Passive Categorisation Training for Tinnitus Management

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Abstract

Background: While sound therapy (ST) is commonly used for tinnitus relief, tinnitus heterogeneity necessitates advancements in such conventional methods. This thesis evaluated tinnitus replica generation and role in tinnitus management, specifically within a novel effortless auditory categorisation-based ST.

Aims:

1. Review/understand mechanisms of auditory categorisation training and its role in tinnitus management.
2. Assess the use of different sounds for appropriate/accurate tinnitus synthesis.
3. Evaluate an effortless personalised categorisation training approach relative to conventional ST using broadband noise (BBN).

Methods:

Three narrative reviews were undertaken regarding:

1. Current knowledge/theories surrounding tinnitus.
2. Psychoacoustic assessment of tinnitus.
3. Auditory categorisation and its potential role in tinnitus perception.

Pilot study (n=22): Evaluated eight tinnitus replicas based on their emotional affect and ability to replicate participant's tinnitus.

Effortless auditory categorisation study (n=29): Compared the effects of an effortless auditory categorisation training (CT) paradigm to conventional white noise (WN) ST.

Results:

Narrative reviews:

1. Tinnitus heterogeneity necessitates a shift to tailor-made, machine-learning informed management methods.
2. Psychoacoustic measures are vital to tinnitus evaluation.
3. Categorisation-based perceptual training paradigms present a promising means of tinnitus management.

Pilot study: Puretone-based replicas had greater negative affect (cf. noise-like replicas). Avatars and pure-tone and localisation replicas accurately capture the tinnitus experience. The uncanny valley phenomenon was not substantiated in tinnitus matching.

Effortless auditory categorisation: WNST resulted in significant improvements in tinnitus impact independent of counselling; CT did not. Acute WN resulted in changes within the default mode network (DMN). Acute CT resulted in overall reduction in activity at the prefrontal cortex (PFC), and a decrease in gamma-band activity within the auditory cortex.

Conclusions:

To effectively address tinnitus heterogeneity, personalised management using psychoacoustic assessments and employing machine-learning may be needed. Tinnitus replica assessment revealed that both simple and complex copies accurately capture tinnitus, indicating that replica complexity should reflect its intended/overall purpose. Reductions in tinnitus complaint were greater with WNST than the experimental CT, however the CT approach showed acute changes in brain areas associated with tinnitus, different from those altered by WNST. This evidence supports further investigation into CT in tinnitus management. While tinnitus relief can be achieved solely using WNST, neural changes within the DMN (following WN) and PFC (following CT) are encouraging as they are directly correlated with tinnitus distress.

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Executive summary

Tinnitus is the perception of sound in the absence of an external auditory stimuli (Baguley, McFerran, et al., 2013) which may progress to become tinnitus disorder characterised by behavioural and functional disability (De Ridder, Schlee, et al., 2021). There is no pharmaceutical cure for tinnitus and no single gold standard for tinnitus management, however sound therapy using white noise and nature sounds to provide tinnitus relief or retrain tinnitus perception are popular approaches. The response to sound therapy varies greatly between individuals, as such there have been calls to improve sound therapy by taking a personalised approach that accounts for underlying variability in tinnitus perception and that apply perceptual approaches more nuanced than masking or habituation to sound. The goal of this thesis was to evaluate the generation of tinnitus replicas and their role in tinnitus management, in particular a novel effortless auditory categorisation-based sound therapy.

Aims:

1. Review and understand the mechanisms of auditory categorisation training and its application within a passive perceptual training paradigm for tinnitus management.

2. Evaluate the use of different sounds for the synthesis of appropriate and accurate tinnitus replicas, discern what constitutes a successful and convincing tinnitus replica, and investigate the emotional ‘affect’ of different tinnitus replicas.

3. Elucidate whether there are any differences and/or benefits in the implementation of an effortless personalised categorisation training approach relative to conventional sound therapy using broadband noise (BBN).

Methods:

Phantom sound: An overview of tinnitus and tinnitus disorder: A narrative review of the current knowledge and theories surrounding the aetiology, manifestation, progression, assessment, and management of tinnitus.

Principles and Methods for Psychoacoustic Evaluation of Tinnitus: A comprehensive narrative review of the psychoacoustic assessment of tinnitus, its relationship to cognitive and behavioral aspects of tinnitus, and its neuropathophysiology.

A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception: A review of auditory categorisation and its potential role in tinnitus perception.

The relationship between psychoacoustic tinnitus matching similarity, affect, and the perceptual uncanny valley phenomenon: A pilot study (n = 22) evaluated eight different tinnitus replicas. These were evaluated based on 1) their ability to successfully replicate and reflect participant's true tinnitus experience, and 2) the degree of affect along a simple dimension of how much the individual disliked the matched sound.

Electrophysiological and behavioural evidence of the effects of white noise and a progressive re-categorisation sound therapy on tinnitus: The main empirical study was a randomised tinnitus sound therapy trial (n = 29) comparing the effects of an effortless auditory categorisation training paradigm to conventional sound therapy using white noise. Tinnitus-relevant behavioural and qualitative measures were obtained at two time points: prior to the study session and following the 30-day training period. Acute neural (electroencephalographic) measures were collected at three time points: baseline (10-minute resting state sitting in silence), during acute sound exposure (10-minute training using either white noise or morphing auditory categorisation sound), and acute post-sound exposure (10-minutes sitting in silence).

Results:

Phantom sound: An overview of tinnitus and tinnitus disorder: The heterogeneity of tinnitus is clear for every dimension of the experience. I provide arguments that this necessitates a shift from 'one-size-fits-all' model of tinnitus therapy to an approach with more personalized, tailor-made methods. There is a need to refine and advance current tinnitus assessment tools by introducing machine learning and modelling techniques that will support researchers and clinicians in moving toward a tailor-made mode of tinnitus therapy through predicting therapeutic success and allowing for real-time delivery and modification of personalised therapies.

Principles and Methods for Psychoacoustic Evaluation of Tinnitus: Psychoacoustic measures of pitch, loudness, minimal masking level, and auditory residual inhibition face several limitations commonly centred around issues regarding protocol standardisation, equipment-based constraints, and tinnitus heterogeneity. Irrespective of these limitations, psychoacoustic measures are vital to the evaluation of tinnitus and found to offer valuable insight into how a participant perceives their tinnitus. It is important to evaluate and consider tinnitus as a holistic experience consisting not only of its acoustic parameters, but also patient personality and activity within auditory and non-auditory tinnitus-related neural networks.

(Vajsakovic, D., Maslin, M., & Searchfield, G. D. (2021). Principles and Methods for Psychoacoustic Evaluation of Tinnitus. In G. D. Searchfield & J. Zhang (Eds.), *The Behavioral Neuroscience of Tinnitus* (pp. 419-459). Springer.)

A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception: In the categorisation review 112 articles were reviewed in full, from which 59 were found to contain relevant information and were included in the review. I concluded that implementation of a categorisation-based perceptual training paradigm might be a promising means of tinnitus management, by reversing the changes in cortical plasticity that are seen in tinnitus, in turn altering the representation of sound within the auditory cortex itself. In the instance that the categorisation training was successful, this would likely mean a decrease in the level of activity within the auditory cortex (and other associated cortical areas found to be hyperactive in tinnitus) as well as a reduction in tinnitus salience.

(Vajsakovic, D., Maslin, M. R., & Searchfield, G. D. (2022). A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception. *Journal of Otorhinolaryngology, Hearing and Balance Medicine, 3*(3), 6.)

The relationship between psychoacoustic tinnitus matching similarity, affect, and the perceptual uncanny valley phenomenon: There was insufficient evidence to support the existence of an uncanny valley in tinnitus matching. Puretone-based replicas had greater negative affect when compared to their noise-like counterparts. The high degree of variability in participant ratings is reflective of the heterogenous nature of tinnitus disorder. Although complex replicas of tinnitus (avatars) offer an accurate representation of participant's tinnitus sensation, simple pure tone and localisation replicas are also highly reflective of the tinnitus experience. While it is evident that tinnitus and its replicas give rise to strong psychological responses, whether these responses are indicative of a low point in the perception of sound equivalent to the uncanny valley in vision or are simply a reaction to generally unpleasant sounds remains unclear.

Electrophysiological and behavioural evidence of the effects of white noise and a progressive re-categorisation sound therapy on tinnitus: White noise sound therapy resulted in significant improvements in tinnitus impact (TFI pre: $M = 53.4$, $SD = 18.0$, TFI post: $M = 39.0$, $SD = 9.9$, $p < 0.01$), severity (TSNS pre: $M = 7.4$, $SD = 1.3$, TSNS post: $M = 6.3$, $SD = 1.0$, $p < 0.002$), and negative emotionality (PANAS negative pre: $M = 21.4$, $SD = 8.0$, PANAS negative post: $M = 17.0$, $SD = 4.9$, $p < 0.009$) independent of counselling. Categorisation training did not give rise to statistically significant changes in tinnitus impact (TFI pre: $M = 47.8$, $SD = 18.2$, *TFI post:* $M = 45.2$, $SD = 20.4$, $p > 0.05$). Nine participants from the white noise group and three from the categorisation training group achieved a clinically meaningful improvement in tinnitus severity (determined by a 13-point reduction in TFI score). Sound therapy using white noise gave rise to changes within the default mode network (specifically within the angular gyrus), while passive auditory categorisation training led to an overall reduction in activity at the level of the prefrontal cortex, as well as a decrease in gamma-band activity within the auditory cortex. Different neural changes observed using white noise sound therapy relative to auditory categorisation training suggest that the two modes of sound therapy likely work through different mechanisms or neural pathways, in turn targeting different neural structures. An artificial intelligence Spiking Neural Network (SNN) efficiently identified and differentiated between therapeutic responders and non-responders with a high level of accuracy (overall classification accuracy was 89.44% for responders and 93.57% for non-responders).

Conclusions:

The findings of the thesis highlight the heterogeneous nature of tinnitus and calls for a shift in tinnitus management strategies away from being ‘one-size-fits-all’ towards personalised tailor-made approaches. These new approaches may leverage machine-learning techniques. Tinnitus replica complexity should reflect its intended purpose; simplistic tinnitus replicas are sufficient for simple tinnitus matching purposes, while tinnitus avatars should be reserved for circumstances requiring long-term sound exposure (e.g., sound therapy). Furthermore, although tinnitus and its replicas give rise to strong psychological responses there was insufficient evidence to support the existence of an uncanny valley in tinnitus matching. The diminished cortical representation that occurs following acute auditory categorisation training makes categorisation-based perceptual training an attractive strategy for tinnitus management by potentially reversing the changes in cortical plasticity that are seen in tinnitus. While sound therapy using conventional white noise offers tinnitus relief independent of counselling, neural changes observed within the default mode network following white noise sound therapy and at the level of the prefrontal cortex following passive auditory categorisation training are encouraging as they are directly correlated with tinnitus distress. The notion that simple (BBN) and complex (categorisation) modes of sound therapy act at these different neural sites is a promising finding that requires further investigation. Targeting multiple tinnitus generating areas through the application of a polytherapeutic sound approach should be explored.

Chapter 1. Introduction

Tinnitus is the perception of sound in the absence of an external auditory stimulus (Baguley, McFerran, et al., 2013). Globally 10-15% of adults experience chronic tinnitus (>6 months duration) and 1% will suffer from tinnitus disorder (emotional distress, autonomic arousal, and/or cognitive dysfunction caused by tinnitus) (De Ridder, Schlee, et al., 2021) resulting in a severely reduced quality of life (Axelsson & Ringdahl, 1989; Heller, 2003; Meikle et al., 1984). Although our understanding of the phantom sound has grown substantially over the past few decades, the sensation itself, its aetiology, pathophysiology, manifestation, progression, and treatment remain largely elusive (for a detailed review of current knowledge surrounding tinnitus see *Chapter 2.2. Phantom sound: An overview of tinnitus and tinnitus disorder*). The difficulties researchers and clinicians are faced with are predominantly a consequence of the heterogeneity of tinnitus (Cederroth et al., 2019). No two tinnitus experiences are identical; they can vary at any dimension of tinnitus presentation, from the psychoacoustic properties and sound description, through to associated comorbidities and treatment response (Beukes, Manchaiah, et al., 2021; Cederroth et al., 2019; Manning, Thielman, et al., 2019; Mohan et al., 2022). Tinnitus heterogeneity introduces hurdles along the many winding paths of tinnitus research and its progress, particularly in tinnitus management. There is currently no known cure for tinnitus, and among the extensive repertoire of trialled remedies and treatments (see *Chapter 2.2.4 Treatment and management of tinnitus* for a detailed review of tinnitus therapies) none offer a high degree of evidence to support their reliability and effectiveness in suppressing the perception of tinnitus (Langguth et al., 2019; Zenner et al., 2017).

While there is no gold standard of treatment for tinnitus, the current recommendations involve the application of sound therapy (and hearing aids/amplification where required) in combination with counselling (Bauer & Brozoski, 2011; Cuesta et al., 2022; Hyun et al., 2022; Makar et al., 2017; Searchfield et al., 2010; Tyler et al., 2020; Zenner et al., 2017). Sound therapy involves the use of external sounds to manage tinnitus by modifying its perception and/or reactions to it (Searchfield, 2021; Searchfield et al., 2012). Current practice typically uses noise (either broadband or narrowband), environmental sounds, or music as therapy sounds, but there is no consensus as to the most clinically appropriate and therapeutically effective choice of sound (Brennan-Jones et al., 2020; Henry et al., 2008;

Hoare, Gander, et al., 2012; Hoare, Searchfield, et al., 2014; Hobson et al., 2012; Li et al., 2019; Wang et al., 2020). There is however a need to move away from ’one-size-fits-all’ treatment paradigms and adopt ‘tailored’ approaches to therapy in which tinnitus management is personalised and uniquely adapted for each individual patient. When considering sound therapies, the psychoacoustic features of tinnitus are often overlooked or disregarded (Vajsakovic et al., 2021); however, more personalised modes of sound therapy which centre the treatment sound in and around tinnitus pitch require accurate representations of the tinnitus sensation (see Chapter 3 *Principles and Methods for Psychoacoustic Evaluation of Tinnitus* for a detailed review on the psychoacoustic parameters of tinnitus). It may be important to provide accurate and perceptually meaningful replicas of tinnitus known as ‘tinnitus avatars’, which serve to aid our understanding of patient’s tinnitus experience and inform future sound-based therapies.

The use of a sound therapy based on the individual’s tinnitus avatar has recently yielded promising tinnitus relief results (Durai, Doborjeh, et al., 2021). Durai, Doborjeh and colleagues (2021) trialled a sound therapy attempting to recategorise tinnitus as a real-world environmental sound. The passive auditory categorisation training resulted in both behavioural and physiological changes; participants experienced a significant reduction in the level of impact that tinnitus had on their lives and its degree of intrusiveness, in addition to developing an improved ability to ignore tinnitus (Durai, Doborjeh, et al., 2021). Furthermore, changes in neural tinnitus networks were observed using artificial intelligence (AI) based Spiking Neural Network (SNN) architecture by mapping, learning, visualising, and classifying meaningful brain patterns. The study identified a recategorisation training-specific increase in bilateral hemispheric involvement concomitant with the morphing of the training sound from the tinnitus replica (avatar) into the real-world natural sound. Changes were observed in regions related to discriminatory judgements and attention (i.e., the dorsal attention network, precentral gyrus, and ventral anterior network). It is likely that this adaptive method of sound therapy offers tinnitus relief through a different pathway or ‘mode’ relative to conventional sound therapies (Searchfield, 2021). Perceptual training paradigms such as categorisation might oppose or altogether reverse the aberrant cortical activity that gives rise to neural hyperactivity seen in tinnitus by reducing the amount of cortical representation for training stimuli representative of the tinnitus experience (i.e., the tinnitus avatar) (for a detailed review on categorisation as a tool for tinnitus management, see

Chapter 2.4 A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception). While Durai, Doborjeh, et al. (2021) illustrated the potential of recategorisation training as a tool for tinnitus management, it is not clear whether the effects and mechanisms of auditory categorisation training differed from conventional sound therapy (using broadband noise (BBN)). Further work is required to compare and contrast the effects of passive categorisation training to the use of BBN for tinnitus relief. Additionally, the importance of tinnitus replicas – and what constitutes a realistic, convincing, and successful tinnitus replica – has not yet been investigated. Given that sound therapy is based on the presentation of an auditory stimuli over a prolonged period of time, it is imperative to understand tinnitus synthesis and the parameters that are important to replica generation, in addition to the emotional impact of sounds, participants response to them, and how they can affect therapeutic success.

Aims

1. Review and understand the mechanisms of auditory categorisation training and its application within a passive perceptual training paradigm for tinnitus management.

2. Evaluate the use of different sounds for the synthesis of appropriate and accurate tinnitus replicas, discern what constitutes a successful and convincing tinnitus replica, and investigate the emotional 'affect' of different tinnitus replicas.

3. Elucidate whether there are any differences and/or benefits in the implementation of a personalised passive categorisation training approach relative to conventional sound therapy using broadband noise (BBN).

Thesis structure

The research conducted for this thesis was of an exploratory nature. At present, there are no studies that have 1) examined the use of different sounds for the purpose of tinnitus synthesis and attempted to discern what parameters are necessary for the creation of a realistic and appropriate tinnitus replica, and 2) evaluated the efficacy of auditory categorisation training in contrast to conventionally prescribed broadband sound therapy. Several literature reviews were undertaken to outline what is currently known about tinnitus – its aetiology, assessment, and treatment – and offer insights into auditory categorisation and its potential as a promising tinnitus therapeutic. These extensive reviews offer support to the theory and design of the undertaken studies: Chapter 2 presents a narrative review providing a general up-to-date overview of tinnitus and tinnitus disorder, Chapter 3 offers a review of the principles and methods commonly implemented for psychoacoustic assessment of tinnitus, and Chapter 4 presents a review of auditory categorisation and its application for tinnitus management. Chapter 5 presents a self-contained pilot study which was used to inform tinnitus synthesis for the subsequent study presented in Chapter 6. A general discussion considering all aspects and components of the thesis are presented in Chapter 7.

Chapter 2. Phantom sound: An overview of tinnitus and tinnitus disorder

2.1. Chapter Introduction

The narrative review presented in this chapter offers an up-to-date overview of tinnitus and tinnitus disorder, succinctly summarising present knowledge and theories surrounding the aetiology, manifestation, and progression of tinnitus, in addition to outlining current modes of assessment and management, and illuminating gaps in tinnitus research which can act to guide the directions of future work in the field. The review illustrates the need to refine and advance current tinnitus assessment tools by introducing machine learning and modelling techniques which support researchers and clinicians in moving toward a tailor-made mode of tinnitus therapy through predicting therapeutic success and allowing for real-time delivery and modification of personalised therapies. One such predictive tool (Spiking Neural Network (SNN) methodology) was applied and evaluated in the auditory categorisation training study described in Chapter 6. The review also reflects upon and considers the impact of COVID-19 on tinnitus management strategies.

2.2. Introduction

Tinnitus is the perception of sound in the absence of a physical sound source (Eggermont & Roberts, 2004). In this review the term tinnitus refers to "true tinnitus" or “subjective tinnitus” rather than what has be called “objective tinnitus” or “somatosounds” (Henry, 2016). Objective/somatosound tinnitus are actual sounds created by the body (e.g., blood pulse, muscular/skeletal/vascular irregularities) that are heard. Tinnitus as used here is created and heard by the auditory system but is never a true sound. While everyone is likely to experience transient tinnitus at some stage in their lives (e.g., following a loud music concert), chronic tinnitus (>6 months in duration) affects 10-15% of the adult population, with approximately 1-5% of individuals enduring a detriment to their quality of life as a result (Axelsson & Ringdahl, 1989; Davis & El Refaie, 2000; Heller, 2003; Meikle et al., 1984; Sindhusake et al., 2003). Tinnitus with associated suffering can be defined as ‘tinnitus disorder’ (De Ridder, Schlee, et al., 2021). It is widely accepted that tinnitus is the result of a series of neuroplastic changes in the auditory pathway following injury to the auditory periphery (Eggermont & Roberts, 2012). The changes that arise following a peripheral lesion alter patterns of activity at cortical (Eggermont & Roberts, 2004) and sub-cortical (Kaltenbach et al., 2005) auditory processing areas. In addition to aberrant changes within the auditory structures, there is increasing evidence to support the involvement of non-auditory structures such as the limbic system in tinnitus perception, suggesting that the experience is more complex than initially thought (Chen, Xia, et al., 2017; Hu et al., 2021; Leaver et al., 2011). Tinnitus severity is determined by the complex interaction between auditory, emotional, distress, motor and attention networks, with several factors, including context, personality, and memory all contributing to the perception and impact of tinnitus (Chen et al., 2016; De Ridder, Elgoyhen, et al., 2011; Hu et al., 2021; Jastreboff, 1990; Kaltenbach, 2006; Muhlau et al., 2006; Searchfield et al., 2012; Welch & Dawes, 2008).

The strong association between tinnitus and psychological distress highlights the importance and urgency for a cure. Tinnitus sufferers often complain of insomnia, anxiety, depression, difficulties in concentrating, feelings of despair, social withdrawal, psychosomatic symptoms, and interpersonal problems (Bhatt et al., 2017; Gul et al., 2015; Langguth et al., 2011). These factors not only act to reduce the quality of life for those individuals, but also increase morbidity and risk of suicide (Han et al., 2018; Lewis et al., 1994).

An issue that comes to light when considering tinnitus therapy is the heterogeneous nature of the percept. Tinnitus is variable in almost every aspect; from its onset, through to the way in which it is manifested, and even to the way in which it may be managed (Cederroth et al., 2019). No two tinnitus cases appear to be the same; they may perceive different sounds (i.e., pitch, loudness, quality, laterality and localisation), they may have different causal risk factors and comorbidities, their psychological reaction to the experience may differ, as may their response to treatment (Cederroth et al., 2019; Coelho et al., 2020).

This review will aim to succinctly summarise what is currently known about tinnitus, providing an overview of the underlying mechanisms and pathophysiology, assessment and measures of tinnitus applied in clinical and research settings, as well as the treatment/management options available. Speculations will also be made about the future of tinnitus research and what it might look like, considering avenues of interest that show promise for further research and exploration.

2.3. The auditory system and tinnitus: from the cochlea to the brain

Tinnitus can be described as a phantom sound, analogous to phantom pain. Tinnitus is not imagined but the perception is not the result of a real-world sound, rather activity in the auditory system that creates the perception that a sound is present. Tinnitus is linked to damage at any point along the auditory pathway; commonly, it is believed that the phantom percept is induced by insult to the auditory periphery, and is maintained by changes in auditory and non-auditory neural networks (Henton & Tzounopoulos, 2021). Tinnitus can also occur with head and neck injury (Folmer & Griest, 2003; Sindhusake et al., 2004). Changes in spontaneous activity, structure and functional connectivity have been observed throughout the auditory pathway from the cochlea (Haider et al., 2018; Henry et al., 2014) to the cochlear nucleus (Coomber et al., 2015; Gu et al., 2012; Martel et al., 2019; Smith, 2012; Vogler et al., 2011; Wu, Martel, et al., 2016; Zhao et al., 2016), inferior colliculus (Henry et al., 2014; Robertson & Mulders, 2012), medial geniculate body (Bartlett, 2013; De Ridder, Vanneste, et al., 2015; Leaver et al., 2011; Rauschecker et al., 2010), and auditory cortex (Basura et al., 2015; Chen et al., 2013; Eggermont & Roberts, 2004; Noreña & Eggermont, 2003; Noreña et al., 2003; Roberts et al., 2010; Schneider et al., 2009; Takacs et al., 2017), and associated networks (De Ridder, Elgoyhen, et al., 2011; Leaver et al., 2011; Searchfield et al., 2012). The following sections will review some of the structures and mechanisms implicated in tinnitus generation and maintenance.

Cochlea

The involvement of the cochlea in tinnitus generation is based on the notion that damage or dysfunction in the auditory periphery leads to aberrant neural activity at the level of the cochlea which is then transmitted through the auditory pathways, in turn giving rise to the perception of sound (Henry et al., 2014). This view is commonly referred to as "peripheral tinnitus" and was favoured by early tinnitus researchers as it firstly explained why tinnitus is often perceived in the ears, and secondly justified the fact that the perceived tinnitus frequency is closely matched to the audiometric profile of hearing thresholds (Henry et al., 2014). It is now generally accepted that peripheral tinnitus is not entirely independent of "central tinnitus" (i.e., auditory perception generated and maintained by aberrant neural activity in auditory brain centres); the transition of tinnitus from being an acute to a chronic experience is defined as the "centralisation" of an initially peripheral tinnitus (Eggermont, 2003). In cases where abnormal hearing is not detected by conventional pure-tone audiometry, there may be a 'hidden hearing loss' that can be detected using auditory brainstem responses (ABR), otoacoustic emissions (OAEs), and/or high-frequency audiometry (Rauschecker et al., 2010; Tang et al., 2019). The lack of a hearing loss does not necessarily reflect lack of a cochlear impairment (Roberts, 2018; Weisz et al., 2006); even individuals who demonstrate normal auditory thresholds show presence of cochlear dead regions or outer hair cell (OHC) damage (Job et al., 2007).

It is now widely acknowledged that while it is unlikely that the cochlea is solely responsible for tinnitus propagation and maintenance (House & Brackmann, 1981), there are several anatomical structures within the cochlea which, when damaged, can contribute to the phantom perception of sound, including (Haider et al., 2018):

- Death of inner hair cells (IHCs) or outer hair cells (OHCs).
- Loss of OHC electromotility.
- Cochlear synaptopathy.

