Soundbites
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Chapter 1
General introduction
What is this?
And how can we help her?

These were the principle thoughts I had, when I was interviewing the first patient, Ms. A. It was 2009 and I was working as a psychiatry resident at the outpatient clinic of the Academic Medical Center (AMC), department of anxiety disorders. I had been asked to examine three patients, who had been referred to Prof. Dr. Damiaan Denys with a preoccupation with certain sounds and similar aversive reactions. When hearing someone eat, drink or sigh they felt intense anger and disgust. These emotions were so strong they felt the urge to attack the other person, to kick or throw a punch. Ms. A. was a Dutch woman in her mid-twenties who explained to me that she was usually able to withhold her aggressive reactions. She would endure the triggering sounds but would not say anything. Only once had she actually screamed and hit someone. The affected person had been her boyfriend at that time, who had been eating potato chips on the couch. She had regretted it immediately. Losing her temper was not acceptable to her. She explained that when hearing someone eat, the anger would arise immediately. It did not build up gradually. The only thoughts she would have at that moment were: ‘Stop smacking!’ and ‘Sound, go away!’ She considered her reaction excessive and unreasonable. She also pointed out that she wasn’t afraid of the sounds themselves, but that it was the loss of control and potential outburst she feared. The emotions and thoughts were so intense, it made her increasingly avoid these situations. She avoided dinners with her family, stopped attending office meetings and couldn’t sleep next to her boyfriend anymore. I could see she felt miserable and could feel her suffering.

The stories of Ms. A. and the other two patients showed striking similarities. Their first memories of feeling annoyed by such sounds were from their childhood, e.g. while having a meal with their parents. Through the years, as they grew older, they had tried various strategies to cope with their complaints: Staying in the situation while trying to endure the tantalizing sounds. Wearing earplugs to block the sound. Having dinner with the radio or television switched on. Nothing seemed to work. They mostly avoided the situations with possible triggers. However, even looking at someone who was producing the sound could be bothersome. The symptoms only got worse. Doctors and psychologists didn’t know what to think of their complaints or how to help them. Some of them suggested exposure therapy, a common technique in psychiatry to relieve anxiety symptoms. This didn’t work. It even seemed to aggravate the symptoms. Others argued that it wasn’t that bad and that they should live with it. All three patients felt...
misunderstood, hopeless, and isolated. I was intrigued by their stories. And puzzled by the two questions: what is this? And how can we help them? I couldn't let it go. I really wanted to find the answers.

When this project was started at the department of anxiety disorders in 2009 little was known about this condition. In audiological literature there was a name for this phenomenon: misophonia, meaning hatred of sound or voice. It was used for strong negative reactions that were not related to the loudness of the sound, which was the case in hyperacusis, nor due to the perception of a noise or ringing sound inside the ears, i.e. tinnitus. Usually, people with misophonia had normal hearing. However, not much else was known about misophonia. The marked similarities between the symptoms of the three patients and their significant functional impairment, led us to believe that misophonia was a distinct condition. Furthermore, the symptoms could not be attributed to any known psychiatric disorder within the current classification systems, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Statistical Classification of Diseases and Related Health Problems (ICD-10). To gain more insight in this phenomenon, it was necessary to find more people with misophonic symptoms. Because in audiological literature misophonia was commonly mentioned with hyperacusis and tinnitus, we posted one small message on a Dutch Internet newsgroup for hyperacusis and tinnitus. Soon we started to receive e-mails from people who suffered from similar symptoms. This was the starting point for investigating misophonia at the AMC. Since then it has become a unique journey in which patients, therapists and researchers have been working together to address the three core issues:

1. **What is misophonia and how can we define it?** Is misophonia a separate disorder or is it a symptom of another underlying psychopathology?

2. **What happens in the brain of someone with misophonia during a misophonic reaction?** How is it possible that something so trivial as a lip smacking sound can trigger such rage in apparently normal people?

3. **How can we treat misophonia?** Is it possible to help misophonia sufferers by developing an effective therapy to attenuate misophonic symptoms?
This thesis focuses on laying a foundation for understanding misophonia. The first question we therefore asked was whether misophonia could be delineated as a distinct mental disorder. In chapter 2 we describe the first 42 patients with misophonic symptoms. We compared their symptoms to the criteria of other psychiatric disorders and posited that misophonia be classified as a separate disorder with a specific set of diagnostic criteria. Additionally, we constructed the Amsterdam Misophonia Scale (A-MISO-S), a concept scale to assess symptom severity.

The second question we raised was whether it was possible to reveal the underlying brain mechanisms involved in the misophonic reaction. Chapter 3 presents our initial study, using electro-encephalography (EEG). EEG enables recording from cortical areas with good temporal resolution. This implies that EEG electrodes can measure small and rapid changes in electric brain currents, which are recorded on the outside of the skull. Because misophonic symptoms are primary triggered by auditory stimuli, we hypothesized that this could be related to some dysfunction of the automatic auditory processing system. This study was carried out with a so-called oddball paradigm.6 In this paradigm, participants were presented with repetitive tones ("standard") with randomly occurring rare deviant tones ("oddballs"), while watching a silent movie. We examined if there were differences in specific components of the auditory event-related potentials (ERPs) – i.e. in the EEG signal - between misophonia patients and controls.

The next step was to investigate what happens in the misophonic brain during the misophonic reaction. The limitation of EEG is that it only records superficial cortical activity with restricted anatomical specificity. However, in misophonia patients the misophonic cues trigger excessive emotional reactions. Thus, the misophonic reaction is likely to additionally engage multiple emotional – limbic – brain regions. These regions are better examined and distinguished with functional magnetic resonance imaging (fMRI). We therefore proceeded with an fMRI study, which is described in chapter 4. In this study we provoked misophonic symptoms inside an MRI scanner by showing misophonic video clips to misophonia patients and healthy controls. We expected different activation in brain regions that belong to the salience network, which segregates important interoceptive and environmental information.7, 8 Furthermore, we expected to find different involvement of regions related to auditory attention. In addition, we expected that these aversive reactions would also be accompanied by increased physiological arousal, as measured with electrocardiography (ECG). Lastly, we hypothesized that possible mood changes would also be reflected in changes on
various mood questionnaires. However, it could not yet be ruled out that the main
difference between misophonia patients and healthy controls would be an increased
general averseness in patients. An aversive reaction to sounds would then be just one
of various sensory triggers eliciting aversion in misophonia patients and hence non-
specific. To control for this possibility, we also showed participants commonly aversive
video clips, i.e. loathsome scenes from different commercial movies. This would reveal
whether misophonic symptoms were specific for misophonia patients or related to
differences in general averseness levels.

The third question we raised was whether it would be possible to treat
misophonia. In cooperation with a first group of misophonia patients seeking
treatment, we assessed which cognitive behavioral therapy techniques could target the
misophonic symptoms. We noticed that mere exposure to misophonic triggers did not
reduce anger or disgust and that it might be better to combine it with other techniques.
These techniques addressed the uncontrollable intensity of the emotions and shifted
attention away from the misophonic cues. Based on this initial pilot we constructed a
group therapy, in which we combined four techniques: task concentration exercises,
counterconditioning, stimulus manipulation, and relaxation exercises. Chapter 5
describes the evaluation of this therapy in a large open-label study with 90 patients. In
addition, we investigated if there were clinical and demographic factors - such as age of
onset or symptom severity – that predicted treatment response.

In the final chapter 6 the main findings of the previous chapters are
summarized. We will put the findings in the context of existing literature, discuss the
clinical implications and suggest directions for future research.
References


