Characterizing the Nature and Features of Misophonia: A Mechanistic Approach

by

Rachel Eliza Guetta

Department of Psychology & Neuroscience
Duke University

Defense Date: March 18, 2024

Approved:

M. Zachary Rosenthal, Supervisor

Timothy Strauman

Rick Hoyle

Andrada Neacsiu

Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Psychology and Neuroscience in The Graduate School of Duke University
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ABSTRACT

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Abstract

Misophonia is a newly defined sound intolerance disorder that implicates the defensive motivational systems across cognitive, affective, attentional, physiological, and behavioral domains (Swedo et al., 2022). The nature of misophonic triggers and reactions is highly variable, necessitating the need for idiographic assessment of relevant mechanisms (Brout et al., 2018). Still, despite prevalence estimates ranging from 5 to 49.1% (Jakubovski et al., 2022; Siepsiak et al., 2020; Vitoratou et al., 2023; Wu et al., 2014; Zhou et al., 2017), and significant distress and functional impairment associated with this condition, the nascency of misophonia literature limits effective assessment and treatment. Existing studies have largely relied on self-report tools based on unvalidated diagnostic criteria that focus on trigger types and frequency, rather than on a more holistic understanding of emotional functioning before, during, and after triggers, impacts to self-concept, coping strategies, and impairment. In addition, few studies have helped to build a mechanistic understanding of processes that can be targeted for change via psychological interventions.

One key challenge to advancing our understanding of misophonia has been developing measurement tools that holistically and dimensionally reflect relevant constructs in this disorder. A second key challenge in developing effective interventions to treat misophonia has been limited granular understanding of maintenance factors and mechanisms of change that can be leveraged in treatment.

This dissertation consists of three original studies that aim to characterize and understand the nature and features of misophonia, and to strengthen a mechanistic approach to assessment and treatment of this condition. Each study utilizes a different community sample of adults across the United States. Chapter 2 details the creation and preliminary validation of the Duke Misophonia Interview (DMI; Guetta et al., 2022a), the first semi-structured clinical interview to assess misophonia in adults. The DMI can be used by both clinicians and researchers to advance our understanding of this understudied disorder and design corollary interventions. Chapter 3 works to further examine components of emotional functioning in misophonia. Findings from this study (Guetta et al., 2022b) suggest that targeting processes of emotion regulation is crucial in treatment for misophonia. Implications from this work also suggest that how individuals perceive and respond to triggers, shaped by learning histories and chronic stress, may impact misophonia severity. Chapter 4 then explores the relationships among perceptions of stress, trauma history, and traumatic stress in adults with misophonia. Results from Chapter 4 (Guetta et al., 2024) indicate that, although there is overlap in transdiagnostic factors between trauma and misophonia (e.g., perceived stress), there is no evidence for a causal link between traumatic events and the development of misophonia. These findings provide further support for integrating idiographic assessment tools to understand individual histories of chronic stress, as well as perceptions of stress related to misophonic triggers and to functioning more broadly.

Taken together, these three studies add to the nascent literature involving mechanistic approaches to assessment and treatment of misophonia in adults. This dissertation concludes with a discussion of future directions and recommendations for research on understudied health phenomena like misophonia.

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1. Introduction: Approaches to and challenges of studying a new disorder

1.1 The advent of misophonia

The emergence of misophonia over the last decade – as a clinical concern, a sociocultural phenomenon, and an area of growing research – is, in and of itself, a process worth studying. When a new condition is observed, it can take decades before the disorder is introduced as a diagnosis in any formal nomenclature. And in the interim, there are both opportunities to conduct careful science to understand it, and opportunities for a sociocultural zeitgeist to define it. In the case of misophonia, there has been fascinating and galvanizing momentum on both fronts since the term misophonia was coined in 2001 (Jastreboff & Jastreboff). Simultaneously, researchers across disciplines are chipping away at understanding this new phenomenon (within the last three years, more studies have been published on misophonia than in all prior years combined), while mentions of and stories about misophonia across social media and news outlets have increased dramatically.

Because misophonia is not yet (nor may ever be) situated firmly in any one discipline, there have been several attempts to define what the condition is and what it is not. The first observations of misophonia occurred within audiological settings (Jastreboff & Jastreboff, 2001), and thus the earliest concept of misophonia was characterized as a condition of decreased sound tolerance; treatment efforts were first

organized around Tinnitus Retraining Therapy (Jastreboff & Jastreboff, 2014). Later, Schröder et al. defined misophonia as a psychiatric condition (2013); Taylor posited that misophonia is a psychological disorder (2017); and Dozier & Morrison suggested misophonia be considered an aversive physical and emotional reflex disorder treated with classical conditioning (2017). Other researchers have dedicated work to examining genetic (Smit et al., 2023), neurodevelopmental (Cavanna & Seri, 2015), and neurobiological features and treatment targets of misophonia (Grossini et al., 2022; Neacsiu et al., 2024; Neacsiu et al., 2023; Neacsiu et al., 2022). Kumar et al. support a model of misophonia based in motor system functioning (2021), while other frameworks link misophonia to broader sensory over-responsivity (Adermane et al., 2022). Given the clear signal from growing literature that there are mechanisms and candidate treatment targets across audiology, neurology, biology, psychiatry, and psychology, it is arguably premature, reductive, and unhelpful to stake a claim about what "type" of disorder misophonia is, and what diagnostic nomenclature it ought to "belong to."

Alongside empirical work, misophonia sufferers, their loved ones, and other stakeholders have taken to news outlets (e.g., New York Times, The Guardian, USA Today) and social media (e.g., Reddit, TikTok, Facebook) to share anecdotes and define themselves what misophonia is and what it is not. Indeed, when a condition like misophonia that is marked by intense distress and impairment has gone understudied for decades, there is a formidable sense of urgency and interest by those affected. The

expanding depth and breadth of conversation and discovery around misophonia, both in the laboratory and on the Internet, poses an opportunity to evaluate the most effective approaches to empirically define, assess, and treat this new disorder.

1.2 Taking a mechanistic approach to studying a new disorder

In studying any new disorder, it is important to consider the benefits and limitations of existing frameworks of nosology and etiology, as the way we derive categorizations and working models hold implications both in theory and practice. When approaching work on misophonia, for example, does it make sense to prioritize research from a diagnostic or non-diagnostic lens, or both? To examine mechanisms from a top-down or bottom-up approach, or both? To create checklists of symptoms or assess processes more dimensionally? How can we best minimize the research to practice gap, particularly for a disorder with literature in early stages?

Since the rise of modern American psychiatry in the 1960s, the integrity and utility of nosological classification has been debated in both academic literature and clinical practice. Originating in the mid-20th century, the Diagnostic and Statistical Manual (*DSM*) has undergone a fascinating evolution, beginning with theory-driven and descriptive approaches to categorization to symptom- and criterion-based categorization. The *DSM* has long stood as the arbiter of classification, offering a structured framework for understanding psychiatric conditions, providing

standardization within the practice of psychiatry, and facilitating communication and research across disciplines.

However, the *DSM* has been vulnerable to numerous critiques, with adversaries of the prevailing system arguing that the generic diagnostic criterion, absence of objective laboratory markers, and correlated measures breed reductionism and tautology (Wolfe et al., 2013). Further, the 2.8-fold increase in number of disorders since the first edition of the *DSM* (with approximately 300 diagnoses across 20 types of disorders; Surís et al., 2016), gives rise to more questions around the limits of the medical model reliance on binary classification, symptom checklists, and diagnostic questionnaires.

Dimensional frameworks, such as the Research Domain Criteria (RDoC; Cuthbert & Insel, 2013) and the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017), represent alternative approaches to accelerating the way psychopathology is examined, classified, and treated. RDoC provides an empirical framework with which to study the transdiagnostic underpinnings of the HiTOP dimensions (e.g., internalizing, externalizing). Both RDoC and HiTOP frameworks place focus on shared mechanisms and dimensional constructs that address the profound heterogeneity within and across psychiatric disorders and reduce the reliance on binary classification (Michelini et al., 2021). Together, RDoC and HiTOP approaches promote synergy between etiology and nosology, wherein clearer understanding of shared

mechanisms across biobehavioral substrates will lead to more refined taxonomy and classification of mental illness.

As diagnostic status of misophonia may take many more years, a mechanistic approach to researching this new condition is warranted in order to (a) identify symptoms that tend to cluster together; (b) develop useful clinical tools to measure the condition, and distinguish from other related but distinct phenomena; (c) understand relevant processes to across biopsychosocial domains that exist dimensionally on a continuum; and (d) identify candidate treatment targets that can be integrated into intervention and implementation work.

1.3 A stepwise process of characterizing the nature and features of misophonia

Responding to the emergent nature of misophonia, this dissertation reflects a stepwise process of scientific discovery. The three studies included in this dissertation explore the nature and features of misophonia, and respond to the imperatives of mechanistic, transdiagnostic research aligned with dimensional frameworks.

The first study aims to both identify symptoms that cluster together within misophonia, and provide a clinically useful and psychometrically validated tool. It details the grassroots, iterative creation of the first semi-structured interview to assess this new condition. Rather than assessing mere presence or absence of symptoms, the interview probes frequency, intensity, and distress of mechanisms across cognitive,

affective, attentional, physiological, and behavioral domains to increase clinical and empirical utility. Dimensional rating systems nested within the interview promote moving beyond dichotomous identification of symptoms to a more idiographic understanding of how particular experiences are realized in an individual's sociocultural system. Administration and initial validation of the interview revealed the complexities of how emotional functioning (i.e., the interplay between emotion regulation, affective lability, chronic and perceived stress) may impact maintenance and severity of misophonia.

The second study aims to better understand facets of emotional functioning dimensionally within misophonia, and to identify possible transdiagnostic treatment targets. Extant literature has evidenced that emotion and emotion regulation are germane to misophonia and that particular emotions (e.g., anxiety, anger, disgust) may be particularly central to the presentation of misophonia (Cassiello-Robbins et al., 2020a; Möllmann et al., 2023; Spencer et al., 2023). However, less is understood about the intensity, duration, and topography of emotion and emotion regulation in misophonia. This study examines mechanisms of emotional functioning in order to provide insight into the relative contributions and differential associations of transdiagnostic processes related to emotion that are relevant in misophonia. This study also considers population-level stressors (COVID-19) to both account for environmental-level influences and to gain a more cohesive picture of distress within a complex sociocultural

landscape. Findings from this study highlight the importance of emotion regulation as a potential treatment target for misophonia. Further, the impact of COVID-19 stress and co-occurring symptoms of depression and anxiety on misophonia severity raise the question of if, and to what extent, general psychological distress may explain the relationship between misophonia and emotion regulation. Indeed, the first two studies suggest the relevance of persistent sympathetic nervous system arousal in misophonia, as well as the role of perceived threat. Thus, understanding the various components of stress within misophonia is warranted.

The third study responds to this question of if and how misophonia may be related to components of stress, ranging from broader perceived stress to cumulative adverse life events to formal diagnosis of stressor- and trauma-related disorders. This study aims to both understand relevant processes of stress and trauma that may exist dimensionally on a continuum, and to identity possible transdiagnostic treatment targets for symptoms relevant to misophonia and co-occurring conditions. Findings from this paper highlight the lack of association between misophonia and any trauma- or stressor-related disorder (e.g. PTSD), again suggesting that the condition may be related to transdiagnostic psychological processes, rather than a specific set of symptoms. Further, the study suggests that perceived stress may be an important treatment target.

1.4 Challenges of studying a new health phenomenon

Understanding, assessing, and treating a new mental health condition such as misophonia is a complicated process that raises many more questions than answers. With neither established diagnostic criteria nor a comprehensive understanding of all the relevant biopsychosocial mechanisms, rigorous empirical query presents significant difficulty. Below are various challenges, though certainly not an exhaustive collection, faced in the process of completing this dissertation.

Lack of valid assessment tools. In nascent literature on any new disorder there are often very few of psychometrically validated measurement tools. In the case of misophonia, most studies to date rely on measures that have little to no demonstrated reliability or validity (Jakubovski et al., 2022; Simner et al., 2021; Schröder et al., 2013; Wu et al., 2014). Further, the tools are often reliant on self-report data, which is vulnerable to response biases, variable and nonspecific interpretations to questions, and reductive responses (Rosenthal et al., 2021; Siepsiak et al., 2020; Vitoratou et al., 2021). Additionally, a lack of validated measurement tools also has implications on sampling, and inclusion and exclusion criteria (i.e., in terms of how to accurately characterize and group prospective participants). The challenges born out of weak assessment tools, in conjunction with the fact that there are varying interpretations across laypeople, psychologists, audiologists, and sufferers about what misophonia is and is not, can lead to drawing tenuous conclusions about this new condition.

Assumptions and biases across the arc of scientific inquiry. Each empirical question, study design, and set of inferences is shaped by assumptions and biases that may be specific to the investigator, discipline, and/or sociocultural context. For example, misophonia within audiological contexts are inevitably shaped by expertise and hypotheses tied to psychoacoustics and neurophysiological pathways (Aryal & Prabhu, 2023; Jastreboff & Jastreboff, 2001); misophonia researchers in the mental health space are likely to assess for biopsychosocial factors and focus on observable behaviors (Holohan et al., 2023). As this condition has underpinnings across neurobiological, psychophysiological, and socioemotional domains, it remains a challenge to conduct research that disrupts discipline-bound silos. Although theoretical written discussion may orient towards the levels of analysis being left out, there remain significant gaps in comprehensive measurement within and across studies. The limited utilization of interdisciplinary teams to study a phenomenon that spans multiple disciplines will continue to constrain our understanding of misophonia.

Balancing dimensional approaches with conventional medical models. One assumption underlying much of the work in this dissertation is that there is utility in characterizing misophonia from a dimensional, mechanistic approach. Although this assumption and guiding principle is based largely on the fact that misophonia is not yet a formal diagnosis, it presents the challenge of how to integrate findings most effectively into conventional settings. Indeed, the *DSM* and medical models still prevail in clinical

contexts. For as long as a goal of this work is to hold value within the current healthcare landscape, it remains a challenge to balance frameworks of psychopathology that consider both medical and dimensional models.

Lack of representative samples. With little epidemiologic data about misophonia (Jakubovski et al., 2022; Rosenthal et al., 2022; Vitoratou et al., 2023), it is crucial to conduct research using representative samples. Research on understudied disorders may often face sampling challenges (e.g., relying on convenience sampling within university settings). In the case of misophonia, and within this dissertation, findings have disproportionately included college-educated White women (Brennan et al., 2024; Dixon et al., 2023; Wu et al., 2014; Zhou et al., 2017). One hypothesis for this skewed sampling is recruitment methods, wherein the way studies have been promoted among networks of misophonia sufferers (e.g., via Reddit, Facebook pages) becomes self-selecting. As such, adequate reach to achieve representative sampling remains a challenge for understudied conditions. The lack of epidemiological data will continue to limit the utility and scalability of findings. Another hypothesis is the low level of misophonia awareness among laypeople, as most of the information deployed about misophonia is being consumed by groups with higher income and education levels (Dixon et al., 2023). The low recognition, awareness, and knowledge of misophonia in the general population remains a challenge not only in empirical work, but also in public policy, public health campaigns, and community-based outreach endeavors.

Lack of clinical control groups. Building a thorough understanding of what misophonia is, and what it is not, is crucial to developing targeted assessment and treatment efforts. Studies on misophonia to date have seldomly used clinical control groups, and the lack of comparisons is a weakness within both dimensional and medical model approaches. Although the work in this dissertation does not include clinical control groups, the studies aim to address this challenge by controlling for clinically relevant features and traits via statistical methods (e.g., in multiple linear regression models, controlling for anxiety and depression when exploring the impact of emotion regulation difficulties on misophonia severity). In order to parse out components that may be unique to misophonia, clinical control groups and/or accounting for transdiagnostic confounding variables (e.g., general distress, neuroticism) must be considered.

Funding. Securing ample funding for any understudied condition is undoubtedly one of the largest practical challenges in conducting rigorous research. Not only is funding from various sources (e.g., philanthropic and private foundations, governmental institutions, institutional mechanisms) a challenge, but this perpetuates the numerous challenges listed above. Limits on funding also limits the ability to engage in translational, prospective, epidemiological, longitudinal, and other experimental designs that will glean the most insight into a new condition, like misophonia.

Balancing rigorous research with dissemination. The creation and dissemination of knowledge about a new phenomenon is impacted by several stakeholders (e.g., funding agencies, institutions and universities, research centers and individual investigators, providers and sufferers, among others). With the growth of any new and understudied health condition, there is both a sense of urgency and responsibility that can hold competing interests. For example, the first study included in this dissertation details the development and preliminary psychometric validation of the first semi-structured interview to assess misophonia in adults. The interview was rigorously and iteratively developed (i.e., using a grassroots approach, integrating feedback from several experts, as well as misophonia sufferers), though tested within a pilot sample. As there is an undeniable need for validated and rigorously developed assessment tools, we prioritized dissemination of the interview for use, and continue ongoing efforts to further validate the interview among larger and more diverse samples. Indeed, a powerful challenge remains balancing the pressures and rewards of responding to urgency and staking a claim, with the imperatives to drive science forward carefully, earnestly, and with integrity.

2. Creating the first semi-structured clinical interview for misophonia

This chapter aims to respond to a central challenge in the study of misophonia to date: the lack of rigorously developed and psychometrically validated assessment tools. Creation of the Duke Misophonia Interview (DMI) utilized an iterative item generation process and integrated feedback directly from individuals with misophonia to increase accessibility, acceptability, and feasibility of this novel assessment tool. This semi-structured interview assesses misophonia across cognitive, affective, attentional, physiological, and behavioral domains, aligned with the consensus definition of misophonia (Swedo et al., 2022). Further, it captures responses via a dimensional rating system (including frequency, intensity, and severity ratings) to increase clinical and empirical utility. The DMI reflected high internal reliability, test re-test reliability, and discriminant validity. Development, administration, and validation of the DMI emphasizes the prevalence of interrelated constructs of emotional functioning (e.g., stress, difficulties with emotion regulation) in adults with misophonia.

Note: Since the publication of this study, the DMI has been iterated to address several of the future directions proposed in the discussion section. Firstly, the interview has been modified with minor word changes to improve clarity and to align with the consensus definition of misophonia (Swedo et al., 2022), including items to probe influences on misophonic reactions (e.g., perceived degree of control over stimulus,

stimulus volume), and more specificity regarding negative emotions during triggers. In addition, some verbiage in the instructions was reduced in order to streamline administration. Average administration time of the DMI is currently around 45 minutes, and thus can be situated within a standard psychotherapy session.

2.1 Development and psychometric exploration of a semi-structured clinical interview for misophonia

The following original research article was published in Personality and Individual Differences (Guetta et al., 2022), with the title, "Development and psychometric exploration of a semi-structured clinical interview for Misophonia." The authors were as follows: Rachel E. Guetta, Clair Cassiello-Robbins, Deepika Anand, and M. Zachary Rosenthal.

2.1.1.1 Introduction

Misophonia is a disorder marked by decreased tolerance, as well as sensory and emotional over-responsivity to repetitive sounds ("triggers") and related stimuli (Jastreboff & Jastreboff, 2002, 2014; Edelstein et al., 2013; Schröder et al., 2013; Swedo et al., 2022; Wu et al., 2014). Triggers are typically human-produced, pattern-based oral and/or nasal noises (e.g., throat clearing, chewing, slurping, sniffing), can be environmentally produced (e.g., pen clicking, keyboard typing, dog drinking), and are not attributable to aversive acoustic features such as volume or pitch (Brout et al., 2018; Swedo et al., 2022; Taylor, 2017). Although auditory triggers are most common in

misophonia, individuals may also report distress in response to visual triggers (e.g., leg shaking, foot tapping, fan spinning; Swedo et al, 2022), as well as visual reminders of auditory triggers (e.g., watching someone open the refrigerator).

The intensity of emotional reactions to triggers is expressed across a range of affective responses (e.g., anger, anxiety, disgust, rage) and physiological reactivity (e.g., muscle tension, increased heart rate, heightened galvanic skin response; Edelstein et al., 2013; Jastreboff & Jastreboff, 2001; Rouw and Erfanian, 2018). Individuals responding to misophonic triggers report difficulty disengaging their attention from the sounds, as well as aversive and negative thoughts (e.g., "I hate this person" or "I can't stand it"), sometimes accompanied by urges toward aggression (Jastreboff & Jastreboff, 2001; Swedo et al., 2022). Common behavioral responses include glaring at or mimicking the person producing the sound, verbal agitation or aggression, and infrequent physical aggression, all of which adversely impact interpersonal functioning (Jastreboff & Jastreboff, 2001). In additional to interpersonal aggression and conflict, escape and avoidance behavior functions to prevent exposure to and distress from misophonic cues.

Intolerance of possible triggering contexts (e.g., family meals and restaurants, certain workplaces) may lead to diminished confidence and ability to regulate emotions over time (Rouw & Erfanian, 2018; Wu et al., 2014). For example, among participants recruited from online support groups with misophonia, 78% reported spending over an hour each day thinking about misophonic sounds and reported moderate to extreme

interference in social and/or academic and work life (e.g., strained relationships, social isolation, inability to perform important work tasks, to keep jobs; Rouw & Erfanian, 2018; Swedo et al., 2022). The level of impairment and distress associated with misophonia makes clear the importance of both developing and utilizing evidence-based assessments that characterize misophonia and treatments that alleviate relevant symptoms.

As the term "misophonia" was coined in the early 2000s (Jastreboff & Jastreboff, 2001), many questions remain regarding onset, etiology, course, biological, genetic, and behavioral mechanisms, phenotypic and syndromal boundaries with other psychiatric and medical conditions (Taylor, 2017). Central to answering these outstanding questions is the development and validation of empirically derived assessments that adequately capture the heterogeneity of misophonic symptom presentations.

Utility of a Clinical Interview

Recent studies have begun to validate self-report inventories assessing symptoms and features of misophonia. For example, the Misophonia Questionnaire (Wu et al., 2014), Amsterdam Misophonia Scale (Naylor et al., 2020), Misophonia Response Scale (Dibb, Golding, & Dozier, 2021), MisoQuest (Siepsak et al., 2020), and Duke Misophonia Questionnaire (DMQ; Rosenthal et al., 2021) each have shown preliminary psychometric validation, and, collectively, provide promising new tools to help clinicians and researchers characterize misophonia. Despite the value of self-report

assessment measures (e.g., brief, accessible, convenient), however, there are inherent problems with relying on subjective measurement approaches.

The focus of most self-report measures has been on types of triggers (e.g., oral, nasal, environmental, etc.), symptoms (e.g., physiological, emotional, and behavioral responses), and subjective appraisals of functional impairment (e.g., social, occupational, academic). Although this is sensible in the context of brief measurement, little attention has been given to a more holistic understanding of the scope of affective, cognitive, behavioral, and physiological processes that occur in response to triggers, or to how misophonia affects one's self-concept. It is important to move beyond subjective assessment of triggers, symptoms, and impairment in order to obtain a more comprehensive understanding of an individual's experience of misophonia. In doing so, assessment can improve treatment by informing how to flexibly apply interventions capable of targeting of idiographic problems using nomothetically derived and empirically supported processes of change (e.g., cognitively, behaviorally, or physiologically-focused interventions).

Existing instruments also have weaknesses common among self-report measures, including response biases (e.g., acquiescence or naysaying biases), variable and nonspecific interpretations of questions, and reductive responses, all of which can be partially overcome using semi-structured clinical interviews (e.g., Widiger & Saylor, 1998). For example, when administering a semi-structured interview, responses can be

followed with probes and prompts in order to enhance the precision and accuracy of responses. Integrating follow-up questions in clinical interviews allows the interviewer to (a) clarify contextual details underlying questions/responses, (b) address ambiguous responses or participant uncertainty, (c) confirm the frequency, intensity, and duration of individual symptoms, and (d) situate symptom severity within the context of both the individual (idiographically) and what is empirically and clinically considered subthreshold versus threshold (nomothetically). Collectively, the advantages of using semi-structured interviews offer greater precision, scope, and treatment utiity than brief self-report inventories in the measurement of misophonia.

2.1.1.2 Current Study

The primary aim of the present study was to develop and conduct exploratory psychometric analyses of a new semi-structured clinical interview to assess misophonia in adults. The *a priori* goals were to create and evaluate items representing an individual's: (a) current frequency of being affected by misophonic triggers, (b) degree of responding to triggers across affective, physiological, cognitive and behavioral domains of functioning, (c) social and occupational impairment caused by misophonia over one's lifetime, as well as (d) impact of misophonia on beliefs about the self. These items were generated rigorously using qualitative and quantitative approaches in the initial validation of the Duke Misophonia Questionnaire (DMQ; for details, see Rosenthal et al., 2021). The present interview was developed to compliment the DMQ

and other self-report measures of misophonia, with the intention of being administered in both research and clinical settings to comprehensively characterize the heterogenous nature of misophonia.

The development of the clinical interview was scaffolded by assessment standards for creating new interview measures (Watson, 1990; Watson et al., 1991), including: (a) correspondence with proposed diagnostic criteria in order to promote generalizability and external validity; (b) inclusion of both dichotomous and continuous ratings to provide critical information about presence or absence of the condition in addition to dimensional characterization of severity; (c) ability to be trainable among paraprofessionals in order to contribute a scalable and broadly useful instrument; and (d) adequate reliability and validity. We also referenced several widely used and psychometrically validated clinical interviews, including the Clinician-Administered PTSD Scale for *DSM*-5 (CAPS-5; Weathers et al., 2018) and the Anxiety Disorders Interview Schedule for *DSM*-5 (ADIS-5; Brown & Barlow, 2014), and incorporated principles articulated by the creators of these instruments.

Firstly, we aimed to craft clear and concise questions. Secondly, we incorporated behavioral anchors derived from clinical experience with misophonia sufferers in the community and pilot data into the rating system in order to improve reliability and reduce rater bias (Blake et al., 1995). We also created dimensional ratings for symptoms that integrate both frequency and intensity in order to capture a more individualized

symptom presentation and provide clinically useful information to researchers and clinicians alike. Such granular analysis of symptom severity affords an idiographic and flexible account of misophonia. For example, one individual may experience relatively frequent but mildly distressing misophonia symptoms, whereas another may experience less frequent symptoms but markedly more distress. This division of frequency and distress into a dimensional severity score may bolster the treatment utility of the assessment (Hayes, 1987; Weathers et al., 2018). Lastly, we incorporated interview questions that assess both current symptomatology and global impact and we were careful to use clear wording to distinguish between time frames.

2.1.1.3 Methods

All study procedures were approved by an IRB and all participants provided informed consent before beginning study procedures. Developed at Duke University's Center for Misophonia and Emotion Regulation, the Duke Misophonia Interview (DMI) was developed in two phases and was designed to overcome the limitations of existing measures of misophonia. In Phase 1, the interview items were generated using a literature review, responses to an initial version of the interview from both misophonia experts and a pilot sample of 10 misophonia sufferers, and iterative feedback from professionals. Phase 2 involved exploratory psychometric assessment among a larger sample of misophonia sufferers (n = 30). A summary of the methodology used to

develop the DMI is depicted in Figures 1a-1c. Details of each element in this flowchart are described below.

2.1.1.4 Phase 1a: Development of Interview

Literature Review to Identify Candidate Items

To identify candidate items for the interview, a comprehensive literature search for existing proposed diagnostic criteria and tools to assess misophonia was conducted. All items across these proposed diagnostic criteria and measures were reviewed and constructs (e.g., emotional, behavioral, physiological) were consolidated into semi-structured interview questions. These steps resulted in an initial pool of 26 candidate interview items.

Creation of Individual Interview

Next, a semi-structured interview was developed to ensure that the included items would comprehensively capture the current experience of individuals with misophonia. Features of the interview included (a) dichotomous (present/absent) responses for each individual symptom in the past month, (b) separate ratings for symptom frequency and intensity, culminating in a dimensional rating, (c) prompts, follow-up probes, and behavioral anchors for each dimensional rating scale in order to increase reliability (Blake et al., 1995), (d) functional impairment ratings for each past-month symptom, and (e) several questions assessing global (lifetime) impact of misophonia on the individual. See Figures 2a-2b for examples of interview items.

The first question established presence or absence of trigger sounds, as well as frequency and distress of the sounds. The next series of questions assessed cognitive, emotional, physiological, and behavioral misophonic responses. The last several questions assessed impact of misophonia on relationships, school, work, and important hobbies, beliefs about the self, and overall quality of life across the individual's lifetime.

2.1.1.5 Scoring of the DMI

Dichotomous Ratings for Current Symptoms. Prompts for each item began with a description of the symptom to assess presence or absence, and if the respondent endorsed the symptom, all follow-up prompts in the item were administered. If the respondent did not endorse presence of the given symptom, the interviewer moved on to the next symptom and the item was scored as a 0.

Dimensional Severity Ratings for Current Symptoms. Each past-month symptom included both frequency and distress ratings, which got converted into a single, dimensional severity rating (Weathers et al., 2018). First, symptom frequency was recorded directly as reported by the individual, and distress was captured using a subjective unit of distress (SUDS) rating from 1-10. Respondents were asked to generate personally-relevant behavioral anchors, with 1 being the level of distress during a moment or event that represented the calmest the individual had been in their life and 10 being the level of distress during a moment or event that represented the height of distress in their life. This allowed the respondent to situate the distress from each

misophonia symptom within the context of their life stressors more broadly. Distress was rated as "*minimal*" (SUDS rating 1-3), "*clearly present*" (SUDS rating 4-5), "*pronounced*" (SUDS rating 6-8), or "*extreme*" (SUDS rating 9-10).

Next, derived from psychometrically validated, clinician-rated scoring rules (Weathers et al., 1999; Weathers et al., 2018), frequency and distress ratings were converted into a 5-point severity rating (0 = *absent*, 1 = *mild*, 2 = *moderate*, 3 = *severe*, 4 = *extreme*). Behavioral anchors were provided next to each severity rating option for the interviewer to refer to. For example, a moderate severity rating for most items required symptom frequency to be at least once a day over the past month and for distress to be clearly present.

Continuous Ratings for Current Impairment. After collecting frequency and distress ratings for each past-month symptom, the interviewer followed prompts to ask about the extent to which that symptom had impacted their relationships with others, their ability to work or quality of work, as well as any other adverse impact on their day-to-day life that month. Impairment was rated by the interviewer on a 3-point Likert scale (0 = *no functional impairment* to to 2 = *functional impairment*), based on the rating system derived in the Structured Clinical Interview for *DSM-5* (SCID-5; First, 2014). Impairment ratings incorporated information such as behavioral observations of the respondent, information gained earlier within that item and throughout interview, and judgment based on respondent reporting style.

Continuous Ratings for Global Impact. After the assessment of past-month symptoms, the interview included several items about the overall impact of misophonia on relationships, school and occupation, self-concept and image, and subjective distress over one's lifetime. Each of these items were rated on a 5-point Likert scale from 0 (absent) to 4 (extreme). Global impact ratings incorporated factors such as degree of subjective distress, behavioral observations and information gained throughout interview, and judgment regarding reporting style.

Outcome Scores. The interview yielded four scores: (a) total DMI score (a sum of all dimensional severity ratings for each past-month symptom and continuous ratings for each global impact item), (b) current severity score (a sum of all dimensional severity ratings for each past-month symptom), (c) current impairment score (a sum of all continuous impairment ratings), and (d) global impact score (a sum of all continuous lifetime effect ratings). A summary of the division of items and DMI outcome scores is depicted in Table 1.

2.1.1.6 Pilot Study

Participants were individuals with misophonia (n = 10) and were included if they were between the ages of 18 and 65, did not meet criteria for current mania, anorexia nervosa, or psychosis, and scored a mean item score of 2 or greater on the Misophonia Symptom Scale and Misophonia Emotions and Behaviors Scale and a score of 7 or higher on the Severity Scale of the Misophonia Questionnaire (Wu et al., 2014).

2.1.1.7 Phase 1b: Refinement of Initial Item Pool

Feedback on Item Wording, Structure, and Applicability from Misophonia Sufferers

In addition to responding to the interview items themselves, the same participants as in Phase 1a (n = 10) provided free response feedback on each item and offered changes or additions to the interview, including length, content, scoring criteria, wording of instructions, and comprehensibility of items. Participant feedback was discussed by the study team, and changes were incorporated to enhance accessibility and/or clarity of the instructions. Items flagged as confusing or redundant were either removed or condensed.

Feedback from Experts

The iterated interview was sent to several clinicians and professional experts. Expert feedback was reviewed and incorporated by the study team. Changes included clarifying instructions and including additional relevant items (e.g., functional impairment items for each misophonic symptom).

Study Team Qualitative Review

As the final step in Phase 1, members of the study team reviewed the iterated interview and made additional refinements to increase clarity and specificity of the interview items. This included further collapsing and/or parsing questions and further simplification of instructions and response options. After completion of all Phase 1b

modifications, 19 items were prepared for Phase 2 data collection and initial psychometric analyses.

2.1.1.8 Phase 2: Scale Refinement Using Preliminary Psychometric Analyses

Phase 2 involved administering the DMI to a larger sample to further assess feasibility and acceptability of the measure and to begin exploratory psychometric analysis of the interview.

Participants

Phase 2 sample (n = 30) was recruited via the same methods as Phase 1. Thirty percent of the current sample (n = 9) was randomized to a follow-up visit in order to compute a preliminary estimate of test-retest reliability and predictive validity of the DMI.

Measures

Misophonia Questionnaire (MQ; Wu et al., 2014). The MQ is a brief, 17-item self-report scale divided into three subscales: the Misophonia Symptom Subscale, the Misophonia Emotions and Behaviors Subscale, and the Impairment Subscale. A cut score of 7 ("Moderate") or higher on the Impairment Subscale indicates clinically significant misophonia symptomology. Initial validation of the MQ demonstrated good internal consistency (α = .86 - .89; Wu et al., 2014). Reliability for the MQ total score in the current sample was acceptable (α = .72; 95% CI [.55, .85]).

Amsterdam Misophonia Scale (A-MISO-S; Schröder et al., 2013). The A-MISO-S is a 6-item semi-structured interview that assesses the following: (1) amount of time occupied by misophonia symptoms; (2) interference in social functioning from misophonia; (3) level of general distress (irritation, anger, disgust) the misophonia symptoms cause the individual; (4) level of effort for the individual to resist or divert attention from misophonia impulses (i.e. sound-related thoughts); (5) how much control the individual feels they have over their misophonia-related thoughts; and (6) how much an individual avoids misophonia situations. In the current study, this measure was administered as a self-report questionnaire rather than an interview. Scores from 0 to 4 are considered subclinical misophonic symptoms, 5–9 mild, 10–14 moderate, 15–19 severe, and 20–24 extreme. A good internal consistency of 0.81 was reported (Naylor et al., 2020). Reliability of the A-MISO-S total score in the current sample was adequate (α = .68; 95% CI [.46, .83]).

Brief Symptom Inventory (BSI-18; Derogatis et al., 2001). The BSI-18 is an abridged version of the 53-item BSI developed to identify self-reported clinically relevant psychological symptoms. The BSI-18 is a checklist developed as a screen for symptoms ranging from depression, panic, to anxiety. Each symptom is rated on a five-point Likert scale with responses ranging from 0 (“Not at all”) to 4 (“Extremely”), with total scores ranging from 0-72. Higher total scores indicate higher global psychological distress. Initial validation of the BSI-18 total score demonstrated good internal

consistency (α = .89; Zabora et al., 2001). Reliability for the BSI-18 total score in the current sample was excellent (α = .91; 95% CI [.86, .95]).

Centrality of Religiosity Scale (CRS; Huber & Huber et al., 2012). The CRS is a 15-item self-report scale assessing the significance of spirituality in individuals' lives, and was included to assess for discriminant validity. The measure was designed to measure five dimensions of religiosity: (1) Intellect, (2) Ideology, (3) Public practice, (4) Private practice, and (5) Experience. The CRS demonstrated good internal consistency (α = 0.73 to 0.83; Abbasi et al., 2019). Reliability for the CRS in the current sample was good (α = .83; 95% CI [.73, .91]).