- Hyperactive cochlear NMDA receptors (primarily in the case of noise-induced tinnitus, a target for cochlear therapies).
- Increase in endocochlear potential (observed in acute phase of tinnitus, induced by transient noise trauma).
- Stereocilliar bundle damage.
- Basilar membrane rupture.
- Alteration in tectorial membrane position.

While cochlear abnormalities might be the initial trigger for tinnitus onset, it is more likely that the subsequent cascade of neural changes observed in the auditory system (and associated areas) are what in turn maintain and progress the condition (Baguley, McFerran, et al., 2013).

Dorsal Cochlear Nucleus

The dorsal cochlear nucleus (DCN), a brainstem nucleus that receives direct input from the auditory nerve, has been identified as a key structure for tinnitus induction (Wu, Martel, et al., 2016). In addition to receiving auditory input from the cochlea, the DCN also receives and filters somatosensory input from the dorsal column nucleus, cervical dorsal root ganglion, spinal trigeminal nucleus, and trigeminal ganglion (Wu, Stefanescu, et al., 2016; Zhan et al., 2006; Zhou & Shore, 2006). Following injury to the auditory periphery (primarily as a result of noise trauma), the fusiform cells of the DCN show an increase in synchrony, bursting, and spontaneous firing rates (SFRs), as well as a change in stimulus-timing dependent plasticity (StDP), all of which correlate with behavioural measures of tinnitus (Martel et al., 2019; Wu, Martel, et al., 2016). It is thought that this hyperactivity is driven by a decrease in auditory nerve input, in turn disinhibiting the DCN and giving rise to the increase in spontaneous activity at the higher-level central auditory system that is seen in tinnitus (Zhao et al., 2016). At a molecular level, it appears that the NMDA receptors (present on DCN fusiform cells and responsible for driving long term potentiation in these cells) undergo changes that lead to a reduction in spontaneous activity of the inhibitory cells of the DCN, in turn resulting in fusiform cell hyperactivity (Criddle et al., 2018). At a structural level, several studies have explored the possibility that the phenomenon is the result of axonal sprouting (Heeringa et al., 2018). A recent study investigating the role of axonal sprouting in driving changes in auditory-somatosensory innervation in rats measured the protein levels of vesicular glutamate transporter 1 (VGLUT1) (marker of auditory input to the DCN), VGLUT2 (marker of somatosensory inputs), and several known axonal sprouting-related factors (including growth-associated protein 43 (GAP43), neuronal growth marker indicative of synaptogenesis and axonal outgrowth, and growth differentiation factor 10 (GDF10), a factor responsible for mediating axonal sprouting) (Han, Mun, et al., 2019). The study found that compared to non-tinnitus rats, the tinnitus rats expressed a significant decrease in VGLUT1 and a significant increase in VGLUT2, as well as significant increases in GAP43 and GDF10 protein expression levels, lending support to the notion that axonal sprouting underlies the altered neural input distribution to the DCN that likely gives rise to tinnitus (Han, Mun, et al., 2019). The last few years have also shown an increased interest in the investigation of voltage-activated (Kv3-like) K^+ currents as another potential culprit of altered DCN fusiform cell activity, with several studies suggesting that DCN fusiform cells suffer a change in firing pattern as a result of a decrease in Kv3.1 K^+ currents following noise-exposure (Olsen et al., 2018). Modulation of these channels appears to suppress spontaneous activity in the auditory system (Glait et al., 2018; Olsen et al., 2018), in turn offering a means of management for noise-induced tinnitus. However, it is likely that the treatment targeting the CN is dependent on the ability to act shortly after tinnitus onset (Mulders & Robertson, 2011); as such, the probability that such strategies will aid chronic tinnitus sufferers is unfortunately slim.

The need to identify and clearly define tinnitus subtypes has led to a surge of research in the areas of protein expression and genetics. While the heritability of tinnitus remains a controversial topic, a recent genome-wide association study aiming to detect loci strongly associated with tinnitus identified a single nucleotide polymorphism (SNP) in the gene WDPCP expressed in the DCN. While the exact role of WDPCP mutations in tinnitus is yet unclear, the authors propose that the gene’s role in ciliogenesis and directional cell migration likely mean that it is also responsible for facilitating the restructuring of synapses and neuronal circuitry within the DCN, in turn posing as a likely mechanism for DCN hyperactivity (Urbanek & Zuo, 2021).

Though the contribution of the DCN in the generation of tinnitus is widely recognised and understood, a secondary ‘supplementary’ role has also been identified for the ventral cochlear nucleus (VCN). While this role appears to be minor, several studies highlight tinnitus-relevant interactions between the auditory and vestibular systems (Coomber et al., 2015; Gu et al., 2012; Smith, 2012; Vogler et al., 2011), encouraging researchers to make efforts to further understand the role of the VCN in tinnitus pathogenesis.

Inferior Colliculus

As we move along the auditory pathway, we start to form a clearer picture of the cascade of events that are set off like a domino effect from the cochlea. Deafferentation at the level of the cochlear nucleus gives rise to increased fusiform cell activity within the DCN which then leads to increased output to the subsequent structure in the auditory pathway; the inferior colliculus (IC) (Henry et al., 2014). The IC has been extensively studied within the context of tinnitus, and is widely regarded as an important structure in the central mechanisms underpinning the phantom percept (Henry et al., 2014; Robertson & Mulders, 2012). The IC primarily consists of excitatory glutamatergic neurons (75%), with only 25% of neurons being GABAergic (inhibitory) (Ito et al., 2011; Merchán et al., 2005). Following an auditory insult, a series of plastic changes arise within the neuronal circuitry of the IC, resulting in an altered balance of excitation and inhibition; it is this aberrant excitatory-inhibitory balance within the IC that is thought to underlie subjective tinnitus (Berger & Coomber, 2015; Ma et al., 2020; Sturm et al., 2017). Using novel optogenetic methods on transgenic mice, a recent paper investigating the effects of noise-exposure on the neuronal circuitry of the IC not only identified an inversion in the balance of excitatory-inhibitory activity between glutamatergic and GABAergic neurons (i.e., an increase in spontaneous activity of the glutamatergic neurons), but also observed an increase in bursting events in glutamatergic neurons and a modification of the spike shapes of both the excitatory and inhibitory neurons, suggesting a change in the expression and/or distribution of postsynaptic K^+ channels (Ma et al., 2020). In addition to the heterogeneous changes in the excitatory-inhibitory balance, results from studies observing animal models of tinnitus have shown that the IC neurons undergo a delayed increase in SFRs, suggesting that IC hyperactivity is more likely associated with chronic rather than acute tinnitus (Bauer et al., 2008; Groschel et al., 2014; Henry et al., 2014; Manzoor et al., 2013; Stolzberg et al., 2012; Vogler et al., 2014; Wang et al., 2013).

While the increase in SFRs of IC neurons is a prevalent finding throughout the literature, there is some controversy with respect to the extent to which they contribute to and drive tinnitus. There is evidence that animals which undergo unilateral noise trauma do not exhibit behavioural signs of tinnitus, however do show increased SFRs at the level of the IC, in turn suggesting that while the phenomenon may be necessary, it is not sufficient to justify tinnitus generation on its own (Berger & Coomber, 2015; Coomber et al., 2014; Ropp et al., 2014). Further work is required however to fully grasp the role and involvement of the IC in the development and maintenance of tinnitus.

Medial Geniculate Body

The medial geniculate body (MGB), a central relay station along the auditory pathway, receives input from the IC and projects to the primary auditory cortex and limbic structures, actively shaping and controlling the processing of information between subcortical and cortical areas (Bartlett, 2013; De Ridder, Vanneste, et al., 2015). The connections of the MGB with both auditory and non-auditory structures (particularly those concerned with emotion and attention) make it a key structure for tinnitus perception (Leaver et al., 2011; Rauschecker et al., 2010). It is well recognised that tinnitus perception and level of distress is in part determined by the emotional reaction to the tinnitus itself (De Ridder, Elgoyhen, et al., 2011; Jastreboff, 1990; Searchfield et al., 2012; Welch & Dawes, 2008). The MGB has projections that pass through to the amygdala and are involved in auditory fear conditioning; this pathway is thought to underlie and reinforce the relationship between tinnitus perception and the negative emotional response it elicits (Rauschecker et al., 2010; Weinberger, 2011). Interestingly, two opposing theories predominate the literature with respect to how the MGB drives tinnitus perception; one stipulates a decrease in GABAergic inhibition, while the other suggests an increase (for a detailed review, see Caspary and Llano (2017)). The Gain Control Theory (also known as Central Gain Theory) of tinnitus is characterised by reduced GABAergic inhibition, and is associated with the general notion of neuronal hyperactivity that has been observed throughout the central auditory system (Auerbach et al., 2014; Noreña, 2011). In contrast, the thalamocortical dysrhythmia model of tinnitus suggests that aberrant oscillations between the MGB and auditory cortex – resulting from a net increase in tonic inhibition in a subset of thalamocortical projection neurons – drive tinnitus pathology (Caspary & Llano, 2017; De Ridder, Vanneste, et al., 2015; Sametsky et al., 2015). The literature is divided, with a substantial level of support being offered to either hypothesis. Studies using animal models of tinnitus to investigate tinnitus-related changes within the MGB have found increased levels of spontaneous firing, bursting, and tonotopic reorganisation within the structure, maintaining the consistent theme of hyperactivity throughout the auditory pathway that is a well-documented hallmark of tinnitus pathology (Basta et al., 2015; Kalappa et al., 2014; Kamke et al., 2003). However, there is also evidence in favour of the thalamocortical dysrhythmia model; increased thalamocortical gamma (50-70 Hz) oscillations have been associated with tinnitus (Llinás et al., 2005), and several studies conducted on animal models of tinnitus have reported increased $GABA_A$-receptor efficacy in affected animals (linked to increased T-type Ca^{2+} channel activity), suggesting that these maladaptive oscillations are what in fact underpins thalamocortical dysrhythmia and in turn drives tinnitus (De Ridder, Vanneste, et al., 2015; Sametsky et al., 2015).

It is important to distinguish and define the mechanisms driving the changes within the MGB so as to understand where and how they come into play within the context of tinnitus, and how they might be manipulated for use in tinnitus therapy. Recent findings have flagged the MGB as an important and promising target for tinnitus therapy, with several studies utilising deep brain stimulation (DBS) reporting residual tinnitus suppression in noise-induced tinnitus rat models following high frequency stimulation (Rammo et al., 2019; van Zwieten et al., 2019; van Zwieten et al., 2021). van Zwieten et al. (2021) propose that DBS acts to suppress tinnitus by desynchronising these thalamocortical beta (20-35 Hz) and gamma (50-70 Hz) oscillations, in turn blocking the flow of this aberrant information. While it is likely that several mechanisms are at play, particularly given the heterogeneous nature of tinnitus, more research is required so as to better understand and define the way in which the MGB contributes to the tinnitus experience.

Auditory Cortex

Tinnitus-related hyperactivity is maintained all the way to the auditory cortex (AC): neurons in the AC exhibit an increase in SFRs, synchrony, and burst firing (Basura et al., 2015; Chen et al., 2013; Eggermont & Roberts, 2004; Noreña & Eggermont, 2003; Noreña et al., 2003; Roberts et al., 2010; Takacs et al., 2017). In addition, there is also evidence of structural changes (Schneider et al., 2009) and reorganisation of the tonotopic maps within the AC (Chen et al., 2016; Chen et al., 2013; Mühlnickel et al., 1998; Roberts et al., 2010). However, while some studies have reported a correlation between the extent of tonotopic reorganisation and the occurrence and severity of tinnitus (Chen et al., 2013; Mühlnickel et al., 1998; Noreña & Eggermont, 2006; Weisz, Wienbruch, et al., 2005; Wienbruch et al., 2006), others claim that this macroscopic reorganisation is not necessary for tinnitus induction (Miyakawa et al., 2019) and is, in fact, not characteristic of tinnitus associated with normal hearing or mild hearing loss (Langers et al., 2012; Yang et al., 2011). A recent study using fMRI techniques on individuals with bilateral high-frequency hearing loss examined the relationship between hearing loss, tinnitus, and tonotopic reorganisation (Koops et al., 2020). The study found that compared to healthy hearing, non-tinnitus controls, individuals with hearing loss in the absence of tinnitus had significantly different tonotopic maps, while those with the additional comorbidity of tinnitus did not. The authors propose that this suggests cortical map reorganisation is a characteristic of hearing loss, not tinnitus, and that tinnitus is likely related to a more conservative form of adaptation rather than excessive cortical plasticity (Koops et al., 2020).

In addition to evidence of enhanced central gain in the auditory cortex, alterations in rhythmic oscillatory activity among tinnitus patients have also been described, with studies reporting a reduction in alpha (8-13 Hz) activity and an increase in delta-theta (1-4 Hz) activity in the auditory cortex (Houdayer et al., 2015; Ortmann et al., 2011; Van Der Loo et al., 2009; Weisz, Dohrmann, et al., 2007; Weisz, Moratti, et al., 2005; Weisz, Müller, et al., 2007) and perisylvian regions in comparison to normal-hearing controls (Weisz, Moratti, et al., 2005). Given that alpha power is an indicator of ongoing inhibition and maintains the excitatory/inhibitory balance within the sensory cortices (Jensen & Mazaheri, 2010; Weisz et al., 2011; Weisz, Moratti, et al., 2005), the significant reduction in alpha activity within the auditory cortex is likely a key component in the cascade of events that give rise to tinnitus (Malekshahi et al., 2020). A recent study conducted by Hayes and colleagues (2021) sought to clarify how much each of the proposed neural correlates of tinnitus (increased central gain and altered rhythmical oscillations) contributed to the phantom sensation, and whether they are in fact sufficient and/or necessary for tinnitus generation. Using rat models of tinnitus, the researchers evaluated whether these known correlates of tinnitus were consistent across several tinnitus induction methods (salicylate, noise exposure), and whether direct pharmacologic induction of increased central gain/modified cortical oscillations would give rise to behavioural evidence of tinnitus (Hayes et al., 2021). The study failed to find an obvious association between tinnitus and the presence of enhanced sound-evoked activity or modified spontaneous cortical oscillations (Hayes et al., 2021). However, impaired GABAergic neurotransmission in the auditory cortex appeared to be sufficient for tinnitus generation, with the researchers suggesting a likely role for impaired cortical inhibition as a driver of the increased spontaneous firing rates observed in tinnitus (Hayes et al., 2021).

With the advancement of scientific methodologies and increasing availability of resources, researchers have been able to investigate potential genes, proteins, and receptors that might be involved in tinnitus. While the role of NMDA receptors has been explored for over a decade (Chen et al., 2013; Guitton et al., 2003; Jang et al., 2019; Ruel et al., 2008), recent studies have identified that nociceptive proteins (Yan et al., 2021), genes (Lopez-Escamez et al., 2016; Vona et al., 2017; Wells et al., 2021; Xie et al., 2021), and even neuroglial activation (Xia et al., 2020) might also contribute to the phantom sensation. Though these findings certainly add pieces to the 'tinnitus puzzle', it is evident that efforts are required to further current understanding of the neural basis of tinnitus and the contributing factors at play within the AC; future research should focus on disentangling and making more sense of the mechanisms thought to underlie tinnitus generation, defining their true relationship with the phantom sound.

Non-auditory areas implicated in tinnitus

It is now well established that tinnitus disorder is not merely the result of a disruption in the auditory pathways, but a reflection of the interaction between auditory networks and non-auditory areas involved in attention, emotion, salience, and memory (De Ridder, Elgoyhen, et al., 2011; Leaver et al., 2011; Searchfield et al., 2012). Involvement of the limbic system in tinnitus perpetuation and maintenance has been recognised for quite some time (Hallam, 1993), with growing efforts being made over the past few decades to understand the exact role of the limbic structures within the context of tinnitus (Jastreboff, 1990; Jastreboff & Hazell, 2008; Leaver et al., 2011; Rauschecker et al., 2010; Shahsavarani et al., 2019). Studies using functional magnetic resonance (fMRI) techniques have identified tinnitus-related changes in functional connectivity of several neural networks involving both auditory and extra-auditory regions, including the frontal cortex, cingulate cortex, caudate nucleus, parahippocampal gyrus, amygdala, and insula (Araneda et al., 2018; Besteher et al., 2019; Cai et al., 2019; Chen et al., 2018; De Ridder, Vanneste, et al., 2011; Henderson-Sabes et al., 2019; Husain & Schmidt, 2014; Lv et al., 2020; Maudoux et al., 2012; Schlee et al., 2009; Schmidt et al., 2013; Vanneste et al., 2018; Vanneste, Focquaert, et al., 2011; Vanneste, van de Heyning, et al., 2011; Xu et al., 2019). Additionally, animal models of tinnitus have also shown evidence of hyperactivity in several of the aforementioned areas (Allan et al., 2016; Chen et al., 2014; Husain et al., 2011; Krick et al., 2017a, 2017b; Plewnia, Reimold, Najib, Reischl, et al., 2007; Schlee et al., 2009; Vanneste & De Ridder, 2012a, 2016), likely contributing to the negative perception of tinnitus. Given the role of these structures in cognition, memory, attention, perception, and emotion, it is hypothesised that central neural alterations at the level of these non-auditory areas likely contributes to – and perhaps maintains – the clinical symptoms of tinnitus (Besteher et al., 2019; Chen, Bo, et al., 2017; De Ridder, Elgoyhen, et al., 2011; Husain, 2016; Joos et al., 2012; Pattyn et al., 2016; Vanneste et al., 2019). Aspects of Jastreboff's (1990) neurophysiological model of tinnitus are widely supported by these findings, and they have been pivotal in setting the foundation for and informing subsequent models of tinnitus generation and severity. More recent models of tinnitus perception formed on the basis of this interplay between auditory and non-auditory networks include – but are not limited to – the Noise-Cancellation model (Rauschecker et al., 2010), Integrative Model of Tinnitus (De Ridder et al., 2014), and Ecological Model of Tinnitus (Searchfield, 2014).

Noise-Cancellation model

The Noise-Cancellation model posits that failure of the limbic structures to filter and block hyperactive signals generated by the auditory structures gives rise to chronic tinnitus (Rauschecker et al., 2010). Proposed by Rauschecker and colleagues (2010), the model speculates that while tinnitus likely arises from lesion-induced plasticity at any point along the auditory pathway, the disorder is propagated and maintained through the aberrant activity of the paralimbic structures. Under normal circumstances, an inhibitory feedback loop involving paralimbic structures (namely the nucleus accumbens and the ventral medial prefrontal cortex) acts to cancel out the phantom signal at the level of the thalamus. In tinnitus, these mechanisms are compromised, in turn eradicating this 'noise-cancelling' ability and allowing the signal to be relayed to higher-level centres such as the auditory cortex, ultimately giving rise to permanent cortical reorganisation and chronic tinnitus.

The Integrative Model of Tinnitus

The Integrative Model of Tinnitus proposed by De Ridder and colleagues (2014) acts as an extension of several well-known models (including the neurophysiological model (Jastreboff, 1990), thalamocortical dysrhythmia model (De Ridder, Vanneste, et al., 2015; Llinás et al., 2005; Llinás et al., 1999), noise-cancellation model (Rauschecker et al., 2010), and central gain theory (Noreña, 2011)), and was designed with the aim of both unifying noise-cancelling and deafferentation-based models of tinnitus and integrating brain areas and networks implicated in tinnitus within a single model. The model posits that a central 'tinnitus core' exists comprised of the auditory cortex, parahippocampus, ventrolateral prefrontal cortex, and the inferior parietal area as the minimal assembly of neural structures required for perception of the tinnitus signal (De Ridder et al., 2014). This core works in concert with several 'multiple, parallel, dynamically changing and partially overlapping subnetworks' to give rise to the final tinnitus percept (De Ridder et al., 2014). Each of the 'subnetworks' exhibits a specific oscillatory pattern and is thought to reflect a specific aspect of the overall tinnitus sensation (for example, the 'tinnitus distress' subnetwork consisting of the frontopolar cortex, dorsolateral prefrontal cortex, precuneus, anterior/posterior cingulate cortex, (para)hippocampus, amygdala, insula, and orbitofrontal cortex, or the 'tinnitus location' network involving the parahippocampus, inferior parietal area, auditory cortex, and the dorsolateral/ventrolateral prefrontal cortex). Structures that are involved in several tinnitus networks simultaneously are termed 'hubs' (e.g., the parahippocampal area involved in both tinnitus distress and location). The implications of the Integrative Model of Tinnitus could be profound; given the unique oscillatory signature of each network involved in tinnitus, the researchers postulate that manipulation of a specific hub would allow for modulation of the feature encoded by that particular hub (i.e., stimulation of the parahippocampal area could in theory enable modification of tinnitus distress or location).

The Ecological Model of Tinnitus

The Ecological Model of Tinnitus emphasises the notion that the tinnitus experience – and in turn management – is shaped by several psychosocial, individual, and contextual factors, meaning that while the onset of tinnitus might be rooted in lesion-induced neuroplasticity, the unified tinnitus sensation is a reflection of the interaction between psychoacoustic, social, and environmental context factors (Searchfield, 2014). The model offers a holistic view of the tinnitus experience (cf. conventional

> psychoacoustic models of tinnitus) and is based on the Adaptation Level Theory (ALT) (Searchfield et al., 2012) which speculates that tinnitus – and an individual's reaction to it – is in fact fluid, continuously varying depending on changes in cochlear outflow, attention, context, and emotion. According to the ALT, the overall perceived magnitude of tinnitus is determined by several factors which act to shape an individual's 'frame of reference', including the tinnitus signal itself, background/contextual stimuli, and residuals/social factors (Searchfield et al., 2012; Searchfield et al., 2019).

In addition to playing a significant role in the induction, maintenance, and even suppression of tinnitus, the importance of these non-auditory regions is also highlighted in the context of their contribution to disentangling and de-coding tinnitus heterogeneity. Recent studies exploring the role of non-auditory networks in tinnitus have identified alterations in brain activity and functional connectivity that are indicative of different forms of tinnitus (Lan et al., 2021; Shahsavarani et al., 2021). If differences in these networks could help discern between the various types of tinnitus thought to exist, it would offer a means of tinnitus sub-typing, furthering current understanding of tinnitus and the mechanisms that drive it. Lan et al. (2021) reported observing different patterns of neural activity and connectivity as the percept transitioned from being an acute event to a chronic experience (Lan et al., 2021). As the duration of the tinnitus increased, and the sensation transitioned from an acute to a chronic state, Lan et al. (2021) identified gradual changes in neural activity in frontal, parietal, and temporal cortices, as well as altered connectivity between the parahippocampal gyrus and other extra-auditory areas. The researchers suggested that tinnitus development is a complex, dynamic process perpetuating from dysfunctional local neural activity to aberrant connectivity in multifunctional neural networks, and that the parahippocampal gyrus is likely to be a key player in tinnitus perception (Lan et al., 2021). Similarly, Shahsavarani et al. (2021) found that the varied functional connectivity of several brain regions – such as the precuneus, cerebellum, primary visual cortex, superior/middle frontal gyrus – and components of the salience network, dorsal attention network, and the amygdala, gave rise to two tinnitus sub-groups characterised by tinnitus severity. Shahsavarani et al. (2021) explored neural correlates of tinnitus distress using a unique jazz music-rest interleaved fMRI paradigm. On average individuals who reported experiencing bothersome tinnitus exhibited stronger inter-network connectivity of the limbic, attention, salience, and default mode networks relative to those who reported mild tinnitus (Shahsavarani et al., 2021). These results not only further our understanding of the role of non-auditory networks in tinnitus perception and the level of their contribution towards the phantom sensation, but also inform tinnitus sub-typing which is presently considered the way forward.

2.4. Assessment and measurement of tinnitus

The difficulty of tinnitus assessment is that there is currently no objective means of measuring the phantom percept; rather, it relies on the subjective characterisation and description of those suffering from it. Given that the tinnitus experience is a reflection of the individual, their personality, experiences – all of which act to shape their perception and therefore response to tinnitus – it becomes difficult to reliably define, measure, and gage the true extent of the sensation. At present, there are two main branches of tinnitus assessment: psychoacoustic measures (see Vajsakovic et al. (2021) for a detailed review) and self-report measures. Psychoacoustic measures evaluate the auditory attributes of tinnitus, such as perceived pitch (frequency), loudness (intensity), and assess how tinnitus behaves and/or interacts with external auditory stimuli by recording minimum masking levels and residual inhibition. Conversely, self-report measures generally utilise psychometric questionnaires to gain a better understanding of not only the psychoacoustic properties of the sensation, but also the type and level of distress associated with it. Commonly used standardised tinnitus questionnaires in the clinical and research setting include the Tinnitus Functional Index (TFI) (Meikle et al., 2012), Tinnitus Handicap Questionnaire (THQ) (Kuk et al., 1990), Tinnitus Reaction Questionnaire (TRQ) (Wilson et al., 1991), Tinnitus Handicap Inventory (THI) (Newman et al., 1996), Tinnitus Primary Function Questionnaire (TPFQ, also referred to as the Iowa Tinnitus Activities Questionnaire) (Tyler et al., 2014), and Tinnitus Questionnaire (TQ) (Hallam et al., 1988) (Table 1).

Table 1. Overview and summary of several commonly used psychometric questionnaires for tinnitus assessment.

