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Analyzing Sensory Gating Capacity in Misophonia

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Abstract

Misophonia is a pattern of aberrant sound perception that is defined by atypical emotional, neurophysiological, and behavioral reactivity to specific pattern-based trigger sounds (Brout et al., 2018). Those with misophonia exhibit increased arousal of the sympathetic nervous system, coupled with emotional distress, when in the presence of trigger sounds (Edelstein et al. 2013). We propose that individuals who experience this phenomenon may have difficulty in filtering out irrelevant stimuli, such that repetitive and otherwise banal sounds cannot be ignored. Thus, the current study recorded responses to pairs of repeated stimuli from participants across the misophonic severity spectrum in order to gain a measure of the degree to which misophonic experiences are associated with the ability to suppress the representation of repeated sounds. We found that misophonic symptom severity was associated with self-reports of early phase inhibition, but evidence of a relationship to objective measures of gating was less clear. These findings lay key groundwork on the relationship between aberrant early phase processing and misophonia from which future studies can expand on.

Keywords: Misophonia, Sensory gating capacity, P50 suppression, Dual-click paradigm, Repetition suppression

Summary for Lay Audience

The role of inhibition can often go unnoticed when doing simple tasks, such as conversing with a friend while at work. In this example, your brain is suppressing irrelevant information, such as other conversations, in order to focus on your friend. While at least part of the mechanism responsible for the suppression is efficient in typical populations, some individuals struggle to successfully filter out irrelevant information, and are described as having poor sensory gating capacity. In the laboratory setting, sensory gating can be assessed by using a dual-click paradigm - a task that can probe an individual's ability to suppress repeated stimuli by presenting repeated identical tones and determining if a participant's brain responds less to the second tone, reflecting effective sensory gating. While this assessment has been used to examine gating capacity in neurotypical individuals and those with disorders like ADHD, it has yet to be used to explore sound processing in people with misophonia. Misophonia is a psychological condition where individuals cannot tolerate certain sounds to the point where they exhibit intense negative emotional reactions coupled with a salient fight or flight response. Misophonic 'triggers', or sounds that elicit the misophonic experience, tend to be repetitive in nature, suggesting that those with misophonia may have difficulty suppressing repetitive sensory information. Accordingly, the current study seeks to bridge the gap in the literature by administering the dual-click paradigm to determine whether those who exhibit more severe misophonic symptoms exhibit sensory gating deficits in comparison to those who do not. Because it is understudied and poorly understood, an individual cannot be formally diagnosed with misophonia, meaning that those suffering cannot follow an empirically supported treatment option. Better understanding the deficits that underlie the experience of misophonia will help establish diagnostic tools and inform therapeutic interventions.

Co-Authorship Statement

Dr. Blake Butler was the primary supervisor of this research and was directly involved in the conceptualization, methodology, writing, and funding of this research. Dr. Yu Karen Du was involved in the coding of the EEGlab and MATlab pipeline for data analysis. Kate Raymond was involved in conceptualization, methodology, and editing of this manuscript. Jamie Jon was involved in literature review, data collection, and data compartmentalization.

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Chapter 1: Introduction

Imagine you are writing a crucial exam that you have been working towards for months. You get into the exam room filled with other students and start writing, but you find it difficult to attend to the questions because you are continuously distracted by the sounds that your classmates are making. The coughing from one classmate to the left, sniffling to the right, and pen clicking behind you cause a deeply negative and aversive reaction, coupled with a feeling of anger, annoyance, disgust, and rage, so much so that you cannot focus on the task at hand. This example highlights an intense case of Misophonia – a sound intolerance condition in which certain sounds can trigger extreme atypically aversive reactions. While misophonic triggers tend to be human-based orofacial sounds such as coughing, sniffling, and heavy breathing, individuals with misophonia routinely endorse repetitive sounds among their most common misophonic triggers, suggesting a potential deficit in inhibiting sensory information (Enzler et al., 2021). Most individuals suppress irrelevant sensory information with little effort; however, some struggle due to poor sensory gating. Sensory gating is an early-phase inhibitory process by which irrelevant stimuli are suppressed by the brain so that more behaviorally relevant stimuli retain priority access to perceptual and cognitive functions (Freedman et al., 1987). Poor early phase inhibition or sensory gating could cause an excess of sensory information in the misophonic brain, leading to aberrant auditory processing and contributing to the atypical reaction to trigger sounds. A pattern of atypical sensory gating has been found to be associated with psychological disorders, including obsessive-compulsive disorder (OCD; Kang et al., 2013; Bannon et al., 2002), attention-deficit/hyperactivity disorder (ADHD; Micoulaud-Franchi et al., 2019; Lei et al., 2015), and schizophrenia (Shen et al., 2020; Shaw et al., 2020). Notably, misophonia has been found to be comorbid with both OCD and ADHD (Schröder et al., 2013), and the condition shares strong similarities with components of the schizophrenic experience. Thus, the current study seeks to assess sensory gating across the misophonic sensitivity spectrum by analyzing self-report data as well as electroencephalographic (EEG) activity in response to an auditory dual-click paradigm (Braff & Light, 2005). This will address the gap in the literature on the relationship between sensory gating and misophonia and will strengthen our understanding of potential neural markers for this understudied condition.

1.1 What is Misophonia?

1.1.1 Characterizing Misophonia

Misophonia is a unique sensory phenomenon in which certain sounds (hereafter referred to as triggers) elicit atypically intense and emotional responses. These responses primarily manifest as anger and/or disgust, but tend to also involve other prevailing emotions, including irritation, stress and anxiety, aggravation, a feeling of being trapped, and impatience (Rouw & Erfanian, 2018). In the presence of trigger sounds, those with misophonia exhibit increased arousal of the sympathetic nervous system, or a “fight or flight” reaction, coupled with the emotions mentioned (Edelstein et al. 2013; Schröder et al., 2019).

Notably, misophonic triggers are predominantly repetitive human-based sounds. Sounds generated during eating, such as chewing, lip smacking, swallowing, and throat noises (Bernstein et al., 2013; Kumar et al., 2014, 2017; Zhou et al., 2017), as well as nasal sounds, like breathing, nose blowing, sniffling, and coughing (Wu et al., 2014; Zhou et al., 2017) comprise the most commonly reported misophonia triggers. Interestingly, different triggers tend to elicit different emotions, the most common one being a feeling of irritation towards loud chewing and heavy breathing (Vitoratou et al., 2023). Additionally, the context in which these triggers occur is noteworthy; misophonic reactions tend to be stronger when the triggers manifest in familiar settings, such as within groups of family and friends, or within occupational and educational environments (McGuire et al., 2015; Schneider & Arch, 2017). This suggests a cognitive link, or a link with appraisals in latter stages of auditory processing, between misophonic trigger sounds and the corresponding aversive reactions.

While many of these orofacial triggers are repetitive in nature, misophonics also endorse a number of other repetitive sounds (e.g., pen clicking, keyboard tapping, fingernail tapping, etc.) as particularly likely to elicit a misophonic reaction and rate them as significantly more unpleasant than control participants (Colucci, 2015; McGuire et al., 2015; Reid et al., 2016; Schröder et al., 2014; Vidal et al., 2017; Wu et al., 2014; Zhou et al., 2017; Enzler et al., 2021). Conversely, these studies typically find no differences between individuals with and without misophonia in ratings of typically pleasant (birds chirping, lake, fountain) and typically unpleasant (fork on a plate, fingernails on a chalkboard) sounds, confirming that the experience of misophonia is unique to trigger sounds, and does not present as an aversion to sound more generally. Indeed, the repetitive nature of so many common triggers raises a question as to whether those with misophonia exhibit differences in processing repetitive stimuli, or faulty sensory gating.

1.1.2 Cognitive Effects of Misophonia

Individuals with misophonia display deficits in cognition and attention in the presence of trigger sounds (Daniels et al., 2020; Frank et al., 2020; Sanchez & Silva, 2019). For example, misophonics show slower reaction times and poorer accuracy on a Stroop task (i.e., are slower/less accurate at attending to and reporting the colour of a word while ignoring its semantic content) than control participants when in the presence of common trigger sounds (Daniels et al., 2020). In contrast, no difference in response time or accuracy is observed between groups in the presence of typically unpleasant or neutral sounds. Additionally, the severity of an individual’s sensitivity to trigger sounds has been shown to uniquely correlate with deficits in reading comprehension in the presence of those sounds (Raymond & Butler, 2024). Collectively, these findings suggest that individuals with misophonia experience impairments to cognitive functions in the presence of trigger sounds. These impairments likely underscore reports that individuals with misophonia feel as though their sound sensitivities impede their overall functioning and sense of well-being (Ferrer-Torres et al., 2022). Moreover, the coping mechanisms that individuals with misophonia often employ (e.g., wearing sound cancelling headphones, mimicry of human-produced sounds, avoidance of environments in which triggers are often present) may further disrupt their ability to perform in professional or educational endeavors, which can lead to substantial impediments in social connections. The social, cognitive, and emotional consequences of misophonia highlight the urgency for further research on the condition.

1.1.3 Onset and Prevalence of Misophonia

The literature is largely undecided regarding the age at which the symptoms of misophonia first appear. An early survey of 42 individuals with misophonia found that the mean age for misophonic onset was 13 years (Schröder et al., 2013). However, more recent reviews suggest that misophonia may onset anytime during childhood, adolescence, or even in adulthood (Aryal & Prabhu, 2022), with a slightly larger proportion of studies suggesting onset occurs during adolescence (from 12 to 18 years of age; Potgieter et al., 2019). However, there remain a number of significant challenges to accurately determining the age of onset and prevalence of misophonia. Foremost, there are no standardized diagnostic criteria for misophonia, and the available literature uses a broad range of measures ranging from self-reports to diagnostic interviews. Additionally, misophonia often occurs alongside other hearing and mental health disorders, and its prevalence may be underestimated due to its potential to mimic other hearing-related conditions (Jastreboff & Jastreboff, 2014). As a result, misophonia is often regarded as an underdiagnosed disorder. The lack of concordance across surveys and the existing challenges to diagnosis further emphasize the need to better understand the nature of this disorder.

Several survey studies have attempted to quantify the prevalence of misophonia in the general population. While results have varied, the available estimates suggest that a significant portion of the population has experienced symptoms. One study of 483 undergraduate students noted that 22.8% of respondents frequently or always experienced sensitivity or irritation due to specific sounds like eating, repetitive tapping, or nasal noises (Enzler et al., 2021; Wu et al., 2014). A more recent study of medical school students reported that 49.1% of their 336 respondents reported misophonia symptoms with clinical significance (Naylor et al., 2021). However, it should be noted that this study found a significantly higher prevalence than previous studies, and that 37% showed mild misophonia, 12% showed moderate, and only 0.3% showed severe levels of misophonia (Naylor et al., 2021). There is no evidence to support sex differences in the prevalence of the misophonic experience (Ferrer-Torres et al., 2022).

