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Review Paper

Misophonia: A Scientific Review on Etiology, Pathophysiology, and Therapeutic Approaches

Yashitha M. P.*, Harshitha Yeshwanth Deshbhandari

PG Student, Department of Pharmacy Practice, Karavali College of Pharmacy Mangalore- 575028.

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ABSTRACT

Misophonia, characterized by intense emotional and physiological responses to specific sounds, represents a complex neurophysiological and behavioral syndrome first identified in 1997. This review synthesizes current understanding of its epidemiology, etiology, pathophysiology, and clinical implications. Population studies indicate prevalence rates of 15-20% in the general population, with 2-3% reporting severe cases, and higher rates among university students (20-25%) and clinical populations (up to 60%). The condition shows female predominance (3:2 ratio) with typical onset between ages 8-12. Neuroimaging studies reveal altered activity in the anterior cingulate cortex, anterior insular cortex, and superior temporal cortex, suggesting disrupted sensory-emotional integration. Multiple factors contribute to its etiology, including neurobiological, genetic, developmental, environmental, and psychological mechanisms. Common triggers include eating sounds, breathing, and repetitive movements, leading to intense autonomic arousal, anxiety, and aggressive impulses. The condition frequently co-occurs with obsessive-compulsive disorder, post-traumatic stress disorder, depression, and anxiety disorders. While standardized diagnostic criteria are lacking, several assessment tools exist, including the Misophonia Assessment Questionnaire and Amsterdam Misophonia Scale. Treatment approaches encompass both non-pharmacological interventions (music therapy, sound management) and pharmacological options (MDMA, β-blockers). The condition significantly impacts daily functioning, often leading to social isolation, academic difficulties, and reduced quality of life. Future research priorities include establishing standardized diagnostic criteria, developing validated treatment protocols, understanding neurobiological mechanisms, and conducting long-term outcome studies.

INTRODUCTION

Misophonia, from the Greek words “miso” (hate) and “phone” (voice) [1], is a complex

***Corresponding Author:** Yashitha M. P.
Address: *PG Student, Department of Pharmacy Practice, Karavali College of Pharmacy Mangalore- 575028.*
Email ✉: bojyash@gmail.com
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neurophysiological and behavioral syndrome that is characterized by intense emotional and physiological responses to specific sounds. The condition was first identified by audiologist Marsha Johnson in 1997 and later termed by Jastreboff and Jastreboff. It has become a distinct clinical entity that challenges traditional classifications of auditory processing disorders [2]. The nomenclature surrounding this condition reflects its changing understanding in the medical community. While initially termed “Ear Rage” or “Mastication Rage”, reflecting its common triggers related to eating sounds, the condition has also been described as "Selective Sound Sensitivity Syndrome" and "Soft Sound Sensitivity Syndrome." These varying terminologies highlight the ongoing debate regarding its classification and underlying mechanisms [3]. Individuals with misophonia report strong emotional and physiological responses to certain acoustic stimuli, most characteristically involving sounds made during ordinary human activities such as eating, breathing, typing, or other repetitive movements [4]. Misophonia is specific in that the reactions are always linked to the sound, but unlike general noise sensitivity or hyperacusis, these reactions have a very significant emotional component. The reaction usually involves more than mere annoyance or discomfort, often an intense anger, anxiety, or panic response triggered by a strong fight-or-flight reaction [5]. The current state of scientific understanding about misophonia presents a number of specific challenges. Unlike most psychiatric or audiological conditions, to date, misophonia has not gained an official standing in systems like the International Classification of Diseases (ICD) or in the Diagnostic and Statistical Manual of Mental Disorders (DSM). Lack of formal recognition leads to certain restrictions: in research funding and in clinical practice, since access to relevant treatment and support could become restricted [6]. The disorder may significantly impact everyday functioning. Individuals often elaborate complex avoidance behaviors, and social, occupational, and academic impairment can be considerable. This condition typically has its onset during childhood or early adolescence, a period when key developmental processes might be impacted, leading to entrenched patterns of social isolation that continue into adulthood [7,8]. Recent advances in neuroimaging and psychophysiological research have started to shed light on the neural substrates of misophonia, indicating alterations in sound processing and emotional regulation networks. These findings are important for understanding the etiology of the condition and developing targeted therapeutic interventions. Studies have shown heightened activation in specific brain regions, including the anterior insular cortex and anterior cingulate cortex, when individuals with misophonia are exposed to trigger sounds [10]. Another aspect of complexity lies in the relationship between misophonia and other psychiatric conditions. High rates of comorbidity with obsessive-compulsive disorder, anxiety disorders, and post-traumatic stress disorder suggest that perhaps there are shared neurobiological mechanisms or risk factors. It is therefore crucial to understand these relationships to develop comprehensive treatment approaches and improve outcomes for affected individuals [11]. Despite growing recognition and research interest, significant gaps remain in our understanding of misophonia's prevalence, natural history, and optimal treatment approaches. The condition appears to affect individuals across cultures and demographics, though precise epidemiological data remains limited. Gender differences have been observed, with some studies suggesting higher prevalence among females, though the reasons for this disparity remain unclear [12].

As more research is undertaken in this field, there will be a necessity for standardized diagnostic criteria, validated assessment tools, and evidence-based treatment protocols. Therefore, the proper development of these resources will have to be undertaken with a well-informed sense of the present state of knowledge regarding misophonia, together with identification of critical areas of future investigation.

This review will synthesize the current knowledge about the clinical presentation, mechanisms, diagnostic approach, and treatment of misophonia. In reviewing the existing literature and focusing on areas in need of further study, we aim to add to the developing knowledge base for this challenging condition and improve the care of individuals with misophonia.

1. Epidemiology

Recent epidemiological studies have been very useful in providing information about the prevalence and distribution of misophonia. According to population-based studies, 15-20% of the general population experiences some degree of misophonia symptoms, with 2-3% reporting severe cases that have a huge impact on their lives. Among university students, the prevalence rates are higher, between 20-25%. This might be because of the presence of environmental stressors like noise exposure in an academic environment and greater sensitivities of young people to certain sounds. It is reported to be as high as 60% among patients with clinical populations such as tinnitus and hyperacusis [12,13]. Regarding the demographic distribution, misophonia has been shown to be a gender-disparity disease with female predominance reported at a ratio of 3:2. This might mean that females are more vulnerable to developing this condition, though the reason behind the disparity needs further research. The age of onset usually lies between the ages of 8 and 12 years. Several people have a history of an early age of onset of their symptoms, usually when they were either in childhood or early adolescence. This may well be connected to the emergence of auditory processing sensitivity along with environmental input during the crucial years. It is also reported from all continents and cultures, implying it is not restricted to one geographic area, rather a universal problem. While widely reported, it has been reported that misophonia was not associated with particular socioeconomic statuses. This points to the fact that the disease crosses all different boundaries of socioeconomic groups. Global spread and representation suggest global awareness about it and a better understanding of how it starts or develops within people [12,13].

2. Etiology And Risk Factors [9,14-16]

Misophonia is a complex condition, with factors influencing it at different levels: neurobiological, genetic, developmental, environmental, psychological, and neurodevelopmental. The development and persistence of the disorder can be traced back to certain risk characteristics, combining all these factors as shown in Figure 1.

1. **Neurobiological Factors:** Misophonia in an individual leads to a state of hyperresponsiveness due to the overactivity in the processing of sound and altered autonomic functions and due to increased connectivity between the anterior insular cortex and emotion regulation networks.
2. **Genetic Factors:** Family clustering indicates a genetic predisposition, especially in relation to auditory processing disorders. A family history of misophonia increases the risk, suggesting a genetic component in the development of the condition.
3. **Developmental Factors:** Patterning of exposure to the sound during periods of critical developmental vulnerability, traumatic event, or emotional conditioning plays a large role in misophonia development. Trauma and stress within the childhood and adolescence years often

4. **Environmental factors:** The other influential environmental factor is chronic stress, repeated exposure to certain precipitating sounds, and learned aversive responses that occur in misophonia. A prolonged exposure to noise or stressful life events might amplify the emotional response to certain sounds and contribute to the likelihood of developing this condition.
5. **Psychological Mechanisms:** Classical conditioning, hypervigilance, maladaptive coping strategies and anxiety sensitivity are important psychological mechanisms that sustain and amplify misophonia symptoms. The heightened levels of anxiety sensitivity can more sensitively react to sound stimuli, thus giving the cycle of distress further thrust.

Risk Factors

Several factors increase the risk of developing misophonia. A family history of misophonia or auditory processing disorders may heighten susceptibility. A history of trauma or significant stress during developmental periods, particularly in childhood or adolescence, can disrupt sensory and emotional processing. Hyperacusis, an increased sensitivity to sound, which is often observed in individuals suffering from other sensory processing disorders, has an increased likelihood of developing misophonia. Concurrent psychiatric conditions, for example, anxiety disorders or obsessive-compulsive disorder (OCD), also contribute to vulnerability through increased sensitivity to emotional triggers and the stimuli of sounds .

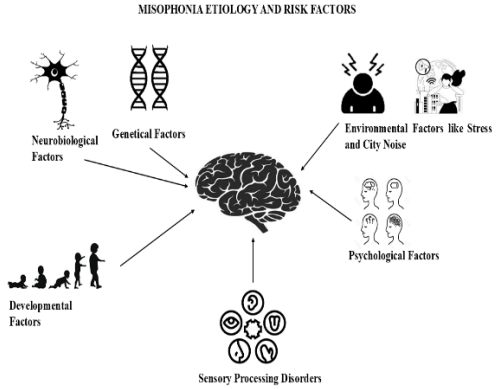

Fig.1: Etiology and risk factors of Misophonia

3. Pathophysiology Of Misophonia

Recent neuroimaging studies have been helpful to understanding the neural mechanisms of misophonia, especially regarding what brain areas are responsible for overresponse to auditory stimuli. These research studies point towards the fact that altered neural processing, particularly concerning emotional regulation as well as sensory integration, characterizes the disorder.

1. Anterior Cingulate Cortex:

Functional neuroimaging has found increased anterior cingulate cortex activity in patients with misophonia when administered trigger sounds. The ACC is significantly implicated in emotional processing, conflict resolution, and the regulation of autonomic responses. This increased activation implies that people with misophonia have exaggerated emotional reactions, such as anger, irritation, or distress, when exposed to certain sounds. The role of the ACC in associating sensory stimuli with emotional responses could account for the exaggerated affective reactions to these auditory stimuli.

2. Anterior Insular Cortex:

The anterior insular cortex is central to the integration of sensory information with emotional and physiological states. Neuroimaging studies have demonstrated that individuals with

misophonia show enhanced activation in the anterior insula when exposed to trigger sounds. This hyperactivation reflects an abnormal integration of auditory stimuli with negative emotional and autonomic responses. The insula's role in interoception and emotional awareness may contribute to the increased distress associated with misophonic episodes, as it processes both sensory input and the emotional salience of the stimuli.

3. Superior Temporal Cortex:

Activation has also been reported in the superior temporal cortex, which is a key area involved in auditory processing. This area is responsible for sound perception and its processing in relation to spatial and emotional contexts. Enhanced activity in the superior temporal cortex in individuals with misophonia suggests that there is an alteration in auditory processing, whereby certain sounds are perceived as more invasive or threatening than they would be to a neurotypical individual. The overactivation of this region may compromise the normal filtering of non-threatening sounds, leading to hypersensitivity to auditory triggers.

Implications of Neural Findings

These findings imply that misophonia is involved in a disturbance in the processing of sensory-emotional integration and that auditory stimuli are processed as not only neutral but also as emotionally threatening. The increased activity in the anterior cingulate cortex, anterior insular cortex, and superior temporal cortex reflects an exaggerated response to auditory cues, likely contributing to the emotional distress, anxiety, and physiological symptoms such as increased heart rate or sweating commonly observed in misophonic individuals. This study points to a neurobiological underpinning of misophonia and helps support the belief that the disorder is driven by alterations in auditory and emotional neural circuits, rather than purely psychological mechanisms.

5. Clinical Manifestations Of Misophonia: Triggers And Responses [17,18]

Triggers

1. **Auditory:** Common auditory triggers include sounds, such as chewing, swallowing, repetitive noises like tapping, or background noises such as the ticking of clocks. These tend to provoke immediate distress.
2. **Visual:** Visual cues like repetitive movements (for example, finger-pointing or leg swinging) and eating-related behaviors, for example, messy eating, can also be triggers, further aggravating sensory overload.

Responses

1. **Autonomic Arousal:** Exposure to triggers has increased autonomic responses such as increased heart rate, elevated blood pressure, heavy breathing, and sweating. The presence of reactions is manifested in the body's stress reaction.
2. **Anxiety and Stress:** Some people react to misophonic triggers with feelings of being overwhelmed by anxiety, stress, or panic attacks which are usually out of proportion to the stimulus.
3. **Physical Sensations:** Some of the common symptoms are a tightened stomach and tingle, showing how the body has reacted strongly to emotional stress.
4. **Aggressive Impulses:** It makes a person angry and irritated. Sometimes it becomes so extreme that they tend to get violent with the sound or become physically aggressive toward the source of the noise.
5. **Avoidance Behavior:** They might avoid areas where the triggers are located or also use earplugs and headphones to block out unwanted noises, continuing the cycle of avoidance

6. Comorbidities In Misophonia [20-23]

Misophonia often occurs in conjunction with a number of mental health and psychiatric

conditions, which can make the symptoms worse. These include:

1. **Obsessive-Compulsive Disorder (OCD):** Misophonia is commonly found in patients with OCD, as both disorders share similar mechanisms of heightened sensitivity to stimuli and intrusive thoughts.
2. **Post-Traumatic Stress Disorder (PTSD):** PTSD is commonly found in conjunction with misophonia, where traumatic experiences contribute to the heightened emotional responses to certain sounds.
3. **Obsessive-Compulsive Personality Disorder (OCPD):** Patients with OCPD can suffer from misophonia, and the rigid and perfectionistic characteristics of OCPD can heighten their response to trigger sounds.
4. **Depression:** Approximately 13% of patients with misophonia suffer from depression, which may be a consequence of the social isolation, stress, and emotional distress that this disorder can provoke.
5. **Anxieties:** Anxiety disorders, such as generalized anxiety and social anxiety, often coexist with misophonia, which means individuals have a greater emotional and physiological response to the triggers.

The comorbidities make it challenging to diagnose and treat patients with misophonia, which calls for comprehensive care that takes care of both misophonia and comorbidities.

7. **Diagnosis [24-25]**

Till now, no standard diagnostic criteria are established for misophonia, but some evaluation tools have been developed to determine the level and effects of this condition. These are the Misophonia Assessment Questionnaire (MAQ), which measures the emotional response to trigger sounds, the Misophonia Questionnaire (MQ), a self-report tool that measures the extent of symptoms, the Misophonia Activation Scale (MAS-1), which assesses the intensity of reactions to triggers, and the Amsterdam Misophonia Scale (A-MISO-S), a comprehensive scale for evaluating misophonic symptoms.

Other tools include an audiological evaluation, which assesses the sensitivity of the individual to sounds. Pure tone thresholds and loudness discomfort levels are measured to determine the presence of other auditory conditions and provide additional context for understanding the misophonia symptoms.

8. **Treatment Approaches Towards Misophonia**

The typical initial approach used to treat the misophonic disorder is with non-pharmacological interventions. Such methods that may be deployed are music therapy, headphones masking noise triggers, earplugs for directly muffling stressful sounds, Tinnitus Retraining Therapy; initially developed in order to rehabilitate patients having tinnitus but incorporates sound therapy together with counselling that makes someone learn to ignore and not even give emotional significance to triggers by habitual learning with time [25-27].

Pharmacological Treatments for Misophonia [28-30]

Pharmacological interventions are considered adjunctive treatments aimed at managing symptoms when non-pharmacological strategies alone are insufficient.

Table 1: Pharmacological Treatments for Misophonia

Medication	Purpose	Effect
MDMA (3,4-methylenedioxy-methamphetamine)	Enhances emotional processing during psychotherapy by diminishing autonomic responses.	Helps in emotional regulation and reduces reactivity to triggers.

β-blockers (e.g., propranolol)	Manages physical symptoms like increased heart rate and anxiety.	Provides symptomatic relief and aids in reducing physiological responses to stress.
Selective Serotonin Reuptake Inhibitors (SSRIs)	Commonly prescribed for anxiety and obsessive-compulsive disorders.	Reduces anxiety and compulsive behaviors associated with misophonia.
Benzodiazepines (e.g., lorazepam, clonazepam)	Used for acute anxiety management in severe cases.	Provides short-term relief of intense anxiety but with potential for dependency.
N-Methyl-D-Aspartate (NMDA) receptor antagonists	Under investigation for emotional dysregulation and sensory processing disorders.	May offer potential benefits for reducing sensory hypersensitivity and emotional response.
Antidepressants (e.g., tricyclic antidepressants)	Used for managing co-occurring depression or anxiety.	Helps stabilize mood and decrease sensitivity to triggers.
Alpha-2 adrenergic agonists (e.g., clonidine, guanfacine)	Reduce sympathetic nervous system activity.	Helps in controlling hyperarousal and autonomic symptoms like increased heart rate. [][
Antipsychotics (e.g., risperidone, aripiprazole)	Occasionally used for managing severe emotional outbursts or impulsivity.	Modulates mood and reduces aggressive responses to triggers.

9. Clinical Implications Of Misophonia [31,32]

1. **Social Isolation:** People may tend to avoid social events or events where they may be exposed to the triggering sounds, which leads to loneliness.
2. **Academic Challenges:** Increased sensitivity to sounds may cause distraction and inability to engage in academic activities, which negatively impacts performance.
3. **Workplace Challenges:** Misophonia may cause an inability to concentrate, strained relationships with colleagues, and avoidance of certain environments, which negatively impacts productivity.
4. **Reduced Quality of Life:** The entire continued strain of trying to tolerate sound triggers leads to extreme emotional and psychological distress, rendering overall well-being futile.
5. **Mental Health Complications:** Misophonia often overlaps with anxiety, depression, and other stress-related disorders that aggravate emotional distress and complicate treatment.

10. Research Gaps And Future Direction

Significant progress has been made regarding misophonia research, yet numerous critical areas exist that would allow for an advancement in the understanding of this disorder, in better diagnosis and, above all, in proper treatment. A principal gap that persists is in diagnostic criteria: presently, no established standard diagnostic tool or standardized set of criteria are available to uniformly diagnose the condition. Standardized diagnostic guidelines would make diagnosis more reliable, ensuring the possibility of correct comparisons between studies and clinical conditions. It could further help in systematically developing treatment protocols.

Validation of treatment protocols is another necessary area that should not be neglected. A variety of interventions, both non-pharmacological and pharmacological, are available; however, there is no well-rounded, evidence-based treatment scheme that has been universally embraced. More clinical trials and studies are needed to establish effective treatment regimens, including the potential benefits of combining therapies like sound therapy, cognitive-behavioral therapy (CBT), and pharmacological interventions. Understanding the neurobiological mechanisms underlying misophonia is also important. This research into specific brain regions and neural pathways will involve, among others, the anterior insular cortex, the anterior cingulate cortex, and other emotion-processing networks that could provide more accurate determination of the exact physiological causes of the condition. It could further pave the way for the design of targeted therapies, addressing the underlying cause rather than merely the symptoms of misophonia.

Long-term outcome studies are essential to determine how misophonia progresses over time, especially in terms of treatment efficacy and symptom development. Currently, there is limited research on how individuals with misophonia fare in the long term, including whether interventions result in sustained relief or if the condition worsens with age or exposure to new triggers. Finally, the investigation of genetic components is an exciting frontier. If a genetic predisposition to misophonia is identified, it could open new avenues for early intervention and personalized treatment. Genetic studies might also reveal the relationship between misophonia and other conditions like anxiety or auditory processing disorders, which would further elucidate the development of this disorder and create tailored therapeutic strategies.

11. CONCLUSION

Misophonia is a complex neurophysiological condition with intense emotional and physiological reactions to specific sounds. Characterized by affecting around 15-20% of the general population, with higher prevalence among university students and clinical populations, gender predominance is female, and the typical age of onset is childhood. Neuroimaging studies are shown to support the existence of sensory-emotional processing disruption, while etiology includes genetic and psychological influences. Common triggers include sounds of everyday activities such as eating and breathing, causing severe distress and functional impairment. Although there are no standardized diagnostic criteria, there are many assessment tools available. Treatment strategies include non-pharmacological therapies and medication. Further research is needed to improve diagnostic standards, treatment efficacy, and understanding of underlying mechanisms.

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