Questionnaire	Author(s)	Purpose	Items/subscales	Validity	Notes
Tinnitus Questionnaire (TQ)	Hallam et al. (1988) Hallam (1996, 2008)	Measures tinnitus severity and evaluates the psychological impact of tinnitus	52 items 5 subscales: • Emotional and cognitive distress • Intrusiveness • Auditory perceptual difficulties • Sleep disturbance • Somatic complaints	High internal consistency, high convergent validity, and high discriminant validity (Zeman et al., 2012) (against the THI, TFI, and Tinnitus Impairment Questionnaire, TBF-12). Good change sensitivity (Jacquemin et al., 2019; Zeman et al., 2012), however is not recommended for use in detecting intervention-related changes as its items are not designed to be specifically responsive to treatment-related changes (Fackrell et al., 2014).	Zeman et al. (2012) found the TQ to be suitable as an outcome measure for evaluating the effects of tinnitus treatments in a cross-cultural context.
Tinnitus Handicap Questionnaire (THQ)	Kuk et al. (1990)	Measures degree of perceived handicap as a result of tinnitus	27 items 3 subscales: • Physical, emotional, and social effect of tinnitus • Hearing and communication ability • Individual's perception of tinnitus	Extremely high internal consistency (as evaluated and critiqued by Fackrell et al. (2014)). High convergent validity (against the TQ, TRQ, and THI) (Henry & Wilson, 1998; Robinson et al., 2003). Low to moderate discriminant validity, suggesting that the instrument may be vulnerable to generalised emotional distress rather than tinnitus-related distress (Fackrell et al., 2014).	
Tinnitus Reaction Questionnaire (TRQ)	Wilson et al. (1991)	Assesses psychological distress associated with tinnitus	26 items	High internal consistency (Wilson et al., 1991), high convergent validity (against THQ, TQ, and THI) (Robinson et al., 2003). Low discriminant validity against	

				several anxiety and depression scales (Andersson et al., 2003; Robinson et al., 2003; Wilson et al., 1991).	
Tinnitus Handicap Inventory (THI)	Newman, Jacobson, & Spitzer (1996)	Measures level of perceived tinnitus severity	25 items 3 subscales: • Functional • Emotional • Catastrophic	High internal consistency, high convergent validity, and high discriminant validity (against the TQ and Tinnitus Impairment Questionnaire, TBF-12) (Zeman et al., 2012). Good change sensitivity (Zeman et al., 2012).	Zeman et al. (2012) found the THI to be suitable as an outcome measure for evaluating the effects of tinnitus treatments in a cross-cultural context.
Tinnitus Functional Index (TFI)	Meikle et al. (2012)	Measures tinnitus severity and treatment-related changes	25 items 8 subscales: • Intrusiveness • Sense of control • Sleep • Cognition • Hearing • Relaxation • Emotional distress • Quality of life	High convergent validity (against the THI, THQ, and TQ) (Fackrell et al., 2015; Jacquemin et al., 2019), and high sensitivity to change (Jacquemin et al., 2019). Moderate discriminant validity against general depression, anxiety and quality of life questionnaires (Fackrell et al., 2014; Fackrell et al., 2015).	Has been validated in New Zealand (Chandra, 2013) Has been translated into 14 different languages (Henry et al., 2016)
Tinnitus Primary Functional Questionnaire (TPFQ)	Tyler et al. (2014)	Evaluates the severity and impact of tinnitus on the quality of life	20 items 4 subscales: • Concentration • Emotion • Hearing • Sleep	High internal consistency, moderate to high convergent validity (against the THQ, Beck Depression Inventory (BDI), State-Trait Anxiety Questionnaire, and Pittsburgh Sleep Quality Index (PSQI) (Tyler et al., 2014; Tyler & Deshpande, 2015), good sensitivity to change (equally sensitive to the THQ).	Has been translated and validated in several different languages (Coradini et al., 2023; Lu et al., 2019; Nahad et al., 2014; Shaurya et al., 2018; Shin et al., 2019; Talaat et al., 2020; Xin et al., 2023).

	Has been adapted into a 12-item version for clinical use (equally valid and reliable) A useful measure for discerning which primary function is most impacted by an individual’s tinnitus (e.g., sleep)

Over the years, these instruments have been evaluated, tested, translated in several different languages and validated across a number of countries (Bouscau-Faure et al., 2003; Coradini et al., 2023; Jun et al., 2015; Kojima et al., 2017; Lu et al., 2019; Müller et al., 2016; Nahad et al., 2014; Shaurya et al., 2018; Shin et al., 2019; Sørensen et al., 2020; Talaat et al., 2020; Vanneste, To, et al., 2011; Wrzosek et al., 2016; Xin et al., 2023). Of the noted questionnaires, the TFI and THI are globally the two most frequently used questionnaires (Baguley et al., 2016). While both questionnaires offer broad assessment of tinnitus impact, the TFI has the additional benefit of detecting change, while the THI was not specifically designed for this purpose and is primarily focused on the psychological impact of tinnitus. While many of the aforementioned measures are being used to measure change in tinnitus-related distress following interventions, only the TFI has been specifically designed and validated for this purpose (National Guideline Centre (UK), 2020). Given its broad assessment of tinnitus impact and ability to measure change, the National Institute for Health and Care Excellence (NICE) have encouraged use of the TFI as an initial assessment of tinnitus in adults (National Guideline Centre (UK), 2020).

Measuring changes in tinnitus

While psychoacoustic measures and psychometric questionnaires are aimed at characterising the tinnitus percept and understanding the psychological impact it may have on an individual, structural and anatomical changes associated with tinnitus are investigated using imaging techniques such as electroencephalography (EEG), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), and magnetoencephalographic imaging (MEGI) (Table 2). These methods help to map the heterogeneous alterations in auditory and non-auditory networks and define structures associated with tinnitus, in turn identifying possible biomarkers of tinnitus and thus informing clinical decision making and the development of management strategies for tinnitus (Adams et al., 2020). While there are advantages and disadvantages to each of the aforementioned neuroimaging techniques, they offer a means of identifying structures of interest, as well as characterising the location, extent, and magnitude of neural activity and connections within the central nervous system (Adams et al., 2020).

Table 2. Overview and summary of several commonly used neuroimaging methods for tinnitus assessment (Adams et al., 2020; Crosson et al., 2010; Kim & Lee, 2016; Tulay et al., 2019)

Neuroimaging method	Use	Advantages	Disadvantages
EEG	Recording electric potentials generated by spontaneous or evoked neural activity	• High temporal resolution (milliseconds) • No radiation • Low cost • Portable • Widely accessible • Fewer motion artefacts	• Low spatial resolution • Does not measure activity below the cortex
fMRI	Spatial mapping of brain activity via changes in blood oxygen level-dependent (BOLD) signal	• High spatial resolution • No radiation • Widely accessible	• Scanner noise interference with auditory processing/resting state • Longer temporal resolution (seconds) cf. EEG/MEGI • Not portable
PET	Spatial mapping of brain activity via increase in regional cerebral blood flow in response to elevation of oxygen and glucose demands	• Quiet • Compatible with ferromagnetic implants (e.g.,	• Inferior spatial/temporal resolution cf. fMRI • Invasive and uses radioactive

		cochlear implants) • Fewer motion artefacts	labels • High cost • Not portable • Not easily available
MEGI	Recording magnetic fields generated by spontaneous or evoked neural activity	• High temporal resolution (milliseconds)	• Low spatial resolution • High cost • Not portable • Not easily available

In addition to the functional neuroimaging methods currently in use, novel techniques are still being explored. A recent study by Shoushtarian et al. (2020) applied a functional near-infrared spectroscopy (fNIRS) technique paired with machine learning in an attempt to objectively measure tinnitus. The authors stated that while the method is incapable of imaging deep cortical regions, it has several advantages over conventional neuroimaging techniques: it is non-invasive and non-radioactive (cf. PET), has better temporal resolution (cf. fMRI), and is quiet, portable, and cost-effective (Shoushtarian et al., 2020). Using fNIRS and machine learning, the study was able to 1) effectively differentiate between tinnitus and non-tinnitus individuals (78.3% accuracy) by identifying fNIRS visual and auditory evoked response and resting state connectivity features, and 2) sub-type patients according to tinnitus severity level (87.3% accuracy, low vs. high severity) by evaluating fNIRS features that were correlated with tinnitus severity (i.e., temporal-occipital connectivity). While each method has its clear advantages and disadvantages for application in tinnitus research, going forward it is interesting – and perhaps crucial – to consider pairing functional imaging with machine learning/artificial intelligence in an effort to advance current understanding. Through this union, it may be possible to 'level-up' and not only build on what is presently known about the structures and networks implicated in tinnitus but disentangle the knot that is tinnitus heterogeneity by applying models/algorithms that can predict and sub-type tinnitus patients accordingly.

2.5. Treatment and management of tinnitus

Treatment of tinnitus is difficult for several reasons, not the least of which is the differential response to treatments that comes as a result of tinnitus heterogeneity (Cederroth et al., 2019). At present, there is no cure for tinnitus but there are management strategies with varying levels of success. The search for a cure has seen a broad range of avenues explored, including acupuncture (Park et al., 2000), pharmacotherapy (e.g., antidepressants, anticonvulsants, nootropics) (Baldo et al., 2012; Beebe Palumbo et al., 2015; Langguth et al., 2019), naturopathic remedies (e.g., gingko biloba) (Hilton et al., 2013; Hoekstra et al., 2011), neuromodulation (e.g., transcranial magnetic stimulation, vagus nerve stimulation[1]) (Meng et al., 2011), auditory stimulation (e.g., hearing aids, sound maskers, sound-based therapies) (Hoare, Edmondson-Jones, Sereda, et al., 2014; Hobson et al., 2012), hyperbaric oxygen therapy (Bennett et al., 2012), and cognitive behavioural therapy (CBT) (Hesser et al., 2011). None of these treatments have high level evidence to support their reliability and effectiveness in suppressing the perception of tinnitus (Langguth et al., 2019; Zenner et al., 2017).

Clinical guidelines recommend targeting potential comorbidities and applying different management strategies such as counselling, hearing aids (where appropriate), CBT, psycho-education, and sound therapy in a personalised patient-specific manner (Simoes et al., 2019; Tunkel et al., 2014). CBT in particular has the most supporting evidence for effectiveness in tinnitus management, but does not reduce tinnitus loudness perception (Hesse, 2016; Martinez-Devesa et al., 2007). CBT has been found to induce a beneficial effect on the quality of life of tinnitus patients (Martinez-Devesa et al., 2007; Robinson et al., 2008), suggesting that perhaps the impact of a treatment on a patient's reaction to their tinnitus is not directly related to their perception of their tinnitus. The current clinical understanding is that while the aforementioned treatments might not be effective for every patient, they might be suitable for some, and as such clinicians should move away from a 'one size fits all' approach and focus on an individualised form of treatment (Langguth et al., 2019; Simoes et al., 2019). Further, it is widely understood that combining some form of counselling with auditory stimulation (and hearing aids/amplification where a hearing loss is identified) is at present the most appropriate first step in alleviating tinnitus-related distress (Baguley, McFerran, et al., 2013; Cuesta et al., 2022; Makar et al., 2017; Tunkel et al., 2014; Zenner et al., 2017). Counselling is an important factor in tinnitus management as it aims to ease a patient's worries and concerns regarding their tinnitus by unpacking the phantom percept and

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[1] The efficacy of vagus nerve stimulation (VNS) for tinnitus treatment has been a topic of debate (De Ridder, Langguth, & Vanneste, 2021; Stegeman et al., 2021); more research is required to fully understand the neural basis of tinnitus and the pragmatics of implementing VNS for therapy.

reassuring the patient that it is not a life-threatening neurological problem (Mazurek et al., 2022; Tunkel et al., 2014). This in turn targets the ‘reaction’ part of the tinnitus experience, and is likely why strategies such as CBT are effective at improving an individual’s quality of life without necessarily lessening the level of tinnitus loudness (Hesser et al., 2011; Martinez-Devesa et al., 2007).

Over the past couple of years, clinical care across the board has been greatly affected by social-distancing and lockdown measures implemented as a result of the COVID-19 pandemic. Clinicians have had to adapt and find ways of offering remote support, often turning to telehealth (Henry et al., 2020) and smartphone apps (Mehdi, Stach, et al., 2020; Nagaraj & Prabhu, 2020; Smith & Sereda, 2020). While there is a need to clinically evaluate and validate the effectiveness of these technology-based ‘vehicles’ for tinnitus management, current findings show promising results for their application in delivering sound-based therapies, CBT, and Progressive Tinnitus Management (PTM) for tinnitus relief (Andersson et al., 2002; Henry et al., 2020; Henry, Thielman, Zaugg, Kaelin, Choma, et al., 2017; Henry, Thielman, Zaugg, Kaelin, Schmidt, et al., 2017; Henry et al., 2010; Jun & Park, 2013; Kaldo et al., 2008; Kaldo-Sandstrom et al., 2004; Kim, Chang, et al., 2017; Mehdi, Dode, et al., 2020; Schmidt et al., 2017; Tyler et al., 2018). Moreover, in addition to taking advantage of personalised devices and adopting an individualised method of tinnitus therapy, it has become increasingly evident that the future of tinnitus management includes using machine learning and modelling to both further our understanding of tinnitus, and predict therapeutic outcomes for those suffering from it (Searchfield, Zhang, et al., 2021). Recent studies have been able to utilize machine learning algorithms in combination with neuroimaging techniques to identify biomarkers of tinnitus and in turn use this to predict therapeutic success in tinnitus patients (Durai, Doborjeh, et al., 2021; Han, Na, et al., 2019). Durai, Doborjeh, et al. (2021) investigated the effects of passive perceptual sound training on tinnitus, identifying meaningful patterns in brain activity using an artificial intelligence (AI) technique known as deep brain-inspired spiking neural network (SNN) architecture which learns from neural networks mapped over time in a 3D space of artificial neurons. The study aimed to recategorize tinnitus as a real-world natural sound, reducing the ambiguity surrounding the phantom sound, relieving cognitive resources, and in turn alleviating tinnitus-related distress (Durai, Doborjeh, et al., 2021). This method has not only enabled researchers to understand the neural networks implicated during the sound training, but also identified changes in these networks as a result of categorisation (altered tinnitus neural network activation and increased bilateral hemispheric involvement as the training sound gradually morphs from the tinnitus sound (avatar) into the real-world natural sound, particularly in regions involved with attention and discriminatory judgements) (Durai, Doborjeh, et al., 2021). While more work is required to establish the use of this computational model in tinnitus research, the ability of this SNN method to identify, map, and continuously learn and build from neural data are what make it a promising tool for the prediction of treatment response and in turn therapeutic success.

2.6. Future of tinnitus: where to from here?

It is clear that the future of tinnitus – from understanding the underlying mechanisms of the phantom percept all the way to identifying appropriate treatment(s) – lies in subtyping, adopting a personalised-medicine approach, and utilising computer modelling methods. These principles could – and should – be applied to every avenue of tinnitus research, from genetics, to all forms of therapy, and even at the earliest stages of tinnitus characterisation. In doing so, we may come to one of three conclusions, either:

- There are different types of tinnitus defined by their differential characteristics across several dimensions (including perception/psychoacoustic properties, causal risk factors and related comorbidities of the patient, level of distress induced, and response to treatment) (Cederroth et al., 2019).

OR

- Tinnitus is a continuum across multiple dimensions meaning that attempting to categorise is futile.

OR

- There is a single common mechanism or structure – a so-called ‘tinnitus perception core’ – present in all of the heterogeneous forms of tinnitus (Henton & Tzounopoulos, 2021).

Whatever the outcome, applying the methods discussed above will mean gaining a better understanding of the mechanisms that underpin the phantom percept and how they might be targeted to alleviate or altogether eradicate the associated distress. Additionally, using these methods enables clinicians and researchers to build profiles for different types of tinnitus, apply modelling to better understand the different tinnitus subtypes, and in turn help determine and/or predict what treatment is most sensible and beneficial for a given patient. Henton and Tzounopoulos (2021) have suggested classifying tinnitus patients using a neuroscience-based 'structure-function' approach, subtyping different forms of tinnitus according to variations in central tinnitus-related plasticity in auditory and extra-auditory centers using EEG, MEG, MRI, and ABR measures. Furthermore, this method of tinnitus classification offers an objective means of measuring and characterising tinnitus; something that is crucial yet still lacking in both the clinical and research environment (currently, only subjective measures of tinnitus perception and severity are available and accepted (Henry, 2016)).

Tinnitus is a complex disorder, one that poses many hurdles and challenges for future research. While efforts are consistently being made to demystify and disentangle the phantom sensation, it is evident that a multidisciplinary approach is necessary to bring alternative perspectives, insights, skills, and techniques from different clinical and academic domains (Cederroth et al., 2019). As an extension, a recent state-of-art review proposed implementing a digital therapeutic system founded on an app-based management tool which uses AI to configure transducers, biosensors, counselling, and ecological momentary assessments (EMA), and relays collected information to clinicians/researchers via cloud computing (Searchfield, Sanders, et al., 2021). The ultimate objective would in turn be the development of a 'smart therapy' platform for tinnitus, in which AI is paired with sensor technology, EMA, and multiple transducers to gain information from a given participant, identify the most appropriate therapy, and potentially deliver real-time modifications to the therapy when/where necessary (Searchfield, Sanders, et al., 2021). Considering the gravity and impact COVID-19 had on limiting access to healthcare services it is imperative, perhaps now more than ever, to be able to offer patients remote support. Interventions rooted in the ecological model of tinnitus (Searchfield, 2014) such as counselling (Beukes et al., 2019), mindfulness (Manchaiah et al., 2020; Rademaker et al., 2019), sound-based therapies (Deshpande & Shimunova, 2019; Durai, Doborjeh, et al., 2021; Mehdi, Stach, et al., 2020; Sereda et al., 2019), CBT (Andersson et al., 2002; Kaldo et al., 2008), meditation (Fitzgerald et al., 2021), and game-based therapies (Wise et al., 2016; Wise et al., 2015) are more easily and readily adaptable for remote application (for a review on the digital technologies that are likely to shape future tinnitus therapies, see Searchfield, Sanders, et al. (2021)). Considering the idea of multi-modal therapy for tinnitus management, Searchfield, Zhang, et al. (2021) advise that these strategies could perhaps form part of a self-directed home-based approach to tinnitus therapy, one that is not independent of other evidence-based tinnitus therapies but rather stands as an option for remote care and management. As such, future strategies for tinnitus management should consider finding ways to incorporate telehealth and app-based services with the aim of increasing access to care and support.

2.7. Summary

While it is clear that decades of research have created a strong foundation of knowledge surrounding tinnitus, there is much work yet to be done in order to sift through that information, make sense of what we currently know, and work together to apply inter-disciplinary methods that can build on that foundation. We possess powerful resources and tools for tinnitus assessment that are capable of evaluating the phantom percept, characterising its psychoacoustical properties, defining its emotional implications, and informing therapeutic success; the next step is refining these tools and coupling them with machine learning and modelling techniques with the aim of moving toward a personalised precision-medicine method of tinnitus therapy through the prediction of therapeutic success and real-time delivery and adjustment of personalised therapies. Additionally, future developers of tinnitus therapies should consider designing treatments that can be easily adapted for remote application in an effort to increase treatment accessibility for all tinnitus patients, in turn knocking down barriers to healthcare services and lending support even in circumstances where face-to-face consultations are not possible.

Chapter 3. Principles and Methods for Psychoacoustic Evaluation of Tinnitus

3.1. Chapter Introduction

The review presented in this chapter provides an overview of the psychoacoustic assessment of tinnitus, its relationship to cognitive and behavioural aspects of tinnitus, and its neuropathophysiology, particularly focusing on the implications of tinnitus heterogeneity on tinnitus matching and assessment. It considers the limitations that psychoacoustic measures of pitch, loudness, minimal masking level, and auditory residual inhibition commonly face, and evaluates the ability of these measures to assess and characterise the tinnitus experience. Furthermore, the paper draws on tinnitus heterogeneity and highlights the importance of evaluating and considering tinnitus as a holistic experience consisting not only of its acoustic parameters, but also patient personality and activity within auditory and non-auditory tinnitus-related neural networks. Steps and protocols used to generate tinnitus replicas in the pilot study (Chapter 5) and auditory categorisation training study (Chapter 6) were informed by the theories and methodologies of psychoacoustic tinnitus evaluation reviewed in this chapter. This review was published in *The Behavioral Neuroscience of Tinnitus* (Vajsakovic et al., 2021) and reprinted in this thesis with permission from Springer International Publishing (2023).

3.2. Abstract

Tinnitus, the perception of sound in the absence of a physical sound in the environment, is highly heterogeneous. It varies in its etiology, characteristics, and impact on an individual's life. The sound is commonly described as "ringing," "buzzing," "crickets," "hissing," "humming." Tinnitus can be acute or chronic, mild or disabling. It can be perceived unilaterally or, more commonly, bilaterally. The sound and its location differ from person to person and fluctuate in the same individual over a certain period of time. This heterogeneity in characterization has important implications for research and clinical practice. Identifying patterns in how tinnitus sounds and its relationship to hearing may aid in identifying different forms of tinnitus and revealing their underlying mechanisms. However, the subjective nature of characterizing tinnitus makes it difficult to reliably define and measure. This chapter will focus on reviewing the psychoacoustic assessment of tinnitus, its relationship to cognitive and behavioral aspects of tinnitus, and its neuropathophysiology. In particular, it will describe the heterogeneity of tinnitus and tinnitus matching, and how individual variability in measures may be used to guide treatment and as a prognostic factor.

3.3. Introduction

Overview of Clinical Characteristics of Tinnitus

It is important to evaluate and quantify tinnitus so as to understand its mechanisms and possible means of treatment (Henry, Flick, et al., 2004). Psychoacoustic measurements have been obtained primarily for two reasons: (1) to define the auditory features related to how it is perceived by the patient and (2) to define to what degree external sounds have an effect on the tinnitus (Henry, 2016). There is now increasing interest in how psychoacoustic measures can inform treatment and serve as prognostic tools. Pitch and loudness measurements aid in determining the auditory attributes of tinnitus, while masking and residual inhibition effects reveal how a patient's tinnitus behaves following the application of an external sound (Henry, 2016). In addition to characterizing the auditory features of tinnitus and its response to auditory stimuli, conducting psychoacoustic measurements is important for a number of secondary reasons: (1) to understand the underlying etiology and mechanisms of tinnitus, (2) to be able to replicate the patient's tinnitus and demonstrate its characteristics and features to both the patient and their family, (3) to reassure the patient and their family that the tinnitus is real, (4) to explore management options and select the treatment most beneficial to an individual patient, (5) to monitor any changes in the tinnitus and its perception, (6) to determine if a patient is likely to benefit from a certain type of treatment, (7) to determine the effects of treatment on tinnitus and its perception, (8) to reproduce the patients tinnitus for use in treatments such as sound therapy, (9) to aid in the exploration and characterization of different tinnitus subcategories, and (10) to assist in legal issues (Henry, Flick, et al., 2004; Henry et al., 2013; Manning, Grush, et al., 2019; Moore, 2014; Nageris et al., 2010; Ristovska et al., 2019; Sandlin & Olsson, 1999; Schechter & Henry, 2002; Switalski & Sanchez, 2019; Tyler, 2000; Vernon & Meikle, 2000).

Table 3. Patients' descriptions of their tinnitus percept. Responses were obtained from the OHSU Tinnitus clinic database 1981-1994 (n = 1625) and Stouffer and Tyler (1990) (n = 528).

Sound	OHSU Tinnitus Clinic 1981-1994 % of responses	Stouffer & Tyler, 1990 % of responses
Ringing	56.9	37.5
Hissing	19.5	7.8
Clear tone	17.3	--
High tension wire	14.2	--
Buzzing	12.0	11.2
Sizzling	7.6	--
Transformer noise	7.1	--
Crickets, insects	6.2	8.5
Pulsating	6.0	3.8
Whistle	6.0	6.6
Hum	6.0	5.3
Roaring	4.8	4.5
Pounding	1.1	0.4
Clicking	0.5	0.6
Music/Musical note*	0.4	4.2*
Other	21.9	9.8

Note. OHSU = Oregon Health and Science University. OHSU data reflects all patients regardless of number of predominant sounds reported, and amounts to a total value greater than 100% as patients were permitted to provide multiple responses (Meikle et al., 2004).

Tinnitus has traditionally been classified as being one of the two general types: (1) the rare objective type (somatosounds) generated as an acoustic signal located in the head or neck as a result of muscular, skeletal, respiratory, or vascular irregularities/disturbances or (2) the more common subjective type (true tinnitus) thought to arise within the auditory and non-auditory pathways as a result of lesion-induced reactive neural plasticity (Douek, 1981; Henry, 2016). This review is focused on subjective tinnitus. Patients describe their tinnitus percept in a number of ways: most commonly as a ringing or hissing sensation, but in some cases as more complex sounds such as crickets and even music (Table 3). It is not uncommon for patients to report hearing more than one sound (together or separately) and/or complex sounds (Douek, 1981; Meikle & Taylor-Walsh, 1984; Tyler, 2000). For example, some individuals might experience a high-pitched whistle and low-pitched "ocean waves" in the same ear, with perhaps one of the sounds fluctuating while the other is continuous (Tyler, 2000), or may describe their tinnitus as sounding like music (Vanneste et al., 2013). Further, tinnitus can have multiple and/or variable localizations, being perceived in the ear (s) or frequently in various locations in/or around the head (Meikle and Taylor-Walsh, 1984; Tyler, 2000).

