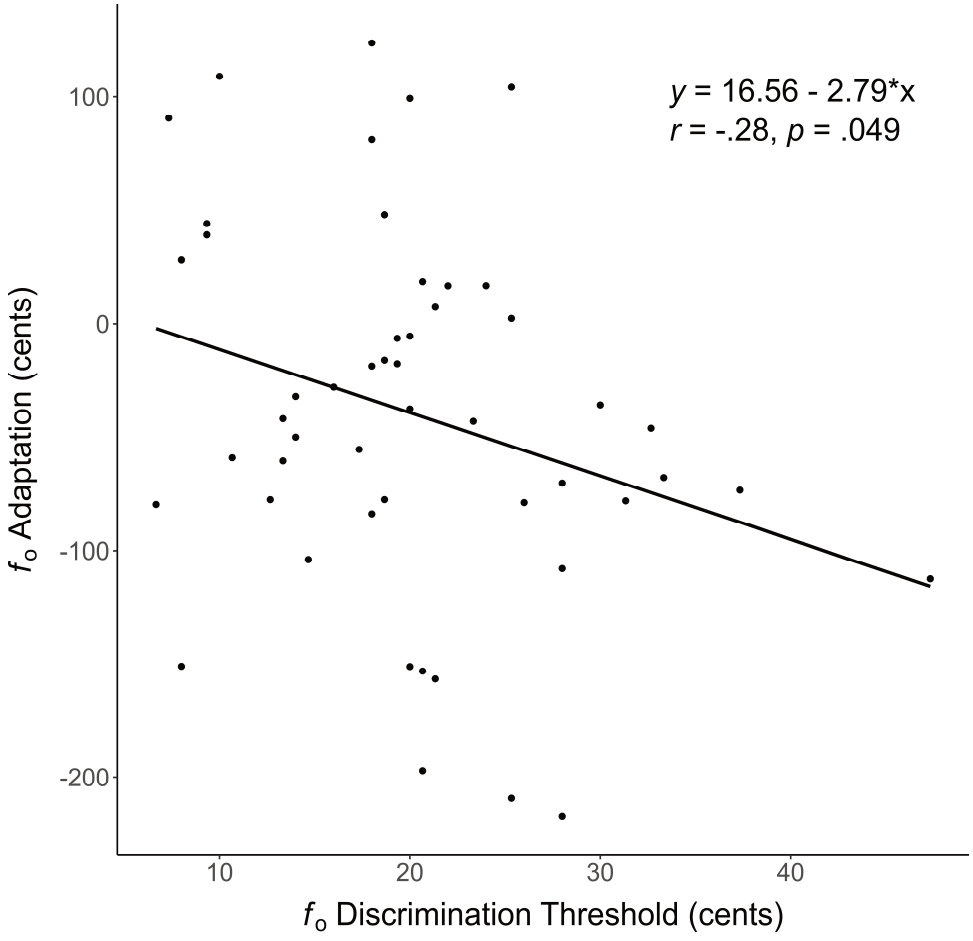
Four *a priori* simple linear regressions were conducted to assess the relationships for the parameters f_o and intensity between discrimination thresholds and CCI during early and late adaptation for the $n = 50$ participants included in the sEMG dataset. Results are given in Table 3-8. There was a significant inverse moderate relationship between f_o discrimination and CCI during the early hold phase ($p = .031$; see Figure 3-9). No other relationships were significant.

Table 3-9. Correlation matrix for variables related to f_o discrimination, adaptation, and CCI.

	1.	2.	3.	4.	5.	6.	7.
1. Pitch JND	–						
2. Baseline CCI	.02	–					
3. Early Hold CCI	-.31*	-.08	–				
4. Mid Hold CCI	-.07	.11	.44*	–			
5. Late Hold CCI	-.019	-.03	.42*	.50*	–		
6. After Effects CCI	-.27	-.26	.46*	.35*	.72*	–	
7. Pitch Adaptation	-.28*	.07	.31*	-.05	-.05	.05	–

*Significant at $p < .05$

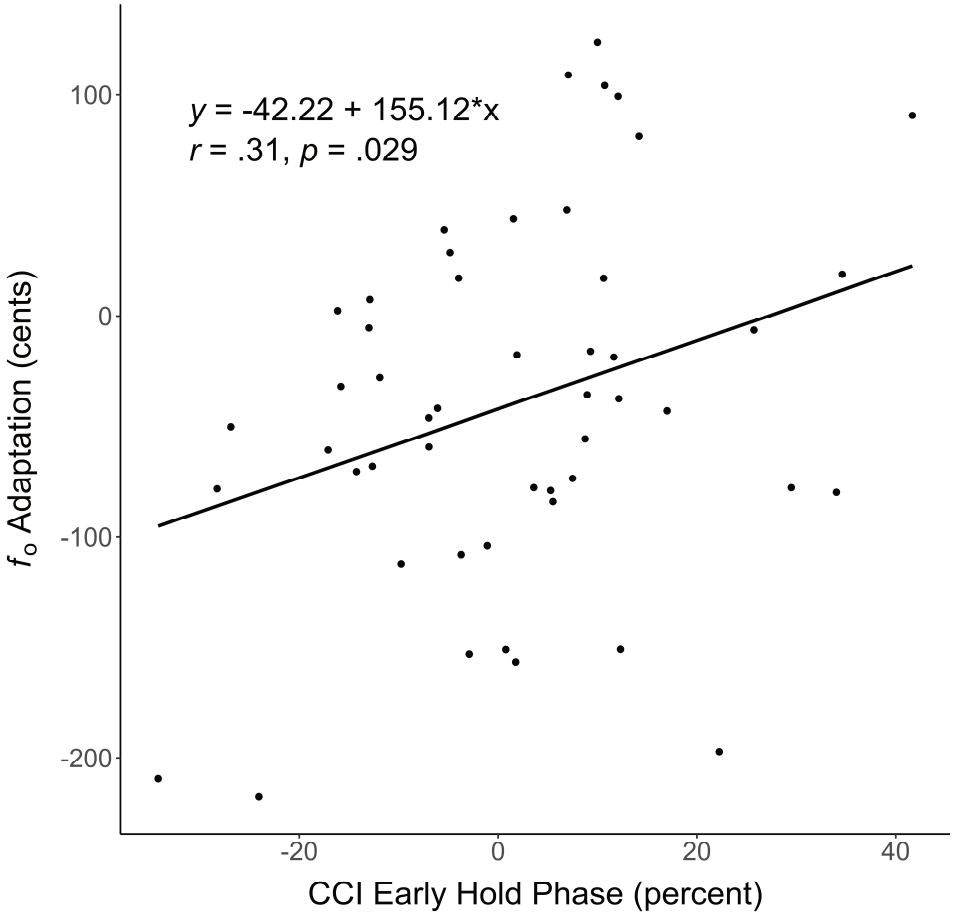
Figure 3-10. Simple linear regression for the relationship between f_o discrimination threshold and f_o adaptation response.



To further examine relationships between variables that might explain the nature of the

relationship between f_o discrimination and perilaryngeal co-contraction during adaptation, a correlation matrix was calculated between f_o discrimination threshold, f_o adaptation responses, and the co-contraction index at all time points (see Table 3-9). Significant positive relationships were found between all CCI measures except baseline. In addition, significant relationships were found between f_o adaptation responses and early hold CCI, and f_o discrimination and f_o adaptation responses. Simple linear regressions were conducted for the latter two relationships, shown in Figures 3-10 and 3-11.

Figure 3-11. Simple linear regression for the relationship between CCI in the early hold phase and f_o adaptation.



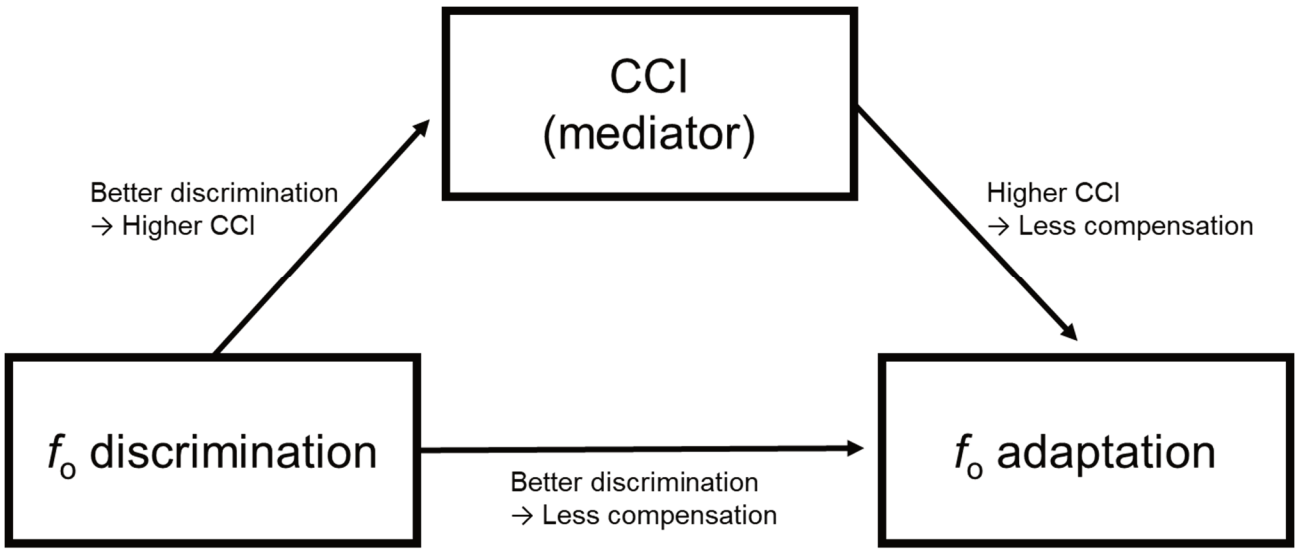
Finally, to test whether the relationship of f_o JND to f_o adaptation was mediated by CCI during the early hold phase, a multiple linear regression was conducted with f_o JND and CCI as predictor variables and f_o adaptation as the outcome variable. The model was significant (F = 3.63, df = 2, p = .034, R^2 = .13), however the individual predictor variables were not (see Table 3-10). Consistent with these results, there was a trend for a mediation effect of CCI on the relationship between f_o JND and adaptation, however it was not statistically significant (average causal mediation effect (ACME) = -0.75, 95% CI = [-2.32, 0.09], p = .106). A schematic of the mediation model is shown in Figure 3-12.

Table 3-10. Multiple linear regression to examine mediation of the relationship between f_o JND and f_o adaptation by CCI.

Predictor	***b***	***r***	***t***	***p***
Intercept	-0.75		-0.02	.981
fo JND	-2.04	-.20	-1.43	.158
CCI (early hold)	123.91	.24	1.74	.089

*Significant at $p < .05$

Figure 3-12. Model of mediation of the effect of f_o JND on f_o adaptation by CCI during the early hold phase.



3.5 DISCUSSION

This study replicates and extends findings from recent studies of auditory-motor function in people with HVDs. We examined adaptive vocal learning responses to perturbations of f_o and intensity of auditory feedback in people with and without HVDs. We simultaneously collected sEMG data from perilaryngeal musculature to investigate a hypothesized laryngeal stabilization response. We also compared these measures with auditory discrimination thresholds for vocal f_o and intensity to develop hypotheses about underlying control mechanisms.

3.5.1 Adaptive vocal learning in people with and without HVDs

Perturbation of f_o auditory feedback can elicit both compensatory (i.e., opposing the perturbation) and following (i.e., following the perturbation) responses in people with typical voices (e.g., Kapsner-Smith et al., 2024; Lester-Smith et al., 2020). Prior studies of vocal adaptive learning in people with HVDs have found increased following responses to f_o perturbation (Stepp et al., 2017) or more extreme responses, in either direction (Abur, Subaciute, Kapsner-Smith, et al., 2021), compared to controls. In the present study, we also found more frequent large following responses to f_o perturbation in people with HVDs than controls (see Figure 3-5). These results replicated findings from previous studies (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017). In contrast, when exposed to perturbations of intensity auditory feedback, there was a trend for participants with HVDs in this study to compensate to a greater degree on average than controls. Neither f_o nor intensity adaptation was significantly predicted by auditory-perceptual ratings of overall severity of dysphonia, suggesting that these findings are related to differences in auditory-motor integration, and not caused by dysphonia itself. This dissociation of impairments (f_o adaptation responses vs. intensity adaptation responses) provides preliminary evidence for the independence of auditory-motor control of

vocal f_o and intensity, at least under certain conditions. It also highlights the importance of refining models of sensorimotor control of speech to account for this independence. The specific nature of the sensorimotor impairments underlying HVDs may provide clues regarding their causal/compensatory relationship with the pathophysiology of HVDs (Hillman et al., 2020). Evidence from ambulatory monitoring studies points to differences in intensity production in people with HVDs (e.g., Toles, Ortiz, et al., 2021). It is possible that this impaired production leads to increased variability and sensitization of the compensatory adaptive response, i.e., an increase in the "gain" (Weerathunge, Alzamendi, et al., 2022). On the other hand, more people with HVDs produced large following responses to perturbations of f_o auditory feedback in this study. Following responses have been suggested to result from an interpretation of the perturbation as external rather than self-produced (Burnett et al., 1998). It has been suggested that some people with HVDs may experience reduced voice-related perceived control (Misono et al., 2019). Further study may be warranted to explore relationships between these factors and auditory-motor function in people with HVDs.

In this study, singers adapted significantly less to intensity perturbations than non-singers (see Table 3-3). One possible explanation for this response may relate to how their sensorimotor control has changed as a result of frequent experiences with external "perturbations" of intensity. This may include use of amplification, different room acoustics, and singing in groups or over instrumental accompaniment or noise. Singers may also have more experience hearing their own voice played back on a monitor. As a consequence of these experiences, responses to intensity perturbations could become desensitized, consistent with a decrease in "gain" of the adaptive response for vocal intensity. Further study is necessary using longitudinal or intervention designs to determine whether intensity adaptation gain is indeed malleable based on experience.

3.5.2 Laryngeal stabilization during adaptive vocal learning tasks

Impedance control has been observed or inferred in studies of sensorimotor learning in the limb (Franklin et al., 2003; Franklin et al., 2004; Huang & Ahmed, 2014) and speech articulation (Nasir & Ostry, 2006) domains. We sought to determine whether co-contraction of the extrinsic laryngeal muscles occurred in response to auditory feedback perturbation, consistent with a laryngeal stabilization response, and whether there were any different patterns observed in people with HVDs. Overall, we did not find significant results for the CCI when analyzed alone during adaptation. This result potentially could be due to large variability in responses across participants, which decreased statistical power. Upon visual inspection of the data, there were qualitative differences between the parameters f_o and intensity in the predicted directions (see Figure 3-6), with increased CCI for f_o only during the hold phase of adaptation; however, these results did not reach statistical significance.

Data from the control conditions provided an opportunity to examine how participants responded to a repetitive, prolonged, tedious speech task in terms of muscle activation. This exploratory analysis revealed two interesting findings that may be relevant for our understanding of vocal hyperfunction. First, all participants significantly increased suprahyoid activation over time (see Figure 3-7 and Table 3-5). Suprahyoid activation, when unopposed, will raise the larynx (Titze, 1994), and interestingly, a high laryngeal position has been associated with vocal hyperfunction (e.g., Saldias, Guzman, Miranda, & Laukkanen, 2019). Second, although it did not reach statistical significance, there was a trend for participants with HVDs to increase suprahyoid activation to a greater degree than controls. This finding may support the notion that vocal hyperfunction is something that everyone experiences, triggered by internal and/or situational conditions. In people with HVDs, it may be qualitatively similar, but can be more severe and

chronic rather than episodic (Hillman et al., 2020). Electrophysiological, kinematic, and/or vocal tract imaging data collected during vocally or cognitively demanding speech tasks in this population may further elucidate these effects.

3.5.3 Auditory discrimination of f_o and intensity in people with and without HVDs

Previous studies of auditory discrimination of f_o have found worse discrimination thresholds in people with HVDs compared to people with typical voices (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022). We sought to replicate and extend prior findings by examining discrimination thresholds for vocal intensity as well as vocal f_o. In contrast with prior studies, we did not find significant differences between people with and without HVDs in auditory discrimination of f_o or intensity. It is likely that our study lacked adequate statistical power for these measures, given the small-to-medium effect size that was detected by Abur, Subaciute, Kapsner-Smith, et al. (2021). However, interesting trends were observed for an interaction of HVD status and singing experience for both f_o and intensity discrimination, such that control singers had better discrimination than control non-singers, but singers with HVDs had worse discrimination than non-singers with HVDs, though the interaction effects were not significant. One hypothesis that could be investigated based on this trend is that individuals with poor auditory discrimination who engage in vocally demanding tasks, like singing, are at greater risk of developing HVDs. This should be interpreted with caution, however, given the lack of statistical significance in this sample, and the lack of causal evidence provided by the current study design. The relationship between these discrimination thresholds and measures of laryngeal stabilization responses and adaptive vocal learning are described in the next section.

3.5.4 Relationships among adaptive vocal learning, laryngeal stabilization, and auditory discrimination of f_o and intensity

In contrast with our hypotheses, f_o discrimination thresholds were not significant predictors of atypical f_o adaptation responses. Similarly, intensity discrimination thresholds were not significant predictors of the magnitude of intensity adaptation responses. However, we found a significant, moderate relationship between f_o discrimination and CCI in the early hold phase (r = -.31; J. Cohen, 1988). People with lower (better) f_o discrimination thresholds tended to increase co-activation of supra- and infra-hyoid musculature more in the first 12 trials in which they were exposed to a +100-cent feedback perturbation, compared to the unperturbed baseline condition. This relationship did not occur in the late hold phase, or for the vocal parameter intensity.

To better understand the nature of the increased CCI seen in participants with better f_o discrimination, we examined relationships among discrimination thresholds, adaptation responses, and CCIs at all stages of the f_o adaptation experiment. In addition to the relationship between f_o discrimination threshold and CCI in the early hold phase, we found moderate relationships between f_o discrimination thresholds and f_o adaptation responses (r = -.28), and between CCIs in the early hold phase and f_o adaptation responses (r = .31). People with better f_o discrimination tended to compensate less or follow the perturbation. This contrasts with prior findings of larger formant adaptation responses in participants with better formant discrimination (Villacorta et al., 2007). However, studies of auditory discrimination and auditory-motor control of articulation and voice suggest mechanistic differences between these two aspects of speech control (Kapsner-Smith et al., 2024; Lester-Smith et al., 2020). In the present study, people who had a greater increase in CCI in the early hold phase compensated less or followed the perturbation. A mediation model was therefore tested with f_o discrimination as the predictor, CCI

during the early hold phase as the mediator, and f_o adaptation as the outcome. The direct relationship between f_o discrimination and f_o adaptation decreased when CCI was included in the model, however the mediation effect did not reach significance.

Following responses in f_o adaptation experiments are not well-understood. It has been suggested that following responses may occur when the speaker perceives a mismatch between expected and actual auditory feedback to be externally rather than internally generated, based on evidence that they occur more frequently when the magnitude of the perturbation is large (Burnett et al., 1998). This evidence comes from reflex-like responses to unpredictable auditory feedback perturbations, rather than adaptation responses to predictable perturbations. However, the relationships found in this study suggest there may be some relevance for f_o adaptation responses. Although the perturbation used in this study (+100 cents) would have been supra-threshold for all participants (f_o discrimination thresholds ranged from 7 – 47 cents), presumably participants with lower discrimination thresholds would have perceived the perturbation as larger in magnitude. These same participants had a larger increase in CCI when the perturbation first occurred, and tended to produce following responses. One interpretation of these relationships is that a laryngeal stabilization response occurs to resist changes in f_o when a perturbation is perceived as externally generated, and that a following response is more likely under these conditions. The trend for mediation of the relationship between f_o discrimination and f_o adaptation by CCI supports this interpretation. People with better discrimination produced a larger change in CCI in the early f_o adaptation hold phase, and in turn adapted less (see Figure 3-12).

In this study, the relationships between auditory discrimination thresholds, adaptation responses, and CCIs in the early hold phase were only found for f_o, and not intensity. This finding also

provides additional evidence that there may be a difference between underlying mechanisms for control of vocal f_o and intensity. It may also relate to more peripheral physiological differences in the production of vocal f_o and intensity. For example, vocal intensity can be altered through a combination of respiratory and laryngeal valving changes to alter subglottal pressure and airflow leading to changes in the amplitude of vocal fold vibration (Titze, 1994). In contrast, although f_o can be altered somewhat by changes in pressure and flow, it is primarily controlled by changes in vocal fold length and tension by intrinsic laryngeal musculature, and indirectly by laryngeal height (Kakita & Hiki, 1976; Maeda, 1976; Sokolowsky, 1943; Sonninen, 1968; Titze, 1994). Thus, laryngeal stabilization may be relevant to stabilize vocal f_o, but not vocal intensity.

3.5.5 Implications for understanding the pathophysiology of HVDs

Our findings generally concur with previous studies of auditory-motor function in people with HVDs, which have found worse f_o discrimination and atypical f_o adaptation responses in terms of magnitude and/or direction (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Stepp et al., 2017). In this set of studies, we found evidence of qualitatively different auditory-motor impairments across the vocal parameters intensity and f_o in people with HVDs compared to people with typical voices. Whereas there was a pattern of more following responses to f_o perturbations, there was a trend for a greater degree of compensation in response to intensity perturbations in people with HVDs. These results suggest differences in the underlying pathophysiology of these auditory-motor integration impairments in people with HVDs. One possible explanation for these differences relates to differences in causal vs. compensatory characteristics of HVDs overall. For example, it is unlikely that poor f_o discrimination would develop as a result of having a voice disorder. However, it could reflect some underlying predisposition to developing one. In contrast, an argument could be made for increased

sensitivity to auditory feedback of intensity as a compensatory mechanism in response to having dysphonia. Disrupted vocal intensity production in people with HVDs could cause greater intensity variability, and in turn sensitize the speaker to vocal intensity feedback (i.e., increase the compensation gain). However, currently available data are not sufficient to support or refute such interpretations. Further study is needed to understand how the differences found in this study between f_o and intensity adaptive responses in people with HVDs relate to the nature of the disorders.

Although we found preliminary evidence of laryngeal stabilization as a potential response to auditory feedback perturbation (specifically related to f_o-perturbed feedback), we did not find differences between people with and without HVDs in this study. However, we did find a trend for differences in suprahyoid activation in tasks with unaltered auditory feedback, which indicates dysregulated muscle activation for voicing. In this study, following responses were associated with larger increases in co-contraction of perilaryngeal musculature in response to auditory feedback perturbation, and significantly more large following responses occurred in people with HVDs than controls. This preliminary evidence suggests the hypothesis of maladaptive stabilization responses in HVDs may still be an avenue to explore. Kinematic evidence and computational modeling point to increased laryngeal stiffness due to muscle activation in people with HVDs (Stepp et al., 2010; Weerathunge, 2024). It is possible the methods used this study were not sensitive enough to capture group differences due to the substantial variability between participants. It is also possible that only a subset of speakers with HVDs display these responses and that they were obscured by group mean analyses.

3.5.6 Limitations

There are several limitations to this set of studies. First, sample size combined with variability between speakers may have limited statistical power to detect differences as a function of voice disorder status and/or musical experience. Second, controlling for variables that may impact auditory-motor function is challenging. For example, although participants were matched for years of singing experience, this metric alone likely does not fully capture the variability in experience and training across singers. Similarly, a variety of voice diagnoses consistent with HVDs were included in a single sample, which could be a source of variability. However, it is noteworthy that participants in the HVD group who displayed atypical f_o following responses were approximately evenly split between PVH and NPVH categories. In addition, our sample of participants with HVDs was skewed toward individuals with mild dysphonia. Although we found no association between overall severity of dysphonia and adaptive vocal learning responses, it is possible that individuals with more severe dysphonia may perform differently. Third, new methods and measures were employed, including use of sEMG during adaptation tasks and adaptation of the co-contraction index for speech (Thoroughman & Shadmehr, 1999). These methods facilitated preliminary evidence of laryngeal stabilization as a method of control of vocal f_o; however, refinement of signal acquisition and processing methods may improve their sensitivity. Finally, the tasks employed in the study were lengthy and somewhat burdensome for participants. Given that the relevant muscle responses occurred early in adaptation, shorter and more efficient tasks likely could be developed to further investigate these phenomena.

3.6 CONCLUSIONS

This study replicates and extends previous findings of impaired auditory-motor function for voice in people with HVDs. People with HVDs appear to be more sensitive to changes in

auditory feedback of vocal intensity, resulting in greater compensation. In contrast, they are more likely than controls to produce a large following response to changes in auditory feedback of f_0. This may reflect underlying differences in control mechanisms and/or causal relationships with the pathophysiology of the disorders. Longitudinal studies are warranted to determine whether auditory-motor impairment precedes or follows development of a voice disorder. These findings also have implications for voice therapy research. Preliminary evidence from a case series of people with HVDs before and after routine voice therapy showed improvements in at least one measure of auditory-motor function in eight of 11 participants (Abur, Hillman, & Stepp, 2023). Future studies should test interventions specifically designed to address auditory-motor impairment. Finally, following responses were also related to evidence of a hypothesized laryngeal stabilization response that involves co-activation of extrinsic laryngeal musculature. These findings have implications for models of vocal sensorimotor control. In addition, further study is warranted to determine whether dysregulated laryngeal stabilization occurs in people with HVDs and impaired auditory-motor integration.

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CONCLUSION

The series of studies presented in this dissertation has been a path to elucidate the pathophysiology of hyperfunctional voice disorders (HVDs) as well as an opportunity to extend our understanding of typical vocal sensorimotor control. Recent studies of auditory perception and vocal sensorimotor control in people with and without HVDs suggest the existence of a sensorimotor subtype of VH (Abur, Subaciute, Kapsner-Smith, et al., 2021; Nguyen et al., 2022; Stepp et al., 2017; Tam et al., 2018; Ziethe et al., 2019). However, questions remain about the nature of these impairments and the methods used to identify them. The specific questions addressed in the present set of studies were:

1) What is the test-retest reliability of behavioral assays of auditory-motor control of articulation and voice (chapter 1)?
2) Can atypical adaptive vocal learning responses in people with HVDs be explained by a broader limitation of volitional control of vocal parameters (chapter 2)?
3) Are auditory-motor impairments in people with HVDs specific to f_o or inclusive of other vocal parameters (chapter 3)?
4) Does auditory feedback perturbation elicit laryngeal stabilization, and is stabilization behavior different in people with and without HVDs (chapter 3)?

4.1 SUMMARY OF MAJOR FINDINGS

In chapter 1, we assessed the test-retest reliability of auditory perturbation methods used to assess feedback and feedforward vocal and articulatory sensorimotor control. We learned that there are key differences in patterns of reliability across these two domains. Namely, responses to assays of reflex-like feedback control of f_o were very reliable, whereas these responses in the

articulatory domain (tested with formant perturbations) were not. In contrast, responses to assays of feedforward vocal adaptive learning using f_0 perturbations were unreliable, whereas articulatory adaptive learning in response to formant perturbations had moderate reliability. This evidence highlights likely differences in the nature of the control mechanisms for voice vs. articulation. Online, reflex-like responses to errors in vocal parameters may be more important than those for articulation due to the different timescales at which they are controlled. Vocal parameters vary over multiple timescales including across phoneme, syllable, and word boundaries (Fujisaki, 2004; Ladd, 2008). Online corrections based on feedback could be used to make meaningful changes to production of these parameters. On the other hand, articulatory parameters vary quickly and likely are not amenable to feedback control in typical speech (Perkell et al., 1997). Because of this, reliable feedforward control of articulatory parameters is likely more important for accurate, fluent speech.

The lack of reliability of f_0 adaptation responses found in chapter 1 could be problematic for studies of vocal sensorimotor control, such as those that have identified auditory-motor impairment in people with HVDs. However, when we assessed test-retest reliability of a categorical method of assessing vocal adaptive learning, as used in Abur, Subaciute, Kapsner-Smith, et al. (2021), we found substantial reliability. This supports the use of categorical measures of vocal adaptive learning as employed in chapter 3 of this dissertation.

In chapter 3, we investigated the specificity of impaired auditory discrimination and vocal auditory-motor integration in people with HVDs, and examined a possible relationship between auditory-motor integration and perilaryngeal muscle activation in response to f_0 perturbations. We found that although there is evidence for differences between people with and without HVDs across both the vocal parameters f_0 and intensity, the nature of these differences is qualitatively

different. Whereas we found a similar pattern of atypical f_o perturbation responses to prior studies (Abur, Subaciute, Kapsner-Smith, et al., 2021; Stepp et al., 2017), with a subset of people with HVDs producing more extreme responses and specifically more following responses, people with HVDs on average tended to compensate more for intensity perturbations than people with typical voices. This finding may represent an impairment of auditory-motor integration of f_o feedback, but a sensitization of auditory-motor integration of intensity feedback. These results are supported by the findings of chapter 2, wherein we saw no significant differences between people with and without HVDs in the ability to make small changes in f_o and intensity in volitional speech tasks. If atypically large adaptation responses were a result of an inability to produce small changes in f_o or intensity, for example due to vibratory impairment, we would expect to see group differences when people with HVDs were asked to produce the smallest possible change in these parameters volitionally. Instead, we saw group differences only during adaptive vocal learning tasks, which are thought to be involuntary responses driven by implicit learning processes (Lametti et al., 2020).

In chapter 3, we also measured perilaryngeal muscle activation during vocal adaptation tasks and examined relationships with auditory discrimination and adaptive vocal learning. Although we did not find clear evidence of a specific relationship between auditory-motor impairment and dysregulated perilaryngeal muscle activation during voicing in people with HVDs, we did find preliminary evidence that laryngeal stabilization may play a role in adaptation to f_o perturbations. This was reflected in increased co-activation of supra- and infrahyoid musculature, measured with a co-contraction index (CCI), in the early hold phase of the f_o adaptation experiment in people who compensated less or followed the perturbation. Interestingly, people with better f_o discrimination thresholds also tended to compensate less or follow the perturbation, and had

greater increases in CCI in the early hold phase. Following has been suggested to occur when speakers perceive a perturbation as externally generated, and occurs more frequently when perturbations are large (Burnett et al., 1998). Taken together, these findings suggest that people with better f_o discrimination thresholds may be more likely to perceive an f_o perturbation as externally generated, and may therefore respond by stabilizing laryngeal height (which contributes to f_o production) by co-contracting the muscles that elevate and depress the larynx. Further research is needed to understand the factors that elicit laryngeal stabilization.

4.2 LIMITATIONS

Many studies of HVDs, including those in this dissertation, are hampered by sample size and statistical power. Although HVDs are quite common, not all individuals seek treatment. It can be challenging to recruit a sufficient number of patients who meet study criteria and are available to participate. The participants with HVDs in this study tended to have mild dysphonia. To some extent this may reflect the fact that the symptoms of HVDs include not only dysphonia but also vocal fatigue and discomfort. It is also possible that people with more severe dysphonia are less likely to volunteer to participate in a vocally taxing study. Furthermore, the methods employed in these studies are time-intensive. Developing sensitive methods to assess vocal auditory-motor function that take less time and ideally less specialized equipment would facilitate larger and more ecologically valid studies of vocal auditory-motor function. In addition, determining the necessity of certain exclusion criteria, such as diagnoses like attention deficit disorder, would enable broader recruitment.

Both chapters 2 and 3 employed novel methods for studying sensorimotor control of speech. In chapter 2, we devised a protocol to measure volitional control of minimal movements for vocal parameters, modeled after Daliri et al. (2013). Although this method did prove sensitive to group

differences related to singing experience, there was a great deal of variability between and within participants. Further assessment of the sensitivity of these tasks is warranted. In chapter 3, we employed surface electromyographic (sEMG) measurements during adaptive learning tasks for speech, something which has not been done before, as well as adapting a measure of co-activation of agonist/antagonist muscles from the limb motor literature (CCI; Thoroughman & Shadmehr, 1999). We did find meaningful patterns of relationships between the CCI and auditory discrimination and adaptive vocal learning for f_o, which support a possible role of laryngeal stabilization in control of vocal f_o . However, variability in CCI measures may have decreased our statistical power for assessing group differences such as HVD status. Potential for refinement of methods, such as tasks and signal acquisition and processing, should be investigated.

4.3 FUTURE DIRECTIONS

This set of studies contributes to a growing body of evidence that there may be a sensorimotor subtype of HVDs, as well as informing theoretical models of speech sensorimotor control. Questions remain about the relationship of impaired auditory-motor function and clinical characteristics of HVDs. Dysregulated laryngeal stabilization could be an explanatory factor, although it was not detected in these studies. Future studies with more sensitive methods of eliciting and measuring laryngeal stabilization would serve to clarify this question. In addition, the different nature of group differences in discrimination and adaptation of f_o versus intensity should be explored further. One possibility is that atypical f_o adaptation reflects an underlying impairment that predisposes individuals to vocal hyperfunction, whereas increased intensity adaptation reflects a sensitization to intensity feedback as a compensation for impaired intensity production. Current evidence cannot answer these questions. Longitudinal studies of at-risk

populations and treatment responses could aid in understanding causal questions about pathophysiology.

Results from chapters 1 and 3 highlight differences in auditory-motor control between voice and articulation, and even between different vocal parameters. However, current models of speech sensorimotor control make limited if any distinctions between these domains. The laryngeal directions into velocities of articulators (LaDIVA) model is a first step in the direction of a physiologically-motivated voice-specific model of sensorimotor control (Weerathunge, Alzamendi, et al., 2022). However, this model does not currently account for specific differences between control of different vocal parameters such as f_o and intensity. Furthermore, impedance-like control via mechanical stabilization is not included in any current models of sensorimotor control of speech (Houde & Nagarajan, 2011; Parrell et al., 2019; Tourville & Guenther, 2011; Weerathunge, Alzamendi, et al., 2022). Future studies should pursue model-driven explanations of differences in control of different parameters of speech, including flexibility (reflected in test-retest variability), differences in gain, causes of following responses, and the nature and significance of control via mechanical stabilization. A more comprehensive understanding of vocal motor control in people with and without HVDs may facilitate development and testing of novel interventions designed to improve auditory-motor function, and ultimately, quality of life.

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APPENDIX A: REPRINT PERMISSION

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