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Misophonia revised

New insights in phenomenology and psychotherapy

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Publication date

2022

Document Version

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Citation for published version (APA):

Jager, I. J. (2022). *Misophonia revised: New insights in phenomenology and psychotherapy*.

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An abstract painting of a face. The face is rendered in warm, earthy tones of yellow, orange, and brown. The mouth is a large, heart-shaped opening, outlined in thick, dark red paint. Inside the mouth, there are several vertical red lines, suggesting teeth or a tongue. The background of the face is a mix of these warm tones, with some darker, more textured areas. The overall style is expressive and somewhat somber.

I.J. Jager

MISOPHONIA REVISED

New insights in
phenomenology
and psychotherapy

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I.J. Jager

Misophonia revised: New insights in phenomenology and psychotherapy
Doctoral thesis, Faculty of Medicine (AMC-UvA), University of Amsterdam

Cover	Marlene Dumas, Teeth, 2018
Layout	Renate Siebes Proefschrift.nu
Printed by	Proefschriftmaken.nl De Bilt
ISBN	978-94-90791-93-3

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Misophonia revised

New insights in phenomenology
and psychotherapy

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. ir. K.I.J. Maex

ten overstaan van een door het College voor Promoties ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
op donderdag 3 februari 2022, te 16.00 uur

door Inge Jeanine Jager
geboren te Eindhoven

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1

General introduction

Bart is 21 years and studies at the university of applied sciences. He lives with his parents and sister. Bart's misophonia started when he was seven. From that period, he remembers especially the sounds of his father as a trigger. His father rubbed his feet together and when Bart saw and heard that rubbing, he got mad at him. Bart was also disgusted by his father's eating manners. "It made me very angry and I just couldn't stand it.", he said. His misophonia has a major impact on his life. Bart is a cheerful and creative person, but he says he is increasingly gloomy because of his symptoms. He didn't graduate from high school due to misophonia and is now afraid to live with his friends because of the risk of developing misophonia to his roommates. Although Bart is a social person, he avoids social contacts. He also no longer dares to get into a relationship. Bart's biggest misophonia triggers are eating sounds, namely loud chewing, swallowing and seeing someone remove leftover food from their molars. Bart's coping is to tell his parents to act normal. If others start to question his comments, Bart may lose control of his anger. He mostly has his anger under control, but sometimes with his parents it can escalate. Then he will throw things in anger and slams his fists against the wall until his knuckles bleed. Once, while eating, Bart has pointed a knife at his father. He was frightened by this incident and is ashamed to report this. Bart has had impulsive breakthroughs in other areas and has been suicidal in the past. ADHD and borderline traits may explain his aggressive outbursts in misophonia.

Because of comorbidity and severity of misophonia there was doubt whether Bart would profit from the eight-weeks group treatment at our psychiatry department. Bart has a very positive influence on the group dynamics and benefits from treatment with group cognitive behavioral therapy (G-CBT). Bart reports at follow-up things are going much better at home. He has no more aggressive outbursts. He also goes to lectures more often and socializes more with his friends. Most triggers do not result in a strong emotional reaction anymore. If a trigger does provoke anger or disgust, the emotional reaction is mild and Bart copes with it in a whole different way, for example by making a joke about his misophonia. As a result of treatment, he shares more with his parents and friends about his symptoms and feels more free and relieved. Bart also mentions that sharing with other patients has dissolved shame and guilt. Following misophonia treatment, Bart is referred now to a specialized center for personality problems in young adults.

1.1 Misophonia

In the last decade the psychiatry department of the Amsterdam UMC, location AMC, has become a world leading expertise center for misophonia. Over 3000 patients were

diagnosed at our center and more than 1300 patients have received treatment. One of these patients was Bart.

Misophonia is a disorder in which patients suffer from extreme anger or disgust when they are confronted with specific human sounds, such as loud chewing or breathing. Non-auditory cues, such as repetitive movements (e.g., wobbling legs), induce these strong emotional reactions as well. Patients experience a profound sense of loss of self-control. They are therefore highly preoccupied with specific misophonia cues and avoid cue related situations, resulting in significant functional impairment (Schröder et al., 2013; Brout et al., 2018). Misophonia patients are often not able to eat, sleep or work in an office and most social- and family relations are negatively affected. Misophonia patients do have the insight their reaction is disproportional and often feel guilty and ashamed of their intense (internal) reaction.

Since the onset of symptoms is around the age of 13 (Schröder et al., 2013; Rouw & Arfanian, 2017), misophonia patients develop a lifelong coping behavior of avoidance affecting both specific situations as well as their life in general. In specific situations misophonia patients walk away or use earplugs to camouflage trigger sounds. In general, misophonia patients make different important life choices such as not living together or working as a freelancer.

Solid epidemiological studies are missing, but some estimates of incidence based on student samples suggest misophonia is possibly a common disorder with an incidence of moderate symptoms and/or impairment from 6 to 12% (Zhou, Wu, & Storch, 2017; Naylor, Caimino, Scutt, Hoare, & Baguley, 2020).

Misophonia received increasing academic attention in the last two decades. It was initially described in auditory literature (Jastreboff & Jastreboff, 2001), and subsequently in psychiatric literature by the group of Denys. There is still debate about the nature of the disorder, some research groups emphasize its audiological or neurological nature and others, among which our research group, its psychiatric nature. The publication of the Amsterdam University Medical Center (Amsterdam UMC, location AMC) research group in 2013 proposing the first diagnostic criteria of misophonia as a psychiatric disorder (Schröder, Vulink, & Denys, 2013) caused a stir in Dutch media (for example Batstra, 2017), as well as in international scientific journals (see for example an overview of criticisms given by Taylor, 2017). Critics were concerned about “the creeping medicalization of quirks of human behavior” (BMJ, 2020; 369: m1843) or questioned the psychiatric nature of the condition (Jastreboff & Jastreboff, 2015). Though the AMC diagnostic criteria for misophonia were much debated in the social and academic field, the research was rewarded with the Ig Nobel Prize in Medicine 2020 (“List of Ig Nobel Prize winners – Wikipedia”, 2021).

1.2 Literature review

1.2.1 Search July 2015

As a start I performed a literature search in July 2015. I used a nonsystematic search strategy with the search term 'Misophonia' in Pubmed. Removing all textbooks and doubles, merely 25 research articles with misophonia as a main topic were found. The low number of articles illustrated the lack of knowledge about misophonia. In the General discussion I will describe the development in misophonia research from the starting point of my thesis until the finalization this year.

Three of 25 articles were from our research group from a psychiatric perspective (Schröder, Vulink, & Denys, 2013; Schröder, et al., 2014; Schröder, Giorgi, van Wingen, Vulink, & Denys, 2015), two from the Jastreboff group from an audiological perspective (Jastreboff & Jastreboff, 2002; Jastreboff & Jastreboff, 2006) and five articles from the Storch group from a psychological perspective (Johnson, Webber, Wu, Lewin, Murphy, & Storch, 2013; Webber, Johnson, & Storch, 2014; Wu, Lewin, Murphy, & Storch, 2014; McGuire, Wu, & Storch, 2015; Webber & Storch, 2015). Half of the found articles consisted of single case studies providing only anecdotal evidence on phenomenology or treatment. My research can therefore be considered as pioneering in a mostly unexplored research area with divergent visions on misophonia.

1.3 Aims of the present thesis

This thesis has two main aims. First, to increase knowledge concerning the phenomenology of misophonia (Part I). Second, to investigate the effect of different treatments for misophonia (Part II).

The following research questions will be addressed in Part I (chapter 2):

1. How many subjects referred with misophonia-like symptoms actually suffer from misophonia?
2. Should misophonia be approached from an audiological or psychiatric perspective?
3. Are specific psychological profiles, namely disgust sensitivity, autism-like traits and perfectionism associated with misophonia?
4. Is misophonia a distinct psychiatric disorder for which the diagnostic criteria, proposed by our research group in 2013 (Schröder et al.), can be confirmed and sharpened in a large sample?

In Part II (chapter 3–5) the following research questions will be addressed:

5. What is the short-term efficacy of group cognitive behavioral therapy (G-CBT) on misophonia symptoms compared to a waiting list control group?
6. Does the reduction in misophonia symptoms achieved by G-CBT remain at one-year follow-up?
7. What is the rationale behind the interventions of G-CBT and what is the design of the treatment protocol?
8. What could be the effectiveness of eye movement desensitization and reprocessing (EMDR) therapy as a trauma-focused approach in treating misophonia symptoms?

Chapter 6 will provide a general discussion based on the findings presented in chapter 2–5. It discusses the conclusions that can be drawn from the former chapters by answering the research questions, strengths and weaknesses of the present study, the development in misophonia research, and offers recommendations for future research.

1.4 Credentials

I believe all scientists should hand over their credentials, especially in a field with such conflicting views. Here are mine:

Before my employment at the A-UMC, I had never heard of misophonia as a condition in mental healthcare. In retrospect I recognized this syndrome in one patient, who I treated for burn-out and who also suffered from obsessive-compulsive personality disorder. He scored positive on an item of the SCL-90 concerning social anxiety, which puzzled me: “Feeling uncomfortable about eating and drinking in public”. Upon inquiry he turned out to be highly bothered by eating sounds of others. He avoided public transport and got caught up in conflicts with his colleagues and wife and children about their eating behavior. He asked me if I could help him with this problem, since it affected so many domains of life. Unfortunately, I could not.

In January 2015, I was the first to start a specialization as a clinical psychologist, with a colleague, at the Psychiatry department of Amsterdam UMC, location AMC, supervised by Arnoud van Loon and Damiaan Denys. Research is a part of this four-year specialization, but in the AMC this part is extended into a PhD project. I had the opportunity to apply clinical research directly to a newly discovered condition. As a scientist practitioner I chose

explicitly for this type of research. Combining clinical work and research has developed my understanding of misophonia.

Starting my PhD mid-2015 I was skeptical about misophonia as an independent disorder and thought it to be a symptom of obsessive-compulsive personality disorder or general neuroticism. I did not see it any different from my compulsive neighbor who gets extremely annoyed with falling leaves in our avenue every fall and with a barking dog living up the street. My neighbor suffers from the same preoccupation, annoyance and anger as was described in misophonia patients. Even though I was reluctant at first to consider misophonia a psychiatric disorder, I was convinced by the strong evidence we found and especially by the patients I met. I started directly as a therapist in our misophonia treatment groups and have spoken to over a hundred misophonia patients during my studies. Particularly in working with adolescents with misophonia and their families I was impressed by the distress caused by misophonia. The research I did on misophonia in children, resulting in the master thesis of Vanja Dubislav 'Misophonia in children; Phenomenology and treatment effect of cognitive-behavioral group therapy' is however beyond the scope of this thesis.

With respect to therapy for misophonia, I was biased. Trained as a cognitive behavioral therapist and CBT supervisor I am convinced of the effect of CBT on all kind of disorders. Whether misophonia would be a distinct disorder or not, I already suspected CBT would be effective on the main symptoms. I was more skeptical about the possible effect of eye movement desensitization and reprocessing (EMDR) therapy for misophonia. Especially patients who had previously received EMDR therapy elsewhere without a positive effect, applied for help at the psychiatry department. Even though I was aware of the selection bias, I was cautious to apply EMDR therapy for other conditions than post-traumatic stress disorder with little evidence. However, I hope my critical and open attitude helped me with my research.

So with regards to both diagnosis and treatment of misophonia, I had underlying presumptions, which changed during my PhD, but which have possibly influenced this thesis. It is up to the reader of this thesis to decide the extent to which my conclusions are substantiated by our findings.

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PART I

**New insights in
phenomenology of
misophonia**



2

Misophonia: Phenomenology, comorbidity and demographics in a large sample

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PloS one, 15(4), e0231390.

Objective: Analyze a large sample with detailed clinical data of misophonia subjects in order to determine the psychiatric, somatic and psychological nature of the condition.

Methods: This observational study of 779 subjects with suspected misophonia was conducted from January 2013 to May 2017 at the outpatient-clinic of the Amsterdam University Medical Centers, location AMC, the Netherlands. We examined DSM-IV diagnoses, results of somatic examination (general screening and hearing tests), and 17 psychological questionnaires (e.g., SCL-90-R, WHOQoL).

Results: The diagnosis of misophonia was confirmed in 575 of 779 referred subjects (74%). In the sample of misophonia subjects (mean age, 34.17 [SD = 12.22] years; 399 women [69%]), 148 (26%) subjects had comorbid traits of obsessive-compulsive personality disorder, 58 (10%) mood disorders, 31 (5%) attention-deficit (hyperactivity) disorder, and 14 (3%) autism spectrum conditions. Two percent reported tinnitus and 1% hyperacusis. In a random subgroup of 109 subjects we performed audiometry, and found unilateral hearing loss in 3 of them (3%). Clinical neurological examination and additional blood test showed no abnormalities. Psychological tests revealed perfectionism (97% CPQ > 25) and neuroticism (stanine 7 NEO-PI-R). Quality of life was heavily impaired and associated with misophonia severity ($r(184) = -.34$, $p < .001$, $p < .001$).

Limitations: This was a single site study, leading to possible selection- and confirmation bias, since AMC-criteria were used.

Conclusions: This study with 575 subjects is the largest misophonia sample ever described. Based on these results we propose a set of revised criteria useful to diagnose misophonia as a psychiatric disorder.

2.1 Introduction

Misophonia is a recently recognized condition, characterized by an impulsive aversive physical reaction of irritation, anger, or disgust when confronted with specific, repetitive stimuli (for instance, eating sounds). The word was first used in audiology literature as a hatred of sounds (Jastreboff & Jastreboff, 2001). In 2013 our research group at the Amsterdam University Medical Centers (Amsterdam UMC, location AMC) proposed the first diagnostic criteria for misophonia as a psychiatric disorder (Schröder, Vulink, & Denys, 2013) (Table 2.1). Thereafter, research on misophonia has increased vastly. The Amsterdam viewpoint is misophonia is definitely a psychiatric disorder, though there’s no agreement among different research teams. For a recent descriptive overview, we refer to Taylor (2017) or Brout et al. (2018).

Table 2.1. AMC 2013 diagnostic criteria for misophonia

AMC 2013 criteria for misophonia
A. The presence or anticipation of a specific sound, produced by a human being (e.g. eating sounds, breathing sounds), provokes an impulsive aversive physical reaction which starts with irritation or disgust that instantaneously becomes anger.
B. This anger initiates a profound sense of loss of self-control with rare but potentially aggressive outbursts.
C. The person recognizes that the anger or disgust is excessive, unreasonable, or out of proportion to the circumstances or the provoking stressor.
D. The individual tends to avoid the misophonic situation, or if he/she does not avoid it, endures encounters with the misophonic sound situation with intense discomfort, anger or disgust.
E. The individual’s anger, disgust or avoidance causes significant distress (i.e. it bothers the person that he or she has the anger or disgust) or significant interference in the person’s day-to-day life. For example, the anger or disgust may make it difficult for the person to perform important tasks at work, meet new friends, attend classes, or interact with others.
F. The person’s anger, disgust, and avoidance are not better explained by another disorder, such as obsessive-compulsive disorder (e.g. disgust in someone with an obsession about contamination) or post-traumatic stress disorder (e.g. avoidance of stimuli associated with a trauma related to threatened death, serious injury or threat to the physical integrity of self or others).

Currently, a total of 797 misophonia subjects has been described in 26 clinical research papers, including five sample studies [Schröder et al., 2013; Wu, Lewin, Murphy, & Storch, 2014; Rouw & Erfanian, 2017; Sanchez & Silva, 2017; Zhou, Wu, & Storch, 2017). Only subjects included in the AMC sample (Schröder, et al., 2013) and a sample study published last year (Erfanian, Kartsonaki, & Keshavarz, 2019) had a systematic medical and psychiatric examination. All other samples (of the papers included in our 2018 search) merely used questionnaires to diagnose misophonia.

Without a systematic clinical interview, which is missing in almost three quarters of all described subjects, misophonia symptoms could possibly be better explained by another disorder or results could be influenced by self-report biases (references in Supplementary Table S2.1 and Supplementary Figure S2.1).

Therefore, we assessed a new sample of subjects with misophonia symptoms who were referred to the AMC by their general practitioner, which is both quantitatively and qualitatively superior to previous research. The first aim of this study was to determine whether referred subjects with misophonia-like symptoms actually suffered from misophonia using a psychiatric interview conducted by three experienced psychiatrists. The second aim was to determine phenomenology, comorbidity, and demographics of the misophonia sample to address three major issues: 1) whether misophonia should be approached from an audiological or psychiatric/psychological perspective; 2) whether specific psychological profiles, which have been associated with misophonia, such as disgust sensitivity (Taylor, Conelea, McKay, Crowe, & Abramowitz, 2014), autism-like traits (Danesh, Lang, Kaf, Andreassen, Scott, & Eshraghi, 2015; Tavassoli, Miller, Schoen, Jo Brout, Sullivan, & Baron, 2017) and perfectionism (Schröder et al., 2013) are still valid; and 3) whether misophonia is a distinct psychiatric disorder for which diagnostic criteria should be determined.

2.2 Methods

2.2.1 Subjects

In this sample study, we analyzed data collected from subjects who were referred with misophonia symptoms from 2013 through 2017 at the Department of Psychiatry at Amsterdam University Medical Center (Amsterdam UMC), the Netherlands. This study has been approved by the ethics committee of Amsterdam UMC and the need for informed consent was waived.

Of the 779 examined subjects, 575 subjects met criteria for misophonia. The 204 subjects excluded from this sample were: subjects with primary autism spectrum conditions (ASC), primary attention-deficit (hyperactivity) disorder (AD(H)D), a primary diagnosis on Axis II (varying from schizotypal personality disorder to obsessive compulsive personality disorder) and subjects without a DSM-IV diagnosis. Hearing impairments or audiological disorders were no exclusion criterion.

2.2.2 Diagnostic procedures

Assessment of current Axis I and Axis II disorders based on the DSM-IV criteria (American Psychiatric Association, 2000) was determined with the MINI-International Neuropsychiatric Interview Plus (Sheehan et al., 1998) (MINI-plus) and sections of the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (First, Gibbon, Spitzer, Williams, & Benjamin, 1997) (SCID II). Based on information obtained from clinical interview, questionnaires or psychiatric history specific sections of the SCID-II relevant to each subject were selected and conducted. DSM-5 was not in use for clinical purposes at our department until 2018. Three psychiatrists, specialized in anxiety disorders and obsessive-compulsive and related disorders, carried out the clinical (medical and psychiatric) interviews.

Somatic assessment consisted of a general physical and neurological examination and a general blood screening. Audiometry was performed with the Hughson-Westlake procedure (Carhart & Jerger, 1959) to obtain hearing thresholds in a random selection of participants ($n = 109$) in the first 300 subjects. Patients were randomly assigned to three psychiatrists. In a period of 20 months the assessment of one psychiatrist was extended with audiometry. Because the results were clear, we stopped performing audiometry in order not to unnecessarily burden subjects. Air conduction thresholds were measured at all octave frequencies from 0.25 to 8 kHz and bone conduction thresholds were measured at 0.25, 0.5, 1, and, 2 kHz, with adequate masking if necessary. The Pure Tone Average (PTA) was obtained by averaging air conduction thresholds 0.5, 1, 2, and, 4 kHz and hearing loss classification was defined according to WHO-classification (WHO, 1991).

Finally, a variety of self-report questionnaires examined the nature and severity of misophonia symptoms, quality of life, anxiety and depressive symptoms, and personality profile of the subjects. Given the naturalistic nature of the sample, the standard battery of questionnaires at our psychiatry outpatient clinic was used (seven questionnaires), with several additional questionnaires to understand the phenomenology of misophonia and the relation with possible correlated constructs. All questionnaires were administered during intake procedure. A random selection of subjects ($n = 56$) completed an additional personality questionnaire (see Supplementary Table S2.2). During 4 months all intakes (60 subjects in total) were approached for this additional personality questionnaire, which was completed by 56 subjects.

2.2.3 Questionnaires

The following questionnaires were administered: Misophonia Screening List (see Appendix 2.1), Misophonia Sound List (MSL; see Appendix 2.2), Amsterdam Misophonia Scale (Schröder et al., 2013) (A-MISO-S), AMISOS Revised (AMISOS-R; see Appendix 2.3), Hamilton Depression Rating Scale (de Jonghe, 1994; Hamilton, 1960) (HDRS), Hamilton Anxiety Scale (Maier, Buller, Philipp, & Heuser, 1988; Hamilton, 1959) (HAS), Symptom Checklist 90 Revised (Arrindell & Ettema, 1986; Derogatis, Lipman, & Covi, 1973) (SCL-90-R), Manchester Short Assessment of Quality of life (van Nieuwenhuizen, Janssen-de Ruijter, & Nugter, 2017; Priebe, Huxley, Knight, & Evans, 1999) (MANSA), Sheehan Disability Scale (Sheehan, 1983) (SDS), WHO Quality of Life-BREF (Trompenaars, Masthoff, Van Heck, Hodiamont, & de Vries, 2005; The WHOQOL Group, 1998) (WHOQoL-BREF), NEO-Personality Inventory-revised (Miller et al., 2008; Costa & McCrae, 1992) (NEO-PI-R), Autism Spectrum Quotient (Hoekstra, Bartels, Cath & Boomsma, 2008; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) (AQ), Inventory of Interpersonal Situations (van Dam-Baggen & Kraaimaat, 2000) (IIS), Clinical Perfectionism Questionnaire (Shafran, Cooper, & Fairburn, 2002) (CPQ), Frost Multidimensional Perfectionism Scale (Frost, Marten, Lahart, & Rosenblate, 1990) (FMPS), Disgust Propensity and Sensitivity Scale Revised (van Overveld, de Jong, Peters, Cavanagh, & Davey, 2006; Cavanagh & Davey, 2000) (DPSS-R), Disgust Scale Revised (van Overveld, de Jong, Peters, & Schouten, 2011; Haidt, McCauley, & Rozin, 1994) (DS-R). For more information, see Supplementary Table S2.2.

2.2.4 Statistical analysis

All statistical analyses were conducted with SPSS statistical package version 24. We report the sample descriptively in terms of means and standard deviations or percentage of the sample, where appropriate. We used independent-samples t-tests to explore whether males and females differed in age of onset and symptom severity (i.e. A-MISO-S or AMISOS-R score). We used multiple linear regression to explore whether certain features were associated with symptom severity. AMISOS-R scores were included as independent variables, and CPQ, FMPS, AQ, DS-R and DPSS-R were included as dependent variables. We confirmed normality of residuals by checking the QQ plot of the model. We treated the full Likert scales as numerical, since assumptions of linear regression were met (residuals were normally distributed) and results are much easier to interpret. Finally, a non-parametric correlation (Spearman's rho) was calculated to determine whether misophonia symptoms (A-MISO-S) correlated with quality of life (MANSA). No missing scores were imputed and no outliers were removed. We considered $p < .05$ to be statistically significant.

2.3 Results

2.3.1 Demographics

Our sample was predominantly Caucasian, 69% were female, and 64% had a relationship. Over 85% were employed or studying and 5% were on sick-leave. Mean age at admission was 34.17 years ($SD = 12.22$) and mean age of onset was 13.17 years ($SD = 7.37$). Onset in females was not significantly earlier than in males ($p = .076$). Most subjects (93%) reported a gradual onset of the misophonia symptoms. Clinical interviews with older subjects indicated a chronic course and 33% reported a positive family history of misophonia.

2.3.2 Comorbidity

The comorbid DSM-IV disorders are shown in Table 2.2. 72% of subjects diagnosed with misophonia had no comorbid Axis I psychiatric disorder, 22% had one comorbid disorder, and 6% had two or more comorbid disorders. Common comorbid disorders were major depressive disorder (6.8%) and obsessive-compulsive disorder (2.8%). Another 5% of the sample had comorbid AD(H)D and 3% was diagnosed with a comorbid ASC.

The majority (59%) had no comorbidity on Axis II. Most prevalent were OCPD (2.4%) and borderline personality disorder (BPD, 1.7%). Obsessive-compulsive personality traits were found in 26%. Subjects exhibited especially high morality and clinical perfectionism.

2.3.3 Misophonia triggers

Almost all subjects reported to be triggered by eating sounds (96%) followed by nasal and breathing sounds (85%). Subjects were also regularly disturbed by sounds of repetitive tapping or mouth/throat sounds. All triggers are shown in Figure 2.1.

Visual triggers were often reported, e.g., repetitive movements (68%). We found visual triggers were often directly associated with auditory triggers (e.g., grinding teeth) in clinical interviews. When visual triggers were reported, they occurred secondary to auditory triggers and had less impact than the auditory triggers. When visual and auditory stimuli occurred simultaneously (e.g., hearing and seeing someone chewing gum), subjects reported a more intense response. 59% were bothered by ambient sounds, particularly by sounds of neighbors.

Table 2.2. Percentage and absolute frequencies of current DSM-IV Axis I & Axis II disorders in misophonia subjects

Comorbidity DSM-IV Axis I	% (N)	Comorbidity DSM-IV Axis II	% (N)
No comorbid diagnosis on Axis I	71.8 (413)	No comorbid diagnosis on Axis II	58.6 (337)
Mood disorders	10.1 (58)	Personality disorder	5.0 (29)
Major depressive disorder	6.8 (39)	Obsessive-compulsive	2.4 (14)
Dysthymic disorder	1.7 (10)	Borderline	1.7 (10)
Bipolar II disorder	0.7 (4)	Avoidant	0.5 (3)
Bipolar I disorder	0.5 (3)	Dependent	0.2 (1)
Depressive disorder NOS	0.3 (2)	Antisocial	0.2 (1)
Anxiety disorders	9.0 (52)	Personality traits	27.1 (156)
Obsessive compulsive disorder	2.8 (16)	Obsessive-compulsive	23.8 (137)
Posttraumatic stress-disorder	1.7 (10)	Avoidant	1.4 (8)
Social phobia	1.2 (7)	Borderline	1.2 (7)
Generalized anxiety disorder	1.0 (6)	Narcissistic	0.2 (1)
Specific phobia	1.0 (6)	Antisocial	0.2 (1)
Panic disorder with agoraphobia	0.9 (5)	Schizoid	0.2 (1)
Separation anxiety disorder	0.2 (1)	Schizotypal	0.2 (1)
Anxiety disorder NOS	0.2 (1)	Mixed personality traits	2.6 (15)
Autism spectrum conditions	2.4 (14)	Obsessive-compulsive and avoidant	1.4 (8)
Autistic disorder	1.2 (7)	Obsessive-compulsive and borderline	0.3 (2)
Pervasive developmental disorder NOS	1.2 (7)	Avoidant and dependent	0.3 (2)
Somatoform disorders	1.4 (8)	Obsessive-compulsive and schizotypal	0.2 (1)
Hypochondriasis/BDD	0.9 (5)	Avoidant and narcissistic	0.2 (1)
Undifferentiated somatoform disorder	0.5 (3)	Avoidant and schizoid	0.2 (1)
Substance related disorders	1.6 (9)	Diagnosis deferred on Axis II	6.6 (38)
Alcohol dependence	0.7 (4)	Total	100 (575)
Cannabis or dependence on sedatives	0.5 (3)		
Abuse of alcohol	0.3 (2)		
Impulse control disorders	2.1 (12)		
Trichotillomania or Excoriation disorder	1.9 (11)		
Intermittent explosive disorder	0.2 (1)		
Tic disorders	1.6 (9)		
Tic disorder NOS	0.5 (3)		
Chronic motor or vocal tic disorder	0.5 (3)		
Gilles de la Tourette	0.3 (2)		
Tic disorder	0.2 (1)		
Attention Deficit (Hyperactivity) Disorders	5.4 (31)		
Attention Deficit Disorder	3.3 (19)		
Attention Deficit Hyperactivity Disorder	1.7 (10)		
Attention Deficit Hyperactivity Disorder combined type	0.3 (2)		
Other disorders	1.4 (8)		
Eating disorder NOS	0.7 (4)		
Neurocognitive disorder	0.3 (2)		
Schizophrenia	0.2 (1)		
Stuttering	0.2 (1)		
Total	106.7 (614)		

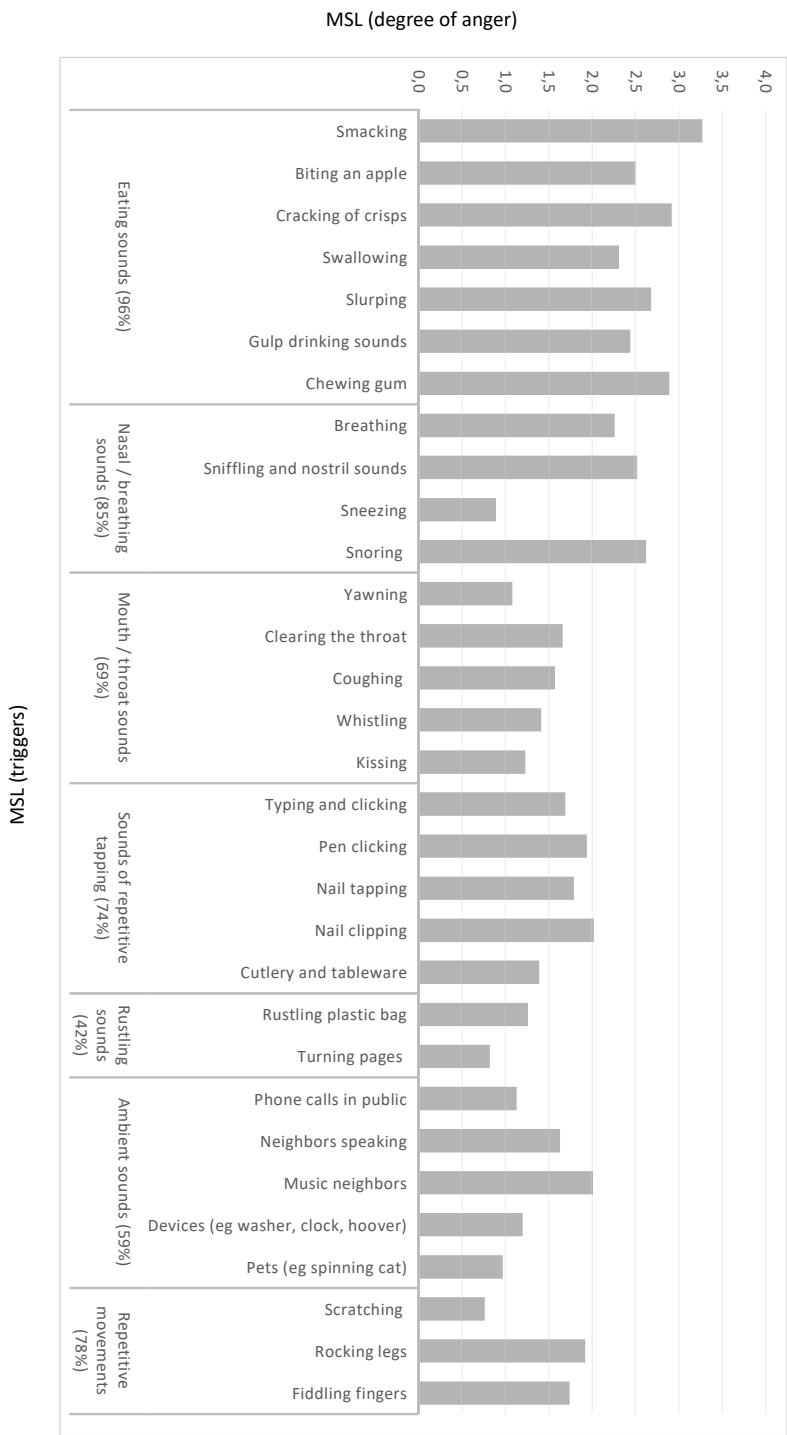


Figure 2.1. Triggers and provoked anger for misophonia subjects.

2.3.4 Nature of the response

Subjects reported extreme irritation, anger, and disgust as primary emotional responses (see Table 2.3). Aggressive outbursts were seldom reported at psychiatric interviews; verbal aggression was common, but physical aggression was rare. Frequency was not assessed with a questionnaire.

Table 2.3. Emotional response and hyper focus to sounds in misophonia subjects

Emotional response to sounds	N = 257 (%)
Irritation	241 (93.8)
Severe to extreme irritation	248 (93.3)
Anger	230 (89.5)
Severe to extreme aggressive feeling	195 (73.8)
Urge to hurt the person	208 (79.1)
Disgust	165 (64.0)
Severe to extreme disgust	167 (63.3)
Other emotional response	37 (13.6)
Synonym Anger	14 (5.1)
Synonym Disgust	2 (0.7)
Sadness	16 (5.9)
Physical reaction	7 (2.6)
Anxiety	5 (1.8)
Loss of control	4 (1.5)
Despair	3 (1.1)
Boredom	1(0.4)
Alienation	1 (0.4)
Perceived loss of control	208 (79.1)
Severe to extreme powerlessness	234 (88.9)
Hyper focus on sounds	N = 263 (%)
Hyper focus	259 (98.1)
Severe to extreme hyper focus	241 (91.3)
Seldom to never able to deviate attention	226 (85.6)

None of the subjects reported anxiety as a primary response, neither at psychiatric examination nor with questionnaires. Only five subjects (1%) reported secondary anxiety, following anger or disgust. The majority of the sample reported anticipatory anxiety, which was mild and related to thinking of future misophonic situations. In clinical interviews, all subjects reported confrontations with triggers as stressful events. Subjects worried about misophonic triggers and their capacity to cope. A perceived loss of control was seen in 81% of the subjects and 90% reported severe to extreme powerlessness. In clinical interviews,

most subjects expressed shame or guilt. Anticipatory anxiety and preoccupation with misophonic triggers appeared simultaneously. Two different scales showed 86 to 91% experienced serious preoccupation.

Most used coping was turning on music (99%) and walking away (99%). Making noise or making noise in the same rhythm, e.g., chewing or typing, was also used frequently, 86% and 77%, respectively. Finally, 86% described using earplugs; the majority of these subjects used them in the last week (73%).

In general, subjects reported to spend a lot of time actively avoiding triggers: 24% 0 to 1 hour each day, 24% 1 to 3 hours, 32% 3 to 8 hours, and 9% avoided over 8 hours each day.

2.3.5 General somatic

76% of the sample reported no diagnosis on Axis III, 20% reported one diagnosis, and 4% had multiple diagnoses. Most common diagnoses were: migraine, irritable bowel syndrome, asthma, and back pain. During physical examination, a primary neurological disorder was never determined, but a mild somatic comorbid disorder was regularly found (e.g., hypertension). Approximately 1% of blood tests results were abnormal (e.g., decreased Hb levels, thyroid abnormalities or increased liver functions).

2.3.6 Audiology

Of the total sample, four subjects (0.7%) were previously diagnosed with hyperacusis only, ten subjects (1.7%) with tinnitus only, and one patient with both. Twenty subjects reported hearing loss or other hearing problems.

The subgroup performing an audiogram consisted of 109 subjects (69% female) with a mean age of 36.70 years (SD = 12.08). 106 subjects had bilateral normal hearing (PTA \leq 25 dB HL). The remaining three subjects had a unilateral hearing loss: one slight conductive hearing loss (25–40 dB HL), one moderate conductive hearing loss (40–60 dB HL), and one profound sensorineural hearing loss (80+ dB HL). This implies all participants had at least one ear with normal hearing.

2.3.7 Severity

Subjects had moderate to moderate-severe symptoms according to the A-MISO-S and AMISOS-R. No significant sex differences were found (respectively $p = .44$ and $p = .29$).

Subjects had mild symptoms on the HAS and HDRS and a high score on the SCL-90-R. Quality of life varied from a low satisfaction on the MANSA, to some impairment in day-to-day life on the SDS, particularly with family relations (Olfson et al., 1996), to a slightly lower perceived quality of life on the WHOQoL-BREF (Masthoff, Trompenaars, van Heck, Hodiamont, & de Vries, 2006). Subjects all described to have made adjustments to their day-to-day life, such as avoiding public transport. Many subjects lost work or relationships because of misophonia. Rarely, subjects were desperate for help or expressed suicidal ideations in the clinical interviews.

2.3.8 Personality profile

Subjects scored average on the AQ and ISS. Subjects scored low on the DS-R and on the DPSS-R (Olatunji, Cisler, Deacon, Connolly, & Lohr, 2007). There was a significant positive correlation between the DPSS-R and DS-R ($r = .545$, $n = 442$, $p < .000$). Further, subjects scored high on the CPQ (healthy controls in an unpublished AMC study have $M = 23.82$). A total of 97% had a score over 25, indicating clinical perfectionism. Subjects scored slightly higher on the FMPS (healthy controls in an unpublished AMC study have $M = 92.70$). A total of 66% had a score over 22 on the scale 'Concern over mistakes', indicating clinical perfectionism (cut off suggested by Egan & Hine, 2008). There was no significant correlation between the CPQ and FMPS ($r = .036$, $p = .571$).

The NEO-PI-R sub-sample showed no sex differences and subjects scored above average (stanine 7) only on Neuroticism, with the facet Angry hostility (stanine 7). All characteristics are shown in Table 2.4.

Using a standard multiple regression, perfectionism (CPQ: $p = .487$; FMPS: $p = .651$), autism traits (AQ: $p = .270$), and disgust sensitivity (DS-R: $p = .628$; DPSS-R: $p = .961$) showed no significant relation to the severity of the misophonia symptoms, measured by the AMISOS-R.

Finally, non-parametric correlation (Spearman's rho) was used to determine whether misophonia symptoms (A-MISO-S) correlated with a decreased quality of life (MANSA). The more severe the misophonia symptoms, the lower the satisfaction with quality of life, $r_s(184) = -.34$ $p < .001$.

Table 2.4. Characteristics of misophonia subjects

Misophonia questionnaires	N	Mean (SD)
AMISOS-R	258	29.78 (6.46)
Female	183	30.00 (6.79)
Male	75	29.04 (5.76)
A-MISO-S	253	14.02 (3.43)
Female	175	14.00 (3.43)
Male	78	14.05 (3.43)
General psychopathology	N	Mean (SD)
SCL-90-R	454	163.35 (53.17)
HAS	495	14.51 (9.54)
HDRS	436	10.97 (6.58)
GAF	516	68.05 (10.04)
Quality of life	N	Mean (SD)
MANSA	220	3.58 (0.73)
SDS total	98	17.79 (5.42)
Work		5.33 (2.54)
Social		5.63 (2.22)
Family		6.79 (2.19)
WHOQoL-BREF	102	
Physical health		14.94 (2.42)
Psychological health		13.20 (2.12)
Social relationships		14.38 (2.47)
Environment		16.28 (1.84)
General (1&2)		7.55 (1.44)
Personality profile	N	Mean (SD)
AQ	109	19.25 (7.62)
IIS	221	76.90 (24.58)
CPQ	268	31.48 (8.99)
FMPS	261	94.67 (20.81)
DS-R	478	39.77 (13.38)
DPSS-R	464	23.35 (10.37)
NEO-PI-R	49	
Neuroticism		152.7 (23.1)
Extraversion		148.3 (18.9)
Openness		156.7 (17.1)
Agreeableness		166.0 (17.4)
Consciousness		164.4 (19.2)

2.4 Discussion

This is the largest qualitative and quantitative description of a sample of misophonia subjects so far ($N = 575$). Our study demonstrates that clinical examination from a medical-psychiatric perspective is invaluable for diagnosing misophonia, as one out of four referred subjects does not suffer from misophonia. Risk of misdiagnosis is high, because misophonia-like symptoms could be explained by comorbid conditions such as OCPD traits, mood disorders, AD(H)D, and ASC. From a somatic perspective, our misophonia subjects do not have specific somatic comorbid disorders. Furthermore, they have normal hearing, which is in contrast to hearing in tinnitus (Jastreboff, 1990). Prevalence of hearing loss found in our population is even less than expected based on the prevalence of disabling hearing loss in normal population for the Netherlands ($PTA > 40$ dB HL in better ear around 5% for adult population, World Health Organisation, 2019). From a psychological perspective, misophonia can be seen as an independent construct. No association was found between misophonia symptoms and ASC, disgust sensitivity, or clinical perfectionism. Clinical perfectionism, however, was seen in 66 to 97% of the subjects. Severity of misophonia symptoms is negatively correlated with quality of life. Family relations especially suffer, but the influence on working life remains limited with only 5% on sick leave.

Overall prevalence rate of comorbid DSM-IV Axis I disorders is similar to general population in the Netherlands, except for mood disorders (twice as prevalent; de Graaf, ten Have, van Gool, & van Dorsselaer, 2012), AD(H)D (two-and-a-half times more prevalent; de Graaf, ten Have, van Gool, & van Dorsselaer, 2012) and the ASC (threefold the prevalence; Roelfsema et al., 2012). Some studies (Rouw & Erfanian, 2017; Kumar et al., 2017) suggest an association with affective disorders, particularly post-traumatic stress disorder. The preliminary results of a new sample study using psychiatric evaluation (Erfanian et al., 2019) even showed a prevalence of 15%. However, prevalence of PTSD in our sample is not higher. The prevalence rate of comorbid DSM-IV Axis II disorders is mildly higher and corresponds with findings of Rouw & Erfanian (2017). We found OCPD traits in one out of four subjects. Regardless, the exact prevalence of personality traits in community samples is unknown, we consider a 26% prevalence of OCPD traits high. 52% of the 2013 AMC sample (Schröder et al., 2013) had a comorbid OCPD. This difference can be explained by a smaller sample size and selection bias in this previous sample.

Development and severity of misophonia symptoms in this large sample are consistent with findings in the 2013 AMC sample (Schröder et al., 2013). In our sample, however, a larger percentage is female. Specifically, age of onset, course, severity of symptoms, and a positive

family history (Edelstein, Brang, Rouw, & Ramachandran, 2013; Rouw & Erfanian, 2017; Sanchez & Silva, 2018) supports misophonia as a distinct disorder (American Psychiatric Association, 2013). Findings from psychiatric, medical, and psychological assessments substantiate this conclusion. Our findings result in a revision of the 2013 criteria, which are illustrated in the next paragraph and marked in Table 2.5. We emphasize that to be diagnosed with misophonia, all criteria should be met. As in all psychiatric disorders a subclinical group probably exists, in most cases lacking criterion E-R.

Table 2.5. Amsterdam UMC 2020 revised diagnostic criteria for misophonia

Amsterdam UMC 2020 revised criteria for misophonia
A-R. Preoccupation ^a with a specific auditory, visual or sensory cue ^c , which is predominantly induced by another person ^d . It is required that oral or nasal sounds are a trigger. ^b
B-R. Cues evoke intense feelings of irritation, anger and/or disgust of which the individual recognizes it is excessive, unreasonable or out of proportion to the circumstances.
C-R. Since emotions trigger an impulsive aversive physical reaction, the individual experiences a profound sense of loss of self-control with rare but potentially aggressive outbursts.
D-R. The individual actively avoids situations in which triggers occur or endures triggers with intense discomfort, irritation, anger or disgust.
E-R. The irritation, anger, disgust or avoidance causes significant distress and/or significant interference in the individual's day-to-day life. For example, it is impossible to eat together, work in an open office space or live together. ^e
F-R. The irritation, anger, disgust and avoidance are not better explained by another disorder, such as an Autism Spectrum Condition (e.g. a general hypersensitivity or hyper arousal to all sensory stimuli) ^f or Attention Deficit Hyperactivity Disorder (e.g. attention problems with high distractibility in general) ^f .

a-f refers to specific paragraphs in section 2.4.1.

2.4.1 Misophonia triggers

Our detailed investigation of triggers leads to new conclusions. Approximately all subjects in our sample report eating sounds as a trigger (96%) and the majority reports nasal or breathing sounds as a trigger (85%). Combined, all subjects report either oral or nasal sounds as a trigger. Therefore, we propose other triggers can be a part of the condition, but an emotional reaction to oral or nasal sounds is required^b. Visual triggers, like scratching, and non-human triggers, like animal sounds or air-conditioning sounds, were occasionally described (Dozier, 2015; Ferreira, Harrison, & Fontenelle, 2013). We indeed found evidence for non-auditory triggers in 78% of our sample, but auditory triggers are primary triggers^c. If combined, these triggers cause a more intense emotional reaction. In a mass experiment which was performed among the general population, adding a corresponding image to a disgusting sound had no effect (Cox, 2008). This interaction effect is probably typical for misophonia subjects.

Ambient sounds are most often reported amongst other misophonia triggers^d (see Supplementary Table S2.2). If subjects are bothered only by ambient sounds (e.g., sounds of neighbors), misophonia should not be diagnosed, even though subjects describe a similar response. Over 8% of the Dutch population reported serious nuisance by sounds of neighbors in the last year and 29% reported mild or moderate nuisance. A much higher percentage is bothered by various traffic sounds (van Poll, Breugelmans, Houthuijs, & van Kamp, 2018). In these cases, symptoms can be seen as a more general disturbance of sounds, such as noise sensitivity or sensory over-responsivity, which also occurs in a normal population (Robertson & Simmons, 2013). We used typical examples of avoidance from our psychiatric assessments^e.

2.4.2 Nature of the response

As in other samples and case studies, we show misophonia is associated with considerable non-expressed aggression, but physical aggressive outbursts are rare (Taylor, 2017). Subjects with a comorbid affective instability, due to for instance comorbid BPD, sometimes reported aggressive outbursts in our clinical interviews. These outbursts were mild in comparison to the internal aggressive thoughts all misophonia subjects described. Anxiety is also frequently described as a response to misophonia triggers (Bruxner, 2016; Dozier & Morrison, 2017; Wu et al., 2014; Zhou et al., 2017). In our sample, subjects do not report anxiety as a prompt reaction to a trigger, but experience anticipatory anxiety and physical stress. Possibly this anticipatory anxiety is elsewhere mistaken for anxiety as a primary response. This emphasizes the value of a thorough psychiatric evaluation once more. We found all subjects consider their reaction to be out of proportion. Interestingly, only one case study describes a patient who perceived her reaction to sounds as inappropriate (Bernstein, Angell, & Dehle, 2013). Subjects with a primary OCPD or ASC often do not consider their reaction to be out of proportion, and OCPD or ASC are possible differential diagnoses^f.

Subjects often stated the emotional response to be far more intense towards loved ones inducing misophonia triggers. Context also influenced the emotional response; when misophonia trigger sounds were made by toddlers, mentally disabled adults, or elderly with dementia, an emotional response seldom occurred.

We consider preoccupation an additional core symptom of misophonia, since approximately all subjects in our sample report hyper focus^a. Hyper focus was also reported in 82% of the sample of Edelstein et al (2013) and an intervention targeting hyper focus has a clear effect on misophonia symptoms (Schröder, Vulink, van Loon, & Denys, 2017).

2.4.3 Limitations

This is the first large sample study of misophonia subjects in which we not only explored the dynamics of misophonia symptoms, but also examined the impact of symptoms on quality of life. However, this research also has its limitations. First, the Amsterdam UMC is the only center in the Netherlands with a specific treatment for misophonia, which could lead to a selection bias. Furthermore, since no other criteria were available, AMC 2013 diagnostic criteria were used for selection of subjects, possibly leading to confirmation bias. However, we believe we limited confirmation bias, because we examined all patients who were referred with misophonia-like symptoms; using questionnaires with a broad scope, and we investigated alternative symptoms, e.g., anxiety, in our psychiatric evaluations. Finally, types or versions of questionnaires administered changed over time in this sample. Some of the questionnaires administered are not yet validated in Dutch translation or lack a norm group, but were the best available. Also, the A-MISO-S is not psychometrically validated and the AMISOS-R is in the process of validation.

2.4.4 Conclusions

In conclusion, this analysis of a large sample confirms that misophonia is a distinct psychiatric disorder characterized by an intense emotional reaction of irritation, anger, and often disgust elicited by specific auditory, visual or sensory triggers predominantly induced by another person, resulting in preoccupation and avoidance. We suggest future studies to use the revised Amsterdam UMC proposed criteria and to conduct international multi-center studies. A multi-disciplinary approach, especially including psychiatry, audiology, and psychology, would be preferable. International confirmation of the Amsterdam UMC revised criteria is needed before next steps in research can be taken. Future research should also include more treatment studies (e.g., a RCT of CBT or a new intervention) and validation of misophonia questionnaires.

Acknowledgments

We thank Arjan Schröder and Arnoud van Loon for their contribution to misophonia research in general at Amsterdam UMC and Arjan for the development of misophonia questionnaires, in particular. We also thank UnYoung Chavez Baldini for textual comments on the manuscript. We thank Martijn Figee for data collection and Isidoor Bergfeld for his advice on the statistics. Finally, we thank all misophonia patients for their contribution.

Conflicts of interests

The authors declare that there are no conflict of interests.

Author contributions

I. Jager: conceptualization, data curation, formal analysis, investigation, methodology, and writing—original draft. P. de Koning: conceptualization and investigating. T. Bost: data curation, formal analysis, writing—original draft. D. Denys: conceptualization, methodology, supervision, and writing—review and editing. N. Vulink: conceptualization, methodology, investigating, supervision, writing—review and editing.

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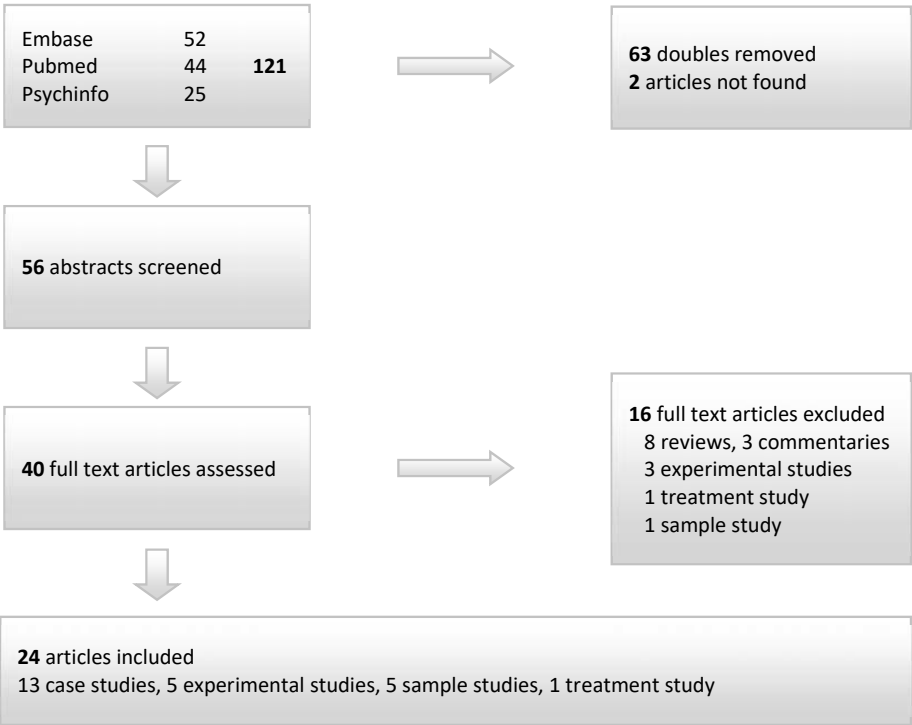
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2.6 Supporting information



Supplementary Figure S2.1. Flowchart search May, 2018.

Supplementary Table S2.1. Results search May, 2018

	Study authors	Study type	Study population	Diagnosis based on
1	Bernstein et al., 2013	Case study	1 misophonia pt	Clinician
2	Bruxner, 2016	Review and case vignette	1 misophonia pt	Clinician
3	Dozier, 2015	Case study	1 misophonia pt	Clinician, questionnaires (MAQ, MCR, MTS)
4	Edelstein et al., 2013	Experimental study	11 misophonia pts, 5 controls	Self-diagnosed
5	Eijsker et al., 2017	Experimental study	21 misophonia pts, 23 controls	Clinician, questionnaire (A-MISO-S)
6	Ferreira et al., 2013	Case study	3 misophonia pts	Clinician
7	Johnson et al., 2013	Case study	4 misophonia pts	Clinician
8	Kamody et al., 2017	Case study	1 misophonia pt	Clinician, questionnaires (A-MISO-S, MAQ)
9	Kluckow et al., 2014	Case study	3 misophonia pts	Clinician, questionnaires (A-MISO-S, MAS-1)
10	Kumar et al., 2017	Experimental study	20 misophonia pts, 22 controls	Questionnaire (unclear: Kumar 2014)
11	McGuire et al., 2015	Case study	2 misophonia pts	Questionnaires (MQ and MSS)
12	McKay et al., 2015	Sample study	121 misophonia pts, 507 controls	Questionnaires (MQ)
13	Neal et al., 2013	Case study	1 misophonia pt	Clinician
14	Reid et al., 2016	Case study	1 misophonia pt	Clinician, Questionnaire (A-MISO-S)
15	Rouw et al., 2017	Sample study	301 misophonia pts	Self-diagnosed Questionnaires (MAS, MPRS, A-MISO-S)
16	Sanchez et al., 2017	Sample study	12 misophonia pts	Self-diagnosed
17	Schröder et al., 2013	Sample study	42 misophonia pts	Clinician, Questionnaire (A-MISO-S)
18	Schröder et al., 2014	Experimental study	20 misophonia pts, 14 controls	Clinician, Questionnaire (A-MISO-S)
19	Schröder et al., 2015	Experimental study	10 misophonia pts, 7 controls	Clinician, Questionnaire (A-MISO-S)
20	Schröder et al., 2017	Treatment study	90 misophonia pts	Clinician, Questionnaire (A-MISO-S)
21	Veale, 2006	Case study	1 possible misophonia pt	Clinician
22	Webber et al., 2014	Case study	1 misophonia pt	Clinician
23	Wu et al., 2014	Sample study	483 students of which 20%: 96 misophonia pts	Questionnaire (MQ)
24	Zhou et al., 2017	Sample study	415 students of which 6%: 25 misophonia pts	Questionnaires (MQ, SDS-M)

Supplementary Table S2.2. Overview questionnaires

Questionnaire	Interpretation	N total	N completed (%)
Misophonia screening list (see Appendix 2.1)	Range 0–56, higher scores (>20) indicating misophonia	275	264 (96)
A-MISO-S* (Schröder et al., 2013)	Range from 0–24, higher scores indicating more severe misophonia. 0–4 subclinical misophonia symptoms, 5–9 mild, 10–14 moderate, 15–19 severe, 20–24 extreme	275	253 (92)
AMISOS-R* (see Appendix 2.3)	Range 0–40, higher scores indicating more severe misophonia. 0–10 subclinical misophonia symptoms, 11–20 mild, 21–30 moderate severe, 31–40 severe to extreme	300	259 (86)
MSL (see Appendix 2.2)	Range 0–4, higher scores indicating more provoked anger	275	135 (49)
HDRS* (De Jonge, 1994; Hamilton, 1960)	Range 0–54, higher scores indicating more symptoms of depression	575	436 (76)
HAS* (Maier et al., 1988; Hamilton, 1959)	Range 0–56, higher scores indicating more anxiety	575	495 (86)
SCL-90-R* (Arrindell & Ettema, 1986; Derogatis et al., 1973)	Range 90–450, higher scores indicating more general psychopathology	575	454 (71)
MANSA (Nieuwenhuizen et al., 2017; Priebe et al., 1999)	Range 0–7, higher scores indicating greater life satisfaction	275	220 (80)
SDS (Sheehan, 1983)	Range 0–10, higher scores indicating more impairment	115	98 (85)
WHOQoL-BREF (Trompenaars et al., 20015; WHOQoL Group, 1998)	Range per domain 4–20, range general health 1–10, higher scores indicating a higher perceived quality of life	115	102 (89)
NEO-PI-R ^o (Miller et al., 2008; Costa et al., 1992)	With scores on five subscales neuroticism, extraversion, openness, agreeableness and consciousness	56	49 (88)
AQ (Hoekstra et al., 2008; Baron-Cohen et al., 2001)	Range from 0–50, higher scores indicating more evidence for Autism Spectrum Conditions	115	109 (95)
ISS (Van Dam et al., 2000)	Range 35–175, higher scores indicating more social anxiety	275	212 (77)
CPQ (CPQ; Shafraan et al., 2002)	Range 12–48, with higher scores indicating more perfectionism	300	268 (89)
FMPS (Frost et al., 1990)	Range 35–175, higher scores indicating more perfectionism	300	261 (87)
DPSS-R* (Van Overveld et al., 2006; Cavanagh et al., 2000)	Range 0–64, higher scores indicating more propensity and sensitivity to disgust	575	464 (81)
DS-R* (Van Overveld et al., 2011; Haidt et al., 1994)	Range 0–100, higher scores indicating more disgust sensitivity	575	478 (83)

* seven questionnaires were presented to all subjects; ^o questionnaire presented to a random sample.

Supplementary Table S2.3. Triggers for misophonia subjects

Reported triggers	Total N	Mean (SD)
Eating sounds	424	
Smacking		3.27 (0.8)
Biting an apple		2.50 (1.4)
Cracking of crisps		2.92 (1.2)
Swallowing		2.31 (1.3)
Slurping		2.68 (1.1)
Gulp drinking sounds		2.44 (1.3)
Chewing gum		2.89 (1.1)
Nasal and breathing sounds	425	
Breathing		2.26 (1.3)
Sniffing and nostril sounds		2.52 (1.3)
Sneezing		0.89 (1.2)
Snoring		2.62 (1.2)
Mouth and throat sounds	418	
Yawning		1.08 (1.3)
Clearing the throat		1.66 (1.3)
Coughing		1.57 (1.3)
Whistling		1.41 (1.4)
Kissing		1.23 (1.3)
Certain vocal sounds	257	
Sounds of repetitive tapping	420	
Typing and clicking		1.69 (1.5)
Pen clicking		1.94 (1.5)
Nail tapping		1.79 (1.4)
Nail clipping		2.02 (1.4)
Cutlery and tableware		1.39 (1.3)
Rustling sounds	420	
Rustling plastic bag		1.26 (1.3)
Turning pages		0.82 (1.1)
Ambient sounds	420	
Phone calls in public		1.13 (1.2)
Neighbors speaking		1.63 (1.4)
Music neighbors		2.01 (1.5)
Devices (e.g., washer, clock, Hoover)		1.20 (1.3)
Pets (eg spinning cat)		0.97 (1.3)
Repetitive movements	166	
Scratching		0.76 (1.1)
Rocking legs		1.92 (1.4)
Fiddling fingers		1.74 (1.5)

Appendix 2.1 Misophonia screening list

Misophonia Screening List

Name: _____
Date of birth: ____-____-____
Date of session: ____-____-____

Choose the answer that is most applicable for you.

1. I am focused on sounds people make	Very much disagree 0	1	2	3	Very much agree 4
2. If people make sounds, I instantly walk away	Very much disagree 0	1	2	3	Very much agree 4
3. I made arrangements to my life to minimize hearing sounds	Very much disagree 0	1	2	3	Very much agree 4
4. I want to hurt the person making sounds	Very much disagree 0	1	2	3	Very much agree 4
5. If I enter a room in which my loved ones are eating, I feel aggression	Very much disagree 0	1	2	3	Very much agree 4
6. If I enter a room in which my loved ones are eating, I feel disgust	Very much disagree 0	1	2	3	Very much agree 4

7. I feel annoyed by sounds all day	Very much disagree 0	1	2	3	Very much agree 4
8. My quality of life is greatly decreased due to sounds of others	Very much disagree 0	1	2	3	Very much agree 4
9. I would be able to relax more if I did not hear any sounds	Very much disagree 0	1	2	3	Very much agree 4
10. I suffer from sounds other people produce	Very much disagree 0	1	2	3	Very much agree 4
11. My relationships are limited by sounds others make	Very much disagree 0	1	2	3	Very much agree 4
12. I feel interference in my day-to-day life by the sounds of others	Very much disagree 0	1	2	3	Very much agree 4
13. After hearing a sound, I experience a sense of loss of self-control	Very much disagree 0	1	2	3	Very much agree 4
14. I feel misunderstood when I suffer from sounds	Very much disagree 0	1	2	3	Very much agree 4
Total score:					

Appendix 2.2 Misophonia Sound List (MSL)

Misophonia Sound List

Name:	_____
Date of birth:	____-____-____
Date of session:	____-____-____

Category A

never	past	last week	Sounds	Degree of irritation/disgust/anger 0 = no 1 = a little (e.g., irritation) 2 = quite 3 = a lot (e.g., anger) 4 = extreme (e.g., rage)
			Smacking	0 – 1 – 2 – 3 – 4
			Biting an apple	0 – 1 – 2 – 3 – 4
			Crunching of crisps	0 – 1 – 2 – 3 – 4
			Swallowing	0 – 1 – 2 – 3 – 4
			Slurping	0 – 1 – 2 – 3 – 4
			Gulping	0 – 1 – 2 – 3 – 4
			Breathing	0 – 1 – 2 – 3 – 4
			Sniffing and nostril sounds	0 – 1 – 2 – 3 – 4
			Yawning	0 – 1 – 2 – 3 – 4
			Clearing the throat	0 – 1 – 2 – 3 – 4
			Footsteps or high heels on the floor	0 – 1 – 2 – 3 – 4
			Chewing gum	0 – 1 – 2 – 3 – 4
			Coughing	0 – 1 – 2 – 3 – 4
			Sneezing	0 – 1 – 2 – 3 – 4
			Whistling	0 – 1 – 2 – 3 – 4
			Typing and clicking	0 – 1 – 2 – 3 – 4

			Pen clicking	0 – 1 – 2 – 3 – 4
			Nail tapping	0 – 1 – 2 – 3 – 4
			Nail clipping	0 – 1 – 2 – 3 – 4
			Cutlery and tableware	0 – 1 – 2 – 3 – 4
			Turning pages	0 – 1 – 2 – 3 – 4
			Scratching the head	0 – 1 – 2 – 3 – 4
			Rustling plastic bag	0 – 1 – 2 – 3 – 4
Total score A:				

Category B

never	past	last week	Other sounds	Degree of irritation/disgust/anger 0 = no 1 = a little (e.g., irritation) 2 = quite 3 = a lot (e.g., anger) 4 = extreme (e.g., rage)
			Snoring	0 – 1 – 2 – 3 – 4
			Phone calls in public	0 – 1 – 2 – 3 – 4
			Kissing	0 – 1 – 2 – 3 – 4
			Neighbors speaking	0 – 1 – 2 – 3 – 4
			Music from neighbors	0 – 1 – 2 – 3 – 4
Total score B:				

Category C

never	past	last week	Non-human sounds	Degree of irritation/disgust/anger 0 = no 1 = a little (e.g., irritation) 2 = quite 3 = a lot (e.g., anger) 4 = extreme (e.g., rage)
			Devices (e.g., washer, clock, Hoover)	0 – 1 – 2 – 3 – 4

			Pets (e.g., dog licking, cat purring, rooster crowing)	0 – 1 – 2 – 3 – 4
Total score C:				

Category D

never	past	last week	Visual triggers	Degree of irritation/disgust/anger 0 = no 1 = a little (e.g., irritation) 2 = quite 3 = a lot (e.g., anger) 4 = extreme (e.g., rage)
			Twitching legs	0 – 1 – 2 – 3 – 4
			Fiddling fingers	0 – 1 – 2 – 3 – 4
Total score D:				

Category E

never	past	last week	Avoidance	Degree of avoidance 0 = no 1 = a little 2 = quite 3 = a lot 4 = extreme
			Putting on music (speakers or headphone)	0 – 1 – 2 – 3 – 4
			Making noise	0 – 1 – 2 – 3 – 4
			Making noise in the same rhythm (e.g., 'chewing along')	0 – 1 – 2 – 3 – 4
			Wearing earplugs	0 – 1 – 2 – 3 – 4
			Walking away	0 – 1 – 2 – 3 – 4
Total score E:				

Appendix 2.3 Revised Amsterdam Misophonia Scale (AMISOS-R)

Amsterdam Misophonia Scale - Revised (AMISOS-R)

2

Name:	_____
Date of birth:	____-____-____
Date of session:	____-____-____

In comparison to others I am sensitive to:

(multiple answers possible)

- ☐ Eating sounds (e.g. chewing, smacking, slurping, swallowing)
- ☐ Nasal sounds (e.g. sniffing, breathing in, breathing out)
- ☐ Throat sounds (e.g. harrumphing, coughing)
- ☐ Specific sounds (e.g. 'k' sound)
- ☐ Repeating clicking sounds (e.g. nails on a blackboard, pen clicking)
- ☐ Crinkling sounds (e.g. paper, plastic)
- ☐ Ambient noises (e.g. clock ticking noise or similar devices)

Which emotions are evoked by listening to those sounds?