The Historic Foundations of Tinnitus Matching

Psychoacoustics is the study of the perception of sound and can trace its roots to Aristotle and later Leonardo De Vinci. However our understanding of psychoacoustics has accelerated with the development of telecommunications (Yost, 2015). The history of tinnitus assessment has followed a similar trajectory (Stephens, 1984). In the early nineteenth century, French physician Jean Marie Itard outlined early attempts at describing tinnitus masking, including piercing a tiny hole in a waterfilled vase and letting the water trickle into a large copper bowl of the same capacity, burning greener or slightly damp firewood, and even advising tinnitus sufferers to take up residence near a water mill (J.M.G. Itard, quoted in Stephens, 1984). As early as 1903, Spaulding acknowledged the advantages of matching a patient's tinnitus to musical notes of the same pitch. His approach included playing musical scales on his violin and instructing patients to indicate when they felt a note best-matched the pitch of their perceived tinnitus (Spaulding, 1903). Spaulding was one of the first along with Josephson (1931) to identify and shed light on the temporary suppression of tinnitus following sound, known as residual inhibition (Vernon & Fenwick, 1984). Building on Spaulding's work, Josephson (1931) designed a method for the measurement of both tinnitus pitch and "intensity." For the evaluation of tinnitus pitch, he employed a pure-tone pitch-matching method in which the pitch of the tinnitus was estimated by stimulation over a range of frequencies. Throughout his masking experiments, Josephson noted that tinnitus did not appear to behave as an external sound. If it did, a summation of the tinnitus and pitch-matched sound loudness would have been observed, instead masking occurred (Josephson, 1931). According to his methods, the "intensity" of tinnitus could be measured by defining the difference between the threshold of the superimposed sound as compared to the normal hearing threshold at that frequency (Josephson, 1931). The pure-tone method was also implemented by Wegel (1931), who used measurements of pitch and loudness to construct masking curves of tinnitus. The work of these researchers both set the scene and laid the foundation for the more detailed investigations that were to follow. Pivotal contributions to tinnitus measurement were made mid-last century by Edmund Prince Fowler, the first researcher to determine tinnitus loudness in dB sensation level (dB SL) by balancing the tinnitus loudness in one ear with the loudness of a tone in the contralateral ear (Fowler, 1936, 1937). Fowler emphasized the importance of psychoacoustic measurements in defining the spectral characteristics of tinnitus. He also considered the possibility that features such as tinnitus tone, frequency, intermittency (or conversely constancy), and reaction to masking and environmental noise might suggest different etiologies and site of lesion (Fowler, 1940). Fowler described methods of pitch and loudness matching that are comparable to what is being used in clinics and research today. He also identified many of the issues and limitations of psychoacoustic measures that clinicians and researchers still remain mindful of when assessing patients.

Goodhill (1952) believed that the validity with which patients described their tinnitus depended to a great degree on their knowledge of musical terms, having observed that a number of his patients had difficulties with defining their tinnitus. Reed (1960) conducted the first large-scale tinnitus study, using audiometric testing to evaluate the spectral features of tinnitus in 200 patients. Instead of applying the tinnitus measurement techniques available (such as those described by Fowler and others), he chose to develop his own method for matching tinnitus "frequency, content, and loudness," commenting on the inability to replicate the methods of others due to the lack of sufficient detail provided. In addition to defining the localization, intermittency (or conversely constancy), degree of hearing loss, description of tinnitus sound, frequency, and loudness, Reed (1960) also noted that the severity of a patient's tinnitus did not appear to be correlated with any of the psychoacoustic measures (central frequency, bandwidth, or loudness). Furthermore, he advised that tinnitus without a degree of hearing loss is rare, occurring in only 7.5% of tinnitus cases. Exploring tinnitus and hearing loss in more depth, Graham and Newby (1962) assessed the characteristics of tinnitus in four different groups of patients; those with normal hearing sensitivity, sensorineural hearing loss, conductive hearing loss, and mixed sensorineural-conductive hearing loss. The study found that the pitch matches for patients with conductive hearing loss were significantly lower in frequency than for patients in the other two hearing loss groups. Graham and Newby (1962) suggested that this might reflect an underlying mechanism for the generation of tinnitus in patients with conductive hearing loss that is distinct from that experienced by patients with other types of hearing loss. The first systematic evaluation of tinnitus masking was conducted by Feldmann (1971), who investigated the effect that sounds of certain frequencies had on the tinnitus sensation of 200 patients. Feldmann (1971) noted that sound-on-sound masking generates five different masking patterns (see The Minimum Masking Level section): one similar to sound-on-sound masking in which the closer the frequency of the masker is to the frequency of the tone being masked, the lower the intensity required to mask it. The others did not follow conventional sound-on-sound masking principles (Feldmann, 1971). Forty years ago efforts were made at a Ciba Foundation Conference in London to promote the standardization of tinnitus characterization procedures, advocating for the routine measurement of four features of tinnitus deemed crucial to its evaluation, namely tinnitus pitch and loudness, the maskability of tinnitus (ability of an external sound to conceal the tinnitus), and residual inhibition (reduction or complete elimination of the perception of tinnitus following auditory stimulation) (Evered & Lawrenson, 1981). Working closely with the Ciba Symposium, Vernon and Meikle (1981) designed a protocol detailing the methods for conducting these four measurements. However, despite these efforts, standardized methods have not been adopted universally (Henry, Flick, et al., 2004). The absence of standardization presents severe limitations to the obtainment of valid and reliable psychoacoustic measurements. It also prevents the collation, comparison, and interpretation of data across clinics and research laboratories on a global scale, in turn impeding progress in the field of tinnitus research.

3.4. Psychoacoustic Measures: Pitch

Pitch is the perceptual equivalent of the frequency of sound. Pitch matching of tinnitus is a fundamental psychoacoustic measure in most clinical or research assessment protocols. This section will consider the values and shortcomings of different measures of tinnitus pitch. Pitch measures:

- Aid in characterizing the perceived tinnitus and can be used as a reference point (useful for monitoring changes in tinnitus, especially during treatment).
- Help/support the clinician in determining an optimal route of treatment for a particular patient.
- Aid in the selection and fitting process for acoustic instrumentation and sound therapy.
- Form a critical component for establishing and implementing therapeutic masking for tinnitus.
- Contribute to our understanding of tinnitus including its origin and aetiology by allowing interindividual comparisons to be made, focusing on patients who experience different tinnitus frequencies, have hearing loss in addition to their tinnitus, or an altogether different comorbidity (Kim, Yakunina et al., 2017; Nageris et al., 2010; Switalski & Sanchez, 2019).

Methodologies of Tinnitus Pitch Matching

Test ear

The ear chosen for the test stimuli is important as it can influence the results of pitch matching and in turn the final tinnitus-matched frequency (Tyler, 2000). If the tone is presented to the same ear where the tinnitus is heard (i.e., ipsilaterally), then the tone could affect the tinnitus perception in some way. Alternatively, if it is presented in the ear opposite to that where the tinnitus is heard (i.e., contralaterally), there is a risk of binaural diplacusis occurring, giving rise to inaccurate pitch matching (Tyler, 2000). If the tester/investigator chooses to present the tone binaurally, the patient might experience confounding by both of these effects, in turn finding it hard to not only define their perceived tinnitus, but do so accurately and reliably from trial to trial.

A number of researchers suggest ipsilateral sound presentation, primarily to avoid any effects of binaural diplacusis. Though the majority of patients have bilateral tinnitus (Meikle & Taylor-Walsh, 1984), recommendations have been made to conduct monaural ipsilateral testing in each ear separately (if they are found to differ), making sure to perform at least seven replications, with the examiner noting down the test ear each time (Tyler & Conrad-Armes, 1983a; Vernon & Fenwick, 1984). Conversely, there are also those who stand in support of contralateral test tone presentation, maintaining that it is less confusing for patients during pitch-matching procedures to have the tone presented in the ear that is free from distracting sound sensations (Evered & Lawrenson, 1981; Sandlin & Olsson, 1999). In most cases it simply does not matter which ear the sound is presented to (Baguley, Andersson, et al., 2013; Vernon & Fenwick, 1984). The best procedure is to play a test tone to the patient separately in each ear and allow them to decide for themselves which ear they would like to have the tones presented (see Vernon and Fenwick, 1984). In the case that they feel more comfortable with the tones being presented to the contralateral ear, it is recommended that the examiner repeats the final pitch-match tone on the ipsilateral side to account for possible diplacusis-related complications and ensure that the tinnitus-matched frequency established in the contralateral ear also holds for the ipsilateral ear (Vernon and Fenwick, 1984). An alternative approach, advocated when there are hearing asymmetries, is to choose the better hearing ear; this is likely to have least disruption of tonotopicity, frequency resolution, and less complications related to cochlear recruitment.

Matching Method

Numerous methods of pitch matching have been developed and tested, with varying levels of success. These methods include, but are not limited to, the adjustment, limits, and adaptive methods (Tyler & Conrad-Armes, 1983a), 2-alternative forced-choice (2AFC) method (Vernon and Fenwick, 1984), binary-2AFC (Henry et al., 2001), forced-choice double-staircase (FCDS) technique (Penner & Bilger, 1992; Penner & Klafter, 1992), heptatonic scale (Ohsaki et al., 1990), subject-guided procedure (Henry, Flick, et al., 2004), and tinnitus likeness ratings (also known as tinnitus spectrum measurements) (Noreña et al., 2002; Roberts et al., 2006) (see Table 4). Tyler and Conrad-Armes (1983a) were among the first to investigate psycho-acoustic measures, developing three methods (adjustment, limits, and adaptive) and evaluating their ability to define the pitch and loudness of tinnitus for ten participants. The adaptive and limits methods share a similar protocol, while the method of adjustment differs primarily in that it is patient-guided; the patient “adjusts” the main frequency dial of a pulsed-tone oscillator to localize the frequency most representative of their tinnitus, before making further adjustments using a fine-control dial to more precisely define and finalize their tinnitus frequency (Tyler & Conrad-Armes, 1983a). Although the methods varied in their respective protocols, no significant differences were observed in either the group means or standard deviations for the pitch matches. Tyler and Conrad-Armes

(1983a) suggested that the adaptive and adjustment methods were superior for use in the clinical setting due to their ability to obtain single pitch matches within 1–2 min (compared with 4–5 min for the method of limits). A second recommendation was to conduct a minimum of seven pitch-match replicates for each patient to account for the large variability in a patient’s ability to accurately reproduce their tinnitus pitch (Tyler & Conrad-Armes, 1983a).

Table 4. Summary of methods used to characterize and evaluate tinnitus pitch.

Method	Studies using this method, number of subjects (n)	Protocol	Test ear (to which sound is presented to)	General comments
Conventional single-tone pitch matching (2AFC)	Vernon and Fenwick (1984), n = --	A tinnitus synthesizer is used to present two loudness-matched tones separated by 1000 Hz in an alternating manner, so that each tone is heard four to five times. The subject is instructed to choose which of the two tones is most like their tinnitus. This is done using a bracketing approach (in which the patient’s decision dictates the subsequent frequencies presented) until the frequency of the tinnitus has been established. Once the tinnitus frequency has been defined, it is verified in the ipsilateral ear to avoid binaural diplacusis.	Ipsilateral and contralateral (determined by patient preference)	N/A
	Ohsaki et al. (1990), n = 55		Not disclosed	Reproducibility of pitch matching is not as good as for the heptachord method
Binary-2AFC	Henry et al. (2001), n = 20	The 2AFC procedure is followed, however binary bracketing is applied, narrowing the testing frequencies down until tinnitus frequency is reached. First, the subject is presented with two frequencies, and is instructed to decide which is closer in pitch to their tinnitus. This initial frequency choice results in binary bracketing, either to the lower or upper frequency range. Movement to new	Contralateral	Pitch matches could be obtained within 20-25 minutes, with response reliability being good for some subjects but not others
	Henry, Flick, et al. (2004), n = 42		Contralateral	Excellent response reliability for about half of the subjects. Defining the range of

		frequencies progresses in octave steps, and the computer further brackets the pitch match to within an octave. Following this, matches are made in $\frac{1}{3}$ octave steps.		pitch matches might be more appropriate than identifying single pitch matches
Recursive 2-interval forced choice (RIFT)	Korth et al. (2020), n = 117	The RIFT procedure is similar to the 2AFC. 17 tones are presented in the range from 1 to 16 kHz in ¼ octave steps. First, the level of the tones is manually adjusted by the participant using a scrolling volume slider until the tinnitus and presented tone is matched in loudness. Following this, the stimulus frequency is then limited to the highest frequency that is audible to the participant. Two tone pairs (2 octaves apart) are presented and the participant is instructed to indicate the frequency most representative of their tinnitus. Based on their decision, further tone pairs are presented, reducing the octave step each time until a decision on the smallest step of a twelfth octave is reached and one final frequency is chosen. If the subject's choices are contradictory twice in a row, the test is cancelled and restarted.	Ipsilateral (unilateral tinnitus) OR Ear with more dominant tinnitus perception/less average hearing loss (bilateral tinnitus)	Reliable estimations of tinnitus pitch can be obtained as long as initial and redundant sessions, and participants with poor pitch match performance are excluded
Tinnitus likeness ratings	Noreña et al. (2002), n = 10	A pure tone with a pseudo-randomly selected frequency is presented and subjects are asked to match the intensity of the tone to the loudness of their tinnitus. If the subject indicates that the pitch of the pure tone corresponds to a component of their tinnitus sensation, they are to rate on a ten-point scale the degree to which this pitch contributes to their overall tinnitus percept.	Ipsilateral	In most cases, the 'internal tinnitus spectra' demonstrated a broad peak sitting within the range of hearing loss
	Roberts et al. (2006), n = 32	Tones are chosen from a set of three stimuli depending on the subjects tinnitus (tonal, ringing, or hissing). Subjects are then instructed to rate the pitch of each presented sound for similarity to their perceived tinnitus using a Borg CR100 scale (0 = not at all similar, 30 = not very similar, 50 = somewhat similar, 70 = very similar, and 100 = identical).	Not disclosed	Results are in agreement with Noreña et al. (2002), however it is important to consider the effect hearing loss has on the perception of sounds used to measure the tinnitus spectrum
	Hoare, Edmondson-Jones, Gander, et al. (2014),	11 tonal or narrowband sound clips are presented to subjects, with each sound being played three times in a random order. Subjects are asked to rate the similarity of the pitch of	Not disclosed	Tinnitus likeness rating across a range of frequencies is highly variable and unpredictable

	n = 28	each of the sounds presented to their tinnitus on an 100-point scale.		
FCDS	Penner and Bilger (1992), n = 11	In the double-staircase, the experimenter selects two starting points for two sequences of trials; one with the comparison stimuli clearly above the patients tinnitus pitch, and the other clearly below it. In the forced-choice procedure, the experimenter presents the tinnitus ("standard") stimulus, accompanied by a 750 msec flash of light, followed by an external comparison tone also marked with a flash of light. The subject is instructed to choose which of the two stimuli is "lower" or "higher" in frequency (depending on the experimenter's instruction). 100-Hz step sizes are employed for obtaining pitch matches.	Ipsilateral	Within-session variability of pitch-matching to the tinnitus pitch for the FCDS procedure is consistent and greater than for a method of adjustment (bracketing technique similar to the Method of Adaptation – not to be confused with the Adjustment method developed by Tyler and Conrad-Armes (1983))
	Penner and Klafter (1992), n = 7	The FCDS procedure is followed, but step sizes are reduced to 0.2%.	Ipsilateral OR Ear in which tinnitus is louder	The step sizes used in the original FCDS procedure (Penner & Bilger, 1992) were substantially larger than the frequency difference limen for normal-hearing subjects. Following step size reduction, the frequency difference limen for tinnitus matches is comparable to that obtained for external stimuli
Subject-guided	Henry, Flick, et al. (2004), n = 42	Loudness-matched test frequency is presented at random (from a selection of 17 frequencies) using an automated computer system. The subject then has the option to respond and alter the tone so that it becomes "higher", "much higher", "lower", or "much lower" in frequency until a tone is presented that is equal in pitch to the subjects tinnitus.	Contralateral	Excellent response reliability for about half of the subjects. Defining the range of pitch matches might be more appropriate than identifying single pitch matches

Heptatonic scale	Ohsaki et al. (1990), n = 55	A heptachord generator is used to present 56 tones in eight octaves. Presentation of the tones is done in ascending runs. A tone is considered representative of the patients tinnitus frequency when it has been obtained twice continuously in increasing runs.	Not disclosed	The heptachord method is more reliable and accurate than the conventional ‘one-octave-interval’ method, with coincidence ratios as high as 100%, 94.8%, and 88.9% respectively for intra-daily variation, intra-weekly variation, and eight consecutive measurements in one test
Method of limits	Tyler and Conrad-Armes (1983a), n = 10	The subject is instructed to state whether their tinnitus is “higher” or “lower” in pitch than the tone presented by the tester. The tester then presents a sequence of pulsed tones and allows the subject to make a decision. The tones are presented in ascending and descending runs, with an ascending run always being accompanied by a descending run (order of presentation is randomised). The last ‘higher’ and ‘lower’ responses (in the respective ascending and descending runs) are averaged to give the overall tinnitus pitch.	Ipsilateral	No significant differences were found in the group means or standard deviations for the tinnitus frequencies obtained using these three methods. For clinical use, it is recommended that the Adaptive or Adjustment method be used due to their time efficiency (only 1-2 minutes per pitch match). Ipsilateral presentation is recommended to avoid binaural diplacusis. Seven to nine pitch matches are recommended per subject due to large variability in pitch reproducibility
Adaptive method		The subject is instructed as per the ‘Method of limits’, with the tester presenting a series of pulsed tones and allowing the subject to make a ‘higher’ or ‘lower’ decision. The first stage includes locating the subjects tinnitus pitch to within a 1-octave band. In the second stage, tones are presented whose frequencies are within the 1-octave range determined in stage 1, with the final pitch being located to within a $\frac{1}{6}$-octave range.		
Adjustment method		The subject is instructed to adjust the pitch of the pulsing tone using a dial on the pitch-matching apparatus, first making wide sweeps with the dial and then gradually narrowing down to the pitch most representative of their tinnitus.		

The 2AFC procedure has received the most attention and gained wide acceptance as the conventional method for tinnitus pitch assessment due to its simplicity for patients and relatively short completion time (Kim, Yakunina et al., 2017). Development of the 2AFC method began as an attempt by Vernon and Fenwick (1984) to provide a standardized measure for tinnitus characterization. Over the years, progressive advances in technology have enabled 2AFC to be applied using different platforms: manual and computer-automated (Henry, Flick, et al., 2004), web-based (Mahboubi, Ziai, Brunworth, et al., 2012), through portable media players (Wunderlich et al., 2015), and iPods (Korth et al., 2020). Korth et al. (2020) used an adaptation of the 2AFC, known as the recursive 2-interval forced-choice test (RIFT), in an iPod-based automated tinnitus pitch-matching procedure. The study found that recursive matching resulted in reliable tinnitus pitch matching in patients with tonal tinnitus once initial and redundant sessions, and patients with poor pitch-matching performance were excluded (Korth et al., 2020).

Penner and Bilger (1992) explored the FCDS procedure (Jesteadt, 1980) as a psychoacoustic measure for tinnitus pitch and loudness, believing it had a number of advantages over measures based on bracketing and sequential presentation of tones. For one, methods which present matching tones in a monotonic series (such as those in which the experimenter adjusts the frequency in equal steps according to a subject's request to raise or lower it) are subject to response bias as a result of sequential effects. FCDS avoids response bias by not presenting successive tones in a predictable sequence, instead forcing the subject to judge each stimulus independent to the judgment of previous stimuli as the stimuli bear no relation to each other (Penner and Bilger, 1992). Further, the FCDS enables the subject to classify comparison stimuli with respect to their tinnitus rather than simply matching pure tones to the percept, as is the protocol applied in most pitch (and loudness) matching measures. Evaluating the pitch-match reliability of the FCDS relative to that obtained using a "method of adjustment[2]" the investigators observed a lower within-session variability with the FCDS procedure. Although the method has been reported as being capable of producing reliable pitch matches, it is rarely used in the clinical setting due to issues regarding comprehension of the testing concept and the lengthy completion time involved (Henry et al., 2013; Kim, Yakunina et al., 2017).

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[2] The "method of adjustment" as referred to by Penner and Bilger (1992) is simply a bracketing method in which the subject attempts to match their tinnitus to tones presented by the experimenter (for more detailed protocol, see Penner and Bilger (1992)). It is not to be confused with Tyler and Conrad-Armes (1984) "method of adjustment."

Most methods available today share a similar basis for pitch matching (namely presenting a series of tones at varying frequencies and adjusting them according to the subject's response until the tinnitus frequency is achieved). They differ only in the finer details such as the instructions given to the subject, sequence in which the tones are presented, or perhaps the frequency differences of test tones. Novel approaches have been trialed including matching using the standard musical "do-re-mi" scale (Ohsaki et al., 1990). The usefulness of this method is limited by the nature of musical tonality which begins to break down above 4,000 Hz. As will be discussed shortly, many patients perceive their tinnitus pitch above this frequency; hence, it becomes difficult to apply methods using music intervals for testing and pitch matching.

Perhaps the most complete pitch-matching procedures are the tinnitus likeness rating methods developed by Noreña et al. (2002) and Roberts et al. (2006). Instead of participants' choosing between test tones in an "all-or-nothing" manner, they were instructed to rate each presented tone for the degree to which the particular tone contributed to the overall tinnitus sensation. What is generated as a result is an "internal tinnitus spectrum" which shows the frequency components of an individual's tinnitus, highlighting dominant frequencies. Roberts et al. (2006) used tinnitus likeness software to evaluate psychoacoustic properties of tinnitus and residual inhibition in 32 tinnitus patients. After identifying the quality of sound of their tinnitus ("tonal," "ringing," or "hissing"), the patients were instructed to match the loudness of 11 "tonal," "ringing," or "hissing" sounds depending on their initial selection (each with increasing center frequency) to the loudness of their tinnitus. Once the loudness was established, the patients were then replayed with each of the 11 sounds at this level, rating the sounds based on their likeness (similarity) to the tinnitus, in turn generating a spectrum of tinnitus frequency components. The most prominent component was replayed to the patients, and they were asked to rate the sound based on its similarity to the tinnitus percept using a Borg CR100 scale approach where 0 = "not at all," 30 = "not very similar," 50 = "somewhat similar," 70 = "very similar," and 100 = "identical." The study revealed a tendency for the tinnitus spectra to span the region of hearing loss in agreement with the results of Noreña et al. (2002) who also found that the majority of their participants displayed a broad peak sitting within the range of hearing loss. Likeness ratings offer more complete account of participants' tinnitus, but the method is time-consuming, limiting its clinical applicability compared to the 2AFC method.

Tinnitus Pitch and Hearing Loss

It is not uncommon for patients to complain about difficulties in hearing as a result of their tinnitus; however, it appears that this is primarily a consequence of an underlying hearing loss rather than the tinnitus itself (Ratnayake et al., 2009). Auditory processing mechanisms do appear to be disrupted by tinnitus in a pitch specific manner; specifically, auditory streaming of tones is disrupted at tinnitus pitch (Durai et al., 2019). As demonstrated by the tinnitus likeness rating measurements, there is a clear relationship between tinnitus pitch and hearing loss. Individuals who suffer from tinnitus are highly likely to have some degree of hearing loss (Axelsson & Ringdahl, 1989; Henry, 2016; Josephson, 1931; Moore, 2010, 2012; Noreña et al., 2002; Ristovska et al., 2019; Roberts et al., 2008; Schechter & Henry, 2002; Vernon, 1977; Ward & Baumann, 2009; Wegel, 1931). While the exact pitch perceived varies from patient to patient, most patients tend to match their tinnitus to a high-frequency tone at or above 3,000 Hz (Meikle & Taylor-Walsh, 1984; Mitchell et al., 1984; Reed, 1960; Roeser & Price, 1980; Sandlin & Olsson, 1999; Stouffer & Tyler, 1990; Tyler, 2000; Vernon & Meikle, 2000). The high-frequency locus of tinnitus has, for some time, been thought to be linked to the idea that tinnitus is closely related to hearing loss, in particular, high-frequency hearing loss, in many cases due to noise induced trauma/exposure (Henry, 2016). Conducting the first large-scale tinnitus study, Reed (1960) found that in 38% of cases the tinnitus was pitch matched to a pure tone within the 3,000–5,000 Hz range; several subsequent studies have observed similar trends (Meikle and Taylor-Walsh, 1984; Roeser and Price, 1980; Sandlin and Olsson, 1999; Stouffer and Tyler, 1990; Tyler, 2000; Vernon & Meikle, 2000). Mitchell et al. (1984) confirmed that most patients suffer from a high-pitch tinnitus, however noted a broader range of reported pitch-match frequencies (1,000–8,000 Hz). The high-frequency nature of tinnitus is not only evident from the results of psychoacoustic testing, but has also been demonstrated by patient complaints (Stouffer and Tyler, 1990; Tyler, 2000).

Although the pitch of tinnitus commonly falls in the high-frequency range, this is not always the case. A study by Pan et al. (2009) identified various trends in pitch matching among 195 tinnitus patients; those who described a tone-like tinnitus reported a higher pitch (mean = 5,385 Hz) relative to those experiencing a noise-like sensation (mean = 3,266 Hz). Further, patients with a flat audiogram demonstrated a higher chance of describing a tinnitus that was noise-like, unilateral, and had a pitch-match frequency < 2,000 Hz. In addition, those with a notched audiogram often identified a pitch ≤8,000 Hz, while those with normal hearing up to 8,000 Hz often matched a pitch ≥8,000 Hz (Pan et al., 2009).

