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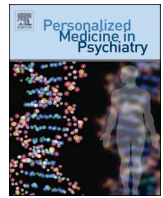
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A systematic review of treatments for misophonia

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ABSTRACT

Research into misophonia treatments has been limited and it is unclear what treatment approaches may be effective. This systematic review extracted and synthesized relevant treatment research on misophonia to examine the efficacy of various intervention modalities and identify current trends in order to guide future treatment research. PubMed, PsycINFO, Google Scholar, and Cochrane Central were searched using the keywords “misophonia,” “decreased sound tolerance,” “selective sound sensitivity,” or “decreased sound sensitivity.” Of the 169 records available for initial screening, 33 studied misophonia treatment specifically. Data were available for one randomized controlled trial, one open label trial, and 31 case studies. Treatments included various forms of psychotherapy, medication, and combinations of the two. Cognitive-behavioral therapy (CBT) incorporating various components has been the most often utilized and effective treatment for reduction of misophonia symptoms in one randomized trial and several case studies/series. Beyond CBT, various case studies suggested possible benefit from other treatment approaches depending on the patient's symptom profile, although methodological rigor was limited. Given the limitations in the literature to date, including overall lack of rigor, lack of comparative studies, limited replication, and small sample size, the field would benefit from the development of mechanism-informed treatments, rigorous randomized trials, and treatment development with an eye towards dissemination and implementation.

1. Introduction

Misophonia is an impairing condition, generally presenting in childhood or early adolescence, characterized by a decreased tolerance to specific sounds or stimuli associated with these sounds, known as “triggers” [50]. The term misophonia was originally coined in 2002 [24] with the literature gradually expanding thereafter. These triggers elicit a range of negative emotional, physiological, and behavioral responses, often leading to avoidance of triggers and significant functional impairment [41,50]. Triggers are typically related to oral and nasal sounds produced by other people, such as chewing and breathing, but can include a broad range of typically benign auditory stimuli, such as tapping or scratching [20,51]. Responses to triggers include agitation, anger, disgust, and/or anxiety, as well as a “fight-or-flight” autonomic response [4,13,41]. Misophonia commonly presents with co-occurring depression and anxiety disorders, and less commonly with OCD, Tourette's syndrome, ADHD, autism, panic disorder, personality disorders, and suicidality [6,30,45,55]. Regarding the underlying pathophysiology, brain-body connectivity mechanisms have been proposed based

on functional neuroimaging findings revealing increased activation of the anterior insula in individuals with misophonia, as well as increased connectivity between cortical sensory and orofacial motor processing pathways Cavanna and Seri [5,26,27].

To date, variable treatment approaches for misophonia have been reported. With several notable exceptions, majority of the literature consists of case reports implementing a range of psychotherapy techniques, and medications either in isolation or combination with psychotherapy [3,8,38,40,54,58]. Psychotherapeutic interventions include various forms of Cognitive-Behavioral Therapy (CBT), Exposure Therapy, Acceptance and Commitment Therapy (ACT), Dialectical Behavior Therapy (DBT), and Eye Movement Desensitization and Reprocessing (EMDR). Medications include selective serotonin reuptake inhibitors (SSRIs), stimulants, anti-psychotics, and β -Blockers. In addition, one randomized controlled trial supported the efficacy of group CBT relative to a waitlist control with treatment components including task concentration, positive affect labeling, stimulus manipulation, and arousal reduction [21–22]. Due to the paucity of experimental trials, protocolized practice parameters for the treatment of misophonia remain

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elusive.

Misophonia research is increasing in breadth and scope, with new research exploring prevalence, symptomatology, phenomenology, demographics, and comorbidities [16,21,31,14]. Methodologically rigorous research on treatment interventions remains limited, and there has not yet been a systematic review to synthesize data and overall effects of extant treatments. This review extracts and synthesizes research from case series, case studies, open trials, and randomized-control trials on the treatment of misophonia to examine the preliminary evidence for various treatment modalities and identify current data trends, which will provide guidance for clinical practice and future research.

2. Methods

This review is reported according to the PRISMA checklist extension for scoping reviews [34]. First, the rationale and study objective were defined. Next, the relevant studies were identified using a broad, comprehensive approach to the literature. Studies were selected based on pre-determined search parameters. The results were summarized, synthesized, and reported. The findings were then reviewed by experts in the field.

2.1. Eligibility criteria (PICO)

Inclusion and exclusion criteria were formulated using the PICO framework.

Population: We included records if they reported case or cohort studies, case series, randomized controlled trials (RCTs) or non-RCTs where the effectiveness of a treatment was documented and tested, and misophonia was the primary complaint/treatment target. All ages and comorbidities were included. Only studies published in English were included.

Intervention: We considered all treatment interventions if the purpose of the study was to describe a patient or patients where the primary or secondary complaint was misophonia. Regardless of whether misophonia was the patient's primary or secondary concern, the treatment had to specifically target misophonia symptoms. Examples of studies we did not include were reviews, non-peer reviewed studies, editorials, manuals, or guidelines. We did not include records without a full-text translation into English.

Comparison: Studies that did and did not include comparison treatments were included.

Outcome: To be included, studies had to have defined misophonia symptom severity and either quantitative or qualitative reporting of treatment outcomes.

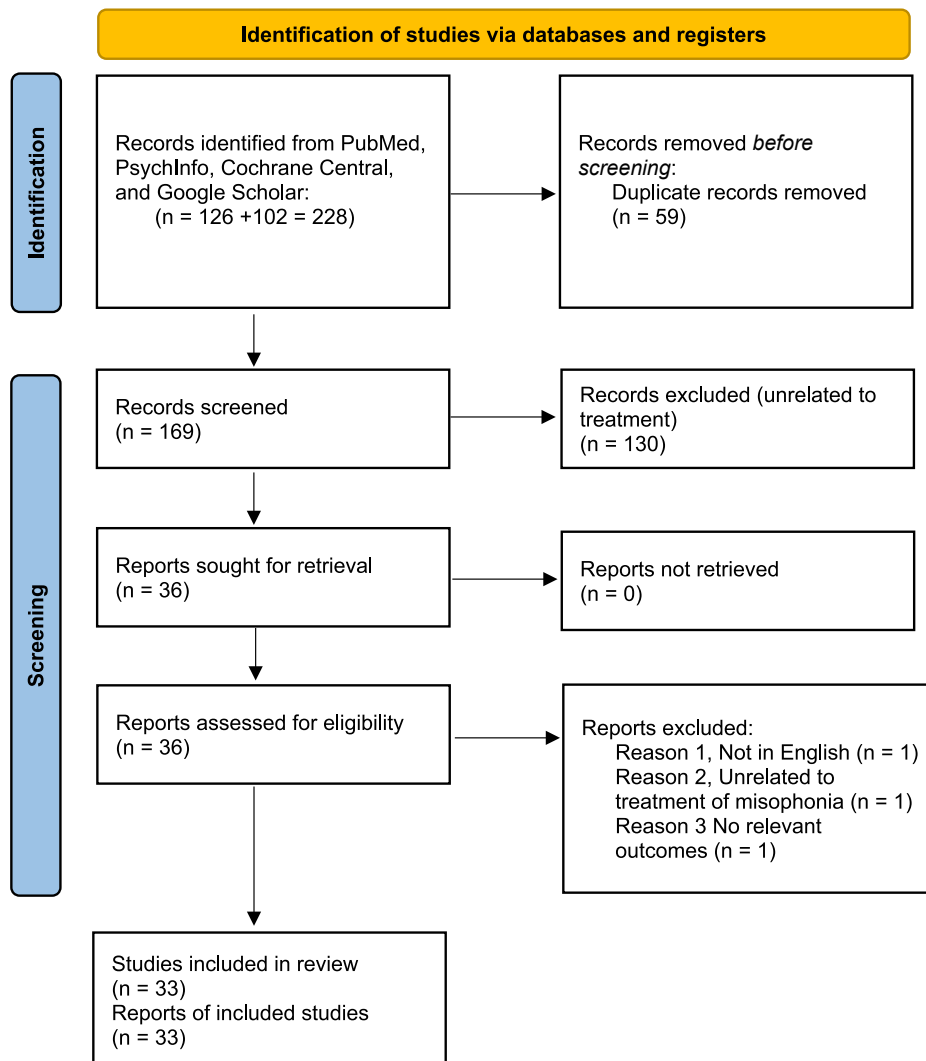


Fig. 1.

2.2. Information sources and search strategy

On May 27th, 2022 we conducted a search of PubMed, PsycINFO, Cochrane Central, and Google Scholar using the keywords “misophonia”, “decreased sound tolerance”, “selective sound sensitivity”, or “decreased sound sensitivity.” Additionally, the reference section of relevant sources was searched to locate other related sources that were not found in the initial primary search.

2.3. Study selection

All abstracts were assessed by an independent reviewer. Only records addressing misophonia treatment were included in the initial screen. This was followed by a full text review, which was checked by a second reviewer to determine if eligibility criteria were met by all included studies (See Fig. 1). Reviewers (3) included a clinical psychologist, a post-doctoral clinical psychology fellow, and a medical student under the supervision of the last author. Discrepancies arose regarding the inclusion of studies where misophonia symptoms were not the direct target of therapy but included as a comorbidity. It was deemed these reports did not meet initial eligibility criteria, leading to a consensus decision to exclude them. One exception to this was the study by Naguy et al. (2022), which was deemed relevant because of the proposed mechanism by which the medication, targeting primary ASD symptoms, also treated secondary misophonia symptoms.

2.4. Outcomes and prioritization

The primary outcome was improvement on standardized misophonia severity questionnaires, where the most commonly utilized measures included the Amsterdam Misophonia Scale (A-MISO-S; [41]), the updated Amsterdam Misophonia Scale-Revised (AMISOS-R; [42]), and the Misophonia Questionnaire [56]. The A-MISO-S and AMISOS-R, which were modeled after the Yale-Brown Obsessive-Compulsive Scales [15,48], are the most widely used measures in the misophonia literature to date. Psychometric properties have been reported including good internal consistency, convergent and divergent validity and treatment sensitivity [22]. The Misophonia Questionnaire has demonstrated good internal consistency, and convergent and divergent validity [56,59]. Other validated outcome measures used included the Clinical Global Impressions Improvement (CGI-I) Scale [17] and the Children’s Global Assessment Scale (CGAS). Outcome measures that were less commonly used in the included studies are the Subjective Units of Distress (SUDS) scale [3], Navaco Anger Scale (NAS) [38], and the Misophonia Assessment Questionnaire (MAQ) [9–11].

3. Results

After removing duplicate records, 169 records were obtained for initial screening. From these, 130 were excluded because they did not study misophonia treatment. Of the remaining 36 papers sought for full-text review, 3 were excluded for various reasons (see Fig. 1). Of the 33 included reports, 1 was an RCT, 1 was an open label study, and 31 were case studies/series. Of the 31 case studies/series, 15 were primarily CBT interventions (9 of which included exposure-based techniques), 3 involved counter-conditioning alone, 1 was DBT, 1 was ACT, 1 was EMDR, 2 were TRT, 6 were primarily pharmacological interventions, and 2 reported a combination of both therapy and pharmacological interventions. The characteristics of included trials are shown in Table 1. All interventions were given to individuals diagnosed with misophonia using various clinical criteria, with most studies utilizing the A-MISO-S [41].

The Cochrane risk of bias tool was used to assess risk of bias in included randomized control trials (Higgins & Green, 2011). The Jager et al. [22] RCT has an overall low risk of bias based on criteria such as the randomization process, deviations from intended interventions,

missing outcome data, measurement of the outcome, and selection of reported results.

3.1. Cognitive-Behavioral therapy

Although results are both preliminary and heterogeneous, of all the treatment approaches studied to date, cognitive-behavioral therapy (CBT) is the most consistently effective. The only randomized-controlled trial published to date, by Jager and colleagues (2020), studied 54 adult patients randomized to either weekly group-based CBT or similar duration wait-list. CBT involved a closed group setting of 9 patients per group, and CBT components included exercises in task concentration, positive affect labeling, stimulus manipulation, and arousal reduction. Stimulus manipulation involved counter-conditioning methods, a form of exposure that will be discussed in detail later. Therapists also provided psychoeducation around eating norms to both the individuals and their families. After 3 months of weekly group therapy, patients showed an average decrease of 9.7 points on the AMISOS-R (95% CI, -12.0 to -7.4 ; $p < .001$, $d = 1.97$), and 37% were rated as treatment responders on the CGI-I. Effects were modest and maintained at 1-year follow-up, suggesting short and long-term benefit for misophonia symptoms. The same research group previously conducted an open label trial with a similar CBT approach. After 7–8 group CBT sessions, 90 total patients reported a mean reduction of 4.5 points on the A-MISO-S. Overall, nearly half of the patients experienced at least a 30% reduction on the A-MISO-S [43]. Lewin et al. [28] published a case series ($N = 4$) from an ongoing RCT examining the effect of a transdiagnostic CBT protocol known as the Unified Protocol. Results indicate mild improvement, especially in severe cases.

Counter-conditioning, a common behavioral technique across case studies, involves pairing a stimulus that evokes a specific behavior with a behavior that is incompatible with it. Counter-conditioning for misophonia involves pairing a positive auditory stimulus (e.g., music) with the negative (often reduced in intensity) conditioned stimulus (e.g., chewing) while inducing physiological relaxation incompatible with the typical tension response evoked when encountering a trigger (e.g., through progressive muscle relaxation). It was first implemented for misophonia by Dozier [11,9–10] in a case series. Anecdotal improvement was reported after anywhere from 7 to 23 treatment sessions of 30 min each [9–11]. Subsequent studies, including the seminal study by Jager and colleagues (2020), have implemented counter-conditioning components in conjunction with other techniques [43,7].

CBT has been shown to be beneficial in multiple case studies, in both in-person [1,2,3,38] and virtual formats [57]. Of the patients in these studies ($n = 7$), all were young females ranging from 16 to 22 years old and the most common reaction was anger [1,2,3,38,57]. There was a wide range of symptom improvement, with one case improving from moderate severity (11 on the A-MISO-S) to subclinical (4) severity [1] while another case showed improvement from extreme (23) to moderate (12) severity [1]. Of the CBT components utilized, Roushani and colleagues (2021) implemented a similar model as described by Schneider and Arch [40]. Others utilized cognitive reappraisal components, behavioral components to move from avoidance to healthy coping strategies, and relaxation exercises [3].

3.2. CBT with exposure therapy

Case studies have also examined CBT protocols that incorporate various exposure techniques. While some report treatment with comorbid OCD, all the exposures in these studies were directed towards misophonia symptoms specifically. Cases were mostly young females although ages ranged widely across all studies (10–35 years). Further, symptom profile as well as primary outcomes varied across the 13 patient cases. In general, length of therapy was longer and more intense compared with the studies of non-exposure-based CBT alone, ranging from 2 to as many as 23 total sessions [8,37]. Therapy was typically

Table 1
Summary of Misophonia Treatments.

Study design + Treatment	Study	Sample Size + Age + Gender	Trigger Sounds + Symptoms	# Of Sessions And/Or Dose	Outcome Measures	Primary Outcome	Components + Techniques Described
<i>RCT</i> CBT	Jager et al. [22]	54 M/F patients, age 18–70	Variable	7 weekly group therapy of 1.5 h psychotherapy and 1.5 h psycho-motor training (PMT)	A-MISO-S CGI-I	A-MISO-S: mean reduction 9.7 points CGI-I: mean 37% improvement	Group CBT in PMT 1) Task concentration shifting to redirect away from exposure trigger sounds 2) Counter-conditioning to undo patterned associations of neutral stimuli with a negative emotional response toward a more positive emotional response 3) Stimulus manipulation to promote patient sense of control 4) Relaxation exercises for arousal reduction. 5) Psychoeducation for families
<i>Open Label Trial</i> CBT	Schneider and Arch [40]	90 adults (65F + 25 M) Ages 18–64 (mean age: 36)	Trigger: Eating sounds in 77% Symptoms: Anger alone in 63%, Anger + Disgust in 37%	7–8 Biweekly group therapy sessions	A-MISO-S CGI-I	48% (N = 42) had both a CGI-I score of 1 or 2 after treatment and at least a 30% reduction on the A-MISO-S, with mean reduction of 4.5 points	1) Task concentration shifting to redirect away from exposure trigger sounds 2) Counter-conditioning to undo patterned associations of neutral stimuli with a negative emotional response toward a more positive emotional response 3) Stimulus manipulation to promote patient sense of control 4) Relaxation exercises for arousal reduction.
<i>Pilot Case Series</i> CBT	Lewin et al. (2020)	4 children/adolescents, ages 8–16	Unspecified	10 sessions of Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Children and Adolescents	A-MISO-S CGI CGAS	Mild improvement in all three domains.	1) Psychoeducation regarding misophonia 2) Personalized cognitive-behavioral model of misophonia 3) Learning “opposite action” strategies to counter misophonia-related avoidance/safety behaviors 4) Cognitive restructuring 5) Developing a hierarchy for trigger sounds 6) Exposure therapy 7) Relapse prevention
<i>Case Studies</i> CBT	Bernstein et al. [3]	19 y.o. female	Disgust and anger to chewing sounds	6 CBT sessions	Subjective Units of Distress (SUDS)	Mild symptoms persisted but functional abilities returned. Effect maintained at 4 months follow up.	1) Cognitive reappraisal component 2) Behavioral components to move from avoidance to healthy coping strategies 3) Relaxation exercises Unspecified
CBT	Alekri & Al Saif [1]	18 y.o. female	Severe symptoms of anger and suicidal ideation	Unspecified	A-MISO-S	A-MISO-S: –23 to 16 at 3 months –12 at 1 year	

(continued on next page)

Table 1 (continued)

Study design + Treatment	Study	Sample Size + Age + Gender	Trigger Sounds + Symptoms	# Of Sessions And/Or Dose	Outcome Measures	Primary Outcome	Components + Techniques Described
CBT	Altunöz et al. [2]	18 y.o. female	Anger in response to drinking sounds	6 CBT sessions	A-MISO-S	A-MISO-S: –11 to 4	Unspecified
CBT	Roushani et al. (2021)	3 females aged 20–22 y. o.	Anger	8 weekly CBT sessions	Navaco Anger Scale (NAS)	NAS: Self-reported decrease in all three cases	Similar as described by Schneider and Arch [40]
Online CBT	Zarotti et al. [57]	16 y.o. female	Temperature increase, anger, and skin crawling sensation in response to nasal sounds	15 weeks of online CBT	A-MISO-S	A-MISO-S: –17 to 10	Online CBT: Emotional regulation 1) Distress tolerance 2) Cognitive restructuring
CBT + Exposure	Hocaoglu [19]	20 y.o. and 29 y.o. females	Comorbid OCD	4–5 months of therapy	Self-reported	Self-reported	Exposure therapy
CBT + Exposure	Hadjipavlou et al. [18]	13 y.o. and 25 y.o. females	13 y.o.: social impairment 25 y.o.: multiple psychiatric comorbidities	Unspecified	Self-reported	Unsuccessful treatment	Multiple medications and Exposure therapy
CBT + Exposure	McGuire et al. (2015)	11 y.o. and 17 y.o. females	No psychiatric comorbidities. Primarily distress/irritability reactions.	Unspecified	MQ MSS	Self-reported	CBT with Exposure therapy
CBT + Exposure	Reid et al. [37]	14 y.o. female	Comorbid OCD, ADHD, MDD, and specific phobia	Intensive 14 sessions over 3 weeks	A-MISO-S	A-MISO-S: –17 to 7 Maintained at 3 months follow up.	CBT + Exposure: only 2/14 total sessions specifically targeted misophonia symptoms
CBT + Exposure	Dover & McGuire [8]	10 y.o. female	Anger and panic to family chewing sounds	23 family-based CBT sessions	A-MISO-S MQ Family accommodation	A-MISO-S: –10 to 3 -MQ: 70% reduction in severity – 75% reduction in family accommodating behaviors	23 total sessions, in three phases: 1) Habit reversal training 2) Parent management training 3) Exposure therapy
CBT + Exposure	Rabasco & McKay [36]	21 y.o. female and 35 y.o. male	Symptoms causing severe social impairment	12 sessions over 6 weeks	SUDS	SUDS: Self-reported increased tolerance to trigger sounds	12 total session, in two phases: 1) Coping skills using Unified Protocol for Emotional Disorders 2) Exposure exercises
CBT + Exposure	Muller et al. [29]	14 y.o. female	Disgust and anger causing avoidance behaviors	Unspecified	SUDS	SUDS: Self-reported increased tolerance to trigger sounds	Unspecified: CBT + Exposure
CBT + Exposure	Cecilione et al. [7]	12 y.o. female	Symptoms causing social impairment	23 sessions	MQ	MQ: Self-reported decreased from 96th percentile severity to 53rd	CBT sessions focused on: 1) Counter-conditioning 2) Task concentration exercises 3) Relaxation exercises 4) Exposure exercises
CBT + Exposure	Singer (2019)	19 y.o. female	Anger, disgust, and anxiety	10 sessions	A-MISO-S MQ	A-MISO-S: –23 to 4 MQ: –54 to 21	CBT sessions focused on: 1) Cognitive restructuring, 2) Relaxation techniques 3) Graded exposure exercises
Counter-conditioning Therapy	Dozier [9–11]	2 Case studies: 21 y. o. and 48 y.o. females	Variable	Ranging from 7 to 23 sessions lasting 20–30 min	MAQ	MAQ: –49 to 12 after one year Case Series: anecdotal	Counter-conditioning: pairing a positive auditory stimulus (music) alongside the negative conditioned stimulus (continued on next page)

Table 1 (continued)

Study design + Treatment	Study	Sample Size + Age + Gender	Trigger Sounds + Symptoms	# Of Sessions And/Or Dose	Outcome Measures	Primary Outcome	Components + Techniques Described
		Case Series: 10 cases of varied age				improvement of symptoms	
Dialectical Behavior Therapy (DBT)	Kamody & Del Conte [25]	16 y.o. female	Comorbid social anxiety with primary anger response.	Partial Hospitalization daily DBT for 7 weeks	A-MISO-S	A-MISO-S: –22 to 10 after 7 weeks	DBT with a focus on mindfulness and distress tolerance skills
Acceptance AND Commitment Therapy (ACT)	Schneider & Arch [40]	17 y.o. male	Anger and disgust as primary response	10 sessions	A-MISO-S	A-MISO-S: –14 to 7, maintained at 6 months	Mindfulness and acceptance based components, in addition to CBT and DBT components
Tinnitus Retraining Therapy (TRT)	Jastreboff & Jastreboff [23]	Variable	28% with comorbid hyperacusis	Unspecified number of sessions	Self-reported impairment scale from 0 to 10	86% reported significant improvement	Create clear hierarchy of trigger noises from most to least distressing, and gradual confrontation of these trigger noises with support
TRT	Vanaja & Abigail (2020)	26 y.o. female	Responses: burning sensation in the ear, headache, and irritability	28 weekly sessions	AMISOS-R	AMISOS-R: –17 to 6, maintained at 3 months	Tinnitus retraining therapy, desensitization techniques, and habituation therapy described by P. J. Jastreboff and Jastreboff [23]
Eye Movement desensitization Reprocessing (EMDR)	Jager et al. (2021)	8 adults	Unspecified	1–4 Sessions of EMDR	A-MISO-S	A-MISO-S: Mean 6-point reduction across all cases (20% reduction)	EMDR: One to four 60–90 min sessions
Pharmacotherapy Case Studies							
SSRI	Sarigedik & Yurteri [39]	14 y.o. female	Anger and avoidance behaviors	Fluoxetine 30 mg/day	A-MISO-S CGA scale	A-MISO-S: –18 to 11 CGA: 70% improvement	Started at 10 mg/day, uptitrated to 30 mg over 2 months
SSRI	Vidal et al. [53]	32 y.o. female	Comorbid OCD	Escitalopram (dose unspecified)	Unspecified	Self-reported partial remission of symptoms	Unspecified dose
SSRI	Zuschlag & Leventhal [58]	32 y.o. female	Comorbid anxiety and depression	Sertraline 150 mg/day	Unspecified	Complete resolution of symptoms after 3 weeks	Started at 50 mg/day, uptitrated to 150 mg/day
β-Blockers	Webb [54]	16 y.o. male	Increased heart rate, sweating, rapid breathing, panic, and aggression	Propranolol 60 mg/day	A-MISO-S	A-MISO-S: –15 to 2	60 mg of propranolol one hour before each meal
Benzodiazepine	Tunç & Başbuğ [52]	22 y.o. male	Disgust and extreme intolerance	Alprazolam 0.5 mg/day	A-MISO-S	A-MISO-S: 23 at baseline. Self-reported symptom improvement	Three-day course of alprazolam (0.5 mg/day)
Atypical antipsychotic	Naguy et al. (2022)	4 y.o. male	Autism with comorbid misophonia	Risperidone 0.25 mL BID	Unspecified	Symptoms resolved	Unspecified
Stimulant + CBT	Osuagwu et al. [32]	14 y.o. male	Distractability symptoms associated with misophonia	methylphenidate (dose unspecified)	Unspecified	Self-reported improvement in ability to focus and distress tolerance	Methylphenidate + CBT
Medication + Therapy	Robinson et al. (2018)	12 children	Comorbid Tourette's Syndrome or Tic disorder	Varied	Varied	Varied	Various combinations of medication and therapy

*A-MISO-S: Amsterdam Misophonia Scale has clinically defined severity categories [41]: Scores from 0 to 4 are considered subclinical; 5–9 mild symptoms; 10–14 moderate; 15–19 severe; 20–24 extreme.

MQ: Misophonia Questionnaire & MSS: Misophonia Severity Scale [56].

MAQ: Misophonia Assessment Questionnaire.

CGI: Clinical Global Impressions Scale.

CGAS: Children's Global Assessment Scale.

divided into distinct phases, with exposure comprising one of the phases. Exposure was defined variably among studies with some utilizing traditional graded exposure [46], while others were grounded in newer inhibitory learning models of extinction learning [8]. For example, Dover and McGuire [8] implemented 23 total sessions of a family-based CBT approach, with distinct phases of habit reversal training, parent management training, and exposure therapy. This report showed a 70% reduction in misophonia symptoms. Family accommodation behaviors also significantly decreased, suggesting some added benefit to a family-based approach.

Tinnitus retraining therapy (TRT) is a type of treatment aimed at decreasing the strength of negative reactions through exposure to a continuous low-level broadband sound in which the patient has variable levels of control over the environment, sounds used, and duration of sound exposure. Jastreboff and Jastreboff [23] report clinical improvement in 86% of 201 total patients based on self-reported measures of functional impairment. Misophonia symptom reduction (from severe (17) to mild (6) based on the AMISOS-R) was also achieved through a combination of TRT, desensitization techniques, and habituation therapy (Vanaja and Abigail, 2020).

3.3. “Third-Wave” therapy approaches

Two case studies implemented “third wave” behavioral approaches, including ACT and DBT. One case study described an adolescent female with a primary response of intense rage who was unsuccessfully treated with exposure-based CBT. While on paroxetine (25 mg) to treat anxiety, the patient received DBT focusing on mindfulness and distress tolerance skills for 5 days a week during a 7-week partial hospitalization program. A-MISO-S scores reduced from extreme (22) to moderate (10) [25]. Another third-wave case study implemented mindfulness and acceptance-based techniques to target high levels of anger and disgust in a 17-year-old male patient [40]. Treatment also integrated DBT and CBT interventions. After 10 sessions, severity ratings on the A-MISO-S scale decreased by 50% from moderate (14) to minimal (7).

3.4. Pharmacotherapy

The most widely reported medication class used to treat misophonia was selective serotonin reuptake inhibitors (SSRIs) [39,53,58]. Three case studies of variable demographics (one adolescent female, one adult female with comorbid OCD and one adult male with comorbid anxiety and depression) showed responses to SSRIs ranging from complete to partial remission of misophonia symptoms [39,53,58]. Sarigedik and Yurteri [39] indicated a response time of one month on fluoxetine 20 mg daily, and continued improvement with increased dose (30 mg) at 3 months. Zuschlag and Leventhal [58] reported remission of symptoms after 3 weeks of sertraline 150 mg daily.

In certain cases with specific comorbidities, treatment of a primary behavioral impairment led to the secondary improvement of misophonia symptoms. For example, in a 4-year-old with autism, low-dose risperidone reportedly resolved misophonia symptoms (Naguy et al., 2022). In a 14-year-old with comorbid ADHD, a combination of methylphenidate and CBT reportedly improved distractibility symptoms in addition to improving distress tolerance to misophonia triggers [32]. Lastly, in a case of misophonia with primarily autonomic symptoms (e.g., increased heart rate, sweating, rapid breathing), propranolol one hour before each meal reduced symptoms from severe (15) to subclinical (2) levels on the A-MISO-S [54].

4. Discussion

To date, there has been a paucity of research on the treatment of misophonia. This systematic review highlights preliminary efficacy for one non-exposure-based CBT protocol [22], as well as preliminary case study-level support for a number of other psychotherapeutic

approaches. The only randomized control trial to date [22] describes a group therapy CBT approach, implementing task concentration exercises, positive affect labeling, stimulus manipulation, and arousal reduction techniques. This approach was significantly superior to a waitlist control in misophonia severity reduction, and improvements were maintained post-CBT treatment and at 1 year follow up. Across this randomized trial and many other case studies, CBT-based interventions with variable core components demonstrated potential in the treatment of misophonia. This is consistent with previous literature on related disorders (e.g., anxiety, OCD) and we posit that this may be due to similar mechanisms (e.g., associative and non-associative learning responses to aversive stimuli) underlying the development and maintenance of symptoms across these conditions [33]. CBT is believed to target maladaptive learned responses to trigger sounds through cognitive techniques such as positive affect labeling and acceptance, as well as behavioral strategies such as exposure and affect regulation skills. However, the high prevalence of anger and disgust responses, as well as the sensory nature of misophonia, suggest the underlying mechanism of misophonia may be related to but distinct from primary anxiety disorders [35,56]. Targeting anger and disgust responses through nuanced therapy approaches beyond CBT may prove to be an effective approach.

Several case reports described benefit from exposure-based CBT protocols utilizing a traditional habituation model of exposure. However, exposure therapy is not widely accepted as a credible intervention among individuals with misophonia [47], and it has been argued that exposure therapy can have deleterious effects [12]. An inhibitory learning model may better target the unique symptoms of misophonia by emphasizing distress tolerance and violating expectancies about triggers by using more adaptive approaches when confronting them (Frank & McKay, 2019). While there is promise in various CBT protocols, it is unclear what components are most effective and contribute to response. For example, the current protocols described by Jager et al. [22] and Schröder et al. [43] include elements that are not classically thought of as exposure, but carry elements of exposure in the introduction of trigger sounds during counter-conditioning procedures, which involve pairing a misophonia trigger with a pleasant stimulus to develop a new positive association with the trigger. It remains unclear which of these modalities contribute to the positive outcomes reported in these initial reports; dismantling studies are needed to understand core treatment components that contribute to outcome.

There is preliminary evidence for third-wave behavioral approaches such as ACT and DBT, suggesting possible benefits from implementing mindfulness and acceptance techniques. Mindfulness techniques may provide patients with an adaptive framework for engaging with distress evoking stimuli by taking a present-centered, non-judgmental perspective. Mindfulness techniques may assist in creating psychological distance from negative thoughts while fostering openness towards a patient's anger [40], allowing them to strategically re-engage in meaningful activities, even if misophonia symptoms are ongoing. Moving beyond case report data is necessary to understand the potential utility of interventions like ACT for misophonia.

While the psychotherapeutic literature is at a relatively early stage, research on pharmacotherapy for misophonia is in its infancy. Case reports provide preliminary directions. For example, the autonomic arousal implicated in misophonic responses [13] can be directly dampened by specific medications such as β -Blockers [54]. As research continues taking steps towards understanding the underlying neurophysiological mechanisms of misophonia [44], future research should focus on understanding how the physiologic response can be targeted with appropriate medications.

While overall response rates to published CBT reports for misophonia were generally positive, the lack of validated measures beyond the single-item CGI-I reveal a gap in the current treatment research paradigm. Psychometrically valid measures of misophonia symptom severity are needed to determine if treatment modalities are consistently efficacious. The A-MISO-S measures, modeled after the Y-BOCS, are most

often used. However, it remains unclear if the self-report nature of this scale is optimal (relative to clinician rated administrations, as the Y-BOCS is done); concerns about self-reported Y-BOCS ratings have been reported, especially items that tap into resistance and control dimensions of symptom severity [49]. Based on our clinical experience, we hypothesize similar issues may exist in self-reported misophonia severity.

Despite the first report of misophonia in the literature almost two decades ago, there exists no single frontline treatment for misophonia to date. This systematic review of misophonia treatments highlights the significant lack of strong empirical support for any interventions for misophonia. Several directions for future research are noted. First, and most broadly, development of mechanistically informed treatment protocols that have meaningful stakeholder engagement are needed. Treatment development efforts should engage multiple stakeholders (i. e., individuals with lived experience, clinicians, researchers) to develop robust and acceptable interventions that will translate well to real-world clinical settings. Second, future studies should focus on further refinements of promising extant interventions (e.g., dose of treatment, isolation of specific components) and replication by a second, independent team. Third, third-wave and pharmacological approaches may hold promise but require considerable additional study. Fourth, as mentioned previously, limitations of the overall literature which impact the present study include a lack of robust comparative trials as well as a lack of psychometrically validated measures for diagnosis and measuring severity. Using the growing pool of psychometrically validated measures of misophonia (both currently published, and measures to be developed) in assessing treatment efficacy is necessary. While the misophonia intervention literature is at an early stage, there is an opportunity to use strong scientific methods to build on the foundational research that has been done to date to develop efficacious treatments that reducing suffering and improve quality of life for children and adults with misophonia.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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