1.1.4 Misophonia and Other Audiological Disorders

Misophonia frequently manifests simultaneously with related audiological conditions such as tinnitus, hyperacusis, and phonophobia. As a result, it is crucial to outline the differences between misophonia and these conditions for accurate investigation, diagnosis, and treatment (Aryal, 2022). Hyperacusis and misophonia both involve sensitivity to sound (Ferrer-Torres et al., 2022), and are sometimes considered under the umbrella of reduced sound tolerance disorders. While hyperacusis and misophonia can co-occur, they are functionally separable in that hyperacusis describes an enhanced sensitivity to a broad range of sound frequencies and volume levels, whereas misophonia centers on the subjective response to specific trigger sounds (Pienkowski et al., 2014). Misophonia is also distinct from phonophobia, which describes individuals who experience anxious and fearful reactions to specific sounds; misophonia most often manifests as anger and/or disgust (Schröder et al., 2013) with misophonics rarely suggesting they are fearful of their triggers. In short, misophonia shares some features with other audiological diagnoses, but presents as a distinct sound tolerance disorder. Additional research surrounding specific biomarkers of misophonia will help further distinguish the disorder and facilitate better differential diagnosis and treatment.

1.1.5 Misophonia and Other Psychological Disorders

The literature shows that misophonia is comorbid with, and is in some ways similar to, both ADHD and OCD (See Potgieter, 2019 for review). For example, one study of over 800 patients suggested that roughly 50% of individuals with misophonia also displayed symptoms of OCD (Cusack et al., 2018). Specifically, both conditions involve an overwhelming preoccupation with certain stimuli that is experienced as intrusive and unwanted thoughts, and individuals often employ strategies to avoid distress triggered by these thoughts (Schröder et al, 2013; Cusack et al., 2018). However, a more recent study of 575 individuals with misophonia documented lower comorbidity rates, reporting that 26% of participants exhibited traits of OCD, 10% showed evidence of mood disorders, 5% had ADHD, and 3% showed traits consistent with autism spectrum disorder (Jager et al., 2020). Importantly, in contrast to OCD, misophonics do not tend to perform compulsions to reduce their negative feelings in response to their trigger sounds, suggesting that while the two disorders may be comorbid, the experience of misophonia is not adequately explained by the presence of OCD.

1.1.6 Diagnosing Misophonia

While a number of tools have been developed over the past two decades, there is currently no agreed-upon measure or battery of measures for the diagnosis of misophonia. Because it is a sound tolerance disorder, many individuals experiencing misophonia may first seek diagnosis and/or treatment from a clinical audiologist. However, because there is no clear audiological discrepancy in those with misophonia, audiological evaluations are not currently considered to be a reliable approach to diagnosis (Ferrer-Torres et al., 2022). Instead, a complete clinical evaluation through a psychologist/psychiatrist is seen as the most comprehensive method for ensuring that what one suffers is truly misophonia and not a related disorder (Palumbo et al., 2018). Tools like the Duke Misophonia Interview (Guetta et al., 2022) help facilitate this type of detailed evaluation, and borrow their structure from widely used and psychometrically validated clinical interviews, including the Clinician-Administered PTSD Scale for DSM-5 and the Anxiety Disorders Interview Schedule for DSM-5. However, these measures are time consuming and require clinical expertise to administer and score. Fortunately, a number of self-report instruments have been developed to measure misophonic sensitivity.

1.1.6.1 The MisoQuest

The MisoQuest (Siepsiak et al., 2020) is a misophonia self-report questionnaire that was constructed to assess the following seven domains of the misophonic experience: reaction to specific sounds, an occurrence of reaction, emotional reactions, control of emotional reactions, attitude to own reactions, avoidance, and daily functioning. The finalized questionnaire comprises 14 items each rated on a scale of 1 (I definitely do not agree) to 5 (I definitely agree; Appendix A), with scores greater than 61/70 being described as clinically meaningful (Siepsiak et al., 2020). Importantly, a recent study suggests that the English translation of the MisoQuest has good discriminant and convergent validity, good test-retest reliability, and demonstrates that individual scores correlate with the scale of the impacts that trigger sounds have on cognitive function (Raymond and Butler, 2024). Scores on the MisoQuest are strongly associated with the Selective Sound Sensitivity Syndrome Scale (S-Five; Vitoratou et al., 2021), reflecting good convergent validity. In addition, the study found that MisoQuest scores are only moderately associated with measures of anxiety and hypersensitivity; however, these associations could be interpreted by comorbidities with these conditions rather than a flaw in the assessment itself. The results of this investigation reinforced that the MisoQuest specifically tests for misophonia and not comorbid conditions such as OCD or more general hypersensitivity conditions (Raymond and Butler, 2024). In this way, the MisoQuest differs from other popular self-report measures (e.g., the Amsterdam misophonia scale [A-MISO-S; Schröder et al., 2013] or the misophonia quotient [MQ; 5 Wu et al., 2014]), which were adapted from OCD assessments based on an early mischaracterization of misophonia.

1.1.7 Summary

The past two decades have provided studies and diagnostic tools that give us an idea of the onset, prevalence, and distinctiveness of the misophonic experience. However, the literature is still growing, and the lack of a formal diagnostic procedure prevents us from drawing conclusions with confidence. This further emphasizes the need for investigations on potential markers for misophonia, including objective measures that may complement self-reports. Although the literature is sparce, a few studies have begun to identify neurological and physiological patterns that seem to be unique to misophonia.

1.2 Physiological Markers of Misophonia and Associated Deficits

1.2.1 Atypical Sound-Emotion Association

Trigger sounds often induce an autonomic response in individuals with misophonia that manifests as increased skin conductance and, in more severe cases, elevated blood pressure and heart rate, feelings of physical pain, and difficulty breathing (Edelstein et al., 2013; Schröder et al., 2019) as well as increased heart rate (Schröder et al., 2019). Importantly, this increased arousal is unique to trigger sounds, and the magnitude of the response is correlated with how intensely aversive the sound was reported to be (Edelstein et al., 2013). Accordingly, functional imaging has revealed that trigger sounds evoke activity in the anterior insular (Kumar et al., 2017; Schröder et al., 2019) and anterior cingulate cortices (Schröder et al., 2019), as well as heightened connectivity between the anterior insula and brain regions responsible for emotion regulation, such as the ventromedial prefrontal cortex (vmPFC), the hippocampus, and the amygdala (Kumar et al., 2017). Additionally, trigger sounds have been associated with the right superior temporal cortex (Schröder et al., 2019), increased orbitofrontal cortex connectivity, and increased interaction between the mid-cingulate and primary auditory cortex in comparison to controls (Cerliani & Rouw, 2020).

The anterior insula is a key component of the salience network, which plays a role in attributing salience to external stimuli and directing attention towards them (Garfinkel & Critchley, 2013). Similarly, the superior temporal cortex and anterior cingulate have both been associated with the allocation of auditory attention. Thus, the increased activity observed across these brain areas points to an overactivation of the network responsible for detecting and selecting emotionally relevant sensory information. Moreover, that patterns of atypical activity/connectivity are specific to trigger sounds further supports the idea that misophonia is characterized by exaggerated responses to specific stimuli rather than a generalized emotion disorder or aversion to sound.

1.2.2 The Potential Role of Aberrant Bottom-up Processing in Misophonia

In individuals with misophonia, trigger sounds evoke increased activity in auditory cortex relative to non-trigger sounds (Kumar et al., 2017), suggesting the system may be hypersensitized to specific sounds. One potential explanation involves a deficit in inhibiting and filtering out behaviorally irrelevant sensory information in early phases of auditory processing, which in turn contributes to aberrant higher-order processing. This idea is supported by the fact that individuals with misophonia endorse repetitive orofacial and non-orofacial sounds among the most common trigger sounds (see section 1.1.1), including many that are easily ignored by individuals without these sensitivities. While the mechanisms underlying this potential hypersensitivity in misophonia remain unclear, analyzing whether misophonics exhibit difficulty in inhibiting irrelevant sounds would progress the notion that poor inhibition in the misophonic brain may be contributing to hypersensitivity.

1.2.3 An Overview of Inhibition

As we move through the world we are constantly bombarded by sensory inputs. In order to focus on the most behaviorally relevant stimuli in our environments, we must suppress the representations of the majority of these inputs. Thus, inhibitory mechanisms are essential to processing and integrating sensory information effectively. With respect to auditory perception, inhibition can occur across several levels within the hierarchy of processing. The earliest form of inhibition involves filtering out unnecessary information before it gets processed extensively by attentional and cognitive functions (Freedman et al., 1987). This process has been termed ‘sensory gating’. Signals that are allowed through the ‘gate’ can subsequently be inhibited via cognitive inhibition (Harnishfeger, 1995) – the mental process of diminishing or eliminating information that has been encoded but has thereafter been deemed irrelevant. This level of inhibition involves cognitive appraisal, while sensory gating is thought to be more automatic. Finally, behavioral inhibition describes the process by which the behavioral response elicited by an external stimulus is inhibited after conscious perception (Harnishfeger, 1995). While each of these processes in critical to selecting and acting upon stimuli in the environment, the current thesis focuses on early sensory gating of sounds.

1.2.4 Measuring Sensory Gating

Reduced sensory gating has been shown to be related to difficulty sleeping (Milner et al., 2009), differences in social skills (Ebishima et al., 2019), cognitive impairments (Park et al., 2015), and attentional difficulties (Jones et al., 2016). Not surprisingly, there has been growing interest in ways to quantify gating across populations and individuals. There are various ways to operationalize sensory gating capacity in humans and in animals; however, there remains a lack of consensus regarding which established physiological measure of sensory gating might best be used for assessing clinical populations (Schulz et al., 2022).

The sensory gating inventory (SGI) is a self-report measure that attempts to capture self-perceived sensory gating capacity. This measure was developed to evaluate an individual’s perceived ability to filter irrelevant sensory information and focus on relevant environmental cues (Bailey et al., 2021). Because sensory gating deficits are known to be associated with psychopathologies, the SGI has been used as a diagnostic tool for disorders such as ADHD, OCD, and ASD.

However, to facilitate more efficient clinical and laboratory use of this inventory, a shortened version was subsequently developed (Bailey et al., 2021). Exploratory factor analysis suggested that the SGI was heavily influenced by a general factor across the original four dimensions; thus, a 10-item unidimensional subset of the SGI (the SGI-B) was created (Bailey et al., 2021). When administered, higher scores on this inventory reflect poorer self-perceived sensory gating capacity.

One way we can objectively operationalize a potential neural mechanism underlying poor self-perceived sensory gating is through the use of electroencephalography (EEG). EEG records the electrical activity of populations of neurons via electrodes placed onto the scalp that capture changes in voltage potential caused by the generation of action potentials in the underlying neural tissue (Müller-Putz, 2021). Event-related potentials (ERPs) are a key component of EEG studies and can be used to measure the brain's response to specific stimuli by examining the average patterns of activity evoked by those stimuli across multiple presentations. The sub-millisecond temporal precision of EEG makes it a particularly valuable tool to study processes like sensory gating, which occur in close proximity to the onset of sounds.

Sound-evoked ERPs are characterized by a sequence of peaks occurring 50ms (P50), 100ms (N100), and 200ms (P200) after stimulus onset (Lijffijt et al., 2009). The P50 peak is thought to reflect the brain’s initial step of safeguarding cognitive processes by preventing irrelevant information from overwhelming and interfering with higher-order thinking (i.e., sensory gating; Freedman, Waldo, Bickford-Wimer, & Nagamoto, 1991; Hsieh, Liu, Chiu, Hwu, & Chen, 2004). In contrast, later components including the N100 and P200 are thought to reflect mechanisms related to the triggering and allocation of attention (Lijffijt et al., 2009). Thus, examining patterns of evoked potentials may inform the nature of any underlying deficits in sound processing.

Several studies have considered group differences in the P50 response as a measure of sensory gating deficits in clinical populations. For example, in individuals with ADHD, high distractibility has been associated with poor sensory gating as evidenced by both the SGI (Sable et al., 2012; Micoulaud-Franchi et al., 2015) and dual-click EEG paradigms (wherein a smaller evoked response to the second click in each pair is taken as a measure of successful gating; Holstein et al., 2013; Micoulaud-Franchi et al., 2015; but see Olincy et al., 2000). Impaired sensory gating has also been shown in adults with OCD using a dual-click paradigm (Hashimoto et al., 2008) as well as a pre-pulse inhibition of the acoustic startle response paradigm (Ahmari et al., 2012).

Relative to ADHD and OCD, the literature on misophonia and auditory-evoked potentials is limited. One study comparing ERPs evoked by infrequent deviant pure tones found that individuals with misophonia showed a smaller average N100 amplitude than control participants but failed to find a group difference in P50 amplitude (Schröder et al., 2014). This suggested that individuals with misophonia may show a deficit in early attentional processing, or 'cognitive inhibition' but did not differ with respect to sensory gating. An additional study that examined ERPs evoked by repeated pure tone bursts found that, while P50 amplitude did not differ between individuals with misophonia and controls, the latency of the P50 decreased with increasing symptom severity (Aryal and Prabhu, 2023). It is worth noting that while these studies provide mixed results, neither was optimized to detect differences in P50 amplitude, which typically involves the use of paired stimuli (Freedman et al., 2020). We believe that the administration of paired stimuli (i.e., repeated, identical sounds), would better reflect the repetitive trigger sounds that misophonics tend to report as aversive. Thus, the literature would benefit from additional, targeted work examining P50 suppression as an index of sensory gating in misophonia.

1.3 The Present Study

The current study aims to determine whether sensory gating deficits are associated with misophonia symptom severity. In addition to self-report measures (the MIsoQuest, SGI-B), participants are presented with a dual-click paradigm that has been shown to be sensitive to differences in P50 suppression among clinical populations (Micoulaud-Franchi et al., 2019). This approach complements previous work that, by design, was more sensitive to differences in later ERP components (e.g., Schröder et al., 2014) and allows for more detailed conclusions to be drawn about the relationship between sensory gating and the misophonic experience. I hypothesize that individuals with more severe sound sensitivity will show larger deficits in suppressing the neural representation of the second of two paired clicks, reflecting a deficit in filtering out irrelevant sensory information. In addition, I hypothesize that higher MisoQuest scores will be associated with poorer self-reported sensory gating capacity, as captured by higher scores on the SGI-B. Similar to previous work (Aryal & Prabhu, 2023) I hypothesize that misophonic severity will be associated with decreased P50 peak latency. Lastly, I hypothesize that objective and subjective measures of sensory gating will be correlated, which will support the idea that P50 suppression is a useful measure of sensory gating capacity.

1.4 Methods

1.4.1 Participants

Participants were mainly recruited through Western University's SONA platform. This platform is open to university students during the school year, and their participation is rewarded with SONA credits that are either required for passing a course or are used for a grade increase in a course. Participants were also recruited through posters placed throughout Western University campus, and through word of mouth. To be included in the study, participants were required to be 18 years of age or older, fluent in English, and have self-reported normal hearing and normal or corrected-to-normal vision. In line with previous studies, exclusion criteria included a history of or current psychological disorder, brain injury, a severe medical disorder, addiction to drugs or alcohol (Micoulaud-Franchi et al., 2019). Additionally, participants were asked to refrain from caffeine or nicotine consumption at least 6 hours prior to the study, as these compounds have been demonstrated to affect the reliability of the P50 response (Choueiry, 2023; Ghisolfi et al., 2006). This study was approved by the Western University Non-Medical Research Ethics Board (NMREB; Appendix A).

1.4.2 Study Procedure

At the start of the session, participants provided informed consent to participate in the experiment. Because there are no agreed-upon diagnostic criteria for misophonia, current best practices for research typically include administering a measure of misophonia symptom severity *and* a battery of other measures that provide evidence that a participant's symptoms are not better explained by a related disorder. Accordingly, participants completed six self-report questionnaires: the MisoQuest, the Sensory Gating Inventory (SGI), the 7-item Generalized Anxiety Disorder Inventory (GAD-7), the Adult ADHD Self-Report Scale (ASRS), the Autism Spectrum Quotient (AQ-10), and the revised Obsessive-Compulsive Inventory (OCI-R). Demographic information such as age and gender were also collected. Following this, participants' heads were measured to ensure an appropriate fit for a 32-channel BioSemi EEG cap. With all electrode sensors in place, participants were seated comfortably in front of a computer monitor and provided with headphones through which they heard the experimental sounds. During the experiment, participants watched a silent film (Pixar's *Wall-E*) and were asked to remain as still as possible. There was no instruction as to whether to pay attention to the sounds or not. Upon completion, electrode caps were removed and participants were provided with debriefing information.

1.4.3 Questionnaires

1.4.3.1 MisoQuest

The MisoQuest was used to assess misophonic severity. As described above, the MisoQuest is a 14-item self-assessment that asks participants to rate a series of statements on a scale of 1 (I definitely do not agree) to 5 (I definitely agree).

The authors of this measure suggest that a score of 61 or greater represents clinically relevant sensitivity; however, in practice, we and others have found this to be quite conservative. Accordingly, MisoQuest scores are used as a continuous measure of sound sensitivity in the current study.

1.4.3.2 Sensory Gating Inventory-Brief (SGI-B)

The SGI-B (Appendix C) is a self-report measure of an individual's ability to ignore irrelevant stimuli in their environment, and was selected for the current study as it has been found to reliably detect sensory gating differences between individuals with and without diagnosed neurodevelopmental disorders (Schulz et al., 2022).

1.4.3.3 Autism Quotient (AQ-10)

The Autism-Spectrum Quotient (AQ) was designed to be a self-administered instrument for measuring the degree to which an adult with normal intelligence displays traits associated with the autistic spectrum (Baron-Cohen et al. 2001). In an effort to create a more streamlined measure, a 10-item version (AQ-10; Appendix D) was generated by selecting the 2 items with the highest discriminatory power in each of the 5 subscales that comprise the AQ (Allison et al., 2012; Booth et al., 2013). Since the purpose here was simply to assess the potential that sound sensitivity could be related to sensory issues prevalent in autistic individuals, the abbreviated measure was selected. This measure was not directly compared with our EEG measure of sensory gating capacity as it was not a continuous measure, and only one participant was found to be at risk for clinical levels of autism.

1.4.3.4 Generalized Anxiety Disorder (GAD-7)

The GAD-7 (Appendix E) is a 7-item inventory used to measure generalized anxiety disorder by assessing the frequency with which an individual experienced symptoms associated with anxiety over the previous two weeks (Spitzer et al., 2006). Symptoms such as nervousness, worrying, having trouble relaxing, finding it hard to sit still, etc. are used to create an overall score between 0-21 which is binned as follows: 0–4: minimal anxiety; 5–9: mild anxiety; 10–14: moderate anxiety; 15–21: severe anxiety (Spitzer et al., 2006). The GAD-7 has been shown to be reliable to have a unidimensional structure that reflects generalized anxiety across a sample of over 5000 subjects (Löwe et al., 2008). This measure was utilized in a linear regression analysis to control for its potential confounding of the relationship between misophonia and sensory gating capacity.

1.4.3.5 Obsessive Compulsive Inventory Revied (OCI-R)

The Obsessive-Compulsive Inventory (OCI) is a 42-item self-assessment composing 7 subscales: Washing, Checking, Doubting, Ordering, Obsessing (i.e., having obsessional thoughts), Hoarding, and Mental Neutralizing (Foa et al., 1998). The OCI was subsequently revised to eliminate the redundant frequency scale, simplify the scoring of the subscales, and reduces overlap across subscales. The revised measure (OCI-R; Foa et al., 2002; Appendix F) comprises 18 items, generates a score between 0 and 72, and has been shown to be a psychometrically comprehensive instrument appropriate for research scenarios in clinical and non-clinical population (Huppert et al., 2007). This measure was utilized in a linear regression analysis to control for its potential confounding of the relationship between misophonia and sensory gating capacity.

1.4.3.6 Adult ADHD Self Report Scale (ASRS)

The ASRS (Appendix G) assesses how often participants experience 18 ADHD symptoms using the following scale: never, rarely, sometimes, often, very often (Kessler et al., 2005). Developed by the World Health Organization, it is primarily used as a tool in the first step of diagnostic evaluation to determine whether a participant requires further assessment for the presence of ADHD (Kessler et al., 2005). This measure was utilized to determine if there was a subgroup of individuals who showed clinical levels of ADHD when assessing misophonic sensitivity across sensory gating capacity.

1.4.4 Assessing Sound-Evoked Neural Activity

To provide an objective measure of sensory gating, identical pairs of brief clicks were delivered in a passive listening task. Each stimulus consisted of a 0.05 ms square wave pulse presented over headphones at an intensity of 100 dB SPL. Each stimulus pair consisted of a conditioning click (S1) and a testing click (S2) presented with an inter-stimulus interval of 500 ms. This interval is thought to encapsulate the gating mechanism better than shorter or longer intervals (Dolu et al., 2001). A total of 100 stimulus pairs were presented with a mean inter-pair interval of 9 s (intervals were drawn randomly from a normal distribution ranging from 8-10 s). These intervals have been shown to be sufficient to reset the sensory gating mechanism between pairs (Dalecki et al., 2011). The averages of the S1 and S2 ERP responses elicited by these 100 pairs were compared to provide a measure of sensory gating.

A 32-channel BioSemi electroencephalographic (EEG) system was used to record stimulus-evoked brain activity (Biosemi; Amsterdam, Netherlands). Electrodes were positioned according to the International 10/20 convention, with Common Mode Sense (CMS) and Driven Right Leg (DRL) used as the reference and grounding electrodes. Electrode impedance was maintained below 20 kΩ and data were recorded with a sampling rate of 512 Hz. A Stimtracker Duo (Cedrus; San Pedro, California) was used to mark stimulus onsets in the EEG recording using the rising phase of the acoustic signal to ensure that event-related potential latencies were reliably recorded.

1.4.5 EEG Preprocessing

Raw data with a recorded sampling rate of 512 Hz were read into EEGlab in MATLab (Mathworks; Natick Massachussetts) and were: 1) re-referenced to the average of all the channels using ‘pop_reref’; and 2) bandpass filtered between 1 Hz and 50 Hz using a hamming-windowed sinc FIR filer via the ‘pop_eegfiltnew’ function (Delorme & Makeig, 2004). Filtered data were then subjected to independent components analysis using the ‘runica’ function, and components deemed unlikely to reflect brain activity were removed on an individual subject basis. Specifically, components judged by the ‘icatype’ function to have a 90% or greater likelihood of being noise (including blinks, eye movements, physiological signals, etc.) were visually inspected and removed. Lastly, channels with kurtosis > 3, or those showing obvious irregularities on visual inspection were identified as bad channels were spherically interpolated using the ‘pop_interp’ function. Unless otherwise specified, the default settings within EEGlab for these preprocessing functions were employed.

1.4.6 Quantifying ERP Amplitudes

Components of the auditory evoked potential, including the P50, are robustly observed over central and frontocentral electrodes (Korzyukov et al., 2007). Accordingly, in the current study we averaged the activity recorded across five frontocentral electrodes (CZ, CP1, CP2, FC1, and FC2). Data were epoched from 0 to 500 ms relative to sound onsets, and separate averages were computed for each of the two paired stimuli (S1 and S2) using the period between -200 and 0 ms as a baseline. The P50 component was identified as the largest positive-going peak occurring between 40 and 80 ms post-stimulus-onset for each of the two paired stimuli. The amplitude of each component was calculated as the difference between the peak and the preceding trough. Peaks and troughs for each participant were manually scanned by a researcher to identify potentially noisy participants. If a participants’ averaged ERP response to the dual-click paradigm did not exhibit discernable peaks around the time windows, or if the S2/S1 ratios were disproportionate (e.g. much higher than 1) then the data of these participants were dropped. A total of five participants met these cutoff requirements and their data were dropped from the analyses entirely, leaving us with our sample of 38 participants. In order to quantify sensory gating, the amplitude of the P50 response elicited by the second stimulus was divided by the amplitude of the response elicited by the first stimulus (hereafter referred to as the P50 S2/S1 ratio). High values (e.g. S2/S1 = 1) suggest minimal gating of the neural response to repeated stimulus, while lower values (e.g., S2/S1 = 0.1) suggest significant gating of the second stimulus relative to the first (Freedman et al., 1987).

1.4.7 Statistical Analyses

Spearman's Rho correlation coefficients were used to quantify the relationships between measures of sensory gating capacity (SGI-B or S2/S1 ratios) and MisoQuest scores, as well as between the measures of sensory gating capacity themselves (SGI-B vs S2/S1 ratios), and finally, between MisoQuest scores and S1, S2, and S2-S1 peak latency. Additionally, linear regression analyses were conducted to determine whether factors including age, GAD-7 scores, and OCI-R scores modified these relationships. Analyses were conducted using JASP (Version 0.18.3). Lastly, an EEG waveform plot of the ERP responses of two sample participants was created for visualization purposes.

1.5 Results

1.5.1 Sample Characteristics

Our total sample consisted of 38 participants (31 F), aged 18-59 (M = 23, SD = 9). Scores on the MisoQuest ranged from 18-64 (M = 37, SD = 11.9), resulting in a good distribution across the broad range of sound sensitivity. Additionally, P50 S2/S1 ratios (M = .36, SD = .24) ranged from 0.01, reflecting substantial suppression of repetitive stimuli, to 0.92, reflecting very little suppression of this response (see Table 1 for summary of measures collected).

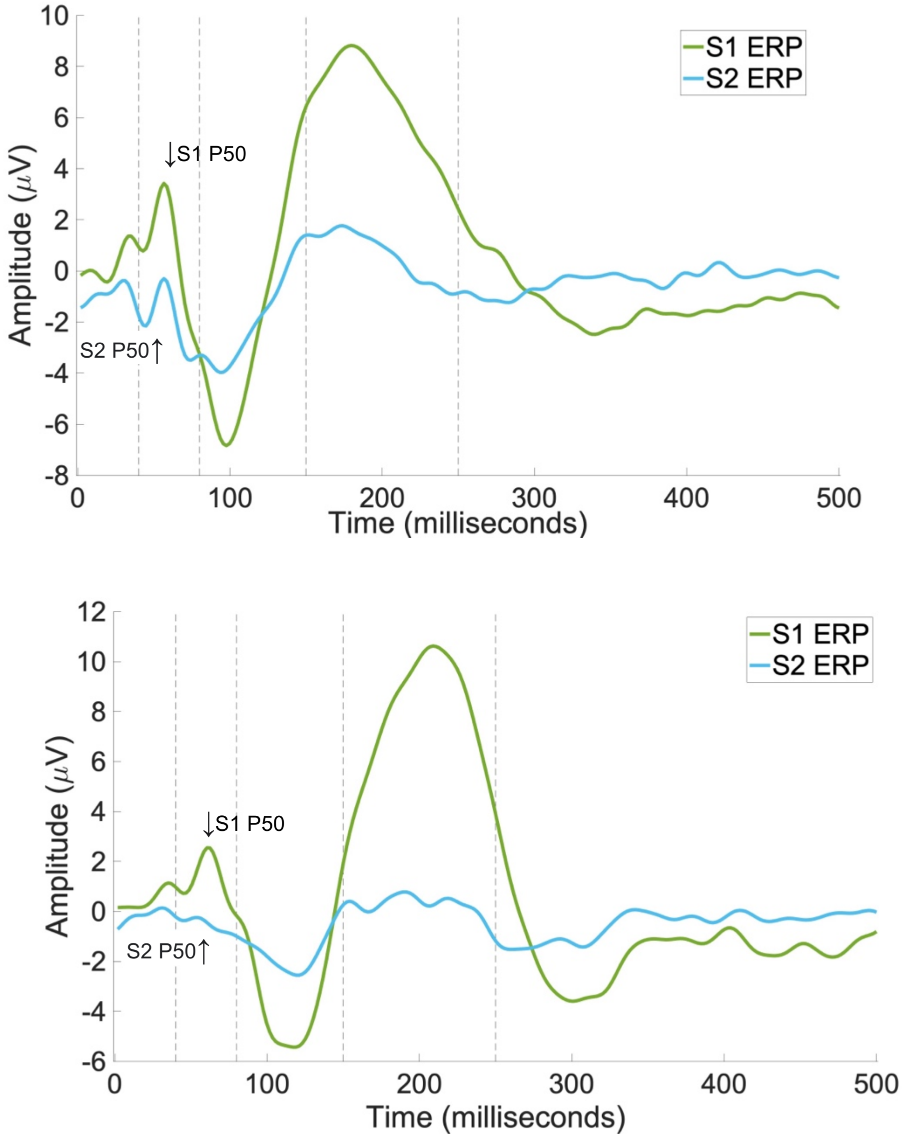
Table 1: Mean and Standard Deviation of Measures Used in This Study (*N* = 38)

Measure	*M*	*SD*
P50 S2/S1 Ratio	0.36	.30
P50 S1 amplitude (μV)	1.42	.63
P50 S2 amplitude (μV)	.62	.60
P50 S1 Latency (ms)	61.18	1.85
P50 S2 Latency (ms)	59.79	3.48
Misoquest Scores	37.29	11.68
SGI-B Scores	21.16	7.68
OCI-R Scores	18.43	8.24
GAD-7 Scores	8.26	3.07

1.5.2 Visualization of Auditory Evoked Responses

Each square wave impulse evoked an event-related response that consisted of a positive-going deflection occurring roughly 50 ms after sound onset (the P50), followed by negative-going and positive-going deflections around 100 ms and 200 ms post-stimulus-onset (the N100 and P200, respectively). Figure 1 illustrates the average responses evoked by the first (S1) and second (S2) of the paired impulses from a participant who showed clinical levels of misophonia (a), and a participant with a milder sound sensitivity (b).

a)



b)

Figure 1: Example ERPs elicited in response to the first (green) and second (blue) or the paired sounds from two participants with differing levels of misophonic severity. (a) a participant who scored 64 on the MisoQuest and exhibited a P50 S2/S1 ratio of 0.700. (b) a participant who scored 30 on the MisoQuest and exhibited a P50 S2/S1 ratio of .067. Dotted lines show timepoints at 40ms, 80ms, 150ms, and 250ms to highlight the P50, N100, and P200 time windows. Waveforms consist the average of the responses at the CZ, CP1, CP2, FC1, and FC2 electrodes.

1.5.3 Relationship Between Sensory Gating and Misophonic Severity

To examine whether there was a relationship between sensory gating and sound sensitivity, the Spearman's correlation was computed between S2/S1 ratio and MisoQuest score. This relationship was not statistically significant ($\rho(37) = 0.23$, $p = 0.164$; Figure 2).

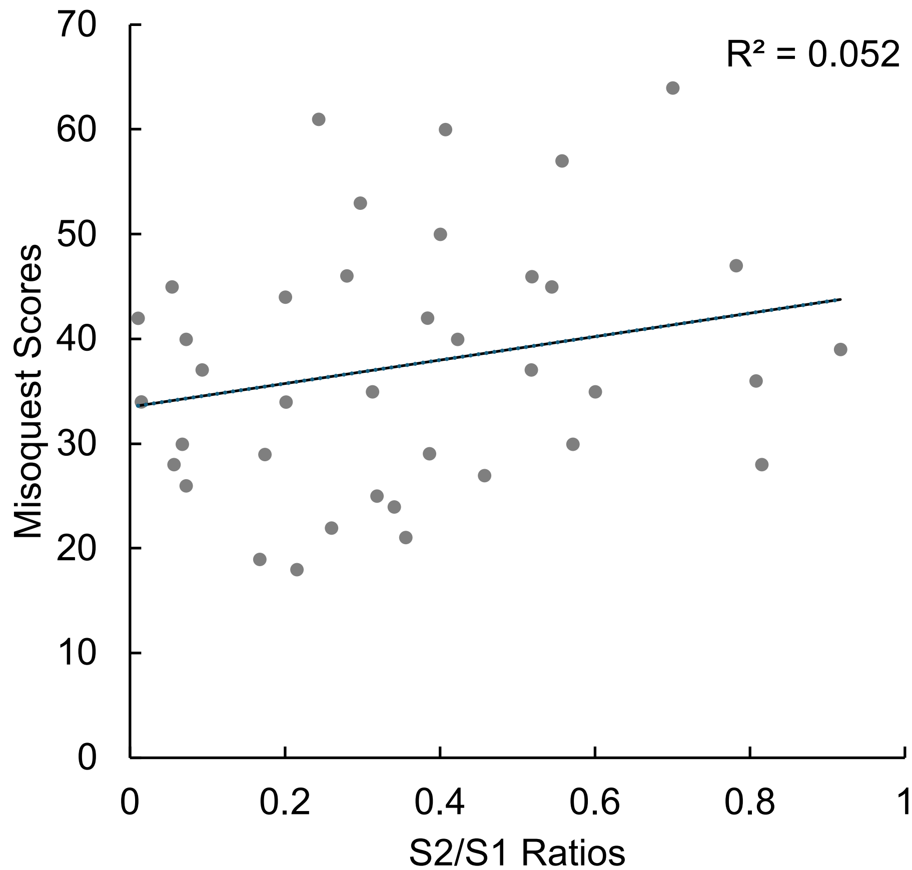


Figure 2: Scatterplot of the relationship between P50 S2/S1 ratios and MisoQuest scores.

In contrast, participants' subjective assessments of their sensory gating abilities (i.e., SGI-B scores; higher scores mean more perceived difficulty) were significantly correlated with symptom severity (ρ(37) = 0.67, *p* = <0.001; Figure 2), suggesting a strong correspondence between SGI-B and MisoQuest scores.

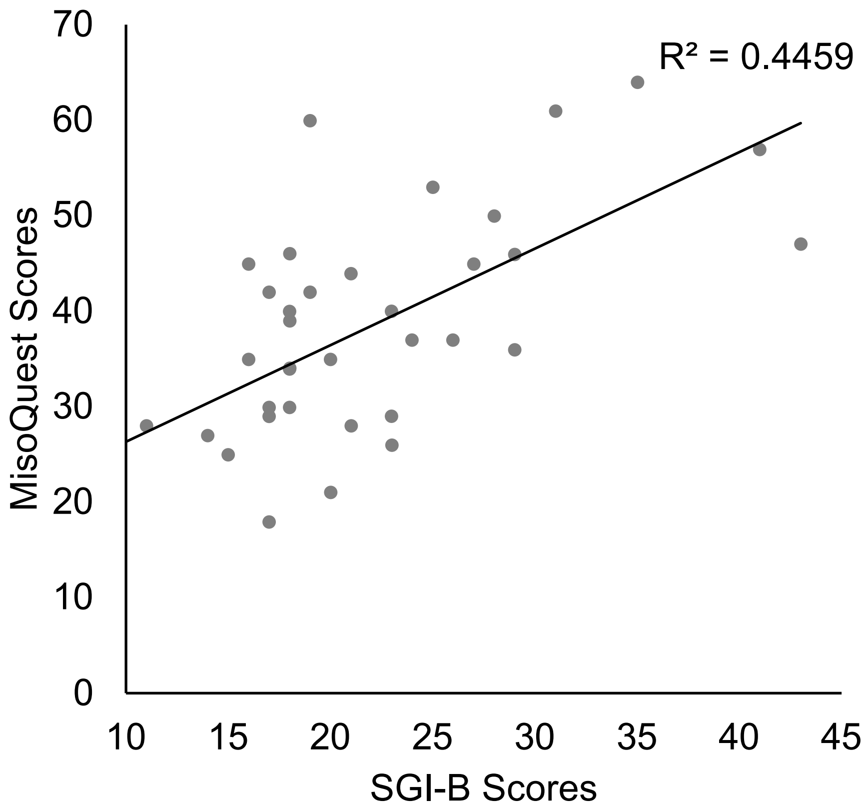


Figure 3: Scatterplot of the relationship between SGI-B scores and MisoQuest scores.

1.5.4 Relationship Between Objective and Subjective Measures of Gating

Additionally, we assessed the degree of correspondence between self-reported sensory gating difficulties and the objective measure assessed here (P50 S2/S1 ratio). The Spearman correlation between the two measures was statistically significant (ρ (37) = 0.35, p = 0.029), suggesting that individuals with low self-perceived sensory gating capacity also showed less suppression of the neural response to repeated sounds (Figure 3).

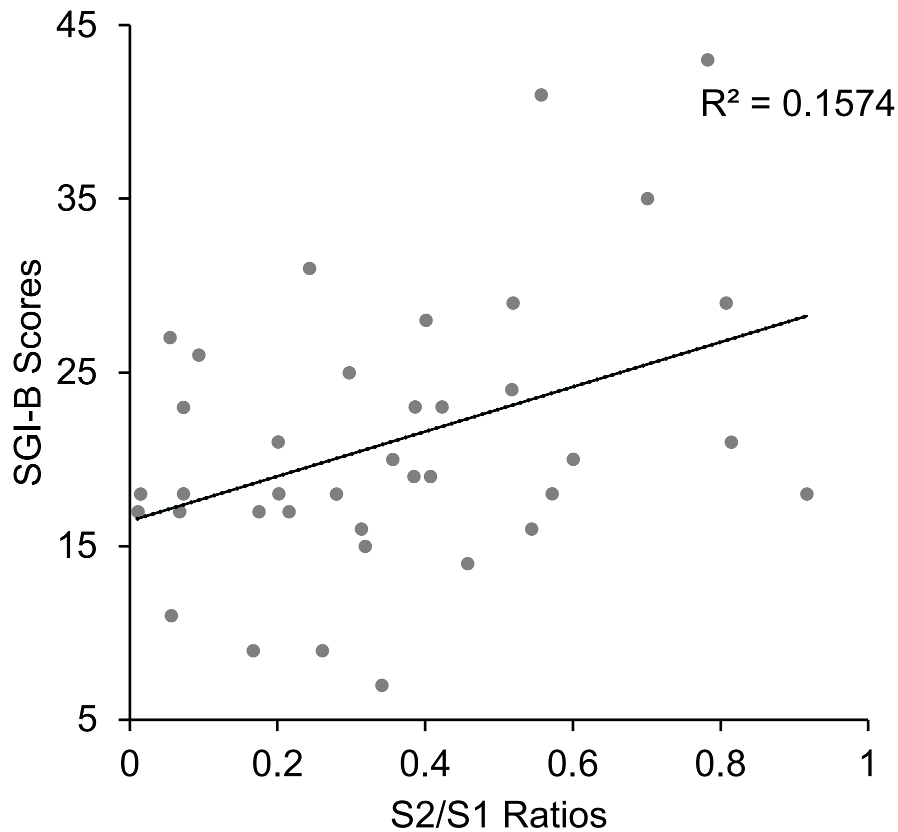


Figure 4: Scatterplot of the relationship between P50 S2/S1 ratios and SGI-B scores.

1.5.5 Relationship Between MisoQuest Scores and ERP Peak Latency

Finally, we analyzed the degree of correspondence between misophonic sensitivity and the latency of the P50 component elicited by each of the paired stimuli. The Spearman correlation between S1 P50 latency and misophonia severity was not significant (ρ (37) = -.177, *p* = 0.280; Figure 5). Similarly, the Spearman correlation between S2 P50 latency and misophonia severity was not significant (ρ (37) = -.151, *p* = 0.358; Figure 6). Lastly, the difference in latency between S2 and S1 peaks was not associated with misophonic severity (ρ (37) = -.182, *p* = 0.275; Figure 7). Taken together, our results do not support that misophonic severity is associated with shifts in the latency of P50 components elicited by stimuli presented in the dual-click task.

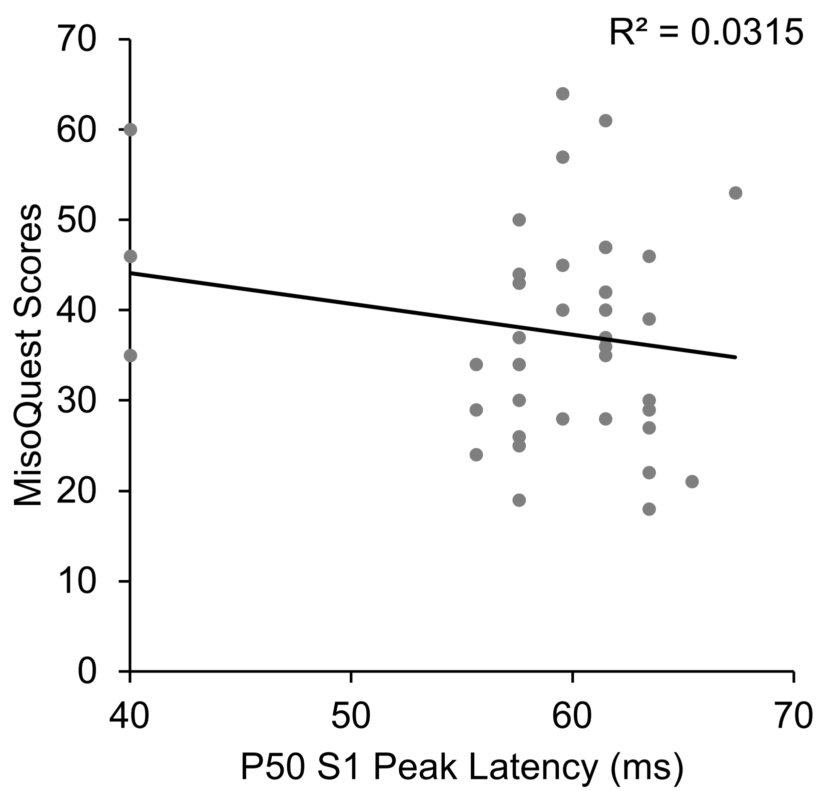


Figure 5: Scatterplot of the relationship between S1 P50 Latency and MisoQuest Scores.

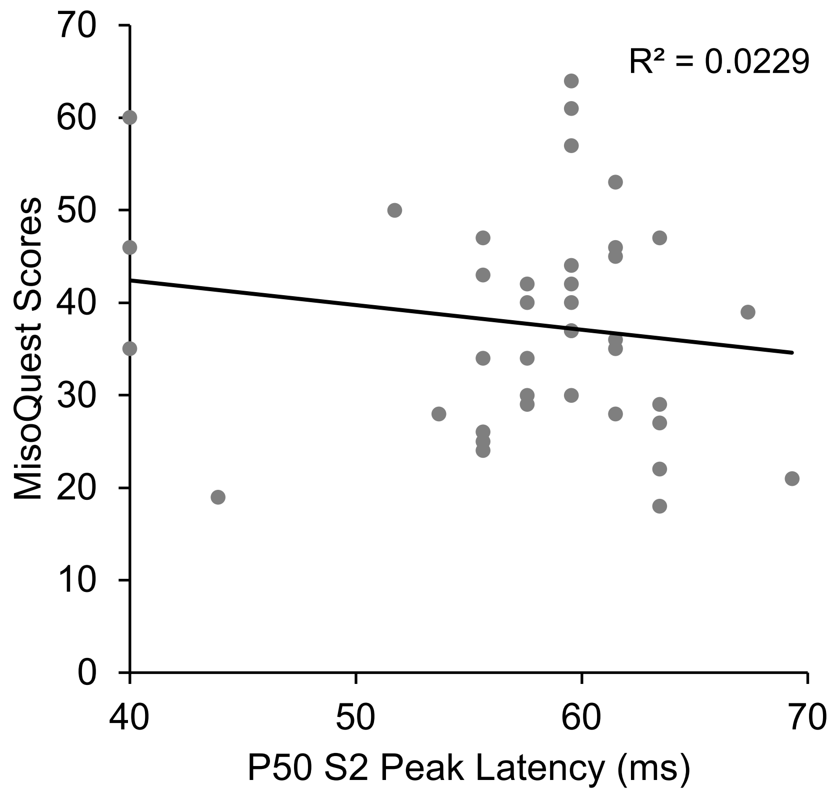


Figure 6: Scatterplot of the relationship between P50 S2 Peak Latency and MisoQuest scores.

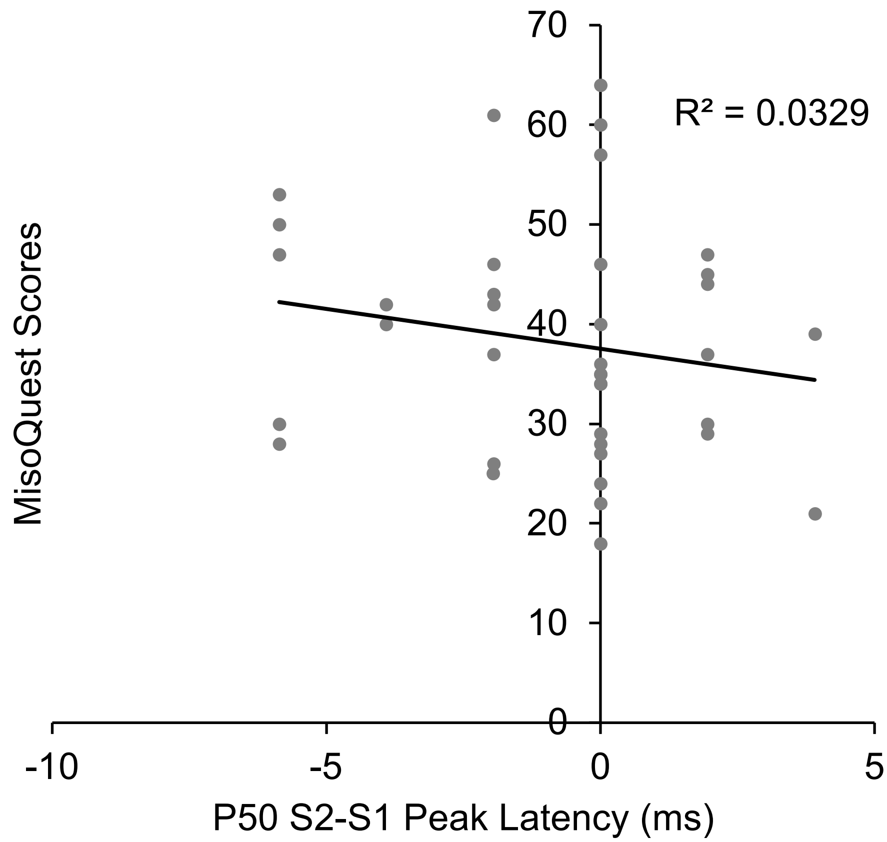


Figure 7: Scatterplot of the relationship between the difference in peak latencies evoked by the first and second of the paired stimuli (S2 latency - S1 latency) and SGI-B scores. Note: one outlier was dropped with a kurtosis > 3.

1.5.6 Linear Regression Analyses

To examine how variables such as age, OCI-R scores, GAD-7 scores, ASRS scores, and AQ-10 scores might modify the relationships explored above, MisoQuest and SGI-B scores were subjected to linear regression analyses to assess their contribution to S2/S1 ratios when controlling for these factors. This approach is similar that of Micoulaud-Franchi et al. (2019), who conducted a similar linear regression model when assessing the relationship between ADHD severity and S2/S1 ratios. SGI-B scores were found to contribute to S2/S1 ratios when controlling for all other factors, with a standardized coefficient of .371 (p = .061), while Misoquest scores failed to reach statistical significance with a standardized coefficient of .321 (p = .101). Both standardized coefficients are moderate in strength and suggest that as S2/S1 ratios increase, misophonic severity and sensory gating deficits both decrease; however, a larger sample size is needed to solidify this interpretation.

Table 2: Effect of MisoQuest scores on S2/S1 ratios controlling for cofactors

Model		Unstandardized	SE	Standardized	t	p
H_0	(intercept)	.37	.04		8.41	<.01
H_1	(intercept)	.30	.23		1.28	.21
	Age	<-.01	.<.01	-.27	-1.3	.2
	OCI-R	<.01	<.01	.03	.14	.89
	GAD-7	<-.01	.01	-.08	-.37	.71
	ASRS (Yes)	.02	.10		.23	.82
	AQ-10 (Yes)	-.09	.22		-.4	.68
	MisoQuest	<.01	<.01	.32	1.75	.1

Table 3: Effect of SGI-B scores on S2/S1 ratios controlling for cofactors

Model		Unstandardized	SE	Standardized	t	p
H_0	(intercept)	.37	.04		8.41	<.01
H_1	(intercept)	.32	.21		1.25	.22
	Age	<-.01	.<.01	-.17	-.85	.4
	OCI-R	<.01	<.01	.02	.08	.93
	GAD-7	<-.01	.01	-.13	-.64	.53
	ASRS (Yes)	.03	.1		.28	.78
	AQ-10 (Yes)	-.07	.22		-.32	.75
	SGI-B	.01	<.01	.37	2.00	.06

1.6 Discussion

The current study sought to analyze the relationship between misophonic sensitivity and an individual's ability to inhibit repeated sounds via sensory gating – an early, inhibitory process by which irrelevant stimuli are suppressed so that more behaviorally relevant stimuli retain priority access to perceptual and cognitive functions. We operationalized sensory gating in two ways: the SGI-B questionnaire provided a measure of self-perceived sensory gating capacity, while a comparison of the electrical potentials evoked a pair of repeated sounds (the P50 S2/S1 ratio) provided a more objective measure. Each of these measures was compared to an individual's MisoQuest score to determine the nature of the relationship between sound sensitivity and gating capacity. While a clinical cutoff value of >61 has been proposed for the MisoQuest, the current study sought to examine this relationship across the broader range of sound sensitivities rather than binarizing the sample into those with and without Misophonia (Raymond and Butler, 2024). Accordingly, the sample included here is broadly distributed across the scale of possible MisoQuest scores.

Misophonics report a range of repetitive oral and non-oral sounds among their most consistent trigger sounds; Accordingly, future studies should continue to focus on low-level auditory processing differences in those with misophonia, an area of study that seems to be disproportionately understudied in the literature in comparison to studies of later-stage processes such as cognitive and emotional appraisal of sound. Overall, our results point toward a potential relationship between sensory gating capacity and misophonic severity, although a larger sample may be necessary to fully understand the nature of individual differences in these measures. Again, these results can provide a framework from which future studies can investigate the role of early auditory processing in the experience of misophonia.

1.6.1 Misophonia May be Associated with Self-Perceived Sensory Gating Capacity

Our results suggest that Misophonia symptom severity is associated with self-perceived sensory gating capacity. The statistically significant, strongly positive correlation between SGI-B scores and MisoQuest scores ($\rho = 0.67$, $p < 0.001$) suggests that as one's sensitivity to specific sounds increases, so does their self-perceived inability to filter out irrelevant sensory stimuli in day-to-day life. Moreover, the statistically significant relationship between this self-report measure of sensory gating capacity and P50 S2/S1 ratios ($\rho = 0.35$, $p = 0.029$) suggests that as our participants' perceived inability to filter out irrelevant stimuli increased, so too did their brain's inability to inhibit repetitive sounds such as those presented in the dual-click paradigm. This reinforces the idea that P50 S2/S1 ratios are significantly related to and can be a predictor of one's subjective sensory gating capacity. The results of the linear regression model strengthen these conclusions, demonstrating that the relationships between measures of sensory gating are similar even when controlling for relevant cofactors ($p < .1$).

We did not find a statistically significant relationship between P50 S2/S1 ratios and misophonia severity ($\rho = 0.23$, $p = 0.168$). In addition, the relationship between misophonia and sensory gating capacity (p = .084) in the linear regression model was not significant. Further, there were no significant relationships between misophonia severity and the time in which either S1 and S2 peaks occurred, or in the difference in latency between peaks. This is somewhat conflicting of the findings from a recent study (Aryal & Prabhu, 2024) that found differences in P1 peak latency between misophonics and controls in response to 500Hz tone burst stimuli. However, as in this study, the authors did not find differences in ERP amplitudes. Resolving these discordant object and subjective measures of the relationship between gating and misophonia will likely require replication.

1.6.2 Interpreting Objective Versus Subjective Sensory Gating Capacity

While the objective and subjective measures of gating obtained in the current study were correlated across individuals, only the SGI-B was significantly associated with the severity of misophonia symptoms. This highlights the potential that the SGI-B and P50 S2/S1 ratio are examining different aspects of sensory gating capacity. The SGI-B is a self-report measure that asks participants to describe the extent to which they notice that their inability to suppress or inhibit irrelevant sensory inputs interferes with their day-to-day life. Thus, this measure assesses the behavioral consequences of sensory gating impairments, which is likely affected by the extent to which individual listeners are able to compensate for their difficulties by, for example, overtly directing their attention away from repetitive stimuli. It is perhaps unsurprising, then, that this subjective measure would show a strong association with the MisoQuest, which inquires about the ways in which trigger sounds impact daily function. The P50 S2/S1 ratio, on the other hand, provides a measure of the auditory system's capacity to inhibit the response to repeated stimuli; this suppression is thought to occur prior to cognitive appraisal or influence, and thus might be more dissociable from misophonia symptom severity. While the two measures of sensory gating were significantly correlated with one another, the amount of variance in one measure explained by the other was only 16% (ρ^2 = 0.16), leaving a considerable amount unexplained. Thus, while low-level sensory gating may explain part of the subjective experience of suppressing irrelevant sounds, there may be additional, higher-level processes involved in subjective sound sensitivity as reflected by the SGI-B that cannot be explained by repetition suppression. Indeed, high-level processes including salience attribution and emotional regulation appear to be involved in the experience of misophonia, and may build upon potential difficulties with low level repetition suppression.

1.6.3 Limitations of the Current Study

A limitation in this study, and in all studies analyzing misophonia, is the rates of comorbidity between misophonia and OCD (11.53%; Erfanian et al., 2019) and ADHD (12%; Rouw & Erfanian, 2018) – each of which have been independently associated with atypical sensory gating. We attempted to mitigate this concern by excluding participants who have been *diagnosed* with a psychological disorder, and by including self-report questionnaires designed to assess symptoms of ADHD and OCD. In addition, we opted to use the MisoQuest to quantify misophonia severity, as this measure was specifically developed to assess misophonia independent of other potential neurological disorders.

The MisoQuest is a validated self-report measure of symptom severity that has been shown to have good test-retest reliability, and discriminant and convergent validity (Raymond and Butler, 2024). However, there remains considerable variability in how misophonia severity is captured in the literature. Some authors have encouraged a semi-structured interview approach to diagnosis, which utilizes the expertise of a clinician in combination with self-report questionnaires (Palumbo et al., 2018). In these interviews, the history of the patient is analyzed in detail by an expert, who uses an empirical approach to investigate the nature and onset of the experience, as well as whether the experience may be better encapsulated by a comorbid condition. The interviewer can obtain a more comprehensive understanding of how their experience with sensitivity to sound is affecting their day-to-day life in a more holistic manner, which can be beneficial for accurate diagnosis. However clinical interviews for the diagnosis of misophonia, are still being developed, and there remains no gold standard for assessment.

Additionally, due to a combination of limited recruitment resources and a small clinical population of misophonia in the real world, we were not able to achieve a sample that included a large number of individuals with clinically-relevant misophonia as defined by the proposed MisoQuest cutoff value. This precluded a groupwise analysis of sensory gating capacity. However, even after contacting local audiologists, and posting recruitment posters and advertisements around the city that specifically targeted individuals who self-identified as experiencing specific sound sensitivities, it was difficult to find participants who scored higher than 61 on the MisoQuest. This is consistent with previous work by our group, and supports the idea that this cutoff may be overly conservative to capture the group of individuals who are significantly affected by trigger sounds in their everyday lives. This diagnostic criterion warrants further examination.

In addition, previous work has suggested that the P50 S2/S1 ratios elicited by dual-click stimuli may be influenced by a number of state-dependent factors that are difficult to control for, such as the arousal or acute stress levels of the participant before and during the study session (Xin et al., 2021) as well as the quality of sleep the participant has been having (Milner et al., 2009). While we attempted to address some of these factors by limiting the consumption of caffeine and nicotine prior to testing, other factors were beyond our control and may have affected our measures. Future studies may want to collect information on acute stress and quality of sleep in order to control for these additional potential confounds.

Finally, since our analyses were mainly correlational measures, a larger sample size would provide a better characterization of individual differences in these measures. Given the modest relationship between the MisoQuest and S2/S1 ratios ($\rho = 0.23$), a sample size of at least 57 would be required to moderately stabilize our effect, while a sample of 250 or more would be required for more complete stability (Lakens & Evers, 2014).

1.6.4 Conclusions and Future Directions

To our knowledge, this study was the first to objectively assess the relationship between sensory gating and misophonia severity using a paradigm tailored to elicit P50 suppression (i.e., the dual-click paradigm). We predicted that those exhibiting higher misophonic severity would have difficulty inhibiting repeated sounds, as evidenced by a deficit in the brains ability to filter irrelevant sensory information and reports of difficulty suppressing irrelevant sensory information in everyday scenarios. We provide mixed evidence for this association; MisoQuest scores were strongly associated with self-reported gating deficits but were not significantly associated with P50 S2/S1 ratios. However, a trend was observed whereby higher S2/S1 ratios (suggesting poor sensory gating) were observed in individuals with more severe misophonia symptoms, which should compel future studies to continue to investigate this relationship. While misophonia has been characterized as a deficit in high level associations of meaning and emotion to otherwise innocuous sounds, the evidence provided here points toward a potential low-level deficit in preventing these sounds from reaching conscious awareness in the first place. Such a deficit would constitute a significant shift in our understanding of the etiology of misophonia, and would open additional lines of inquiry and potential therapeutic interventions to alleviate symptoms.

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Appendix A

Western Research

Date: 27 March 2023

To: Dr. Blake Butler

Project ID: 121365

Study Title: Assessing repetition suppression across the range of specific sound sensitivity using EEG

Short Title: Repetition Supression & Sound Sensitivity

Application Type: NMREB Initial Application

Review Type: Delegated

Full Board Reporting Date: 14/Apr/2023

Date Approval Issued: 27/Mar/2023 14:40

REB Approval Expiry Date: 27/Mar/2024

Dear Dr. Blake Butler

The Western University Non-Medical Research Ethics Board (NMREB) has reviewed and approved the WREM application form for the above mentioned study, as of the date noted above. NMREB approval for this study remains valid until the expiry date noted above, conditional to timely submission and acceptance of NMREB Continuing Ethics Review.

This research study is to be conducted by the investigator noted above. **All other required institutional approvals and mandated training must also be obtained prior to the conduct of the study.**

Documents Approved:

Document Name	Document Type	Document Date	Document Version
ASRS	Paper Survey	06/Feb/2023	1.0
SensoryGatingInventory	Paper Survey	06/Feb/2023	1.0
OCI-R	Paper Survey	06/Feb/2023	1.0
MisoQuest	Paper Survey	06/Feb/2023	1.0
RecruitmentEmail	Recruitment Materials	06/Feb/2023	1.0
OurBrainsCAN_Miso_Gating	Recruitment Materials	06/Feb/2023	1.0
Demographic Survey	Paper Survey	06/Feb/2023	1.0
Protocol_miso_2023	Protocol	06/Feb/2023	1.0
DebriefingLetter_gating	Debriefing document	27/Mar/2023	1.1
SONA_Miso_Gating	Recruitment Materials	06/Feb/2023	1.1
LOIconsent_Gating	Written Consent/Assent	27/Mar/2023	1.1
Gating_Posters	Recruitment Materials	27/Mar/2023	1.1

The Western University NMREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the Ontario Personal Health Information Protection Act (PHIPA, 2004), and the applicable laws and regulations of Ontario. Members of the NMREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB. The NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Ms. Zoë Levi, Research Ethics Officer on behalf of Dr. Randal Graham, NMREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Appendix B

MISOQUEST – A QUESTIONNAIRE FOR ASSESSING DECREASED SOUND TOLERANCE

authors: Siepsiak, M., Śliwerski, A., Dragan, W. Ł

Some people are less sensitive to certain sounds, while other people are more sensitive to certain sounds. Are there any sounds which you find particularly burdensome? Please indicate how much you agree or disagree with the following statements using the following scale:

1 – I definitely do not agree

2 – I do not agree

3 – Hard to say

4 – I agree

5 – I definitely agree

1	Some sounds bother me so much that I have difficulty controlling my emotions.	1	2	3	4	5
2	Unpleasant sounds make me feel overwhelmed.	1	2	3	4	5
3	I become anxious at the mere thought of an unpleasant sound.	1	2	3	4	5
4	I believe that my reactions to sounds are exaggerated, but I can't get rid of them.	1	2	3	4	5
5	When I hear unpleasant sounds, I start sensing emotions in my body (e.g. I sweat, feel pain, feel pressure, my muscles tens).	1	2	3	4	5
6	I start feeling anger the moment I see a thing/animal/person that might make an unpleasant sound at any time.	1	2	3	4	5
7	I put a lot of effort into controlling emotions when I hear an unpleasant sound.	1	2	3	4	5
8	If I can, I avoid meeting with certain people because of the sounds they make.	1	2	3	4	5
9	I find some sounds made by the human body unbearable.	1	2	3	4	5
10	I feel that my mental state worsens if I cannot leave a place where there's an unpleasant sound.	1	2	3	4	5
11	I often think about how to drown out unpleasant sounds.	1	2	3	4	5
12	Some unpleasant sounds make me instantly angry.	1	2	3	4	5
13	I am scared that unpleasant sounds may impact my future.	1	2	3	4	5
14	When meeting with other people, I am sometimes irritated because of unpleasant sounds that are present.	1	2	3	4	5

Appendix C

Sensory Gating Inventory-Brief

Participant: **Date:**

Age: **Sex:** **Score:**

Notes:

Never True	Almost Never		Sometimes True	Almost Always	Always True
0	**1**	**2**	**3**	**4**	**5**

Please circle your response

1. There are times when I can't concentrate with even the slightest sounds going on.	0	1	2	3	4	5
2. For several days at a time I have such heightened awareness of sights and sounds that I cannot shut them out.	0	1	2	3	4	5
3. When I am in a group of people I have trouble listening to one person.	0	1	2	3	4	5
4. I have feelings of being flooded by visual experiences, sights, or colors.	0	1	2	3	4	5
5. There have been times when it seems that sounds and sights are coming in too fast.	0	1	2	3	4	5
6. Background noises are just as loud or louder than the main noises.	0	1	2	3	4	5
7. I cannot focus on visual images when I am tired or stressed.	0	1	2	3	4	5
8. Maybe it's because I notice so much more about things that I find myself looking at them for a longer time.	0	1	2	3	4	5
9. Everything grips my attention even though I am not particularly interested in any of it.	0	1	2	3	4	5
10. When I'm tired sounds seem amplified.	0	1	2	3	4	5

Appendix D

National Institute for Health Research

AQ-10

Autism Spectrum Quotient (AQ)

A quick referral guide for adults with suspected autism who do not have a learning disability.

	Please tick one option per question only:	**Definitely Agree**	**Slightly Agree**	**Slightly Disagree**	**Definitely Disagree**
1	I often notice small sounds when others do not				
2	I usually concentrate more on the whole picture, rather than the small details				
3	I find it easy to do more than one thing at once				
4	If there is an interruption, I can switch back to what I was doing very quickly				
5	I find it easy to 'read between the lines' when someone is talking to me				
6	I know how to tell if someone listening to me is getting bored				
7	When I'm reading a story I find it difficult to work out the characters' intentions				
8	I like to collect information about categories of things (e.g. types of car, types of bird, types of train, types of plant etc)				
9	I find it easy to work out what someone is thinking or feeling just by looking at their face				
10	I find it difficult to work out people's intentions				

SCORING: Only 1 point can be scored for each question. *Score 1 point for Definitely or Slightly Agree on each of items 1, 7, 8, and 10. Score 1 point for Definitely or Slightly Disagree on each of items 2, 3, 4, 5, 6, and 9.* If the individual scores **6 or above**, consider referring them for a specialist diagnostic assessment.

This test is recommended in 'Autism: recognition, referral, diagnosis and management of adults on the autism spectrum' (NICE clinical guideline CG142). www.nice.org.uk/CG142

Key reference: Allison C, Auyeung B, and Baron-Cohen S, (2012) *Journal of the American Academy of Child and Adolescent Psychiatry* 51(2):202-12.

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Appendix E

GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Column totals _____ + _____ + _____ + _____ =

Total score _______

If you checked any problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

Scoring GAD-7 Anxiety Severity

This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day."
GAD-7 total score for the seven items ranges from 0 to 21.

0–4: minimal anxiety

5–9: mild anxiety

10–14: moderate anxiety

15–21: severe anxiety

Appendix F

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Obsessive-Compulsive Inventory - Revised (OCI-R) (OCI-R)

Instructions:

The following statements refer to experiences that many people have in their everyday lives. Select the option that best describes how much that experience has distressed or bothered you during the PAST MONTH.

		Not at all	A little	Moderately	A lot	Extremely
1	I have saved up so many things that they get in the way.	**0**	**1**	**2**	**3**	**4**
2	I check things more often than necessary.	**0**	**1**	**2**	**3**	**4**
3	I get upset if objects are not arranged properly.	**0**	**1**	**2**	**3**	**4**
4	I feel compelled to count while I am doing things.	**0**	**1**	**2**	**3**	**4**
5	I find it difficult to touch an object when I know it has been touched by strangers or certain people.	**0**	**1**	**2**	**3**	**4**
6	I find it difficult to control my own thoughts.	**0**	**1**	**2**	**3**	**4**
7	I collect things I don't need.	**0**	**1**	**2**	**3**	**4**
8	I repeatedly check doors, windows, drawers, etc.	**0**	**1**	**2**	**3**	**4**
9	I get upset if others change the way I have arranged things.	**0**	**1**	**2**	**3**	**4**
10	I feel I have to repeat certain numbers.	**0**	**1**	**2**	**3**	**4**
11	I sometimes have to wash or clean myself simply because I feel contaminated.	**0**	**1**	**2**	**3**	**4**
12	I am upset by unpleasant thoughts that come into my mind against my will.	**0**	**1**	**2**	**3**	**4**
13	I avoid throwing things away because I am afraid I might need them later.	**0**	**1**	**2**	**3**	**4**
14	I repeatedly check gas and water taps and light switches after turning them off.	**0**	**1**	**2**	**3**	**4**
15	I need things to be arranged in a particular way.	**0**	**1**	**2**	**3**	**4**
16	I feel that there are good and bad numbers.	**0**	**1**	**2**	**3**	**4**

Appendix F

NovoPsych

		Not at all	A little	Moderately	A lot	Extremely
17	I wash my hands more often and longer than necessary.	**0**	**1**	**2**	**3**	**4**
18	I frequently get nasty thoughts and have difficulty in getting rid of them.	**0**	**1**	**2**	**3**	**4**

Developer Reference:

Foa, E. B., Huppert, J. D., Leiberg, S., Langner, R., Kichic, R., Hajcak, G., & Salkovskis, P. M. (2002). The Obsessive-Complusive Inventory: Development and validation of a short version. Psychological Assessment, 14(4), 485–495. https://doi.org/10.1037//1040-3590.14.4.485

Appendix G

ADULT ADHD SELF-REPORT SCALE (ASRS-V1.1) SYMPTOM CHECKLIST

Patient: ______________________________ Date Completed: ____________

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during your appointment.	Never	Rarely	Sometimes	Often	Very often
PART A					
How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
How often do you have difficulty getting things in order when you have to do a task that requires organization?					
How often do you have problems remembering appointments or obligations?					
When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
How often do you feel overly active and compelled to do things, like you were driven by a motor?					
PART B					
How often do you make careless mistakes when you have to work on a boring or difficult project?					
How often do you have difficulty keeping your attention when you are doing boring or repetitive work?					
How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?					
How often do you misplace or have difficulty finding things at home or at work?					
How often are you distracted by activity or noise around you?					
How often do you leave your seat in meetings or in other situations in which you are expected to stay seated?					
How often do you feel restless or fidgety?					
How often do you have difficulty unwinding and relaxing when you have time to yourself?					
How often do you find yourself talking too much when you are in social situations?					
When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish it themselves?					
How often do you have difficulty waiting your turn in situations when turn taking is required?					
How often do you interrupt others when they are busy?					

CV

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EDUCATION

Western University , *MSc., Neuroscience* Sept. 2022 – Apr. 2024

- Current student and researcher in the neuroscience department at Western University

Western University , *Honours BSc., Specialization in Psychology* Sept. 2018 – Apr. 2022

- Honours thesis student
- Dean's Honor List (2018, 2020-2021)

SCHOLARSHIPS AND AWARDS

UWO In-Course Scholarship (Year 3) , $700.00 Sept. 2021

- Awarded to select students with exceptional cumulative averages within the Social Science faculty and Psychology program

UWO Faculty of Social Science Alumni Award , $1500.00 Nov. 2021

- Awarded to 8 undergraduate students in Western's social science faculty who are thriving academically

NSERC Undergraduate Student Research Award , $6000.00 May 2019

- Awarded to full time undergraduate students who display academic success and are interested in conducting research over a summer term

The Western Scholarship of Excellence , $2000.00 Sept. 2018

- Awarded to incoming undergraduate students for achieving academic excellence

RESEARCH EXPERIENCE

Author & Primary Researcher , *Neuroscience Masters Thesis* Sept. 2022 – Present

- Project title: "Analyzing Sensory Gating Capacity in Misophonia"
- Currently analyzing if sensory gating is a potential neural correlate for the misophonic experience as deduced by anomalies in EEG activity during an auditory task
- Supervised by Dr. Blake Butler

Author & Primary Researcher , *Psychology Undergraduate Thesis* Sept. 2021 – Apr. 2022

- Project title: "Analyzing the Perceptual and Neural Correlates of Misophonia"
- Conducted an online study analyzing misophonia and perceptual narrowing, and completed a research paper expanding the literature pertaining to neural and perceptual markers of misophonia disorder
- Supervised by Dr. Blake Butler

Lab Assistant, *Neuroplasticity in Sensory Systems Lab* May 2021 – Sept. 2021

- Shadowed fMRI procedures involving felines

CV

- Helped ensure that medical devices were securely attached to the sedated felines and were functioning throughout the scanning process
- Trained to socialize and handle felines under the supervision of a veterinary technician
- Was additionally responsible for emailing and recruiting potential participants for an online study
- Supervised and hired by Dr. Blake Butler

Author & Primary Researcher , *Independent Study Program* Jan. 2021 – Apr. 2021

- Project title: "A Review on the Use of 'Compensatory Neuroplasticity' and Related Terms"
- Worked individually with Dr. Blake Butler to conduct and complete a literature review
- Focused on how past authors interpreted or alluded to the mechanisms underlying compensatory neuroplasticity
- Received substantial personal feedback on how to analyze scientific literature and how to write an academic paper

Primary Researcher, *Neuroplasticity in Sensory Systems Lab* May 2020 – Sept. 2020

- Project title: "Computational analysis and cell counting of cells in visual and association areas"
- Was trained to discriminate between different cells found in neuroimages of visual cortex.
- Developed efficient skill in the three-dimensional drawing of cells through an online platform.
- Participated in data collection for the project which was supervised by Dr. Blake Butler and Dr. Daniel Miller.

Lab Assistant, *Neuroplasticity in Sensory Systems Lab* Sept. 2020 – Apr. 2021

- Hired by Dr. Blake Butler through Western University's work study program
- Continued collecting data and increasing the power of Dr. Blake Butlers and Dr. Daniel Millers study
- Continued enhancing skills in Python
- Attended weekly lab meetings that consisted of research related topics and discussion

LEADERSHIP EXPERIENCE & CO-CURRICULAR ACTIVITIES

Teaching Assistant , *Deparment of Psychology at Western University* Sept. 2022 – Apr. 2023

Podcast Host , *Gradcast Student Podcast at Western* Sept. 2022 - Present

Director of Events , *Distributive Education Clubs of America* Sept. 2020 – May 2022

Club Member , *Western Psychology Association* Sept. 2019 – May 2022

RELEVANT SKILLS & COURSES TAKEN

- Skills: Python, R, SPSS, Microsoft Office (Word, Excel, PowerPoint), Qualtrics, Slack,
- Courses: Introductory Neuroscience, Sensation and Perception, Introductory Physiology, Abnormal Psychology, Social Psychology, Cognitive Psychology, Statistic in Psychology, Research Methods in Psychology, Evolution and Psychology, Biochemistry, Organic Chemistry

REFERENCES: Available upon request