Alongside the fairly universal acceptance of a general relationship between the frequency of hearing loss and tinnitus pitch, specific theories relating the degree of hearing loss to tinnitus have been proposed to explain tonal pitch matches. The two most widely recognized theories are the “edge frequency” and “region of maximal hearing loss” theories. The edge frequency theory posits that the pitch of a patient’s tinnitus corresponds to the “edge frequency” of the audiogram; more specifically, the frequency at which hearing loss transitions from normal to abnormal hearing relatively abruptly (Josephson, 1931; Moore, 2010, 2014). Moore (2010) found that patients’ final pitch matches were generally at the lower end of the spectrum (1,630 Hz) with a strong correlation ($r = 0.94$) between the matches and edge frequency of the audiogram. The edge theory is concordant with the tonotopic reorganization model of tinnitus; when a certain frequency region is affected as a result of hearing loss, there is a lack of inhibition from neurons that were once tuned to that particular region. This then leads to a downstream release of lateral inhibition and resultant increase in neural activity in adjacent regions where there is less or no hearing loss; the consequence is tinnitus with a dominant frequency that corresponds to the audiometric edge (Moore, 2010).

Several psychoacoustic studies have failed to find strong support for the edge frequency theory (Pan et al., 2009; Ristovska et al., 2019; Sereda et al., 2011). Ristovska et al. (2019) reported a clear relationship between tinnitus pitch and hearing loss, however found no relationship between tinnitus pitch and the edge frequency of the audiogram. The tinnitus pitch corresponded to the edge frequency in only 16.5% of patients; comparatively, the tinnitus frequency corresponded to the frequency range of hearing loss and greatest region of hearing loss in 70.8% and 37.3% of cases, respectively. Pan et al. (2009) and Sereda et al. (2011) found a subset of participants in which the tinnitus pitch was associated with the audiometric edge. Sereda et al. (2011) reported that these participants exhibited a narrow tinnitus bandwidth. It is possible that a relationship between tinnitus pitch and the audiogram edge exists, but perhaps only in certain subgroups, possibly alluding to different underlying mechanisms involved (Pan et al., 2009).

A number of researchers believe that tinnitus pitch corresponds to a frequency range where the hearing loss was greatest, giving rise to the “region of maximal hearing loss” theory (Moore, 2012; Sandlin & Olsson, 1999). This theory is supported by the homeostatic plasticity hypothesis which posits that tinnitus is the result of homeostatic mechanisms acting to compensate for the reduced sensory input that occurs in hearing loss by reducing inhibitory and/or increasing facilitatory mechanisms (Schecklmann et al., 2012). Changes in neuronal activity take place in the frequency ranges where there is sensory deprivation, in turn leading to ongoing increased neuronal activity and/or synchrony in the affected central auditory pathways. This increase in central gain and resultant neuronal hyperactivity are thought to represent a neural correlate of tinnitus, with the frequency of tinnitus corresponding to the frequency of hearing loss (Noreña, 2011; Schaette & Kempter, 2009; Schecklmann et al., 2012).

Patients with hearing loss generally face challenges when performing tinnitus pitch matches as their ability to hear and discriminate between the matching tones presented is limited to frequency regions of normal hearing (Ward & Baumann, 2009). Considering the fact that the tinnitus frequency is often found in regions of hearing loss, it is important to accommodate for this by presenting the matching sound at a level that is safe but audible to the patient (Mitchell et al., 1984). It has also been noted that patients with significant hearing loss can experience difficulties in pitch matching due to the testing tone not having a clear pitch. This is often the case when the frequency of the sound used for pitch matching leads to maximum basilar membrane vibration in the region of the cochlea where the number of functioning inner hair cells and/or neurons is scarce or even nonexistent; this is known as the cochlear dead region (Moore, 2014). Even with training, these patients are still limited in their ability to make appropriate pitch matches (Henry et al., 2001).

Although there is a clear link between tinnitus pitch and hearing loss, it does not explain the tinnitus experienced by individuals clear of any hearing difficulties. Recent findings have demonstrated that even individuals with a normal/healthy audiogram are likely to have some small degree of hearing injury (“hidden hearing loss”) which might in turn give rise to the tinnitus (Plack et al., 2014).

Reliability of Pitch-Matching Measures

Pitch-matching measures are complicated by the fact that pitch matching reliability varies widely across patients. As such, it becomes difficult to discern whether the reliability of a measure has been compromised by the method itself or is simply a reflection of the heterogenous nature of the patient’s tinnitus. The reliability of pitch matching is also complicated due to the oversimplification of a patient’s tinnitus through the use of single tones during psychoacoustic testing. Even in cases where tinnitus is described as “tonal,” it is often comprised of a spectrum of frequencies, in turn intrinsically limiting pitch-match reliability (Hébert, 2018). Hébert (2018) investigated individual test–retest reliability of the 2AFC and tinnitus likeness rating methods in 31 patients over a one-month period. The study reported a superior test–retest reliability for the tinnitus likeness rating relative to the 2AFC protocol, with at least one of three dominant tinnitus frequencies being reproducibly identified at the second session by the majority of participants (>80%), and two dominant frequencies being reproducibly identified by half of the patients. Only 13% of patients could reproducibly identify as many as three dominant tinnitus frequencies; this is similar to the proportion of patients in whom the final tinnitus frequency could be determined at the same ear using the 2AFC method (Hébert, 2018). Though the tinnitus likeness rating protocol has been praised for its ability to offer a more complete view of an individual's tinnitus, it is not immune to problems and complications; in particular relating to its methodology. Unlike in the case of conventional methods where the complexity of tinnitus can be severely underestimated by use of single-tone pitch matches, tinnitus likeness ratings risk the tinnitus sensation being described as having a broad spectral pattern, when in fact it may be narrow (Noreña et al., 2002). This could occur due to patient laxity or perhaps misunderstanding of the protocol. For instance, a broad spectral pattern would arise if a patient is not strict enough in their likeness-rating criteria, in turn simply rating the overall similarity between the presented tone and their tinnitus sensation rather than the degree to which the presented tone contributed to their overall tinnitus percept. Neff et al. (2019) found that the 2AFC and tinnitus likeness rating (as well as the adjustment method) all had good reliability, with participants being less satisfied with the 2AFC method, and the likeness rating protocol being more time-consuming.

A source of pitch-match inaccuracy and complication comes from octave confusion, where patients find it difficult to differentiate frequencies one octave apart from each other, considering them to be identical (Graham & Newby, 1962; Kim, Yakunina et al., 2017). Though the effect is widely recognized and has been identified in a number of studies (Graham & Newby, 1962; Kim, Yakunina et al., 2017; Ristovska et al., 2019), there are researchers who have failed to observe octave confusion among patients (Penner, 1983; Tyler & Conrad-Armes, 1983a) or have identified the effect in only a small subset of patients (Ristovska et al., 2019). Even so, testing for octave confusion has been recommended as an integral part of a standard tinnitus evaluation battery and should be performed to ensure patients are generating reliable matches true to their tinnitus pitch (Evered & Lawrenson, 1981). The protocol involves presenting the matching sound one octave above and below the initial match and allowing the patient to determine which – if either – of the tones appears to be a better match to their tinnitus relative to the initial frequency chosen (Hazell & Wood, 1981). In addition to test reliability, the heterogeneous nature of tinnitus – and its perceived pitch – must also be considered. Conducting an "in-depth" tinnitus characterization study on 528 patients, Stouffer and Tyler (1990) noted approximately 36% of patients reporting regular fluctuation in pitch of their tinnitus varying from day to day (Stouffer & Tyler, 1990). It was not uncommon for patients to report noticing a change in their tinnitus since its onset; while 76% reported they experienced no change, 19% of patients found their tinnitus pitch increased, and 5% observed a decrease in pitch (Stouffer & Tyler, 1990). The majority of patients (73%) reported that their tinnitus has always been constant, while those who indicated that their tinnitus changed to a completely different sound noted that this change either occurred suddenly (16%) or gradually (11%) (Stouffer & Tyler, 1990).

The 2AFC method is widely used due to its easy-to-follow instructions and efficient time to complete; however, its pitch-matching reliability has been questioned (Hébert, 2018; Neff et al., 2019). The FCDS procedure has been found to demonstrate a good degree of pitch-matching reliability as have the likeness tests; however, these methods are time-consuming; as such, they are rarely implemented in the clinical setting. Those conducting psychoacoustic evaluations should be mindful of the high level of pitch-matching variability across patients – whether it be due to daily fluctuations in tinnitus pitch, changes in pitch over time, or even difficulties in discerning an accurate and reflective pitch match – and consider the importance of obtaining several pitch-match replications (Tyler, 2000).

3.5. Psychoacoustic Measures: Loudness

The two most common methods of defining the loudness of tinnitus are loudness matching and loudness rating. Although it has been suggested that loudness ratings are the more useful measure, loudness matching appears to be the more widely used technique, with loudness being determined by having the patient adjust an external pure tone stimuli so that it is equal in loudness to their tinnitus (Henry, 2016; Moore, 2014; Tyler, 2000). Loudness rating is based on a more holistic approach, with ratings reflecting the impact of tinnitus rather than the perception itself (Henry, 2016). Most of the measures available for the assessment of tinnitus pitch have been developed in such a way that they can be implemented for the determination of tinnitus loudness, including the adaptive, limits, and adjustment methods (Tyler & Conrad-Armes, 1983a), 2AFC method (Vernon & Fenwick, 1984), and the FCDS protocol (Penner & Bilger, 1992; Penner & Klafter, 1992).

There appears to be a lack of correlation between loudness matching and loudness rating (Henry, 2016; Henry et al., 1999). This is likely due to the two methods assessing slightly different aspects of loudness perception. Psychoacoustic matching is primarily based on the sensory judgment of tinnitus loudness, while loudness rating also depends on emotional and cognitive factors, perhaps being more reflective of what the subject is experiencing and feeling (Adamchic et al., 2012). Incorporation of cognitive and behavioral aspects by both the psychoacoustic match and ratings may be required to achieve effective evaluation of tinnitus loudness. It is essential to validate a loudness measurement method that is accurate, reliable, and capable of detecting changes in tinnitus loudness. While tinnitus loudness matching typically demonstrates good reliability, with the great majority of loudness matches achieved between 0 and 20 dB SL (Goodwin & Johnson, 1980; Graham & Newby, 1962; Meikle & Taylor-Walsh, 1984; Ristovska et al., 2019; Roeser & Price, 1980; Sandlin & Olsson, 1999; Tyler & Conrad-Armes, 1983b; Vernon & Meikle, 2000), it is not immune to the effects of interindividual variability (Burns, 1984; Schechter & Henry, 2002). Still, it must be noted that the reliability of loudness matching procedures is far superior to that observed in pitch matching (Henry et al., 1999; Penner, 1983). Loudness ratings may be more easily influenced by factors such as annoyance or impact on quality of life than loudness matches (Henry, 2016; Manning, Grush, et al., 2019) but loudness matches are also not immune from psychological modifiers (Searchfield et al., 2012).

Tinnitus Loudness Matching and Choice of Units

There are a number of ways in which the magnitude of the matching tone can be specified, but there are questions as to their test–retest reliability (Hall et al., 2017). The simplest way of expressing tinnitus loudness is using intensity matches in either dB hearing level (HL) or dB sound pressure level (SPL); these reflect the dial values of equipment. The most common method is to use dB sensation level (SL), the difference between the loudness match and threshold to the same sound. The dB HL or dB SPL method is not independent of the listener's hearing threshold, so a person with hearing loss will have a higher dB HL match than a person with normal hearing, even if the perceived loudness were the same. The test–

retest reliability of the SL measure may be less than SPL and HL methods, as it is the difference between the loudness match (dB HL on an audiometer) and auditory threshold (dB HL) meaning two measurements are required, increasing the chance of error. None of the intensity matches, whether it be dB HL, dB SPL, or dB SL, may truly reflect tinnitus loudness (Stevens & Davis, 1938). Individuals can report different loudness to the same physical intensity of sounds, and loudness perception is influenced by context, memory, and personality (Searchfield et al., 2012).

In addition to the measure not representing loudness, Tyler and Conrad-Armes (1983b) found that the dB SL of a tinnitus loudness-matched tone depended on the pure-tone frequency used during matching. More specifically, tinnitus loudness matches are generally greater in frequency regions of normal hearing sensitivity, whereas loudness matches in frequency regions where hearing thresholds are elevated are often matched to only a few decibels above threshold (generally between 0 and 20 dB SL) (Goodwin & Johnson, 1980; Graham & Newby, 1962; Meikle & Taylor-Walsh, 1984; Penner, 1986; Reed, 1960; Ristovska et al., 2019; Roeser & Price, 1980; Sandlin & Olsson, 1999; Tyler & Conrad-Armes, 1983b; Vernon & Meikle, 2000). This may be explained by loudness recruitment (Tyler & Conrad-Armes, 1983b). In an attempt to resolve this issue and offer a means of better understanding the loudness of tinnitus, Tyler and Conrad-Armes (1983b) converted dB SL measures into tinnitus loudness in sones, a conventional psychoacoustic unit of loudness. One sone is the loudness of a 1,000 Hz tone with a level of 40 dB SPL (Moore, 2014). Tyler and Conrad-Armes (1983b) believed that there were several advantages to using the sone as a measure of tinnitus loudness: (1) it has diagnostic significance and can help identify those who complain of a very loud tinnitus but match their loudness to a soft tone, (2) presentation at the same sone for another listener (e.g. in demonstrating the percept to family and supplement counseling) should be the equivalent loudness, (3) it allows for comparisons to be made across patients, (4) it can be used as a quantitative measure to monitor changes in tinnitus with treatment, and (5) it offers a more meaningful psychoacoustic measure of the discomfort and annoyance that results from tinnitus (Tyler & Conrad-Armes, 1983b).

Although Tyler and Conrad-Armes (1983b) suggested that using the sone was a more appropriate way of measuring tinnitus loudness, using the measure in the clinical setting presents two challenges. First, the sone scale is unfamiliar to many clinicians and as such makes it difficult for them to conceptualize the result (Matsuhira et al., 1992). This in turn presents a challenge with respect to not only validating and making sense of a patient's tinnitus percept, but providing the patient (and their family) with effective counseling. Secondly, the sone is based on loudness functions that represent complete loudness recruitment (see Tinnitus loudness, recruitment, and hyperacusis section); as such, the measure tends to result in the overestimation of tinnitus loudness as it assumes complete recruitment, which is not always the case in tinnitus patients (Matsuhira et al., 1992). In addition, loudness growth formulas are likely too general for application to specific individuals, in turn suggesting individualized functions need to be established at each loudness matching frequency (Henry & Meikle, 2000).

Highlighting a number of these limitations, Matsuhira et al. (1992) proposed a method to account and correct for the effect of recruitment in tinnitus loudness matches using information obtained from standard clinical evaluation. The investigators devised an "average loudness function" which converted measures in dB SL into an estimate of the effective loudness level and corrected for abnormally rapid loudness growth by adjusting the mean loudness function for each participant using data generated by the individual (Henry & Meikle, 2000; Matsuhira et al., 1992).

The measure was essentially the same as the phon scale, an alternative measure of loudness level, except for the difference in reference level (Matsuhira et al., 1992). However, the results of the study (Matsuhira et al., 1992) were highly variable, probably due to the large inter-subject variability in loudness recruitment between participants, even with the same level of hearing loss. The method has not been widely adopted.

Another method for quantifying tinnitus loudness is to use the personal loudness unit (PLU) developed by Hinchcliffe and Chambers (1983). They proposed calculating individualized loudness functions for each tinnitus patient and specifying the loudness match in terms of this loudness function. Much like the sone and phon measures, the PLU uses a loudness function at 1,000 Hz as the reference level; however, instead of using dB SL as unity, it employs the "most comfortable loudness level." Though the authors promoted the use of this method in the clinic, it has not been widely used likely due to clinical time constraints and difficulty in comprehension (Henry & Meikle, 2000).

In summary, the measurement of dB SL has become the de facto unit for tinnitus loudness matching. It does have flaws, but its limitations should be considered in light of tinnitus being a complex concept. The need for precision in the measurement of loudness should also be balanced against time and benefits. At present: a precise loudness match is unnecessary for demonstrating the experience of tinnitus to a third party (i.e. family member/partner); loudness is not diagnostic or prognostic, and no treatment currently requires the measurement to be effective. As new treatments are developed precision of loudness match may become more important.

Tinnitus Loudness, Recruitment, and Hyperacusis

Tinnitus loudness tends to be matched to a relatively low intensity tone, often only a few decibels above threshold. The majority of matches have been reported to be within the 0–20 dB SL range (Goodwin & Johnson, 1980; Graham & Newby, 1962; Meikle & Taylor-Walsh, 1984; Reed, 1960; Ristovska et al., 2019; Roeser & Price, 1980; Sandlin & Olsson, 1999; Tyler & Conrad-Armes, 1983b, 1983b; Vernon & Meikle, 2000). Meikle and Taylor-Walsh (1984) evaluated the tinnitus percept of over 1,800 patients, reporting extensive fluctuations in loudness in 24% of cases (17% reported fluctuations from time to time, 55% reported a constant tinnitus, and 4% were not able to answer the question). Similar analyses were conducted by Stouffer and Tyler (1990) in 528 participants; loudness fluctuated in 56% of the tinnitus patients, changing either suddenly (25%) or gradually (31%). Further, half of the patients reported that the loudness of their tinnitus varied daily, while the remaining half did not notice daily fluctuation. Changes in tinnitus loudness since onset were also observed, with 33% of patients noticing an increase in loudness and 7% experiencing a decrease (there was no change for 60%).

Fowler, a pioneer in loudness measurement, was the first to note a paradoxical relationship between loudness matches as measured using psychoacoustic methods and subjective patient report (Fowler, 1944). He found that although tinnitus loudness was matched only a few dB above the threshold of hearing, the subjectively perceived loudness of tinnitus has often been described by patients as being intolerable (Fowler, 1944). Fowler (1944) suggested clinicians use the loudness matched tinnitus as a “factual foundation” for counseling patients, demonstrating that their perceived tinnitus is in fact a very soft sound. Fowler did not consider loudness recruitment, which has since been identified as a significant contributor to low-level loudness matches (Goodwin & Johnson, 1980; Henry et al., 1999; Tyler & Conrad-Armes, 1983b). Loudness recruitment is a phenomenon associated with hearing loss, in which there is disproportionately rapid loudness growth following increases in sound intensity (Goodwin & Johnson, 1980; Penner, 1986; Raj-Koziak et al., 2019; Tyler & Baker, 1983). In turn what is found is that the growth of loudness for an external tone is more rapid when matches are made at the tinnitus frequency versus at frequencies outside of the tinnitus region (Eggermont & Roberts, 2004; Mitchell et al., 1993; Penner, 1986). As such, it comes as no surprise that large differences have been reported between loudness matches obtained at the tinnitus frequency, and at frequencies very different from the tinnitus pitch (Goodwin & Johnson, 1980; Mitchell et al., 1993; Tyler & Conrad-Armes, 1983b). Specifically, recruitment results in tinnitus being matched to a tone at a lower sensation level in regions affected by hearing loss (often the tinnitus frequency) than in regions of normal hearing (Penner, 1986; Vernon & Fenwick, 1984). In an attempt to avoid recruitment and better represent true tinnitus loudness, Vernon and Fenwick (1984) suggested routinely conducting loudness matches both at the tinnitus frequency and at a second frequency distinct from tinnitus in the normal hearing portion of the patient's audiogram. However, a number of researchers have noted that even when this method is applied, mean dB SL values are still too low to correspond to patient complaints (Henry & Meikle, 1996; Jakes et al., 1986). A study by Hulshof (1986) considered the effects of recruitment by evaluating and comparing tinnitus loudness in those who are affected by the phenomenon versus those who are not (at least in one ear). The results demonstrated that although loudness recruitment has an effect on the measurement of tinnitus loudness, its effects are very small. Similarly, Henry and Meikle (1996) conducted measures of loudness growth at both reference and tinnitus frequencies, finding that the recruitment phenomenon is only responsible for 25% of the variability in loudness matching. The source of the remaining 75% of that variability remains unsolved.

Tinnitus is also associated with hyperacusis, a reduced tolerance to everyday sounds that cause significant discomfort, distress, and even pain (Baguley, 2003; Moore, 2014). It has been reported that approximately 85% of those with hyperacusis also suffer from tinnitus (Anari et al., 1999; Sheldrake et al., 2015). Often in cases where tinnitus is accompanied by hyperacusis, loudness discomfort measures are performed as part of the test battery. As in the case of psychoacoustic tinnitus measures, these testing protocols for hyperacusis evaluation vary and are not standardized (Goldstein & Shulman, 1996). Loudness discomfort levels (LDL) are most frequently used to assess hyperacusis, defining the intensity level at which a sound is reported as being uncomfortable. Patients with hyperacusis will have lower LDLs than normal due to increased sensitivity to sound (Pienkowski et al., 2014). Generally, LDLs of 95 dB or greater are considered normal, whereas LDLs between 80 and 90 dB reflect mild hyperacusis, those between 65 and 75 dB imply moderate hyperacusis, and below 60 dB signify severe hyperacusis (Goldstein & Shulman, 1996). More work is required to establish universally agreed upon frequencies for assessment and number of repetitions per judgment, as well as to determine norms for the range of LDLs for those with specific degrees and types of hearing loss (Goldstein & Shulman, 1996; Pienkowski et al., 2014).

Tinnitus Loudness: Annoyance and Severity

A frequent complaint by tinnitus patients is the annoyance and distress experienced as a result of the perceived loudness of the tinnitus (Hallam et al., 1988). Several researchers have failed to identify a significant relationship between tinnitus loudness and annoyance, proposing that loudness is not a significant contributor to the perceived distress caused by tinnitus (Andersson, 2003; Rosito et al., 2013; Sandlin & Olsson, 1999). Andersson (2003) noted the lack of a relationship between loudness in dB SL and tinnitus annoyance, but reported a correlation when the loudness was expressed in dB HL, proposing that the degree of hearing loss was an important factor to consider when evaluating the impact of loudness on the perceived tinnitus distress. Meikle and Taylor-Walsh (1984) also reported that tinnitus severity was not correlated with loudness in dB SL, instead finding that loudness judgments are influenced by emotional factors. Loudness ratings, which reflect tinnitus impact (reactions) rather than actual loudness (percept), are found to significantly correlate with the severity of annoyance and distress reported by the patient (Henry, 2016; Hiller & Goebel, 2006; Schechter & Henry, 2002; Stouffer & Tyler, 1990; Tyler, 2000; Ward & Baumann, 2009). Factors other than loudness determine the perceived annoyance and in turn severity of tinnitus, including the duration since tinnitus onset (habituation factors) and the psychological state of the patient (Tyler, 2000). Although tinnitus perceived at a greater loudness is generally more likely to be annoying, it does not necessarily mean that a softer tinnitus is any less severe of an issue for certain patients; in other words, it is often the case that the perceived intensity of tinnitus does not dictate how a patient reacts to their tinnitus and in turn how distressing they find it (Folmer et al., 1999; Tyler, 2000). Ward and Baumann (2009) aimed to clarify the relationship between loudness and perceived distress using annoyance caused by aircraft noise near airports as an example. What is apparent is that although the relationship between aggregated loudness of flyovers and community annoyance is generally stable, there still remains a large amount of variability after the day-night noise level is accounted for (Ward & Baumann, 2009). A subset of this variability is the result of differences in annoyance thresholds, which are also influenced by a number of variables such as fear of crashes and political interactions with airports; however, there are other unknown factors that are likely community-specific, as well as hypersensitive people who get annoyed by noises that are negligible to most people (Ward & Baumann, 2009). As such, it appears that though loudness might influence tinnitus annoyance and distress, it is likely to be one of many factors defining overall tinnitus severity. For example, a low-level tinnitus might not be bothersome for one individual, but for another presenting with hyperacusis it might be highly disruptive (Hiller & Goebel, 2006). The incorporation of cognitive and behavioral aspects (such as memory, attention, context, and personality) may provide a more meaningful understanding of a patient's tinnitus (Hiller & Goebel, 2006; Searchfield et al., 2012; Welch & Dawes, 2008).

Tinnitus Loudness, Magnitude, and the Adaptation Level Theory

Some of the variability in loudness matching could potentially be ascribed to auditory context, attention, and individual psychology (e.g., personality, memories, emotional state) (Searchfield et al. 2012). The adaptation level theory (ALT) of tinnitus (Searchfield et al. 2012) is founded in a psychoacoustical model proposing that stimuli do not act as singular entities, but instead interact with and influence each other (Helson, 1964). In the context of tinnitus, it is proposed that the perceived tinnitus intensity is governed by several factors, not the least of which is the personality of the patient (Searchfield et al. 2012). The attitudes, ideals, experiences, learning, interpersonal relations, and intellectual and emotional behavior of an individual shape an individual's "frame of reference," which in turn dictates their response to stimuli. This is supported by findings suggesting a patient's response on a visual analogue scale (VAS) is correlated with the extent to which the individual is impacted by their tinnitus (Zenner et al., 2005). Helson (1964) defined the adaptation level as the weighted product of focal, background, and residual stimuli, using a simple mathematical equation to demonstrate the ALT:

$$A = \overline{X}^{p} B^{q} R^{r}$$

where tinnitus audibility in the environment is the combined result of tinnitus magnitude (X), background sound (e.g. sound therapy, B), and residual factors (R) such as personality, as influenced by weighting factors related to attention and auditory scene analysis (ASA). By adopting this theory, Searchfield et al. (2012) hypothesize that the variability in loudness matching and individual patient's overall response to tinnitus may be attributable to their internal reference for tinnitus loudness and be determined by interactions among many affecting factors.