(multiple answers possible)

- ☐ Irritation
- ☐ Anger
- ☐ Disgust
- ☐ Other:

Review your experience from hearing your misophonia sounds *in the last 3 days*.
Read instead of “sounds” your most disturbing misophonia sounds and instead of
“emotion” your typical emotion. Choose the answer that is most applicable for you.

1. How many time do you spend a day (thinking about) these sounds?	0 hour 0	< 1 hour 1	1-3 hour 2	3-8 hour 3	>8 hour 4
2. To what extent do you focus on these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
3. To what extent do you experience impairment due to these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
4. How intense is your feeling of irritability/anger when you hear these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
5. To what extent do you feel helpless against these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
6. To what extent are you suffering from these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
7. To what extent are you suffering from the avoidance of these sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
8. To what extent are the sounds limiting your life (work, household etc.)?	not 0	mild 1	moderate 2	severe 3	extreme 4
9. To what extent are you avoiding specific places or situations because of the sounds?	not 0	mild 1	moderate 2	severe 3	extreme 4
10. To what extent can you shift your attention when you are hearing these sounds?	always 0	usually (75%) 1	sometimes (50%) 2	seldom (25%) 3	never 4
Total score:					

PART II

**New insights in
psychotherapy
for misophonia**



3

Cognitive behavioral therapy for misophonia: A randomized clinical trial

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Depression and Anxiety, 38(7), 708–718.

Background: Patients with misophonia suffer from anger or disgust confronted with specific sounds such as smacking or breathing. Avoidance of cue-related situations results in social isolation and significant functional impairment. This is the first randomized, controlled cognitive behavioral therapy (CBT) trial for misophonia, evaluating the short- and long-term efficacy.

Methods: The evaluator-blinded, randomized clinical trial was conducted from May 2017 until December 2018 at an academic outpatient clinic. Misophonia patients were randomly assigned to 3 months of weekly group-CBT or a waiting list and tested at baseline, 3 months (following CBT or waiting list), 6 months (after cross-over), and 15/18 months (1-year follow-up). CBT consisted of task concentration and arousal reduction, positive affect labeling, and stimulus manipulation. Co-primary outcomes were symptom severity assessed by the Amsterdam Misophonia Scale-Revised (AMISOS-R) and improvement on the Clinical Global Impression-Improvement (CGI-I). Secondary outcomes were self-assessed ratings of general psychopathology (Symptom Checklist-90-Revised [SCL-90-R]) and quality of life (five-dimensional EuroQoL [EQ5-D], Sheehan Disability Scale [SDS], WHO Quality of Life-BREF [WHOQoL-BREF]).

Results: In all, 54 out of 71 patients were included (mean age, 33.06 [SD, 14.13] years; 38 women [70.4%]) and 46 (85%) completed the study. In the randomized phase, CBT resulted in statistically significant less misophonia symptoms in the short-term (-9.7 AMISOS-R; 95% CI, -12.0 to -7.4; $p < .001$, $d = 1.97$). The CBT group had an observed clinical improvement (CGI-I < 3) in 37% compared to 0% in the waiting list group ($p < .001$). The effect of CBT was maintained at 1-year follow-up on primary and secondary outcomes.

Conclusions: This first randomized control trial shows both short-term and long-term efficacy of CBT for misophonia.

3.1 Introduction

Patients with misophonia suffer from irritation, anger, or disgust confronted with specific sounds, such as eating sounds or breathing. Avoidance of cue-related situations and preoccupation with possible triggers result in social isolation and significant functional impairment. Misophonia patients are often not able to eat, sleep, or work in company, and most social and family relations are negatively affected. Especially when avoidance (e.g., walking away or wearing earplugs) is not possible, patients suffer. For example, detecting an apple at the desk during a meeting can already cause an extreme emotional response.

A growing scientific interest in misophonia has emerged within the last two decades (Brout et al., 2018). Research has mainly focused on clinical features, leading to the proposal of diagnostic criteria (Dozier et al., 2017; Jager et al., 2020; Schröder et al., 2013). There is no consensus about the nature of the disorder, other research groups emphasize its audiological or neurological nature. Incidence and prevalence are unknown, though a Chinese student sample indicates an incidence of 6% (Zhou et al., 2017). Misophonia is often found among family members, suggesting a hereditary component (Jager et al., 2020; Sanchez & Silva, 2018). The exact etiology of misophonia still remains unclear, but misophonia is possibly associated with neurodevelopmental conditions. Jager et al. (2020) found comorbid DSM-IV Axis I diagnoses in 28%, most commonly, mood disorders (10%) and anxiety disorders (9%). Autism spectrum disorders and attention-deficit/(hyperactivity) disorder (AD(H)D) were both common comorbid disorders, and important differential diagnoses for misophonia. Specific sample studies for misophonia prevalence among these neurodevelopmental conditions are yet to come. Though the nosography is not yet established, misophonia is widely recognized as an impairing condition (Taylor, 2017).

There are little well-established, empirically supported treatments for misophonia. A few case studies were published in which misophonia patients were treated with cognitive behavioral therapy (CBT) using various techniques (Bernstein et al., 2013; Dozier, 2015; McGuire et al., 2015) and with dialectical behavior therapy (Kamody & Del, 2017). Our research group conducted an open-label trial involving 90 patients with misophonia (Schröder et al., 2017), which showed promising results for CBT. In this trial, 48% of patients improved after eight sessions of CBT on the Clinical Global Impression-Improvement (CGI-I), and misophonia symptoms improved by 4.5 points on the Amsterdam Misophonia Scale; range from 0 to 24. Besides this trial, three case reports (total $n = 4$) showed anecdotal evidence for CBT. Bernstein et al. (2013) showed six sessions of CBT improved social and occupational functioning. Dozier (2015) showed after 14 sessions of counterconditioning

misophonia symptoms were decreased. McGuire et al. (2015) showed 10–18 sessions of CBT (exposure) reduced misophonia symptoms in two youths and improved school and family functioning. No randomized clinical trials for any treatment have been published yet.

The current study is the first randomized controlled trial of CBT for misophonia and examines the efficacy of CBT compared to a waiting list control group. CBT is mainly concentrated on the preoccupation and associated arousal with misophonia triggers, since hyperfocus is considered a core symptom. Interventions also target the associated negative response by overwriting this and examining underlying assumptions. The study has two goals: first, to examine the short-term efficacy and second, to examine the effect of CBT at follow-up. We hypothesized a reduction in symptoms and improvement in quality of life (QoL) in the CBT group compared to the waiting list control group and the effects to persist at 1-year follow-up.

3.2 Materials and methods

The study site was the outpatient clinic of the department of psychiatry of the Amsterdam University Medical Center (Amsterdam UMC, location AMC). The study was registered in the Netherlands Trial Register (www.trialregister.nl) under number NL6304. The authors assert that all procedures contributing to this study comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving patients were approved by AMC Medical Ethics Committee. Written informed consent was obtained from all patients.

3.2.1 Participant selection, recruitment, and enrollment

A total of 71 patients were recruited from the outpatient clinic at the Amsterdam UMC. All patients were referred by their General Practitioners for treatment of impairing misophonia symptoms. All had received a psychiatric assessment and were on the waiting list for treatment. A research assistant approached all patients on the waiting list by telephone to inform them about the study, screened them, and sent written information by email or post.

Inclusion criteria were the presence of misophonia (as proposed by Schröder et al., 2013) diagnosed by a psychiatrist during a structured diagnostic interview at the intake of our psychiatric center and aged between 18 and 70 years. Exclusion criteria were the presence of major depression or anxiety disorder as primary diagnosis, bipolar disorder, autism spectrum disorders, schizophrenia, or any other psychotic disorder, substance-related

disorder during the past 6 months, any structural central nervous system disorder or stroke within the last year, currently taking benzodiazepines or stimulants, patients at risk for suicide, and patients with language barriers or illiteracy.

3.2.2 Randomization

Patients were randomized to treatment condition groups using a computerized randomization procedure (www.randomizer.org) with a 1:1 allocation ratio. Patients learned their treatment assignment directly after randomization. The independent researcher (IJ) was naive to randomization status. We assessed the fidelity of masking, which was found to be poor (78% of the assessments of treatment allocation were correctly guessed at the second clinical interview).

3.2.3 Treatment condition

The intervention was a manualized group treatment fairly similar to CBT used in our previous open-label study (Schröder et al., 2017). The treatment manual was refined for this study with the elaborate input of the participating therapists. The manual (Van Loon et al., 2019) had specific instructions for each session (e.g., with a set time for each intervention, fully written exercises, and instruction videos for the therapists) to optimize equivalence among the different treatment groups. All interventions were checked after applying.

CBT was given in combined psychotherapy and Psychomotor Therapy (PMT) and consisted of four components: task concentration exercises, positive affect labeling, stimulus manipulation, and arousal reduction. Two elements were added: re-evaluating (eating) norms and stress reduction. Family and friends were seen in groups in one separate session for psychoeducation and sharing experiences, and one family session for practicing the learned techniques together (see Table S3.1 and Appendix S3.1).

Group therapy was conducted in a closed group of nine patients with seven weekly meetings of 1.5 h of psychotherapy and 1.5 h of PMT, and one follow-up meeting of 1.5 h after 3 weeks.

3.2.4 Waiting list condition

Patients in the waiting list condition received no treatment in the first 3 months. After 3 months, they received the same treatment as patients in the treatment condition, as described above.

3.2.5 Therapist training and quality assurance

Therapists for group CBT were licensed clinical psychologists with extensive training and experience in CBT for obsessive–compulsive and related disorders and misophonia in particular. Co-therapists were licensed clinical psychologists, registered psychiatric nurses, and psychomotor therapists with CBT training. The department has so far diagnosed 1800 misophonia patients and treated over 1100 in this team. Therapists were provided with ongoing peer supervision throughout the randomized control trial (RCT) every 2 weeks. A research assistant attended the team-meetings of each therapy group before and after sessions 1, 4, 7, and 8 to evaluate treatment adherence with detailed feedback, to maintain treatment fidelity and to ensure all measures were taken.

All raters (therapists and the independent investigator) were trained in April 2017 in scoring the clinical interview measuring misophonia severity and improvement. This interview was co-rated until they demonstrated at least a 0.80 inter-rater reliability.

3.2.6 Assessments

Patients were assessed at baseline (T1), 3 months (T2, post-CBT or waiting list), 6 months (T3, 3 months after cross-over), and 15/18 months (T4, 1-year follow-up). At T1, T2, and T3 the blinded investigator assessed all patients in a clinical interview by phone. In addition to the study assessments, two symptom-questionnaires were administered after CBT sessions 4 and 7.

3.2.7 Primary outcomes

Misophonia symptoms were measured using the Amsterdam Misophonia Scale-Revised (AMISOS-R; see the Supplementary Appendix; Jager et al., 2020). This improved version of the A-MISO-S (Schröder et al., 2013) is in the process of validation; it consists of 10 items with scores ranging from 0 to 40. Higher scores indicate more severe misophonia; 0–10: normal to subclinical misophonia; 11–20: mild misophonia; 21–30: moderate–severe misophonia; 31–40: severe to extreme misophonia. Preliminary results of the validation show reliability of the scale was good ($\alpha = .84$), as well as its validity ($r = .87, p < .01$). The co-primary outcome was the CGI-I (Guy, 1976) as blinded observer ratings. The CGI-I is a clinical interview to answer the question: “Compared to the patient’s condition at admission to the project this patient’s condition is 1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change from baseline (the initiation of treatment); 5 = minimally worse; 6 = much worse; 7 = very much worse since the initiation of treatment.”

3.2.8 Secondary outcomes

Secondary outcomes included the CGI Severity scale (CGI-S), which was scored by a blinded rater and independently by group therapists who were not blind to treatment allocation. The CGI-S score ranges from 1 to 7 with higher scores indicating more severe illness. General mental and physical dysfunction was assessed with the Symptom Checklist-90-Revised (SCL-90-R; Arrindell & Ettema, 1986; Derogatis et al., 1973). The total score is 90–450, with higher scores indicating more general psychopathology. QoL and impairment was assessed with three questionnaires: the five-dimensional EuroQoL (EQ5-D; Lamers et al., 2006), Sheehan Disability Scale (SDS; Sheehan, 1983), and WHO Quality of Life-BREF (WHOQoL-BREF; Trompenaars et al., 2005; WHOQoL Group, 1998). The EQ5-D score represents a health state between 0 (worst imaginable condition) and 1 (perfect health). The SDS has three domains; Work, Social, and Family and the range per domain is 0–10. The total score is 0–30, with higher scores indicating more impairment. The WHOQoL-BREF has four domain scores: physical health, psychological health, social relationships, and environment, each with scores ranging from 4 to 20, and a score for general health, ranging from 1 to 10, with higher scores indicating a higher perceived QoL. At last, post-treatment, all diagnostic criteria of misophonia were examined systematically by the blinded investigator.

3.2.9 Statistical analysis

Treatment groups were compared on baseline characteristics using χ^2 tests for binary and categorical variables and two-tailed *t* tests for continuous variables.

We tested symptom severity in the randomized phase with a linear mixed model, which is suitable for longitudinal data and can handle missing values appropriately (Molenberghs et al., 2004). The dependent variable was AMISOS-R total score; independent fixed factors were assessments (T1, T2), condition (CBT, waiting list), and their interaction, with a random intercept with subject as grouping variable. Clinical improvement (CGI-I scores < 3) were tested with a χ^2 test, with condition as the independent variable.

Continuous secondary outcomes in the randomized phase were analyzed with linear mixed models similar to the one used for AMISOS-R, except for the dependent variable (SCL-90 [after log transformation to ensure normality of residuals], SDS, EQ5-D, and WHOQoL scales). The CGI-S was analyzed with a Mann–Whitney U test with condition as independent variable.

To test long-term efficacy, we used linear mixed models with AMISOS-R, log-transformed SCL-90, EQ5-D, SDS, or the WHOQOL domains as dependent variables. Independent fixed

factors were Assessment (baseline [T1], post-CBT [i.e., T2 in the CBT group and T3 in the waiting list group] and 1-year follow-up [T4]), Condition (CBT or waiting list), and their interaction, and a random intercept with subject as grouping factor was included. CGI-S was analyzed with a Mann–Whitney U test with time as the independent variable.

The sample size was set to be able to detect 4 points' mean difference in the AMISOS score, with an assumed SD of 3.5 points (based on previous research) and a power of 90%. After accounting for expected dropout rates, we aimed to recruit 45 patients in total. To account for possible small differences of the revised version (the AMISOS-R), we planned to enroll 27 patients in each group before the start of the study. Power calculations and all analyses were all based on two-tailed t tests. For co-primary outcomes $p < .025$ was considered to be statistically significant, because of multiple testing (conform Bonferroni). For secondary outcomes we considered $p < .05$ to be statistically significant. Data were analyzed using IBM SPSS Statistics version 25 and R Version 3.5.

3.3 Results

3.3.1 Participant flow and characteristics

A total of 54 patients (38 [70.4%] female; mean [SD] age, 33.06 [14.13] years) were included (Table 3.1). No significant differences were found between the two groups at baseline on main characteristics. Comorbid medical disorders were comparable amongst the two groups, including irritable bowel syndrome ($n = 3$), migraine ($n = 2$), and hypothyroidism ($n = 2$). Three patients reported tinnitus, previously confirmed by an otorhinolaryngologist. Hyperacusis, hearing loss, or other hearing problems were not reported. In each group one patient used medication (venlafaxine 225 mg daily and risperidone 0.5 mg daily) for comorbid obsessive–compulsive disorder and depressive disorder. Doses of medication were stable for at least 3 months at time of inclusion and were not changed during treatment.

Twenty-seven patients (50.9%) were randomized to the treatment group (CBT) and 26 patients (49.1%) randomized to the waiting list control group (WL). All of them completed 1 or more post-baseline assessment (Figure 3.1). All completers attended at least six CBT sessions. There was no difference in treatment participation between the two groups.

During treatment/waiting period (T1–T3) eight patients dropped out ($n = 3$ in the CBT, $n = 5$ in WL, $\chi^2(1) = 0.6$, $p = .70$). Reasons for dropout were comorbid psychiatric disorders, for example, relapse depression (3), stressors, for example, deceased family member (2),

comorbid somatic disorders (1), and planning problems (1). At last follow-up (T4) nine patients had dropped out in each condition (18 in total). Partly due to dropout some scores are missing, see Tables 3.2 and 3.3 for the actual number of observations. No difference in number of missing values was found between conditions (see Table 3.2, biggest difference: 8 vs. 5 missings: $\chi^2(1) = 0.9$, $p = .53$).

Table 3.1. Demographic and clinical baseline characteristics of the ITT group by condition

Variable	CBT group (n = 27)	WL group (n = 27)	Total (N = 54)
Gender (Female)	21 (77.8)	17 (63)	38 (70.4)
Age, mean (SD), y	31.30 (12.80)	34.81 (15.38)	33.06 (14.13)
Marital status (in a relationship)	15 (55.6)	17 (63)	32 (59.3)
Level of education			
Low (primary or secondary)	10 (37)	14 (51.9)	24 (44.4)
High (college or university)	17 (63)	13 (58.1)	30 (55.6)
Employment			
Employed or studying	24 (88.9)	25 (92.6)	49 (90.7)
Unemployed	3 (11.1)	2 (7.4)	5 (9.3)
Axis I disorder			
Mood	3 (11.1)	1 (3.7)	4 (7.4)
Anxiety	1 (3.7)	1 (3.7)	2 (3.7)
Axis II disorder			
OCPD	1 (3.7)	0 (0)	1 (1.9)
Obsessive-compulsive traits	8 (29.6)	7 (25.9)	15 (27.8)
Other traits	1 (3.7)	2 (7.4)	3 (5.6)
Axis III disorder			
Tinnitus	1 (3.7)	2 (7.4)	3 (5.6)
Other	7 (25.9)	7 (25.9)	14 (25.9)
Age of onset misophonia	10.7 (4.00)	11.89 (5.40)	11.3 (4.74)
Primary outcomes			
CGI-S score, mean (SD)	5.56 (0.75)	5.00 (0.83)	5.28 (0.83)
AMISOS-R score, median (95% CI)	30.00 (20–36)	27.50 (19–38)	29.00 (19–38)

Abbreviations: AMISOS-R, Amsterdam Misophonia Scale-Revised; CBT, cognitive behavioral therapy; CGI-S, CGI Severity scale; ITT, intention-to-treat; OCPD, obsessive-compulsive personality disorder; WL, waiting list.

3.3.2 Short-term efficacy; primary outcomes

Compared with baseline (T1), the mean scores decreased after 3 months (T2) by 9.7 (95% CI, -12.0 to -7.4) in the CBT group and by 0.8 (95% CI, -2.1 to 0.4) in the waiting list control group (Table 3.2). The standardized effect-size was very large ($d = 1.97$).

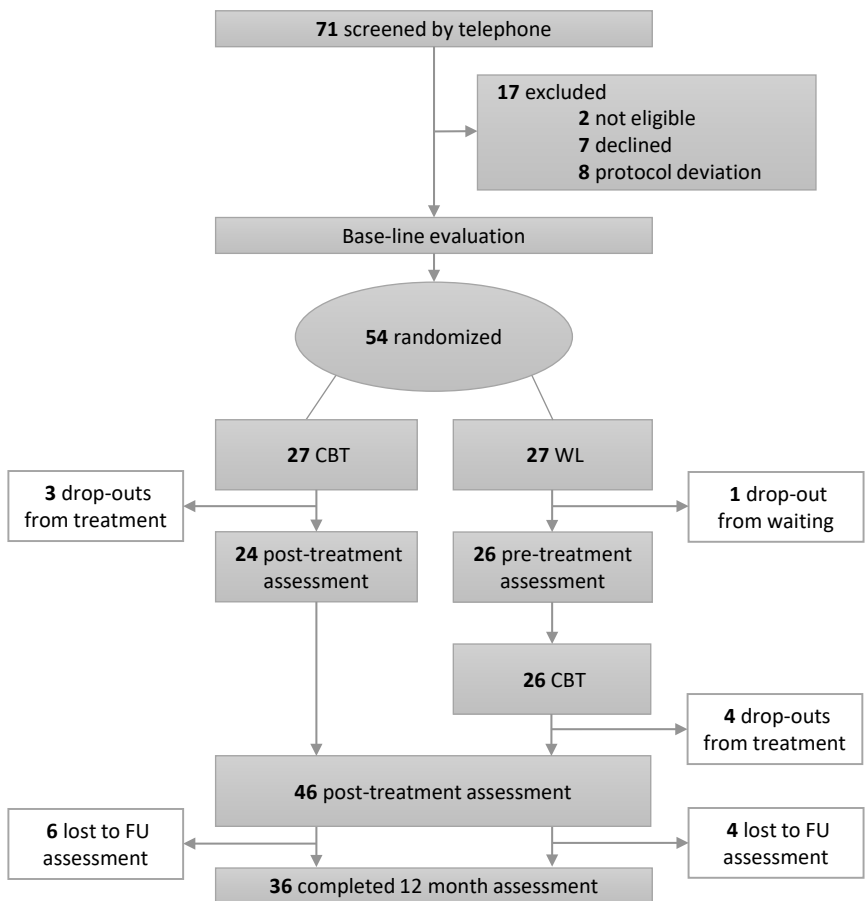


Figure 3.1. CONSORT diagram of participants in a study of CBT for misophonia.

The CGI-I showed a significant difference between the two groups: 37% of the CBT group and 0% of the WL group was much or very much improved (CGI-I < 3) in the intention-to-treat group ($\chi^2(4) = 19.37, p < .001$).

Compared to the waiting list condition, patients in the CBT condition showed a significantly larger decrease of AMISOS-R scores ($F(1, 48.6) = 49.8, p < .001$).

3.3.3 Secondary outcomes

A Mann–Whitney U test showed that the CGI-S (scored blinded) was significantly reduced by CBT, $U = 507.00, p = .000$. In addition, CBT significantly reduced the SCL-90-R score with -30.9 (-46.6 to -15.1) points mean difference (95% CI) versus a decrease of -1.2 (-13.6 to

11.2) in the waiting list condition ($F(1, 44.8) = 14.3, p < .001$). Results for the blinded CGI-S showed an effect of $d = 1.39$, and results for the SCL-90 showed an effect size of $d = 0.86$.

Table 3.2. Outcome measures of ITT by condition T2–T1

			WL group (n = 27)	CBT group (n = 27)	d
Co-primary variables					
AMISOS-R (MD; 95% CI)			-0.8 (-2.1 to 0.4)	-9.7 (-12.0 to -7.4)***	1.97
	n missing	0		1	
CGI-I (n)					
Very much improved			0	1***	
Much improved			0	9***	
Minimally improved			4	8	
No change			14	8	
Minimally worse			9	1	
Much worse			0	0	
Very much worse			0	0	
	n missing	0		0	Na
Secondary variables					
CGI-S (MD; 95% CI)			0.0 (-0.1 to 0.2)	-1.0 (-1.4 to -0.6)***	1.39
	n missing	1		3	
SCL-90-R (MD; 95% CI)			-1.2 (-13.6 to 11.2)	-30.9 (-46.6 to -15.1)***	0.86
	n missing	4		4	
EQ5-D (MD; 95% CI)			0.0 (-0.1 to 0.1)	0.0 (0.0 to 0.1)	-0.13
	n missing	7		5	
SDS Total (MD; 95% CI)			0.2 (-2.1 to 2.6)	-6.0 (-7.9 to -4.2)***	1.33
Work			-0.3 (-1.5 to 0.8)	-1.8 (-2.7 to -0.8)	0.60
Social			0.9 (-0.2 to 2.0)	-2.0 (-2.7 to -1.3)***	1.42
Family			-0.3 (-1.3 to 0.6)	-2.3 (-2.9 to -1.7)***	1.12
	n missing	8		5	
WHOQoL (MD; 95% CI)					
Social relationships			0.8 (0.2 to 1.3)	1.0 (0.0 to 1.9)	-0.11
Environment			0.3 (-0.4 to 1.0)	1.0 (0.0 to 1.9)	-0.33
Physical health			0.1 (-0.9 to 1.0)	1.3 (0.5 to 2.1)	-0.60
Psychological health			0.1 (-0.7 to 1.0)	1.1 (0.5 to 1.6)	-0.59
General health			0.2 (-0.3 to 0.7)	0.0 (-0.7 to 0.7)	0.14
	n missing	7		5	

Abbreviations: AMISOS-R, Amsterdam Misophonia Scale-Revised; CBT, cognitive behavioral therapy; CGI-I, Clinical Global Impression-Improvement; CGI-S, CGI Severity scale; EQ5-D, five-dimensional EuroQoL; FU, follow-up; NaN, Not a Number; QoL, quality of life; SCL-90, Symptom Checklist-90; SDS, Sheehan Disability Scale; WL, waiting list; WHOQoL-BREF, WHO Quality of Life-BREF.

*** $p < .001$.

Table 3.3. Treatment efficacy at post-treatment and 12-month follow-up

Outcome and time	N	Mean (SD) [95% CI] ^a		Time effect F (df)	Within-group p-value		
		WL	CBT		Pre to Post	Pre to FU	Post to FU
Primary outcome							
AMISOS-R							
Pre	54	27.5 (4.8) [25.6–29.3]	30.4 (4.2) [28.8–32.0]	48.76 (2,86.6)***	***	***	.383
Post	48	19.7 (6.8) [16.8–22.6]	21.9 (7.0) [19.2–24.6]				
Follow-up	37	22.3 (8.3) [18.4–26.1]	22.2 (8.4) [18.4–26.0]				
Secondary outcomes							
CGI-S							
Pre	54	5.0 (0.8) [4.7–5.3]	5.6 (0.8) [5.3–5.8]	NaN			
Post	49	3.5 (1.4) [2.9–4.0]	4.7 (1.0) [4.3–5.0]				
Follow-up	‡	‡	‡				
CGI-S therapist							
Pre	53	5.7 (0.7) [5.4–5.9]	5.7 (0.6) [5.5–5.9]	NaN			
Post	48	2.8 (1.0) [2.3–3.2]	3.5 (1.4) [2.9–4.0]				
Follow-up	‡	‡	‡				
SCL-90							
Pre	54	147.0 (42.5) [130.8–163.1]	182.8 (62.7) [159.0–206.5]	31.00 (2,81.9)***	***	***	.107
Post	47	116.5 (22.8) [106.7–126.3]	156.5 (75.0) [127.6–185.5]				
Follow-up	37	133.6 (55.1) [108.0–159.1]	142.2 (54.9) [117.4–167.0]				
EQ5-D							
Pre	53	0.8 (0.2) [0.8–0.9]	0.8 (0.1) [0.7–0.8]	1.57 (2,84.9)	.431	.229	.659
Post	44	0.8 (0.2) [0.7–0.9]	0.8 (0.2) [0.7–0.9]				
Follow-up	37	0.9 (0.1) [0.8–0.9]	0.8 (0.2) [0.7–0.9]				

Outcome and time	N	Mean (SD) [95% CI] ^a		Time effect F (df)	Within-group p-value		
		WL	CBT		Pre to Post	Pre to FU	Post to FU
SDS Work							
Pre	54	4.0 (3.0) [2.8–5.1]	6.0 (2.3) [5.1–6.9]	10.76 (2,82.6)***	***	***	.914
Post	46	2.6 (2.3) [1.6–3.6]	4.2 (2.7) [3.1–5.3]				
Follow-up	37	2.3 (2.4) [1.2–3.4]	4.3 (2.7) [3.1–5.5]				
SDS Social							
Pre	54	6.0 (2.0) [5.2–6.7]	6.9 (1.7) [6.2–7.5]	27.60 (2,80.6)***	***	***	.841
Post	46	3.4 (2.1) [2.5–4.3]	5.0 (2.7) [4.0–6.1]				
Follow-up	37	4.6 (3.0) [3.2–5.9]	4.6 (3.1) [3.2–6.0]				
SDS Family							
Pre	54	6.4 (2.8) [5.4–7.5]	8.0 (1.4) [7.5–8.6]	29.20 (2,82.7)***	***	***	*
Post	46	4.0 (2.9) [2.8–5.3]	6.1 (1.9) [5.4–6.9]				
Follow-up	37	4.4 (3.3) [2.9–6.0]	4.6 (2.8) [3.4–5.9]				
SDS Total							
Pre	54	16.4 (5.8) [14.2–18.6]	20.9 (3.9) [19.4–22.3]	37.00 (2,80.3)***	***	***	.310
Post	46	10.1 (5.9) [7.6–12.6]	15.4 (6.1) [13.0–17.8]				
Follow-up	36	10.9 (7.0) [7.6–14.3]	13.5 (8.0) [9.9–17.2]				
WHOQoL Social relationships							
Pre	53	14.3 (2.8) [13.2–15.3]	12.9 (2.5) [12.0–13.9]	4.44 (2,79.1)*	*	.074	.767
Post	43	15.3 (2.2) [14.4–16.2]	14.1 (3.0) [12.8–15.3]				
Follow-up	37	13.9 (2.9) [12.6–15.3]	14.0 (2.8) [12.8–15.3]				
WHOQoL Environment							
Pre	53	16.7 (1.9) [16.0–17.5]	14.9 (2.1) [14.1–15.7]	4.11 (2,80.3)*	*	***	.140
Post	43	16.8 (1.9) [16.0–17.6]	15.8 (2.6) [14.7–16.8]				
Follow-up	37	16.8 (1.9) [15.9–17.7]	16.4 (2.3) [15.4–17.5]				

Table 3.3 continues on next page.

Table 3.3. Continued

Outcome and time	N	Mean (SD) [95% CI] ^a		Time effect F (df)	Within-group p-value		
		WL	CBT		Pre to Post	Pre to FU	Post to FU
WHOQoL Physical health							
Pre	53	14.9 (2.5) [13.9–15.9]	13.1 (2.5) [12.1–14.0]	13.07 (2,79.1)***	**	***	.216
Post	44	16.3 (1.6) [15.6–17.0]	14.1 (2.7) [13.0–15.3]				
Follow-up	37	16.3 (2.4) [15.3–17.4]	14.9 (3.3) [13.5–16.4]				
WHOQoL Psychological health							
Pre	53	13.6 (2.0) [12.8–14.4]	12.1 (2.3) [11.3–13.0]	12.74 (2,79.4)***	**	***	.225
Post	44	14.7 (1.2) [14.2–15.3]	13.1 (2.6) [12.0–14.1]				
Follow-up	37	14.0 (2.6) [12.7–15.2]	13.6 (2.5) [12.5–14.8]				
WHOQoL General health							
Pre	53	7.5 (1.4) [7.0–8.0]	7.1 (1.5) [6.6–7.7]	1.99 (2,78.9)	.968	.420	.453
Post	44	8.2 (1.1) [7.7–8.7]	7.1 (1.9) [6.4–7.9]				
Follow-up	36	8.2 (1.3) [7.6–8.8]	7.5 (1.9) [6.6–8.3]				
CGI-I				NaN			
Pre	NaN	NaN	NaN				
Post	49 ^b	2.3 (0.8) [2.0–2.6]	3.0 (1.0) [2.6–3.3]				
Follow-up	^b	^b	^b				
CGI-I therapist				NaN			
Pre	NaN	NaN	NaN				
Post	48 ^b	2.0 (0.8) [1.7–2.4]	2.3 (0.9) [1.9–2.7]				
Follow-up	^b	^b	^b				

Abbreviations: AMISOS-R, Amsterdam Misophonia Scale-Revised; CBT, cognitive behavioral therapy; CGI-I, Clinical Global Impression-Improvement; CGI-S, CGI Severity scale; EQ5-D, five-dimensional EuroQoL; FU, follow-up; NaN, Not a Number; QoL, quality of life; SCL-90, Symptom Checklist-90; SDS, Sheehan Disability Scale; WL, waiting list; WHOQoL-BREF, WHO Quality of Life-BREF.

^a For the waiting list condition in “Pre” data of T2 was used.

^b There was no CGI assessment at FU.

* $p < .05$. ** $p < .01$. *** $p < .001$.

CBT significantly increased SDS total score compared to WL, especially in two subscales (Social: $F(1, 45.3) = 21.8, p < .001$ and Family life: $F(1, 39.1) = 13.02, p < .001$). No significant differences were found between CBT and WL on other quality of life scales (EQ5-D and WHOQoL-BREF).

The course of decrease in misophonia symptoms during treatment was similar for both groups and is shown in Figure S3.1. The SCL-90-R showed a comparable pattern of decrease during treatment.

A structured diagnostic interview showed 37% of the completers did not meet diagnostic criteria for misophonia any more post-treatment. Most patients (70.6%) failed to meet more than one criterion. Improvement was found particularly in experiencing more self-control (38.9% no longer meeting criterion B) and less problems in day-to-day life (25% no longer meeting criterion E).

3.3.4 1-year follow-up

The analysis of all data (CBT and delayed CBT combined) for three time points: baseline (T1), after CBT (T2/T3), and 1-year follow-up (T4), showed a main effect of time, but no condition or interaction effects were found for the AMISOS-R scores (Time: $F(2, 86.6) = 48.76, p < .0001$). Improvement on the primary outcome was sustained, since no significant changes were found at follow-up compared to post-treatment (see Table 3.3 and Figure 3.2).

A Mann–Whitney U test revealed significant differences in CGI-S scores pre- (MD = 5, $n = 54$) and posttreatment (MD = 4, $n = 49$), $U = 631.50, p = .000$.

For the other secondary outcomes group-by-time interaction effect was not statistically significant, except for the SCL-90 ($p = .028$) and WHOQoL-BREF Environment ($p = .032$). There were significant between-group differences on the SCL-90 ($p = .042$), SDS Work ($p = .004$), SDS Total ($p = .003$), and WHOQoL-BREF Physical and Psychological health scores ($p = .014$ and $p = .042$).

Main effect of time was significant for all variables, except for EQ5-D and WHOQoL-BREF General health. The pattern of scores was similar to the primary outcomes; differences between pre- and post-intervention were significant, except for the WHOQoL-BREF Environment. Improvement on all secondary outcomes was sustained at follow-up, with no significant differences between post-treatment and follow-up, except for SDS subscale Family. At follow-up the SDS subscale Family was further improved.

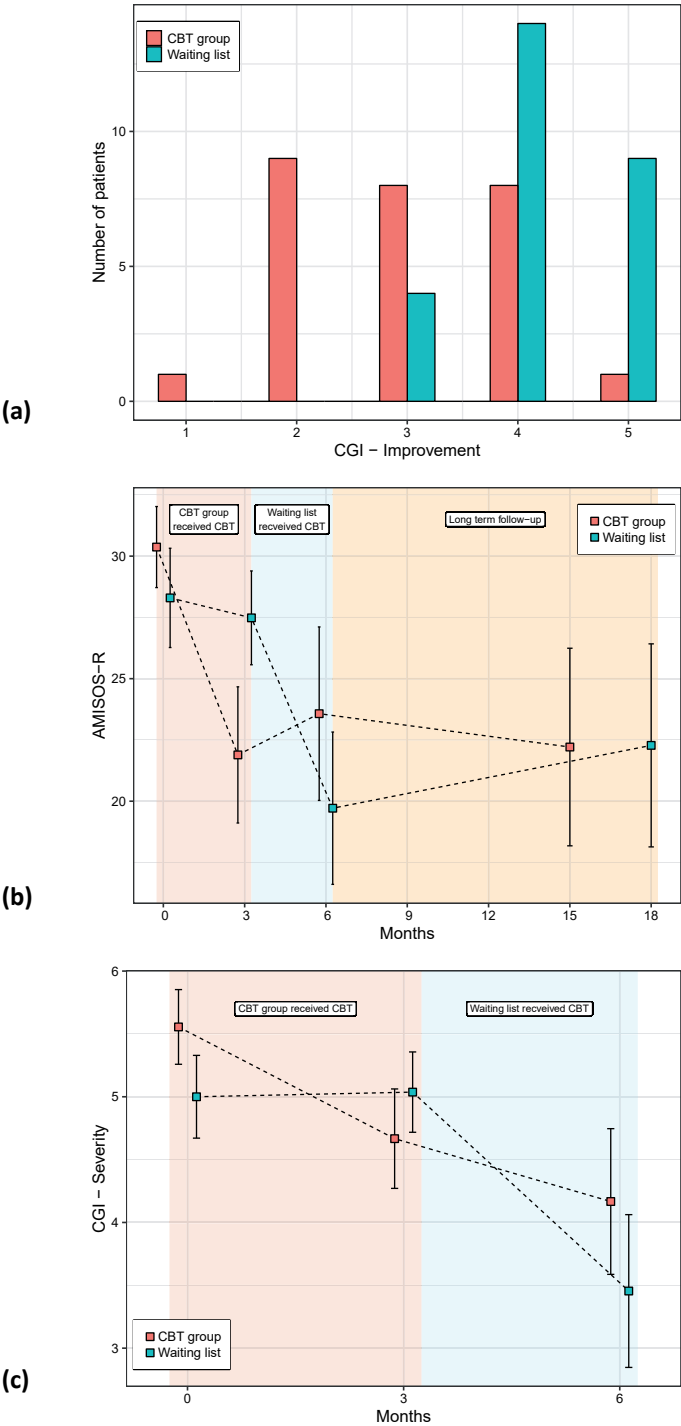


Figure 3.2. Results for co-primary outcomes at all assessments (PP).

3.3.5 Adverse events and treatment acceptability

Five patients expressed their concern to adopt trigger-sounds from fellow group members at the start of CBT. At the end of treatment none of the patients reported to have obtained new trigger-sounds. During treatment/waiting period (T1–T3) eight patients dropped out. One reported an adverse event as a cause of dropout. This subject had increased misophonia symptoms and anxiety and explained this by an inability to open up in a group. No serious adverse events were reported.

Treatment acceptability ($n = 43$) was measured by satisfaction and a report mark for the therapy. Post-treatment, 65.1% were (very) satisfied, 25.6% were neutral, 7% were not satisfied, and 2.3% were very dissatisfied ($n = 1$). Treatment was rated by patients with a mean (SD) of 6.72 (1.59).

3.4 Discussion

This first randomized trial with CBT for misophonia showed both short- and long-term efficacy. Three months of CBT reduced misophonia symptoms compared to a waiting list. Clinical improvement was found in 56% of all completers (37% intention-to-treat) compared to 0% in the waiting list. General mental and physical dysfunction decreased and patients reported less disabilities in family and social functioning after CBT than after waiting list as well. Importantly, 12 months after the end of treatment, the considerable improvement in misophonia symptoms was sustained. On top of these measurements, group therapists rated 74% of all completers clinically improved ($\text{CGI} < 3$).

These results confirm the positive effect of CBT previously found in case reports and a previous open-label trial in our center (Bernstein et al., 2013; Dozier, 2015; McGuire et al., 2015; Schröder et al., 2017) and extends its findings. This RCT provides evidence for the efficacy of CBT for misophonia and can serve as a stepping stone to implement CBT in clinical practice. We have published our protocol, so more misophonia patients can benefit from this treatment.

In clinical practice and future trials, these results could be improved. Patients gradually improved in time. Since there was no plateau effect (see Figure S3.1), there is room for further improvement. By adding more sessions, we could possibly even reach a better outcome. This notion is supported by detailed feedback of patients, who endorsed a prolonged treatment. Future studies should investigate whether additional sessions lead to additional improvement.

As opposed to the strong symptom improvement after CBT, we did not find a meaningful effect on QoL in the primary analysis. There are several reasons; first of all, a ceiling effect is probable, given the high pretreatment score on both questionnaires. We doubt misophonia has no effect on QoL, so these two questionnaires are probably not suitable for this population. Possibly, a different questionnaire, the Manchester Short Assessment of Quality of Life (MANSA; Priebe et al., 1999), would have been more sensitive, since patients with misophonia score low on the MANSA (Jager et al., 2020). Misophonia has a clear impact on social and family functioning. The MANSA has more focus on the social domain (e.g., with several items concerning the quality of relationships with friends, family, and colleagues) than the EQ5-D or WHOQoL-BREF.

In this first RCT for misophonia, the highly controlled intervention (Van Loon et al., 2019) is a major strength. The interventions were highly comparable in all treatment groups, because the study was situated in one center. Furthermore, only a few experienced therapists were involved and monitored by regular intervention. Another strength are the assessments. Assessments were thorough with the use of blinded observer ratings, clinical interviews by both therapists and observer, diverse self-reports, multiple measures during treatment, and a measure at 1-year follow-up.

3.4.1 Limitations

However, this study has several limitations. A first potential study limitation is the lack of a fully validated misophonia questionnaire. Although the AMISOS-R is a good scale and is almost fully validated (publication in preparation), we used the CGI-I as a co-primary outcome to aid interpretation of the clinical results. Second, there were missing data, especially at 1-year follow-up (33%), even though we went to great lengths to complete the data. This is common in treatment studies and percentages of dropout in other CBT studies with 1-year follow-up were comparable to our dropout rates. For instance, Segal et al. (2020) had a dropout of 23%–33% at 1 year follow-up ($n = 460$), and Wiltink et al. (2017) dropout rates at 1 year follow-up were 25%–36% ($n = 109$). Third, our study missed a condition controlling for nonspecific effects of treatment. Future research should compare the current CBT to an active control group, for example, a support group. Because of this comparison with a waiting list, the fidelity of masking was poor. The assessor guessed the majority correctly based on the reported improvement, despite the fact that patients managed to keep their allocation secret during the blinded assessment (merely two patients used terms obviously learned in therapy). This could have led to a bias.

3.4.2 Conclusions

This RCT evaluating the immediate and long-term effects of manualized CBT compared with a waiting list control group demonstrated CBT is effective for reducing misophonia symptoms in adults and for improving social and family functioning. Future work should include an active control group.

Acknowledgements

We are very grateful to our colleagues from the AMC misophonia treatment team. We thank Michel H.P. Hof of the AMC Dept. Clinical Epidemiology, Biostatistics, and Bioinformatics for his advice at the beginning of this study. Finally, we thank all misophonia patients for their contribution.

Conflict of interests

The authors declare that there are no conflict of interests.

Author contributions

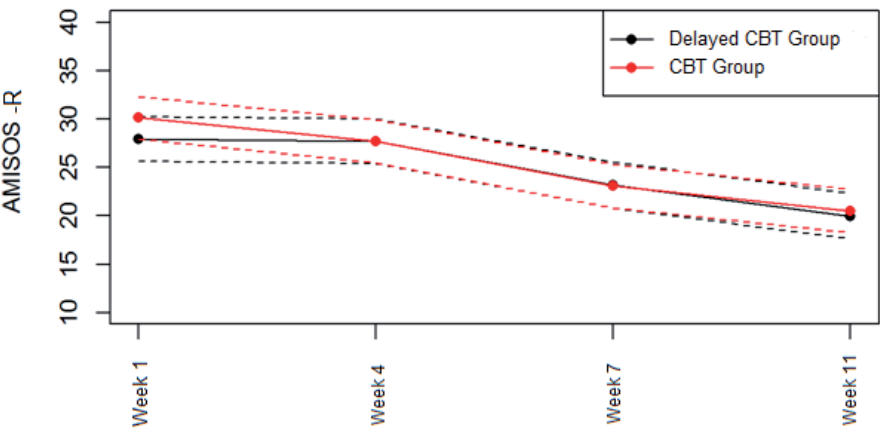
I. Jager: conceptualization, data curation, formal analysis, investigation, methodology, and writing—original draft. N. Vulink: conceptualization, methodology, supervision, and writing—review and editing. I. Bergfeld: data curation, formal analysis, and writing—review and editing. A. van Loon: conceptualization and investigation. D. Denys: conceptualization, methodology, supervision, and writing—review and editing.

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3.6 Supporting information



Supplementary Figure S3.1. Decrease of misophonia symptoms during treatment.

Supplementary Table S3.1. Overview treatment protocol

	Psychoeducation	Work in sessions	Homework assignments
Session 1	CBT model and rationale Misophonia model Attention	Treatment planning Goal setting Sharing misophonia origin PMT: Task concentration exercises and applied relaxation	Psychoeducative material Task concentration exercises* Applied relaxation*
Session 2	Classical conditioning	Completion personal misophonia model Association exercise PMT: Task concentration exercises and applied relaxation	Moodboard (misophonia triggers and positive) Task concentration exercises Applied relaxation
Parallel: session with psychoeducation and sharing for family/friends			
Session 3	Perception	Completion moodboards Stimulus manipulation PMT: Task concentration exercises and applied relaxation	Stimulus manipulation* List of resembling sounds Task concentration exercises Applied relaxation
Session 4	Stress reduction Breathing	Completion stimulus manipulation Positive affect labeling PMT: Task concentration exercises, breathing exercise and applied relaxation	Positive affect labeling* Stress reduction Task concentration exercises Breathing exercise Applied relaxation
Session 5	Misokinesia	Positive affect labeling Functional analysis of (eating) norms PMT: Task concentration exercises with triggers, applied relaxation	Positive affect labeling Behavioral experiment for high (eating) norms Task concentration exercises Breathing exercise Applied relaxation
Session 6		Positive affect labeling PMT: exercises with family/friends	Exercise plan family/friends List of misophonia behavior Daily practice of the main techniques*
Session 7		Monitoring practice Goal setting for FU PMT: exercises in public space	Daily practice of the main techniques*
Session 8 (FU)		Monitoring practice Goal evaluation	Daily practice of the main techniques*



4

Synopsis of a treatment protocol to guide group-cognitive behavioral therapy for misophonia

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ABSTRACT

Misophonia is a disorder in which patients suffer from anger or disgust when confronted with specific sounds such as those associated with eating or breathing, causing avoidance of cue related situations resulting in significant functional impairment. Functional magnetic resonance imaging studies suggest misophonia is associated with increased activity in the auditory cortex and salience network, which might reflect increased vigilance towards specific misophonia triggers. New treatments have been developed and investigated in the last years in which this vigilance plays an important role. This is a synopsis of the first group protocol for Cognitive Behavioral Therapy (G-CBT) for misophonia. We discuss the model of CBT for misophonia, provide a detailed guide to the treatment illustrated with a clinical case study, discuss advantages, limitations and possible pitfalls, and review evidence for the protocol.

4.1 Introduction

Misophonia is a term which has been used first in 2001 (Jastreboff & Jastreboff). It's characterization as a potential psychiatric condition was first discussed by the Denys group in 2013 (Schröder, Vulink & Denys, 2013). Research in the last two decades has been focused primarily on its phenomenology. The diagnosis has not been added to psychiatric classification systems as DSM-V or ICD-10 yet. Misophonia is characterized by the symptoms described in Table 4.1 which are consistent with the symptoms observed in a group of 575 patients (Jager, de Koning, Bost, Denys, & Vulink, 2020a).

Table 4.1. Revised diagnostic criteria for misophonia (Jager et al., 2020a)

Amsterdam UMC 2020 revised criteria for misophonia	
A-R.	Preoccupation with a specific auditory, visual or sensory cue, which is predominantly induced by another person. It is required that oral or nasal sounds are a trigger.
B-R.	Cues evoke intense feelings of irritation, anger and/or disgust of which the individual recognizes it is excessive, unreasonable or out of proportion to the circumstances.
C-R.	Since emotions trigger an impulsive aversive physical reaction, the individual experiences a profound sense of loss of self-control with rare but potentially aggressive outbursts.
D-R.	The individual actively avoids situations in which triggers occur or endures triggers with intense discomfort, irritation, anger or disgust.
E-R.	The irritation, anger, disgust or avoidance causes significant distress and/or significant interference in the individual's day-to-day life. For example, it is impossible to eat together, work in an open office space or live together.
F-R.	The irritation, anger, disgust and avoidance are not better explained by another disorder, such as an Autism Spectrum Condition (e.g. a general hypersensitivity or hyper arousal to all sensory stimuli) or Attention Deficit Hyperactivity Disorder (e.g. attention problems with high distractibility in general).

Common triggers are: eating sounds (e.g., food chewing or swallowing) and nose - and breathing sounds (e.g., sniffing and heavy breathing). The intensity of the emotional response varies in different contexts and the level of stress in general. In the phenomenology of misophonia preoccupation with specific triggers is a main criterion (A). Two functional magnetic resonance imaging studies found evidence for this vigilance by showing increased activity in the auditory cortex and left amygdala in misophonia patients (Schröder et al., 2019; Schröder, San Giorgi, van Wingen, Vulink, & Denys, 2019).

Prevalence and incidence still remain unclear, but first estimations of its prevalence suggest misophonia to be a common condition. In a sample of Chinese students, 6% was assessed to have misophonia (Zhou, Wu, & Storch, 2017) and in a sample of English students 12%

reported moderate to severe misophonia symptoms (Naylor, Caimino, Scutt, Hoare, & Baguley, 2020). The origin of misophonia is a current topic of research. For now, we know at least a third of patients report a family history of misophonia (Sanchez & Silva, 2017; Jager et al., 2020a). Misophonia symptoms usually arise gradually in peri puberty, around the age of thirteen (Schröder, Vulink, & Denys, 2013; Rouw & Arfanian, 2017; Jager et al., 2020a).

Research on treatment for misophonia started in audiology with the altered intervention of tinnitus retraining therapy (TRT; Jastreboff & Jastreboff, 2014). Currently, treatment studies exist mainly within the domain of mental health. Cognitive behavioral therapy has been investigated most often and has shown promising results in treating misophonia in single case studies (Bernstein Angell & Dehle, 2013; McGuire, Wu, & Storch, 2015; Reid, Guzik, Gernand, & Olsen, 2016; Altinoz, Ercan, & Altinoz, 2018; Muller, Khemlani-Patel, & Neziroglu, 2018).

In this article we present the first protocol for group- cognitive behavioral therapy (G-CBT) for misophonia. This is a synopsis of the Dutch manual for group (G-)CBT for adults with misophonia developed by van Loon et al. (2019), which contains a protocol for individual therapy and a protocol for youth (age 12 to 18 years) as well. The main aims of the misophonia protocol are to decrease misophonia symptoms, improve quality of life, and to provide a greater sense of personal control. The highlights of this protocol have been succinctly described in the methods section of the randomized controlled trial (Jager, Vulink, Bergfeld, van Loon & Denys, 2020b). The aim of the present study is to present a model for G-CBT for misophonia through the description of a single clinical case. This clinical case study will serve as a running example throughout this article. We provide a detailed guide to the treatment by describing all interventions and providing timing and illustrations for the procedures. We review evidence for the protocol and will discuss advantages, limitations, and possible pitfalls. This article is intended as a practical guide, instead of a discussion of theoretical learning principles of CBT for misophonia.

4.2 Methods

4.2.1 Misophonia model

Misophonia is best understood as a conditioned response (of disgust and anger) to an originally neutral stimulus (sounds). In the course of time specific sounds have received a negative meaning which is stored as an associative memory. This concerns mostly human sounds which are disliked by some people, like food chewing or slurping. For instance, if

a child is annoyed by the sounds of his father eating, but is not allowed to leave the table and has to listen to these sounds, he or she may feel disgusted and powerless. The next meal this child will focus on the eating sounds of father again and the feelings of the last meal will come to mind. Gradually the stimulus will robustly and repeatedly evoke aversive thoughts or emotions. The hyper focus on (possible) triggers causes sensitization to these sounds. Even the softest sounds are noticed and cause an extreme reaction. The intense emotional reaction to triggers can be described as reflexive in nature as patients do not appear to be able to inhibit their prompt response. A commonly used model for characterizing misophonia is the biopsychosocial model, presented in Figure 4.1.

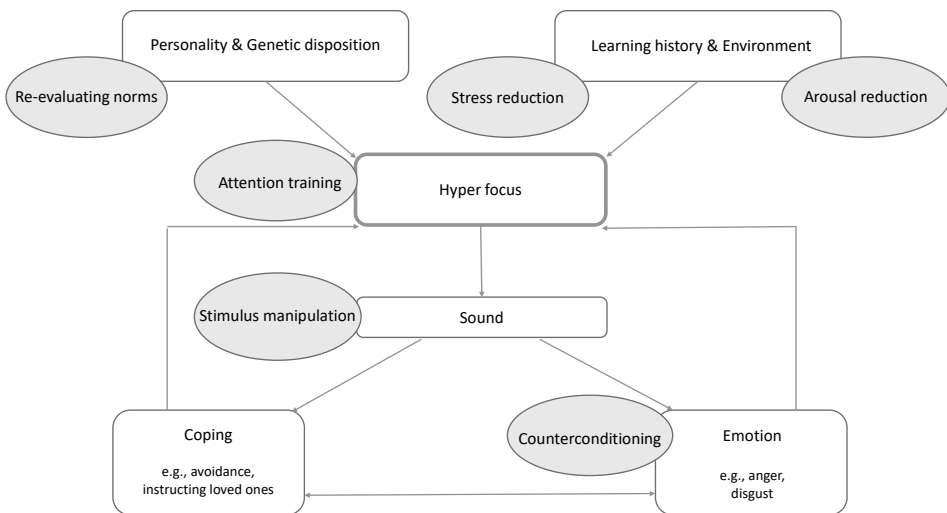


Figure 4.1. Biopsychosocial model of misophonia.

This model assumes that *hyper focus*, characterized by preoccupation with trigger sounds and a high arousal, has a central role in the onset and maintenance or aggravation of misophonia symptoms. Almost all patients report a hyper focus (Edelstein, Brang, Rouw, & Ramachandran, 2017; Jager et al., 2020a). This hyper focus implies that patients are trained to notice trigger sounds much sooner than others. And other triggers may be added if they also are attended to easily. For example, when the sound of a spouse chewing gum is the trigger for a misophonia patient, this patient will notice this sound made by the spouse before anyone else can notice this. But it is probable this patient will then notice a colleague eating gum, and may assess if this is just as disturbing. The hyper focus then will lead to a more generalized sensitization. Besides trigger sounds, non-auditory triggers (like seeing someone chewing gum) can then cause a strong aversive emotional reaction as well.

Since all misophonia patients report sounds as a trigger (Jager et al., 2020a; Swedo et al., 2021), it is safe to say that *sound* is the primary trigger modality in the misophonia model.

Several factors can influence the development of a hyper focus. Specific *personality* traits can include clinical perfectionism which has been found in 66 to 97% of patients (Jager et al., 2020a), and the setting of high norms, as a trait of obsessive-compulsive personality disorder are found in 26–52% (Schröder et al., 2013; Jager et al., 2020a) of patients. These traits increase the chance of developing a hyper focus. Furthermore, many of the misophonia patients report a *family history* of misophonia.

Besides factors within the patients, external factors such as learning history and environment can also contribute in the development of a hyper focus. The *learning history* of a patient with misophonia is one in which specific sounds have been associated with negative experiences by the process of classical conditioning during life. Finally, *environmental factors* influence hyper focus more directly. When patients experience stress or are tired they experience more hyper focus than when they are in good condition.

To *cope* with the trigger sounds and provoked emotions, patients develop maladaptive strategies, such as avoiding trigger sounds (e.g., they work, travel, sleep or eat alone or use earplugs), using camouflaging sounds (e.g., an extractor or music), or compulsory instructing their social environment (e.g., forbid partner to eat crisps). These strategies implemented in turn have effect on the hyper focus as depicted by the return arrow in Figure 4.1. For instance, a strategy such as using headphones with music, may counterintuitively lead to increased vigilance over whether the sound is still present and even greater focus on the trigger sounds despite the overlaying music. This increases hyper focus.

Trigger sounds provoke strong *emotions* of irritation and anger, and in most cases disgust (Schröder et al., 2013; Rouw & Erfanian, 2017). The intensity of the aggression is mostly very strong (Jager et al., 2020a). Patients quite often report the urge to harm their loved ones, because of the (eating) sounds they produce. To avoid being overwhelmed and feeling powerless by these emotions, patients pay more attention to detect trigger sounds. This is depicted by the return arrow from emotion to hyper focus in Figure 4.1.

4.2.2 Case conceptualization

As an illustration of the misophonia model we use the case conceptualization of an actual patient given the anonymized name of ‘Charlotte’. The labels in parentheses are links to the main elements of Figure 4.1 again.

Charlotte is a 37-year-old woman, who works as a lawyer and has a family with two children. Charlotte signed up for treatment, because she wants to avoid a divorce. She considers treatment as “her last straw to save her marriage”. Charlotte developed her symptoms at the age of twelve, when she started puberty. She has always had high standards as a child (*personality*), but she started judging people who made more eating sounds and even disliked them. Now she considers people who make eating sounds as “people who have a defect” and refuses to interact with them. Her parents do not have misophonia, but she found out her father’s mother had similar symptoms (*genetic disposition*). Charlotte grew up in a prosperous family as an only child. Her first and main trigger sound was the sound of food chewing her mother made. During her adolescence all joint meals were in a tense atmosphere, with her mother expressing she was hurt by the non-verbal aggression of Charlotte, and her father “trying to mediate between them”. Sometimes Charlotte was allowed to listen to a portable music player during dinners, but more often she was told by her father to stay at the table and control herself. This made her feel extremely powerless and she felt guilty for ruining dinner (*learning history*). During holidays, without her busy schedule of extracurricular activities, misophonia symptoms were less present. With lower stress and, as such, less sensitivity to misophonic triggers, she could enjoy her mother’s company more (*environment*). Later in life she felt annoyed by nearby eating behaviors of students or colleagues, but misophonia symptoms were not disabling, because she could avoid her major triggers. When she visited her parents however, misophonia symptoms returned to levels that were present at puberty. The first six years of her relationship with her husband, she did not experience him as a misophonia trigger. But during the pregnancy of their firstborn child, she started to respond with disgust and aggression (*emotion*) to his eating sounds and breathing or snoring. She also had a strong reaction to the sounds of doors closing loudly, whispering, sniffing, ‘s’ and ‘t’ sounds, glasses being put on the table, ringing keys and the dishwasher during nighttime (*trigger sound*). She developed a strong focus on these sounds, which made it impossible to engage in social interaction or sleep during these sounds (*hyper focus*). Subsequently Charlotte avoided eating together with her family and started sleeping alone. She tried to correct her husband when he was eating, even though she realized he did not produce too much sound, and she picked many fights about his breathing sounds (*coping*).

4.2.3 Phases of the protocol

The phased structure of this G-CBT protocol for misophonia is outlined below.

(A) Assessment and engagement phase

Firstly, patients in the group are invited to get acquainted with each other, possibly with the use of introductory games (i.e., ice-breakers). Within the first session, group therapy rules concerning presence, confidentiality and between session tasks are explained and the focus is to create a safe context for patients to share personal experiences. Therapists give psychoeducation about misophonia, validate the patients' experiences, normalize symptoms such as internal rage and emphasize similarities between the patients in the group. The biopsychosocial model for understanding misophonia is explained and filled with patients' experiences. Patients are motivated to share the onset of their symptoms to the best of their knowledge as the origins might not be clear and the effect on their life and life choices. Experiences are shared when patients present their 'mood boards' (a personal collage consisting of images, texts and samples of objects in a composition), an in-between-session task, with current negative associations with triggers and their desired associations.

A pretreatment measurement for misophonia symptoms can be performed at the first session with the revised Amsterdam Misophonia Scale (AMISOS-R; Schröder & Spape, 2014). We advise adding a questionnaire for general psychopathology, such as the Symptom Checklist-90 (SCL-90; Derogatis, Lipman, & Covi, 1973). Further, the Sheehan Disability Scale (SDS, Sheehan, 1983), used for other psychiatric and general medical conditions, can be applied to misophonia to determine the effect of treatment.

In the first phase effects of misophonia symptoms on work, social life and family life are discussed, as well as the pros and cons of being open about the diagnosis to family, friends or colleagues. Patients are encouraged to invite their loved ones to actively participate in the treatment. In this phase loved ones are invited for a separate meeting without the patients to provide psychoeducation about misophonia and the treatment, to share experiences, to manage expectations (e.g., no symptom reduction should be expected before week four) and to motivate them to participate actively and support their loved ones.

Expectations of treatment of all patients are discussed and information is provided about scientific research, as well as clinical experiences with the misophonia group protocol. Patients must be willing to devote the time needed for weekly sessions, as well as to devote energy to out-of-session work (e.g., homework). Goals are set within the first two

sessions. Once goals have been identified and prioritized, they are operationalized, which involves defining the goals and all the steps that it will take to achieve them in concrete, observable/measurable cognitive or behavioral terms (SMART). Finally, patients are invited to examine their tension and attention as a first step towards reduction of arousal and stress with the body scan procedure (Davis, Eshelman, & McKay, 2008).

(B) Change strategy phase

Once the secure base of the group is formed and goals are formulated in a SMART manner, various interventions to change are applied. Each group session has a theme matching the main intervention with corresponding psychoeducation and exercises (e.g., Misophonia models, Perception & attention, Stress, Conditioning, and Norms).

Patients learn to gain control over their (internal) reactions to misophonia triggers and practice new behavior and adaptive coping strategies. The interventions are described in detail below in the section 'Overview of the protocol'. Since patients first need to practice the various techniques before they can apply them to misophonia trigger situations, actual change often only emerges after session four. In this stage avoidance behavior is phased out, which means patients are gradually exposed to misophonia triggers situations. Please note, this is not the same as the intervention of prolonged exposure used as a behavioral technique for anxiety disorders and trauma- and stressor-related disorders.

This phase ends with a session including loved ones to practice all the learned techniques together under supervision of the therapists.

(C) Consolidation phase

The aim of the final two sessions is to develop a plan of action for the maintenance of gains and for relapse prevention. Patients practice with their misophonia triggers and exercises are done in real-life situations (e.g., visiting a food court). A list of remaining safety and avoidance behavior is made and patients make a roadmap to reduce their maladaptive misophonia behavior. This phase involves collaboration of the system. For example, patients and their loved ones practice together at home. Treatment is evaluated by discussing the effect of the different interventions, providing feedback for the therapists and a final measure of the misophonia symptom questionnaire (AMISOS-R) and possibly of general psychopathology (SCL-90) or quality-of-life (SDS) questionnaires.

4.2.4 Principles and values within the protocol

Patients with misophonia as primary diagnosis can be treated with this protocol. A clinical examination from a medical-psychiatric perspective is invaluable for diagnosing misophonia before treatment can be initiated.

Knowledge of and experience with cognitive behavioral therapy are required to apply this protocol with care and adjusted to the patient. Therefore, we refer to the handbooks of Wenzel (2019) and Beck (2020).

The (CBT) principles of learning are used to maximize the transfer of information during psycho-education. Learning from experience is more powerful than learning from verbal explanation. For instance, in classical conditioning two stimuli are associated to produce a new learned response. This is explained to the group by using a volunteer, linking a bell and a plant sprayer. All given information is repeated and patients are asked to explain the provided information in their own words with their own experience. Finally, the therapists invite patients to be creative in their fight against misophonia and use their own imagination and associations instead of dictating common associations from previous group therapy.

Throughout therapy, there is a strong emphasis on between-session-tasks in order to facilitate change and to focus on active participation. An explicit discussion about the importance of such tasks in achieving goals occurs in Phase A. Between-session-tasks take patients on average 30 to 60 minutes each day during treatment. At each session sufficient time should be devoted to both reviewing previous tasks and setting new ones. For psychotherapy between session tasks are given, such as practicing relaxation exercises or producing a mood-board with desired associations with misophonia triggers.

Misophonia is a problem with significant impact on interpersonal interactions. Therefore, therapy in group is very suitable for misophonia patients. This principle is central to this protocol. Often misophonia patients are embarrassed and reluctant about sharing their symptoms. In G-CBT they find recognition and support for their symptoms. Also, in G-CBT patients have a unique chance to experience both being the victim, and offender. Knowledge of group dynamics is obviously needed to use this factor therapeutically. Our systemic approach of misophonia is evidenced by the role of loved ones in this protocol. Loved ones receive psychoeducation, share experiences amongst each other, give support with between-session-tasks and practice the learned techniques together. For further reading about fundamental principles of group psychodynamics and couple therapy we suggest: Yalom & Leszcz (2020) and Gurman, Lebow, & Snyder (2015).

Lastly, the therapeutic attitude is first of all validating and supporting. However, we believe that the use of humor in the group sessions is an important element with positive results. Most often patients tend to take their symptoms (and their opinions on others) extremely serious since misophonia has put them and their social environment in a trap. Humor creates a distance towards the symptoms and helps patients to revise their high norms. It provides room to be more flexible and try out new behavior.

4.2.5 Overview of the protocol

The protocol is designed for a closed group of maximum nine patients with seven weekly meetings and one follow-up meeting after three weeks. Therapy sessions last 180 minutes with a short break. The manual has specific instructions for each session (e.g., with a set time for each intervention and fully written exercises). CBT consists of four main components: *stimulus manipulation*, *positive affect labeling*, *arousal reduction*, and *task concentration exercises*. In the most recent version two smaller elements are added: *re-evaluating (eating) norms* and *stress reduction*. Matching themes are respectively Perception, Conditioning, Stress, Attention, and Norms. In our center, the practical exercises, like task concentration exercises, are guided by psychomotor therapists in an exercise room, but this is not a necessity. Table 4.2 offers an overview of the sessions including themes, psychoeducation, in session work and homework assignments. The time of each procedure is provided in minutes. It should be noted there is a need for flexibility and the manual should be used as a guide.

In the next section we will discuss each intervention and illustrate the interventions with the clinical case vignette of Charlotte. All interventions are displayed within the biopsychosocial model in Figure 4.1.

1. Stimulus manipulation

In stimulus manipulation the ambiguity of sounds is used as stimulus control. The ambiguity of sounds confuses and/or produces humor. This property of sound is illustrated by a quiz in which patients have to guess different (trigger-)sounds. Patients learn other interpretations of their trigger sounds and manipulate their trigger sounds, by editing volume or speed or merging it in different sounds or music.

For example, the sound of sniffing resembles the sound of scratching a record much like a musical DJ would do, so Charlotte mixed her colleagues' sniffing sounds into a scratched music number. When she could not see the 'sniffer' but hears a sniff, she learned to imagine it was paper ripping. See for an illustration of stimulus manipulation supplementary fragment 4.1.

Table 4.2. Overview treatment protocol per session

Session 1	Theme: Attention	Time
Psychoeducation	CBT & Misophonia model	30
	Attention	10
Work in sessions	Treatment planning	5
	Goal setting	10
	Sharing misophonia onset (<i>patients read aloud their first misophonia memory</i>)	30
	Introduction games	40
	Task concentration exercises	45
	Bodyscan	5
Homework assignments	Psycho educative material (<i>sharing with family/ friends</i>)	5
	Task concentration exercises*	
	Applied relaxation*	
Session 2	Theme: Stress	Time
Psychoeducation	Stress reduction	20
	Breathing	10
Work in sessions	Completion misophonia models (<i>patients share their own model</i>)	45
	Task concentration exercises	45
	Applied relaxation	25
	Breathing exercises	20
Homework assignments	Mood boards (<i>one of misophonia and one of positive associations</i>)	15
	Stress reduction (<i>patients make a self-control program for stress reduction</i>)	
	Task concentration exercises	
	Applied relaxation	
	Breathing exercises	
Parallel to Session 2: Session with psychoeducation and sharing for family/friends		90
Session 3	Theme: Perception	Time
Psychoeducation	Perception	10
Work in sessions	Completion stress reduction	10
	Completion mood boards (<i>patients present their mood boards</i>)	40
	Stimulus manipulation (<i>sound quiz and start with digital trigger sound manipulation</i>)	25
	Task concentration exercises	45
	Applied relaxation	30
	Breathing exercises	15
Homework assignments	Stimulus manipulation* (<i>patients produce soundtracks with their triggers</i>)	5
	List of resembling sounds (<i>patients search for resembling sounds for their triggers</i>)	
	Task concentration exercises	
	Applied relaxation	
	Breathing exercises	

Session 4	Theme: Conditioning	Time
Psychoeducation	Classical conditioning	25
Work in sessions	Completion stimulus manipulation (<i>patients present their soundtracks</i>)	40
	Positive affect labeling (<i>brainstorm counterconditioning</i>)	15
	Task concentration exercises	45
	Applied relaxation	30
	Breathing exercises	15
Homework assignments	Positive affect labeling* (<i>patients make an audiovisual production</i>)	10
	Task concentration exercises	
	Applied relaxation	
	Breathing exercises	
Session 5	Theme: Norms	Time
Psychoeducation	Misokinesia / other triggers	20
Work in sessions	Completion positive affect labeling (<i>patients present their audiovisual production</i>)	25
	Functional analysis of (eating) norms (<i>panel discussion of high norms</i>)	40
	Task concentration exercises combined with triggers	45
	Exercises for easing high standards	45
	Positive affect labeling (<i>patients make new productions or extend their productions to an advertising campaign</i>)	5
Homework assignments	Behavioral experiment for high (eating) norms	
	Task concentration exercises combined with triggers	
	Applied relaxation	
Session 6	Theme: Real life	Time
Psychoeducation	-	-
Work in sessions	Positive affect labeling (<i>patients present advertising campaign or new productions</i>)	90
	Task concentration exercises with family/friends producing triggers	80
Homework assignments	Exercise plan family/friends	10
	List of misophonia behavior	
	Daily practice of the 4 main techniques*	
Half of Session 6: Patients practice under guidance with family/friends		
Session 7	Theme: Relapse prevention	Time
Psychoeducation	Relapse prevention	20
Work in sessions	Monitoring practice	45
	Goal setting for FU	25
	Task concentration exercises and applied relaxation in public space	90
Homework assignments	Daily practice of the 4 main techniques*	-
Session 8	Theme: Plan of action	Time
Psychoeducation	-	-
Work in sessions	Monitoring practice	45
	Goal evaluation	20
	Goal setting for the future	25
Homework assignments	Daily practice of the 4 main techniques*	-

2. Counterconditioning

The intervention of counterconditioning is used to neutralize the negative affective-evaluation of misophonia triggers. This intervention shows similarities with the procedure of COMET (Korrelboom, Jong, Huijbrechts, & Daansen, 2009). Patients produce videos where powerful personal positive images (e.g., two favorite nieces with rain boots jumping up and down in a mud puddle) are combined with the aversive misophonia trigger (e.g., food chewing) emerging with their favorite music. These videos are part of a large ‘campaign’ with images, slogans, messages on their phone, in their house and at work, to maximize the positive affect labeling. For stimulus manipulation and counterconditioning different digital editing programs for sounds and videos can be used, for instance the free audio editing software ‘Audacity’. Patients who are not digitally skilled or do not have access to these programs, are encouraged to ask their loved ones for help. During therapy the group members often help each other as well. And it is almost always possible to improvise with the use of mobile phones.

Charlotte produced a video of taped breathing sounds of her spouse and edited a personal diving video of her favorite holiday with the song ‘A beautiful day’ from the band U2. She watched the video every day, but was also reminded and counter conditioned by coral next to her bed, a picture of her wearing a diving mask as background on her phone and a quote with positive self-verbalization (‘Just breathe!’) with lipstick on her mirror. See for an illustration of counterconditioning supplementary fragment 4.2 and 4.3.

3. Arousal reduction

Arousal reduction consists of breathing techniques, progressive muscle and passive relaxation, applied relaxation techniques and mindfulness techniques (Hayes & Hofmann, 2018). Initially, patients learn to reduce arousal in a normal state, later they learn to relax in a state of arousal caused by misophonic triggers. Throughout the entire treatment arousal reduction is a part of the sessions.

Whereas breathing sounds of her spouse were a trigger for Charlotte, she learned to relax by listening to her own breathing sounds with diaphragmatic breathing. She became very skilled in applied relaxation, as she practiced this during all her lunch breaks at her work at the law firm.

4. Task concentration exercises

With task concentration exercises patients learn to control their attention and to shift their focus from the misophonia triggers towards the task. Difficulty of exercises gradually

increases, as in the CBT protocol for social anxiety (Wild & Clark, 2015). First patients learn to switch their attention in situations not related to misophonia to gain experience with controlling their focus. Then, when patients are more skilled, they practice being confronted with misophonia triggers in controlled situations. Finally, they apply the attention training in real-life misophonia situations.

Charlotte first used her love for classical music to control her attention. Switching between the different instruments was easy. She practiced with shifting focus from the environment (sounds of the clock, pen clicking or the ventilation system) to the task, for example playing badminton. At home she practiced with shifting focus from her husbands' breathing sounds to a horror movie and from eating sounds of commuters on the train to a Sudoku puzzle.

5. Stress reduction

Stress reduction is based on an intervention for symptom reduction from the burn-out protocol (van Dam, Keijsers, Kriens, Boelaars, & Vossen, 2017). Patients learn through self-control techniques (e.g., Mahoney & Thoresen, 1972) to recognize symptoms of stress and manage their stress levels by either taking relaxing measures or by reducing (work-)load. Mild stress levels require small measures and higher levels require more drastic measures. Patients are made aware of the, often precarious, balance between relaxation and stress and are, if necessary, invited to make more structural changes in their work-life balance.

Charlotte noticed by registering her levels of stress that her perceived average stress level was too high. Because of her perfectionism and high standards, she often worked late after putting her children to bed. This resulted in little time to relax. She discovered the impact of stress on her misophonia; dinners on Fridays following a busy week were more difficult than on Wednesdays, when she had the afternoon off. She was convinced she had to reduce stress and made a self-control program, with signals of increasing stress (such as tension headache) and increasing measures for more relaxation (for example taking a massage or bath) or less load (such as postponing a deadline), resulting in more spare time and lower stress levels.

6. Re-evaluating (eating) norms

This intervention consists of different exercises to challenge, unconscious, assumptions and norms about eating habits or other misophonia triggers, such as sniffing. Decisional balance exercises or discussions about norms are done. Patients debate about for example the proposition: "Making eating sounds is never allowed!". To experience the burden of

high norms and (other people's) rules, a ball game 'the game without rules' is introduced. Patients can introduce new game rules, by stopping the game and putting the rule to the vote. This often results in discussion and there's no room left for playing and having fun. Finally, patients are also challenged to break their own (eating) norms in a behavioral experiment, since these norms maintain the hyper focus on triggers.

Charlotte always avoided public transport, because she detested and judged commuters who were eating in the train. She was challenged to eat a bag of her favorite crisps on the train when she was hungry. Even though she felt like a criminal at first (which amused her), she could really enjoy the crisps and could therefore slightly imagine why commuters eat while traveling.

4.3 Results

4.3.1 Development and effectivity of the protocol

The original manual for G-CBT was the result of years of clinical practice. Between 2011 and 2021 over 1200 patients with misophonia were treated within our psychiatry department. Different CBT interventions, among which cognitive therapy, exposure and imagery rescripting, were investigated, but did not show a positive effect on the symptoms. Years of trial and error finally resulted in a mix of CBT interventions who were fine-tuned for treating misophonia in the most effective way. This protocol has been used in the treatment of over 1200 patients in clinical practice so far.

This G-CBT manual has been used in two clinical trials by our research group where it has been efficacious in treating misophonia in Dutch adults (Schröder, Vulink, van Loon, & Denys, 2017; Jager et al., 2020b). The effectiveness of the first version of this protocol for group treatment has been examined with good results (Schröder et al., 2017). Almost half of the patients studied had over 30% symptom reduction and were clinically assessed as "much improved" or "very much improved" on the Clinical Global Impression-Improvement (CGI-I; Guy, 1976).

The protocol, with the addition of stress reduction and re-evaluating (eating) norms, has also been studied in a randomized controlled trial with positive effects which were preserved at one-year follow-up (Jager et al., 2020b). In comparison with a waiting list control group treatment was effective with much to very much clinical improvement in 37% of the studied patients; on average symptoms were reduced with 28% after treatment and one year after treatment symptoms were reduced with 24%. On top of these meas-

urements, group therapists rated 74% of all completers clinically improved. 37% of the completers did not meet diagnostic criteria for misophonia any more post-treatment. Treatment acceptability was quite high; 65% was (very) satisfied and 25% was neutral, and treatment was rated by patients with a mean of 6.7 out of 10.

4.3.2 Results clinical case study

Results of the protocol are illustrated by the case study of Charlotte. Even though Charlotte was anxious at first to adopt new triggers from other patients, she did not. After treatment she experienced a large reduction in misophonia symptoms. Although she was still experiencing some symptoms, the relationship with her husband improved significantly. After treatment Charlotte was able to eat and sleep together again. She could make jokes with her husband about her misophonia (for example saying 'Just breath!', when she got annoyed) and the tension at home decreased. She lost the hyper focus on most trigger sounds. The eating sounds of her mother remained a trigger for Charlotte, but she no longer avoided eating with her parents. She was able to cope in a functional manner when an emotional reaction was provoked. Charlotte stated she felt more relaxed and free in social interactions with other people.

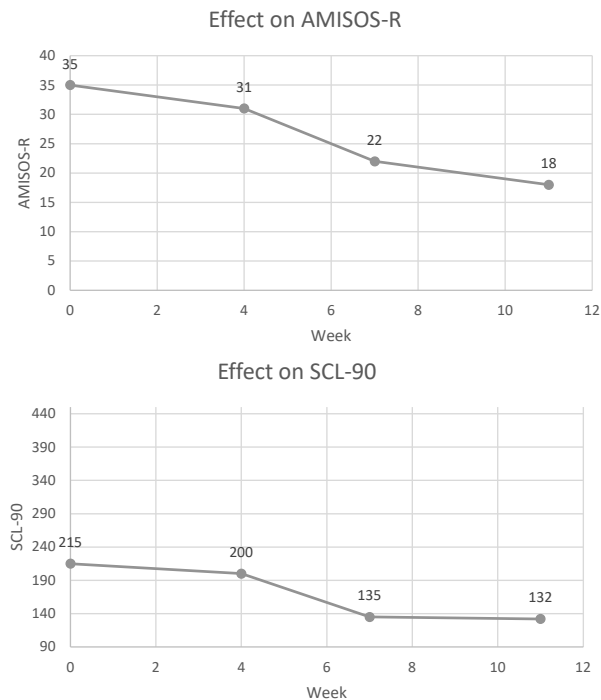


Figure 4.2. Symptoms Charlotte during G-CBT.

At session 1, 4, 7 and 8 progress was monitored by two questionnaires; the AMISOS-R and SCL-90. Charlotte started treatment with severe to extreme misophonia (range 31–40) and at the end of treatment her symptoms were reduced to mild misophonia (range 11–20). Also, general psychopathology decreased from a very high level to a level above average (see Figure 4.2).

4.4 Discussion

This paper introduced the protocol for G-CBT for misophonia. The interventions are based on the biopsychosocial explanatory model for misophonia with hyper focus as a core symptom. The G-CBT protocol includes six interventions: stimulus manipulation, counterconditioning, arousal reduction, task concentration exercises, stress reduction and re-evaluating (eating) norms. While the case study described in this paper responded to all interventions and was successfully treated by G-CBT, most patients benefit from various combinations of the interventions. Since misophonia is an interpersonal problem with a large impact on all interactions, group therapy is very suitable. Loved ones are involved throughout the treatment, so patients are motivated to fight their misophonia together instead of fighting with each other or fighting internally.

The advantages of group treatment for misophonia consists of peer support, more opportunity to practice under guidance, more natural exposure and cost effectiveness. Compared to, for example, the case study of Muller et al. (2018) with a duration of 24 sessions of 45 minutes of individual therapy (18 hours per patient) our treatment is brief with a duration of 8 sessions of 180 minutes using less time per patient (6 hours per patient, in a group of 8 patients with two therapists).

A first limitation of group treatment is the requirement of a minimum number of misophonia patients. At least eight patients are needed to form a psychotherapeutic group (Koks, Steures, & Ter Haar, 2021). In our experience misophonia patients only admit themselves in large numbers to a center when this facility identifies itself as a misophonia treatment center. A second limitation is the limited possibility to adjust to individual needs of patients. For example, if a patient has misophonia-related emotionally disturbing memories adding eye movement desensitization and reprocessing (EMDR) therapy as a trauma-focused approach may be considered (Jager, Vulink, de Roos, & Denys, 2021). Such an additional intervention can more easily be integrated in individual therapy.

The protocol has been used by one other research group so far; in a single case study by Roushani & Honarmand (2021). Three patients were treated individually conform our protocol instead of in a group, with positive effect. Two of the three patients had a recovery percentage of 42–43% on anger. Further, the proposed treatment paradigm for misophonia by Frank & McKay (2019) is largely based on the present protocol and includes (besides exposure using inhibitory learning): counter conditioning, stimulus manipulation and stress management in 12 sessions. Preliminary results of the 18 patients enrolled in their RCT have not been published yet. Hopefully this synopsis will contribute to the implementation of G-CBT in clinical trials for misophonia, as well as in clinical practice.

4.4.1 Conclusion

In this article we have presented our treatment protocol for G-CBT for misophonia, which has been evaluated in two clinical trials and has been used in clinical practice for treating over 1200 patients. This protocol is based on the biopsychosocial explanatory model for misophonia with hyper focus as a core symptom. Knowledge of the principles and values of CBT, as well as a phased approach should help to maximize results. With this treatment manual, which is illustrated with a clinical case study, we hope to encourage other investigators for more clinical trials and to inspire clinicians working with misophonia patients to implement G-CBT.

Acknowledgements

We are very grateful to all misophonia patients for their contribution in the development of this protocol. We also thank our colleagues from the AMC misophonia treatment team.

Conflict of interests

The authors declare that there are no conflict of interests.

Author contributions

I. Jager: conceptualization, and writing—original draft. N. Vulink: conceptualization, supervision, and writing—review and editing. A. van Loon: conceptualization. A. Schröder, conceptualization, writing—review. M. van der Pol: conceptualization. S. Slaghekke: conceptualization. D. Denys: conceptualization, supervision, and writing—review and editing.

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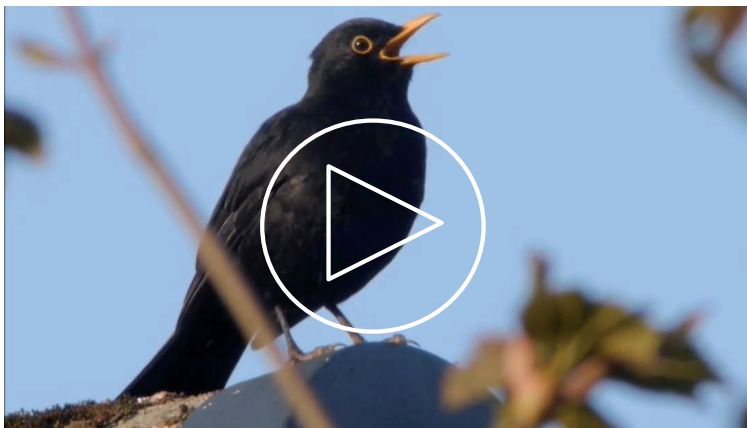
4.6 Supporting information



Supplementary fragment 4.1. Example of stimulus manipulation: Audio fragment DJ sniffing.



Supplementary fragment 4.2. Example of counterconditioning: Video fragment Baby sniffing.



Supplementary fragment 4.3. Example of counterconditioning: Video fragment Bird coughing.



5

EMDR therapy for misophonia: A pilot study of case series

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European Journal of Psychotraumatology, 12(1).

ABSTRACT

Background: Misophonia is a disorder in which patients suffer from anger or disgust when confronted with specific sounds such as loud chewing or breathing, causing avoidance of cue-related situations resulting in significant functional impairment. Though the first treatment studies with cognitive behavioral therapy (CBT) showed promising results, an average of 50% of the patients has not improved much clinically.

Objective: The aim of this pilot study was to assess the effectiveness of eye movement desensitization and reprocessing (EMDR) therapy as a trauma-focused approach in treating misophonia symptoms.

Method: A sample of 10 adult participants with misophonia was studied at the outpatient clinic of the Academic Medical Center in Amsterdam. Participants were either on the waiting list for CBT or non-responders to CBT. EMDR was focused on misophonia-related emotionally disturbing memories and delivered in a mean of 2.6 sessions of 60–90 minutes. Pre- and post-treatment self-assessed ratings of misophonia symptoms (AMISOS-R, primary outcome), of general psychopathology (SCL-90-R) and of quality of life (SDS) were administered. The co-primary outcome was the Clinical Global Impression Improvement scale (CGI-I).

Results: A paired t-test ($n = 8$) showed improvement on the primary outcome (-6.14 [MD], 5.34 [SD]) on the AMISOS-R ($p = .023$). Three of the eight patients showed clinically significant improvement measured with the CGI-I. No significant effect on secondary outcomes was found..

Conclusions: These preliminary results suggest that EMDR therapy focused on emotionally disturbing misophonia-related memories can reduce misophonia symptoms. RCTs with sufficient sample sizes are required to firmly establish the value of EMDR therapy for misophonia.

5.1 Background

Misophonia is a disorder in which patients suffer from anger or disgust when confronted with specific sounds such as loud chewing or breathing, causing avoidance of cue-related situations resulting in significant functional impairments (Jager et al., 2020; Schröder, Vulink, & Denys, 2013). Misophonia patients can often not eat, sleep or work in company and most social and family relations are negatively affected. Since the onset of symptoms is around the age of 13 (Jager et al., 2020; Schröder et al., 2013), misophonia patients develop a lifelong coping behavior of avoidance, like walking away or using music or earplugs to camouflage trigger sounds. There is debate about the nature of the disorder, other research groups emphasize its audiological or neurological nature. Recently, a Delphi Process study led to an agreement of experts of at least 80% on the consensus definition of misophonia (Swedo et al., 2021).

Estimates of the incidence of misophonia in adults vary (Naylor, Caimino, Scutt, Hoare, & Baguley, 2020; Zhou, Wu, & Storch, 2017). Solid epidemiological studies are missing, also as a consequence of the ongoing debate about the definition of misophonia. Comorbidity is relatively low: 40% (Erfanian, Kartsonaki, & Keshavarz, 2019) to 72% (Jager et al., 2020) of subjects diagnosed with misophonia do not report another Axis I psychiatric disorder. Hence, misophonia is an impairing and common disorder for which effective treatment is urgently needed, given the huge impact on family and social relations.

The Amsterdam University Medical Center of Psychiatry, location AMC (Amsterdam UMC) has developed the first protocolled treatment with cognitive behavioral therapy (CBT) for misophonia (Van Loon et al., 2019). CBT consists of four main components: task concentration exercises, positive affect labelling, stimulus manipulation, and arousal reduction. The first treatment studies with CBT showed promising results, respectively, 48% (Schröder, Vulink, Van Loon, & Denys, 2017) and 37% of the patients (Jager et al., 2021) showed significant clinical improvement with CBT post treatment. However, CBT is ineffective for more than half of misophonia patients, who therefore require alternative treatments. Except for CBT, some data suggest Tinnitus Retraining Therapy offers an 83% success rate for misophonia (Jastreboff & Jastreboff, 2014).

EMDR therapy is an evidence-based psychological treatment that is effective for post-traumatic stress disorder (PTSD) and its comorbid symptoms (De Jongh, Amann, Hofmann, Farrell, & Lee, 2019; International Society of Traumatic Stress Studies [ISTSS], 2019; National Institute for Health and Care Excellence, 2018). In the last decades, the insight that unprocessed traumatic memories (not only criterion A events) play an important role

in the development and maintenance of a variety of mental health conditions led to the use of EMDR therapy as a trauma-focused treatment for a broader spectrum of disorders (Shapiro, 2018). Evidence for its effectiveness for disorders beyond PTSD is growing, such as for major depressive disorder, bipolar disorder, psychosis, anxiety disorders, obsessive compulsive disorder, substance use disorder, and pain (Matthijssen et al., 2020; Maxfield, 2019). In a recent meta-analysis of RCTs (Cuijpers, Veen, Sijbrandij, Yoder, & Cristea, 2020), significant results were found for EMDR in phobias and test anxiety, but with a high risk of bias. Overall, the authors concluded that there is not enough evidence for the use of EMDR for mental health problems other than PTSD (Cuijpers et al., 2020). More research on EMDR and larger RCTs with clear-cut results are needed, as in the majority of the RCTs EMDR is merely used for comorbid PTSD or as an add-on to treatment-as-usual (Meyerbröker, Emmelkamp, & Merckx, 2019).

The theoretical model behind EMDR, the adaptive information processing model (AIP), suggests that 'dysfunctionally stored' memories may have an etiological and maintaining role for a broad spectrum of symptoms and problems, not limited to PTSD (Hase, Balmaceda, Ostacoli, Liebermann, & Hofmann, 2017; Shapiro, 2018). Desensitization and reprocessing of these disturbing memories and images with EMDR will result in reduction of the vividness and emotionality of unpleasant mental representations (Gunter & Bodner, 2008).

Up to date it is unknown if there might be a connection between misophonia symptoms and related disturbing experiences or memories. Only one case description found a decrease in misophonia symptoms after EMDR treatment (Vollbehr & ten Broeke, 2017). When relevant memories are found a trauma-focused approach such as EMDR therapy could reduce misophonia symptoms. This pilot study aimed first to identify relevant experiences related to misophonia symptoms and secondly to reduce misophonia symptoms with EMDR therapy for reprocessing maladaptive implicit memories. Therefore, with this pilot study we assess the feasibility and preliminary effectiveness of EMDR in reducing misophonia symptoms and improving general mental functioning and quality of life.

5.2 Methods

The study site was the outpatient clinic of the department of psychiatry of the Amsterdam University Medical Center (Amsterdam UMC, location AMC, the Netherlands). All patients gave written informed consent. The study was approved by the AMC medical ethics committee and carried out in accordance with the Declaration of Helsinki.

5.2.1 Participant selection, recruitment, and enrolment

A total of 14 patients were selected from September 2015 to July 2017 from the outpatient clinic at the Amsterdam UMC (see Figure 5.1). All patients were referred by their General Practitioners for treatment of invalidating misophonia symptoms. All had received a psychiatric assessment at our clinic. Presence of comorbid Axis I disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) diagnostic criteria was validated at baseline by the MINI-International Neuropsychiatric Interview Plus (MINI-plus) (Sheehan et al., 1997; Sheehan et al., 1998; Van Vliet & De Beurs, 2007).

Recruited patients were either on the waiting list for treatment or non-responders to CBT. Ten subsequently referred patients, who were most recently added to the waiting list, were approached in order of registration. Six were included, four patients were not willing to participate. We also included four non-responders; patients who completed CBT without positive results at the AMC in the period of this study and searched for help and further treatment.

Inclusion criteria were diagnosis of misophonia (Schröder et al., 2013) and aged between 18 and 65 years. Exclusion criteria were: previous EMDR treatment for misophonia, the presence of depression and anxiety disorder as a primary diagnosis, bipolar disorder, autism spectrum disorders, schizophrenia or any other psychotic disorder, substance-related disorder during the past 6 months, any structural central nervous system disorder or stroke within the last year, currently taking benzodiazepines or stimulants, patients at risk for suicide and patients with language barriers or illiteracy.

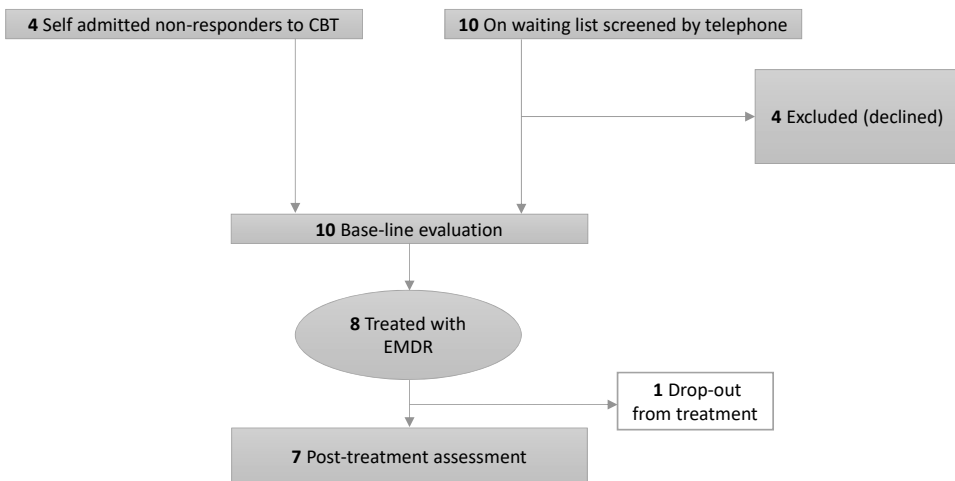


Figure 5.1. Consort diagram.

5.2.2 EMDR therapy

The EMDR therapy was conducted according to the standard eight-phase protocol by Shapiro using the Dutch translation of the EMDR protocol (De Jongh & ten Broeke, 2019; Shapiro, 2001). The standard EMDR treatment protocol (Shapiro, 2018) consists of the following phases: 1. History Taking (including discussion of the rationale for therapy and case conceptualization/idiographic formulation of the patient's difficulties); 2. Preparation (preparation for reprocessing of target trauma memories and equipping patients with strategies to better self-regulate during trauma reprocessing work); 3. Assessment (the identification of a specific target memory/image as well as associated negative cognitions, disturbing emotions or bodily sensations; a positive cognition that is preferable to the negative one is also identified); 4. Desensitization and reprocessing (involving the repetitive use of bilateral stimulation, for example, the tracking of a moving object, while the patient is asked to simultaneously focus on the image, the negative cognition, and the disturbing emotion or body sensation until he/she reports a marked reduction in distress associated with these experiences); 5. Installation (in which the patient is encouraged to associate the trauma memory with the positive cognition previously identified, or a new more adaptive positive cognition); 6. Body scan (designed to target any residual negative/uncomfortable physical sensation or bodily tension associated with the trauma memory); 7. Closure (generally involving the use of distress management and tolerance strategies before the end of the session); 8. Re-evaluation (where the patient and therapist reassess the previous target to evaluate whether additional work is necessary before proceeding further with the intervention).

The memories EMDR focused on were identified (phase 1) following a standardized search strategy called time-line path in the first session (first method; de Jongh et al., 2010). This strategy is used for a broad spectrum of symptoms beyond PTSD and helps to develop a case conceptualization in terms of a relationship between memories of significant events, on one hand, and clients' current symptoms, on the other hand. It is also suggested for the case conceptualization for EMDR for misophonia (Vollbehr & ten Broeke, 2017). The time-line path deals with symptoms whereby memories of the etiological and aggravating events can be specified on a time line. For this pilot study, the main questions of the therapist were: 'When did your misophonia symptoms start and when did they get worse?'. The events or experiences found were target memories for EMDR and processed with EMDR. The order of targets was set; starting with targets that were related to the onset of the misophonia symptoms and subsequently, the memories of the events after which symptoms worsened. For all identified events a Subjective Units of Distress Scale (SUD)

score was given between 0 and 10 (0 meaning no distress to 10 meaning highest distress) that was felt when the memory was kept in mind. Hereafter, the standard protocol was first applied to the first target memory in time. A substantial reduction in SUD was required to move to the next memory. In all the following sessions, memories were processed. Eye movements were applied as a dual-attention stimulus. Each EMDR session lasted 60–90 minutes. Treatment was ended when the Subjective Units of Distress Scale (SUD) score was zero for all indexed misophonia-related memories identified on the time-line. All patients were equally involved in the eight phases of the standard protocol. The total number of sessions varied across patients depending on the number of targets and the speed of desensitization.

The therapist was a licensed clinical psychologist (IJ) with appropriate training (level II trained) in EMDR and extensive experience in CBT for obsessive-compulsive and related disorders and misophonia in particular.

5.2.3 Assessments

Patients were assessed at baseline (T1), and post treatment (T2). At T2 an independent assessor rated all patients in a clinical interview. This independent assessor was a cognitive behavioral worker with extensive experience in CBT for misophonia.

5.2.4 Primary outcomes

Misophonia symptoms were measured using the revised Amsterdam Misophonia Scale (AMISOS-R) (Schröder & Spape, 2014). It consists of 10 items with scores ranging from 0 to 40. Higher scores indicate more severe misophonia; 0–10: normal to subclinical misophonia; 11–20: mild misophonia; 21–30: moderate severe misophonia; 31–40: severe to extreme misophonia. (see supplementary appendix). This improved version of the A-MISO-S (Schröder et al., 2013) is in the process of validation; Preliminary results of the validation show reliability of the scale was good ($\alpha = .84$), as well as its validity ($r = .87$, $p < .01$).

The co-primary outcome was CGI-Improvement (CGI-I) (Guy, 1976) as objective observer ratings. The CGI-I consists of one question: ‘Compared to the patient’s condition at admission to the project this patient’s condition is: 1 = very much improved since the initiation of treatment; 2 = much improved; 3 = minimally improved; 4 = no change from baseline (the initiation of treatment); 5 = minimally worse; 6 = much worse; 7 = very much worse since the initiation of treatment.’

Responses are defined by a CGI-I scale score <3 , usually used to define response (Bandelow, Baldwin, Dolberg, Andersen, & Stein, 2006). Full response was defined by 25% reduction (or more) in the AMISOS-R and a CGI-I score < 3 . Partial response was defined by either a 25% reduction (or more) on the AMISOS-R or a CGI-I score < 3 .

5.2.5 Secondary outcomes

General mental dysfunction was assessed with the Symptom Checklist-90-R (SCL-90-R; Arrindell & Ettema, 1986; Derogatis, Lipman, & Covi, 1973). The total score is 90 to 450, with higher scores indicating more general psychopathology. Quality of life was assessed with the Sheehan Disability Scale (SDS; Sheehan, 1983). The SDS has three domains; Work, Social and Family, and the range per domain is 0 to 10. The total score was 0 to 30, with higher scores indicating more impairment.

5.2.6 Qualitative outcome

The perceived intensity of disturbance or distress of an image or an emotional memory being recalled is measured with the Subjective Units of Distress (SUD) scale. This score is indexed on an 11-point Likert scale, ranging from 0 ('no disturbance at all') to 10 ('greatest level of disturbance') (Shapiro, 2018). Participants were requested to indicate the SUD score verbally to the therapist for all identified events at the start, during and after EMDR therapy. The SUD scores are displayed at Table 5.4.

The severity of posttraumatic stress symptoms was measured on indication (if the presence of these symptoms was assumed) with the Impact of Events Scale (IES; Brom & Kleber, 1985; Horowitz, Wilner, & Alvarez, 1979; van der Ploeg, Mooren, Kleber, van der Velden, & Brom, 2004). The Impact of Events Scale has two subscales (avoidance and intrusions) and a total score ranging from 15 to 60, with higher scores indicating more PTSD symptoms and a cut-off score of 33 or more (Creamer, Bell, & Failla, 2003).

5.2.7 Statistical analysis

Since this is a pilot study no formal sample size calculations were performed. We tested the decrease in symptom severity with a paired t-test; the dependent variable was AMISOS-R total score, and independent factors were assessments (T1, T2). An additional intention-to-treat analysis was performed, including all patients who received EMDR therapy, irrespective of whether they completed the therapy. Missing values were hereby imputed by the last observation carried forward (LOCF).

All analyses were all based on 2-tailed t-tests. For both co-primary and secondary outcomes $p < .05$ was considered to be statistically significant. All results should be considered as exploratory. In all analyses for normal distribution was controlled by Shapiro–Wilk and a visual check of the histogram. Data were analyzed using IBM SPSS Statistics version 25.

5.3 Results

5.3.1 Participant flow and characteristics

A total of 10 patients (9 [90%] female; mean [SD] age, 35 [14,53] years) were included (Table 5.1). Mean (SD) age of onset was 13.10 (9.75). Fifty percent of the patients fulfilled criteria (measured with the MINI-plus) for comorbidity on Axis I, none of patients suffered from comorbid PTSD, and AXIS II personality traits were found in 60% of the patients.

In eight of the 10 patients, misophonia-related emotionally disturbing memories were identified; the other two patients were excluded from the study. Seven patients completed EMDR-therapy and the post-treatment measures. Only one patient dropped out after the first EMDR session. Despite several attempts to approach the patient, she declined to attend treatment appointments and post-treatment measures were missing.

Table 5.1. Demographic and clinical characteristics of the 10 patients with misophonia

Patient	Sex	Age (years)	Age onset (years)	Family history	Previous CBT	Comorbidity Axis I	Comorbidity Axis II
1	F	49	6	Misophonia	No	Specific phobia	No diagnosis
2	F	19	11	Clear	No	Anxiety disorder NOS	No diagnosis
3	F	55	39	Misophonia	No	No diagnosis	No diagnosis
4	F	23	7	Clear	No	No diagnosis	Avoidant traits
5	F	26	15	Misophonia	No	No diagnosis	OCPD traits
6	M	56	6	Misophonia	No	No diagnosis	No diagnosis
7	F	40	13	Clear	Yes	Trichotillomania	Borderline traits
8	F	27	14	Misophonia	Yes	No diagnosis	OCPD traits
9	F	37	7	Clear	Yes	Eating disorder NOS	OCPD
10	F	18	13	Clear	Yes	Social phobia	Avoidant traits

5.3.2 Primary outcomes

On average, 2.6 sessions of EMDR were provided to each participant ($n = 7$). A paired t-test for the completers showed significant improvement on the primary outcome (-6.14 [MD],

5.34 [SD]) on the AMISOS-R ($p = .023$) (Tables 5.2 and 5.3). On average, the AMISOS-R total scores were reduced by 20%. In Figure 5.2 the decrease in AMISOS-R is shown for the completers. An additional intention-to-treat analysis showed the same significant difference and direction of the effect on the AMISOS-R (-5.37 [MD], 5.40 [SD], $p = .026$).

Table 5.2. Paired samples t-test statistics for the mean changes between baseline and end-of-treatment in completers (n = 7)

	Pre treatment means (SD)	Post treatment means (SD)	N	t	Sig.
AMISOS-R	30.43 (4.28)	24.29 (9.05)	7	3.046	.023
SCL-90	172.83 (22.09)	154.83 (32.32)	6	1.402	.220
SDS work	4.57 (2.99)	3.14 (2.91)	7	1.369	.220
SDS social	5.00 (2.38)	4.00 (1.63)	7	.882	.412
SDS family	6.29 (3.04)	4.86 (2.48)	7	.946	.381
SDS total	15.86 (3.81)	12.00 (5.89)	7	1.218	.269

Table 5.3. Paired samples t-test statistics for the mean changes between baseline and end-of-treatment. Intention-to-treat analysis with the last observation carried forwards (n = 8).

	Pre treatment means (SD)	Post treatment means (SD)	N	t	Sig.
AMISOS-R	30.50 (3.96)	25.13 (8.71)	8	2.817	.026
SCL-90	181.57 (30.68)	166.14 (42.02)	7	1.383	.216
SDS work	4.38 (2.83)	3.13 (2.70)	8	1.357	.217
SDS social	5.38 (2.45)	4.50 (2.07)	8	.884	.406
SDS family	6.50 (2.88)	5.25 (2.55)	8	.947	.375
SDS total	16.25 (3.69)	12.88 (5.99)	8	1.213	.265

Three patients (#3, #7, #9) were found to be clinically improved, two of them with much improvement ($\text{CGI-I} < 3$). One patient (#4), who showed large improvement on the AMISOS-R, was not considered clinically improved, since the improvement seemed to be related to temporary reduction of specific misophonia triggers.

In conclusion, the full response rate was 25%; two of the eight included patients had both 25% symptom reduction and a maximum CGI-I score of 2 ('much improved' (2) or 'very much improved' (1)). Two other patients were considered as partial responders with at least 25% symptom reduction on the AMISOS-R or a maximum CGI-I score of 2 (see Table 5.4).

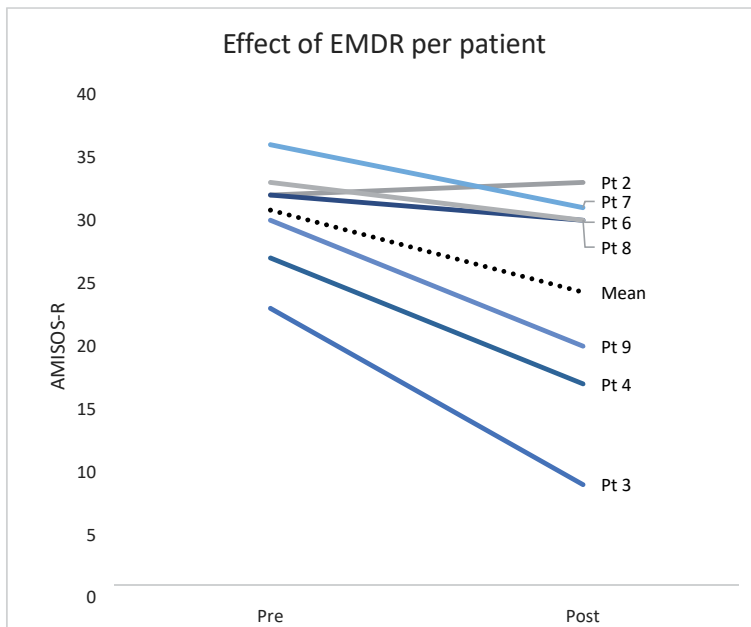


Figure 5.2. Effect of EMDR therapy on misophonia symptoms per treatment completer (n = 7).

5.3.3 Secondary outcomes

No significant effect was found on secondary outcomes (see Tables 5.2 and 5.3). However, SCL-90 mean scores decreased with 33% and patients reported fewer disabilities in all SDS subscales (work, family and social functioning) after EMDR-therapy.

In one patient who experienced neglect and aggression as negative childhood experiences, the IES was administered pre- and post-treatment. The scores of 23 (pre) to 3 (post) were mild and not indicative for PTSD. The difference in total score between pre and post was large, but IES was not used as an outcome measure in this study.

5.3.4 Qualitative outcomes: misophonia-related memories

In total 14 target misophonia-related memories were identified in eight patients, of which seven reported one or two targets and one patient reported three targets (for an overview of the targets, see Table 5.4). The number of EMDR sessions varied from 1 to 4 sessions of 60–90 minutes. Subjective Units of Distress (SUD) Scale scores at the start of the EMDR therapy varied from 5 to 10 and at the end of the therapy all SUD scores were decreased to 0. Two examples of target memories are: firstly, as an 11-year-old girl on holiday sharing a tent with her father, she had a panic attack after hyper focusing on his

Table 5.4. EMDR treatment information of the 10 included patients with misophonia

Patient	Included	EMDR sessions	Target memories	SUD scores PRE	AMISOS-R PRE	AMISOS-R POST	CGI-I
1	No	0	-	-	28	-	-
2	Yes	2	Misophonia related panic attack on holiday (onset) Suicidal ideations following a misophonia related fight (increase)	7 4	32	33	4
3	Yes	4	Tension during meal caused by aggressive father (onset) Misophonia symptoms during the silence following death of caring grandmother (onset) Fight with friend about binge eating as coping (increase)	10 8 8	23	9	2
4	Yes	1	Misophonia related fight in school and being punished by teacher (onset)	5	27	17	4
5	No	0	-	-	36	-	-
6	Yes	2	Misophonia related fight on holiday (onset)	9	32	30	4
7	Yes	3	Misophonia related fight at dining table followed by pulling hair and snacking (onset) 8-hour drive to a holiday destination with snacking family (increase)	10 7	36	31	3
8	Yes	3	Misophonia related fight with father (prototypical situation) Overhearing parents judgmental comments on misophonia (increase)	8 7	33	30	4
9	Yes	3	Misophonia triggered by a disabled child who sniffed in class (onset) Misophonia-related snapping at sibling during grandmothers' funeral (increase)	9 9	30	20	2
10	Yes	1	Almost choking on a candy on holiday (onset)	7	31	-	-

snoring with the experience she could not escape from the tent in the middle of the night (negative cognition: 'I am powerless'). Secondly, as a 10-year-old girl who could not grieve at her grandmother's funeral, because she was so bothered by the breathing sound of her crying brother that she snubbed him and felt terrible about herself (negative cognition: 'I am a bad person').

5.3.5 Adverse events and side effects

No adverse events were reported. Three patients showed misophonia symptoms during EMDR (e.g. expressing anger in reaction to the ticking of the clock or to breathing sounds of the therapist). Other mild side effects included fatigue or headaches in three patients, lasting for two days maximum. One patient suffered from suicidal ideations with intrusions of suicide during EMDR treatment after the first session. After the second EMDR session, the suicidal ideations disappeared. In the end, this patient (#3) profited most of all patients from EMDR.

5.4 Discussion

This is the first clinical sample study which examines the feasibility and effectiveness of EMDR for misophonia in eight patients. The results showed that EMDR focused on desensitizing emotionally disturbing memories related to the onset or worsening of misophonia symptoms and significantly reduced these symptoms.

Our positive outcome is in line with the results of the case report of Vollbehr and ten Broeke (2017). However, comparisons with their findings is difficult, because pre- and post-treatment assessments were missing and extra targets were used during EMDR therapy. Nevertheless, though no questionnaires were administered, Vollbehr and ten Broeke observed alleviation of symptoms of misophonia without full remission. Their patient was still sensitive to misophonia triggers, but his/her emotional reaction and avoidance behavior diminished substantially. Apart from desensitization of the identified misophonia-related target memories, their patient was also instructed to create an extremely inflated image of present triggers in imagination, after which desensitization of this image took place (Shapiro, 2018). In our study, no present triggers, nor an inflated image of present triggers were targeted. However, after having treated all misophonia-related target memories, the 'future template' procedure was used (Shapiro, 2018) to help patients visualizing successfully managing an anticipated future event with misophonia triggers.

In our trial, for two out of 10 patients, no explicit disturbing misophonia-related memories could be identified. For the remaining patients, their memories of the first (onset) misophonic experience and/or aggravating experiences were treated. The nature of these experiences were not evidently traumatic (corresponding to Criterion A of the DSM 5 PTSD criteria; American Psychiatric Association, 2013). They may be classified as unpleasant and disturbing, as is described in previous clinical case series (Ferreira, Harrison, & Fontenelle, 2013; Johnson et al., 2013). Target memories related to the onset or worsening of misophonia in childhood consisted in our pilot of situations of fierce arguments caused by their misophonia, maladaptive coping incidents such as bulimic outrage, suicidal ideations, or panic attacks when misophonia triggers could not be avoided (feeling overwhelmed and powerless). Target memories of the two full responders were easier to identify with the time-line method and had a higher level of observed distress than in the other patients. This could be one of the reasons why EMDR was more successful in these cases, as it is known that EMDR is more effective when the level of disturbance at the start of the session is high (Littel, Remijn, Tinga, Engelhard, & van den Hout, 2017). We did not examine predictors of treatment outcomes because of the small sample, but we hypothesize that the nature of target memories, participant characteristics or type of misophonia symptoms such as disgust, might predict treatment outcomes. Hypothesizing about a treatment mechanism is beyond the scope of this article.

Since we used only the time-line procedure to identify the target-memories for EMDR therapy, it remains unclear whether the two patients without target memories could have benefitted from EMDR. It would be interesting to add more explicit desensitization of 'present triggers' following desensitization of misophonia-related target memories, or use the creation of an extremely inflated image of present triggers (Rijkeboer, ten Broeke, & Koekbakker, 2016). We advise clinicians working with patients with misophonia to select and desensitize different types of targets, such as past traumatic or disturbing events, present triggers (e.g. inflated image), and future targets as well.

Treatment options are still limited for misophonia. So far, the only well-studied intervention for misophonia is G-CBT (Jager et al., 2021; Schröder et al., 2017). Compared to the results of the recent RCT of G-CBT, EMDR was less effective with a decrease of -6.14 vs -9.7 points (G-CBT) on the AMISOS-R post treatment, respectively, though an equal percentage of patients clinically improved, 38% with EMDR vs 37% with G-CBT on the CGI-I post treatment (Jager et al., 2021).

G-CBT and EMDR both have pros and cons. G-CBT as a multicomponent intervention offers more techniques from which patients can profit, extensive psychoeducation, more opportunity to practice under guidance, peer support, and support of loved ones. The empirical level of evidence is higher for G-CBT including a RCT with one 1-year follow-up, no adverse events were reported and patient's acceptability is high (Jager et al., 2021; Schröder et al., 2017). In this pilot study, EMDR therapy time was limited by a mean of 2.6 sessions of 1 to 1.5 hours (mean total of 3.9 hours) versus 8 (group) sessions of CBT of 3 hours (mean total of 24 hours) and could therefore be more cost-effective. As a con, apart from this case study, there is no empirical evidence for its effectivity. So far, indication to use EMDR was conditional, depending on the presence of emotionally disturbing target memories related to the onset or worsening of the symptoms.

Our results suggest as well that EMDR is an attractive alternative for non-responders to G-CBT. In this pilot study, patients on the waiting list for G-CBT ($n = 6$) and non-responders to G-CBT ($n = 4$) were included. Patients from both groups profited from EMDR (one patient waiting for CBT and 2 non-responders), but no post-hoc analyses could be performed because of the small sample size. We might speculate in which cases EMDR or G-CBT should be considered. First, EMDR might be preferred in cases where clear and emotionally disturbing target memories for EMDR can be identified. Secondly, when therapists can not provide (G-)CBT or patients are reluctant to participate in group therapy. Finally, if patients are in need of a quick fix for example, when a final exam in 2 weeks is hindered by misophonia symptoms.

5.4.1 Limitations and strengths

This is a small case series without a control group and therefore our study suffers from several important limitations. The lack of a control group prevents us from assessing the effects of time and of non-specific factors on misophonia symptoms. The small sample warrants caution in the generalization of the results. There was no follow-up assessment since half of the patients were on the waiting list for CBT and received CBT following EMDR, making it impossible to determine whether treatment gain was maintained over time. The inclusion of two subpopulations can be considered a limitation in this small sample. However, this does resemble clinical practice. All participants received EMDR from one therapist, the evaluator was not blind to treatment and treatment fidelity measures were not carried out, possibly leading to bias. More and larger studies are needed to confirm the effectiveness of EMDR therapy and to determine the average number of EMDR sessions needed to significantly reduce misophonia symptoms. Finally, because of the small sample

size, some tantalizing questions regarding prediction or comparative efficacy with CBT could not be answered.

On the other hand, our study is innovative, and the use of a case series was considered appropriate given the exploratory nature of the study. The sample had baseline characteristics comparable to larger misophonia samples (Jager et al., 2020; Rouw & Erfanian, 2018), leading to adequate external validity. We used a diagnostic clinical interview to assess the presence of disorders, an objective diagnostic assessment (CGI) and a manualized treatment. Data were also analyzed under restrictions of intention-to-treat analysis and missing values were imputed by LOCF, resulting in a conservative estimation of the effect.

5.4.2 Conclusions

In conclusion, the results of this study suggest that EMDR therapy is a promising and time-limited intervention in reducing misophonia symptoms, also in patients who were previously unable to benefit from evidence-based treatment (G-CBT). No adverse events were reported. Given the limitations due to the study design, the results should be considered preliminary. The next step would therefore be replication of the results in a larger RCT comparing EMDR therapy (with an extended target selection) with CBT and a waiting list or EMDR therapy as an add-on intervention to CBT, with a long-term follow-up.

Acknowledgments

We are very grateful to the 10 participating misophonia patients who relied on our expertise to try an innovative treatment. We thank Steven Meijer for his advice on the EMDR techniques at the beginning of this study. We thank Annemieke Polling for conducting the clinical interviews. Finally, we thank Isidoor Bergfeld for his advice on the statistics.

Conflicts of interests

The authors declare that there are no conflicts of interests.

Author contributions

I. Jager: conceptualization, data curation, formal analysis, investigation, methodology, and writing—original draft. N. Vulink: conceptualization, methodology, supervision, and writing—review and editing. C. de Roos: conceptualization, writing—review and editing. D. Denys: conceptualization, methodology, supervision, and writing—review and editing.

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6

General discussion

In this thesis I studied misophonia as a psychiatric disorder with corresponding diagnostic criteria and its psychological treatments. The overall objective of this thesis was to broaden our knowledge of this relative newly investigated phenomenon, by assessing a large sample, and increase treatment options for misophonia patients. The latter was done by evaluating an established treatment (G-CBT), as well as an innovative treatment for misophonia (EMDR therapy), and providing our treatment manual for G-CBT for clinicians and researchers.

I addressed the following research questions:

1. How many subjects referred with misophonia-like symptoms actually suffer from misophonia?
2. Should misophonia be approached from an audiological or psychiatric perspective?
3. Are specific psychological profiles, namely disgust sensitivity, autism-like traits and perfectionism associated with misophonia?
4. Is misophonia a distinct psychiatric disorder for which the diagnostic criteria, proposed by our research group in 2013 (Schröder et al.), can be confirmed and sharpened in a large sample?
5. What is the short-term efficacy of group cognitive behavioral therapy (G-CBT) on misophonia symptoms compared to a waiting list control group?
6. Does the reduction in misophonia symptoms achieved by G-CBT remain at one-year follow-up?
7. What is the rationale behind the interventions of G-CBT and what is the design of the treatment protocol?
8. What could be the effectiveness of eye movement desensitization and reprocessing (EMDR) therapy as a trauma-focused approach in treating misophonia symptoms?

This final chapter provides a summary of the main findings by answering the research questions and considers these findings in a broader perspective, including methodological considerations. The chapter concludes with the clinical implications of the results for clinical practice, an overview of the development in misophonia research and discusses possible directions for future research.

6.1 Summary of main findings

6.1.1 Summary - Part I

In chapter 2, I reviewed research on misophonia phenomenology for hypotheses to reevaluate the AMC 2013 misophonia criteria in a substantially larger sample. Previous research was limited, with 26 clinical research papers describing a total of 797 misophonia subjects. In our sample of referred subjects, the diagnosis of misophonia was confirmed in 74% (*research question 1*). In the other 26% diagnoses varied from primary autism spectrum conditions (ASC), primary attention-deficit (hyperactivity) disorder (AD(H)D), various primary diagnoses on Axis II and subjects without a DSM-IV diagnosis. Subjects with a primary obsessive-compulsive personality disorder (OCPD) or ASC often do not consider their reaction to be out of proportion, and therefore OCPD or ASC are important differential diagnoses for misophonia.

In the misophonia subjects no somatic disorders were found with a physical and neurological examination and a blood screening. Audiometry performed in a random subgroup showed normal hearing and a low percentage of comorbid disorders such as tinnitus (2%) and hyperacusis (1%) was found. These results do not support an approach from a somatic (audiological) perspective, but evidence was found for an approach from a psychiatric approach (*research question 2*).

Our thorough psychiatric clinical assessment showed a psychiatric comorbidity of Axis I disorders similar to the general population in the Netherlands, except for mood disorders, AD(H)D and the ASC (each 2–3 times as prevalent). The prevalence rate of comorbid DSM-IV Axis II disorders was higher, OCPD traits were found in a quarter of the subjects. This latter finding was supported by questionnaires; clinical perfectionism was seen in 66–97% of the subjects. Furthermore, from a psychological perspective, misophonia can be seen as an independent construct. I investigated associations between misophonia symptoms and specific psychological profiles, which have been suggested in the literature to have a link with misophonia (Schröder et al., 2013; Taylor et al., 2014; Danesh et al., 2015; Tavassoli et al., 2017). No association was found between misophonia symptoms and disgust sensitivity, misophonia symptoms and autism like traits, or misophonia and perfectionism (*research question 3*).

The analysis of this large sample confirmed misophonia as a distinct psychiatric disorder on account of: similar phenomenology amongst subjects, similar age of onset around the age of 13, uniform course with a gradual onset and heavy impairment in quality of life (especially impaired functioning in family relations), severity of misophonia symptoms (which was

negatively correlated with quality of life), absence of psychiatric comorbidity, and positive family history for similar symptoms in one third of the sample. The detailed investigation of misophonia triggers and analysis of the nature of the responses in the sample led to a confirmation and sharpening of the AMC 2013 criteria, see Table 6.1 (*research question 4*).

Table 6.1. Amsterdam UMC 2020 revised diagnostic criteria for misophonia

Amsterdam UMC 2020 revised criteria for misophonia	
A-R.	Preoccupation with a specific auditory, visual or sensory cue, which is predominantly induced by another person. It is required that oral or nasal sounds are a trigger.
B-R.	Cues evoke intense feelings of irritation, anger and/or disgust of which the individual recognizes it is excessive, unreasonable or out of proportion to the circumstances.
C-R.	Since emotions trigger an impulsive aversive physical reaction, the individual experiences a profound sense of loss of self-control with rare but potentially aggressive outbursts.
D-R.	The individual actively avoids situations in which triggers occur or endures triggers with intense discomfort, irritation, anger or disgust.
E-R.	The irritation, anger, disgust or avoidance causes significant distress and/or significant interference in the individual's day-to-day life. For example, it is impossible to eat together, work in an open office space or live together.
F-R.	The irritation, anger, disgust and avoidance are not better explained by another disorder, such as an Autism Spectrum Condition (e.g. a general hypersensitivity or hyper arousal to all sensory stimuli) or Attention Deficit Hyperactivity Disorder (e.g. attention problems with high distractibility in general).

The most important finding is the confirmation of the main criteria of Schröder et al. (2013). In our larger sample we identified similar emotional reactions (irritation, anger and disgust with a sense of loss of self-control with rare but potentially aggressive outbursts), a similar egodystonic view on these reactions and similar coping behavior and impairment in day-to-day life.

Two significant alterations in the diagnostic criteria were made based on our results (criterion A-R). First, I found evidence for non-auditory triggers in 78% of our sample, but auditory triggers remained primary triggers. All subjects reported either oral or nasal sounds as a trigger. This led us to conclude other triggers, such as visual triggers (e.g., scratching) or non-human triggers (e.g., air-conditioning sound), can be a part of misophonia, but the presence of oral or nasal trigger sounds is mandatory for diagnosing misophonia. Oral and nasal triggers are also described as the most important triggers in the onset of misophonia. Furthermore, this requirement enables clinicians to better distinguish misophonia patients with subjects with a more general disturbance of sounds, such as noise sensitivity

or sensory over-responsivity (which also occurs in a normal population). Secondly, even though anxiety was frequently described as a response to misophonia triggers (Bruxner, 2016; Dozier, 2017; Wu et al., 2014; Zhou et al., 2017), our subjects did not report anxiety as a prompt reaction to a trigger. Only five subjects (1%) reported secondary anxiety, following anger or disgust. They did however experience anticipatory anxiety and physical stress. These symptoms were potentially misinterpreted as a primary response, because other samples were merely investigated with the use of questionnaires instead of clinical psychiatric assessments. The anticipatory anxiety and physical stress were associated with preoccupation with misophonia triggers. Approximately all subjects in our sample reported hyper focus (previous also described by Edelstein et al., 2013), which led to our appraisal of preoccupation as a core symptom of misophonia.

In sum, based on the largest qualitative and quantitative description of a sample of misophonia subjects so far (N=575), I define misophonia as a psychiatric disorder characterized by an intense emotional reaction of irritation, anger, and often disgust elicited by specific auditory, visual or sensory triggers predominantly induced by another person, resulting in preoccupation and avoidance.

6.1.2 Summary – Part II

In chapter 3, the efficacy of group-CBT on misophonia symptoms was studied. In this first randomized trial for misophonia a sample of Dutch misophonia outpatients (N=54) were randomly assigned to 3 months of weekly G-CBT or a waiting list. Assessments were carried out at baseline, after 3 months (following G-CBT or waiting list), 6 months (after cross-over), and 15/18 months (1-year follow-up). G-CBT consisted of task concentration and arousal reduction, positive affect labeling, and stimulus manipulation. Co- primary outcomes were: symptom severity (assessed by the Amsterdam Misophonia Scale-Revised, AMISOS-R) and clinical improvement (on the Clinical Global Impression- Improvement, CGI-I). Secondary outcomes were: self-assessed ratings of general psychopathology (Symptom Checklist-90-Revised, SCL-90-R) and quality of life (five-dimensional EuroQoL, EQ5-D; Sheehan Disability Scale, SDS; WHO Quality of Life-BREF, WHOQoL-BREF).

I found three months of G-CBT reduced misophonia symptoms compared to a waiting list. Clinical improvement was found in 56% of all completers (37% intention-to-treat) compared to 0% in the waiting list. General mental dysfunction decreased and patients reported less disabilities in family and social functioning after G-CBT than after waiting list as well (*research question 5*). On top of these measurements, group therapists rated

74% of all completers clinically improved ($\text{CGI-I} < 3$). 37% of the completers did not meet diagnostic criteria for misophonia any more post-treatment. Treatment acceptability was quite high; 65% was (very) satisfied and 25% was neutral, and patients rated the treatment with an average of 6.7 out of 10.

Importantly, twelve months after the end of treatment the considerable improvement in misophonia symptoms was sustained. The effect of G-CBT was maintained at 1-year follow-up on both primary and secondary outcomes (*research question 6*). One of the secondary outcomes showed even further improvement; patients reported less problems in family functioning after one year than directly post treatment.

Our findings were in line with the positive effect of CBT for misophonia previously found in case reports (Bernstein et al., 2013; Dozier, 2015; McGuire et al., 2015; Muller, Khemlani-Patel, & Neziroglu, 2018), a previous open-label trial for G-CBT in our center (Schröder, et al., 2017), a single case study based on our G-CBT protocol (Roushani & Mehrabizadeh Honarmand, 2021) and extends their findings. This RCT provides evidence for the efficacy of G-CBT for misophonia and can serve as a stepping stone to implement CBT in clinical practice.

Chapter 4 consists of the treatment protocol for G-CBT for misophonia with the aim of further implementation in clinical practice and research. This chapter presents the biopsychosocial explanatory model for misophonia with hyper focus as a core symptom, through the description of a single clinical case. An overview of the protocol is provided with the description of the four main components: stimulus manipulation, positive affect labeling, arousal reduction, and task concentration exercises. Also, two smaller elements are described: re-evaluating (eating) norms and stress reduction. The treatment has three phases; the assessment and engagement phase, the change strategy phase and the consolidation phase. The phased structure is outlined and therapeutic principles and values are illustrated. Throughout this chapter the single clinical case is used to illustrate all six interventions, as well as the specific therapeutic principles in the phased structure. Last, a detailed description of each session is provided (*research question 7*).

In chapter 5, I studied an innovative treatment for misophonia in a pilot study of case series. The aim of this pilot study was to assess the feasibility and effectiveness of eye movement desensitization and reprocessing (EMDR) therapy as a trauma-focused approach in treating misophonia symptoms. A sample of Dutch misophonia outpatients ($N=10$) were assessed pre- and post-treatment. Participants were either on the waiting list for G-CBT or non-responders to G-CBT. EMDR therapy was focused on misophonia-related emotionally

disturbing memories and conducted according to the standard eight-phase protocol by Shapiro using the Dutch translation (Shapiro, 2001; De Jongh & ten Broeke, 2019). Memories were processed until Subjective Units of Distress Scale (SUD) scores were zero, using eye movements as the dual-attention stimulus. The memories EMDR focused on were identified following a standardized search strategy called time-line path in the first session (first method; de Jongh et al., 2010). Co-primary outcomes were: symptom severity assessed by the Amsterdam Misophonia Scale-Revised (AMISOS-R) and clinical improvement on the Clinical Global Impression-Improvement (CGI-I). Secondary outcomes were: self-assessed ratings of general psychopathology with the Symptom Checklist-90-Revised (SCL-90-R) and quality of life with the Sheehan Disability Scale (SDS).

In two out of ten patients, no explicit disturbing misophonia-related memories could be identified. The results of eight remaining patients showed that EMDR, focused on desensitizing emotionally disturbing memories related to the onset or worsening of misophonia symptoms, significantly reduced these symptoms in a mean of 2.6 sessions of 60–90 minutes. Three of eight patients showed clinically significant improvement measured with the CGI-I, including patients who were previously unable to benefit from evidence-based treatment (G-CBT). No significant effect on secondary outcomes was found. The target memories related to the onset or worsening of misophonia in childhood were not evidently traumatic, but were unpleasant and disturbing, for example: situations of fierce arguments caused by their misophonia, maladaptive coping incidents such as bulimic outrage, suicidal ideations, or panic attacks when misophonia triggers could not be avoided. Target memories of the responders were easier to identify with the time-line method and had a higher level of observed distress than in the other patients. These results suggest that EMDR therapy focused on emotionally disturbing misophonia-related memories can reduce misophonia symptoms in limited time (*research question 8*).

6.2 Strengths and methodological considerations

This thesis includes one controlled clinical study in the form of a RCT with a controlled intervention using a manualized treatment protocol. All participating therapists were highly familiar with the protocol, because it was used in all clinical misophonia care at our department, and furthermore held regular intervention. This led to high treatment fidelity. The intervention was comparable in all treatment groups, because the study was situated in one center and only a few, experienced therapists were involved. The treatment team was fairly similar to the team involved in our previous open-label study and included some

of the authors of the manualized treatment protocol (van Loon et al., 2019). Assessments were thorough with the use of blinded observer ratings, clinical interviews by both therapists and an observer, diverse self-reports, multiple measures during treatment, and a measure at 1-year follow-up. The other clinical study included in this thesis is a pilot study with an exploratory nature, providing a much lower level of evidence. This small case series without a control group suffers from several important limitations due to the study design. Finally, this thesis includes a sample study, which is superior to all phenomenological studies on misophonia so far. It is exceptional in both quantity, considering the sample size of 575 misophonia subjects and the use of 17 psychological questionnaires, as in quality, considering the thorough clinical psychiatric examinations and somatic assessment with audiometry. For the specific methodological strengths and weaknesses of each study I refer to the discussion section of chapter 2, 3 and 5. I will hereby point out the most important methodological considerations of this thesis in general.

As mentioned in the general introduction, the international research field of misophonia is divided. The misophonia treatment facility of the Amsterdam UMC Psychiatry department is the only center in Europe with the expertise of diagnosing and treating misophonia. Even though patients from all over the Netherlands (and regularly from surrounding countries, such as Belgium or the United Kingdom as well) seek help at our center, all studies are performed at one site. Participation in international misophonia research consortia has been hindered by the conflicting views on misophonia. The lack of (international) cooperation could have led to confirmation bias and limits generalization of the results.

When I started my treatment studies, no validated questionnaires for misophonia symptom severity existed. For all of our studies I used the AMISOS-R, which was developed at our department from the revision of the A-MISO-S (Schröder, Vulink, & Denys, 2013). The A-MISO-S is translated and validated in English (Naylor, Caimino, Scutt, Hoare, & Baguley, 2021). The AMISOS-R is a good scale, is almost fully validated (publication in preparation) and I used the CGI-I as a co-primary outcome in our clinical studies to aid interpretation of the clinical results. In the last years the AMISOS-R was translated into five different languages. A limitation of all studies in this thesis however, is the lack of a fully validated Dutch misophonia questionnaire. While the AMISOS-R was still in the process of validation, several new misophonia symptom questionnaires have been developed and validated, such as the MisoQuest (Siepsiak, Śliwerski, & Łukasz Dragan, 2020) and the S-Five (Vitoratou, Hayes, Uglik-Marucha, & Gregory, 2020). Validated questionnaires contribute to the maturation of misophonia research.

Finally, the scope of this thesis is misophonia in adults, so our research on misophonia in children and adolescents is excluded. Our department has extensive experience with misophonia in children and especially in adolescents in the age of 12–18 years. We have diagnosed and treated over 300 teenagers and their family. The findings of our research (e.g. the master thesis on the efficacy of G-CBT in children) and my own clinical experience treating misophonia in this age group has broadened my knowledge and enriched my view on misophonia. Especially in my role as therapist of our ‘miso-kids’ groups I have gained knowledge on the phenomenology in children, but also witnessed the impact misophonia can have on family life with parents feeling powerless by recurring conflicts and on self-image in these children. Unfortunately, this scientific knowledge and clinical experience is not included in this thesis.

6.3 Clinical implications

Despite the mentioned limitations, this thesis allows us to explore some clinical implications. We have a decade of experience in diagnosing and treating misophonia at our center. Our study of the phenomenology of 575 misophonia patients has confirmed the leading role of the center in misophonia research worldwide. The clinical implication of the indisputable evidence for misophonia as a psychiatric disorder is significant. Due to the absence of a diagnosis for the symptoms of misophonia until 15 years ago, the suffering of misophonia patients was hidden. As long as misophonia is not included in our current diagnosis system, the identification of the disorder will remain limited, and therefore the suffering of misophonia patients will remain partly hidden. The recognition of misophonia as a distinct diagnosis will hopefully lead to more treatment options for misophonia patients. In psychiatric assessments, as well as in the psycho-education phase in group therapy, I have witnessed the impact of the recognition of misophonia symptoms. Patients realize they are not ‘crazy’ or ‘hard to deal with’, but instead suffer from a specific disorder of which the symptoms are maintained by hyper focus, maladaptive coping behavior and systemic consequences.

On the other hand, I am aware of the disadvantages of over-diagnosing and of the current paradigm change. The development from evidence-based practiced symptom reduction, with emphasis on DSM classification, towards tailored trans-syndromal symptom reduction is interesting and valuable, but still in its infancy. Although important research already has been done, e.g., Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2017) or the Research Domain Criteria (RDoC; Insel, 2014) which has been, to some extent, also

translated into clinical practice (for instance Hayes & Hofmann, 2018), still the majority of research and clinical work is diagnosis-based. Therefore, it is suitable to add misophonia as a psychiatric diagnosis, in order for clinicians to identify the clinical phenomenology and treat misophonia, and for researchers to see eye to eye. Despite the progression towards process-based interventions, as a scientist practitioner and CBT supervisor, I would not let go of our valuable diagnosis-based interventions.

Our clinical trials add substantial evidence to the effectiveness of G-CBT for misophonia and feasibility and potential effectiveness of EMDR therapy. The impact of misophonia on patients' day-to-day life is undeniable. Even though the influence on working life remains limited with only 5% on sick leave (chapter 2), family - and social life suffer substantially. Misophonia patients often have an intense emotional response towards loved ones inducing misophonia triggers. Conflicts with their loved ones and avoidance of social gatherings effect the quality of life of misophonia patients. Our clinical trials have improved treatment options for misophonia patients. The publishing of our treatment manual for G-CBT contributes to this aim as well.

6.4 Misophonia research

6.4.1 Search July 2015

As described in the General introduction, as a starting point for my research I performed a literature search in July 2015. I used a nonsystematic search strategy with the search term 'Misophonia' in Pubmed. Removing all textbooks and doubles, merely 25 research articles with misophonia as a main topic were found (see Figure 6.1).

6.4.2 Search May 2018

For the purpose of our article about the phenomenology and possible revision of the diagnostic criteria, I performed a more systematical search for a review with the research question: What is the phenomenology of misophonia and are there indications for a revision of the 2013 AMC criteria? I searched Embase, Pubmed and Psycinfo info to identify studies published in English in scientific journals (no textbooks or retracted papers). The search term was 'Misophonia'.

In total I found 121 studies and after the removing of 63 doubles, 58 articles remained. I first screened titles and abstracts and excluded based on relevance and language. Then

the remaining full text articles were screened. In the end, 40 articles were included (see Figure 6.1).

In this search I merely focused on the available research on the phenomenology and nature of misophonia and the diagnostic criteria. I only included articles providing descriptions of misophonia subjects with a transparent procedure for diagnosing. Finally, 26 articles were included in the semi systematic search used for the article describing 797 misophonia patients in total (see Supplementary Table S2.1, chapter 2). A fifth was examined by the AMC group (Eijsker et al., 2017; Schröder et al., 2013; 2014; 2015; 2017) using a systematic medical and psychiatric examination and questionnaires. In most described subjects a systematic clinical interview was missing. Various misophonia symptom questionnaires were used, none of which were validated. The conclusions from most studies, especially concerning psychiatric co-morbidity, should consequently be interpreted with caution.

The AMC diagnostic criteria were confirmed in the majority of studies. They were partially confirmed in other studies, with the addition of anxiety and/or physical discomfort. In several studies other trigger stimuli, in particular visual triggers or non-human triggers, were mentioned. These results provided the base of our research on the phenomenology (Thesis Part I).

6.4.3 Search March 2021

Using the same search strategy in March 2021, 228 articles are found. After removing 106 doubles, 122 articles remained, of which 91 include 'misophonia' in the title. After screening titles and abstracts, the remaining full text articles were screened. Reasons for exclusion were: other languages with only an English abstract (6), audiological research concerning tinnitus or hyperacusis (13), dissertations (3), a column (1), manuscript not available (3) and other main topics (9). Finally, 86 articles were included (see Figure 6.1). In Appendix 6.1 all included articles are displayed.

The 86 articles found, have been classified according to the previous searches in 2015 and 2018. Noticeable is the development in research in the last years from the description of the phenomenology of misophonia (e.g., Wu, Lewin, Murphy, & Storch, 2014) to investigating associated symptoms (e.g., McKay, Kim, Mancusi, Storch, & Spankovich, 2018), underlying mechanisms (Cassello-Robbins et al., 2020) and possible treatment interventions (e.g., Wiese, Wojcik, & Storch, 2021).

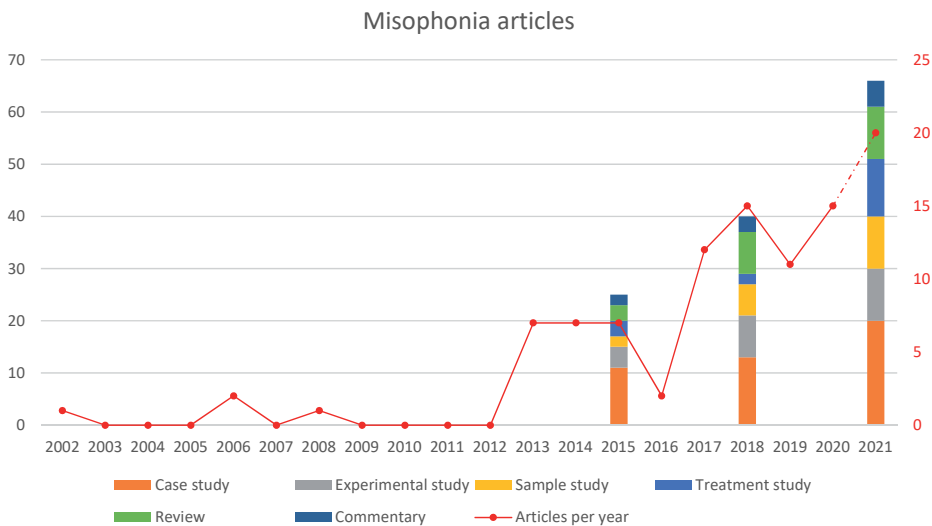


Figure 6.1. Three searches of misophonia literature.

Concerning the diagnostics (Thesis Part I), it is striking that from different specialized psychiatric settings, for example tic disorders, eating disorders or autism specter disorders, research articles have emerged with the question whether misophonia is really a distinct disorder (Robinson, Hedderly, Conte, Malik, & Cardona, 2018; Kluckow, Telfer, & Abraham, 2014; Williams, He, Cascio, & Woynaroski, 2021) or with the suggestion to apply corresponding specific treatments, for example the use of schema focused therapy (Natalini, Dimaggio, Varakliotis, Fioretti, & Eibenstein, 2020). The most remarkable finding was from Jastreboff & Jastreboff (2014) who diagnosed 55% (92% of the 60% with comorbid decreased sound tolerance) of his tinnitus patients with misophonia as well. Unfortunately, it was unclear on what grounds these misophonia diagnoses were established. I have discovered no evidence in the found articles to question misophonia as a distinct disorder. Since the prevalence rate of misophonia is possibly 6 to 12%, misophonia is also present in other psychiatric patient groups. I do not consider coincidental comorbidity a sound reason to question misophonia as a distinct disorder and/or to adjust treatment.

Recently a Delphi Process study tried to settle the disagreement amongst misophonia researchers about the definition of misophonia (Swedo et al., 2021). This led to an agreement of experts on at least 80% of the consensus definition. Although there was criticism on our proposed criteria and other definitions have been proposed as well (e.g., Dozier, Lopez, & Pearson, 2017), eventually this consensus definition corresponds highly

to the Amsterdam UMC 2020 revised criteria. Comparing our proposed revised diagnostic criteria with this definition I find our criteria (see Table 6.1) are mostly adopted:

- Criterion A-R is similar to the consensus definition, accept our requirement of oral or nasal sounds is stronger defined than the definition of Swedo et al: “Sounds associated with oral functions are among the most often reported ... Nasal sounds, such as breathing and sniffing, often serve as triggers as well.”
- Criterion B-R is extended in the consensus definition with two emotional reactions, anger and rage. Again, our criterion is defined stronger; Swedo et al. describe some (instead of all) individuals with misophonia are aware that their reactions are disproportionate.
- Criterion C-R is also included in the consensus definition, accept for the ‘profound sense of loss of self-control’.
- Criterion D-R is fully included in the consensus definition. Swedo et al. also describe several additional specific behavioral strategies individuals with misophonia use to mitigate their reactions to triggers.
- Criterion E-R is also fully included in the consensus definition. Swedo et al. describe misophonia can result in significant distress, interfere with day-to-day life, and may contribute to mental health problems. Also various functional and social impairments that range from mild to severe are described.
- Criterion F-R is included as well. Swedo et al. however do not provide differential diagnoses, but describe ASC and ADHD (amongst other disorders) as possible comorbid disorders.

In conclusion, almost all of our revised criteria are a part of this consensus definition, but the psychiatric nature of the disorder is not included. This has a political background, caused by resistance of some research groups and patient associations. However, the definition is a confirmation of our research and serves as a premise for future research and more collaboration amongst the conflicting research groups.

The main findings concerning the treatment of misophonia (Thesis Part II) were as follows. In 22 of the 86 articles psychotherapeutic treatment interventions were described. The 22 selected studies varied in the extent in which the interventions were described. Results of the experimental studies are beyond the scope of this paragraph, although some findings have implications for treatment, for instance Samersmit, Saal, & Davidenko (2019). Some descriptions of misophonia treatment were brief, as in some case studies (e.g., Lugg, 2021; Kamody & Del Conte, 2017) and in short commentaries (Schneider & Arch, 2015; Webber &

Storch, 2015) and some were extensive (e.g., Frank & McKay, 2019). Treatment strategies varied consisted mostly of CBT, DBT, or a combination of both CBT and DBT, for example described by Wiese, Wojcik, & Storch (2021). Also some specific treatment strategies used for comorbid disorders were proposed, such as exposure and response prevention (ERP) for misophonia combined with OCD (Reid, Guzick, Gernand, & Olsen, 2016) or applied behavioral analysis (ABA) therapy for misophonia combined with autism spectrum disorder (Haq, Alresheed, & Tu, 2020). Particularly the treatment paradigm of Frank & McKay (2019) was very similar to and partly based on our treatment protocol, applying exposure with inhibitory learning strategies, using counterconditioning and stimulus manipulation, and applying stress management. Furthermore, only two articles described drug treatment in misophonia. None of the found treatment studies used a trauma focused approach.

The three searches I performed on misophonia research in the last six years illustrates the increased scientific interest in misophonia. Figure 6.1 shows the exponential growth of research articles concerning misophonia as major topic. Also, in the last years more articles have been published in journals with a higher impact factor, and my sample study (chapter 2) was singled out by NEJM Journal Watch (Yager, 2020). The almost 160,000 views of the first sample study of our research group (Schröder, Vulink, & Denys, 2013) underlines the impact of misophonia research as well. However, considering the below level of qualitative research much more and better research is needed.

6.5 Future research

This thesis builds on the founding research on misophonia at the psychiatry department of the Amsterdam UMC, by my predecessor Schröder, and my supervisors Vulink and Denys. I wish to think I have contributed to the level of evidence with this thesis, including the first RCT worldwide on G-CBT for misophonia as a milestone and the revision of the diagnostic criteria based on a profound qualitative and quantitative misophonia patient sample.

International confirmation of the Amsterdam UMC revised criteria is needed, using international multi-center studies. A multi-disciplinary approach, especially including psychiatry, audiology, and psychology, would be preferable to reach agreement concerning the etiology, which is still missing in the consensus definition of Swedo et al. (2021).

The lack of knowledge regarding the treatment of misophonia is striking. Most evidence is anecdotal or preliminary. In future research attention should especially be paid to treatment studies. The results presented in this doctoral dissertation are encouraging, but only provide

a first support for these treatments. Since we were the only research group to report on G-CBT, the results of our clinical trial should be replicated in other samples of misophonia patients. Therefore, I have also published our treatment manual (chapter 4). Additionally, more and larger studies are needed to confirm the effect of EMDR therapy on misophonia symptoms. Replication of the results in a larger RCT is needed to gain understanding of predictive factors, comparative efficacy and long term effects. In the discussion sections of our two trials I have made specific recommendations for future research on G-CBT and EMDR therapy. Also other proposed treatments, like tinnitus retraining therapy for misophonia (Jastreboff & Jastreboff, 2014) should be investigated in well-designed studies. Research should focus on other innovative interventions as well. Lastly, it is important to investigate misophonia treatment in children. Hopefully, this will lead to further improvement of care for misophonia patients and their families.

6.6 Concluding remarks

This thesis has two main aims. First, to review and increase knowledge concerning the phenomenology of misophonia, with a particular focus on comorbidity and demographics in order to formulate revised diagnostic criteria (Part I). Second, to investigate different treatments for misophonia, specifically group cognitive behavioral therapy (G-CBT) and eye movement and desensitization reprocessing (EMDR) therapy, and describe the treatment protocol for G-CBT (Part II).

This project has been a combination of pioneering, reevaluation and perseverance. My initial assumptions, which I have described in the credential section of the General introduction of this thesis, developed in hypotheses which I tested and finally I have revised my opinion on misophonia. Perhaps this also applies to the reader of this thesis.

6.7 References

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Appendix 6.1 Search March, 2021

Year	Authors	Title	Type	Journal	DOI
2002	Jastreboff MM, Jastreboff PJ	Decreased sound tolerance and tinnitus retraining therapy (TRT)	Treatment study	Austr and New Zealand J Audiology	doi: 10.1375/audi.24.2.74.31105
2006	Jastreboff PJ, Jastreboff MM	Tinnitus retraining therapy: A different view on tinnitus	Treatment study	ORL J Otorhinolaryngol Relat Spec	doi: 10.1159/000090487
2006	Veale D	A compelling desire for deafness	Case study	J Deaf Stud Deaf Educ	doi: 10.1093/deafed/enj043
2008	Hadjipavlou G, Baer S, Lau A, Howard A	Selective sound intolerance and emotional distress: What every clinician should hear	Case study	Psychosom Med	doi: 10.1097/PSY.0b013e318180edc2
2013	Bernstein, Rosemary E, Angell KL, Dehle CM	A brief course of cognitive behavioural therapy for the treatment of misophonia: A case example	Case study	Cogn Behav Ther	doi: 10.1017/S1754470X13000172
2013	Edelstein M, Brang D, Rouw R, Ramachandran VS	Misophonia: Physiological investigations and case descriptions	Experimental study	Front Hum Neurosci	doi: 10.3389/fnhum.2013.00296
2013	Ferreira GM, Harrison BJ, Fontenelle LF	Hatred of sounds: Misophonic disorder or just an underreported psychiatric symptom?	Case study	Ann Clin Psychiatry	PMID: 24199217
2013	Johnson PL, Webber TA, Wu MS, Lewin AB, Murphy TK, Storch EA	When selective audiovisual stimuli become unbearable: A case series on pediatric misophonia	Case study	Neuropsychiatry	doi: 10.2217/npv.13.70
2013	Neal M, Cavanna AE	Selective sound sensitivity syndrome (misophonia) in a patient with Tourette syndrome	Case study	J Neuropsychiatry Clin Neurosci	doi: 10.1176/appi.neuropsych.11100235
2013	Schröder A, Vulink N, Denys D	Misophonia: diagnostic criteria for a new psychiatric disorder	Sample study	PLoS One	doi: 10.1186/1744-7061-0054706

Year	Authors	Title	Type	Journal	DOI
2013	Schroder AE, Mazaheri A, Petropoulos D, Soto V, Smolders R, Vulink NCC, et al	A diminished mismatch negativity response in misophonia, a potential marker for aggressive impulsivity	Experimental study	Eur Neuropsychopharmacol	doi: 10.1016/S0924-977X%2813%2970269-4
2014	Cavanna AE	What is misophonia and how can we treat it?	Review	Expert Rev Neurother	doi: 10.1586/14737175.2014.892418
2014	Duddy DF, Oeding KAM	Misophonia: An overview	Review	Semin Hear	doi: 10.1055/s-0034-1372525
2014	Jastreboff PJ, Jastreboff MM	Treatments for decreased sound tolerance (hyperacusis and misophonia)	Treatment study	Semin Hear	doi: 10.1055/s-0034-1372527
2014	Kluckow H, Telfer J, Abraham S	Should we screen for misophonia in patients with eating disorders? A report of three cases	Case study	Int J Eat Disord	doi: 10.1002/eat.22245
2014	Schröder A, van Diepen R, Mazaheri A, Petropoulos-Petalas D, Soto de Arnesti V, Vulink N, Denys D	Diminished n1 auditory evoked potentials to oddball stimuli in misophonia patients	Experimental study	Front Behav Neurosci	doi: 10.3389/fnbeh.2014.00123
2014	Webber TA, Johnson PL, Storch EA	Pediatric misophonia with comorbid obsessive-compulsive spectrum disorders	Case study	Gen Hosp Psychiatry	doi: 10.1016/j.genhosppsych.2013.10.018
2014	Wu MS, Lewin AB, Murphy TK, Storch EA	Misophonia: incidence, phenomenology, and clinical correlates in an undergraduate student sample	Sample study	J Clin Psychol	doi: 10.1002/jclp.22098
2015	Boyce PM	A young woman with noise intolerance	Case study	Med Today	ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed16&NEWS=N&AN=605373508
2015	Cavanna AE, Seri S	Misophonia: Current perspectives	Review	Neuropsychiatr Dis Treat	doi: 10.2147/NDT.S81438

Year	Authors	Title	Type	Journal	DOI
2015	Dozier TH	Counterconditioning treatment for misophonia	Case study	Clin Case Stud	doi: 10.1177/1534650114566924
2015	McGuire JF, Wu MS, Storch EA	Cognitive-behavioral therapy for 2 youths with misophonia	Case study	J Clin Psychiatry	doi: 10.4088/JCP.14cr09343
2015	Schneider RL, Arch JJ	Letter to the editor: Potential treatment targets for misophonia	Commentary	Gen Hosp Psychiatry	doi: 10.1016/j.genhosppsych.2015.03.020
2015	Schroder A, San Giorgi R, Van Wingen G, Vulink N, Denys D	Impulsive aggression in misophonia: Results from a functional magnetic resonance imaging study	Experimental study	Eur Neuropsychopharmacol	ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed16&NEWS=N&AN=72129465
2015	Webber TA, Storch EA	Toward a theoretical model of misophonia	Commentary	Gen Hosp Psychiatry	doi: 10.1016/j.genhosppsych.2015.03.019
2016	Bruxner G	Mastication rage': A review of misophonia - an under-recognised symptom of psychiatric relevance?	Review	Australas Psychiatry	doi: 10.1177/1039856215613010
2016	Reid AM, Guzik AG, Gernand A, Olsen B	Intensive cognitive-behavioral therapy for comorbid misophonic and obsessive-compulsive symptoms: A systematic case study	Case study	J Obsessive Compuls Relat Disord	doi: 10.1016/j.jocrd.2016.04.009
2017	Dozier TH, Lopez M, Pearson C	Proposed diagnostic criteria for misophonia: A multisensory conditioned aversive reflex disorder	Review	Front Psychol	doi: 10.3389/fpsyg.2017.01975
2017	Dozier, Thomas H, Morrison, KL	Phenomenology of misophonia: Initial physical and emotional responses	Experimental study	Am J Psychol	doi: 10.5406/amerjpsyc.130.4.0431
2017	Eijlker N, Schroder A, Van Wingen G, Denys D	Response inhibition in misophonia	Experimental study	Eur Neuropsychopharmacol	ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed18&NEWS=N&AN=619298701

Year	Authors	Title	Type	Journal	DOI
2017	Kamody RC, Del Conte GS	Using dialectical behavior therapy to treat misophonia in adolescence	Case study	Prim Care Companion CNS Disord	doi: 10.4088/PCC.17l02105
2017	Kumar S, Tansley-Hancock O, Sedley W, Winston JS, Callaghan MF, Allen M, Cope TE, Gander PE, Bamiou DE, Griffiths TD	The brain basis for misophonia	Experimental study	Curr Biol	doi: 10.1016/j.cub.2016.12.048
2017	Kumar S, Griffiths TD	Response: Commentary: The brain basis for misophonia	Commentary	Front Behav Neurosci	doi: 10.3389/fnbeh.2017.00127
2017	Schneider, Rebecca L, Arch JJ	Case study: A novel application of mindfulness- and acceptance-based components to treat misophonia	Case study	J Contextual Behav Sci	doi.org/10.1016/j.jcbs.2017.04.003
2017	Schröder A, van Wingen G, Vulink NC, Denys D	Commentary: The brain basis for misophonia	Commentary	Front Behav Neurosci	doi: 10.3389/fnbeh.2017.00111
2017	Schröder AE, Vulink NC, van Loon AJ, Denys DA	Cognitive behavioral therapy is effective in misophonia: An open trial	Treatment study	J Affect Disord	doi: 10.1016/j.jad.2017.04.017
2017	Taylor S	Misophonia: A new mental disorder?	Review	Med Hypotheses	doi: 10.1016/j.mehy.2017.05.003
2017	Tunc S, Basbug HS	An extreme physical reaction in misophonia: Stop smacking your mouth!	Case study	Psychiatr Clin Psychopharmacol	doi.org/10.1080/24750573.2017.1354656
2017	Zhou X, Wu MS, Storch EA	Misophonia symptoms among Chinese university students: Incidence, associated impairment, and clinical correlates	Sample study	J Obsessive Compuls Relat Disord	doi.org/10.1016/j.jocrd.2017.05.001

Year	Authors	Title	Type	Journal	DOI
2018	Aazh H, Knipper M, Danesh AA, Cavanna AE, Andersson L, Paulin J, Schecklmann M, Heinonen-Guzejev M, Moore BCJ	Insights from the third international conference on hyperacusis: Causes, evaluation, diagnosis, and treatment	Review	Noise Health	doi: 10.4103/nah.NAH_2_18
2018	Altinoz AE, Unal NE, Altinoz ST	The effectiveness of Cognitive Behavioral Psychotherapy in misophonia: A case report	Case study	Klinik Psikiyatri Dergisi	doi: 10.5505/kpd.2018.18480
2018	Brout JJ, Edelstein M, Erfanian M, Mannino M, Miller LJ, Rouw R, Kumar S, Rosenthal MZ	Investigating misophonia: A review of the empirical literature, clinical implications, and a research agenda	Review	Front Neurosci	doi: 10.3389/fnins.2018.00036
2018	Cusack SE, Cash TV, Vrana SR	An examination of the relationship between misophonia, anxiety sensitivity, and obsessive-compulsive symptoms	Sample study	J Obsessive Compuls Relat Disord	doi: 10.1016/j.jocrd.2018.06.004
2018	Eijsker N, Schroder A, Van Wingen G, Denys D	Response bias on the stop-signal task: An endophenotype of misophonia?	Experimental study	Biol Psychiatry	ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed19&NEWS=N&AN=621901731
2018	Hocaoglu C	A little known topic misophonia: Two case reports	Case study	Dusunen Adam	doi: 10.5350/DAJPN2018310109
2018	Janik McErlean AB, Banissy MJ	Increased misophonia in self-reported autonomous sensory meridian response	Sample study	PeerJ	doi: 10.7717/peerj.5351
2018	McKay D, Kim SK, Mancusi L, Storch EA, Spankovich C	Profile analysis of psychological symptoms associated with misophonia: A community sample	Sample study	Behav Ther	doi: 10.1016/j.beth.2017.07.002
2018	Muller D, Khemlani-Patel S, Neziroglu F	Cognitive-behavioral therapy for an adolescent female presenting with misophonia: A case example	Case study	Clin Case Stud	doi: 10.1177/1534650118782650

Year	Authors	Title	Type	Journal	DOI
2018	Palumbo DB, Alsalmán O, De Ridder D, Song JJ, Vanneste S	Misophonia and potential underlying mechanisms: A perspective	Review	Front Psychol	doi: 10.3389/fpsyg.2018.00953
2018	Quek TC, Ho CS, Choo CC, Nguyen LH, Tran BX, Ho RC	Misophonia in Singaporean psychiatric patients: A cross-sectional study	Sample study	Int J Environ Res Public Health	doi: 10.3390/ijerph15071410
2018	Robinson S, Hedderly T, Conte G, Malik O, Cardona F	Misophonia in children with tic disorders: A case series	Case study	J Dev Behav Pediatr	doi: 10.1097/DBP.0000000000000563
2018	Rouw R, Erfanian M	A large-scale study of misophonia	Sample study	J Clin Psychol	doi: 10.1002/jclp.22500
2018	Sanchez TG, Silva FED	Familial misophonia or selective sound sensitivity syndrome: Evidence for autosomal dominant inheritance?	Sample study	Braz J Otorhinolaryngol	doi: 10.1016/j.bjorl.2017.06.014
2018	Seaborne A, Fiorella L	Effects of background chewing sounds on learning: The role of misophonia sensitivity	Experimental study	Applied Cognitive Psychology	doi: 10.1002/acp.3387
2019	Aazh H, Landgrebe M, Danesh AA, Moore BC	Cognitive behavioral therapy for alleviating the distress caused by tinnitus, hyperacusis and misophonia: Current perspectives	Review	Psychol Res Behav Manag	doi: 10.2147/PRBM.S179138
2019	Alekri J, Al Saif F	Suicidal misophonia: A case report	Case study	Psychiatr Clin Psychopharmacol	doi: 10.1080/24750573.2019.1597585
2019	Eijsker N, Schröder A, Smit DJA, van Wingen G, Denys D	Neural basis of response bias on the stop signal task in misophonia	Experimental study	Front Psychiatry	doi: 10.3389/fpsyg.2019.00765
2019	Erfanian M, Kartsonaki C, Keshavarz A	Misophonia and comorbid psychiatric symptoms: A preliminary study of clinical findings	Sample study	Nord J Psychiatry	doi: 10.1080/08039488.2019.1609086

Year	Authors	Title	Type	Journal	DOI
2019	Frank B, McKay D	The suitability of an inhibitory learning approach in exposure when habituation fails: A clinical application to misophonia	Treatment study	Cogn Behav Pract	doi: 10.1016/j.cbpra.2018.04.003
2019	Potgieter I, MacDonald C, Partridge L, Cima R, Sheldrake J, Hoare DJ	Misophonia: A scoping review of research	Review	J Clin Psychol	doi: 10.1002/jclp.22771
2019	Samermit P, Saal J, Davidenko N	Cross-sensory stimuli modulate reactions to aversive sounds	Experimental study	Multisens Res	doi: 10.1163/22134808-20191344
2019	Schröder A, van Wingen G, Eijsker N, San Giorgi R, Vulink NC, Turbyne C, Denys D	Misophonia is associated with altered brain activity in the auditory cortex and salience network	Experimental study	Sci Rep	doi: 10.1038/s41598-019-44084-8
2019	Siepsiak M, Dragan W	Misophonia - A review of research results and theoretical concepts	Review	Psychiatr Pol	doi: 10.12740/PP/92023
2019	Silva FED, Sanchez TG	Evaluation of selective attention in patients with misophonia	Experimental	Braz J Otorhinolaryngol	doi: 10.1016/j.bjorl.2018.02.005
2019	Van Ameringen M, Patterson B, Turna J, Simpson W	Selective sound sensitivity (misophonia): Characteristics of an online sample	Sample study	Eur Neuropsychopharmacol	doi: 10.1016/j.euroneuro.2019.09.499
2020	Osugwu FC, Osugwu VC, Machoka AM	Methylphenidate ameliorates worsening distractibility symptoms of misophonia in an adolescent male	Case study	Prim Care Companion CNS Disord	doi: 10.4088/PCC.19102553
2020	Cassio-Robbins C, Anand D, McMahon K, Guetta R, Trumbull J, Kelley L, Rosenthal MZ	The mediating role of emotion regulation within the relationship between neuroticism and misophonia: A preliminary investigation	Sample study	Front Psychiatry	doi: 10.3389/fpsy.2020.00847

Year	Authors	Title	Type	Journal	DOI
2020	Daniels EC, Rodriguez A, Zabelina DL	Severity of misophonia symptoms is associated with worse cognitive control when exposed to misophonia trigger sounds	Experimental study	PLoS One	doi: 10.1371/journal.pone.0227118
2020	Eijsker N, Schroder A, Smit DJA, van Wingen G, Denys D	Structural and functional brain abnormalities in misophonia	Sample study	Biological Psychiatry	doi: 10.1016/j.biopsych.2020.02.585
2020	Frank B, Roszyk M, Hurley L, Drejai L, McKay D	Inattention in misophonia: Difficulties achieving and maintaining alertness	Experimental study	J Clin Exp Neuropsychol	doi: 10.1080/13803395.2019.1666801
2020	Haq SS, Alresheed F, Tu JC	Behavioral treatment of problem behavior for an adult with autism spectrum disorder and misophonia	Case study	J Dev Phys Disabil	doi: 10.1007/s10882-020-09780-8
2020	Jager I, de Koning P, Bost T, Denys D, Vulink N	Misophonia: Phenomenology, comorbidity and demographics in a large sample	Sample study	PLoS One	doi: 10.1371/journal.pone.0231390
2020	Jager IJ, Vulink NCC, Bergfeld IO, van Loon AJJM, Denys DAJP	Cognitive behavioral therapy for misophonia: A randomized clinical trial	Treatment study	Depress Anxiety	doi: 10.1002/da.23127
2020	McGeoch PD, Rouw R	How everyday sounds can trigger strong emotions: ASMR, misophonia and the feeling of wellbeing	Review	Bioessays	doi: 10.1002/bies.202000099
2020	Natalini E, Dimaggio G, Varakliotis T, Fioretti A, Eibenstein A	Misophonia, maladaptive schemas and personality disorders: A report of three cases	Case study	J Contemp Psychother	doi: 10.1007/s10879-019-09438-3
2020	Naylor J, Caimino C, Scutt P, Hoare DJ, Baguley DM	The prevalence and severity of misophonia in a UK undergraduate medical student population and validation of the Amsterdam Misophonia Scale	Sample study	Psychiatr Q	doi: 10.1007/s11126-020-09825-3

Year	Authors	Title	Type	Journal	DOI
2020	Sharan R, Sharma V	A case of bipolar disorder and misophonia	Case study	Prim Care Companion CNS Disord	doi: 10.4088/PCC.19102523
2020	Siepsiak M, Śliwerski A, Łukasz Dragan W	Development and psychometric properties of MisoQuest - A new self-report questionnaire for misophonia	Sample study	Int J Environ Res Public Health	doi: 10.3390/ijerph17051797
2020	Siepsiak M, Sobczak AM, Bohaterewicz B, Cichoński Ł, Dragan Wł	Prevalence of misophonia and correlates of its symptoms among inpatients with depression	Sample study	Int J Environ Res Public Health	doi: 10.3390/ijerph17155464
2020	Vanaja CS, Abigail MS	Misophonia: An evidence-based case report	Case study	Am J Audiol	doi: 10.1044/2020_AJA-19-00111
2021	Cassello-Robbins C, Anand D, McMahon K, Brout J, Kelley L, Rosenthal MZ	A preliminary investigation of the association between misophonia and symptoms of psychopathology and personality disorders	Sample study	Front Psychol	doi: 10.3389/fpsyg.2020.519681
2021	Wiese AD, Wojcik KD, Storch EA	Assessment and intervention for individuals with misophonia	Treatment study	J Health Service Psychol	doi: 10.1007/s42843-021-00025-6
2021	Lugg W	Misophonia in pregnancy - A case report	Case study	Australas Psychiatry	doi: 10.1177/1039856220986719
2021	Raj-Koział D, Gos E, Kutymba J, Skarzynski H, Skarzynski PH	Decreased sound tolerance in tinnitus patients	Sample study	Life (Basel)	doi: 10.3390/life11020087
2021	Roushani K, Mehrabizadeh Honarmand M	The effectiveness of cognitive behavioral therapy on anger in female students with misophonia: A single-case study	Case study	Iran J Med Sci	doi: 10.30476/ijms.2019.82063
2021	Williams ZJ, He JL, Cascio CJ, Woynarowski TG	A review of decreased sound tolerance in autism: Definitions, phenomenology, and potential mechanisms	Review	Neurosci Biobehav Rev	doi: 10.1016/j.neubiorev.2020.11.030



7

Appendices

Summary

Dutch summary / Nederlandse samenvatting

PhD portfolio

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Acknowledgements / Dankwoord

Summary

When I started my PhD project in 2015 only 25 research articles on misophonia had been published. Even though misophonia can usually be considered as a rather mild condition compared to most severe mental disorders, still many patients experience substantial impact from misophonia on their work, social and family life. This impairment in quality of life of misophonia patients deserves more scientific attention.

In the introduction of this thesis (**chapter 1**), I address the diagnosis of misophonia which is illustrated by a case study of one of my patients and I discuss the controversies surrounding this relatively new disorder. Further, I describe the objectives of this thesis; first to increase knowledge concerning the phenomenology of misophonia and second to investigate the effect of different treatments for misophonia. In this thesis I revise the previous research done by our research group by answering eight research questions. Finally, I provide my credentials and describe the development of my personal understanding of misophonia.

Part I (chapter 2): New insights in phenomenology of misophonia

Chapter 2 describes a large sample of patients, referred with a suspicion of misophonia, from a medical-audiological and a psychiatric-psychological perspective. This chapter shows that the diagnosis of misophonia, using the diagnostic criteria proposed by the AMC in 2013, is confirmed in 575 of 779 (74%) referred subjects (*research question 1*).

In the sample of misophonia subjects medical examination shows no abnormalities. Psychiatric comorbidity is absent in 72%. Main secondary comorbid disorders are: traits of obsessive-compulsive personality disorder (26%), mood disorders (10%), attention-deficit (hyperactivity) disorder (5%), and autism spectrum conditions (3%) (*research question 2*).

Psychological tests show perfectionism in almost all misophonia subjects (97%) and increased neuroticism. Disgust sensitivity and autism-like traits are not associated with misophonia. Quality of life is heavily impaired and associated with misophonia severity (*research question 3*).

The majority of the 2013 AMC criteria for misophonia are confirmed in this sample. Misophonia is considered a psychiatric disorder, which is characterized by anger and disgust provoked by human sounds in particular. Two significant alterations in the diagnostic criteria are made, namely the presence of preoccupation with misophonia triggers and the presence of mouth or nose sounds as trigger. Based on the results chapter 2 proposes a set of revised criteria useful to diagnose misophonia as a psychiatric disorder (*research question 4*).

Part II (chapter 3–5): New insights in psychotherapy for misophonia

Chapter 3 investigates the effectiveness of group cognitive behavioral therapy (G-CBT) on misophonia symptoms compared to a waiting list control group in the first randomized controlled trial (RCT) for misophonia worldwide. Three months of G-CBT reduces misophonia symptoms compared to the waiting list condition. Clinical improvement is found in 56% of all completers (37% intention-to-treat) compared to 0% in the waiting list control group. General mental dysfunction decreases and patients report less disabilities in family and social functioning after G-CBT compared to the waiting list condition (*research question 5*).

One year after the end of treatment, the reduction in misophonia symptoms sustains. In addition, the improvement in general mental functioning and quality of life remains. Chapter 3 concludes that this RCT shows both short-term and long-term efficacy of G-CBT for misophonia (*research question 6*).

Chapter 4 focuses on the rationale of G-CBT and describes the interventions of this treatment protocol. The phased structure is outlined, and therapeutic principles and values are discussed. Throughout this chapter a single clinical case study is used to illustrate all interventions and the specific therapeutic principles of the group treatment (*research question 7*).

Chapter 5 explores the effectiveness of eye movement desensitization and reprocessing (EMDR) therapy focused on emotionally disturbing misophonia-related memories in a pilot study of case series. Significant reduction in misophonia symptoms is found in three of eight participating patients, including patients who had previously been unable to benefit from evidence-based treatment (G-CBT). No significant effect on general mental functioning and quality of life is found. Chapter 5 concludes that EMDR therapy is a promising intervention for misophonia (*research question 8*).

In the discussion (**chapter 6**) I reflect on the results from the three studies and the synopsis of G-CBT protocol described in this thesis, by discussing the eight research questions. Subsequently, I describe strengths and weaknesses of the studies and clinical implications for mental healthcare for patients with misophonia. Additionally, I provide a description of the development in misophonia research through the discussion of three literature searches in time. Finally, I propose suggestions for future research.

In conclusion, in this thesis the phenomenology of misophonia is studied in a highly qualitative and quantitative sample. This leads to new insights and an important revision of the

diagnostic criteria. The first randomized controlled trial of G-CBT for misophonia worldwide and publication of the treatment manual for G-CBT, constitute a milestone in misophonia research. G-CBT is determined an effective treatment for misophonia. Moreover, a pilot study shows that alternative treatment options, notably EMDR therapy, can be considered. The new insights from this thesis contribute to a further development of scientific research into misophonia.

Dutch summary / Nederlandse samenvatting

Bij de start van mijn promotietraject in 2015 waren slechts 25 onderzoeksartikelen over misofonie gepubliceerd. Hoewel misofonie kan worden beschouwd als een overwegend milde aandoening in vergelijking met ernstige psychische aandoeningen, ervaren veel patiënten een aanzienlijke negatieve invloed van misofonie op hun werk, sociale leven en gezinsleven. Deze verminderde kwaliteit van leven misofoniepatiënten verdient meer wetenschappelijke aandacht.

In de inleiding van dit proefschrift (**hoofdstuk 1**) ga ik in op de diagnose misofonie, aan de hand van een casusbeschrijving van één van mijn patiënten, en bespreek ik de controverses rond deze relatief nieuwe aandoening. Verder beschrijf ik de doelstellingen van dit proefschrift: ten eerste het vergroten van de kennis over de fenomenologie van misofonie en ten tweede het onderzoeken van het effect van verschillende behandelmethoden voor misofonie. In dit proefschrift beantwoord ik acht onderzoeksvragen waardoor eerdere bevindingen van onze onderzoeksgroep worden herzien. Ten slotte overhandig ik mijn geloofsbrief en beschrijf ik de ontwikkeling van mijn persoonlijke visie op misofonie.

Deel I (hoofdstuk 2): Nieuwe inzichten in de fenomenologie van misofonie

Hoofdstuk 2 beschrijft een grote groep proefpersonen, verwezen met het vermoeden van misofonie, vanuit een medisch-audiologisch en een psychiatrisch-psychologisch perspectief. In dit hoofdstuk blijkt dat de diagnose misofonie middels de in 2013 door het AMC opgesteld diagnostische criteria bevestigd wordt bij 575 van de 779 (74%) verwezen proefpersonen (*onderzoeksvraag 1*).

In de groep met misofonie komen er bij medisch onderzoek geen bijzonderheden naar voren. Psychiatrische comorbiditeit is afwezig bij 72%. De belangrijkste secundaire comorbide stoornissen zijn kenmerken van obsessieve-compulsieve persoonlijkheidsstoornis (26%), stemmingsstoornissen (10%), aandachtstekortstoornis (met hyperactiviteit) (5%) en autismespectrumstoornissen (3%) (*onderzoeksvraag 2*).

Bij bijna alle misofoniepatiënten (97%) wordt met psychologische tests perfectionisme vastgesteld en tevens een verhoogd neuroticisme. Gevoeligheid voor walging en autistische eigenschappen blijken niet geassocieerd met misofonie. De kwaliteit van leven is sterk verminderd en hangt samen met de ernst van misofonie (*onderzoeksvraag 3*).

De meerderheid van de 2013 AMC-criteria voor misofonie wordt in deze patiëntgroep bevestigd. Misofonie wordt gezien als een psychiatrische diagnose met woede en walging

bij met name geluiden van anderen. Er zijn twee belangrijke wijzigingen in de diagnostische criteria, namelijk aanwezigheid van preoccupatie met misofonietriggers en aanwezigheid van mond- of neusgeluiden als trigger. Op basis van de resultaten stelt hoofdstuk 2 herziene criteria voor om misofonie als een psychiatrische stoornis te diagnosticeren (*onderzoeksvraag 4*).

Deel II (hoofdstuk 3–5): Nieuwe inzichten in psychotherapie voor misofonie

Hoofdstuk 3 beschrijft de eerste gerandomiseerde gecontroleerde studie (RCT) voor misofonie ter wereld. Hierin wordt de effectiviteit van groeps-cognitieve gedragstherapie (G-CGT) op symptomen van misofonie in vergelijking met een wachtlijstcontrolegroep onderzocht. Drie maanden G-CBT vermindert de symptomen van misofonie in vergelijking met de wachtlijstconditie. Bij 56% van alle behandelde patiënten (37% intention-to-treat) wordt een klinisch relevante verbetering gevonden vergeleken met 0% van de wachtlijst. Algemene psychische klachten nemen af en patiënten rapporteren minder beperkingen in het gezins- en sociaal functioneren na G-CGT in vergelijking met de wachtlijstconditie (*onderzoeksvraag 5*).

Een jaar na het einde van de behandeling is de behaalde vermindering van misofonieklaarten onveranderd. Bovendien blijft de verbetering van het algemeen mentaal functioneren en de kwaliteit van leven behouden. Hoofdstuk 3 concludeert dan ook dat deze RCT zowel de korte- als langetermijneffectiviteit van G-CGT voor misofonie aantoont (*onderzoeksvraag 6*).

Hoofdstuk 4 richt zich op de rationale van G-CGT voor misofonie en beschrijft de interventies van het behandelprotocol. De gefaseerde opbouw komt aan bod en therapeutische principes en waarden worden besproken. In dit hoofdstuk wordt een casusbeschrijving gebruikt om alle interventies en de specifieke therapeutische principes van de groepsbehandeling te illustreren (*onderzoeksvraag 7*).

Hoofdstuk 5 onderzoekt de effectiviteit van eye movement desensitization and reprocessing (EMDR-) therapie gericht op emotioneel verontrustende misofonie-gerelateerde herinneringen in een pilotstudie (case series). Er wordt een significante vermindering van misofonieklaarten gevonden bij drie van de acht deelnemende patiënten, inclusief patiënten die eerder geen baat hadden bij een evidence-based behandeling (G-CGT). Er wordt geen significant effect gevonden op het algemeen psychisch functioneren en de kwaliteit van leven. Hoofdstuk 5 concludeert dat EMDR-therapie een veelbelovende interventie is voor misofonie (*onderzoeksvraag 8*).

In de discussie (**hoofdstuk 6**) reflecteer ik op de resultaten van de drie studies en de synopsis van het G-CGT-protocol beschreven in dit proefschrift, aan de hand van de acht onderzoeksvragen. Verder beschrijf ik de sterke en zwakke punten van de studies en klinische implicaties voor de geestelijke gezondheidszorg voor patiënten met misofonie. Daarnaast geef ik een beschrijving van de ontwikkeling in de wetenschappelijke literatuur van misofonie aan de hand van drie zoekopdrachten in de tijd. Ten slotte doe ik aanbevelingen voor toekomstig onderzoek.

Concluderend, in dit proefschrift wordt de fenomenologie van misofonie bestudeerd in een kwantitatief en kwalitatief hoogwaardige steekproef. Dit leidt tot nieuwe inzichten en een belangrijke herziening van de diagnostische criteria. De eerste gerandomiseerde gecontroleerde studie van G-CGT voor misofonie ter wereld en publicatie van het behandelprotocol voor G-CGT, zijn een mijlpaal in het wetenschappelijk onderzoek naar misofonie. G-CGT blijkt een effectieve behandeling voor misofonie. Bovendien wordt met een pilotstudie aangetoond dat alternatieve behandelvormen, zoals EMDR-therapie, overwogen kunnen worden. De nieuwe inzichten van dit proefschrift dragen bij aan een verdere ontwikkeling van wetenschappelijk onderzoek naar misofonie.

PhD portfolio

Name: Drs. I.J. (Inge) Jager

Institution: Amsterdam University Medical Center – University of Amsterdam

PhD period: Part time: January 2015 – May 2019
In own time: May 2019 – October 2021

Promotor: Prof. dr. D.A.J.P. (Damiaan) Denys

Copromotor: Dr. N.C.C. (Nienke) Vulink

List of peer reviewed publications

Accepted

Jager, I., Vulink, N., Bergfeld, I., van Loon, A., & Denys, D. (2021). Cognitive behavioral therapy for misophonia: A randomized clinical Trial. *Depression & Anxiety*, 38(7), 708–718.

Jager, I., Vulink, N., de Roos, C., & Denys, D. (2021). EMDR therapy for misophonia: A pilot study of case series. *European Journal of Psychotraumatology*, 12(1).

Jager, I., de Koning, P., Bost, T., Denys, D., & Vulink, N. (2020). Misophonia: Phenomenology, comorbidity and demographics in a large sample. *PLoS one*, 15(4), e0231390.

Under review

Jager, I., Vulink, N., van Loon, A., Schröder, A., van der Pol, M., Slaghekke, S., & Denys, D. Synopsis of a group treatment protocol to guide cognitive behavioral therapy for Misophonia.

Book

Van Loon, A., Van der Pol, M., Slaghekke, S., Van der Meer, C., Schekman, E., Nieuwendijk, E., Jager, I. (2019). *Misofonie: Behandelprotocol in 8 sessies [Misophonia: Treatment protocol of 8 sessions]*. Boom Publishers.

Teaching

Supervising

Vanja Dubislav – Master thesis Health sciences: ‘Misophonia in children; Phenomenology and treatment effect of cognitive-behavioral group therapy’ 2017

Mentoring

- Tutoring eleven psychologists in data management during the Misophonia Sample study, 2016–2018
- Tutoring and mentoring two research assistants during the Misophonia RCT, 2017

Workshop

A two-day course for therapists: *Treating Misophonia*, Psychiatry department, Amsterdam, 2019

Presentations

- Oral: ‘*EMDR for Misophonia: a pilot study*’, EMDR Europe Conference, Dublin, 2021
- Oral: ‘*CBT for Misophonia*’ Academic workplace Outpatient Clinic for Affective disorders, GGZ inGeest, Amsterdam, 2020
- Oral: ‘*Misophonia: assessment and treatment*’, Annual Congress of Dutch Association of Behavioral and Cognitive Therapy (VGCT), Veldhoven, 2019
- Oral: ‘*CBT for misophonia: a RCT*’, World Congress of Behavioral and Cognitive Therapy (WCBCT), Berlin, 2019
- Poster: ‘*CBT for Misophonia: a RCT*’, Annual Congress of Dutch clinical psychologists and clinical neuropsychologists (KP&KNP), Utrecht, 2019
- Oral: ‘*Misophonia: a sample study from a psychiatric, somatic and psychological perspective*’, Grand Round Psychiatry department, Amsterdam, 2018

Other

- Interview in the *New Scientist*, www.newscientist.nl/nieuws/ig-nobelprijs-voor-nederlands-onderzoek-dat-misofonie-ontdekte, 2020
- One-hour interview on Misophonia research on national radio, www.NPORadio1.nl/radio-focus/uitzendingen/655696-2019011-15, 2019

Clinical work / studies

- Clinical psychology 1999–2005
- Licensed Health psychologist 2007–2009
- Specialization Clinical Psychologist-Psychotherapist 2015–2019

Curriculum Vitae

The author of this dissertation, Inge Jeanine Jager, was born on September 16, 1981 in Eindhoven. In September 1999 she started clinical psychology at Radboud University in Nijmegen. During her study she participated in the Honours Program: a two-year program consisting of supplementary interdisciplinary courses on top of the regular program. In December 2005 she received her doctor degree with merit.

After obtaining her degree, she was first employed as a psychologist at HSK, in Amsterdam where she finished her two-year training for a licensed health care psychologist in 2009. She was also trained in EMDR and as a cognitive behavioral therapist and now is a supervisor and on the members' council of the association for behavioral and cognitive therapy. After working as a clinician and team manager for HSK Zaandam for almost five years, she started in January 2015 with her specialization as a clinical psychologist at the Psychiatry department of Amsterdam UMC, location AMC. This four-year specialization was combined with her PhD research under supervision of Prof. dr. Damiaan Denys and Dr. Nienke Vulink. She did research on the phenomenology and assessment of misophonia as a psychiatric disorder and conducted several treatment studies for misophonia. In May 2019 she completed her studies and started working as a licensed clinical psychologist at the Outpatient Clinic for Affective Disorders at GGZ inGeest in Amsterdam. She combines her clinical activities with education, as deputy head of training health care psychologists at Cure & Care Development. Inge is married with Gerben and lives in Hilversum with their two daughters, Julia and Lotte.

Acknowledgements / Dankwoord

Graag wil ik hier een aantal mensen bedanken voor hun hulp en steun bij het tot stand komen van dit proefschrift. Ten eerste wil ik de patiënten die deelnamen aan de verschillende studies van harte bedanken voor hun medewerking. De grote testbatterij aan extra vragenlijsten, afgenomen bij de intake, is door honderden patiënten ingevuld en een groep van ruim honderd patiënten heeft ook audiologisch onderzoek ondergaan. Daarnaast had ik binnen een mum van tijd voldoende patiënten geïncludeerd voor de wachtlijstgecontroleerde studie naar het effect van cognitieve gedragstherapie, ook al hadden deelnemers een 50/50 kans om ingedeeld te worden in de wachtlijstgroep. Tenslotte ben ik de tien patiënten, die ik experimenteel met EMDR-therapie heb behandeld, dankbaar voor hun vertrouwen.

Dan wil ik graag mijn promotor Prof. dr. Damiaan Denys bedanken. Beste Damiaan, dank voor je prikkelende visie. Door jouw kritische feedback heb ik geleerd wetenschappelijker te denken en te schrijven en bleef ik gemotiveerd om dit traject met succes af te ronden.

Mijn co-promotor, Dr. Nienke Vulink: Beste Nienke, bedankt voor je grote steun en je enthousiasme. Die had ik nodig om dit project naast mijn opleiding tot klinisch psycholoog en alle uitdagingen die het leven verder in deze periode voor me in petto had, vol te houden. Dank voor al je tijd en aandacht die je aan mijn begeleiding hebt besteed. En ik denk nog met veel plezier terug aan onze ervaringen en ontmoetingen tijdens het WCBCT in Berlin!

Het misofonie diagnostiek- en behandelteam van AMC Psychiatrie wil ik bedanken voor hun inzet als intaker, verwijzer of behandelaar in de verschillende studies. Met name Pelle de Koning wil ik bedanken voor zijn bijdrage aan de sample study. Ook mijn dank aan de 11 psychologiestagiaires die mij hebben geholpen bij het monnikenwerk om alle vragenlijsten van de grote testbatterij in SPSS te krijgen voor de sample study. Nog speciale dank voor Vanja Dubislav, Nina Koopmans en Babet Wezenberg voor hun hulp rondom de organisatie van de RCT.

Prof. dr. Claudi Bockting, allereerst mijn dank voor het beoordelen van mijn proefschrift als lid van mijn promotiecommissie. Maar nog meer wil ik je bedanken voor alle andere rollen waarin ik in de afgelopen tijd veel van je geleerd heb. Als mijn supervisor psychotherapie tijdens de KP-opleiding spraken we over de behandeling van ernstige stemmingsstoornissen, zingeving en rouw. Ik ben blij om nu met je samen te mogen werken als opleider voor de GZ-opleiding van CCD. Dank voor je adviezen en het met me meeleven, van publicaties tot moederzorgen.

Ook de andere leden van de promotiecommissie, Prof. dr. Patricia van Oppen, Prof. dr. Lisbeth Utens en Prof. dr. Guido van Wingen wil ik graag bedanken voor het kritisch beoordelen van mijn proefschrift en de prettige samenwerking bij het AMC en GGZ inGeest.

Ik wil Tim Bost bedanken voor de analyse van de audiologische data en het schrijven van deze sectie van de grote sample study. Steven Meijer, dank voor het meedenken bij de opzet van de EMDR-studie. En Michel Hof, dank voor je adviezen bij de data-analyse van de sample study.

Carlijn de Roos wil ik bedanken voor het meeschrijven aan een van de studies van dit proefschrift. Bedankt voor het delen van je expertise over de toepassing van EMDR op andere gebieden dan post-traumatische stress-stoornis. Bedankt voor de fijne samenwerking bij het schrijven en je steun tijdens het EMDR Europe congres.

Isidoor Bergfeld, ontzettend bedankt voor de data-analyse van de RCT. Maar meer nog dank voor je geduldige uitleg en adviezen over de analyses en conclusies van mijn andere studies en voor je motiverende mails als ik weer een ellenlange review terug kreeg!

Arnoud van Loon, dank voor de introductie met misofonie en mijn opleiding bij AMC Psychiatrie. Dankzij jou heb ik de combinatie gemaakt van mijn promotie-onderzoek naar misofonie en de KP-opleiding. Ik heb van jou als mijn praktijkopleider en als leidinggevende geleerd van je creativiteit en vertrouwen. Je bent als grondlegger van de misofoniebehandeling een voorbeeld van innovatie in de praktijk.

Arjan Schröder, bijzonder dat jij – de enige die mij voorging in onderzoek naar misofonie – nu mijn collega bent bij de poli Depressie van De Nieuwe Valerius. Bedankt voor al je collegialiteit tijdens dit project.

Mijn oud-collega's van het AMC afdeling Stemningsstoornissen, met name Dominique Scheepens en Anja Lok, wil ik bedanken voor jullie begrip voor de combinatie van alle taken tijdens mijn KP-opleiding en voor de waardevolle klinische lessen die ik van jullie allen heb geleerd. Van de afdeling Angststoornissen wil ik Simone, Christianne, Ellen, Eveline en Iris bedanken als medeauteurs (naast Arnoud en Marthe) van het misofonie protocollenboek en de samenwerking bij de behandelingen. Marthe, jou wil ik bedanken voor het delen van de KP-opleiding met mij en alles wat daarbij hoorde. En natuurlijk lieve Charlotte, je waarschuwingen en adviezen bij de keuze van mijn onderwerp, als ook al je steun bij iedere moeilijke meeting of review, zal ik niet vergeten! Ontzettend bedankt voor je betrokkenheid en je humor. Tenslotte veel dank voor alle praktische ondersteuning van Ditte, Karin en Ingeborg en van de planningscollega's voor de hulp bij de RCT.

Dan mijn vriendinnen uit mijn studententijd in Nijmegen en uit het Hilversumse, vooral lieve Saskia, lieve Barbara, lieve Suzan, Wobke en Marjolijn, lieve Marjan en lieve Bianca, dank voor jullie vriendschap. En mijn 'werk-vriendinnen' Evelien en Jetske: het is heerlijk om met jullie te sparren en te lachen!

Mijn paranimf Floortje Vlemmix: dank voor de vanzelfsprekendheid waarmee jij je ambities in werk waarmaakt. Dat helpt mij enorm om een zelfde keuze te maken. Sinds de disco-kelder in Nijmegen tot nu in 't Gooi sta je naast me. Mijn paranimf Floor de Wit: bedankt voor je scherpe blik en steun met humor, drank, crisisbox of stiekeme snacks tijdens mijn hele KP-opleiding bij het AMC.

Mijn ouders wil ik bedanken voor het grote vertrouwen en alle liefde waarmee ze me hebben groot gebracht. Voor al hun steun in de afgelopen moeilijke jaren. En voor het enthousiasme voor elke mijlpaal van mijn promotietraject. Ook mijn schoonouders wil ik erg bedanken voor hun steun en hulp. Mijn broer: dank voor de mooie herinneringen aan onze gedeelde studententijd en je zorg. En mijn zus: bedankt voor je lieve hulp en steun, je vrolijkheid en voor het zo nu en dan mogen bijkomen van alles in je appartement.

Tenslotte, mijn man en meisjes. Lieve Gerben, bedankt voor al je hulp om dit proefschrift voor elkaar te kunnen krijgen. *Ik heb je lief, en liefde stijgt tot boven de gedeelde daken, waaronder wij het samen maken, wat anderen eronder krijgt.*¹ Bedankt dat je het leven met mij deelt. Mijn liefste Julia en mijn liefste Lotte, het boek van mama is inderdaad "nu eindelijk klaar"!

¹ Nico Scheepmaker