Marlowe-Crowne Social Desirability Scale (MCSD; Reynolds, 1982). This 13-item tool utilizing a true-false response format that assess the impact of social desirability, the tendency to report answers in a way that individuals deem to be socially acceptable. The MCSD was included to assess for discriminant validity. Total scores range from 0-13, with higher scores indicating a social desirability response tendency. The MCSD was validated in a large college sample and evidenced acceptable reliability α = 0.76; Reynolds, 1982). Reliability for the MCSD in the current sample was good (α = .83; 95% CI [.72, .91]).

Data Analytic Plan

Data analyses were conducted in SPSS version 27 (IBM Corp, 2020). Descriptive statistics were calculated for all measures administered. Acceptability and feasibility

ratings for the DMI were also evaluated. We assessed presence or absence of each DMI interview item using a rule of severity score rating ≥ 1 to examine patterns of endorsement rates. Prevalence rates were also used to flag potential items to eliminate in future iterations of the interview.

Internal Reliability

To refine the DMI using exploratory psychometric analyses, we examined means and standard deviations for each individual item, as well as for each DMI outcome score. We calculated total and summary scores on the DMI and evaluated internal consistency and inter-scale correlations in order to describe the relationships between assessed constructs and further explore conceptual groupings of the DMI outcome scores. Cronbach's alphas were computed for all interview items (total DMI score), as well for the three subscores (current symptom severity, current impairment, and global impact scores). In addition, confidence intervals were calculated for the coefficient alphas (Cooper, 2018). Item-total correlations were examined for all outcome scores. Items with item-total correlations less than .30 were removed from subsequent analyses (Brzoska & Razum, 2010; Cristobal et al., 2007; de Vaus, 2004; Maltby et al., 2007; Pedhazur & Schmelkin, 1991).

Test Re-test Reliability

We evaluated one month test-retest reliability among the 30% of the sample (n = 9) that was randomized to a follow-up visit in order to quantify test consistency over

time. Bivariate correlations were computed between baseline and follow-up timepoints for DMI outcome scores.

External Validation Using Existing Measures

Concurrent validity was examined by estimating correlations with external measures of misophonia and symptoms of broader psychopathology. Pearson bivariate correlations were conducted between DMI total score and subscores with the MQ and A-MISO-S for measures of misophonia, as well as the BSI-18 for a measure of general psychopathology.

Discriminant Validity

Discriminant validity was examined among the same 30% of the sample (n = 9) by estimating correlations with external constructs. Pearson bivariate correlations were conducted between DMI total score and the CRS and the MCSD, as neither religiosity nor social desirability are constructs with theoretical overlap with misophonia.

Predictive Validity

Predictive validity was examined by estimating correlations with external constructs. Pearson bivariate correlations were conducted between the DMI total score and subscores with the MQ, A-MISO-S, and BSI.

2.1.1.9 Results

Descriptive Statistics

Most participants in the current sample identified as female (n = 23, 76.6%), White (n = 27, 90%), and non-Hispanic (n = 27). The average age of the sample was 35.90 years (SD = 12.67). Forty percent of participants indicated they were single, never married (n = 12), had completed college (n = 12), and had a salary range of above $40,000 ($n$ = 17, 57%).

The mean score on the MQ Symptom Scale was 21.60 (SD = 4.87) and on the MQ Emotions and Behavior Scale was 25.60 (SD = 5.79), suggesting that on average participants marked responses between "sometimes true" and "often true" when asked how often they were sensitive to various potential sound triggers, and how often they experienced certain emotional and behavioral responses to these triggers. Responses to the MQ Impairment Scale (M = 8.73, SD = 1.82) suggest that on average the sample reported "moderate sound sensitivities." Twenty-nine participants (96.67%) reported "clinically significant symptoms" on the MQ (i.e., ≥ 7 on the impairment subscale (Wu et al. 2014). The mean total score on the A-MISO-S was 13.87 (SD = 3.10), suggesting that on average participants marked responses between "mild" and "moderate" when asked about the frequency, interference, and distress, as well as levels of resistance, control, and avoidance of misophonic cues in the past week. Responses to the BSI-18 (M = 13.83, SD = 10.51) suggest that on average participants had mild anxiety, depression, and/or somatization symptoms. Acceptability and feasibility ratings for the DMI were, on

average, both rated between "very acceptable" and "extremely acceptable" (*M* = 4.63, *SD* = .56 and .62, respectively).

Prevalence of DMI Item Endorsement

To examine endorsement of DMI interview items, we computed frequencies of all 19 items. Current misophonia items on the DMI were endorsed by 100% of the current sample (symptom presence defined by severity rating ≥ 1; Table 2), suggesting strong face validity of the DMI items.

Preliminary Internal Reliability

In order to explore preliminary internal reliability of the DMI, we calculated summary scores on the DMI interview and examined inter-item and item-total correlations, as well as Cronbach's alphas among DMI outcome scores. Internal reliability of the total DMI score was excellent: Cronbach's alpha coefficient for all 19 interview items was α = .90 (95% CI [.84, .95]). Item-total correlations among all interview items were strong, as all items except one had item-total correlations between .32 and .76 (see Table 3). Item #7, assessing worry for a lot of the time about future noises, had an item-total correlation of -.04 and produced a higher Cronbach's alpha when the value was deleted. As such, Item #7 was excluded from remaining analyses; 18 of the 19 items were retained in subsequent analyses.

Inter-item correlations between each of the retained 18 items are displayed in Table 4. Mean total score of all retained 18 items on the DMI was 31.67 (*SD* = 10.98), out of a

maximum of 72 points. Cronbach's alpha for the total DMI score was excellent (α = .91; 95% CI [.86, .95]; see Table 5), and average inter-item correlation (AIC) for the DMI was .36. Mean current severity score was 18.40 (*SD* = 7.34), out of a maximum of 48 points for the 12 items. Cronbach's alpha for the current severity score items was strong (α = .86; 95% CI [.78, .92]) and AIC was .33. Mean current impairment score was 10.30 (*SD* = 6.57), out of a maximum of 24 points for the 12 items. Cronbach's alpha for the current impairment score items was strong (α = .86; 95% CI [.78, .92]) and AIC was .33. Mean global impact score was 8.60 (*SD* = 3.45), out of a maximum of 16 points for the four items. Cronbach's alpha for the global impact score items was excellent (α = .88; 95% CI [.81, .93]) and AIC was .68. Further, inter-scale correlations between the DMI total score and current severity, current impairment, and global impact scores were all significant (*r*s = .96, .74, .78, respectively, *p*s < .001). Correlations among the three scores were also significant (see Table 6).

Taken together, the (a) high endorsement of DMI interview items, (b) strong Cronbach's alphas across the four DMI outcome scores, (c) AICs for the DMI total, current severity, and current impairment scores within recommended range (Clark & Watson, 1995), and (d) inter-scale correlations between the DMI outcome scores provide preliminary evidence of internal reliability for the DMI.

Test Re-test Reliability

Test-retest reliability of the DMI was explored by computing bivariate correlations between DMI scores from the baseline assessment and the follow-up visit among the 30% of participants randomized to follow-up. Pearson correlation coefficients between the DMI total scores ($r = .95$, $p < .0001$), current severity scores ($r = .94$, $p < .0001$), current impairment scores ($r = .88$, $p = .002$), and global impact scores ($r = .995$, $p < .0001$) at both time points were all strongly and positively correlated. Consistent with large correlation coefficient effect sizes (Cohen, 1988), these findings support preliminary evidence of test re-test reliability for the DMI.

External Validation

Next, to assess preliminary concurrent validity between the DMI and existing measures of misophonia, bivariate correlations were conducted. Pearson correlations indicated that the MQ total score and A-MISO-S total score in the current sample were positively correlated with each other ($r = .50$, $p = .005$). As hypothesized, preliminary evidence of convergent validity was observed in correlations between the MQ and DMI (see Table 7). Similarly, there was evidence of significant, positive correlations between the A-MISO-S and some DMI scores. In order to examine convergent validity between the DMI and general psychopathology, correlations were computed between the DMI and BSI-18. Bivariate correlations between BSI-18 and DMI total ($r = .42$, $p = .020$), current impairment ($r = .49$, $p = .006$), and global impact ($r = .54$, $p = .002$) scores were consistent with moderate correlation coefficient effect sizes (Cohen, 1988). DMI current severity

score was not correlated with BSI-18 total score. Taken together, these results indicate preliminary evidence of concurrent validity for the DMI.

Discriminant Validity

To examine preliminary discriminant validity, correlations were conducted between the DMI and the CRS and MCSD. Results suggest that the DMI was not significantly related to either religiosity (r = .05, p = .912) or social desirability (r = -.03, p = .868). These findings suggest preliminary discriminant validity for the DMI.

Predictive Validity

Lastly, bivariate correlations were conducted between DMI at initial assessment visit and self-report measures of misophonia and general psychopathology for the subset of the sample that was randomized to the follow-up visit (n = 9). Pearson correlations indicated that DMI total score was positively correlated with MQ emotions and behavior subscale (r = .81, p = .008), MQ severity score (r = 73, p = .025) and A-MISO-S total score at follow up (r = .71, p = .032). DMI total score was not correlated with MQ total score at follow up or BSI-18 total score at follow up. These findings provide preliminary evidence of predictive validity of the DMI.

2.1.1.10 Discussion

The overarching aim of this study was to develop and begin to psychometrically validate a semi-structured clinical interview to assess misophonia in adults. In addition to establishing symptom presence, as well as severity and impairment in functioning

from misophonia, we also incorporated items that capture a broad spectrum of responses to triggers across affective, cognitive, physiological, and behavioral domains. The interview assesses ways in which these response strategies are effective and/or ineffective, as well as dysfunctional beliefs related to misophonia. There were two phases of interview development. In Phase 1, interview items were generated and iteratively refined from both a scientific literature review and qualitative feedback from misophonia sufferers and experts. In Phase 2, a separate sample of adults was recruited to complete the DMI and other measures in order to assess exploratory psychometric properties. A third of participants were randomized to a follow-up visit in order to assess test-retest reliability and predictive validity. Iterative analytic procedures (e.g., estimated item-total correlations) were used to derive proposed final DMI items. From the overall item pool, the final DMI consists of 18 items, and includes four outcome scores: (1) Total DMI score (all 18 items), (2) Current severity score (12 items), (3) Current impairment score (12 items), and (4) Global impact score (4 items).

The DMI is the first semi-structured clinical interview for misophonia developed using iterative, grassroots methods integrating suggestions and feedback directly from key stakeholders (i.e., individuals with misophonia and experts in the field). Our approach to interview development was conducted to both optimize interview accessibility and applicability in both research and clinical settings, and to limit investigator biases or assumptions about misophonia that could influence the inclusion

or exclusion of interview items. The DMI includes reliable and valid scores reflecting a wide range of responses to misophonia. Intercorrelations between DMI scores indicated strong relationships between constructs. For example, the current severity, current impairment, and global impact scores correlated strongly with DMI total score.

As hypothesized, the DMI was significantly positively correlated with extant self-report measures of misophonia, including the MQ (Wu et al., 2014) and A-MISO-S (Schröder et al., 2013), and a general measure of psychopathology (BSI; Derogatis et al., 2001), supporting the preliminary convergent validity of the DMI. Further, the DMI was not correlated with measures of religiosity and social desirability, two constructs with no *a priori* theoretical overlap with misophonia, suggesting preliminary discriminant validity of the DMI. Test-retest reliability between the two assessment timepoints were strong. Correlations between the DMI at baseline and the A-MISO-S as well as certain MQ subscales were significantly positively correlated, indicating preliminary adequate predictive validity of the DMI.

The full DMI may be used to assess misophonia symptoms, functional impairment, response patterns to triggers, beliefs associated with the disorder, and the global impact of misophonia symptomatology. In addition, DMI subscores can be utilized to investigate changes in specific processes during treatment for misophonia. Researchers and/or clinicians examining intervention outcomes on patterns of thinking and physiological responses in misophonia could use the DMI current severity score as

an endpoint. Similarly, the impact of interventions on impairment could be investigated using the DMI impairment score.

The results of this study should be considered within the context of its limitations. First, it should also be noted that, despite the iterative, grassroots approach taken for item generation and inclusion, in light of the heterogeneity of misophonia, any given individual completing the DMI may report other features not captured by the DMI. Second, our sample in Phase 2 was small (n = 30) and largely homogenous (i.e., mostly White, female participants). Future research should replicate an extend our preliminary findings and evaluate the DMI using larger, more diverse clinical and general population samples. The inclusion of comparison samples of non-misophonic participants may also function to validate the face validity of the interview items as discriminating between those with and without misophonia. Third, preliminary psychometric examination of the DMI was limited in our ability to conduct inter-rater reliability. Validation studies of the DMI should include administration by multiple clinicians, researchers, and/or paraprofessionals, and include inter-rater reliability findings. Lastly, there were weak but positive correlations between the DMI scores with existing measures of misophonia, likely due to sample size and lack of power to detect stronger correlations. In the next phase of validation studies of the DMI, inclusion of other self-report measures of misophonia with stronger psychometric properties (e.g., DMQ; Rosenthal et al., 2021) is warranted.

Future Directions

The consensus definition of misophonia (Swedo et al., 2022) was released after completion of the present study. Future iterations of the DMI should ensure consistency with the recently published expert definition. Specifically, additions to the interview that reflect the consensus definition may include: more in-depth questions about influences on misophonic reactions (e.g., perceived degree of control over stimulus), attentional reactions (e.g., hyperfocus or obsession), and coping strategies to manage misophonia. Relatedly, additional input from interdisciplinary subspecialities (e.g., audiology, occupational therapy, neuroscience, otolaryngology) should be considered in future iterations to continue limiting investigator bias, and increasing accessibility, feasibility, and clinical utility of the DMI.

Additional future directions for the interview may include creation of a shorter version. DMI administration in this study took between 45 to 90 minutes. A briefer version of the DMI may be preferred in some contexts. In addition to developing a briefer version of the DMI for adults, adaption of the DMI to individuals under the age of 18 is warranted, as emerging evidence highlights that the onset of misophonia may be during childhood (Jager et al., 2020). In addition to iterative changes to the interview and adaptations of the DMI, future studies should focus on training paraprofessionals to administer the DMI in order to increase both clinical and research utility.

Conclusions

The DMI was developed as the first semi-structured clinical interview for misophonia to overcome the limitations of existing measures for this new disorder. Although preliminary, initial results evaluating the DMI satisfy the majority of proposed interview standards (Watson, 1990), including correspondence with proposed diagnostic criteria, inclusion of both dichotomous and continuous ratings, and adequate reliability and validity. Although validation and research on the integration of the DMI into varied clinical and research settings is needed, preliminary findings suggest the DMI may have excellent internal consistency, test re-test reliability, convergent validity, discriminant validity, and predictive validity. This study offers promising preliminary evidence for a clinically and empirically useful tool to understand misophonia, a new and understudied disorder.

3. Emotional functioning in misophonia

Creation and administration of the DMI evidences the heterogeneity in emotional functioning within misophonia, not only across types of emotions (e.g., anger, anxiety, disgust), but also across temporality of affect (e.g., shifts in moods) and regulation of emotion (e.g., difficulties coping). Although existing literature suggests an association between negative emotionality and deficits in emotion regulation in misophonia, less is known about the relationships among specific components of emotional functioning (e.g., emotion regulation, affective lability) in misophonia, as well as which processes of misophonia are associated with difficulties in emotional functioning. More insight into this area can further benefit idiographic assessment and treatment-development.

As such, one reasonable next step is to parse out the relationships among affective lability, difficulties with emotion regulation, and various components of misophonia. This study (Guetta et al., 2002b) controls for clinically relevant symptoms of anxiety and depression, as well as population-level stress (COVID-19, via statistical methods in order to account for transdiagnostic confounding variables. Findings indicate that when controlling for depression, anxiety, and COVID-19 impact, (a) difficulties with emotion regulation may be correlated with misophonia severity, and (b) the emotional and behavioral responses when triggered (rather than frequency of sound triggers), are most strongly associated with difficulties with emotion regulation; results

suggest that processes of emotion regulation may be crucial misophonia treatment targets.

3.1 Examining emotional functioning in misophonia: The role of affective instability and difficulties with emotion regulation

The following original research report was published in PLoS ONE (Guetta et al., 2022b), with the title, "Examining emotional functioning in misophonia: The role of affective instability and difficulties with emotion regulation." The authors were as follows: Rachel E. Guetta, Clair Cassiello-Robbins, Jacqueline Trumbull, Deepika Anand, and M. Zachary Rosenthal.

3.1.1 Introduction

Misophonia is a newly described sound intolerance condition characterized by atypical sensory over-responsivity and emotional reactivity to repetitive, pattern-based sounds. These trigger sounds are typically human-produced oral or nasal noises (e.g., throat clearing, chewing, slurping), can be environmentally produced (e.g., pen clicking, clock ticking; Brout et al., 2018; Jastreboff & Jastreboff, 2001), and are not attributable to aversive acoustic features such as volume or pitch (Rouw & Erfanian, 2018). The intensity, uncontrollability, and disproportionality of emotional reactions to trigger sounds is expressed across a range of affective responses (e.g., anger, anxiety, disgust; Rouw & Erfanian, 2018). Common behavioral responses include glaring at or mimicking the person producing the sound, verbal aggression, and infrequent physical aggression

(Taylor, 2017), all of which adversely impact interpersonal functioning. Recent research suggests that distress from trigger noises may be influenced by context. For example, many people with misophonia report more intense reactions when the sound is produced by family members and loved ones, or in contexts where the noises are deemed socially inappropriate (e.g., chewing with one's mouth open, pen-clicking in an exam setting (Edelstein et al., 2013; Taylor, 2017), highlighting the importance of context in both the perception of and response to triggers. In additional to interpersonal aggression and conflict, escape and avoidance behavior functions to prevent exposure and distress associated with misophonic cues. Such intolerance and avoidance of possible triggering contexts (i.e., family meals and restaurants, certain workplaces; Brout et al., 2019; Taylor, 2017) may maintain misophonic distress and, over time, lead to diminished capabilities with confidence and capability coping or regulating emotions.

Misophonia, as currently assessed using self-reported and clinical interview measures (e.g., Guetta et al., 2022a; Wu et al., 2014) can be operationalized using a tripartite symptom presentation: (a) presence of bothersome sounds and related sensory cues (i.e., visual stimuli related to the sounds, such as seeing someone chewing from afar in the absence of hearing chewing); (b) heightened physiological, affective, and cognitive distress with accompanying behavioral reactions in response to one (or more) of the auditory and visual cues; and (c) associated impairment in work, academic, or social functioning. As such, emotions (conceptualized as including physiological, cognitive,

and behavioral responses in order to fulfill context-dependent needs (Campos et al., 1994) and the way in which emotions are experienced and managed are central to the clinical presentation and severity of misophonia.

Emotions are typically managed through emotion regulation: the ability to both automatically and consciously apply sets of strategies that influence emotional experience, intensity, and expression (Gross & Muñoz, 1995). Successful emotion regulation, given the reported intensity of negative emotions in the face of aversive auditory and related stimuli, is essential to adaptive coping and management of misophonia. Chronic dysregulated emotions, particularly in the moments of being activated by triggers, can exacerbate overall impairment and subjective distress. Individuals with misophonia may attempt to disengage from the aversive stimuli and associated internal experiences via escape or avoidance. These strategies, while effective in the short-term to ease contact with the discomfort, are ineffective over time among emotional disorders broadly (Campbell & Barlow, 2007; Hayes et al., 1996; Sauer-Zavala & Barlow, 2014). For example, dysregulated anger or disgust in response to misophonic sounds could result in repeated avoidance of interpersonal situations leading to isolation and loneliness, thereby contributing to impairment caused by misophonia. Although speculative, difficulties with emotion regulation may have an important role in the development, maintenance, and treatment of misophonia. To date, however, very little scientific research has been conducted in this area.

Preliminary evidence suggests that emotion regulation deficits mediate the relationship between trait neuroticism, negative affect, and misophonia (Cassiello-Robbins et al., 2020a). These findings suggest that a reciprocal relationship between the tendency to frequently experience intense emotions and deficits in emotion regulation may confer risk for development and maintenance of misophonia. However, this study was preliminary, limited by small sample size, and did not control for the presence of other emotional problems that are known to co-occur with misophonia (i.e., depression, anxiety (Frank & McKay, 2019; Jager et al., 2020). As such, the relationship between emotion regulation and misophonia needs to be replicated and clarified in larger samples.

Furthermore, emotional functioning is a complex and multi-dimensional construct that includes trait features of emotional reactivity as well as those more directly related to emotion regulation. For example, affective lability (the speed, frequency, and range of changes in affective states) is an important emotional process observed in those with certain psychiatric disorders (e.g., bipolar disorder, borderline personality disorder). More generally, affective lability is a feature underlying trait neuroticism (Fettich et al., 2015) in non-clinical samples and may be a vulnerability factor for psychopathology. Affective lability is a specific process that can be examined as part of a broader effort to phenotypically characterize emotional functioning in misophonia.

No studies have examined the relative contributions and differential associations of affective lability and difficulties with emotion regulation with misophonia. Determining the relationships of these emotional processes with misophonia can help clarify intervention targets for clinicians and treatment researchers. This clarification is important, as there are currently no evidence-based interventions designed for adults with misophonia, and few randomized trials have been conducted (Jager et al., 2001; Lewin et al., 2021). Further, despite empirical evidence that mood and anxiety disorders co-occur with misophonia (Frank & McKay, 2019; Jager et al., 2020; Wu et al., 2014), investigation of misophonia thus far has not controlled for depression and anxiety symptoms. For research to elucidate factors specifically underlying misophonia, it is necessary to increase the scientific rigor by controlling for general psychopathology. In addition, no studies have dismantled whether specific components of misophonia (i.e., frequency of exposure to triggers, ineffective emotional or behavioral responses, or severity of functional impairment caused by misophonia) are differentially related to difficulties with emotional functional within this population. Determining which components may be associated with the greatest problems with emotional functioning could further efforts for treatment development (i.e., mindfulness or acceptance-based approaches for sound tolerance versus emotion regulation strategies to target ineffective behavioral responses).

This study begins to disambiguate the relationships among affective lability, difficulties with emotion regulation, and the components of misophonia. Data were collected over the first few months of COVID-19, and due to the heightened stress and presence of anxiety and depression during the pandemic (Huang & Zhao, 2020) we account for this psychological impact in our hypotheses and data analytic approach. First, replicating and extending the finding that misophonia-related impairment is associated with emotional functioning (Cassiello-Robbins et al., 2020a) we hypothesized that misophonia would be significantly associated with (a) difficulties regulating emotions in moments of distress and (b) rapid shifts in emotional state (i.e., affective lability). We further hypothesized that difficulties managing emotions may be related to severity of misophonia over and above affective lability. We expected these relationships would hold when controlling for symptoms of anxiety and depression and the impact of COVID-19. Lastly, because avoidance and escape are common in misophonia and have been more generally associated with emotion regulation difficulties across a range of psychopathology, it was hypothesized that, among the three components of misophonia, ineffective emotional and behavioral responses to triggers would be differentially associated with greater trait difficulties regulating emotions.

3.1.2 Methods

Participants

We evaluated these aims in a nonclinical sample of 297 adults recruited using the online Amazon Mechanical Turk (MTurk) platform. Inclusion criteria required participants to (a) be able to read and understand English, (b) be between 18-65 years old, and (c) have an MTurk participant approval rating of at least 99%. In line with recommended strategies when conducting research within MTurk, our study included three attention checks (Chandler & Shapiro, 2016). Attention checks were interspersed throughout the study and consisted of brief multiple-choice questions aimed to differentiate attentive from inattentive participants. Of the 384 participants who completed the study, we utilized data from the 297 participants who responded correctly to all three attention checks.

Demographic information for the final sample is displayed in Table 1. Overall, the sample predominantly identified as male, White, and non-Hispanic. The majority reported completing college or a higher level of education and had a household income over $40,000 per year.

Procedures

The Duke Health Institutional Review Board approved study procedures and participants provided written assent before beginning the study. All participants completed a battery of self-report questionnaires related to emotional functioning, mental health symptoms, COVID-19-related stress, and misophonia. Data were collected

online via REDCap and MTurk, and participants received $5.00 for completing the surveys.

Measures

Misophonia Questionnaire (MQ; Wu et al., 2014). The MQ contains 17 items across three subscales: Symptom Subscale, Emotions and Behaviors Subscale, and Impairment Subscale. The Symptom Subscale assesses frequency of bothersome noises (i.e., people eating, repetitive tapping). The Emotions and Behaviors Subscale assesses emotional (e.g., feeling anxious/distressed, becoming angry) and behavioral (e.g., escaping or avoiding situations, covering ears) responses to trigger noises. Response options for the first two subscales are rated from 0 ("not at all true") to 4 ("always true") and are summed for a MQ total score of 0-68. The Impairment Subscale consists of a single self-reported rating of sound sensitivity and impairment, ranging from 0 (minimal) to 15 (severe). As per Wu et al. 2014, a cut score of seven on this item indicates clinically significant misophonia symptomology. Initial validation of the MQ demonstrated good internal consistency (α = .86 - .89; Wu et al., 2014). Cronbach's alpha in the current sample was also good for the MQ total score (α = .89), as well as for the Symptom Subscale (α = .87) and the Emotions and Behaviors Subscale (α = .86).

Difficulties in Emotion Regulation Scale – Short Form (DERS-SF; Kaufman et al., 2016). The DERS-SF is an 18-item version of the widely used 36-item DERS (Gratz & Roemer, 2004). The DERS-SF assesses six processes associated with difficulties

regulating emotions when distressed: (1) Non-acceptance of emotional responses, (2) Difficulties engaging in goal directed behavior, (3) Difficulties controlling impulsive behaviors, (4) Lack of emotional awareness, (5) Limited access to emotion regulation strategies, and (6) Lack of emotional clarity. Item responses are scored from 1 ("almost never") to 5 ("almost always"), with higher scores indicating greater difficulty with emotion regulation. The DERS-SF total score was used in the present study, is commonly used as a global measure of difficulties regulating emotions, and is the sum of the six subscales. This score ranges from 18-90, with higher scores indicating greater difficulty regulating emotions. The DERS-SF total score had high internal consistency in the validation study (α = .89; Kaufman et al., 2015) as well as in the current sample (α = .93).

The Affective Lability Scale – 18 Item (ALS-18; Oliver & Simmons, 2004). This self-report measure assesses rapid shifts in affective experience and emotional expression. Each item is rated on a scale from 0 ("very uncharacteristic of me") to 3 ("very characteristic of me"). Higher total scores indicate more affective lability. The measure demonstrates good internal consistency (α = .87; Oliver & Simmons, 2004). Chronbach's alpha in the current sample was excellent (α = .97).

Generalized Anxiety Disorder 7-Item Scale (GAD-7; Spitzer et al., 2006). This brief self-report questionnaire assesses generalized anxiety. Each item is scored on a 4-point Likert scale from 0 ("not at all") to 3 ("nearly every day") to assess frequency of

symptoms. Higher total scores reflect more severe anxiety. The GAD-7 has excellent internal consistency (α = .92) and test-retest reliability (intraclass correlation = 0.83; Spitzer et al., 2006). Chronbach's alpha in the current sample was .92.

The Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001). The PHQ-9 is the depression module of the larger Patient Health Questionnaire, a self-administered questionnaire that assesses each of the nine *DSM-IV* criteria for depression (i.e., feeling down, hopeless, lack of appetite). The nine items assess symptom frequency from 0 ("Not at all") to 3 ("Nearly every day"). Higher total scores reflect higher depression severity. The PHQ-9 has excellent internal reliability (α = .89). Internal consistency was also high in the current sample (α = .89).

The COVID-19 Exposure and Family Impact Survey (CEFIS; Kazak et al., 2020). The CEFIS is designed to assess the impact of the COVID-19 pandemic. The CEFIS includes 25 dichotomous ratings ("yes" or "no") of how COVID-19 may have impacted that individual and their family, including financial stress, education and work disruptions, family or individual exposure to COVID-19, hospitalizations, and deaths. In order to obtain an indicator of the overall impact of COVID-19, we summed the 25 items; higher total scores indicate more severe impacts of the pandemic. Due to the recent onset of COVID-19 at the time of this study, however, there were no psychometrically validated measures of pandemic stress. We chose to include this

unpublished measure in order to control for the effects of COVID-19 on individuals' daily functioning.

Data analytic plan

All analyses were conducted in SPSS 26.0 (IBM SPSS, 2019). First, data were screened for normality using Shapiro-Wilk tests and any data that were non-normally distributed were log transformed. To conduct this transformation a value of "1" was added to each score because the lowest possible score on these measures was zero, and the value of zero cannot be log-transformed. Preliminary exploration of the relationships among misophonia, depressive and anxiety symptoms, and COVID-19 impact was conducted using bivariate correlations. Next, a multiple linear regression was conducted to explore the relationship between misophonia symptoms and difficulties with emotion regulation and affective lability, controlling for anxiety, depression, and COVID-19 impact. In order to examine if emotional functioning predicts misophonia symptoms broadly, a z-score was computed to derive an overall misophonia severity variable (each of the three MQ subscales was z-scored and the three z-scores were summed to create a standardized composite variable reflective of overall misophonia severity). This analytic plan enabled exploration of the relationships among study variables accounting for potentially confounding variables.

Lastly, the relationships among specific components of misophonia (i.e., MQ Symptom, Emotions and Behaviors, and Impairment Scales) and emotional functioning

were examined. This analysis was conducted using a multiple linear regression with significant predictors from the previous model entered in step two to determine which MQ subscale(s) accounted for emotional functioning over and above the a priori covariates (i.e., anxious and depressive symptoms, and COVID-19 impact) in step one.

3.1.3 Results

The total scores for the DERS-SF, PHQ-9, GAD-7, and ALS-18 all deviated from a normal distribution (as indicated by $p < .05$ on Shapiro-Wilk tests) and were log transformed to reduce bias[1]. Following logarithmic transformations, all variables approximated normal distributions (corrected skewness ranged from -1.78 to .34; corrected kurtosis ranged from -1.31 to 2.76 (Gravetter & Wallnau, 2014; Trochim & Donnelly, 2006).

Descriptive statistics

Descriptive statistics for all measures are included in Table 1. On average, the sample obtained a mean item score of 3.63 ($SD = 2.51$) on the Impairment Subscale, suggesting that the sample reported mild sound sensitivity on average. Over a tenth of the sample (13.47%, $n = 40$) reported clinically significant misophonia symptoms that cause impairment in their everyday lives, as indicated by a score of seven or higher on

[1] Findings are presented using the transformed variables due to the *a priori* decision to log transform variables that were not normally distributed. Analyses were conducted both with and without transforming the variables and results remained the same.

the MQ Impairment Subscale (Wu et al., 2014). In addition, the sample's total scores on the DERS-SF, PHQ-9, and GAD-7 fell within one standard deviation of the scores reported in their respective validation studies in non-clinical samples (Kaufman et al., 2016; Kroenke et al., 2001; Spitzer et al., 2006). The mean score on the ALS-18 was 1.80 standard deviations above that reported in the validation study (Oliver & Simmons, 2004), which used a nonclinical college-aged sample.

Table 1: Demographics and sample characteristics

Variable	*M (SD)*	N (%)
Age	39.13 (11.52)	
Male		156 (52.5)
Female		141 (47.5)
Race		
White		247 (83.2)
Black or African-American		21 (7.1)
Other Asian or Other Asian American (includes India, Malaysia, Pakistan, Philippines)		10 (3.4)
More Than One Racial Group		6 (2.0)
Korean or Korean American		6 (2.0)
Other		3 (1.0)
Chinese or Chinese American		2 (0.7)
Japanese or Japanese American		1 (0.3)
Native American, American Indian, Alaska Native		1 (0.3)
Ethnicity		
Hispanic		19 (6.4)
Non-Hispanic		278 (93.6)
Education Level		
Some High School		1 (0.3)
GED		10 (3.4)
High School Graduate		28 (9.4)
Bus/Tech Training Beyond High School		12 (4.0)
Some College		79 (26.6)
College Graduate		120 (40.4)

Some Graduate School		7 (2.4)
Masters Degree		35 (11.8)
Doctoral Degree		5 (1.7)
Household Income		
0 - $10,000		26 (8.8)
$10,000 - $20,000		29 (9.8)
$20,001 - $40,000		70 (23.6)
$40,001 – $65,000		63 (21.2)
$65,001 - $100,000		56 (18.9)
More than $100,000		53 (17.8)
MQ Symptom Subscale	1.30 (.87)	
MQ Emotions and Behaviors Subscale	0.93 (.61)	
MQ Severity Rating	3.63 (2.51)	
DERS_SF Total Score	35.43 (13.61)	
ALS-18 Total Score	40.63 (14.46)	
GAD-7 Total Score	4.35 (4.73)	
PHQ-9 Total Score	4.35 (5.14)	
CEFIS	6.78 (2.87)	

Note. MQ = Misophonia Questionnaire; DERS-SF = Difficulties with Emotion Regulation Scale Short Form; ALS-18 = Affective Lability Scale; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; PHQ-9 = Patient Health Questionnaire; CEFIS = COVID-19 Exposure and Family Impact Survey.

Correlations between misophonia, mental health symptoms, and emotion regulation

Pearson zero-order correlations indicated there were significant, positive correlations between misophonia severity (MQ total) and (a) depressive symptoms, (b) anxiety symptoms, and (c) COVID impact. As such, we included these variables as covariates in the remaining analyses. Additional Pearson correlations were conducted to examine associations between MQ total and the two planned measures of emotional functioning. MQ total was significantly correlated with both DERS-SF and ALS-18. All correlations are displayed in Table 2.

Table 2: Bivariate correlations between measures of misophonia, difficulties with emotion regulation, affective lability, COVID-19 impact, anxiety, and depression

Variable	DERS-SF	ALS-18	CEFIS	GAD-7	PHQ-9
MQ Total Score	.45**	-.16**	.30**	.43**	.42**

Note. $^{**}p < .01$, $N = 265$, Correlations used logarithmically transformed variables as indicated in text. MQ = Misophonia Questionnaire; DERS-SF = Difficulties with Emotion Regulation Scale Short Form; ALS-18 = Affective Lability Scale; CEFIS = COVID-19 Exposure and Family Impact Survey; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; PHQ-9 = Patient Health Questionnaire.

Relationship among components of misophonia and emotional functioning

First, we examined the relationship between emotional functioning and misophonia symptoms with a multiple linear regression (Table 3). Step 1 controlled for age and gender, as well as symptoms of depression and anxiety, and the impact of COVID-19. Step 2 included two measures of emotional functioning: the DERS-SF, measuring specific difficulties with regulating emotions when distressed, and the ALS-18, measuring strength of variability in affective experiences. The model indicated that, together, the variables in Step 2 (difficulties with emotion regulation and affective lability) accounted for a significant proportion of the variance in overall misophonia severity, even after controlling for severity of anxiety and depression symptoms and the impact of COVID-19 ($F(7,257) = 14.45$, $p < .0001$, $R^2 = .28$, R^2 change = .04). More specifically, the model indicated that the DERS-SF but not the ALS-18 evidenced a significant association with the MQ severity score (standardized $\beta = .26$, $t(3.69)$, $p < .0001$).

Next, we conducted a multiple linear regression to examine the specific component(s) of misophonia related to difficulties regulating emotions (Table 3), after controlling for age, gender, depression and anxiety symptoms and the impact of COVID-19 in Step 1. Only DERS-SF was included in this model, as ALS-18 was not a significant predictor in the prior model. Step 2 of the model accounted for 50% ($p <$ .0001) of the variance in DERS-SF total score ($F(8, 256) = 33.41$, $p < .0001$, $R^2 = .51$, R^2 change = .07), and revealed that the Emotions and Responses Subscale but not the Symptoms or Impairment Subscales evidenced a significant association with DERS-SF total score (standardized $\beta = .38$, $t(5.68)$, $p < .0001$).

Table 3: Multiple linear regressions examining emotional functioning in misophonia

Dependent Variable		Variables	β unstd.	SE	β std	*p*	R^2	$R^2\Delta$
MQ composite severity	Step 1	Age	.01	.01	.04	.520	.24	.24
		Gender	.03	.18	.01	.870		
		GAD-7	1.43	.49	.26	.004		
		PHQ-9	.97	.47	.18	.040		
		CEFIS	.13	.05	.16	.005		
	Step 2	Age	.01	.01	.06	.280	.28	.04
		Gender	.09	.18	.03	.602		
		GAD-7	1.07	.48	.19	.028		
		PHQ-9	.31	.49	.06	.523		
		CEFIS	.13	.04	.17	.003		
		DERS-SF	3.96	1.07	.26	<.0001		
		ALS-18	-.29	.44	-.04	.520		
DERS-SF total	Step 1	**Age**	.00	.00	-.11	.023	.44	.44
		Gender	-.02	.01	-.08	.107		
		GAD-7	.09	.03	.24	.002		
		PHQ-9	.16	.03	.46	<.0001		

	CEFIS	.00	.00	-.04	.457		
Step 2	Age	.00	.00	-.09	.058	.51	.07
	Gender	-.02	.01	-.07	.112		
	GAD-7	.07	.03	.18	.016		
	PHQ-9	.13	.03	.37	<.0001		
	CEFIS	.00	.00	-.06	.203		
	MQ Reactions	.10	.02	.40	<.0001		
	MQ Symptoms	-.02	.01	-.09	.097		
	MQ Impairment	.00	.00	-.07	.259		

Note. Variables with *p*-values less than .05 are shown in bold. MQ = Misophonia Questionnaire; GAD-7 = Generalized Anxiety Disorder 7-item scale; PHQ-9 = The Patient Health Questionnaire; CEFIS = The COVID-19 Exposure and Family Impact Survey; DERS-SF = Difficulties in Emotion Regulation Scale – Short Form; ALS-18 = Affective Lability Scale – 18 Item.

3.1.4 Discussion

The primary aim of this study was to examine the relationships among difficulties with emotional functioning and specific components of misophonia. A community sample was used, with 13.5% of individuals reporting moderate or higher impairment in functioning due to sound sensitivities. This result is notable, given that the sampling procedure did not selectively recruit individuals self-identifying with misophonia. The prevalence of misophonia is unknown, with previous studies estimating approximately 17% of undergraduate students reporting moderate or higher impairment caused by misophonia (e.g., Wu et al., 2014). Accordingly, findings from our study represent a somewhat lower estimate of the prevalence of clinically significant misophonia compared to earlier studies with college student samples.

As hypothesized in the present study, misophonia severity was correlated with anxiety, depression, COVID-19 impact, difficulty regulating emotions, and affective lability. These results are in line with previous findings suggesting misophonia may be associated with higher depression, anxiety, and difficulty regulating emotions (Cassiello-Robbins et al., 2020a; Siepsiak et al., 2020; Wu et al., 2014). This is the first study to examine the relationship of misophonia with affective instability. The association of misophonia with affective lability is consistent with earlier suggestions that misophonia may be characterized by heightened negative emotional reactivity (Brout et al., 2018). To the best of our knowledge, this is also the first study to examine the relationships among misophonia, emotion regulation, and the impact of COVID-19. Given growing literature highlighting the relationship of COVID-19 with increased rates of depression and anxiety (e.g., Huang & Zhao, 2020), which are also associated with misophonia, it is unsurprising that the impact of the ongoing pandemic is also associated with greater misophonia severity.

Additionally, results supported our hypothesis that difficulties regulating emotions would account for misophonia severity after controlling for the presence of anxiety, depression, and COVID-19 impact. One other study has noted a relationship between misophonia and difficulties regulating emotions (Cassiello-Robbins, 2020a); however, this study did not control for the presence of other mental health symptoms. Thus, the results of the current study replicate and extend those findings by suggesting

difficulties with emotion regulation remain significantly related to misophonia even when controlling for anxiety and depressive symptoms. Importantly, although the amount of variance in misophonia symptoms explained by difficulties with emotion regulation was statistically significant, it was much smaller than that accounted for by the impact of COVID-19 and symptoms of depression and anxiety. Nonetheless, this finding raises the question of if, and to what extent, general psychological distress may explain the relationship between misophonia and emotion regulation. One hypothesis is that individuals with misophonia may have problems regulating emotions irrespective of current anxiety, depression, or the impact of COVID-19. Responses to the DERS-SF represent more trait-like difficulties with emotion regulation, whereas the PHQ-9 and GAD-7 represent distress in the two weeks prior to assessment. As such, these findings suggest that an individual's perception of their ability to regulate emotions broadly may be associated with misophonia above and beyond the distress they experienced close to the time of assessment. Still, because symptoms probed on the PHQ-9 and GAD-7 may also be correlated with emotion regulation, it is important to conduct research that can investigate and ultimately elucidate the roles that these constructs have in the etiology and maintenance of misophonia.

In contrast to the role of difficulties with emotion regulation, findings using a multivariate model indicated that affective lability did not account for misophonia severity when co-varying the impact of COVID-19, anxiety, and depressive symptoms.

This finding points to the possibility that affective lability, though correlated with misophonia, is not as useful of an indicator of severity compared to difficulties regulating emotions. When considering this pattern of results, it is possible that the experience of strong and variable emotions is less related to misophonia symptom severity than how emotions are regulated when one is distressed. Because this is the first study to explore the relationship between affective lability and misophonia, this result should be considered preliminary until replicated. Future studies, particularly research using ecological momentary assessment and longitudinal designs, can further disambiguate the temporal relationships among affective lability and emotion dysregulation in naturalistic contexts including trigger sounds.

An additional goal of this study was to explore whether specific aspects of misophonia were differentially associated with emotional functioning difficulties. To the best of our knowledge, no study has explored whether the frequency of exposure to misophonic sounds, emotional and behavioral responses to sounds, or reported impairment due to sound sensitivity is uniquely associated with emotional functioning. Our results are congruent with the hypothesis that emotions and responses when hearing a bothersome noise, rather than the frequency of exposure to bothersome sounds, may be associated with greater difficulties regulating emotions. Put differently, emotion regulation difficulties may be associated with how one responds to triggering stimuli rather than how often they are exposed to such stimuli. This finding may be

useful for clinicians treating misophonia. Specifically, in an effort to reduce difficulties with emotion regulation when treating individuals suffering from misophonia, it may be important to target problems with emotional and behavioral responses to trigger sounds.

These findings add to the emerging literature indicating emotion regulation is relevant to understanding misophonia and has potentially important implications for intervention development (Cassiello-Robbins, 2020a). Evidence-based cognitive behavioral therapies that target processes related to emotion regulation are well established for depressive, anxiety, and emotional disorders (Cassiello-Robbins, 2020b; Hofmann et al., 2012; Sakiris & Berle, 2019). It is possible that the application of these treatments can help remediate symptoms of misophonia. Although there are no evidence-based treatments specifically for misophonia, an emerging clinical literature suggests the application of a range of interventions within the broader family of cognitive behavioral therapies may be useful when treating misophonia (Cassiello-Robbins, 2020a; Sakiris & Berle, 2019). Without more randomized controlled trials or controlled experimental studies testing interventions for misophonia, it is clear that more research is needed to establish the acceptability and efficacy of any treatment approaches for misophonia.

These results should be considered in the context of the limitations of this study. First, the sample was recruited from Amazon's MTurk and had a higher percentage of

White participants (83.2%) than is representative of the United States population (76.3%; https://www.census.gov/quickfacts/fact/table/US/PST045219), limiting the generalizability of study results. Future studies with diverse and under-represented samples are needed. There may also be associated limitations and concerns regarding data collection and sampling using MTurk, including less sustained attention and fidelity to survey procedures, perhaps in part due to the remote, anonymous nature of study administration. There may also be individual differences among MTurk participants that contribute to limited generalizability of results. For example, MTurk participants scored lower on extraversion and emotional stability than community participants on a measure of the Big Five Personality traits (Schröder et al., 2017) a finding reflected in the current sample's ALS-18 scores. Although our sample passed all three attention checks throughout the study, and numerous empirical studies have suggested MTurk participants produce reliable results consistent with decision-making biases present in control groups (Goodman, 2012) replicability among in-person community samples are warranted.

Second, although the MQ has been used in recent studies (Daniels et al., 2020; Frank et al., 2020; Frank & McKay, 2019; McKay et al., 2018; Zhou et al., 2017), it was developed and validated using an undergraduate student sample (Wu et al., 2014). Limited validity data have been published for the MQ, and its applicability to non-student samples remains unclear. Additionally, impairment on the MQ is assessed by a

single item, limiting reliability of this assessment. Third, our data were cross-sectional, liming our ability to draw conclusions about causal relationships between the relevant constructs over time. Future research should aim to collect longitudinal data (e.g., ecological momentary assessment) to further elucidate the relationship between emotions and behaviors in the context of misophonia and emotion regulation strategies. This knowledge can lead to targeted intervention development.

A final limitation to consider is that emotion regulation is a multifaceted construct. For example, Gratz and Roemer (2004) who developed the measure on which the DERS-SF is based, proposed emotion regulation includes components such as awareness and understanding of emotions, acceptance of emotions, engaging in goal directed behavior when experiencing strong emotions, inhibiting impulsive behavior, and accessing effective emotion regulation strategies. In this study, we assessed emotion regulation in a global manner, but did not examine the relationships among specific components of emotion regulation with misophonia. The finding indicating a significant relationship between misophonia and emotion regulation even when controlling for other psychological difficulties (e.g., anxiety, depression, COVID-19 impact) highlights the need for future research designed to parse apart components of emotion regulation that contribute to misophonia severity. When considering the small amount of variance accounted for in the present study by difficulties with emotion regulation over and above the impact of COVID-19, anxiety, and depressive symptoms, it is especially

important for future studies to discern whether and which specific difficulties with emotion regulation are most germane to understanding misophonia. Further, components of depression and anxiety, assessed in the PHQ and GAD respectively, remained significantly associated with difficulties regulating emotions when misophonia variables were included in regression analyses. This result highlights the challenges associated with exploring the relationship of emotion regulation and misophonia while controlling for other psychopathology that is also characterized by difficulties with emotion regulation. On one hand, the significant relationship of misophonia with difficulties in emotion regulation while controlling for depression and anxiety suggests further exploration of misophonia and emotion regulation is warranted. On the other hand, the significant relationship of all three constructs with emotion regulation raises the potential that the relationship of misophonia with emotion regulation is driven by the fact that people with more severe misophonia symptoms often report more depression and anxiety, but that misophonia is neither uniquely associated with emotion regulation alone nor with symptoms of depression or anxiety alone. One way to disentangle the relationships among depression, anxiety, and emotion regulation in misophonia would be to conduct prospective studies (e.g., ecological momentary assessment) that examine the variability of these phenomena longitudinally.

Despite these limitations, this study is among the first to explore and disentangle the relationships among misophonia and emotional functioning broadly. We hope that

these findings will help pave the way for future research to continue examining the role of emotion regulation in the etiology, maintenance, and treatment of misophonia.

4. The role of stress and trauma in misophonia

Taken together, Chapters 2 and 3 highlight areas for future inquiry around mechanisms and experiences that may shape emotional functioning before, during, and after misophonia triggers. Responses in the DMI section about earliest memories of misophonia often included anecdotes about unpleasant childhood events (e.g., growing up with a parent experiencing alcoholism) that individuals paired over time, via associative learning, with related aversive sounds (e.g., swallowing, smacking sounds). There becomes a hypothesis, then, that there exist complex interactions between early social and situational contexts, physiological and emotional arousal and regulation, and vigilance and attentional fixation. Extant literature has suggested the possibility that stress may be a causative factor in the development of sound intolerance, and the possibility that misophonia may be related to trauma and PTSD (Mazurek et al., 2010; Rouw & Erfanian, 2018). Indeed, in both cases of stress and misophonia there are (a) patterns of chronic, aversive stimulation, (b) themes of inescapability, unpredictability, and uncontrollability of threat cues and triggers, and (c) low hums of persistent sympathetic nervous system arousal and hypervigilance to triggers (trauma- or misophonia-related).

Chapter 4 works to further understand the interplay between misophonia, stress, and trauma, as well as identity additional possible mechanisms that may hold implications for both assessment and treatment. The work in this area to date has been

limited by self-reported diagnosis of *DSM* conditions. Utilizing more rigorous assessment tools and probing mechanistic processes is an important avenue to characterizing possible targets for change in misophonia treatment. No studies have explored perceptions of stress, or the impact of broader population-level stressors (e.g., COVID-19), in relation to misophonia. Chapter 4 assesses both the influence of trauma-related diagnoses and stressful life event histories on misophonia, as well as whether traumatic stress specifically or perceived stress more generally accounts for misophonia severity. This study balances both medical model approaches (i.e., integrating comprehensive diagnostic interviewing using the SCID-5) and dimensional, mechanistic frameworks (i.e., assessing transdiagnostic processes of perceived stress, hyperarousal).

Results from Chapter 4 indicate that, although there is overlap in transdiagnostic factors between trauma and misophonia (e.g., perceived stress), there is no evidence for a causal link between traumatic events and the development of misophonia. These findings provide further support for integrating idiographic assessment tools to understand individualized histories of chronic stress, as well as the perceptions of stress during misophonic reactions and in emotional functioning more broadly. Chapter 4 findings also imply that effective treatments for misophonia could involve a process-based approach that targets mechanisms across biological, social, cognitive, and behavioral levels.

4.1 Misophonia is related to stress but not directly with traumatic stress

The following original research report was published in PLoS ONE (Guetta et al., 2024), with the title, "Misophonia is related to stress but not directly with traumatic stress." The authors were as follows: Rachel E. Guetta, Marta Siepsiak, Yanyan Shan, Emily Frazer-Abel, and M. Zachary Rosenthal.

4.1.1 Introduction

Misophonia is a sound intolerance disorder marked by strong aversion and heightened multi-modal (i.e., physiological, cognitive, behavioral) emotional reactivity to certain repetitive auditory stimuli usually produced by other humans (e.g., oral or facial cues such as chewing, sniffing, throat clearing; Erfanian et al., 2019; Swedo et al., 2022). First described by Jastreboff & Jastreboff in 2001, misophonia is a newly studied phenomenon that is gaining empirical and clinical attention across health disciplines. Emotional responses in anticipation or response to aversive cues can include anxiety, anger and disgust, increased sympathetic nervous system activation (e.g., heart rate, muscle tension), and behavioral urges and actions that function as freeze (e.g., hypervigilance), flight (e.g., escape or avoidance), and fight (e.g., confrontation, verbal aggression, indirect aggression; rarely physical aggression) reactions. These patterns collectively contribute to chronic and significant psychological distress and impairment in social, academic, or occupational functioning. Contextual factors (e.g., certain social

settings, particular people, affective state) may influence the severity of misophonic responses (Swedo et al., 2022). Early studies using self-report questionnaires pointed to the possibility that misophonia co-occurs with obsessive compulsive disorder (Schröder et al., 2013) and other specific psychiatric disorders. However, the most recent research using structured diagnostic interviews has observed different results, indicating that (a) there do not appear to be any specific psychiatric disorders uniquely associated with misophonia and (b) the most commonly associated psychiatric disorders, when assessed carefully and comprehensively, may be current anxiety disorders, features of obsessive compulsive personality disorder, and a lifetime history of mood disorders (Guzick et al., 2023; Jager et al., 2021; Rosenthal et al., 2022).

One approach to investigate the relationship between misophonia and other conditions is to examine transdiagnostic mechanisms that may either be shared or can explain differences between disorders. Mechanisms of stress, defined broadly, are of particular interest, given the prevalence of stress reactions in misophonia across affective over-reactivity (e.g., anger, aggression), flight or fight behaviors, physiological arousal (e.g., activation of the sympathetic nervous system), attentional difficulties (e.g., hypervigilance to triggers), and overall distress (Swedo et al., 2022).

There is a growing body of evidence indicating that stress may be a causative factor in the development of sound over-responsivity. Mazurek et al. demonstrated that behaviorally induced stress, including acoustic stress, can result in transient auditory

sensitivity in rats, which may be viewed as an adaptive process of hypervigilance in an insecure environment (Mazurek et al., 2010). Recently, Manohar et al. showed that chronic stress induced pharmacologically with corticosterone hormones caused an increase in sound over-responsivity and auditory cortex hyperactivity in rats (2023). Similar effects of stress on sound perception have also been observed in humans. For instance, in an experimental study, Hasson et al. found that sound sensitivity reflected in uncomfortable loudness levels (ULL) significantly increased in a group of women after stress exposure (Hasson et al., 2013). Emotional exhaustion was also negatively correlated with ULL and hyperacusis in non-clinical participants (Wallén et al., 2012). Nevertheless, the relationships between misophonia and stress has not yet been carefully examined.

Stress, however, is a complex and multi-faceted construct that implicates biological and psychological systems, necessitating specificity in measurement to glean empirically and clinically useful findings. At the broadest level, reactions to everyday stressors manifest in physiological and biological changes (e.g., increases in heart rate, galvanic skin response, activation of the sympathetic nervous system), though the impact of reactions are mediated by subjective appraisals of the stressors (Lazarus, 1984). Perceptions of stress can vary greatly based on individual differences in factors ranging from information processing to cognitive style, and attentional biases to coping strategies (Chang, 1998; Graves et al., 2021). Perceived stress, or the degree to which

individuals appraise their lives and everyday situations as unpredictable, uncontrollable, or overloading (Cohen et al., 1983) is a transdiagnostic factor associated with risk for development of psychiatric, behavioral, and physical health problems (Cohen et al., 2007; Miller et al., 2007; Monroe, 2008), highlighting the importance of subjective appraisals in understanding short- and long-term consequences of situational and chronic stress. Decades of research have evidenced distinct biological pathways that mediate the relationships between traumatic events and perceived stress on various health outcome measures (Cohen et al., 1983; Monroe, 2008). The differences in explanatory and mechanistic pathways between perceived stress, presence of stressful life events, and adverse health outcomes further highlights the need for specificity in measuring stress as a multidimensional construct.

In addition to probing perceived stress, it is important to measure history of traumatic life events. To move towards an objective consensus definition of trauma, the stressor criterion (Criterion A) used to assess and diagnose posttraumatic stress disorder (PTSD) includes specific categories of events that one can experience directly, witness, or learn about via repeated and extreme exposure (Friedman, 2013). Endorsement of these events can be catalogued in self-report measures, such as the Life Events Checklist for *DSM-5* (LEC-5; Wilson & Keane, 2004). Still, the development of PTSD is broadly conceptualized as an interruption to natural recovery from a trauma, as the majority of individuals will not meet criteria for a PTSD diagnosis three months following exposure

to a Criterion A event (Bonanno & Mancini, 2012). Stated differently, epidemiological work indicates that most adults have experienced at least one potentially traumatizing event across their lifetimes, but under 10% develop PTSD (Bonanno & Mancini, 2012; Kessler et al., 2005). As such, traumatic stress, including PTSD and its various symptom clusters, must be measured in addition to the pure presence and frequency of traumatic life events. In addition to presence of a Criterion A event, PTSD symptoms fall into four clusters: re-experiencing (e.g., intrusive thoughts, flashbacks, nightmares), avoidance (e.g., suppression of trauma-related thoughts, avoidance places or people that are reminiscent of the trauma) negative cognitions and mood (e.g., persistent negative emotions, increased guilt and shame, negative belief about self and others), and hyperarousal (e.g., hypervigilance, startle reaction). Some of these symptoms may not be distinct to PTSD, and may reflect transdiagnostic factors unrelated to trauma specifically (e.g., avoidance, negative alterations in mood and cognition).

Lastly, large scale stressors affecting individuals at a population level are an additional dimension of stress that is important to capture empirically. Studies implementing self-report measures of stress and traumatic stress may at times be confounded by cohort-level current or state stress. The COVID-19 pandemic is a good example of this, wherein self-reported stress may at times be confounded by state level stress that is ongoing for individuals. As such, it is important to not ignore population-level stressors that may contribute to or account for self-reported stress.

The question of if and how misophonia may be related to these various components of stress, however, has been largely unaddressed. Most studies to date assessing the relationships between misophonia and stress have focused on the prevalence of traumatic stress, particularly the comorbidity with participant self-reported diagnosis (Rouw & Erfanian, 2018) of PTSD or diagnostic conclusions from structured interviews (Jager et al., 2021; Rosenthal et al., 2022). Among these studies, there have been mixed findings on the extent of the relationship between PTSD and misophonia.

On the one hand, some work suggests that misophonia may be related to PTSD (Rouw & Erfanian, 2018). In an online study among a sample of 301 adults with self-reported misophonia, Rouw and Erfanian (2018) found that PTSD was the most frequently self-reported co-occurring diagnosis (12% of sample) of 10 conditions probed with self-report items (PTSD, OCPD, tinnitus, hyperacusis, auditory processing disorder, attention deficit disorder, exploding head syndrome, phonophobia, eating disorders, and selective mutism). Findings from that study indicate that only PTSD was significantly related to misophonia severity. Of note, however, this study relied solely on self-reported assessments of 10 idiosyncratically chosen psychiatric and medical co-occurring disorders and did not use as comprehensive of an assessment approach as more recent studies (Guzick et al., 2023; Jager et al., 2021; Rosenthal et al., 2022). In the

absence of more rigorous diagnostic approaches, it is not possible to draw definitive conclusions about the relationship between misophonia and PTSD.

With that caveat in mind, several recent studies have found relatively low rates of PTSD in misophonia when using structured psychometrically valid assessment measures to explore the relationships among misophonia and associated mental health conditions (Jager et al., 2021; Rosenthal et al., 2022; Siepsiak et al., 2022). In one study in Amsterdam, 1.7% of adults (*N*= 575) seeking treatment for misophonia met criteria for PTSD when assessed with the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) which assesses 15 current psychiatric problems (Jager et al., 2021). In another study in Poland, Siepsiak et al. (2022) used the M.I.N.I. and found that 11.9% of adults with misophonia met criteria for PTSD. Rosenthal et al. (2022) conducted the first study to characterize *DSM-5* (APA, 2013) disorders using the Structured Clinical Interview for *DSM-5* (First, 2014) in a sample of 207 adults in the U.S. with high misophonia symptoms. Results indicated that 2.9% had concurrent PTSD, with 15.5% having PTSD at some point in their lifetime (Rosenthal et al., 2022). Based on the findings in these three carefully conducted studies, misophonia appears to be associated with relatively low or modest rates of PTSD at a prevalence somewhat congruent with what may be observed in the general population (between 6.8-10%; Bonanno & Mancini, 2012; Kessler et al., 2005).

Accordingly, from these recent studies one could conclude that people with misophonia may not be particularly likely to be diagnosed with current PTSD, raising doubt about whether misophonia should be conceptually related to a history of traumatic stress. However, we believe that conclusion is premature, and that more research is needed to help better understand whether and how misophonia may be related to traumatic stress. No studies have examined whether misophonia is associated with stressful events across the lifespan. It is possible that PTSD itself may not be related to misophonia, but rather that cumulative adverse life events may, as is the case with many physical and mental health problems, be associated with the etiology and/or course of misophonia (Karam et al., 2014; Turner & Lloyd, 1995).

A diagnosis of current PTSD does not appear to be directly linked with misophonia, but what about the broader construct of stress? One recent study investigated the relationship between misophonia symptoms and dimensional aspects of traumatic stress (Siepsiak et al., 2020). These findings suggested a moderate positive correlation between misophonia symptoms and arousal and intrusions, and a low correlation with avoidance. However, it should be noted that this study was conducted on a sample of hospitalized patients with depression; additional research using a similar approach is needed with outpatient and community samples before clear conclusions can be made.

No studies have explored the perceptions of stress in relation to misophonia, or broader population-level stressors. Certainly, some clusters of PTSD symptoms (e.g., avoidance, negative alterations in mood and cognition) are also transdiagnostic factors, unrelated to trauma specifically, but associated with other mental health problems (e.g., mood disorders). It is unknown to what extent some of these shared processes are also related to misophonia outside of the context of trauma. For example, hyperarousal is central to the clinical picture of misophonia, both in heightened physiological reactions to trigger sounds (e.g., increased heart rate, sweating), and in hypervigilance towards trigger sounds and related contextual cues. Avoidance of potentially triggering situations and individuals is also central to maintenance and impairment of misophonia. As such, investigating how specific components of PTSD overlap or diverge from misophonia, over and above PTSD diagnosis, is warranted. One possible explanatory model may be that certain symptom clusters of PTSD could be related to misophonia severity.

Another possibility is that perceived stress more broadly, that does not result in chronic traumatic stress, may be related to misophonia severity. Firstly, given the empirical evidence that perceived stress is transdiagnostic and associated with greater psychological distress, and medical and psychiatric problems broadly (Cohen et al., 2007; Monroe et al., 2008; Miller et al., 2007). it makes conceptual sense that subjective appraisals of stress would be related to misophonia severity as well. Further, the

anecdotal experiences of misophonia often involves a profound sense of unpredictability, uncontrollability, and inescapability (Swedo et al., 2022), suggesting the importance of subjective appraisal of stress reaction in misophonia.

Understanding the ways in which cumulative adverse life events, PTSD diagnosis, PTSD symptomatology, and perceptions of stress are related to misophonia may help shed light on the etiology and maintenance of misophonia, as well as inform treatment recommendations. The primary aim of the current is to better understand the relationships among misophonia, stress, and trauma in a community sample. A secondary aim is to preliminarily examine mechanisms of trauma and stress-related sequalae (i.e., clusters of PTSD symptoms via the PCL-5) that contribute to misophonia severity.

We hope to deepen an understanding of whether traumatic life experiences are associated with misophonia, as well as how perceptions of stress interact with misophonia severity. Because this study was conducted during the peak of COVID-19, we also measured stress in the context of the pandemic in order to account for this population-level stressor and to reduce the possibility confounding results of stress related to COVID-19. Based on the relatively low prevalence of PTSD in prior studies (Jager et al., 2021; Rosenthal et al., 2022; Siepsiak et al., 2022). The theoretical and empirical associations between mechanisms of stress and psychological distress broadly, we hypothesized that specific components of stress (e.g., perceived stress, certain

clusters of PTSD) rather than PTSD diagnosis itself would be more strongly related to misophonia severity.

4.1.2 Materials and methods

Participants and study design

A sample of 143 adults (average age = 36.89 years; females = 67.8%; see Table 1 for demographic information) residing in the U.S. and who identified as having auditory sound sensitivity enrolled in the current study via a REDCap link posted to the Duke Center for Misophonia and Emotion Regulation website (Harris et al., 2009). The Duke Health Institutional Review Board (IRB) approved study procedures and all participants provided written informed consent before participation. Study visits were conducted between December 9, 2019 and December 2, 2022, and included administration of the SCID-5 by trained assessors, followed by several self-report questionnaires that participants were asked to fill out on their own (see below).Exclusion criteria for enrollment included current psychotic disorder, current mania, and current anorexia nervosa; eligibility was confirmed via a phone screening using the M.I.N.I. following completion of the REDCap online screening form. Participants received $75 USD for completion of structured clinical interviews and self-report assessments.

Table 4: Demographic characteristics of the current sample

Characteristic	*n*	%
Age in years (*M, SD*)	36.88	12.84
Sex		
Male	43	30.1
Female	100	69.9
Gender Identity		
Male	43	30.1
Female	97	67.8
Genderqueer	1	.7
Other	2	1.4
Sexuality		
Straight	109	76.2
Gay	8	5.6
Bisexual	14	9.8
Something else	6	4.2
Don't know	5	3.5
Did not disclose	1	.7
Race		
White	106	74.1
African American	6	4.2
Native American	2	1.4
Chinese or Chinese American	7	4.9
Other Asian	6	4.2
Other	3	2.1
More than one race	13	9.1
Hispanic/Latinx		
Yes	23	16.1
No	120	83.9
Income Level		
0-$10,000	21	14.7
10,001 - $65,000	39	27.27
65,001 – more than $100,000	83	58.04
Marital Status		
Single	58	40.6
Married	61	42.7
Separated	4	2.8
Divorced	5	3.5

Living with partner	14	9.8
Missing	1	.7

N = 143

Measures

Misophonia Questionnaire (MQ; Wu et al., 2014): The MQ is a three-part self-report questionnaire that consists of: (a) presence of misophonic triggers (subscale 1), (b) emotional and behavioral responses to misophonic triggers (subscale 2), and (c) a single-item self-rated impairment of sound sensitivities. Participants completed the MQ as part of the online screen posted on our Center's website before enrolling in the study visit. Self-rated MQ impairment ranged from 1 to 12, indicating a sample with misophonia impairment across the spectrum from mild to severe; average self-rated impairment was 7.53 (*SD* = 2.03) corresponding with "moderate sound sensitivities." Cronbach's alpha in the current sample was α = .84 (McDonald's omega = .83)

Structured Clinical Interview for Diagnostic and Statistical Manual-5th research edition (SCID-5; First, 2014). The SCID-5 is a widely used, validated semi-structured interview designed to assess diagnostic symptoms of *DSM-5* disorders (APA, 2013). Trained assessors included licensed clinical psychologists, as well as clinical psychology postdoctoral fellows and doctoral students. Interviewers assessed for categorical diagnoses of current (e.g., past month, past six months) and lifetime disorders. Composite variables were also created to capture whether participants met criteria for current or lifetime categories of disorders (i.e., any mood, anxiety, substance use, or

trauma-related disorder). Diagnostic variables were coded as either 0 (below threshold of meeting clinical criteria) or 1 (meeting full criteria for the presence of disorder). Validation studies for the SCID-5 have evidenced strong internal consistency ($\alpha s > .80$; Shankman et al., 2018). Inter-rater reliability for the SCID-5 interviews was assessed by a blind rater randomly rating 8% of recorded interviews. Significant Cohen's κ ranged from 0.63 to 1.00 ($ps < 0.05$) for all trauma- and stressor-related disorders.

Stressful Life Events Checklist for *DSM-5* (LEC-5; Wilson & Keane, 2004): The Life Events Checklist for the *DSM-5* (LEC-5) is a self-report measure designed to screen for potentially traumatic events over an individual's lifetime. The LEC-5 is often used to establish exposure to a PTSD Criterion A traumatic event. This self-report tool assesses for the 16 events known to potentially result in PTSD (e.g., natural disaster, physical or sexual assault, combat).

Posttraumatic Stress Disorder Checklist for *DSM-5* (PCL-5; Blevins et al., 2015): The PCL-5 is a 20-item, psychometrically validated self-report measure that assesses symptoms of PTSD in accordance with the *DSM-5* diagnostic criteria. The PCL-5 is often used to screen for the possible presence of PTSD and/or severity of PTSD symptoms. Respondents are asked to rate each item in terms of how much they were bothered by that symptom. Each item is captured on a Likert scale ranging from 0 ("not at all") to 4 ("extremely"). A total symptom severity score ranges from 0-80, calculated by summing each item's 0-4 response. Preliminary research suggests PCL-5 score between 31-33

indicates probable PTSD across samples (Bovon et al., 2016). Validation studies reflect strong internal consistency (α = .95; Blevins et al., 2015). Cronbach's alpha in the current sample was α = .93 (McDonald's omega = .93).

Perceived Stress Scale (PSS; Cohen et al., 1983): The PSS is a widely used self-report tool that measures perceptions of stress in the past month. The 10 items probe frequency of perceived stress and associated experiences (e.g., confidence in handling the stressful situation, ability to overcome stressful situations). Each item is captured on a 5-point Likert scale, ranging from 0 ("never") to 4 ("very often"). Total scores on the PSS range from 0-40 with higher scores indicating greater levels of perceived stress. Scores ranging from 0-13 are considered low perceived stress, scores between 14-26 are considered moderate perceived stress, and scores 27-40 are considered high levels of perceived stress. Validation studies reflect strong internal consistency (α = .91; Mitchell et al., 2008). Cronbach's alpha in the current sample was α = .89 (McDonald's omega = .90).

Acute Stress Disorder Scale – Adapted for COVID. The Acute Stress Disorder Scale (ASDS-C) was designed to assess the psychological impact of the COVID-19 pandemic. This adapted version for COVID-19 was adapted from the Acute Stress Disorder Scale (ASDS; Bryant et al., 2000), a self-report measure of acute stress disorder symptoms following a traumatic event. The ASDS-C frames all stress-related questions as they relate to COVID-19 (i.e., "Have you tried not to think about [COVID-19]?"). The

ASDS-C consists of 20 total items, each rated a 5-point scale from 1 (“not at all”) to 5 (“very much”). Total scores on the ASDS-C can range from 20-100; total scores above a 56 indicate significant reactions to COVID-19. Although the adapted ASDS-C has not been psychometrically validated, the original ASDS has strong internal consistency (α =.96; Bryant et al., 2000). Cronbach’s alpha in the current sample was α = .94 (McDonald’s omega = .94)

Duke Misophonia Questionnaire (DMQ; Rosenthal et al., 2021). The DMQ is a psychometrically validated self-report measure of misophonia using factor analytic procedures combined with IRT in an English-speaking sample. The DMQ has 86 items and includes subscales: 1) trigger frequency (16 items), affective responses (8 items), 3) physiological responses (5 items), 4) cognitive responses (10 items), 5) coping Before (6 items), 6) Coping During (10 items), 7) Coping After (5 items), 8) Impairment (12 items), and Beliefs (14 items). Composite scales are derived from overall Symptom Severity (combined Affective, Physiological, and Cognitive Subscales) with scores ranging from 0-83 and Coping (which combined the three coping subscales: before, during, and after being triggered), with scores ranging from 0-78. Clinical impairment scores, derived from the Impairment Subscale, ranging from 0-13 are considered "minimal-mild impairment,” scores between 14-38 are considered "moderate impairment," and scores between 39-48 are considered "severe to very severe impairment.” Internal consistency results indicated that subscale intercorrelations were all within the range of .43 - 0.84,

evidencing strong relationships between the proposed constructs. The mean clinical impairment score in the current sample was 13.43 (*SD* = 10.18), indicating that on average impairment in this sample is on the high end of mild impairment. In frequency of trigger sounds, 39.9% endorsed being triggered between 2-5 times per day on average. The mean symptom severity composite score, combining affective, physiological, and cognitive subscales, was 43.76 (*SD* = 17.73). The mean coping composite score was 35.72 (*SD* = 14.04).

Data analytic plan

All analyses were conducted in SPSS 27.0 (IBM, 2020) and JASP 17.1 (Love et al., 2019). First, we explored the frequency of current and lifetime PTSD diagnoses via the SCID-5 in the current sample, as well as the frequency of potentially traumatic events (LEC-5). Bivariate correlations were conducted to examine if frequency of stressful events across the lifespan (via the LEC-5) was associated with misophonia. Next, Pearson's bivariate correlations were conducted to examine the relationships among misophonia symptoms (via the DMQ) and (a) PTSD symptoms, including clusters of reexperiencing, avoidance, negative alterations in mood and cognitions, and hyperarousal (PCL-5), (b) acute stress disorder scale, adapted for COVID-19 (ASDS-C), and (c) perceived stress (PSS total score). In order to examine misophonia severity most comprehensively, we created a composite DMQ severity score by summing the

standardized z-scores of the DMQ symptom subscale and the DMQ impairment subscale.

We then conducted multiple linear regressions in order to explore if (a) diagnosed trauma-related disorders and (b) particular components of stress and trauma (PCL-5, PSS) predict misophonia severity (DMQ), controlling for age, sex, and frequency of traumatic events across the lifespan.

Last, in order to visualize the partial correlation network among our variables of interest, we conducted network analysis in JASP which makes use of the R package qgraph (Epskamp et al., 2012). We applied a graphical least absolute shrinkage and selection operator (gLASSO; Friedman et al., 2008) regularization, which sets small or unstable correlations within the network to zero to better interpret a parsimonious network. The Extended Bayesian Information Criterion (EBIC; Chen & Chen, 2008) was applied to select the optimal network model derived from the gLASSO solutions. The tuning parameter was set to .5 for increased parsimony and interpretability (i.e., higher sensitivity and specificity, and fewer edges). The accuracy of edge weights was assessed by calculating 95% confidence intervals based on non-parametric bootstrapping (n = 1,000 boots), in line with the recommendation for LASSO regularized edges (Epskamp et al., 2012).

4.1.3 Results

Descriptive statistics

In the current sample, 32.9% (n = 47) of participants met criteria for at least one lifetime trauma and stressor-related disorder, including PTSD, ASD, adjustment disorder, or another specified trauma- and stressor-related disorder. As shown in Table 2, 11.9% (n = 17) met current criteria for any trauma-related disorder (PTSD, ASD, adjustment disorder, other specified trauma- and stressor-related disorder). Among current diagnoses of trauma and stressor related disorders, only 3.5% met full criteria for PTSD, whereas Other specified trauma disorder was most commonly diagnosed.

Table 5: Frequency of SCID-5 trauma- and stressor-related disorders

		Frequency (N = 143)	Percentage
Current			
	PTSD	5	3.5%
	ASD	0	0%
	Adjustment disorder	4	2.8%
	Other specified trauma disorder	8	5.6%
	Any trauma disorder	17	11.9%
Lifetime			
	PTSD	31	21.7%
	Other specified trauma disorder	17	11.9%
	Any trauma disorder	47	32.9%

Note: PTSD = Posttraumatic Stress Disorder; ASD = Acute Stress Disorder

Descriptive results from the LEC-5 reflect that the most frequently reported potentially traumatic events experienced directly were transportation accidents (51.7%), unwanted or uncomfortable sexual experiences (36.4%), natural disasters (32.2%), sexual assault (21.7%), and sudden and unexpected death of a loved one (29.4%). Additionally,

30.1% of participants self-reported experiencing other highly stressful events. See Table 3 for more details. Bivariate correlations evidenced that frequency of lifetime stressful events was not associated with misophonia across DMQ symptoms score (r = .02, p = .799), DMQ impairment score (r = .09, p = .325), and the composite DMQ severity score (r = .06, p = .499).

Table 6: Prevalence of traumatic events experienced via the Life Events Checklist for *DSM-5*

LEC-5 event	Frequency (N = 143)	Percentage
Transportation accident	74	51.7
Other unwanted sexual experience	52	36.4
Natural disaster	46	32.2
Other very stressful event	43	30.1
Sudden, unexpected death of loved one	42	29.4
Physical assault	31	21.7
Sexual assault	31	21.7
Work or recreation accident	16	11.2
Assault with a weapon	14	9.8
Life-threatening illness or injury	13	9.1
Fire or explosion	9	6.3
Exposure to toxic substance	7	4.9
Severe human suffering	3	2.1
Sudden, violent death	3	2.1
Combat or exposure to warzone	1	.7
Captivity	1	.7
Personally causing serious injury, harm, or death	1	.7

Note: LEC-5 = Life Events Checklist for *DSM-5.*

Correlations between misophonia and variables of stress and trauma

In order to explore the relationships between measures of stress and trauma with misophonia, we conducted bivariate correlations among DMQ symptoms score, DMQ

impairment score, and the composite DMQ severity score measures of current PTSD symptoms (PCL-5 total and subscale scores), perceived stress (PSS), and COVID-related stress (ASDS-C); see Table 4. DMQ symptoms, impairment, and severity were significantly correlated with PCL-5 total score and several subscales, particularly the hyperarousal subscale. DMQ scores were also significantly correlated with perceived stress and COVID-related stress.

Table 7: Bivariate correlations among misophonia severity and variables of trauma and stress

	DMQ symptoms	DMQ impairment	DMQ severity
PCL-5 total	.194*	.293**	.266**
PCL-5 reexperiencing	.136	.204*	.186*
PCL-5 avoidance	.102	.122	.123
PCL-5 negative alterations	.146	.252**	.218*
PCL-5 hyperarousal	.262**	.364**	.342**
PSS total	.322**	.363**	.374**
ASDS-C total	.226**	.258**	.264**

Note: DMQ = Duke Misophonia Questionnaire; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*; PSS = Perceived Stress Scale; ASDS-C = Acute Stress Disorder Scale – Adapted for COVID-19. **= $p < .001$; * = $p < .05$

Relationship among misophonia and components of stress and trauma

First, we conducted a multiple linear regression to examine if either a current or lifetime diagnosis of a trauma-related disorder via the SCID-5 predicted misophonia severity (DMQ severity composite). Neither a current nor lifetime diagnosis of a trauma related disorder predicted misophonia severity ($F(4, 138) = 1.57$, $p = .186$). Models with

DMQ symptom score and DMQ impairment score entered as the dependent variables were also not significant.

Next, we examined the relationship among misophonia severity and variables of stress and trauma with a multiple linear regression (Table 5). As has been done in previous studies using similar analyses to characterize misophonia (Eijsker et al., 2021), Step 1 controlled for age and sex. Step 2 included current PTSD symptoms (PCL-5), COVID-related acute stress (ASDS-C), and perceived stress (PSS). This model accounted for a significant proportion of the variance in overall misophonia severity ($F(5, 129) = 4.56$, $p < .001$, $R^2 = .15$, R^2 change = .13). However, only PSS (standardized $\beta = .30$, $t(2.97)$, $p = .044$) total score predicted misophonia severity.

In order to examine if number of stressful life events impact the relationship between perceived stress and misophonia severity, we added total events endorsed via the LEC-5 as a covariate in Step 1 of another model (Table 6). Perceived stress remained a significant predictor of misophonia severity, over and above the presence and/or frequency of traumatic stress ($F(6,128) = 3.78$, $p = .002$, $R^2 = .15$, R^2 change = .12).

Table 8: Multiple linear regression examining variables of stress and trauma on misophonia severity

Dependent Variable		Variables	SE	β std	*p*	R^2	R^2 change
DMQ Severity	Step 1	Age	.01	.02	.803		
		Sex	.34	.14	.107		
	Step 2	Age	.01	.06	.451	.15	.13
		Sex	.33	.09	.281		
		PCL-5	.02	.02	.863		
		ASDS-C	.01	.10	.349		
		PSS	.03	.30	.004		

Note: DMQ = Duke Misophonia Questionnaire; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*; ASDS-C = Acute Stress Disorder Scale – Adapted for COVID-19; PSS = Perceived Stress Scale.

Table 9: Multiple linear regression accounting for number of stressful life events and misophonia severity

Dependent Variable		Variables	SE	β std	p	R^2	R^2 change
DMQ Severity	Step 1	Age	.13	-.01	.942		
		Sex	.35	.15	.086		
		LEC	.01	.10	.292		
	Step 2	Age	.01	.07	.425	.15	.12
		Sex	.34	.09	.315		
		LEC-5	.02	-.03	.785		
		PCL-5	.02	.03	.823		
		ASDS-C	.01	.10	.335		
		PSS	.03	.30	.004		

Note: DMQ = Duke Misophonia Questionnaire; LEC-5 = Life Events Checklist; PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM-5*; ASDS-C = Acute Stress Disorder Scale – Adapted for COVID-19; PSS = Perceived Stress Scale.

Network analysis to visualize relationships among misophonia, stress, and trauma

The EBICGlasso network including misophonia severity (DMQ severity composite score), PTSD symptoms (PCL-5 re-experiencing, avoidance, negative alterations in mood and cognitions, and hyperarousal clusters), perceived stress (PSS), and stress during COVID-19 (ASDS-C), is displayed in Figure 1. There were seven nodes and 15 non-zero edges in the network. Thicker links ('edges') represent stronger correlations and thinner edges reflect weaker correlations; blue lines represent positive correlations, and orange lines reflect negative correlations. Nodes with stronger connections are placed closer together than nodes with weaker connections. Perceived stress and hyperarousal both had positive associations with misophonia severity (*r*s = .19, .18, respectively). Acute stress in the context of COVID-19 had a weak association with misophonia severity (*r* = .07) and avoidance had both a weak and negative association with misophonia severity (*r* = -0.08).

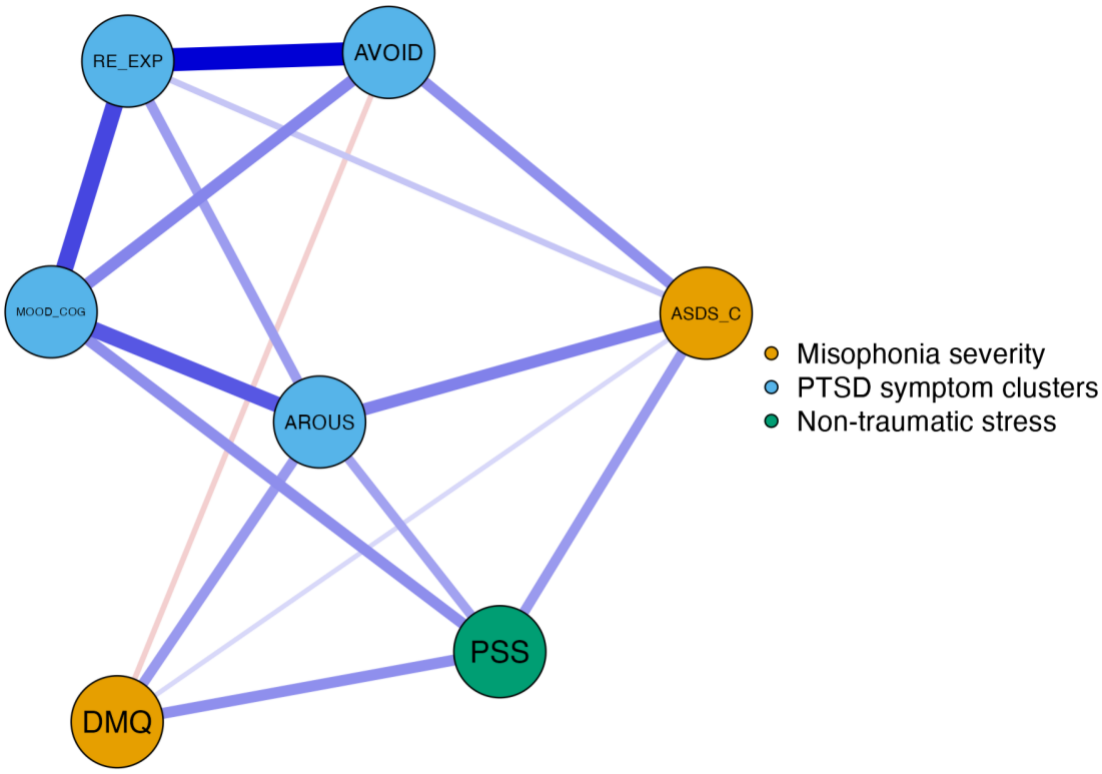

Figure 1: Network plot of variables of misophonia, stress, and trauma.

Last, to further our secondary aim of exploratory analyses to understand how symptoms of stress and trauma relate to symptoms of misophonia, we conducted a forced entry regression to examine which cluster(s) of PTSD via the PCL-5 most account for misophonia severity (DMQ severity; see Table 7). Because earlier analyses indicated that perceived stress predicted misophonia severity over and above PTSD symptoms, we included PSS total score as a covariate in Step 1 of the model. Of the four subscales representing the four clusters of PTSD symptoms (reexperiencing, avoidance, negative alterations in mood and cognition, and hyperarousal), only hyperarousal significantly

accounted for variance in misophonia severity ($F(7,128) = 4.20$, $p < .001$, $R^2 = .19$, R^2 change = .04).

Table 10: Regression examining contribution of current PTSD symptom clusters on misophonia severity

Dependent Variable		Variables	SE	β std	*p*	R^2	R^2 change
DMQ Severity	Step 1	Age	.01	.07	.379		
		Sex	.33	.13	.1086		
		Perceived stress	.02	.35	**<.001**		
	Step 2	Age	.01	.05	.569	.19	.04
		Sex	.33	.13	.111		
		Perceived stress	**.03**	**.27**	**.007**		
		Re-experiencing	.07	.02	.888		
		Avoidance	.12	-.10	.399		
		Alterations	.04	-.07	.576		
		Hyperarousal	**.05**	**.27**	**.022**		

Note: DMQ = Duke Misophonia Questionnaire.

4.1.4 Discussion

The primary aim of this study was to better understand the relationships among misophonia, stress, and traumatic stress in a community sample of U.S. adults. We examined (a) the prevalence of trauma-related disorders using structured diagnostic interviews (e.g., PTSD, ASD, adjustment disorder) and history of stressful life events, (b) the impact of trauma-related diagnoses and stressful life event histories on misophonia, and (c) whether traumatic stress specifically or perceived stress more generally accounts for misophonia severity. A secondary aim was to conduct exploratory analyses to begin parsing apart mechanisms of trauma and stress-related sequalae (i.e., clusters of PTSD symptoms via the PCL-5) that contribute to misophonia severity.

Only 3.5% of participants met diagnostic criteria for current PTSD, with 21.7% meeting criteria for a lifetime diagnosis of PTSD. These results are generally consistent with previous studies using structured diagnostic interviews (Jager et al., 2021; Rosenthal et al., 2022; Siepsiak et al., 2022) and do not suggest a causative or unique association between misophonia and PTSD. The lifetime prevalence rate of PTSD within the current sample is, however, higher than the lifetime prevalence rate in a normative U.S. sample (estimated at 6.8-8%; Kessler et al., 2005; Schein et al., 2021). This discrepancy may in part be explained by the characteristics of our sample. Females are at higher risk for PTSD than males, and the majority of the current sample is female (74.4%), possibly contributing to higher lifetime prevalence. Another possible explanation for the higher prevalence of lifetime PTSD within the current sample could be that misophonia is associated with a lifetime history of PTSD, but not with a current diagnosis. This is speculative and would need to be replicated and explored more carefully, but it is plausible that people with misophonia may experience a diagnosis of PTSD at some point in their lifetime at a rate higher than the general population. Another hypothesis is that misophonia is a developmental risk factor for various psychiatric disorders, and not with PTSD specifically. Indeed, Rosenthal et al. reported that many lifetime psychiatric disorders (e.g., anxiety disorders, mood disorders) were observed at a higher rate than would be expected in a general population (Rosenthal et

al., 2022). As such, it may be that PTSD is not unique in being one of many mental health problems higher in lifetime prevalence than in the general population.

Neither PTSD nor other trauma-related diagnoses accounted for misophonia in the current study. However, perceived stress explained a significant amount of the variance in misophonia severity, even after controlling for age, sex, and frequency of stressful life events across the lifespan. Misophonia is associated with factors known to be related to vulnerability to stress, including anxiety, neuroticism, and difficulties with emotion regulation (Cassiello-Robbins et al., 2021; Cassiello-Robbins et al., 2020; Guetta et al., 2022b). One possibility is that the tendency to experience higher stress in general is associated with misophonia severity through these or other transdiagnostic factors. Another possible explanation for the relationship between higher misophonia and the tendency to generally experience greater stress (but not PTSD-related traumatic stress, per se) could be relatively simple: Individuals with misophonia symptoms experience higher stress because it is stressful to live with this disorder. There is no scientific evidence in the present study or elsewhere suggesting that traumatic stress or PTSD is a causal factor for misophonia. But perhaps misophonia is a causal factor for increased stress. Taking this hypothesis one step further, health problems associated with misophonia could be caused, in part, by transdiagnostic and treatable biological, social, and behavioral mechanistic factors underlying heightened stress. Future work exploring the components of stress and trauma as they relate to misophonia should also include

dispositional factors and characterological features (e.g., neuroticism, difficulties with emotion regulation, *p* factor) in order to further our understanding of shared mechanisms.

It should be noted that in this study, we did not control for the temporality of stressful life events in relation to the onset of misophonia. As misophonia typically begins in childhood (Swedo et al., 2022), it is important for future studies to examine the occurrence of childhood adverse events and the potential impact or overlap in development of misophonia. It is possible that there are shared transdiagnostic processes underlying both traumatic and misophonic etiology and sequelae. Just as unpleasant, inescapable, and uncontrollable situations are risk factors for PTSD, situations with misophonia triggers that are perceived as unpleasant, inescapable, and uncontrollable (i.e., in certain social or work settings, in childhood with limited autonomy) may exacerbate misophonia. Trauma and misophonia both lead to hyperarousal, efforts to avoid and/or escape, as well as pervasive attentional biases and interpersonal sensitivities. Taken together, there is clinically meaningful overlap in transdiagnostic factors between trauma and misophonia (e.g., perceived stress), but there is no evidence for a causal link between traumatic events and the development of misophonia.

In assessment and treatment of misophonia, then, it is important to understand idiographic *processes* related to stress more broadly (e.g., perceived stress), rather than

simply probing trauma histories and related diagnoses. Further, our findings that PTSD symptomatology may be present even in the absence of a diagnosed trauma disorder imply that effective interventions for misophonia could involve a process-based approach with idiographic assessment and tailored interventions to target processes across biological, social, cognitive, and behavioral domains, rather than prescribing treatment that is specifically related to a history of traumatic stress. For example, if perceived stress is indeed a relevant mechanism for a patient, then interventions that are evidence-based and transdiagnostic for perceived stress could be considered as one part of a broader treatment strategy (e.g., implementing mindfulness-based stress reduction strategies that have been empirically tested for perceived stress (Deckro et al., 2002; Stillwell et al., 2017). It will be valuable for future research to directly test evidence-based transdiagnostic interventions (i.e., stress reduction strategies for perceived stress) within misophonia samples to thoughtfully determine how to modify interventions for this population. For instance, mindfulness interventions largely have health benefits, but given sensitivities to sound in misophonia, the application of guided meditations, for example, need to be carefully modified for misophonia so that the mindfulness practices are not undermined by trigger sounds.

Considering processes of trauma sequalae that are often present in misophonia and not exclusively related to Criterion A events (e.g., hyperarousal) may be central to effective courses of treatment. Indeed, through analyzing individual symptom clusters

of PTSD and their relationships to misophonia, this study also identified hyperarousal as a candidate transdiagnostic mechanism to assess and treat in misophonia populations. For example, if a patient presents for treatment of misophonia that has worsened in the context of a recent car accident, a first step may be to idiographically assess and develop a treatment plan given what that individual is willing and able to do in order to reduce hyperarousal that is maintaining heightened misophonic reactions. In collaboration with that patient, the provider may offer examples of process-based interventions that have been empirically supported to treat hyperarousal, such as applying progressive muscle relaxation before getting in a car with a family member or using emotion exposures from the Unified Protocol while driving or thinking about driving (Ehrenreich-May et al., 2012; Varkovitzky et atl., 2018; Toussaint et al., 2021). In line with the literature on effective process-based therapy, priority should be given to the intervention(s) that the patient is both able and willing to do, as well as to the intervention(s) that target processes of change that may be related to other relevant problems for that individual (Hayes & Hofmann, 2018). For example, a therapist and client may collaboratively decide to target hyperarousal first if functional analysis and ample assessment of the patient's context suggests that decreasing hyperarousal before being triggered will then influence other associated processes (e.g., anger, irritability, aversive cognitions, anticipatory anxiety, avoidance behavior).

In any case, the complexity of interrelated constructs that contribute to misophonia severity underscore the importance of idiographic assessment and treatment development that thoughtfully apply either existing evidence-based treatments (e.g., the Unified Protocol; Barlow et al., 2017) or more tailored, idiographic interventions using a process-based approach (Hayes & Hofmann, 2018). Further, it is important in both assessment and treatment of misophonia to differentiate between PTSD and other trauma-related disorders, traumatic stress, and stress reactions more broadly. Interventions based on comprehensive assessment and that are designed to sequentially target features of a patient's network across cognitive, affective, physiological, and attentional domains may work to target both misophonic and other stress or trauma-related suffering.

This study should be considered in the context of the limitations of the study. First, the sample was not representative of the U.S. population (https://www.census.gov/quickfacts/fact/table/US/PST045219), as the current sample had a higher percentage of White female participants, limiting generalizability of the results. Future research with more diverse and cross-cultural samples is needed to increase generalizability. Second, despite interviewing participants to gather both current and lifetime diagnoses, our data were cross-sectional, limiting definitive conclusions about causal relationships between relevant constructs over time. Future work that is longitudinal and prospective in nature will be crucial for bolstering our understanding

of how misophonia, stress, and trauma interact, and for better accounting for the temporality of trauma exposure and onset of misophonia, increases in stress, and any trauma-related sequalae. Additionally, there is a need for more multi-trait multi-mode assessment of stress to better capture idiographic experience. Future work could incorporate behavioral tasks, as well as psychophysiology (e.g., galvanic skin response, heart rate), eye tracking, and facial behavior tracking to increase a granular understanding of mechanisms of stress and trauma (e.g., attentional biases, state-level distress). In addition, it is possible that participants in the current study misconstrued items on the PCL-5 self-report scale (Kramer et al., 2023) and it is important to not conflate scores on the PCL-5 with a clinician-administered diagnosis of PTSD (Bovin & Marx, 2023). Results of the current study should be interpreted with this caveat in mind, and future work should incorporate clinician-rated tools to assess PTSD and trauma-related disorders more comprehensively. Despite these limitations, this study enhances our understanding that neither trauma history itself nor PTSD is directly related to misophonia, but transdiagnostic features of stress (e.g., perceived stress, hyperarousal) may contribute more strongly to misophonia severity.

The findings from the current study add to the nascent literature on the relationships among misophonia, stress, and trauma, and provide clinically meaningful implications for treatment of this understudied disorder. Prior studies have predominantly relied on self-report tools rather than rigorous clinical interviews to

assess trauma diagnoses, and have not disentangled how varied elements of stress and trauma (e.g., perceived stress, cohort-level stressors, frequency of adverse life events, particular clusters of PTSD symptomatology) may differentially contribute to misophonia severity (Jager et al., 2021; Rouw & Erfanian, 2018; Siepsiak et al., 2022). This study is the first to begin parsing apart mechanisms of stress broadly using both self-report and structured clinical assessment to assess how elements of perceived stress, stress during the ongoing COVID-19 pandemic, symptoms related to PTSD, and diagnosis of other trauma-related disorders (e.g., adjustment disorder, other specific trauma- and stressor-related disorder) are associated with misophonia. Further, we measured misophonia with the Duke Misophonia Questionnaire (Rosenthal et al., 2021), a psychometrically validated tool that assesses misophonia holistically across trigger frequency, affective, physiological, cognitive and behavioral responses, as well as coping responses and impairment. The current study has implications for the development of more effective treatments for misophonia that take into account the complexities across stress, trauma, and misophonic reactions.

5. Conclusions: Summary and future directions

In this dissertation, I took a mechanistic approach to understanding the nature and features of misophonia. Chapter 2 outlines the development and initial validation of the DMI, the first semi-structured interview to assess misophonia in adults. The DMI can be used as a tool in both research and clinical settings to gain insight into idiographic presentations of misophonia. In Chapter 3, I explore the relationships among misophonia, emotion regulation, and the impact of COVID-19. Findings from Chapter 3 suggest that difficulties regulating emotions account for misophonia severity over and above presence of anxiety, depression, and level of COVID-19 impact. Further, multivariate model findings suggest that affective lability, although correlated with misophonia, is not as useful of an indicator of misophonia severity as difficulties with emotion regulation. In Chapter 4, I explore the relationships among misophonia and components of stress and trauma. Findings from Chapter 4 do not support a causal link between traumatic events and the development and/or maintenance of misophonia. Rather, findings suggest there is a significant impact of current perceived stress on misophonia severity, highlighting the role of appraisal and perceptions of coping ability as candidate treatment targets for misophonia. Collectively, the studies have several implications for assessment and treatment of misophonia and pave the way for future research.

8.1 Future directions

Since publication of the first version of the DMI, the interview has been iterated to (a) ensure consistency with the consensus definition of misophonia (Swedo et al., 2022), and (b) decrease administration time to both diminish interviewer burden and increase utility within research and clinical contexts. The DMI can now be administered in approximately 45 minutes to fit within a standard therapy session. In addition, the DMI has begun to be translated into other languages (e.g., Polish), and is being integrated into research groups internationally (e.g., in Poland, the UK). Ongoing work should aim to psychometrically validate the iterated version of the DMI within larger, more diverse samples. In addition, feedback from various disciplines (e.g., audiology, occupational therapy, otolaryngology) should continue to be integrated in future iterations of the DMI to further limit investigator bias, and increase accessibility, feasibility, and clinical utility of the DMI. Other future directions include adapting the DMI to individuals under the age of 18, and training paraprofessionals to administer the DMI to increase utility and scalability across both clinical and research contexts.

Chapters 3 and 4, with findings offering promising candidate treatment targets for misophonia (e.g., emotion regulation, perceived stress), promote future work oriented around a process-based, transdiagnostic approach to assessment and intervention with a focus on emotional responses. Evidence from this dissertation suggests that misophonic triggers are associated with a range of emotional responses

(e.g., anger, anxiety, disgust) and may be impacted by perceptions of controllability and ability to cope. As such, one reasonable approach in future treatment work is to target changes in emotional functioning and associated processes (e.g., attentional control and hypervigilance, psychophysiological regulation) in ways aligned with individuals' values and goals. In studying these questions, future research should incorporate both laboratory-based and ecologically valid naturalistic methods. Paradigms that incorporate ecological momentary assessment, for example, can help to identify candidate mechanisms that are both sensitive and specific to misophonia, and that may be considered feasible and acceptable to those suffering with misophonia.

Another conclusion drawn from this dissertation is the level of heterogeneity in the presentation of misophonia, which lends itself to testing individualized approaches to treatment. One promising model of an intervention for misophonia is Process-Based Therapy (PBT; Hoffman & Hayes, 2019), which offers a framework that integrates evidence-based processes of change rather than a prescribed sequence of interventions applied to all patients. PBT is guided by principles and processes of change that are: (a) theory-based (i.e., each evidence-based intervention is explicitly linked to testable hypotheses with transdiagnostic, mediating variables affecting change); (b) dynamic (there may be non-linear feedback loops born out of processes of change to then target); (c) progressive (i.e., evidence-based interventions are sequenced in line with idiographic assessment, such that skills build off of each other to optimize treatment gains), (d)

contextually bound and modifiable (i.e., evidence-based interventions should be adapted to the individual), and (e) multi-level (i.e., some processes of change may be nested within others, and create downstream impacts that will then be integrated dynamically into the treatment).

This type of transdiagnostic, mechanistic approach to treatment holds promise for a new phenomenon like misophonia that shares underlying mechanisms with many co-occurring psychiatric disorders (Rosenthal et al., 2022). A PBT approach requires thoughtful and flexible application of evidence-based interventions that support both what we know nomothetically about misophonia (i.e., as represented in the consensus definition; Swedo et al., 2022) and idiographically via rigorous, individualized assessments (e.g., via the DMI). Finally, PBT is a promising approach that mitigates against the practical challenges that accompany treating a novel condition. Indeed, randomized control trials can take decades to complete before refined protocols are developed. Further, when presenting problems do not fit neatly into a diagnostic category and do not yet have widely disseminated, evidence-based treatments that are likely to be effective, it remains a challenge for clinicians to determine how to help. This can lead to providers being unwilling to treat the patient or attempting to use a pre-existing manualized protocol to treat a condition that, on the surface, seems to be related (i.e., using exposure therapy for misophonia, using the logic that habituation works for

anxiety disorders). A PBT approach circumvents these treatment interferences by flexibly tailoring assessment and interventions to the individual.

8.1.1 Recommendations for future research on newly defined phenomena

Considerably more rigorous research is needed to continue understanding the etiology, underlying mechanisms, correlates, and course of misophonia. There are several principles that can guide future research for phenomena not yet included in any diagnostic nomenclature, and one that is simultaneously being shaped by both scientific and sociocultural bodies. Below are suggested principles to incorporate into future work:

Be aware of and challenge biases and assumptions. Both questions and conclusions about new health phenomena are influenced by numerous stakeholders. Indeed, the scientific process is rarely untouched by the varying interests of researchers within specific disciplines, funding agencies, sufferers, and healthcare providers, among other players. When designing a research protocol and interpreting findings, bias can shape both what data is collected, and how results are interpreted and presented (Hammersley & Gomm, 1997; Wilholt, 2009). Prejudgments, sociocultural postures, political, and/or practical commitments can all color scientific inquiry and dissemination. In the case of misophonia, the original descriptions of this phenomenon were observed in audiological settings (Jastreboff & Jastreboff, 2001) unrelated to psychiatric care, which gave shape to

the earliest definitions and research questions. Later research suggested relevance of other disciplines across psychiatry, psychology, and neurobiology, among others (e.g., Neacsiu 2022; Schröder et al., 2013; Taylor, 2017). Awareness of scientific and other external biases is crucial to performing sound research. Given the potential relevance of misophonia across several disciplines (e.g., audiology, neuroscience, psychiatry, occupational therapy, otolaryngology), it is wise to continue integrating scientific practices to combat infiltration of biases and assumptions. For example, researchers can integrate multidisciplinary perspectives, combine bottom up (e.g., laboratory-based paradigms) and top down (e.g., clinical observations) approaches (Achenbach, 2020), and continue questioning how to categorize misophonia, as well as the utility of categorization to begin with. Continued awareness of assumptions on the part of researchers, providers, funders, and laypeople can help to mitigate against perpetuating discipline- and stakeholder-specific biases. We must always maintain humility around what we believe we know as "truth," and accept the real possibility of fallibility.

Further, acknowledging the role of publication bias within the context of an emerging literature is crucial. Indeed, there exists a relationship between study results and publication probability that is fueled by the academic currency of citations and visibility (Dwan et al., 2013). Harmful albeit common practices of (a) nonpublication of the entire study, (b) selective publication of results within a study, (c) reporting bias, and (d) *p*-hacking all perpetuate publication bias (Jamieson et al., 2017). In order to attenuate

these biases, misophonia researchers are encouraged to register their studies (e.g., via ClinicialTrials.gov), report summary results, present null results, make data available, and publish in open access journals. In addition, open acknowledgment of incentive structures for publishing as well as disincentive structures for not reporting full studies and/or selectively reporting results is warranted.

Engage in multidisciplinary work. A guiding principle in future work on misophonia should be integration of interdisciplinary expertise, and not assuming this phenomenon neatly fits into one discipline. As early evidence suggests misophonia is implicated across many domains, translational studies that explore and integrate components across levels of analysis are necessary. Collaborations between researchers and providers across fields can offer rich and diverse perspectives that not only can drive science forward, but also can protect against falling prey to assumptions and biases that may exist within any given field. One corollary example to the trajectory of misophonia research could be the development of knowledge around Attention-deficit/Hyperactivity disorder (ADHD). Early physicians characterized the phenomenon as a hyperkinetic disease of infancy (Kramer & Pollnow, 1932), while others posited the phenomenon could be understood by postencephalitic behavior and organic neural underpinnings (Tredgold 1908). Only through interdisciplinary work across neurobiological, psychiatric, and other behavioral disciplines across the lifespan, did the

complexity and multifactorial nature of ADHD become understood (Martinez-Badía & Martinez-Raga, 2015).

Think transdiagnostically. Given the levels of comorbidity with misophonia (Rosenthal et al., 2022), and the relevance of candidate treatment targets (e.g., perceived stress, difficulties with emotion regulation, hypervigilance, physiological arousal) to co-occurring conditions, misophonia research should not rely on theoretical models that assume isolated presence of a singular psychiatric disorder. There is increasing recognition that diagnosis-specific interventions for single disorders hold less value and effectiveness than approaches addressing coexisting mechanisms (Martin et al., 2018; McManus et al., 2010; Sauer-Zavala et al., 2017). In developing assessment and treatment tools for misophonia, we must strive to optimize clinical relevance. Researchers and practitioners should give thought to (a) dimensionality of misophonic symptom space, (b) comorbidity of seemingly related and unrelated disorders, (c) presence of phenotypic heterogeneity, and (d) the possibility of evolving trajectory across the lifespan (Dalgleish et al., 2020). That said, studies should also consider how to balance dimensional approaches to characterizing misophonia with existing conventions of medical models to optimize the scalability and generalizability of findings and implications.

Ensure face and content validity of findings. In the ongoing process of cultivating a comprehensive and nuanced understanding within a nascent literature, it is essential that findings are attributable to the phenomenon itself, and not to related but dissimilar

conditions. As a sound intolerance and sensory-related disorder, it is not uncommon for misophonia to be conflated with other related conditions (e.g., hyperacusis, noise and sensory over-responsivity; Aazh et al., 2022; Aazh et al., 2023; Henry et al., 2022). It is imperative to not inappropriately and/or prematurely draw inferences, but rather to give considerable thought to if findings can indeed be ascribed to misophonia rather than related but distinct phenomena. In a similar vein, importance should be placed on (a) using psychometrically validated assessment tools and (b) assessing for readability and correcting verbiage as necessary to both limit unsound characterization of misophonia as well as to limit variability in respondents' interpretation of items. Input from stakeholders (e.g., misophonia sufferers, clinicians, experts across disciplines) and iteration at the item-level of assessment tools can lead to greater specificity and more granular discrimination between and across misophonic processes, as well as increased content and face validity downstream (Connell et al., 2018).

Recruit large, diverse samples. Representative sampling is imperative to build a full understanding of a new health phenomenon, particularly one that seems to have high prevalence across populations (Jakubovski et al., 2022; Siepsiak et al., 2020; Vitoratou et al., 2023; Wu et al., 2014; Zhou et al., 2017). Given the difficulty of meeting adequate sampling needs with the limited resources that often accompany understudied disorders, it is critical to place the utmost effort on studying underrepresented and minoritized individuals with misophonia. Studies with larger, representative, and

diverse samples will help build nuanced understanding of misophonia across identities, variability of presentations, and will increase feasibility, accessibility, and generalizability of results. Research should also be conducted cross-culturally to understand possible variations in etiology, maintenance, course, and expression in other countries and cultural contexts. Recruitment efforts should be deliberate and incorporate empirically supported suggestions to diversify sampling, such as leveraging recruiter experience and involving senior-level researchers in recruitment (Patel et al., 2003; Yancey et al., 2006), and adapting recruitment scripts to invoke either institutional affiliation or scientific evidence (Sugden & Moulson, 2015).

Balance effectiveness across individual and population level. Findings from larger studies hold implications across both individual and population levels. The RE-AIM framework, which emphasizes five dimensions (reach, efficacy/effectiveness, adoption, implementation, and maintenance; Glasgow et al., 2006), reminds us that highly effective interventions on the individual level may not always hold the same impact at a population level. For example, data from two trials comparing approaches to preventing PTSD reflected that the protocol with a smaller effect size on the individual level had a 9.5-fold greater cumulative reduction in PTSD incidence at a population level (Zatzick et al., 2009). In the case of misophonia treatment development, approaches like PBT may be highly effective at an individual level but may be less effective and/or scalable at a

population level for various reasons (e.g., resources required to train in PBT, time and cost to implement the treatment, attitudes on the part of providers and/or patients).

D*esign prospective and longitudinal studies.* In the early stages of understanding a new phenomenon, little is known about the onset, course, variability, or lifetime prevalence of a disorder (current prevalence estimates range dramatically from 5 to 49.1%; Jakubovski et al., 2022; Siepsiak et al., 2020; Vitoratou et al., 2023; Wu et al., 2014; Zhou et al., 2017). Additionally, little existing work has focused on the development of misophonia in childhood and adolescence, and the course of the disorder across the lifespan (Swedo et al., 2022). To gain an understanding of the scope and variability of misophonia, it is imperative to integrate prospective and longitudinal work, not to mention the importance of experimental designs that are capable of inferring causality. Epidemiological work should also be conducted to understand population-wide relevance. More accurate prevalence estimates may also have important downstream impacts on public health (i.e., in raising awareness among laypeople and varied healthcare disciplines, as well as in procuring funding for future work).

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