A straightforward example of the ALT is its use in the context of chronic pain. Patients who suffer from chronic pain (Boureau et al., 1991; Rollman, 1979) or have been severely injured in the past (Dar et al., 1995) have higher unpleasantness thresholds and find experimental pain less intense and more bearable than pain-free individuals. According to the ALT, chronic pain (as well as severe acute pain) can alter the internal anchor points for the subjective evaluation of pain; this in turn results in patients having a different adaptation level than a normal subject, which is demonstrated by the observed increase in pain threshold. Searchfield et al. (2012) considered the plausibility of this scenario in the context of tinnitus, using it to potentially explain the loudness match discrepancy. According to Searchfield et al. (2012), the experimental condition itself, as well as the introduction of a comparison sound (such as that used in loudness matching), can easily bias the adaptation level and in turn give rise to variability. Specifically, when a patient is asked to rate or describe the loudness of their tinnitus, they are often comparing their tinnitus to the quiet environment of the consultation room or research facility. However, when that same patient is instructed to perform tinnitus loudness matches using an external matching stimulus, they are no longer comparing loudness to the absence of sound, but rather to a new adaptation level which includes the test sound and the existing perceived tinnitus magnitude of tinnitus (Searchfield et al. 2012). In turn, it is the interaction between the stimulus (loudness matching sound) and the tinnitus itself which governs the overall magnitude of the tinnitus percept. Hence, adding the matching sound changes the internal anchor point for the subjective evaluation of tinnitus magnitude and results in tinnitus being matched to a tone at a level that is lower than expected (Searchfield et al. 2012). In addition to this interaction with the external matching stimulus, subjective loudness estimates vary from patient to patient as they are likely to have different concepts of tinnitus loudness relative to their own adaptation level (Mitchell et al., 1984). It is possible that ALT could offer a more holistic approach to understanding tinnitus. For example, it could:

- Help determine the relative contributions of psychoacoustic, emotional, and cognitive aspects to tinnitus.

- Clarify why patients perceive their tinnitus in a certain way – what factors actively contribute to the intolerability of their tinnitus, and how these factors might be influenced in an attempt to "shift" the response to tinnitus.
- Identify attributes or elements that are potential risk factors for perceiving tinnitus in a negative and distressing manner, which could aid in grouping of tinnitus patients.
- Help form predictions for the success of tinnitus treatment for a given patient.
- Help identify the optimal route of treatment for a given patient, in turn not only forming a more rounded treatment approach, but also one tailored at the individual level.

3.6. Confusion of Pitch and Loudness: The Circular Problem

One of the most common issues that surfaces when performing psychoacoustic tinnitus matching is the confusion between pitch and loudness. Patients often find it difficult to conduct pitch matches if the matching sound differs in loudness from the tinnitus sound to which it is being matched; the same applies in the case of loudness matching to a sound distinct in pitch from the tinnitus (Mitchell et al., 1984; Moore, 2014; Vernon & Fenwick, 1984). Consequentially, this leads to patients deciding against a tentative tinnitus frequency match on the basis of loudness differences, or confirming an inappropriate pitch match simply because the loudness was comparable to the tinnitus (Vernon & Meikle, 1981). This leads to the circular problem; in order to accurately measure pitch, the stimulus tone should be presented at the loudness of tinnitus, but in order to obtain an accurate measure of loudness, the tone should be presented at tinnitus pitch (Fowler, 1940; Vernon & Meikle, 1981). Further research disentangling pitch from loudness is needed.

3.7. The Minimum Masking Level

Tinnitus loudness and changes to it are often determined by the presence or absence of external auditory stimuli; for instance, tinnitus can be rather audible in quiet conditions, but less obvious in a noisy environment (Fowler, 1944). Masking involves using an external sound to reduce or even fully conceal the tinnitus and is performed with the aim of determining how the addition of external stimuli might affect tinnitus and its perception. Often considered as the most critical aspect of psychoacoustic testing, masking can aid clinicians in deciding whether or not a patient will be a good candidate for sound therapy (Switalski & Sanchez, 2019). It has been suggested that the lower the minimum level of broadband noise required to completely conceal a patient's tinnitus (known as the minimum masking level, MML), the more likely they are to benefit from masking therapy (Henry, 2016).

Tinnitus is maskable in the large majority of cases (Roeser & Price, 1980; Sandlin & Olsson, 1999; Vernon & Meikle, 2003), but tinnitus masking does not behave the same way as sound-on-sound masking does (Mitchell, 1983; Mitchell et al., 1993; Searchfield et al., 2016; Tyler & Conrad-Armes, 1984). There is a great degree of individual variability with respect to the frequency and sensation level (SL) required to mask tinnitus (Feldmann, 1971; Tyler & Conrad-Armes, 1984). A broadband sound cannot be masked by a pure tone, but a broadband tinnitus can be masked by a pure tone. Neither the pitch nor loudness of the tinnitus percept correlates with its maskability (Mitchell, 1983). These findings have led to the realization that the neural processes underpinning tinnitus masking differ greatly from those responsible for the masking of external auditory stimuli (Vernon & Meikle, 2000) (see Table 5).

Table 5. Differences between tinnitus and sound-on-sound conventional masking (Mitchell, 1983; Switalski & Sanchez, 2019; Tyler & Conrad-Armes, 1984; Vernon & Meikle, 2000)

	Sound-on-sound conventional masking	**Tinnitus masking**
Frequency	• It is difficult for a pure tone to mask a band of noise • There is an orderly frequency relationship: sounds that are higher in frequency than the masking sound are easier to mask than those below it	• Noise-like tinnitus can be masked by pure tones • Individual variability is high in terms of the frequency and intensity of sound required for effective masking of tinnitus
Critical band	• There is a "critical band" of frequencies surrounding the sound that is to be masked; frequencies within this band are effective maskers, while those outside are not	• There is no "critical band" for tinnitus masking – any frequency could be effective for a given patient
Beats	• In monoaural conventional masking, it is easy to generate the sensation of "beats" when two sounds of identical loudness are similar, but not exact, in regard to frequency and phase	• In the case of pure tone tinnitus it is very rare to generate "beats"
Sound presentation (ear)	• Contralateral masking has limited effect	• Strong contralateral masking is possible

Level of sound being masked	- Upon masking cessation, the sound being masked is perceived as being at its original (pre-masking) level unless auditory fatigue is experienced	- Upon masking cessation, the patient will often experience residual inhibition (a temporary reduction or even absence of their tinnitus sensation)

Tuning curves are an additional source of evidence that tinnitus differs from an external sound. While psychophysical tuning curves (PTC) depict the level of narrowband masker required to mask an acoustic narrowband signal of a fixed level (e.g., sinewave or narrow band of noise), tinnitus tuning curves (TTC) reveal the masker level that is needed to mask tinnitus (Moore, 2014). For normal-hearing individuals, the PTC typically exhibits a V-shaped pattern, revealing a sharp tip at the signal frequency in normally hearing individuals; specifically, the closer the frequency of the masker is to the target, the lower the level required to mask the target (Fournier et al., 2019). This pattern is thought to arise from cochlear mechanisms; if tinnitus is processed in the same way as an external sound, a similar pattern would be observed. However, little similarity has been found between PTCs and TTCs; often the distinctive V-shape can only be observed for PTC, indicating tinnitus is unlikely to have a cochlear origin (Burns, 1984; Penner, 1987; Tyler & Conrad-Armes, 1984). However, a recent study by Fournier et al. (2019) examining the shapes of PTCs and TTCs in 32 tinnitus patients found that 30% of cases demonstrated a V-shaped pattern for both PTC and TTC, suggesting that there is perhaps a subset of patients for whom tinnitus-related activity may share similar processing pathways with external sounds. The authors proposed that this might have implications for tinnitus research and treatment in terms of subtyping tinnitus and acoustic therapies (in particular those based on tinnitus frequency) (Fournier et al., 2019). Furthermore, the discrepancy between the conventional V-shape and the patterns observed in some TTC could simply reflect the fact that tinnitus, for some, is not narrowband in nature, but represents a broadband complex sound (Noreña et al., 2002).

Fowler (1940) noted subgroups with respect to TTC profiles, claiming that his participants fell into one of the three groups: (1) tinnitus could be masked by tones at low SLs irrespective of its frequency, (2) high masker SPLs were required for all frequencies, and (3) tinnitus could not be masked at all. Feldmann (1971) replicated and extended these findings, exploring the effects that tones of selected frequencies had on the perception of tinnitus. Pure tones, narrow-band noise, and white noise were presented to 200 patients both ipsilaterally and contralaterally, plotting the intensities of the tones and noises just sufficient to mask the tinnitus so as to generate masking curves (Feldmann, 1971). Feldmann identified five different tinnitus profiles based on masking pattern: convergent, divergent, congruent, distant, and persistent (Table 6). Results similar to that of Feldmann (1971) have been reported by others (Mitchell, 1983; Penner, 1987; Tyler & Conrad-Armes, 1984). The heterogeneous nature of tinnitus, in particular with respect to its response to masking, suggests that tinnitus does not arise in the cochlea; it requires central involvement and higher-order processing (Tyler, 2000).

3.8. Auditory Residual Inhibition

Auditory Residual Inhibition (ARI) reflects the temporary suppression or complete elimination of the tinnitus sensation that takes place following auditory stimulation (Henry, 2016). Josephson (1931) was one of the first to describe what we now know to be ARI. The effect was initially named residual inhibition (RI) by Vernon and Schleuning (1978) in recognition of Feldmann's reporting that tinnitus "remains silent for a certain period of time after cessation of the inhibitory stimulus" (Feldmann, 1971). To avoid confusion between acoustical RI and that observed in non-acoustical contexts, such as in neural transcranial magnetic stimulation (van Zwieten et al., 2016; Vanneste & De Ridder, 2012b), "auditory" is recommended to be routinely added to residual inhibition (auditory residual inhibition, ARI).

Table 6. Feldmann's tinnitus masking profiles and their prevalence among tinnitus patients as reported in several studies (Feldmann, 1971 (n = 200), Mitchell, 1983 (n = 32), and Tyler & Conrad-Armes, 1984 (n = 10))

Masking pattern		Prevalence
Type I: convergence	Common. Found in patients with high pitch tinnitus and high frequency hearing loss. Threshold and masking curves converge from low to high frequencies, meeting at the frequency corresponding to the tinnitus pitch and coinciding for higher frequencies. Occurs mostly in industrial deafness and sensorineural hearing loss associated with high-pitched tinnitus. Most like the masking of true sounds.	• Feldmann (1971): 34% of patients • Mitchell (1983): 53% of patients • Tyler and Conrad-Armes (1984): 80% of patients
Type II: divergence	Very rare. Defined by threshold and masking curve diverging from low to high frequencies. No clear pathologies associated.	• Feldmann (1971): 3% of patients

Type III: congruence	Common. Threshold and masking curve coincide within an intensity range of maximally 10 dB; any tone or narrowband noise raised at a level just above threshold will mask the tinnitus. Found in cases with a flat threshold curve, particularly in Meniere's disease, sudden deafness, and otosclerosis. Tinnitus may be tonal or noise-like.	• Feldmann (1971): 32% of patients • Mitchell (1983): 19% of patients • Tyler & Conrad-Armes (1984): 10% of patients
Type IV: distance	Relatively common. Masking sound has to be considerably louder than threshold in order to mask the tinnitus. Threshold curve and masking curve are therefore distant from each other. Present in cases of various pathologies of the middle and inner ear.	• Feldmann (1971): 20% of patients • Mitchell (1983): 22% of patients • Tyler & Conrad-Armes (1984): 10% of patients
Type IVa: dispersion	In type I-III the intensities required for masking with pure tones and narrowband noises are generally equal. In type IV however there can be differences in that higher intensities of pure tones are needed than for narrowband noises. This gives rise to type IVa.	--
Type V: persistence	Tinnitus cannot be masked irrespective of the stimulus. Often occurs in patients with severe sensorineural hearing loss or complete deafness.	• Feldmann (1971): 11% of patients • Mitchell (1983): 6% of patients

The clinical test for ARI is usually the presentation of broadband noise (2–12 kHz) binaurally to patients at 10 dB above their minimum masking level (MML). Exposure to the noise lasts 60 s before abrupt termination, at which time the participant is asked to report any perceived changes to their tinnitus percept (Henry, 2016). In cases where tinnitus is suppressed, the patient is asked to describe any changes to the tinnitus sensation as it recovers and resumes its initial level. Changes to the tinnitus percept, as well as duration of the ARI, are noted and classed according to four categories (Henry, 2016; Switalski & Sanchez, 2019):

1. Positive-complete: Tinnitus is entirely absent, ARI may vary from 1 s to several hours; ARI has been reported to last <2 min in 60% of patients, and <4 min in 80% of patients (Meikle et al., 2004).

2. Positive-partial: Tinnitus is still present, but less audible than prior to the testing procedure. Changes in the quality of the tinnitus might be reported.

3. Negative: No change in tinnitus loudness.
4. Rebound or Exacerbation: Increase in tinnitus loudness level in response to masker presentation (in these cases, the time taken for the tinnitus to return to its initial "original" level is recorded).

ARI has been reported in around 70% of tinnitus patients (Ristovska et al., 2019; Roberts et al., 2008), with some claiming an even higher prevalence of nearly 90% (Vernon & Meikle, 2000). However, results are variable. A study by Roeser and Price (1980) evaluated the efficacy of tinnitus masking, reporting either partial or complete ARI in around 64% of their sample, no effect in 23%, and exacerbation in around 5% (masking was ineffective in 8% of the sample). Mitchell et al. (1984) also examined changes in tinnitus following masking, observing ARI in only 42% of participants. Of those who did not experience ARI, 26% noted that the masking sound alleviated their tinnitus (while it was being presented), while the rest felt the sound was simply "one more noise on top of the tinnitus," in some cases even aggravating the tinnitus. Though the prevalence of ARI is somewhat variable, it appears that those who experience ARI tend to do so consistently (Henry et al., 2013).

The duration of the effect can last anywhere between 1 s and several hours, in some cases even days (Sandlin & Olsson, 1999; Switalski & Sanchez, 2019). The magnitude and duration of ARI are dictated by several factors, including the intensity, duration, and frequency of the masker (Terry et al., 1983; Vernon & Meikle, 1981). High-intensity and long duration maskers have been found to produce longer relief from tinnitus through extending post-masking effects (ARI) (Tyler, 2000). Terry et al. (1983) maintained that the greater the masker intensity, the greater the period of ARI. Evaluating the relationship between masker composition (frequency, bandwidth, intensity, and duration) and the magnitude and duration of ARI, the investigators found that ARI was proportional to the masker intensity given the tinnitus was fully masked (partial masking will result in little or no ARI). In addition, the time course of ARI demonstrates a linear increase as a function of the logarithm of masker duration for durations between 10 s and 10 min (Terry et al., 1983). The duration of the effect, measured as time taken to achieve complete recovery of tinnitus, increased to around 100 s for maskers presented for a period of 100 s, but only increased to 200 s for maskers presented at tenfold greater durations (Terry et al., 1983). Tyler and Conrad-Armes (1984) evaluated the perception of tinnitus following termination of a masker in 10 participants with sensorineural tinnitus, noting several different responses: low-level and short-duration maskers generally resulted in the tinnitus being heard immediately following masker termination, while higher-level and higher-duration masker presentation (and subsequent termination) led to (1) a silent period followed by an abrupt return to the pre-masking level, (2) a silent period followed by a more gradual return, (3) an increase in tinnitus loudness, (4) a reduction in tinnitus loudness, (5) a "wobbling" of the tinnitus, and (6) no ARI effect.

In addition to the well-known influence of masker intensity and duration on ARI, a number of studies have proposed that the post-masking effect is also, to some degree, frequency-dependent (Fournier et al., 2018; Sockalingam et al., 2007). Terry et al. (1983) found that ARI is in general maximal when the frequency of the masker is lower than the tinnitus frequency. Sockalingam et al. (2007) and Fournier et al. (2018) proposed that the closer the masker frequency is to the patient's tinnitus, the greater the ARI. Sockalingam et al. (2007) also noted that while the duration of ARI increased with increasing duration of frequency-matched stimuli, no such correlation was identified for non-frequency-matched stimuli.

Cautions and Application

There is limited evidence to suggest that temporary threshold shift (TTS) is produced during ARI (Terry et al., 1983; Vernon & Fenwick, 1984); however, use of the test with persons who experience reduced sound tolerance is not recommended. ARI has some, limited, potential prognostic value in terms of masker-based therapies, determining the likelihood that a patient will benefit from sound therapy (Vernon, 1977). In addition, it gives many individuals a feeling of renewed hope that their tinnitus can be managed and is not intractable. The demonstration that tinnitus can be altered – even if only for a brief moment – can be particularly rewarding if the patient is someone who has suffered from constant, unremitting tinnitus for a long period of time (Vernon & Meikle, 2000). Further, it shows patients that tinnitus relief might be possible by using external sounds to modify the percept.

3.9. The Future of Psychoacoustic Measures: Methods and Application to Therapy

Methods

Tinnitus evaluation is currently most commonly conducted using a standard audiometer primarily due to the availability, simplicity, and familiarity of the equipment. However, there are well-known limitations associated with assessing tinnitus using a conventional pure-tone audiometer (McFadden, 1982; Vernon & Fenwick, 1984). Audiometers are restricted in the range of frequencies they present, allowing only gross estimates of tinnitus to be obtained (Kostek & Poremski, 2013). Frequencies above 8,000 Hz are often not available, resulting in those with tinnitus frequencies above 8,000 Hz not being appropriately and accurately pitch matched (McFadden, 1982; Schechter & Henry, 2002). Additionally, the typical 5 dB intensity level increments of audiometers may be too large to enable precise loudness matching of tinnitus (Kostek and Poremski, 2013). While some audiometers allow for smaller increments (1 to 2 dB) to be used, this extends test duration (Kostek and Poremski, 2013). The flexibility of digital platforms (software, apps) should free clinicians from the limitations of pure-tone audiometers, but with new innovative methods comes the potential for even less standardization. Kostek and Poremski (2013) evaluated the use of a multimedia-based synthesizer for measuring the psychoacoustical properties of tinnitus, noting its superiority over conventional audiometer use. The tinnitus synthesizer has many benefits above the use of an audiometer: (1) it obtains results more quickly, (2) it has a greater capacity for allocating the acoustic parameters of sound (in turn representing it more accurately), and (3) the participant does not have to be in close cooperation with the examiner or verbally describe the perceived listening experience, which is often challenging for a number of people.

The current pitch and loudness match of tinnitus offer a limited “cartoon-like” representation of the sensation. The use of pure tones as comparison stimuli has limitations, as the majority of individuals describe a broader more complex tinnitus spectra (Table 3). Patients and research participants are instructed to match to the prominent pitch of their tinnitus; however, this is often difficult to do (Henry et al., 2013; Moore, 2014). Though the use of pure tones as comparison stimuli is not ideal, there are claims that it is still a reasonable methodological choice, having a number of advantages over the use of complex tones or noise bands (Noreña et al., 2002). The pitch of pure tones is defined almost exclusively by their frequency;

conversely, the perceptual attributes of complex tones and noise bands are defined by various physical parameters, including their fundamental frequency, center frequency, bandwidth, and spectral shape (which is in turn governed by the amplitude of their frequency constituents) (Noreña et al., 2002).

Tinnitus likeness measures appear a compromise as they use tonal stimuli, but across a wide spectrum (Noreña et al., 2002; Roberts et al., 2006). TLR have demonstrated a greater degree of reliability relative to several alternative methods (Hébert, 2018; Kay & Searchfield, 2008) and have tentatively been shown to improve the validity of pitch matching (Roberts et al. 2006). However, these methods still only offer a simplified representation of the global tinnitus experience, focusing solely on frequency and intensity components; two aspects that contribute to, but do not wholly define the sensation. They are also time-consuming. However, the use of complex and noise stimuli for tinnitus matching need not be a difficult and lengthy procedure. Kostek and Poremski (2013) recommended that for a patient reporting noise-like tinnitus a narrowband noise be presented with a center frequency equal to tonal pitch match. If the patient feels that the pure tone more closely resembles their tinnitus than the noise, this tone is the final match and no further testing needs to be conducted. If the patient feels the noise was a closer match to their tinnitus, the most appropriate form of noise should be determined by comparing broadband noise (speech noise or white noise) with narrowband noise.

More complex approaches such as tinnitus likeness ratings (TLR) are a step towards a more “complete” representation of the tinnitus sensation. Future methods of assessment may require more accurate and/or “realistic” replicas of tinnitus (Searchfield, 2014). There appear to be two approaches to creating realistic copies of tinnitus. One is to start and build on basic building blocks of sound (frequency and intensity), the other is to start with complex sounds (real world) and modify them to match tinnitus (Kay and Searchfield, 2008). In order to achieve appropriate tinnitus avatars (complex replicas of the tinnitus experience), future matches may need to incorporate several different sounds (Drexler et al., 2016), using real-world or complex sounds (Kay and Searchfield, 2008), and defining tinnitus in 3-dimensional space (Searchfield et al., 2015).

Application to Treatment

Tinnitus heterogeneity may be responsible for the variable treatment responses seen among tinnitus patients (Cederroth et al., 2019; Simoes et al., 2019). Until recently, treatments have been largely independent of psychoacoustic measures. However, the increase in management strategies requiring accurate pitch and loudness matches including desynchronization with patterned tones (Reavis et al., 2010), tonotopic reorganization using sound and vagus nerve stimulation (De Ridder, Kilgard, et al., 2015), active discrimination (Roberts & Bosnyak, 2011; Wise et al., 2016), and categorization training tasks (Jepsen et al., 2010) has been a driving force for the need for accurate measurements. A treatment based on sound presentation in and around tinnitus pitch is likely to be compromised if the treatment sound is inaccurately prescribed.

Therapies currently attempting to personalize tinnitus therapy often only focus on one aspect of the percept such as pitch, loudness, sound preference, or maskability rather than considering the percept as the complex combination of these factors (Searchfield, Durai, et al., 2017).

3.10. Summary

Psychoacoustic measures are crucial for characterizing and evaluating the perceptual properties of tinnitus. However, common approaches to the psychoacoustic matching of tinnitus are faced with a number of limitations, including:

- Lacking standardized protocols for psychoacoustic measures.
- Pitch-matching issues: equipment-based limitations, octave confusion, effects of cochlear dead regions, and tinnitus complexity.
- Loudness-matching issues: ample choice of loudness units of questionable relevance and appropriateness, effects of loudness recruitment.
- Masking based issues: variability and unpredictability of tinnitus behavior in response to an external sound.
- Residual inhibition-based issues: unpredictability in terms of whether or not a patient will demonstrate residual inhibition.

Despite these limitations, the current measurements are likely to be sufficiently accurate for counseling and as adjunct measures to questionnaires in research. Throughout this chapter we have discussed and critiqued current psychoacoustic methods, offering suggestions for their improvement and a view of what successful tinnitus evaluation might look like and encompass. It is clear that a broader comprehension of tinnitus is required, taking into consideration not only its acoustic parameters and underlying pathophysiology, but also factors such as patient personality and activity within the neural networks (auditory, attention, memory, and emotion centers) affected by tinnitus. The heterogeneous nature of tinnitus should be taken into consideration at every stage of tinnitus assessment.

Chapter 4. A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception

4.1. Chapter Introduction

The narrative review presented in this chapter explores the categorisation of sound and considers its application within a perceptual training paradigm for tinnitus management. The review compares and contrasts the categorisation phenomenon across several different modalities, reflects upon controversies surrounding the effect, and describes the neurophysiological changes that underpin a reduction in the ability to differentiate between sounds following categorisation training. The principles and basis of these neural changes are identified by the review as being valuable in the treatment of conditions that arise from maladaptive neuroplasticity such as tinnitus. Theories surrounding the reduced cortical representation for a training sound seen following perceptual categorisation training set the foundation upon which the research in the auditory categorisation training study was subsequently based on (Chapter 6). This narrative review was published in the Journal of Otorhinolaryngology, Hearing and Balance Medicine (Vajsakovic et al., 2022) and reprinted in this thesis with permission from the Journal of Otorhinolaryngology, Hearing and Balance Medicine (2023).

4.2. Abstract

Auditory categorisation is a phenomenon reflecting the non-linear nature of human perceptual spaces which govern sound perception. Categorisation training paradigms may reduce sensitivity toward training stimuli, decreasing the representation of these stimuli in auditory perceptual maps. Reduced cortical representation may have clinical implications for conditions that arise from disturbances in cortical activation, such as tinnitus. This review explores the categorisation of sound, with a particular focus on tinnitus. The potential of categorisation training as a sound-based tinnitus therapy is discussed. A narrative review methodological framework was followed. Four databases (PubMed, Google Scholar, Scopus, and ScienceDirect) were extensively searched for the following key words: categorisation, categorical perception, perceptual magnet effect, generalisation, and categorisation OR categorical perception OR perceptual magnet effect OR generalisation AND sound. Given the exploratory nature of the review and the fact that early works on categorisation are crucial to the understanding and development of auditory categorisation, all study types were selected for the period 1950–2022. Reference lists of articles were reviewed to identify any further relevant studies. The results of the review were catalogued and organised into themes. In total, 112 articles were reviewed in full, from which 59 were found to contain relevant information and were included in the review. Key themes identified included categorical perception of speech stimuli, warping of the auditory perceptual space, categorisation versus discrimination, the presence of categorisation across several modalities, and categorisation as an innate versus learned feature. Although a substantial amount of work focused on evaluating the effects of categorisation training on sound perception, only two studies investigated the effects of categorisation training on tinnitus. Implementation of a categorisation-based perceptual training paradigm could serve as a promising means of tinnitus management by reversing the changes in cortical plasticity that are seen in tinnitus, in turn altering the representation of sound within the auditory cortex itself. In the instance that the categorisation training is successful, this would likely mean a decrease in the level of activity within the auditory cortex (and other associated cortical areas found to be hyperactive in tinnitus) as well as a reduction in tinnitus salience.

4.3. Introduction

It is well-known that human perceptual systems group stimuli into behaviourally relevant categories (Guenther et al., 2004; Kuhl, 1991). Our ability to categorise sounds is governed by the fact that our perceptual spaces are warped in such a way that we are better able to discriminate between-category rather than within-category differences in sounds (Guenther & Bohland, 2002). This phenomenon has been defined using several terms throughout the literature; namely, categorisation, categorical perception, and generalisation (Guenther & Bohland, 2002; Guenther & Gjaja, 1996; Harnad, 1987). Similar to categorisation is the "perceptual magnet effect" which refers to the warping of the perceptual space for speech sounds (specifically some synthetic vowels and semi-vowels). According to Kuhl (1991), who coined the term, what makes the magnet effect distinct from categorisation is that it is characterised by disparities in discriminability for prototypical versus non-prototypical stimuli belonging to the same phonemic category. Discriminability is far greater near non-prototypical members of a category than near prototypical members. The claim that categorisation and the perceptual magnet are different entities has been questioned by other researchers who prefer to think about the two as being one and the same (Beale & Keil, 1995; Burns & Ward, 1978; Goldstone, 1994; Guenther et al., 1999; Lane, 1965). Though the perceptual space appears to be more notably warped for vowels and semi-vowels, the effect is also present for consonants and non-speech stimuli (Beale & Keil, 1995; Burns & Ward, 1978; Goldstone, 1994; Guenther et al., 1999; Lane, 1965). As such, this review will consider categorisation and the perceptual magnet effect as interchangeable terms pertaining to the same phenomenon.

Liberman (1957) was one of the first to contemplate the idea of categorisation, proposing two learning processes likely to underpin it: *acquired distinctiveness* and *acquired similarity/equivalence. Acquired distinctiveness* describes a rise in perceptual sensitivity for sounds that are constantly categorised differently in a learning situation. Conversely, in *acquired similarity,* sounds that were once distinct from each other become difficult to distinguish following repeated categorisation to the same group (Liberman, 1957). Guenther et al. (1999) expanded on these processes by examining the effect they had when used in auditory perceptual space training. The study investigated the possibility of inducing *acquired similarity* for category-relevant non-speech sounds using categorisation training and evaluated whether the resulting magnet effect was a consequence of the distribution of the training stimuli, or the type of training used by comparing the results with those obtained by discrimination training. According to Guenther et al. (1999), categorisation and discrimination training paradigms have opposite effects, whereby categorisation training results in a reduction in the ability to distinguish between heavily experienced training sounds, whilst discrimination training leads to an increase in this ability. Furthermore, these effects translate into changes at the level of auditory maps within the brain, with the size of neural representation for the training sounds being determined by the type of training used (Guenther et al., 1999). Specifically, categorisation of the training sounds leads to a reduction in the number of cells coding these sounds in the auditory map, in turn decreasing the ability of an individual to differentiate sounds in this area of acoustic space, whilst the opposite effect is seen when using discrimination.

The diminished cortical representation that occurs as a result of categorisation training may have clinical implications for conditions that arise from disturbances in cortical activation, such as tinnitus. Tinnitus (ringing of the ears) appears to be the consequence of a series of neuroplastic changes in central auditory pathways that lead to hyperexcitability and an increase in the spontaneous firing rate in these pathways (Eggermont & Tass, 2015; Noreña & Eggermont, 2003; Roberts, 2018). Categorisation training might offer a means of tinnitus management by decreasing the area of cortical representation for trained sounds. If successful, categorisation training could be used to reduce activity within the auditory cortex by changing the representation of sound within the cortex itself and in turn reversing the changes in cortical plasticity that are seen in tinnitus, thus reducing tinnitus severity and related distress.

While the notion of perceptual—specifically, categorisation—training is not novel, there are few reviews that offer a concise, up-to-date overview of categorisation within the context of both speech and non-speech sounds, and no reviews known to date that contemplate its potential role in tinnitus perception and management. Given that the cortical changes that occur as a result of categorisation training could oppose or even “reverse” those observed with tinnitus, it is essential to review what is currently known about this form of perceptual training, identify its role in sound perception, and offer insight into the rationale for investigating it as a potential mode of tinnitus therapy. This review will firstly explore the categorisation of sound, providing a general historic overview before expanding on the phenomenon and describing the neural basis believed to underpin it. Secondly, it will discuss its presence across several modalities and evaluate innate vs. passive instances of categorisation. Thirdly, it will bring awareness to the controversies surrounding categorisation and will contemplate its feasibility as a training paradigm. Lastly, this review will consider the clinical implications of categorisation as a tool for tinnitus management, drawing on what is currently known about the cortical effects of categorisation training, as well as the sparse but encouraging evidence emerging from tinnitus studies implementing perceptual training regimes.

4.4. Methods

The Green et al. (2006) narrative review methodology was followed in conducting this narrative review. The advantage of using this framework is that it offers a broad and comprehensive overview of a specific topic. Furthermore, it allows various pieces of information to be pooled and ordered to form an understanding of the history and evolution of the topic, and enables speculations to be made based on the scope of current findings (Green et al., 2006). The key words (categorisation, categorical perception, perceptual magnet effect, generalisation, and categorisation OR categorical perception OR perceptual magnet effect OR generalisation AND sound) were extensively searched on four databases: PubMed, Google Scholar, Scopus, and ScienceDirect. Given the exploratory nature of the review and the fact that early works on categorisation are crucial to the understanding and development of auditory categorisation, all study types were selected for the period 1950–2022 and had the following exclusion criteria applied: article not available in English. Reference lists of articles were reviewed to identify any further relevant studies. The results of the review were catalogued and organised thematically according to common idea threads. The results and discussion section is divided into sections dedicated to each common idea thread.

In total, 112 articles were reviewed in full, from which 59 were found to contain relevant information and were included in the review. Each article was read in depth, identifying key information and evaluating the main findings, as well as defining how these findings inform auditory categorisation and its potential role in the perception of tinnitus. Several key themes identified include categorical perception of speech stimuli, warping of the auditory perceptual space, categorisation versus discrimination, the presence of categorisation across several modalities, and categorisation as an innate versus learned feature. Although a substantial amount of work focused on evaluating the effects of categorisation training on sound perception, only two studies investigated the effects of categorisation training on tinnitus.

4.5. Results and Discussion

4.5.1 **Categorisation: The What, When, and Where**

Categorisation and Its Origin

Categorisation became a widely used term following the experiments of Liberman et al. (1957), who showed that the discrimination of synthetic speech sounds was predominantly governed by the categories to which these sounds were allocated to by the individual. Specifically, if the two sounds belonged to different categories, the participants could discriminate between the stimuli quite quickly and with relative ease, whereas if the sounds belonged to the same category, participants found it harder to discriminate between them. Participants tended to display good discriminability for between-category stimuli, and poor discriminability for within-category stimuli, even though the stimulus pairs used in these scenarios were equidistant in frequency space (Guenther & Gjaja, 1996; Liberman et al., 1957).

The idea of "prototypes" and "non-prototypes" was added to categorisation lexicon. A prototype was considered to be the "best" or "ideal" representative of a category, whilst a non-prototype was regarded as a poor exemplar of the same category (Kuhl, 1991). For example, consider the category "bird"; this category is represented by a prototypical member such as "sparrow" or several prototypical properties such as "feathers". Some prototypes will be better than others in reflecting their parent category; although sparrows and ostriches are both birds, sparrows are considered to be better examples of birds as they share more similarities to other birds. As such, it can be said that sparrows are more ideal approximations of the prototype for birds, as they have more of the crucial features for determining "birdness" (Lively & Pisoni, 1997; Samuel, 1982).

Warping of the Auditory Perceptual Space

Ease of discrimination for between-category stimuli was believed to be due to the assimilation of exemplars found near the prototype by the prototype itself. Strictly speaking, good exemplars of a category appear to draw similar members towards themselves comparatively more often than poor exemplars of the same category (Iverson & Kuhl, 1995; Samuel, 1982). These observations lead to the realisation that the human perceptual system is warped, so that one's ability to discriminate between two stimuli is not linearly related to the physical distance between the stimuli as measured by dimensions such as frequency or time (Aaltonen et al., 1997; Guenther et al., 1999). Guenther and Gjaja (1996) proposed a neural model based on auditory map formation that is thought to underlie this nonuniformity (Figure 1).

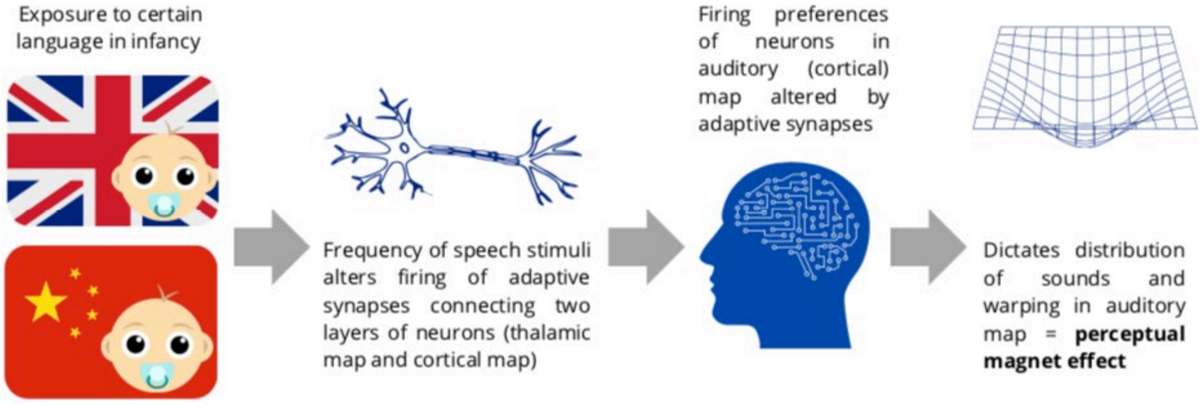


Figure 1. Simplified overview of the neural model underlying the perceptual magnet effect proposed by Guenther and Gjaja (1996). The model employs two layers of neurons (formant representation and auditory map) that are connected through adaptive synapses. The adaptive nature of the synapses determines what cells will become activated in the auditory map. During early exposure to speech stimuli, the strength of the synapses will be altered in such a way where it changes the firing preferences of the neurons in the auditory map, in turn reflecting the distribution of these sounds. The nonuniformity that comes about as a result of this preferential cell firing results in the magnet effect in this model.

The model is founded on the notion that exposure to a certain language in infancy results in nonuniformities in the distribution of neuronal firing preferences in the auditory neural map, leading to the magnet effect (Guenther & Gjaja, 1996). Specifically, the warping occurs because more cells in the map become tuned to the sounds most experienced by the infant. In other words, it is the distribution of the sounds heard by the infant that influences the firing preferences of neurons, giving rise to the warping observed in the auditory map and leading to the respective reduction in perceptual space close to phonemic category centres, and increase in this space away from centres (Guenther & Gjaja, 1996; Guenther et al., 1999). Performing a series of experiments aimed at defining the effects of categorisation versus discrimination training, Guenther et al. (1999) discovered that the sensitivity of their participants for the training stimuli differed depending on the training regime used; namely, categorisation training resulted in a decrease in this sensitivity, whilst discrimination training gave rise to an increase in sensitivity. Based on these findings, the researchers hypothesised that in categorisation training, repeated exposure to the selected training stimuli likely results in a smaller number of cells preferentially coding these sounds in the map, leading to a reduced cortical representation which ultimately weakens the listener's ability to differentiate between the stimuli in that region of acoustic. Conversely, discrimination training results in more neurons becoming tuned to the stimuli to which the listener was most frequently exposed to, leading to an increase in the cortical representation and thus an improved ability to differentiate between the sounds.

Neural Changes Resulting from Categorisation Training

To further explore categorisation and its effects on sound representation within the auditory cortex of human adults, Guenther et al. (2004) used functional magnetic resonance imaging (fMRI) and identified the cortical changes that occur as a result of categorisation training. Their study revealed a significantly higher level of cortical activation for non-prototypical stimuli than for prototypical stimuli, particularly within the temporal lobe (Heschl's gyrus and planum temporale areas) (see Figure 2), lending support to the hypothesised neural changes thought to occur as a result of perceptual (categorisation/discrimination) training, as previously proposed by the researchers. Discrimination was believed to be more difficult between sounds located at the centre of a category compared to those found near category boundaries, as there are fewer cells representing these sounds in the auditory cortical areas (Guenther et al., 2004). Taking the findings of their study in addition to what was already known about categorisation, Guenther et al. (2004) proposed that the brain in fact re-distributes neural resources away from areas of acoustic space where the ability to differentiate between sounds lacks behavioural importance (for example, at the centre of a sound category) and shifts the resources toward areas where precise discrimination is required.

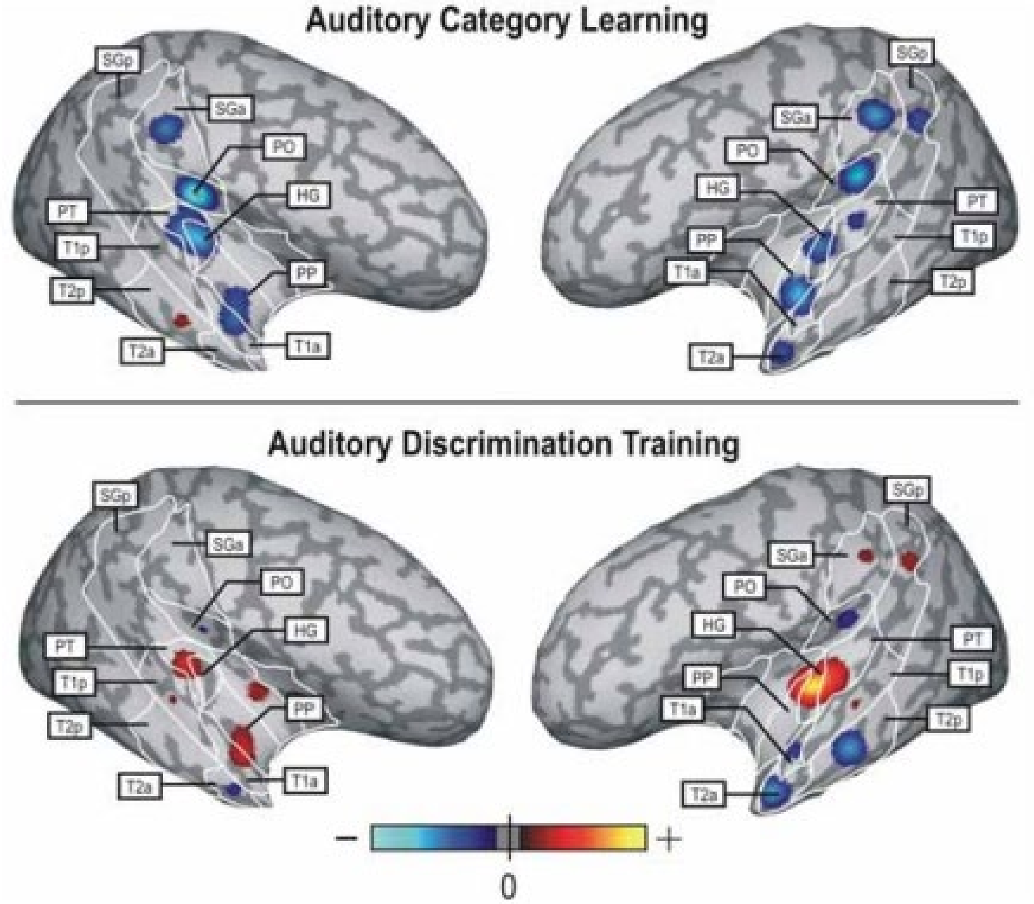


Figure 2. Results of categorisation training (upper panels) and discrimination training (lower panels) on cortical activation. Differences between post- and pretraining cortical activations for the training stimuli minus the control stimuli are shown on the cortical surface models. Regions in which training has resulted in a relative reduction in activation for stimuli within the trained category are shown in blue, whilst those regions in which a relative increase of activation was observed for the training stimuli are marked red. Categorisation training results in a decrease in cortical activation, while discrimination training leads to an increase in this activation in the perisylvian cortical regions. HG = Heschl's gyrus; PT = planum temporale; PP = planum polare; T1a/T1p = anterior/posterior superior temporal gyrus; T2a/T2p = anterior/posterior middle temporal gyrus; PO = parietal operculum; SGa/SGp = anterior/posterior supramarginal gyrus. Figure adapted from Guenther et al., 2004 with permission from ASHA.

Passive Categorisation: A Consequence of Evolution?

For many years, the nature and origin of categorisation have been argued, with some researchers putting forth evidence for the feature being innate, whilst others have proposed that it is induced by learning (Bornstein, 1987; Harnad, 2003). The two hypotheses upon which these arguments are built are primarily the "relativist" hypothesis formulated by Whorf (1956), which suggests that language and culture determine how we categorise, and the "universalist" hypothesis, which posits that category boundaries are a feature innate to humans (Harnad, 1987, 2003). Though initially the Whorf hypothesis was more commonly recognised and adopted amongst researchers, over the years it has been supplanted by universalism (Bornstein, 1987). Evidence from psychophysical studies conducted on adults of different cultural backgrounds, categorisation in infancy studies, and animal studies lend support to the universalist view (Abramson & Lisker, 1970; Berlin & Kay, 1969; Boynton & Gordon, 1965; Eimas et al., 1971; Guenther & Gjaja, 1996; Kuhl, 1979; Kuhl & Miller, 1978; Miyawaki et al., 1975; Sandell et al., 1979; von Frisch, 2014; Werker et al., 1981; Werker & Tees, 1984; Wright, 1972; Wright & Cumming, 1971; Xu et al., 2006).

4.5.2 **Categorisation as an Innate Feature**

Cross Cultural Studies

The innate ability for humans to passively categorise sound has been demonstrated by psychophysical and perceptual studies investigating the categorisation of sound in adults of diverse cultural and linguistic backgrounds. Stevens et al. (1969) explored the discrimination and identification of synthetic vowels by English and Swedish speakers, concluding that vowel perception is not a consequence of experience with linguistic categories, but rather a function of human auditory mechanisms. Building on these results, Guenther and Gjaja (1996) employed their neural model in a simulation-based study investigating the perception of stimuli within or near the American English phonemic categories /r/ and /l/ in Japanese and American adults. The outcomes indicated that American adults, who have been exposed to many instances of /r/ and /l/ in their native language, show perceptual warping around the phonemic categories. Conversely, Japanese adults, who presumably have had less exposure to /r/ and /l/ phonemes as these categories do not have direct correlates in Japanese, do not display this perceptual warping. Their study demonstrated the presence of passive categorisation in humans, suggesting that categorisation and the perceptual magnet effect are a result of neural map formation in the auditory system.

Infancy Studies

Eimas et al. (1971) evaluated the extent to which categorisation is an innate feature through examining the perception of voice-onset time in infants between one- and four-months of age. Using a high-amplitude sucking procedure as a measure of response to sound stimuli, the infants were exposed to three different pairs of sounds of varying voice-onset times; 20 and

40 milliseconds, 0 and 20 milliseconds, and 60 and 80 milliseconds. The 20 and 40 millisecond pair represented stimuli on opposite sides of the category boundary, whilst the remaining two test pairs both fell within the same category. Specifically, the category boundary pair has been found to sound like the syllables BAH and PAH, respectively, to adult speakers of English and other languages, whereas the two within-category pairs were both instances of BAH or PAH. The results of the study indicated that infants, just like adults, perceive differences in voice-onset time categorically, suggesting that categorisation is an innate mechanism tuned to the properties of speech. Expanding on this outcome, Eimas et al. (1971) proposed that the mechanism acts as a precursor for phonemic categories that later in development enables the conversion of speech signals into phonemes that can be then used to form words and meanings. To date, several other studies using the same voicing distinction methods have demonstrated the ability for infants to perceive differences in voice-onset time in a categorical manner, with investigators advocating for an underlying genetic predisposition for speech sound perception and categorisation (Lasky et al., 1975; Streeter, 1976; Trehub & Rabinovitch, 1972).

Moving away from the voicing distinction experiments, Kuhl (1979, 1980, 1983) examined the ability of 6-month-old pre-verbal infants to categorise speech sounds from the same phonetic category without receiving formal training and with a lack of productive skill. Kuhl's studies demonstrated that human infants possess perceptual abilities that enable both the discrimination of phonetically different signals, and the categorisation of those found within the same phonetic category, in turn also supporting the notion of innate mechanisms in speech perception. In concert with these findings, Jusczyk et al. (1977) reported evidence of passive categorisation for non-speech stimuli in early infancy. Using a high-amplitude suckling technique to determine the perception of rise-time differences for sawtooth stimuli in 2-month-old infants, the investigators concluded that infants, like adults, possess the ability to perceive non-speech sounds in a categorical manner.

Animal Studies

Nonhuman studies serve as another line of evidence for passive categorisation of sound as they exhibit work done on species that are capable of sound perception but have no possibility of culture or language. Studies using primates constitute the majority of the work to date with mixed evidence supporting/contradicting categorisation. Studies by Sinnott et al.

(1976) and Kuhl (1991) failed to find evidence of categorical perception in Old World and rhesus monkeys, respectively, proposing that the phenomenon is a unique species-specific speech processing mechanism. However, several other experiments conducted on macaques (Kuhl & Padden, 1982; May et al., 1989), rhesus monkeys (Waters & Wilson, 1976), and owl monkeys (Recanzone et al., 1993) have identified the presence of categorical mechanisms underlying sound perception in these animals. Kuhl and Miller (1978) conducted voicing distinction experiments using chinchillas, testing the animals in a categorisation paradigm in which they were trained to respond differently to the endpoints of a synthetic speech continuum (0 ms voice-onset time and +80 ms voice-onset time). The ability of the chinchillas to perceive the stimuli categorically was almost identical to that seen in adult English-speaking listeners, suggesting the mechanism is an innate non-species-specific property. Similar conclusions were drawn from studies undertaken on house mice. Mice were able to categorically perceive ultrasound vocalisations (Ehret & Haack, 1981). Other studies that have demonstrated the presence of passive categorisation in animals include work done on quails (Kluender et al., 1987), wild swamp sparrows (Nelson & Marler, 1989), songbirds (Hulse & Cynx, 1985), budgerigars (Dooling & Brown, 1990), rats (Eriksson & Villa, 2006), and gerbils (Ohl et al., 2001; Wetzel et al., 1998).

Passive Categorisation in Vision

Though categorisation was first observed for speech sounds, it has since been found that it is not a phenomenon unique to hearing, but one that is present for a variety of stimuli from a number of modalities; perhaps the most important being vision. Numerous human and animal studies have demonstrated the categorical perception of colour (Berlin & Kay, 1969; Bornstein et al., 1976; Boynton & Gordon, 1965; Sandell et al., 1979; Wright, 1972; Wright & Cumming, 1971), shapes (Gaißert et al., 2012; Livingston et al., 1998), and even more complex stimuli such as facial identity (Angeli et al., 2008; Beale & Keil, 1995; Kikutani et al., 2008; Stevenage, 1998; Viviani et al., 2007) and facial expression (Calder et al., 1996; Etcoff & Magee, 1992).

Just as in sound, the perception of visual stimuli has been found to be nonuniform. For example, we do not perceive continuous gradations along the visible light spectrum, but rather a range of discrete hues (Bornstein, 1987; Livingston et al., 1998). Boynton and Gordon (1965) conducted a study in which they asked participants to identify single wavelengths of colour using solely four basic colour terms—yellow, blue, green, and red, or a combination of two of these hues. The results of their colour-naming experiment revealed that participants could easily describe the wavelengths presented to them using one to two of the four basic colour terms, with a high level of agreement among participants. However, when the participants were allowed to use a broader range of colour terms (e.g., violet or orange), they admittedly struggled to define the observed wavelengths, leading to a reduction in agreement.

The findings of the Boynton and Gordon (1965) study serve as perhaps a simple yet effective example of categorisation, in that the four primary terms represent a mutually contrastive set that can be used to describe the colour space exhaustively as a result of our discrete categorical perception of wavelengths (Bornstein, 1987). Because we deconstruct this spectrum of different wavelengths into a limited number of distinct colour bands, we struggle to distinguish between colours within the same category (for instance, mahogany red and scarlet red), yet have no issue with discriminating between those colours that fall on the category boundary (such as green and yellow). Hence, instead of the spectral continuum being homogenous, the neural representation of it is not. Rather, it is warped in the same way as described previously with respect to sound; specifically, a larger change in wavelength is required to produce a just-noticeable difference (JND) in some regions in comparison to others (Livingston et al., 1998). Furthermore, a smaller relative change in wavelength is sufficient to generate a JND for colours that sit on category boundaries, whilst the opposite is true for those found within a colour category. The same principle applies to shapes; we find it easier to generalise and group a set of shapes under a familiar umbrella term than to classify them by specific names (e.g., rhombus, rectangle, trapezium shapes are classified as "square" shapes) (Figure 3) (Bialystok & Olson, 1987; Gaißert et al., 2012).

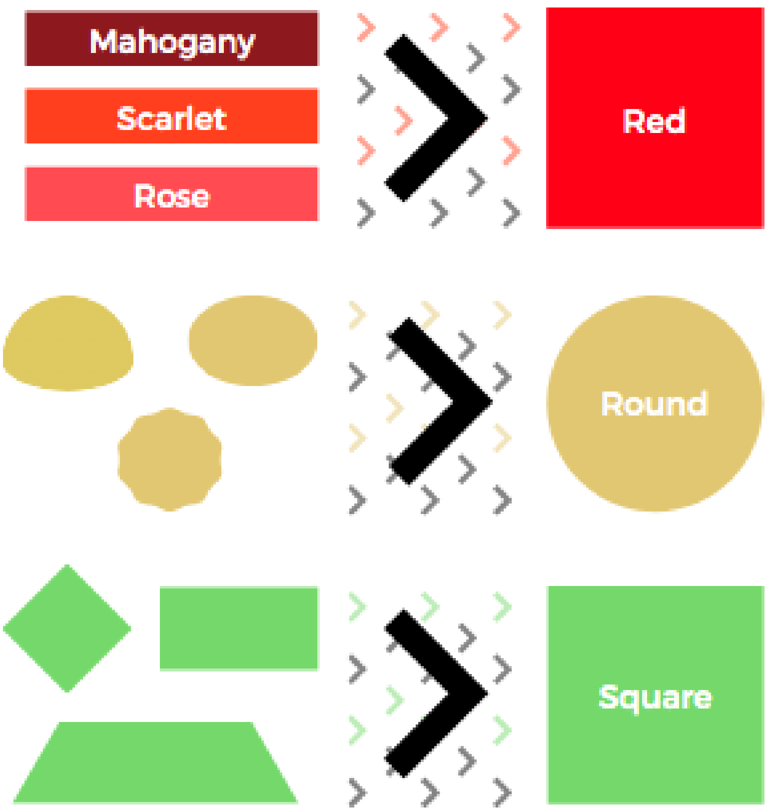


Figure 3. Categorisation explained in the context of colour and shape. Instead of distinguishing between shades of red such as mahogany, scarlet, and rose, individuals often 'categorise' these colours into one group: red. The same principle applies to shapes; instead of specifying what each specific shape is, individuals will group or 'categorise' shapes that share similar properties together. Hence, rounded shapes are simply seen as round, whereas those with sharp edges (such as the rhombus, rectangle, and trapezium) are seen as square.

As in the case of sound categorisation, the innate nature of visual categorisation is strongly supported with evidence from numerous cross-cultural, infancy, and animal studies. Berlin and Kay (1969) demonstrated that basic colour categorisation transcends culture and language. Bilingual adults from 20 different language communities determined the ideal representations of a limited selection of basic colour terms (chosen from a collection of 320 colours). Irrespective of the linguistic differences between the participants, there was high agreement among the group with respect to which colours they identified as being ideal exemplars, reflecting a universal uniformity in the categorical perception of colour (Berlin & Kay, 1969).

Developmental studies are useful for the exploration of categorisation as they allow for observations to be made prior to the acquisition of language and culture. Human infants regularly partition the spectrum of different wavelengths into categories of hue (Bornstein, 1987). Infants as young as four months are capable of categorising the visible spectrum into the basic psychological hues in the absence of any experience or formal training, with the formed categories being almost identical to those seen in adults (Bornstein et al., 1976). The fact that infants, unaffected by learned experiences such as culture or language, possess the ability to perceive colours in a categorical manner offers undeniable support to the notion that categorisation is a phenomenon innate to humans.

In addition to infancy studies, a number of investigations have presented evidence of hue categorisation in non-human species. Irrespective of the variations present in the general perception of the visible spectrum among different species, it has been demonstrated that categorisation of hues is common and universal across species. Pigeon (Wright, 1972; Wright & Cumming, 1971), the European honeybee (von Frisch, 2014), and the monkey (Sandell et al., 1979) perception studies indicate that colour-sensitive species have the ability to categorically perceive the colour spectrum in some way, even if they might not replicate exactly what is seen in humans. Work conducted on species that are capable of categorical perception of colour but have no possibility of culture or language stands as another source of support for the innate and universal mechanisms of categorisation.

4.5.3 **Categorisation as a Learned Feature**

Decades of research lending support to both “passive” and “learned” views of categorical perception has led to the two joining forces and offering a new perspective on categorisation and its origin, proposing that the phenomenon is both an innate feature and one which can be learned through experience. The idea that categorisation is a passive trait underpinning speech perception and comprehension that is fine-tuned through training is one that dominates the literature. Studies of speech perception in infants have demonstrated that although categorisation is in most part ascribed to biological influences, it is also a feature capable of modification through experience with the parental language (Eimas, 1981). Developmental studies documenting the effects of experience on speech perception have demonstrated that infants as young as 6 months of age already show alterations in speech perception dictated by exposure to a specific language (Kuhl et al., 2005; Kuhl et al., 1992). Specifically, an infant’s perception of speech reflects the phonetic structure of the language it has been exposed to (Kuhl, 1993). Though phonetic discrimination is a language universal feature in newborns, by the end of the first year of life, infants experience a reduction in this discrimination for non-native phonemes (Kuhl et al., 2005). Over the course of 30 months, infants demonstrate an increasingly negative correlation between native and non-native phonetic perception; the more the infants improve in their ability to perceive native-language phonemes, the worse they become at perceiving non-native phonemes (Kuhl et al., 2005). These results have been replicated by numerous cross-cultural studies exploring the effect that experience and learning has on the ability of infants of various cultural/lingual backgrounds (including English, Japanese, Spanish, Hindi, Salish, Thai, and Mandarin) to categorise speech (Abramson & Lisker, 1970; Guenther & Gjaja, 1996; Lasky et al., 1975; Miyawaki et al., 1975; Werker et al., 1981; Werker & Tees, 1984; Xu et al., 2006). As such, it appears that the abilities we as humans possess that allow us to categorise information originate from a bountiful and crucial set of biological constraints that are supplemented in their function by an equally important set of environmental constraints (Quinn & Eimas, 1986).

In addition to speech categorisation, Lynch et al. (1990) have demonstrated a role for learning in non-speech categorisation using musical articulation experiments. Evaluating the ability of American 6-month-old infants and adults to detect mistunings along native major and minor scales, and non-native Javanese pelog scales, has revealed that while infants can equally perceive both native and non-native musical scales, adults show improved perception of native scales relative to their non-native counterparts. Reflecting on these findings, the investigators proposed that infants possess an innate equipotentiality for culturally universal scale perception, and that the culturally specific experience that takes place throughout development into adulthood shapes their perception and categorisation of music.

4.5.4 **Controversy Surrounding Categorisation**

The categorical nature of categorisation, along with the robustness of the phenomenon, has been called into question. Though numerous researchers have demonstrated its presence in a variety of domains, including the perception of speech (Guenther & Gjaja, 1996; Guenther et al., 1999; Guenther et al., 2004; Kuhl, 1991; Liberman et al., 1957; Samuel, 1982), colour (Davidoff et al., 1999), familiar faces (Beale & Keil, 1995), and facial expressions (Etcoff & Magee, 1992), some have expressed concerns relating to the existence of the effect. Massaro (1998) labels categorisation as a “lasting myth”, suggesting that the use of multiple sources of information in perception requires these sources to be continuous rather than categorical. Challenging the logic of categorisation, Massaro (1998) outlined the difficulty with which information from various sources would be integrated if even a single source of information was perceived categorically. If we consider the perception of speech, for example, sentential context would either agree or disagree with the categorisation of the speech stimuli. If the context of the sentence agrees with the input, no further information will be obtained; conversely, if it disagrees with the categorisation of the speech signal, the individual is put in a position in which there is conflict and inconsistency between the context and acoustic input (Massaro, 1998). In addition to this argument, the identification-based methods commonly used to demonstrate categorical perception were also criticised by Massaro (1998) as being weak/questionable and guilty of indicating a categorisation effect even where it does not exist.

Massaro (1998) was not the only one to raise questions with respect to categorisation and the extent of its effect. Lively and Pisoni (1997) evaluated the phenomenon with respect to the perceptual magnet effect (PME), replicating the original set of experiments conducted by Kuhl (1991). The three experiments were designed to assess two results deemed by Kuhl as essential to the generation of the PME; namely, (1) whether some examples of a phonetic category are rated as being better representations of that phonetic category than others, and (2) whether category members that approximate an idealised prototype are less discriminable than those not resembling the prototype. Failing to replicate Kuhl's results, and in turn fulfil the requirements of the PME, the authors found that the effect was not as robust as Kuhl had suggested.

Though this controversy cannot be overlooked, it should not stand to mean that categorisation as a concept should be entirely abandoned or ignored. Numerous empirical studies have demonstrated modifications in cortical plasticity following categorisation training, building on the methods previously used to explore categorisation and lending a great deal of support to the phenomenon (Guenther et al., 1999; Guenther et al., 2004). As such, it should merely draw awareness and stand as a reminder for researchers to be mindful of their methodologies so as not to generate an effect where it does not exist.

4.5.5 **Categorisation for Tinnitus**

The notion that tinnitus is the consequence of a series of neuroplastic changes taking place in the central auditory pathways following peripheral injury is one that currently predominates in the literature. Many tinnitus treatments attempt to disrupt or modify tinnitus related neural activity through passive sound exposure over weeks or months (for a review, see Searchfield (2021)). What makes auditory perceptual training paradigms attractive is the use of active participatory learning, which should result in more efficient learning, and plastic brain changes, rather than the usual passive sound exposure (Hoare et al., 2010; Jepsen et al., 2010). The auditory perceptual training programme that has received most interest for tinnitus therapy has been frequency discrimination training (FDT) (Hemanth & Vipin Ghosh, 2022; D. J. Hoare et al., 2012). The goal of FDT is to teach listeners to differentiate between tones matched closely in pitch with a greater degree of precision. Several studies investigating FDT have reported neuroplastic changes in the auditory cortex as a result of the training; specifically, FDT regimes giving rise to an increase in the cortical representation for trained frequencies (Menning et al., 2000; Noreña et al., 2006; Recanzone et al., 1993). The premise underlying the use of FDT for tinnitus is that it has the potential to disrupt the tinnitus-generating network through this tonotopic reorganisation of the primary auditory cortex (Hemanth & Vipin Ghosh, 2022). A recent study employing FDT through a game module as a means of tinnitus management noted a change in pitch and reduced loudness for over 70% of the participants, as well as a reduction in the perceived severity and handicap of tinnitus (Hemanth & Vipin Ghosh, 2022). However, there are still speculations with respect to the strength and robustness of the effect, highlighting the need for high-quality, unbiased, randomised controlled studies (Brown et al., 2004; Hoare et al., 2010).

An alternative to FDT is categorisation training (CT). CT teaches listeners to categorise tones within a certain frequency range and identify them as being members of the same category (Jepsen et al., 2010). Although FDT has received the most research interest in tinnitus, the observation that CT reduces cortical activity for trained tones (Guenther et al., 2004) suggests that it may be a more promising strategy. Guenther et al. (1999) conducted a series of psychophysical experiments to determine the effect of discrimination and categorisation training paradigms on the auditory perceptual space of adults with no history of speech, language, or hearing disorders. Their study found that while discrimination training using non-speech stimuli led to an increase in sensitivity to differences in the training stimuli, categorisation training with the same sounds resulted in a decrease in their discriminability (Guenther et al., 1999). Further investigations using functional magnetic resonance imaging have shown that this decrease in discriminability following categorisation training is the result of a reduction in the size of cortical representation of the training tones (Guenther et al., 2004). The authors postulated that this reflects the redistribution of neural resources by the brain away from areas where distinction between sounds is not behaviourally important, and toward areas where precise discrimination is necessary (Guenther et al., 2004).

While much work has been conducted on the principle of categorisation, it is evident that there is a relative dearth of tinnitus research on categorisation. The available studies investigating categorisation within the context of tinnitus are sparse (only two studies were identified in this review as containing relevant information) and limited to work by the corresponding authors lab. Recognising the promising nature of CT, Jepsen et al. (2010) applied the findings of Guenther et al. (2004) to study the effects of CT (and FDT) on tinnitus and late auditory evoked potentials (AEP). Using a handheld personal digital assistant (PDA) device, 24 participants underwent three weeks of either CT or FDT at pitch match. Prior to and following the training period, the participants attended test sessions in which AEPs were measured (in addition to several other assessments, including the tinnitus handicap inventory (THI)). In concert with the findings of Guenther et al. (2004), the results of the Jepsen et al. (2010) found a reduction in AEP amplitude following CT, and an increase following FDT, with the two perceptual training paradigms having equal but opposite effects. In addition to this, post-intervention examinations found that FDT led to a slightly greater reduction in THI score than CT, however participants were marginally more likely to find ignoring their tinnitus easier following CT than following FDT.

These findings lend support to the ability of categorisation training to modify cortical plasticity and reduce the area of tonotopic representation for trained tones, in turn acting as a potential means of tinnitus management. Jepsen et al. (2010) suggested that CT be used in conjunction with some form of counselling or cognitive based methods to enhance the benefits of CT and further reduce tinnitus severity. Taking a step back, appropriate methods of CT administration must first be considered if it is to be used by patients in an everyday setting. Jepsen et al. (2010) issued PDA devices to patients which meant that they could perform the CT task anywhere, anytime. However, the training involved a series of trials during which participants had to either hear examples of training sounds without responding (‘listening trials’) or identify one sound from a list of presented sounds as belonging to the training group by pressing a button on the PDA screen (“identification trial”). Though the method is straightforward, its simplicity and lack of an “end goal” might prevent its success in the long term as patients start to lose interest. Strategies for categorisation training must be considered to ensure compliance and increase efficacy. Perhaps taking a passive approach, in which the listener can be trained to categorise the stimuli without needing to physically attend to the training programme would be reasonable. This could be useful for individuals leading busy lifestyles, offering a means of management that does not require time to be dedicated specifically to completing the training. Durai, Doborjeh, et al. (2021) attempted to recategorize tinnitus from a sound that represents the sensation in its entirety to a natural real-world sound using such a passive training paradigm. The study involved acute (30 min) and chronic (3 month) exposure to a training sound that matched the individual's tinnitus (i.e., their tinnitus avatar) cross-faded to a chosen nature sound (cicadas, birds, fan, water sound/rain, water and bird). Durai, Doborjeh, et al. (2021) reported several behavioural findings, including a significant reduction in the tinnitus functional index score and subscales of intrusiveness of the tinnitus signal and ability to concentrate with tinnitus. While the participants did not report a change in tinnitus loudness, they observed changes in pitch, uniformity, and location. At a physiological level, the researchers reported changes in the activation of neural tinnitus networks and greater bilateral hemispheric involvement, specifically relating to attention and discriminatory judgments (dorsal attention network, precentral gyrus, ventral anterior network). The absence of a control group means that it is unclear whether these outcomes are the result of recategorization induced by the passive auditory training, or simply a reflection of the benefits of masking and/or any emotional benefit gained from listening to pleasant nature sounds. As such, further efforts are required to determine the role of passive perceptual training as a means of tinnitus management, as well as to better understand how it compares to conventional sound therapy (e.g., broad-band noise).

An alternative to using passive methods is to take an active training approach, one in which listener involvement is required in order to complete the training tasks. For example, categorisation training could be incorporated into a video game, necessitating the interaction between the listener and the training itself through a series of tasks in which the listener is required to respond in some way or another in order to progress through the training programme (Searchfield, Kobayashi, et al., 2017). By designing a categorisation training game with well-defined aims and multiple levels of increasing difficulty, players are inherently motivated to participate and in turn aid in the success of the training (Neal, 1990). However, active training paradigms are more time consuming to design and create, are prone to issues of a technical nature (e.g., glitches in gaming software), and require the participant's full attention, a greater level of technology use and knowledge, and a time slot dedicated to performing the tasks. As such, the next step in evaluating categorisation training for tinnitus management might be to undertake a more basic passive approach in a proof-of-concept trial, in combination with aspects of counselling and more cognitive based methods (as per the recommendation of Jepsen et al. (2010)), prior to taking the leap to more complex resource-intensive approaches such as active training.

4.6. Conclusions

Categorisation is a phenomenon which presents itself as both an innate feature and one which can be learned over time through experience. While the effect has been observed in several different modalities, its presence in hearing and sound is of particular interest due to the implications it may have for conditions such as tinnitus. Implementation of a categorisation-based perceptual training paradigm could serve as a promising means of tinnitus management by reversing the changes in cortical plasticity that are seen in tinnitus, in turn altering the representation of sound within the auditory cortex itself. In the instance that the categorisation training is successful, this would likely mean a decrease in the level of activity within the auditory cortex (and other associated cortical areas found to be hyperactive in tinnitus) as well as a reduction in tinnitus salience, thus giving rise to a reduction in tinnitus severity and related distress. Whether passive or active training paradigms are applied, categorisation training is an avenue worth exploring. While the phenomenon is founded on relatively simple principles, it builds on current methods of sound-based therapies and offers a “next step/level” within this subset of tinnitus management strategies.

Chapter 5. The relationship between psychoacoustic tinnitus matching similarity, affect, and the perceptual uncanny valley phenomenon

5.1. Chapter Introduction

The pilot study (n = 22) presented in this chapter evaluated eight different tinnitus replicas based on 1) their ability to successfully replicate and reflect participant's true tinnitus experience, and 2) the degree of affect along a simple dimension of how much the individual disliked the matched sound. Methods and theories described in Chapter 3 were used to inform tinnitus matching and replica synthesis in this study. The purpose of this pilot study was to firstly establish the parameters vital to the generation of appropriate and realistic tinnitus replicas, and secondly understand the emotional affect of tinnitus replicas and investigate the uncanny valley effect in tinnitus matching. Insufficient evidence was obtained to support the existence of an uncanny valley in tinnitus matching. Pure tone based replicas had greater negative affect when compared to their noise-like counterparts. The high degree of variability in participant ratings reflected the heterogenous nature of tinnitus disorder; the study proposed that this highlights the need to adopt a tailored, personalised approach to tinnitus management. Although complex replicas of tinnitus (avatars) offered an accurate representation of participant's tinnitus sensation, simple pure tone and localisation replicas were also highly reflective of the tinnitus experience. While it was evident that tinnitus and its replicas gave rise to strong psychological responses, whether these responses were indicative of a low point in the perception of sound equivalent to the uncanny valley in vision or were simply a reaction to generally unpleasant sounds is unclear. The findings of this study informed the generation and implementation of the tinnitus avatar for sound therapy in the subsequent auditory categorisation training study (Chapter 6).

5.2. Introduction

Tinnitus is the perception of sound in the absence of an external physical source (Andersson et al., 2005; Henry et al., 2005). It is now widely understood that tinnitus is the result of plasticity of the central auditory and non-auditory pathways following injury to the auditory periphery (Eggermont & Tass, 2015; Kaltenbach et al., 2004; Noreña & Eggermont, 2003; Seki & Eggermont, 2003). After a peripheral lesion, a series of events within the auditory pathways commence that in turn lead to altered cortical activity and the perception of sound (Roberts, 2018). The magnitude of tinnitus is determined by differences in personality and activity within auditory, attention, memory, and emotion networks (Searchfield, 2014; Searchfield et al., 2012). About 10-15% of adults will experience chronic tinnitus (>6 months duration), with approximately 1% having a severely reduced quality of life (Axelsson & Ringdahl, 1989; Heller, 2003; Meikle et al., 1984) that can be described as "tinnitus disorder" (De Ridder, Schlee, et al., 2021). The heterogeneous nature of tinnitus makes it difficult to characterise and define (Cederroth et al., 2019). While a substantial proportion of the adult population suffers from tinnitus, no two individuals are likely to experience the exact same sensation. One person's tinnitus can sound different to another's (i.e., crickets, hissing, ringing). Tinnitus may be perceived to originate from different locations in or around the head (Baguley, Andersson, et al., 2013). The pitch or loudness may differ and the number of sounds perceived may not be the same (Cederroth et al., 2019). Various causal risk factors and related comorbidities contribute to tinnitus heterogeneity and the level of tinnitus related distress experienced by individuals (Cederroth et al., 2019). Furthermore, the effect of tinnitus management strategies varies substantially from person to person (Cederroth et al., 2019), and even between genders (Van der Wal et al., 2020), making it difficult for clinicians to determine the best treatment with confidence and anticipate its success.

Psychoacoustic measures such as pitch and loudness help to characterise a patient's tinnitus and understand its auditory attributes. Tinnitus characterisation is important for many reasons: to be able to demonstrate the patient's tinnitus and its features to both the patient and their family, to reassure the patient and their family that the tinnitus is real, to monitor possible changes in the tinnitus and its perception, to explore management options and discuss the route most beneficial for a given patient, to determine if a patient is likely to benefit from a particular treatment and/or the possible effects of that treatment on tinnitus and its perception, to reproduce the patients tinnitus for use in sound therapy and other such sound-based treatments, to aid in the understanding of the underlying aetiology and mechanisms of tinnitus, and to further the exploration and characterisation of different tinnitus subcategories (Henry, Flick, et al., 2004; Henry et al., 2013; Manning, Grush, et al., 2019; Nageris et al., 2010; Ristovska et al., 2019; Sandlin & Olsson, 1999; Schechter & Henry, 2002; Tyler, 2000; Vernon & Meikle, 2000).

While the importance of tinnitus characterisation is widely recognised, generating psychoacoustic matches or ‘replicas’ of tinnitus that are a true reflection of tinnitus is a challenge. Tinnitus is a complex sensation and as such is difficult to recreate. Tinnitus matching relies on the subjective response of the participant and ability to replicate the tinnitus experience using synthetic sounds (Bertet et al., 2013). Often a patient’s tinnitus will be ‘synthesised’ using simple methods that involve adjusting the frequency and intensity of a pure tone to match the pitch and loudness of the tinnitus (Graham & Newby, 1962; Henry & Meikle, 2000; Mitchell et al., 1993; Nageris et al., 2010; Penner & Klafter, 1992; Reed, 1960; Tyler & Conrad-Armes, 1983a). However, this form of matching may be too simplistic; it fails to identify the spatial location of the sensation and characterise important sound properties such as timbre and sound quality. Moreover, it only captures tonal tinnitus which is experienced by some – but not all – individuals; patients often describe a ringing or hissing sensation, and in some cases as more complex sounds like crickets (Meikle et al., 2004). Given the large degree of variability in the way in which people perceive and describe their tinnitus, there is a need for more complex replicas that encompass the tinnitus experience in its entirety. Attempts have been made to create a more ‘complete’ representation of the tinnitus sensation by using localisation techniques to define tinnitus in 3D space (Searchfield et al., 2015), incorporating several different sounds (Drexler et al., 2016), and using real-world or complex sounds (Kay & Searchfield, 2008).

An important dimension in developing clinically useable tinnitus replicas is the time required to create them. There must be a pragmatic trade-off between the detail possible versus time invested. Tonal matching is reasonably quick and easy to perform, however it offers a less precise reflection of the tinnitus sensation for some people. Generation of a complex replica of tinnitus (its “avatar”) may offer a more realistic copy of a patient’s tinnitus, but it may be more time consuming and difficult to perform. It is also possible that current simple “cartoon-like” tinnitus matches may be more readily accepted as a copy of tinnitus than very close avatars of tinnitus due to a phenomenon that has become known as “the uncanny valley”.

The uncanny valley theory was first proposed by robotics professor Masahiro Mori following his observation that robots that increasingly approach a human-like visual appearance, but fail to appear fully human-like, induce feelings of revulsion and uncanniness among people (Figure 4) (Mori et al., 2012). The uncanny valley has been of interest to the fields of robotics, film production, digital animation, and video gaming. The phenomenon can be an unwanted consequence of unconvincing computer-generated imagery (CGI), resulting in incidental eeriness and compromising the success of the production. An example of this has been observed in the films *Rogue One: A Star Wars Story (2016)* and *The Irishman (2019)* where CGI was used to recreate aging and/or deceased actors. A prequel to the original *Star Wars* movie filmed in 1977, *Rogue One* used CGI to digitally de-age the character of Princess Leia (Carrie Fisher), and recreate the character of Governor Wilhuff Tarkin, originally played by Peter Cushing who passed away in 1994. Similar techniques were used to de-age and adjust the faces of Robert De Niro, Al Pacino, and Joe Pesci in Martin Scorsese's *The Irishman.* Both films were criticised for an inadequate CGI which resulted in a failure to completely and accurately capture human behaviour, in turn giving rise to feelings of eeriness and unease among viewers (Haridy, 2016; Malone, 2019). In auditory perception the uncanny valley describes a low point in negative perception that a sound induces as it imperfectly resembles a real-life sound (MacDorman & Ishiguro, 2006; Mori et al., 2012). It appears that when a sound is close to reflecting a real-world natural sound, but fails to replicate it in its entirety, individuals experience feelings of uneasiness (MacDorman & