Prevalence of Laryngoresponders in the General Population

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Introduction: Over four decades ago Aronson proposed that some individuals are *laryngoresponders*, i.e., their voice and/or larynx is uniquely vulnerable to stress, and that this status might predispose them to certain voice disorders. It remains unknown what proportion of the population would report that their larynx and/or voice is vulnerable to stress. The current study aimed to determine the prevalence of self-identified laryngoresponders in the general population. Based on preliminary data from the Helou Laboratory for Vocal Systems Anatomy and Physiology Research, we hypothesized a prevalence of 20%. We also hypothesized that more females would identify as laryngoresponders than males, based on the higher prevalence of functional voice disorders in women than in men. Finally, we hypothesized that laryngoresponders would report higher stress levels than non-laryngoresponders based on past evidence that individuals with muscle tension dysphonia self-report higher stress levels and stress-reactive personality traits. ***Methods:*** We recruited 1,217 participants between age 18 and 65 to complete an online survey of where in the body they tend to physically manifest stress. To avoid biasing participants toward our region of interest (i.e., the larynx) or its functions (e.g., voice, swallowing), the entire body was surveyed. On a line-drawn figurine, participants selected all general bodily regions in which they experienced physical stress symptoms (e.g., abdomen, head) in the past month. Then, for each region, they reported the severity of symptoms in this region and were invited to describe their symptoms in a free-text format. Next, participants completed the

Perceived Stress Scale (PSS), a validated measure of perceived stress over the past one month. Lastly, we directly asked participants if they experience voice, swallowing, and/or laryngeal symptoms in response to stress. Data for all participants who selected the front-of-neck/throat region was used post-hoc to manually code laryngoresponders. Symptomology was thematically coded to determine the prevalence of laryngeal symptoms among self-identified laryngoresponders.

Results*:* A total of 1,217 adults (77.5% assigned female at birth, mean age 36.1 years [*SD* = 13.7]) completed the demographics questionnaire. Of these, 1,145 participants responded to the figurine and 995 finished the survey in its entirety. We identified four categories of laryngoresponders based on survey response patterns. The prevalence of self-identified laryngoresponders in the general population was determined to be 16.86% unprompted, and 45.42% when participants were asked directly about the larynx. Of the unprompted laryngoresponders, 54.92% rated their symptom severity at a 5 (moderate) or higher (more severe). These unprompted laryngoresponders reporting moderate to severe symptoms made up 9.25% of the participants who responded to the figurine. Reported symptoms varied widely. Unprompted responses largely included reports of tightness/tension in the throat region, while prompted responses also included voice and swallowing symptoms. Contrary to our hypothesis, being assigned female at birth was not significantly correlated with laryngoresponsiveness. Compared to non-laryngoresponders, laryngoresponders reported statistically significantly higher (worse) scores on the PSS.

Conclusions: This study estimated the point-prevalence of self-identified laryngoresponders (16.86% unprompted) and characterized their symptom profiles for the first time. The study indicates that laryngoresponders report higher levels of stress than non-laryngoresponders. It

also supports the popularly-cited relationship between voice and stress. Implications of these findings and suggestions for future work are discussed.

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Preface

It has been an absolute honor to work on this project with the Helou Laboratory for Vocal Systems Anatomy and Physiology Research. The lessons I have learned about research, the voice, and working as a team are gifts that I will cherish throughout my career as a speech-language pathologist. My endless thanks go out to my academic mentor, committee chair, co-author, teacher, and mentor Dr. Leah Helou, without whom I surely would never have found myself on this exciting and challenging path. I would also like to extend my deepest gratitude to Brett Welch, who answered all my novice questions with eloquence, patience, and humor; and to Dr. Jackie Gartner-Schmidt, whose generously shared clinical wisdom provided me a roadmap to navigate laryngeal symptomology. Thank you as well to Dr. Jim Coyle, for all the time and expertise he so graciously spent on this project. And finally, thank you to the rest of the team at the Helou Laboratory; you are all such hard workers and truly far too wonderful for words.

1.0 Introduction

Stress is defined as a psychological and physiological response to a challenge or demand (Epel, 2018). When the body detects physical danger, threat, or excessive emotional or cognitive demands, that signal is detected in the amygdala. The amygdala interprets the threat and sends a distress signal to the hypothalamus. The hypothalamus then signals activation of the autonomic nervous system to release adrenaline into the bloodstream, causing a quickened heartrate and breath rate, increased blood pressure, and increased absorption of oxygen in the lungs. The oxygen content of the brain is also elevated, which sharpens the senses. Prolonged perception of stress initiates a release of cortisol from the pituitary gland, which keeps the body alert for a prolonged period until cortisol levels fall (Yaribeygi et al, 2017).

Although some elements of the fight-or-flight response seem more universal than others, such as increased heart rate, individuals also exhibit idiosyncratic and distinct physical manifestations of stress. It is both popular clinical wisdom and experimentally evident (Cabrera et al. 2018), that people demonstrate unique stress responses (gut responders and headache responders among others). Some refer to these idiosyncratic and distinct manifestations as being reflective of "vulnerable pathways" in that they involve specific areas and systems of the body that consistently respond to stress (Butcher et al., 2007). The premise for this school of thought is that when a person reaches a certain threshold of stress, areas of the body already rendered vulnerable by an unrelated factor (such as an illness or past injury) will physically respond to that stress. The APA's 2010 survey of 1,134 people, *Stress in America*, determined the prevalence of various stress manifestations in the general population, including general muscle tension (23% of respondents), upset stomach (26%), teeth grinding (15%), and more (Anderson et al, 2010).

The laryngeal region was not included in the *Stressed in America* study in terms of either structure or function. It is also omitted from other similar work on the basis that it is not an autonomic effector *per se* (Cabrera et al., 2018). However, it is reasonable to expect that our area of interest, the larynx, might be a vulnerable pathway for some individuals. This possibility is reflected in clinical anecdote as well as empirical evidence. For example, data from Helou et al. (2013) demonstrated that the laryngeal muscles of a cohort of vocally healthy females exhibited significantly greater electrical activity while being exposed to a psychosocial stressor as compared to baseline. On average, the increase was 5-to-10-fold for each intrinsic laryngeal muscle, but a subset of those women showed an up to 25-fold increase in muscle activity when exposed to the stressor. These findings suggest that a minority of participants exhibit dramatic laryngeal stress response as compared to the majority of participants, in alignment with the notion that some people might be uniquely classified as laryngeal responders.

Stress is a powerful risk factor for numerous diseases and disorders, in every area and system of the body. According to the American Psychological Association, the fight-or-flight response can cause changes (both short- and long-term) in most if not all systems within the body, including the musculoskeletal, endocrine, respiratory, cardiovascular, gastrointestinal, nervous, reproductive, and immune systems (American Psychological Association, 2018). How an individual's distinct vulnerable pathways are linked to their current medical status or risk for development of certain diseases and disorders, however, remains unknown. For instance, it is unclear whether self-identified "gut responders" are more likely than "head responders" to be living with a functional gastrointestinal disorder (e.g., irritable bowel syndrome) or to develop one in the future. Likewise, it is unclear whether people who are aware of a predictable or reliable stress manifestation in their laryngeal region or its functions (voice, swallowing, breathing) are at a higher risk of developing a functional voice, swallowing, or laryngeal breathing disorder. The

following was posited by Aronson in 1990: “Those who are prone to develop voice disorders might be called laryngo-responders to designate their predisposition to developing laryngeal and voice disorders as their unique avenue for the expression of emotional distress.” (484).

Despite evidence of the prevalence of a wide range of physical manifestations of stress, and despite a substantial body of evidence that stress impacts the voice (e.g. Besser et al., 2020; Dietrich et al., 2008; Dietrich & Verdolini Abbott, 2012; Giddens et al., 2013; Helou et al., 2018; Helou et al., 2013; Lauka et al, 2008; Van Houtte et al., 2011; van Puyvelde et al., 2018; Wittels et al., 2002), no data exists regarding the prevalence of a known or predictable larynx-based stress response (i.e., the prevalence of laryngoresponders) in the general population. The aforementioned *Stress in America* survey did not include the larynx/voice as a response option, and to our knowledge, no other published survey has either. A study of 29 otherwise healthy females by Becker et al. (2019), currently under review, used a line-drawn figurine of the body to prompt participants about their individualized physical stress responses. This study reported a laryngoresponder prevalence of 20.7%, defining laryngoresponders as those with “sore throat,” “swallowing trouble, “uncomfortable feeling in throat,” and “my throat clenches” during stressful events. The current study aims to build on this preliminary evidence by prospectively quantifying the statistical prevalence of self-reported laryngoresponders in the general population. In the current study, we define the term laryngoresponder as a person whose reported response to stress or strong negative emotions involves distinct laryngeal and/or vocal symptoms, e.g., globus sensation, feelings of throat constriction, or any type of dysphonia.

2.0 Background: Stress and the Voice

Stress can impact the most basic physiology of vocal production. A significant positive correlation exists between salivary cortisol levels and the presence of vocal symptoms as well as increased fundamental frequency (Holmqvist-Jämsén et al., 2017; Pisanski et al., 2016; Perrine & Scherer, 2020), linking stress hormonal production with vocal function and perception. The electromyographic activity both in and around the larynx has been studied in relation to stress as well. Dietrich and Verdolini Abbott (2012) reported significantly increased muscle activity in the infrahyoid muscles of introverts faced with a public speaking task, as measured by surface EMG. Helou et al. (2012, 2018, 2020) found that electrical activity in the intrinsic laryngeal muscles changed significantly during stress reactions to both a physical stressor (the cold pressor test) (Helou, 2013), and a social stressor (Helou, 2018 and 2020) as compared to baseline. Stress clearly and significantly impacts the acoustic and perceptual properties of the voice as well. Significant changes in frequency, intensity, roughness, and other spectral properties of the voice have been observed in individuals under stress (Laukka, 2008; Bachorowski, 1999; Wittels, 2002; Pisanski, 2016; Cardoso et al., 2020; Dahl & Stepp, 2010). Additionally, untrained listeners can detect stress in a speaker's voice (Giddens, 2013).

2.1 The Pathogenesis and Problem of Stress in Voice Disorders

At any given time, between 3% and 9% of the population has a voice disorder, and 29.9% of the population will experience a voice disorder at some point in their lifetime (Roy, 2005).

These disorders are typically characterized as structural (physical changes to the body of the vocal fold tissue), neurogenic (issues in the central and/or peripheral nervous system that interfere with innervation of the larynx), and/or functional. Functional Voice Disorders (FVDs) often present themselves as dysphonia or aphonia, though their symptomatology often includes and can also center principally on aberrant phonatory sensations. The causes of FVD are not fully understood. Individuals who previously used their voices effectively may develop an FVD later in life. Some level of crossover between so-called functional and organic disorders has been established. Specifically, some propose that vocal hyperfunction, if left unaddressed and occurring with high levels of vocal dose as are often exhibited by highly extraverted individuals, may lead to structural changes like benign lesions on the vocal folds (Hillman, 2020; Millar et al., 1999).

Previous research suggests a strong link between stress and the development of functional voice disorders. Specifically, emotionally disturbing events have been known to precede the onset of voice disorders (Aronson et al., 1966; Aronson, 1969; Baker, 2003; House & Andrews, 1988). One functional voice disorder significantly correlated to stress is muscle tension dysphonia (Altman et al., 2005; House & Andrews, 1987). MTD is the commonest functional voice disorder and is characterized by "excessive tension of both the internal and external laryngeal muscles" (Hocevar-Boltezar et al, 1998). Van Houtte et al. (2011) showed that individuals diagnosed with muscle tension dysphonia were more likely to self-report prolonged, high stress levels. For this reason, relaxation techniques and stress management are often included in a multi-disciplinary treatment plan (Altman et al., 2005). However, not everyone with high stress levels develops MTD. We theorize that laryngoresponders, in particular, may be at higher risk for developing a functional voice disorder like MTD than those with differing vulnerable pathways.

The variability in voice changes under stress may point to highly individualized vocal responses to stress, and perhaps the complex relationship between state (e.g., stress vs. baseline)

and certain personality traits as they pertain to vocal symptoms (Dietrich et al., 2008; Dietrich & Verdolini Abbott, 2012). Multiple studies (Roy et al., 2010; Dietrich & Verdolini Abbott, 2012; van Mersbergen et al., 2008) have found that individuals with FVDs demonstrate higher levels of stress-reactivity on measures like the Multidimensional Personality Questionnaire (Tellegen, 1990). Individuals with higher stress reactivity, on this personality measure, are likely to be more tense, easily upset, and worried than those with lower stress reactivity (Patrick et al., 2002).

It is estimated that only 22% of people who experience dysphonia receive treatment (Cohen, 2010). Of those treated, many are never seen by a speech-language pathologist and are managed medically (e.g., antibiotics, anti-inflammatories, antiallergy or anti-reflux medications from their primary care doctors) or told simply to rest (Cohen, 2010). The American Speech-Language and Hearing Association (ASHA) stresses that one of the most important roles of speech-language pathologists is to advocate for their patients (ASHA Practice Portal, n.d.) The principles of patient-centered care dictate that medical and behavioral health professionals determine (through use of a thorough and well-informed patient history) when referrals to specialists are appropriate (Berry et al., 2003). This includes referrals to voice-specialized speech-language pathologists when vocal symptoms are present.

2.2 Sex Assigned at Birth and Voice Disorders

Research shows that a disproportionate number of women seek treatment for functional voice disorders versus men. Estimates of this ratio range from 1.5:1 to 3:1 (Lyberg-Ahlander & Rydell, 2019; Roy, 2005). Women made up a mean 76% of patient caseloads at voice centers in

the late 1990's (Morton & Watson, 1998), and anecdotally no shift in this disproportionate representation has been noted. Specifically, they are more likely than men to report chronic voice disorders (Roy, 2004). This disproportionate representation is likely due to many factors. Anatomical and endocrinological differences might be at play, though these have not been comparatively studied in women versus men. Research points to behavioral risk factors such as an overall greater dosage of voice use both at work and at home for women as compared to men (Hunter et al., 2012). Psychosocial risk factors also likely play a role. Women are significantly more likely than men to report high levels of stress (Anderson, 2010), and are more likely to develop anxiety and depression (Kessler, 1993). Given the established role of stress in the development of voice disorders, elevated levels of stress in women may be associated with elevated risk for voice disorders. Additionally, women may be more likely to seek treatment for a variety of functional disorders throughout the body. Some have attributed this to more finely attuned body awareness in females than males, as a result of interacting physiological and cultural factors (Cabrera et al., 2018).

2.3 Functional Swallowing Disorders, Globus Pharyngeus and Stress

Within the last decade, there has been an increase in research in the field of speech-language pathology into the etiology and treatment of functional swallowing disorders. This includes research into as their overlap with functional voice and upper airway disorders, including MTD, inducible laryngeal obstruction, and chronic cough. Kang et al. (2016) proposed the diagnostic term "muscle tension dysphagia" (MTDg) to describe a subset of patients with functional dysphagia whose idiopathic swallowing symptoms correlate with measurable laryngeal

tension and who show no organic etiology for dysphagia on videofluoroscopic exam. A number of studies (McGarey et al., 2018; Hamdan et al., 2019; Krasnodębska et al., 2019; Krasnodębska et al., 2021) interrogated the prevalence of breathing and swallowing symptoms in patients with a muscle tension dysphonia (MTD) diagnosis, as well as the prevalence of dysphonia and dyspnea in patients with a muscle tension dysphagia (MTDg) diagnosis and found significant overlap. Data from these studies suggest that this overlap points to a shared underlying etiology of both MTD and MTDg that has yet to be fully elucidated.

Preliminary data from Kang's (2016) study found voice therapy effective in relieving muscle tension dysphagia. The suggested mechanism of action of this therapeutic approach was the unloading of laryngeal tension. This efficacy was replicated by an overlapping group of researchers in 2021 (Kang et al.). Significant outcomes were observed not only on laryngeal EMG, but also on the EAT-10 survey. The Kang studies are preliminary in nature; the

The psychosocial history of the patients included in Kang's 2016 retrospective study were not well documented; it is impossible to know if stress contributed to the onset of MTDg in the sixty-seven patients studied. One case study described in detail in the 2021 Kang study, however, highlights the important role that stress management (and body awareness during stress) played in the success of voice therapy with a female patient with muscle tension dysphagia. Presumably, this element of her treatment was included because of the established link between stress and increased laryngeal muscle tension. Although a causal relationship between self-reported laryngeal stress response and muscle tension dysphagia has not been explored, the MTDg theoretical framework leaves room for stress as a possible contributing factor.

Stress has also been attributed as a major etiology for globus pharyngeus, a sensation reported in up to 46% of otherwise healthy individuals (Jones & Prowse, 2015; Drossman et al.,

1993; Harris et al., 1996). One study found that up to 96% of individuals who experience globus report exacerbation during times of stress (Thompson & Heaton, 1982). Although globus symptoms are equally prevalent in healthy men and women, women are more likely to seek treatment (Batch, 1988). Esophageal pathology is a common etiology of globus pharyngeus.

Additionally, the role of stress and anxiety in the onset, development, and severity of functional disorders of the esophageal phase of the swallow has been well documented (Carlson et al., 2020; Drossman, 2006). Drossman (1993) found in a survey study of sample of the general population that between 7% and 8% of the population report idiopathic dysphagia, however the role of stress is unclear.

3.0 Study Aims and Hypotheses

In this study, we primarily aimed to determine the prevalence of laryngoresponders in the general population using web-based survey methods, and to characterize the symptoms of laryngoresponsiveness. Based on pilot work in the Helou Laboratory, we hypothesized that up to 20% of people would report stress responses that would qualify them as laryngoresponders.

A second aim of the present study was to determine the likelihood of laryngeal responsiveness as a function of sex assigned at birth. Based on the female-to-male preponderance on clinical voice caseloads, we predicted that women would be more likely to self-report as laryngoresponders compared to men. The final aim of this study was to determine if laryngoresponders report higher stress levels in the past month than the general population. Given the established etiology of stressful events in the onset of FVDs and evidence of high levels of stress-reactivity in the personality profiles of individuals with FVDs, we hypothesized a positive correlation between laryngoresponder status and scores on the Perceived Stress Scale (PSS).

Past research on the prevalence of voice disorders in "men" versus "women" has generally not differentiated between sex assigned at birth and gender. The current study applied modern conventions related to sex and gender.

We intend for the data collected in this study to serve as a foundation for future research into the phenomenology of laryngoresponsiveness, specifically in regard to whether laryngoresponders are indeed more prone to develop voice disorders, as Aronson suggests.

4.0 Study Methods

4.1 Participants

Because this study aimed to determine the prevalence of laryngoresponders in the general population, people of all backgrounds were encouraged to participate. This study was fully web-based. Exclusion criteria were (1) unwillingness to disclose the information requested by the survey questions (which are fully outlined in the study's consent form, see Appendix C) and (2) being under the age of 18 years old or over the age of 65. Those under the age of 18 were excluded from this study because it included administration of the Childhood Trauma Questionnaire (not included in this thesis project), which includes questions about experiences of trauma before the age of 18. Those over 65 were excluded to somewhat control for the element of age-related changes to the larynx, known as presbylaryngeus. Although participants were screened for age at the top of the survey, the age of participants could not technically be verified given the online survey format. Participants were recruited via social media, through the platform Reddit using subreddits (topic specific pages) with stress-related topics (e.g., r/stress), flyers in the community, and through the recruitment platform Pitt+Me. Pitt+Me is a university-based research recruitment tool supported by the National Institutes of Health through Grant Number UL1 TR001857, KL2 TR001856, and/or TL1 TR001858. See Appendix B for a copy of the recruitment flyer. As compensation for participation in the study, participants were given the option to enter their name for an opportunity to receive an iPad (this required participants to provide an email address). Alternatively, participants could participate as volunteers (which would not require them to provide an email address).

4.2 Sample Size

A sample size of 1,000 participants was determined using the sample size formula proposed by Daniel (1999) for use in population prevalence studies. The margin of error was set at 3%; confidence interval at 98% to yield a critical value of normal distribution (Z-score of 2.326); expected sample proportion at an estimated 20% based on preliminary data from the Helou laboratory; and population size at the standard value, 100,000 (used in this calculation when population size is unknown). These calculations resulted in a target sample size of 953 participants.

4.3 Survey Content

Because no validated measures for establishing laryngoresponder status exist, we designed an online survey similar in structure to other physical stress response and bodily pain prevalence studies conducted in the past, for example the validated body map for pain report by the Collaborative Health Outcomes Information Registry (CHOIR) (Scherrer et al., 2021). Unlike other body perception studies in the extant literature, we ensured that the larynx was encoded in our battery of perceived vulnerable pathways. See Appendix A for the full survey content.

We created this survey using the REDCap online platform. REDCap is a secure, web-based platform designed to collect and manage data for research studies (National Institutes of Health support through Clinical and Translational Sciences Institute (CTSI) at the University of Pittsburgh (Grant Number UL1-TR-001857). This survey was accessible via link or QR scan to anyone with internet. To ensure that only human participants could access this survey, the study screened participants using the reCAPTCHA feature. Further screening included a consent form, the text of

which was presented on the first survey webpage (see Appendix C), and verification that the participant is between the ages of 18 and 65 years old.

Following consent, participants completed a demographic questionnaire that required answers for each of the following variables: age; race/ethnicity (participants could choose more than one); sex assigned at birth; gender identity; socio-economic status; highest level of education; and current primary residence as well as primary residence during their youth.

Next, participants were presented with a line-drawn figurine divided into separate regions and shown in both front and back profiles (Figure 1). Participants first selected from a checklist of major body regions to indicate those they considered to be reliably responsive to stress. Then,

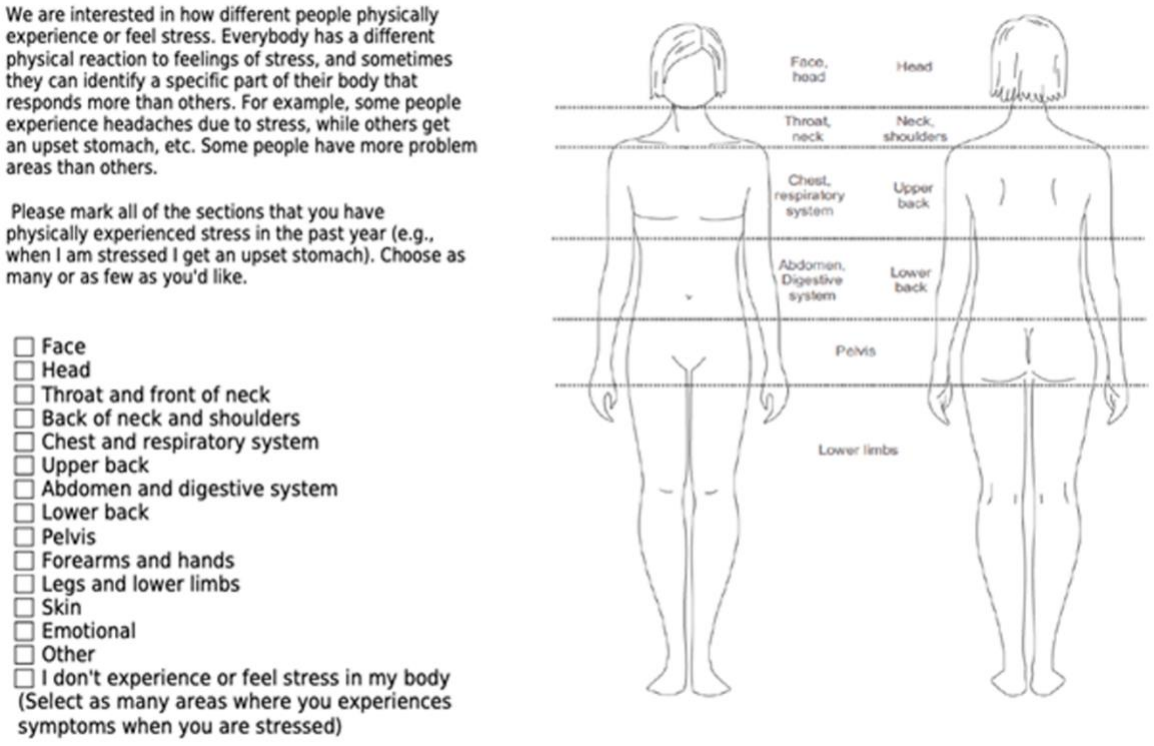

Figure 1 Figurine

for each region that a participant identified as stress-responsive, they were subsequently directed to a page (one per selected body region) that prompted them to (a) describe the symptoms they

experience in that region during times of stress (free text format); (b) define the combined severity of those symptoms on a vertical 9-point anchored scale where 1 (at the top) corresponds with mild, 5 (at the middle) with moderate, and 9 (at the bottom) corresponds with severe; and (c) identify any of their known current/active medical diagnoses that are relevant to that region.

Participants then completed the Perceived Stress Scale (PSS), a commonly used scale designed to measure one's global perceived stress in the prior one month (1988). Participants responded to each of its 14 self-report items on a 5-point likert scale (0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often and 4 = very often). Scores from the PSS range from zero to 40. A score between 0 and 13 indicates low perceived levels of stress, 14 to 26 moderate stress, and 27 to 40 high stress. This measure has been made free to the public by the American Sociological Association with permission from the author and is used verbatim in our survey. The PSS has been validated in a number of studies. A systematic review of 19 articles evaluating the validity of the PSS found well-reported internal consistency reliability, hypothesis validity and factorial validity, but found that criterion validity and test-retest reliability have rarely been assessed (Lee, 2012). Higher scores on the PSS have been found to associate with higher rates of depression, anxiety and negative affect (Ezzatti et al., 2014). PSS scores are also significantly associated with failure to quit smoking, more frequent upper respiratory infections, and life-event-elicited symptoms of depression (Cohen, 1983). The questions and response options were designed to be simple enough for anyone with at least a junior high school education to understand and complete. By asking respondents general questions about the frequency of thoughts and feelings of stress during the last month, the PSS aims to determine how "unpredictable, uncontrollable, and overloaded" participants perceive their lives to be. The questions are general and are designed to be applicable to any subpopulation (Cohen, 1998).

Next, participants were directed to an additional survey page which included the Childhood Trauma Questionnaire (Bernstein et al., 2003), which they were free to opt in or out of completing. The information gathered on this page contributed to our lab's previous preliminary investigations into the link between voice and trauma but was not used in this study.

Survey respondents were then asked what shall be defined hereafter as "the confrontation question." This question read as follows: "Some people find that stress has an impact on their larynx (their voice box) or causes changes in their voice. These symptoms might appear in the way it feels to use your voice, or the way your voice sounds, changes in how it feels to swallow, or other sensations in your throat. Do you have any of these symptoms when you are stressed?" If participants answered yes, they were then prompted, "How would you characterize these symptoms?" with the following checkbox options presented: "how it feels to use my voice," "what my voice sounds like," "changes in my swallowing," "lump or other sensation in my throat." If a participant clicked the first option, they were asked, "How does your voice FEEL different when you are stressed?" If they clicked the second option, they were asked, "How does your voice SOUND different when you are stressed?" If they clicked the third option, they were prompted, "Please describe the changes in your swallowing that you notice when you are stressed." If they chose the last option, they were asked, "What other THROAT SENSATIONS do you feel when you are stressed?" Participants were invited to enter their symptoms as free text response. For these questions as well as for that corresponding with the throat region on the figurine, we opted for free text responses so as not to limit or bias individual responses. These free text responses required manual coding, described subsequently.

The final page of the survey, titled "Final Thoughts," invited participants to share anything else they felt important for the study authors to know about their individual stress response and/or relevant medical history, or anything they forgot to share previously.

4.4 Data Reduction

All data were imported to R (v4.0.2, R Core Team, 2020) from REDCap using REDCap's secure Application Programming Interface. In total, 1,488 entries were imported. We manually inspected the data for irregularities and duplicates and will report changes to the final sample size in section 6.1. One entry appeared twice and the duplicate was removed. One observation was a lab member testing the live survey and their responses were removed. The complete data set was exported from REDCap into Excel for data reduction and coding. The following procedures were conducted by the PI and an undergraduate research assistant under the guidance of the PI's research mentor, and with input from a co-investigator (JGS) as needed to ensure consensus and reliable coding methods.

4.4.1 Creating Gender Categories

On the demographic page, participants were invited to enter their gender into a free text response box. An undergraduate research assistant supervised by Welch read through these responses and organized them into categories. For example, "non-binary" and "nonbinary" were grouped together into a single non-binary category. We grouped responses to be both as inclusive and as specific as possible. For example, a response of "genderqueer" was not changed to non-binary to respect and honor this person's gender identity. However, responses such as "male" and "man" were changed to "cisgender male."

4.4.2 Defining and Classifying Laryngoresponders

At the broadest level, we operationalized a laryngoresponder as one who reported that their anterior throat/laryngeal region is negatively impacted in feeling or function (specifically, that related to voice, swallowing, throat sensations or breathing) during times of stress. However, there were two time points at which a respondent could meet these criteria – by selecting the front-of-neck region on the figurine early in the survey, or by selecting "yes" to the confrontation question at the end of the survey. Therefore, four categories of laryngoresponder were created *a priori* and each participant was binned into one of them depending on their response patterns. Participants who selected front of neck/throat on the figurine were required to describe their symptoms in the free response box, whereas those responding "yes" to the confrontation question were invited but not required to report their symptoms in their free response; these responses *were* however vetted to eliminate any non-laryngeal responses. Examples of qualifying symptoms were any that referenced negative changes in laryngeal-region sensation or function, e.g., tight throat, sense of effort to talk or swallow, dysphonia or pitch changes; these are described in greater detail subsequently. Examples of non-qualifying symptoms were heartburn or development of blotchiness/hives on the skin in the neck region. These non-qualifying symptoms are also described in greater detail subsequently. In cases where the confrontation question was marked "yes" but no symptoms were reported in the text box, entries were not modified.

Table 1 Classifying Laryngoresponders

Laryngoresponder Type	Figurine Selection	Confrontation Question
A	+ Laryngeal Response	+ Laryngeal Response
B	- No Laryngeal Response	+ Laryngeal Response
C	+ Laryngeal Response	- No Laryngeal Response
D	+ Laryngeal Response	N/A
Nonlaryngoresponders	- No Laryngeal Response	- No Laryngeal Response

The laryngoresponder categories can be viewed at a glance in Table 1 and are described as follows. Laryngoresponders A were defined as those who selected the front of neck/throat on the figurine and responded yes to the confrontation question; they also provided qualifying symptoms in their free-text response to the figurine prompts and no non-qualifying symptoms in response to the confrontation question. Laryngoresponders B would *not* select the front of neck/throat on the figurine but would respond *yes* when confronted directly about stress's impact on the larynx and its major functions. Laryngoresponders C were defined as participants who selected the front of the neck/throat on the figurine and reported qualifying symptoms, but then responded "no" to the confrontation question. Laryngoresponders D were defined as participants who selected the front of neck/throat on the figurine and reported qualifying symptoms but did not complete the entire survey.

4.4.3 Thematic Coding of Free-Text Laryngeal Responses

We applied thematic coding analysis (Braun & Clarke, 2006) of the free text data to identify similarities, differences, and patterns in the language that participants used and the physiology that language likely represented. Based on clinical expertise of thesis committee members Helou and

Gartner-Schmidt, on preliminary data (Becker, 2019), and on widely used clinical tools like the Voice Handicap Index (Jacobson et al, 1997), we coded individuals as laryngoresponders when they reported qualifying symptoms on the front-of-neck figurine item such as throat tightness, pain, globus sensation, dysphonia/aphonia, vocal quality changes, strain, dryness, dysphagia, and other front of throat/laryngeal symptoms. Generally, we counted qualifying symptoms as any of those that are commonly reported by patients with functional voice disorders. Responses were first binned into the maximal number of cohesive and descriptive "thin-slice" categories such as those just listed, then they were thematically coded into the following four broad categories: *voice sound, voice feel, swallowing changes*, and *other throat sensations including globus.*

In the confrontation question at the end of the survey, participants who responded yes were presented directly with these four broad categories. For this question, participants first checked a yes/no option to indicate that stress "has an impact on their larynx (their voice box) or causes changes in their voice" and then were prompted to select one or more of these categories. As a reminder, participants were not required to list any symptoms to be categorized as a laryngoresponder here. However, if they responded "Yes" and then they reported only clear non-laryngeal symptoms, they were removed. Free-text data from the reported symptoms on this questionnaire was coded into the same symptom categories in order to observe patterns in the data with and without priming.

Finally, any laryngeal symptoms reported in the "Other" area on the figurine were added into the umprompted laryngoresponder data set. Laryngeal symptoms reported in the "Final Thoughts" section of the survey were added to the prompted laryngoresponder data set.

5.0 Statistical Analysis

Data were imported from Excel and analyzed using R Studio (version 4.0.2, Vienna, Austria). Descriptive statistics were obtained for all demographic variables. A logistic regression was used to determine the relationship between sex assigned at birth and laryngoresponder status. A simple linear regression was performed to determine if PSS scores were significantly different between laryngoresponders and non-laryngoresponders. A linear regression was also used to determine if PSS scores differed significantly between each type of laryngoresponder and non-laryngoresponders.

6.0 Results

6.1 Survey Completion

A total of 1,217 participants began the survey, were screened eligible to participate, and completed the demographic questionnaire. A group of 995 participants completed the entire survey including the confrontation question. Figure 2 illustrates where participants discontinued the survey, and how many participants completed each section. In the figure, "laryngeal response" refers to the confrontation question.

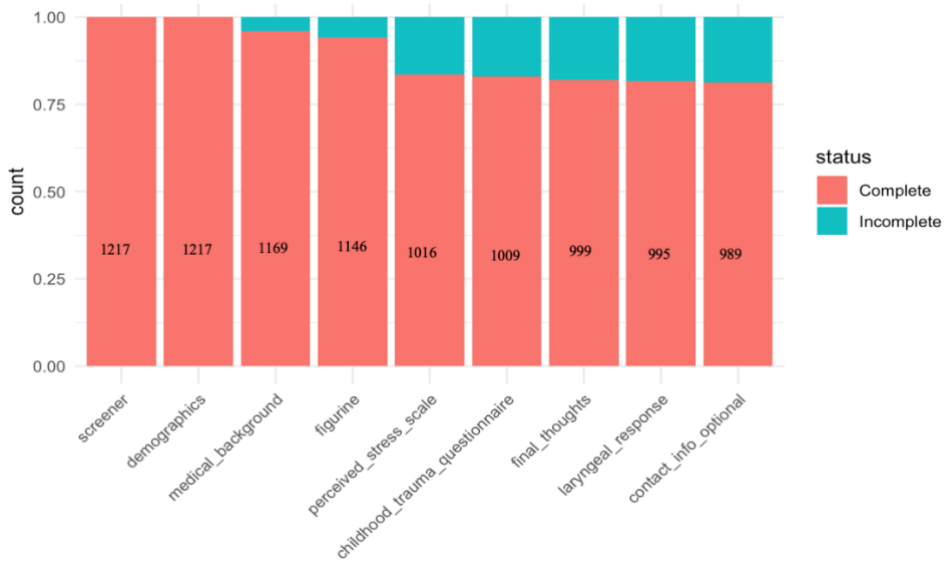

Figure 2 Complete and Incomplete Questionnaires

Of those that did not complete the survey, 7 of these participants were binned as Laryngoresponders D (they selected the front of neck/throat on the figurine and reported laryngeal symptoms but did not complete the survey).

Out of the 1,146 figurine responses, one participant's data was included twice due to a technical issue. Therefore, the official reported total of figurine responses is 1,145. Eight people took the survey twice (resulting in 16 responses for only eight people). In seven of these eight pairs, one response per pair was incomplete (participant stopped taking the survey before filling out the figurine), and therefore one of their responses had already been eliminated from analysis prior to prevalence calculation. One duplicate pair, however, included two complete but slightly different surveys completed by the same individual. The data from the survey that this individual took at an earlier date was kept and the later one removed, given the fact that when the participant took the survey the second time, they had already been primed by reading the confrontation question, which may have influenced their response on the figurine the second time they completed the survey.

6.2 Demographics

A total of 1,217 participants completed the demographics questionnaire. Age distribution for the 1,217 respondents is illustrated in Figure 3. Table 2 illustrates the ages of participants for those 1,217 respondents as well as the ages of the 995 participants who completed the entire survey. Table 3 illustrates other demographic information of participants. Participants were able to check multiple boxes when reporting their race. Table 4 illustrates a more detailed gender breakdown based on free responses.

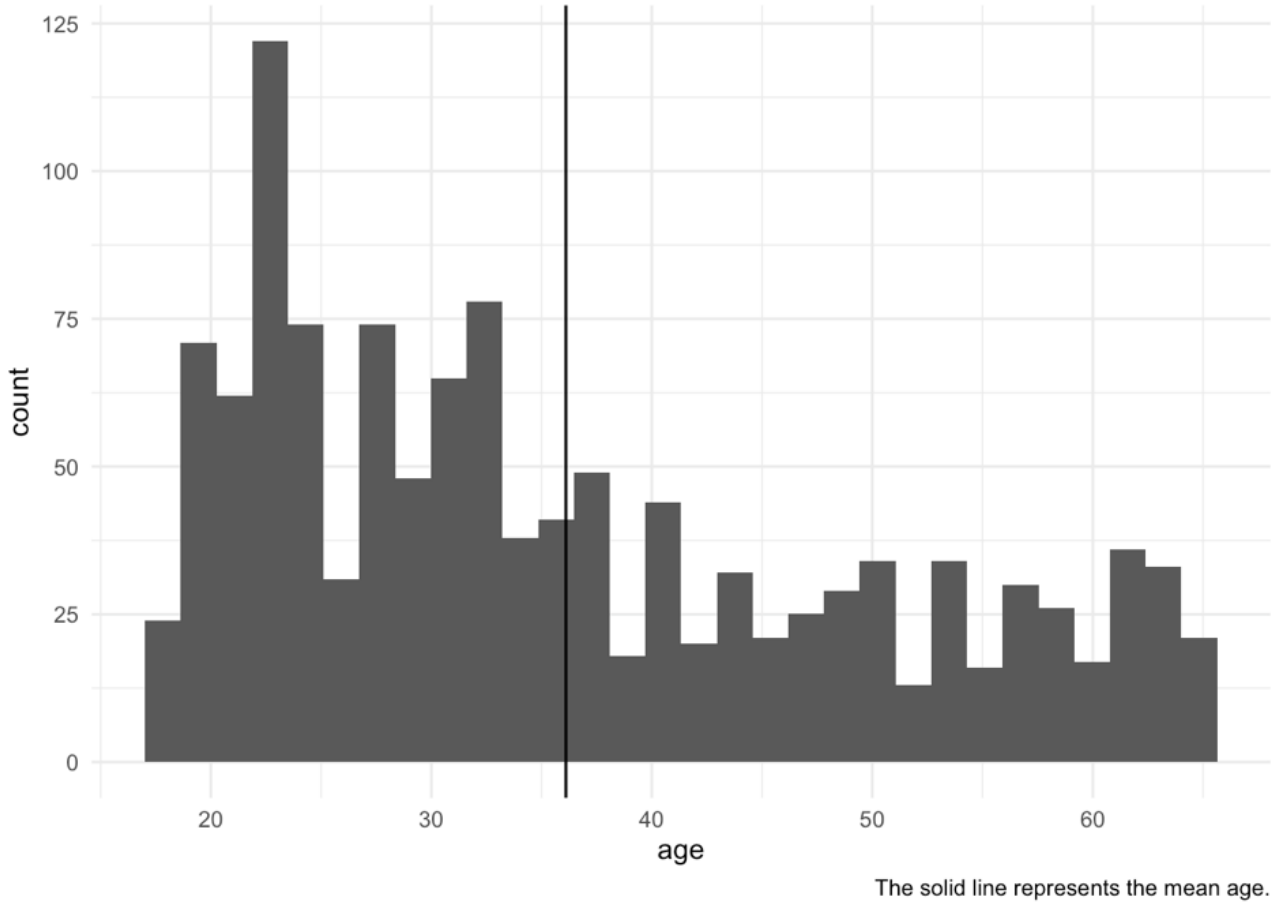

Figure 3 Distribution of Participants by Age (n=1,217)

Table 2 Age of Participants

Minimum	18.0
Maximum	65.0
M	36.1
SD	13.7

n = 1,217

Minimum	18.0
Maximum	65.0
M	36.7
SD	13.8

n = 995

Table 3 Sex Assigned at Birth, Basic Gender, Race, SES, Living Situation, Education Level

	***n* = 1,217**	**% (*n* = 1,217)**	***n* = 995**	**% (*n* = 995)**
Sex Assigned at Birth				
Male	272	22.40	214	21.50
Female	943	77.50	779	78.30
Intersex	2	0.17	2	0.20
Gender *(see figure 5.3 for full gender breakdown)*				
Cisgender	1,173	96.4	960	96.5
Gender expansive	44	3.6	35	3.5
Race				
White/Caucasian	1041	85.50	855	85.90
Hispanic	62	5.09	49	4.92
Black	70	5.75	56	5.63
Asian	75	6.16	62	6.23
Native American	8	0.66	6	0.60
Pacific Islander	4	0.33	4	0.40
Other	15	1.23	12	1.21
Prefer not to say	8	0.66	6	0.60
Socio-economic Status				
I don't know	55	4.52	45	4.52
I prefer not to say	24	1.97	19	1.91
Lower class	86	7.07	63	6.33
Middle class	488	40.10	410	41.20
Upper class	40	3.29	33	3.32
Upper-middle class	268	22.00	218	21.90
Working class	256	21.00	207	20.80
Living situation				
"I currently live in a(n) _____environment."				
Rural	118	9.70	90	9.05
Suburban	524	43.10	440	44.20
Urban	551	45.30	447	44.90
Other	16	1.31	12	1.21
I prefer not to say	8	0.66	6	0.60
"I spent my childhood in a(n) _____ environment."				
Rural	254	20.90	213	21.40
Suburban	735	60.40	605	60.80
Urban	199	16.40	157	15.80
Other	21	1.73	15	1.51
I prefer not to say	8	0.66	5	0.50
Highest level of education achieved				
No high school education	2	0.16	1	0.10
Some high school education	11	0.90	5	0.50
High school diploma	80	6.57	51	5.13
Trade or technical certificate	17	1.40	15	1.51
Some college	223	18.30	170	17.10
Associate's Degree	66	5.42	59	5.93
Bachelor's Degree	416	34.20	345	34.70
Master's Degree	299	24.60	255	25.60
Doctoral/terminal degree	100	8.22	91	9.15
I prefer not to say	3	0.25	3	0.30

Table 4 Gender Breakdown (based on free responses)

Gender	n = 1,217	% (n = 1,217)	n = 995	% (n = 995)
Cisgender Female	917	75.30	757	76.10
Cisgender Male	270	22.20	212	21.30
Non-binary	20	1.64	17	1.71
Agender	2	0.16	2	0.20
Genderqueer	2	0.16	2	0.20
Male/non-binary	2	0.16	2	0.20
Gender non-conforming female	1	0.08	1	0.10
Genderflux	1	0.08	1	0.10
Transmasculine non-binary	1	0.08	1	0.10
Two-spirit	1	0.08	0	0.00

6.3 Prevalence of Laryngoresponders

Although 1,217 participants completed the demographics portion of the survey, only the 1,145 who completed the figurine questions could be used to calculate the prevalence of self-identified laryngoresponders without the prompting that occurred later in the survey during the confrontation question. This total was used to calculate prevalence of Laryngoresponders A through D as described above. Figure 4 illustrates the point in the survey at which participants reported a qualifying laryngeal response and were classified (Laryngoresponder Type or Non-Laryngoresponder). As a reminder, Laryngoresponders A reported laryngeal response to both the figurine and confrontation question, Laryngoresponders B did not select front of neck/throat on the figurine but responded yes to the confrontation question, Laryngoresponders C reported laryngeal stress symptoms in response to the figurine but responded no to the confrontation question, and Laryngoresponders D reported a laryngeal stress response when presented with the figurine but did not complete enough of the survey to answer the confrontation question.

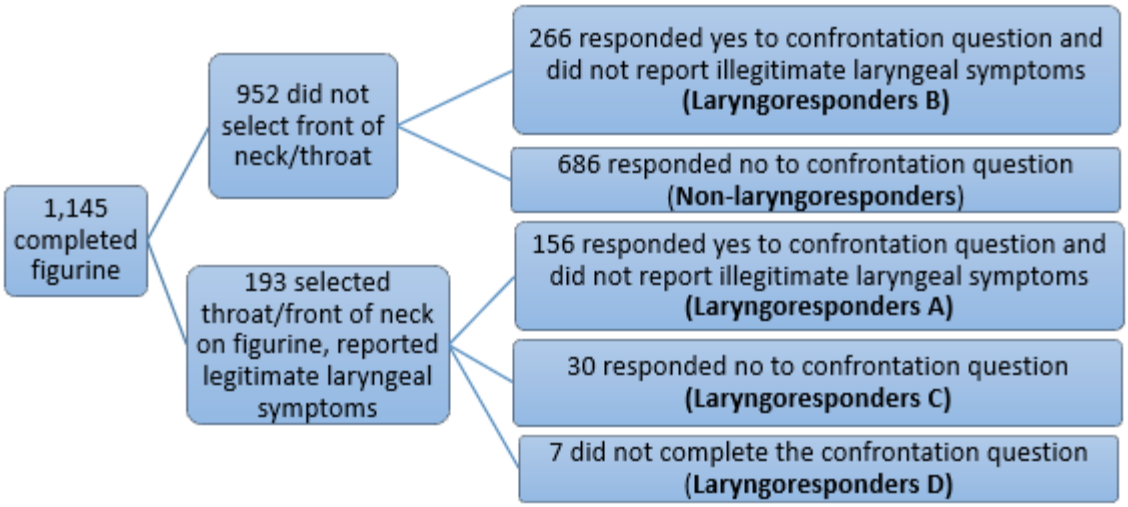

Figure 4 Laryngoresponder Classification

Table 5 illustrates the prevalence of unprompted laryngoresponders and non-laryngoresponders. These results are based solely on participants' responses to the figurine. Unprompted laryngoresponders selected the front of neck/throat and reported laryngeal symptoms. Unprompted non-laryngoresponders either did not select the front of neck/throat or did select it but reported non-laryngeal symptoms. The prevalence of unprompted laryngoresponders was 16.86% of our sample.

Table 5 Unprompted Laryngoresponders (n=1,145)

Responder Type	n = 1,145	%
Unprompted Laryngoresponders	**193**	**16.86**
Unprompted Non- Laryngoresponder	952	83.14

995 participants completed the entire survey. These participants included Laryngoresponders type A, B and C as well as Non-Laryngoresponders. The total maximum prevalence of

laryngoresponders was 45.42%, combining all Laryngoresponder types that completed the survey (prompted and unprompted) (see Table 6).

Table 6 Prompted Laryngoresponders (n=995)

Responder Type	n = 995	%
Laryngoresponder A	156	15.67
Laryngoresponder B	266	26.73
Laryngoresponder C	30	3.02
Prompted Laryngoresponders	**452**	**45.42**
Prompted Non- Laryngoresponders	543	54.57

6.4 Preliminary Symptomatology Results

As a reminder, participants listed and described their laryngeal symptoms at two points in time on the survey: (1) in response to the figurine early in the survey, at which point they wrote whatever came to mind; and (2) in response to the confrontation question at the very end of the survey, at which point they were specifically prompted to respond to each of four broad categories: *voice sound, voice feel, swallowing changes,* and *other throat sensations including globus.* All reported symptoms underwent manual thematic coding before being imported into R to determine the prevalence of the four types of laryngeal symptoms (see Figure 5).

The broad category *voice sound* was subdivided into the maximal number of cohesive and descriptive "thin-slice" categories: dysphonia/aphonia, higher pitch, lower pitch, louder, quieter, weaker sounding, strained (or pushed, forced) sounding, shaky sounding, inflection changes, and "other voice sound changes." The broad category *voice feel* was subdivided into the following

"thin-slice" categories: hoarseness, scratchiness (this included glottal fry and "raspiness"), weakness, tightness when using the voice, strain, effort, shakiness when using the voice, difficulty with projection, need to clear the throat to speak, lack of control over the voice, vocal fatigue, general difficulty speaking, and a "dry" voice feel. A few responses which could not be binned into these categories were put in an "other voice feel" category. *Voice-feel* differed from the *other throat sensations* category in that symptoms were task-specific; participants indicated that they observed them during voice use rather than at rest. As the current study was focused on vocal symptoms, the category *swallowing changes* was not broken down further in the thematic coding process. The broad category *other throat sensations including globus* was broken down into the following categories: globus, general tightness and tension, constriction, sore throat, dryness, pressure, heat, heaviness, burning, laryngopharyngeal reflux symptoms, choking/gagging, throat clearing, cough, and changes to breathing (felt specifically in the throat).

Sometimes, participants reported symptoms in non-corresponding places. For example, a few people reported swallowing symptoms in general throat sensations. Because all thematic coding was done manually in Excel before being imported into R, we were able to correct these types of errors and place symptoms into their appropriate bins. If a symptom could theoretically be categorized in more than one bin, such as "scratchiness," we left it in the place it was reported (if scratchiness was reported as sound, it stayed there; if it was reported as feel, it stayed there.)

Of the 193 participants who selected the front of neck/throat on the figurine (out of 1,145 who responded to the figurine), 11 people reported *voice sound* symptoms, 14 reported *voice feel* symptoms, 22 reported *swallowing* symptoms, and 181 reported symptoms relating to *other throat sensations*. Of the 422 participants who responded yes to the confrontation question (out of 995 who responded to the confrontation question), 204 participants reported voice sound symptoms,

136 reported voice feel symptoms, 160 reported swallowing changes, and 170 reported globus and/or other throat sensations. These results are illustrated in Figure 5.

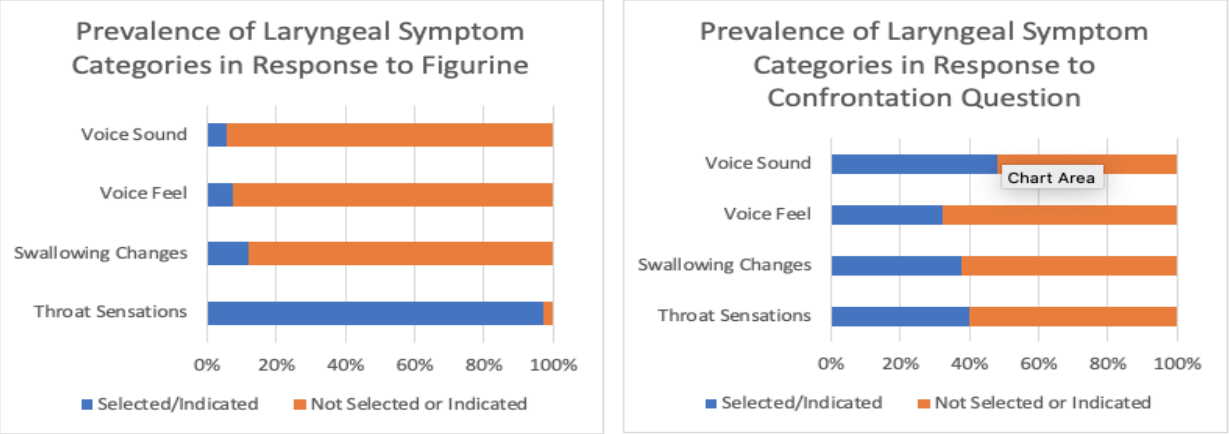

Figure 5 Prevalence of Laryngeal Symptom Categories

Table 7 parses each of the four broad categories further into their constituent symptoms.

Table 7 Free Response Symptoms

	Symptom	*Figurine* Total (*n*=193)	Percentage	*Confrontation* Total (*n* = 422)	Percentage
Voice Sound	Dysphonia/aphonia	9	4.66	60	14.22
	Pitch increase	0	0.00	74	17.54
	Pitch decrease	0	0.00	31	7.35
	Louder	0	0.00	19	4.49
	Quieter	0	0.00	26	6.16
	Shaky sounding	1	0.52	32	7.58
	Inflection changes	1	0.52	4	0.95
	Weaker sounding	0	0.00	6	1.42
	Strained/pushed/forced sounding	0	0.00	16	3.79
	Other voice sound	1	0.52	48	11.37
	Vocal weakness	0	0.00	11	2.61
Voice Feel	Tightness when talking	3	1.55	22	5.21
	Vocal strain	1	0.52	15	3.55
	Scratchiness/glottal fry	0	0.00	17	4.03
	Shaky voice feel	0	0.00	10	2.37
	Projection difficulty/changes	0	0.00	7	1.66
	Lack of voice control and voice "cracking"	1	0.52	20	4.74
	Need to clear throat to use voice	0	0.00	3	0.71
	Hoarseness	1	0.52	6	1.42
	Vocal effort	0	0.00	13	3.08
	Vocal fatigue	1	0.52	0	0.00
	Dry voice feel	0	0.00	6	1.42
	Difficulty speaking/inability to speak	7	3.63	36	8.53
	Pain with talking	0	0.00	8	1.90
	Other voice feel	0	0.00	32	7.58
	Swallowing changes	22	11.40	160	37.91
Front of Neck and Throat Sensations	General tension/tightness	101	52.33	65	15.40
	Closing/constriction	27	13.99	22	5.21
	Front of neck muscle pain/discomfort	23	11.92	0	0.00
	Sore throat	33	17.10	24	5.71
	Dryness	15	8.06	38	9.00
	"Scratchy" throat	12	6.22	0	0.00
	Globus	27	13.99	121	28.67
	Choking/gagging feeling	9	4.84	5	1.18
	Heaviness	5	2.59	5	1.18
	Heat	4	2.07	0	0.000
	Burning	0	0.00	5	1.18
	Pressure	4	2.07	5	1.18
	Laryngopharyngeal Reflux	7	3.63	5	1.18
	Breathing difficulties/changes	13	6.74	14	3.32
	Cough and throat clearing	5	2.59	4	0.95
	Sensory flashback to past trauma	3	1.55	0	0.00
	Other throat sensations	31	16.06	45	10.66

6.4.1 Eliminating Non-Laryngeal Symptoms

Some individuals who clicked the front of neck/throat region on the figurine or responded yes to the confrontation question were not categorized as laryngoresponders (or were categorized as Type B instead of A, Type C instead of A, etc.) because the only symptoms they listed indicated a non-laryngeal response. Some of these responses were very clearly not laryngeal (or related to voice, swallowing, or breathing) in nature. For instance, some individuals reported susceptibility to blotchiness, hives, or other skin irritation in response to stress. If participants identified front of neck/throat as a vulnerable pathway but listed skin symptoms, they were re-coded during the data reduction/preparation phase as dermatological responders and therefore were categorized as "non-laryngoresponders". Other responses that disqualified participants from the laryngoresponder group included symptoms which explicitly named other parts of the body, for instance "back of neck pain," "dry mouth," "teeth grinding," or "jaw clenching." Respondents who selected front of neck/throat on the figurine but did not enter any symptoms or wrote "N/A" were labeled non-laryngoresponders because they did not provide enough information for the symptom to be reliably categorized. Finally, there were a handful of participants who selected front of neck/throat and then wrote in the symptom response textbox something akin to, "Sorry I did not mean to click this;" these participants were not included as laryngoresponders in the survey results.

Although some symptom responses such as the ones previously listed were clearly not laryngeal in nature, others required some deliberation among the study authors. Whenever there was uncertainty about a symptom and whether it qualified as laryngeal, we discussed that symptom to achieve consensus. The following symptoms (paraphrased into categories) were reported as front of neck/throat symptoms on the figurine but were deemed non-laryngeal via author consensus:

- Nausea and heartburn: These are physiological events in the digestive system and are therefore not laryngeal by nature.
- Lymph node swelling attributed to acne scarring
- Heightened awareness of pulse or blood pressure in neck: Although this sensation may be felt in the neck, it is a result of cardiovascular activity.
- Hiccups: Hiccups can be felt in many areas of the body but are diaphragmatic spasms by physiological definition, not laryngospasms.
- Speech, language and cognition changes: There were multiple responses which involved reports of stuttering, word-finding difficulties, changes to speech rate, "disjointed" speech, "rambling," or difficulty formulating sentences. These were determined to be non-laryngeal in nature for the purposes of this study.
- Emotional qualifiers and analogies: A handful of participants wrote that they "sound annoyed" or "sound sad" or sound "like [they are] in pain" when stressed. These descriptions were deemed emotional responses to stress rather than laryngeal responses.

6.5 Severity of Laryngeal Symptoms

Severity ratings of all unprompted physical stress symptoms were reported on a 9-point scale, with 1 representing mild, 5 moderate, and 9 severe. The reported severity ratings of unprompted laryngoresponders ranged from 1 to 9, with a mode of 5. Within this group, 106 (54.92%) of participants reported a laryngeal symptom severity rating of 5 (moderate) or higher (more severe). These unprompted laryngoresponders who reported moderate to severe symptoms made up 9.26% of the 1,145 participants who responded to the figurine. Severity ratings are reported in Table 8.

Table 8 Severity Ratings of Laryngoresponders

Minimum	1
Maximum	9
Mode	5
Reports of 5 and above	54.92%
Reports of 4 and below	45.08%

6.6 Laryngoresponder Status as a Function of Sex Assigned at Birth

We hypothesized that being assigned female at birth would be a significant predictor of laryngoresponder status. We performed a logistic regression to determine the effect of sex assigned at birth on the likelihood that someone will be a laryngoresponder versus a non-laryngoresponder (including both unprompted and prompted laryngoresponders). The logistic regression model was not statistically significant, thus no relationship was identified between sex assigned at birth and laryngoresponder status. These results are illustrated in Figure 6, where LR “0” corresponds with non-laryngoresponders and LR “1” corresponds with laryngoresponders. (Within the unprompted

laryngoresponder group, 79.69% of participants were assigned female at birth. 75.3% of the 1,217 participants who filled out the demographic survey were assigned female at birth.)

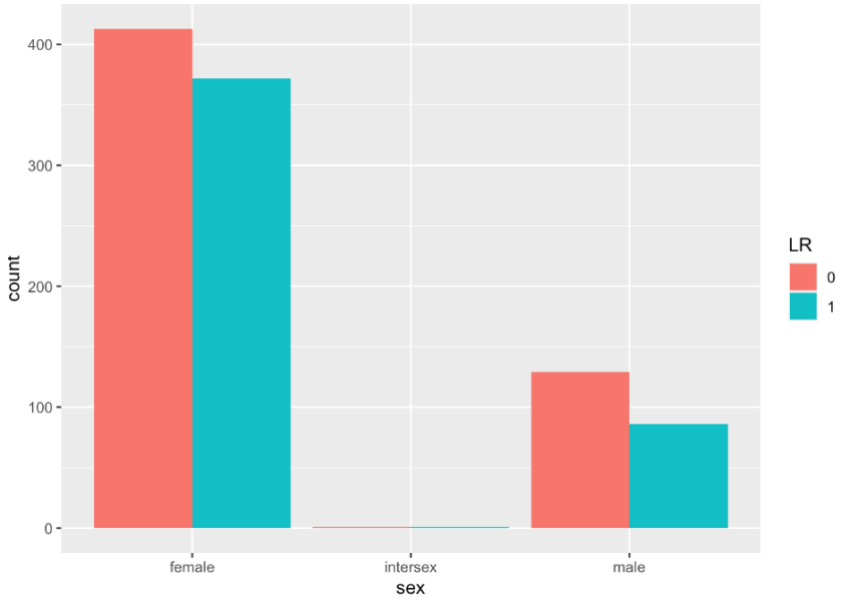

Figure 6 Laryngoresponders by Sex Assigned at Birth (*n* = 995)

6.7 PSS Score as a Function of Laryngoresponsiveness

The mean PSS score for Non-laryngoresponders was 17.7 and the mean score for laryngoresponders across types A, B, C and D was 20.9. The regression coefficient (β = 3.2, 95% CI [2.3, 4.1]) indicated that Laryngoresponder status would correspond with a PSS score of, on average, 3.2 points? higher than that of a non-laryngoresponder. This difference is statistically significant ($p < .001$). These results indicate that laryngoresponder status accounts for 4.91% of the variance between PSS scores. This model was significant, F(1, 998) = 50.99. Effect size (r) = 0.2241.

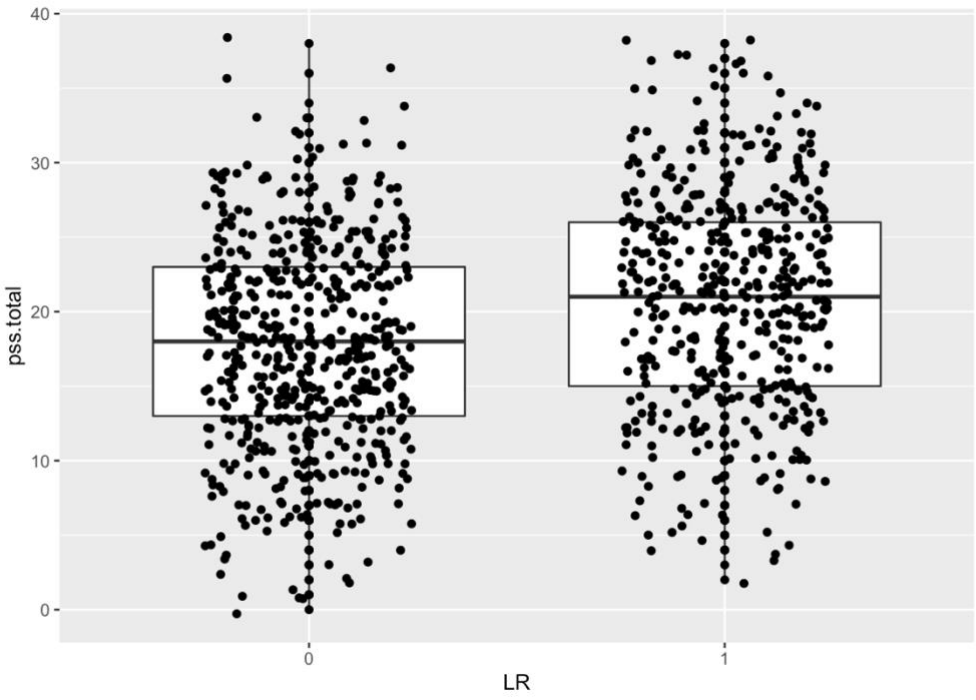

Figure 7 PSS Scores of LRs vs. Non-LRs

6.8 PSS Score as a Function of Laryngoresponder Type

The mean PSS score for each Laryngoresponder subgroup, illustrated in Figure 6, were as follows: A= 22.4; B =20.0; and C = 20.8 The regression coefficient (β = 4.79, 95% CI [3.54, 6.03]) indicated that Laryngoresponder A status would correspond with a PSS score of, on average, 4.79 points higher than that of a non-laryngoresponder. The regression coefficient (β = 2.44, 95% CI [1.39, 3.49]) indicated that a Laryngoresponder B status would correspond with a PSS score of, on average, 2.44 higher than a non-laryngoresponder. The regression coefficient (β = 2.59, 95% CI [0.31, 4.86]) indicated that a Laryngoresponder C status would correspond with a PSS score of, on average, 2.59 higher than a non-laryngoresponder. These differences are statistically significant (p < .001). These results indicate that laryngoresponder type accounts for 6.04% of the variance in

PSS scores in comparison to non-laryngoresponders. This model was significant, F(3, 978) = 21.3. Effect size (r) = 0.2476.

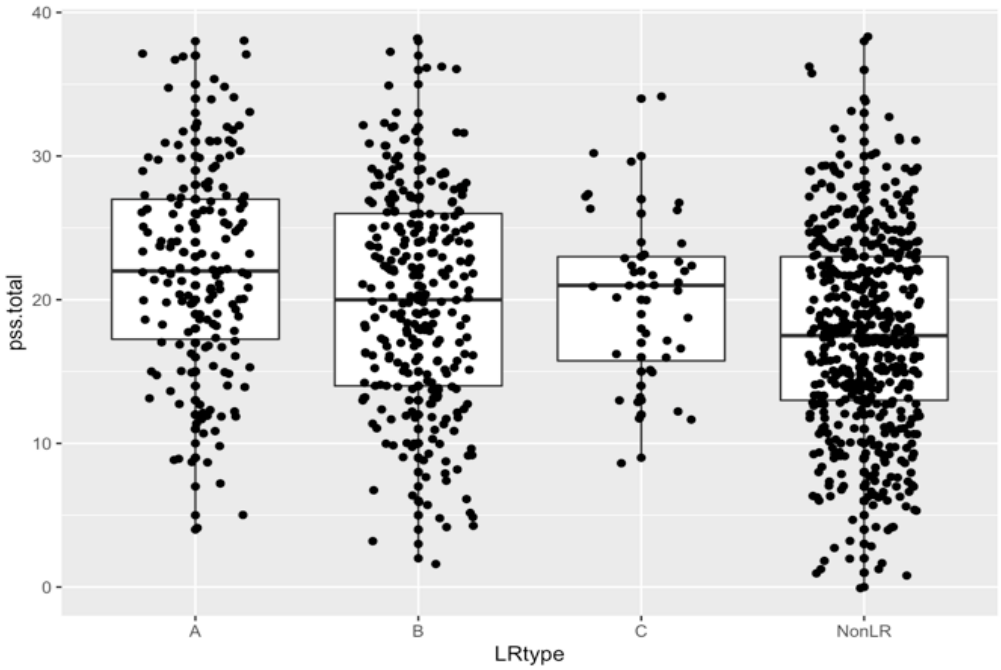

Figure 8 PSS by Laryngoresponder Type

7.0 Discussion

7.1 Prevalence of Laryngoresponders in a Non-Treatment Seeking Population

Results of the current study indicate a prevalence of laryngoresponders in the general population of up to 45.42%. This number is notable when compared with the prevalence of other physical stress responses reported in other surveys like *Stress in America* (Anderson et al., 2010), which indicated upset stomach as a stress response in 26% of (prompted) survey respondents and general muscle tension in 23%. However, a prevalence of nearly half the surveyed population would suggest that laryngoresponsiveness is widespread. Clearly our estimate was heavily influenced by us directly confronting participants with questions about their "voicebox" at the end of the survey. The substantially lower prevalence of only those people who independently recalled qualifying laryngeal symptoms without us prompting them, or 16.86% of the 1145 respondents who completed the figurine, maps more closely onto previous studies by this group (Helou et al., 2013), that some individuals are disproportionately prone to laryngeal stress response than others. This prevalence number also aligns with our hypothesis based on preliminary data of a similar prevalence (20.7) in a smaller sample size (Becker et al., 2019).

The most frequently reported *voice sound* symptoms in laryngoresponders were increase in pitch (17.54% in response to the confrontation question), dysphonia/aphonia (4.66% in response to the figurine and 14.22% to the confrontation question), and shakiness (7.58% to confrontation question). The most reported *voice feel* symptoms were difficulty speaking/inability to speak, tightness when talking and lack of voice control (8.53%, 5.21% and 4.74% respectively, in response to the confrontation question).

According to our data, there is a notably wide variety in laryngoresponder experience. This is evidenced by similar prevalence of seemingly opposite symptoms. Although 17.54% reported an increase in pitch in response to the confrontation question, 7.35% reported a *decrease* in pitch. Prevalence of louder voice and quieter voice as stress responses were also similar (4.49% and 6.16%, respectively), and 11.37% of *voice sound* symptoms were individual enough that they were binned as *other voice sound* symptoms. Generally, *voice feel* symptoms were widely variable as well; 7.58% of laryngoresponders were characterized as *other voice feel,* more than almost any other *voice feel* category. The prevalence of almost all *voice feel* symptoms was relatively equally distributed.

This wide variety in laryngoresponder *voice sound* symptoms is not surprising considering inconsistent evidence regarding the acoustic properties of the voice under stress versus at baseline (Giddens et al., 2013). Variability in *voice feel* symptoms is also unsurprising based on past research of common voice complaints as well as clinical reports.

Prevalence of globus sensation in the current sample (13.99% unprompted and 28.67% prompted) supports previous research regarding this symptom's prevalence. Similarly, the prevalence of swallowing changes in our data (11.40% unprompted) aligns with past survey research indicating a prevalence of idiopathic dysphagia (also unprompted in the Drossman et al. 1993 study) of around 8%. Significantly more prompted laryngoresponders reported swallowing changes (37.91%) than unprompted, which is likely a result of the nature of survey research.

7.2 Impact of Priming on Prevalence of Laryngeal Response

There was a marked difference in prevalence of self-reported laryngeal stress response when participants filled out the figurine unprompted versus when they answered the confrontation question. A total of 422 out of 995 participants answered yes to the confrontation question while only 193 out of 1,145 selected the front of neck/throat on the figurine (and reported laryngeal symptoms). This discrepancy may reflect people's general lack of self-awareness of their bodies' responses to stress. However, it is also possible that asking participants directly about laryngeal response inflated prevalence results, which would track with what we observe clinically during intake and therapy for voice disorders. Thus, most conservative readers of this data may choose to classify only those who selected the front of neck/throat on the figurine *and* responded yes to the confrontation question (Laryngoresponder Type A) as "true" laryngoresponders.

Although overall more people responded yes to the confrontation question than selected the neck/throat region in the figurine, not all reported symptoms followed the same trend. We do not see a higher prevalence of every symptom in response to the confrontation question than we see on the figurine. For those classified as laryngoresponders based on the figurine (unprompted), the vast majority of participants (roughly 97%) reported muscular tension, throat soreness, and other throat sensations. A notable 11.4% reported *swallowing changes*. Only 7.25% and 6.22% reported *voice feel* and *voice sound* symptoms, respectively. Asked directly, far fewer (about 40%) of participants reported throat sensations, while 48% reported *voice sound* changes, 32% *voice feel* and 37.91% *swallowing changes*. This reflects what we often see in the clinical setting, that when patients are asked more targeted questions, the language they use to describe their symptomology becomes more refined.

It is possible that priming participants with not just body *regions*, but *functions* of those regions led to higher symptom reporting rates. The chest area on the figurine, for instance, was labeled "Chest and Respiratory System," and the abdomen was labeled "Abdomen and Digestive System." The front of neck and throat, however, was not labeled with words like "voice" or "swallowing" on the figurine; it was simply titled "front of neck/throat." This area's proximity to regions like the back of neck and trapezius muscle, highly and repeatedly responsive to cognitive stress (Willman & Bolmont, 2012), may have also primed participants to be thinking more about muscular discomfort than about functional deficits. Although it is impossible to confirm or deny whether labeling the front of neck/throat with function words on the figurine would have impacted symptom data, future research into prevalence of vulnerable pathways may benefit from doing so. Further research into how people respond to various question types may also be beneficial.

7.3 Sex Assigned at Birth and Laryngoresponsiveness

We hypothesized that those assigned female at birth would be more likely than those assigned male at birth to self-identify as laryngoresponders based on past evidence indicating a disproportionate number of women compared to men with functional voice disorders (Lyberg-Ahlander & Rydell, 2019; Roy, 2004; Roy, 2005). However, no statistic relationship was found in our study between sex assigned at birth and the likelihood that one would self-identify as a laryngoresponder. Although our data indicates that assigned-at-birth females are not more likely than those assigned male or intersex to self-identify as laryngoresponders, it is possible that historically greater incidence of higher stress levels in women than men (Anderson, 2010) as well as higher rates of anxiety and depression diagnosis in women than in men (Kessler, 1993) may put

assigned-at-birth females at higher risk for stress-induced functional voice than assigned-at-birth males when laryngeal symptoms do arise. It is also possible that those assigned female at birth are more likely than others to seek help for laryngeal symptoms given the documented higher vocal demands on women both at work and at home (Hunter et al., 2012). Additionally, it could be that although those assigned female at birth are simply more likely to seek *help* for a voice problem (Cabrera et al., 2018), sex representation among voice center referrals does not necessarily represent the distribution of stress-induced laryngeal *symptoms* across the sexes. In short, perhaps it is not prevalence of laryngeal symptoms but rather a difference in how assigned-at-birth females react to those symptoms versus assigned-at-birth males that accounts for the functional voice disorder gender preponderance. Finally, there may be value in performing the analysis with only those people classified as laryngoresponders based on the figurine prompt (~17% of 1,145 participants) rather than based on the maximum prevalence estimate of laryngoresponders (~45%), or only with those whose severity of laryngeal symptoms was moderate to severe (9.25% of our sample).

7.4 Stress Levels in Laryngoresponders

Data from the current study supports our hypothesis that laryngoresponders would report higher levels of stress on the Perceived Stress Scale. Mean scores of laryngoresponders on the PSS were 3.2 higher than mean scores of non-laryngoresponders. The effect size varied slightly across laryngoresponder groups, with the Type A cohort averaging 4.8 points higher than the average for non-laryngoresponders. Without controlling for any other features of the respondent, laryngoresponder type accounted for 6.1% of the variance in PSS scores in comparison to non-

laryngoresponders. Considering that there are likely scores of other variables that influence one's perceived stress over the past month, the fact that laryngoresponder type can account for 6% this variation is not negligible. While these group-level differences are not particularly high-magnitude and might not translate to clinically meaningful differences, they generally align with previously discussed research that showed higher self-reported stress levels in MTD patients than in healthy normal (Van Houte et al., 2011). Additionally, these findings may relate to previous reports of increased stress-reactivity in the personalities of patients with functional voice disorders (Roy et al., 2010; Dietrich & Verdolini Abbott, 2012; van Mersbergen et al., 2008), though we did not set out to study a voice-impaired cohort here.

7.5 Limitations

Although this study provides useful information about the prevalence of laryngoresponders and their reported symptoms, the sample is not an accurate representation of the US population. Despite recruitment efforts, the survey participants were mostly female (75.4%). According to national census data, the US population is 50.8% female. (U.S. Census Bureau, 2019). Additionally, 85.5% of survey participants were white. This is not quite an accurate representation of the US population (which is 76.3% white according to census data). Black, Asian, and Hispanic participants were underrepresented in our sample. Although the mean age of our participants was about 36 years (and the mean age of a US citizen was 38.4 in 2019 according to the U.S. Census Bureau), the current study included far more participants in their early to mid-twenties than any other age group. By contrast, the lower half of the US population age groups are evenly distributed, with close to equal populations in their twenties, thirties, and forties. This may reflect past evidence

that younger individuals (< 25) are more likely than older adults to engage in computer-based survey research (Larson et al., 2011). Our sample also consisted of more individuals that identified as upper class and upper-middle class and less individuals who identified as working or lower class than is seen in the distribution of the United States population (U.S. Census Bureau, 2019). Individuals with lower SES may have been limited in their computer/internet access, which could have prevented them from knowing about or participating in our study. Finally, our sample had an overall higher educational level than the general US population. Roughly 25% of our sample reported having a master's degree and 10% a doctorate or terminal degree. Recent census data indicates that only 10% of the US population (over age 25) has a master's degree and only 2% a doctorate. The disproportionately high educational attainment of our sample may have impacted results in many ways, including factors of health literacy, self-awareness, and prior education about the physiological impacts of stress.

Another limitation of our study is simply that it was an online survey. There is an inherent lack of control in a survey study (Rickards et al., 2012; Coughlan et al., 2009). The environment and circumstance in which participants take an online survey cannot be controlled. There is no way to ensure that respondents are taking the time to thoughtfully respond to questions. Participants may withhold information that they find embarrassing while disclosing other information in order to portray themselves in the best light. They may even give inaccurate answers to "help" with whatever they may perceive to be the researcher's intent. It is a common suspicion among researchers that people willing to participate in a survey are likely to have certain personality traits, an interest in research, etc.; this may inherently bias the sample. In our case, for example, we cannot account for the possibility that people who are willing to take a survey study could be more or less likely to report high stress levels, or be more or less likely to have multiple

health problems, mental health disorders, etc. All these potential participant traits and behaviors are confounding variable which may have impacted the validity of our data. Although we did our best to manage these inherent limitations with our recruitment methods, data quality control, and carefully worded survey content (reviewed by multiple authors and contributors), they are limitations which should not be completely ignored.

Another possible limitation of this study in its current form was the decision not to require free response symptoms following the confrontation question. There is an inherent inconsistency in including participants as (prompted) laryngoresponders when they responded "Yes" to the confrontation question but provided no symptoms, but removing them if they responded "Yes" and then only reported non-laryngeal symptoms. Although these participants only made up a small subset of our sample, they represent a flaw in our study design only seen in hindsight. Similarly, it may have been useful to prompt for severity ratings at the confrontation question.

One other limitation of our study relates to the nature of globus and dysphagia symptoms. Globus pharyngeus and perception of pharyngeal dysphagia can be caused by supraclavicular pathology or dysfunction such as achalasia or esophageal motility disorders. We did not have access to the medical records of our survey participants, nor did we perform instrumental laryngeal or swallowing exams on any of them. Therefore, we cannot conclusively report that globus or changes in swallowing during times of stress were directly caused by laryngeal dysfunction in our participants. We can, however, state that a number of participants in our study have perceived an increase in globus sensation and/or swallowing changes during times of stress in the past month, and that deglutition inherently involves superior and anterior movement of the larynx. Therefore, although the relationship of laryngeal stress response with swallowing changes and globus

pharyngeus remains relatively unclear, our preliminary data provides directions for further research.

Despite the attempts of the study authors to use clear concise language, survey participants may have interpreted questions differently from one another. We purposefully elected not to define "stress" for participants, instead allowing each respondent to interpret and apply the term in the most natural and logical way for them. We wanted the survey to conjure the notion of stress and invite participants to share how their body tended to respond in moments of stress. Some participants' descriptions of their symptoms clearly pointed to more acute emotional reactions, such as crying. This lack of specificity is certainly a limitation of our study, and future work in this domain should begin to more tightly control for terminology.

7.6 Clinical and Research Significance

The results of this study suggest a high prevalence of *prompted* laryngoresponders and a relative minority of *unprompted* laryngoresponders in the general population. It also empirically supports a relationship between stress and certain vocal/throat/front of neck symptoms. By Aronson's *laryngoresponder* definition, individuals in the unprompted *voice feel* and *voice sound* group (roughly 7% and 6%) are likely to present at a voice center with a functional voice disorder at some point in their life. By the same principle, one might expect the unprompted *swallowing changes* group (roughly 11%) to present clinically with a functional swallowing disorder, however our evidence is preliminary and quite limited in the area of swallowing and should be viewed as a direction for future inquiry into the relationship between stress and functional swallowing disorders rather than a clear statistical relationship. It is possible that those unprompted

laryngoresponders reporting moderate to severe laryngeal stress symptoms (roughly 9% of the sample), are most likely to present with a functional laryngeal disorder; this is, similarly, an area for potential further study.

As previously discussed, the tenets of patient-centered care point to the importance of generally well-informed healthcare providers. This extends to understanding the role of stress in the development of a wide range of health problems, including voice disorders. Considering our results, it seems a worthy use of time and effort for providers to inquire about physical stress symptoms in their patients using a systematic approach and validated instruments, and to consider a referral to a voice center if laryngeal symptoms of stress are having a noticeable impact.

The language that participants used to report their laryngeal stress symptoms in this study could potentially lay the foundation for a patient-reported outcome measure aimed specifically at indexing the relationship between voice/larynx and stress. For example, patients might be prompted, "My voice feels 'tight' when I talk," and then prompted to select a number on a rating scale for both "all the time" or "when I'm stressed." Although the Voice Handicap Index uses similar language, it does not differentiate ratings between situations of stress and a patient's baseline. A questionnaire like this may be useful for working with patients for whom stress plays a major role in the fluctuation of symptoms. Clinicians may find it helpful for efficient interviewing, formation of clinical hypotheses, and creating patient goals and self-awareness.

Some of the most reported symptoms in the current study are not represented in the most common questionnaires used in voice clinics (the VHI for example). The data from our study indicate that it may be valuable to add some of these symptoms into the language we use in a patient interview when asking about stress, especially tightness in the muscles in and around the

larynx (at rest and/or specifically when talking), changes in pitch and intensity, shakiness, lack of control, general difficulty speaking/an inability to speak.

When broaching the topic of stress with voice patients, the authors of this study have found it difficult in their own clinical practice to avoid the implication that the patient's problem is "all in their head." Patients who have seen multiple specialists without receiving a diagnosis can be naturally defensive about possible accusations of hypochondria or general mental instability. We hope that clinicians will utilize the data from this study to assure patients that laryngeal stress response is quite common, and that stress playing a role in their legitimate medical problems does not make them "crazy."

7.7 Future Research

We intend to further analyze data from this study to determine common areas of crossover between the larynx and other vulnerable pathways to stress, e.g., to determine if laryngoresponders also tend to be headache or gut responders, or if they report more vulnerable body regions than do non-laryngoresponders overall. We will also examine the relationship between self-report of childhood trauma and laryngoresponder status. We also intend to analyze follow-up data from the ~1/4 of our cohort who completed the figurine and confrontation questions a second time, to determine intra-responder reliability of laryngoresponder status. Other future directions may include thematic coding of swallowing data from this study. Swallowing changes may be broken down further into difficulty swallowing, swallowing frequency, etc. This may prove clinically significant in the study of muscle tension dysphagia.

A major next step in this line of work will involve recruiting cohorts of self-identified laryngoresponders and nonlaryngoresponders using classification methods described here, then investigating whether groups differ in terms of their short-term physiological response to experimental stressors. If this is the case, future research on the pathogenesis of voice disorders will benefit from more sensitive and selective recruitment techniques (and in turn, fewer wasted resources) than the current approach of taking all-comers from the general population. This study suggests that 55-83% of the general population might be nonlaryngoresponders, which would substantially impact the effect sizes in voice-stress psychophysiology work.

Later iterations of this kind of research may benefit from more interactive technology, perhaps a clickable figurine or a specialized operating system application. It will also be improved by standardized language regarding stress, body area, and functional systems associated with each area.

Finally, future studies might follow laryngoresponders longitudinally to determine whether those with vocal symptoms are more likely to be diagnosed with a voice disorder in the future. To further enrich this program of research, given the breadth of research on the link between personality and voice disorders (especially neuroticism and extroversion), there may be value in establishing common personality traits among laryngoresponders.

Appendix A Full Survey Content

See attached.

Appendix B Recruitment Materials

Laryngoresponders – Website/Social Media Script

Our laboratory at the University of Pittsburgh is conducting a research study to measure how people experience stress. If you are between the ages of 18-65 years old, you are eligible to participate! The study involves filling out some questionnaires about how stress manifests itself in your body. Depending on your unique stress response, the survey could take as little as 5 minutes or up to approximately 15 minutes to complete. To compensate you for completing the survey, you can choose to have your name entered for the opportunity to receive an iPad. You may also elect to do the survey as a volunteer without compensation (i.e., without having your name entered to receive an iPad).

Some respondents may be invited to fill out the survey a second time at a later date, and will again have the opportunity to receive compensation.

If you'd like to participate, please click this link:
https://www.ctsiredcap.pitt.edu/redcap/surveys/?s=YEFFMMK9PF

Laryngoresponders – Email Script

Hello [name],

We are conducting a research study in our laboratory at the University of Pittsburgh. We are investigating how people experience stress. We are seeking subjects between the ages of 18-65 years old. If you would be interested in participating, please let us know! The study would require that you fill out a few questionnaires. Depending on your unique stress response, the survey could take as little as 5 minutes or up to approximately 15 minutes to complete. To compensate you for completing the survey, you can choose to have your name entered for the opportunity to receive an iPad. Alternatively, you may do the survey as a volunteer (i.e., without entering your name for the opportunity to win an iPad).

Some respondents may be invited to fill out the survey a second time at a later date and will again have the opportunity to receive compensation in the same form as above.

If you would like to participate, please enter this URL into your browser:
https://www.ctsiredcap.pitt.edu/redcap/surveys/?s=YEFFMMK9PF

Best wishes,
[Lab team member]

Subjects Needed for University of Pittsburgh Survey Study about Stress in the Body

If you are between the ages of 18 – 65 years old, you may be eligible for a research study to examine how people experience stress symptoms in different regions of their body.

The research study will take place entirely through an online survey. Depending on your unique stress response, the survey could take as little as 5 minutes or up to ~15 minutes to complete. This study will involve the completion of some questionnaires related to your demographics, your current medical status, and the ways and areas of your body in which you experience the physical symptoms of stress. This survey can also be taken anonymously.

To compensate you for completing the survey, you can choose to have your name entered for the opportunity to receive an iPad. Alternatively, you may elect to participate as a volunteer (i.e., without having your name entered for the opportunity to receive an iPad).
If interested, use the link https://redcap.link/4xmow88n to participate in this study, or the QR code at bottom right! We appreciate your time.

Principal Investigator: Leah B. Helou, Ph.D., Communication Sciences and Disorders, School of Health and Rehabilitation Sciences, University of Pittsburgh, 6080 Forbes Tower, Pittsburgh, PA 15260, (412) 383-6541, lbh7@pitt.edu.

Scan QR code with your smart phone's camera:

https://redcap.link/4xmow88n Use this link to navigate to the survey.

https://redcap.link/4xmow88n Use this link to navigate to the survey.
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ATTENTION STUDY TEAMS: If the IRB requests any changes to this document, please forward IRB comments to Pitt+Me communications manager Heather Rockwell at htr2@pitt.edu for assistance.

PITT+ME ONLINE STUDY ADVERTISEMENT

PITT+ME TITLE

Survey Study about Stress in the Body

AGE: 18-65

STUDY BASICS *(400-character limit)*

Are you 18-65 years old and live in the United States? You may be able to participate in an online research study to learn more about how people experience symptoms of stress in different areas of the body. This study involves online questionnaires that will take about 5-15 minutes to complete.

DURATION:
5-15 minutes

LOCATION:
Online

STUDY PURPOSE

Stress can have an impact on physical health, but researchers do not fully understand this relationship. The purpose of this study is to learn more about how people experience symptoms of stress in different parts of the body.

COULD THIS STUDY BE RIGHT FOR YOU?

- Ages 18-65
- Live in the United States
- Have access to an internet-connected device (smartphone, desktop, laptop, tablet) to complete online questionnaires

COMPENSATION:
Some participants will be chosen at random drawing to receive an iPad

WHAT PARTICIPANTS CAN EXPECT *(1500-character limit)*

The study requires the completion of online questionnaires. Depending on your unique stress response, the survey could take anywhere from 5-15 minutes to complete.

STUDY LOGO:
If you have a study logo, please send a file in email

IRB: STUDY20120051: Self-Reported Physical Manifestations of Stress in the General Population

MEET THE RESEARCHER

Leah B. Helou, PhD, CCC-SLP, is an Assistant Professor of Communication Science and Disorders in the School of Health and Rehabilitation Sciences at the University of Pittsburgh. A graduate of East Carolina University, Dr. Helou's research interests include mind-voice pathways and how psychological states and traits impact the voice and vocal motor behaviors.

PRE-SCREENING QUESTIONS

Are you 18-65 years old? YES

Do you live in the United States? YES

ATTENTION STUDY TEAMS: If the IRB requests any changes to this document, please forward IRB comments to Pitt+Me communications manager Heather Rockwell at htr2@pitt.edu for assistance.

PITT+ME ONLINE STUDY ADVERTISEMENT

If you pass this screening, you will receive the link to a screening survey at the email address that we have on file in Pitt+Me. Is that OK? YES (will receive link: https://www.ctsiredcap.pitt.edu/redcap/surveys/?s=YEFFMMK9PF)

Do I have your permission to forward your contact information onto the study team? YES

SOCIAL MEDIA POSTS

Check here to opt out of social media recruitment: ____

Twitter

Adults ages 18-65 needed to participate in an online research study to learn more about how people experience symptoms of stress. Visit pittplusme.org.

Facebook

Are you 18-65 years old and live in the United States? You may be able to participate in an online research study to learn more about how people experience symptoms of stress in different regions of the body. This study involves online questionnaires that will take about 5-15 minutes to complete. Visit pittplusme.org for details.

SOCIAL MEDIA ENGAGEMENT (optional)

If you and/or your department have professional social media accounts and would like to be tagged in posts about your study, please provide information below:

Professional Twitter handle: @HelouLab
Study/department Facebook page:

Appendix C Consent Form

University of Pittsburgh | School of Health and Rehabilitation Sciences

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

STUDY TITLE: Self-Reported Physical Manifestations of Stress in the General Population

Principle

Leah B. Helou, PhD. CCC-SLP
Department of Communication Science & Disorders
University of Pittsburgh
6080 Forbes Tower, Pittsburgh PA 15260
Telephone: 412-383-6541
Email: lbh7@pitt.edu

This study is supported by departmental funds associated with the Department of Communication Science and Disorders at the University of Pittsburgh.

Why is this research being done?

We are interested in learning more about how individuals experience stress and about stress's impacts on different regions of the body.

Who is being asked to take part in this research study?

You are invited to participate in this study because you are an adult between the ages of 18 and 65 who has indicated interest and meets study criteria from the pre-screening. We will enroll up to 1,000 individuals in this study.

What procedures will be performed for research purposes?

If you are eligible and decide to take part in this research study, you will undergo the following procedures. All procedures will take place via the survey software RedCap.

Experimental Procedures:

1. You will begin by filling out a questionnaire that asks about you and your demographic information.
2. You will then be asked to list any medical conditions or diagnoses that you currently have or suspect that you have.
3. You will next be asked to identify areas (referencing an illustrated map of the human body divided into regions) that you feel are impacted when you are under stress.
4. For each body region that you select, you will be asked a series of questions about the symptoms you experience in that area as a result of stress, the severity of symptoms, and any medical diagnoses/conditions that impact that area.
5. You will be prompted to fill out the PSS (Perceived Stress Scale), which will ask you a series of questions about your general stress levels.
6. Finally, you will be prompted to complete the Childhood Trauma Questionnaire, which will ask you a series of questions about any trauma you have experienced in your life.

These procedures will take about ten minutes to complete. You are permitted to stop the research procedures at any time and withdraw from the study. If you are invited, and are both willing and able, you may have the option to take further part in this research at a later date.

The body map portions of the survey may also be re-distributed to you approximately 3 months after your initial responses; you will be under no pressure to engage a second time.

What are the possible risks, side effects, and discomforts of this research study?

The possible risks of this research study are minimal. You may find the task boring. A minor risk of breach of confidentiality exists, and we will protect against this by assigning you a special identification number instead of using your personally identifying information. Finally, some questions are sensitive in nature, as you will be asked about abuse, traumatic experiences, and sexual and emotional trauma.

What are possible benefits from taking part in this study?

You will receive no direct benefit from taking part in this research study, however you may find that answering questions about how stress manifests in your body brings you greater self-awareness of your response to stress, which you may view as a benefit. Some people find that understanding how their stress impacts their body can help them to better manage symptoms. Furthermore, this study will contribute to a greater body of work dedicated to understanding the physical manifestations of stress.

Who will know about my participation in this research study?

Any information about you obtained from this study will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet or on encrypted and secured servers. Your identity on these records will be indicated by a subject ID rather than by your name, and the information linking subject IDs with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results.

Will this research study involve the use or disclosure of my identifiable medical information?

Volunteering identifiable information is not necessary in order for you to participate in this study. If you wish to be eligible for an opportunity to receive an iPad, or if you would like to be contacted about future research, you may disclose your email address at the end of the survey. All email addresses given will be kept confidential in the manner noted above. The medical information you provide will be kept separate from your email address when data is exported from RedCap.

Who will have access to identifiable information related to my participation in this research study?

The investigator listed on the first page of this authorization (consent) form and their trained research staff will have access to your email address only for the purposes to which you consent (eligibility for the opportunity to receive an iPad or to be contacted for future studies). In the scenarios listed below, we are obligated to release information, which may include identifiable information:

Authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable research information for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform the appropriate agencies, as required by Pennsylvania law.

Additionally, although we do not have any current plans to share de-identified data, we may share de-identified data in the future with proper approvals.

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?

The investigators may continue to use and disclose, for the purposes described above, identifiable information related to your participation in this research study for a minimum of seven years after final reporting or publication of a project.

Is my participation in this research study voluntary?

Your participation in this research study is completely voluntary. Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh.

May I withdraw, at a future date, my consent for participation in this research study?

You may withdraw, at any time and for any reason, your consent for participation in this research study. If you withdraw consent before survey submission, your information will not be recorded. Any identifiable research recorded for, or resulting from, your participation in this research study prior to the time that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above. Any information submitted

anonymously cannot be withdrawn. To formally withdraw your consent for those data to be used, you should provide a written request to helou_lab@groups.pitt.edu.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh.

Who can I contact if I have questions about this research study?

If you have any questions about your rights as a research subject, please contact the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office, 1.866.212.2668. Authorized representatives from the University of Pittsburgh Office of Research Protections may review your data solely for the purpose of monitoring the conduct of this study. If you have any additional questions about the study, please email them to helou_lab@groups.pitt.edu.

Will I be compensated if I take part in this research study?

Upon completion of this survey, you will be eligible for the opportunity to choose compensation for your participation in this study. To compensate you for completing the survey, you can (1) choose to have your name entered for the opportunity to receive an iPad, which will require that you share a valid email address, or (2) participate as a volunteer (i.e., without entering your name for an opportunity to receive an iPad), which can be done anonymously if you choose. You do not need to participate in any further research other than this initial survey to be eligible.

Will I be contacted again about this study in the future?

At the end of this survey, we will ask you if you are willing to be contacted for a second completion of this survey in the future. Obtaining repeat measures from a small portion of individuals will help us understand how consistent individuals' responses are over time. If you consent to being contacted for another completion in the survey and provide your email address for that purpose, we may invite you to complete the study again within 3 months of your first completion. If we do invite you to complete the survey again, you are under no obligation to do so. However, if you do elect to participate a second time, you will again have the opportunity to receive compensation.

Will this research study involve the use or disclosure of my identifiable information?

If you wish to be eligible for the opportunity to receive an iPad, you will need to provide an email address. Your identifiable information will not be used as a part of the study; only your responses to questions will be used. When data is exported from the survey software, your email address will be kept entirely separate from your answers. Your email address will only be used for the purposes to which you consent (eligibility for the opportunity to receive an iPad or to be contacted for future studies).

What can I do if I no longer want to participate?

You may discontinue participation in this study at any time by closing your web browser and discontinuing your engagement in the experimental activities. If you choose to discontinue, data already collected from your responses will be used in our analysis. If you discontinue your participation before finishing the survey, you will not be eligible to win the aforementioned iPad. You may be withdrawn from the study without your consent if your responses are indicative of carelessness, poor engagement, or not following the instructions.

Will my responses be shared with anyone?

The survey feedback may be published, but without any link to your identifying information. Any results published in this study will remain anonymous.

VOLUNTARY CONSENT FOR EXPERIMENTS

I have thoroughly read and understood the above information. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the email address given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator by email.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation.

I have read, understood, and consent to participating in this research study.

☐ ☐ Yes No

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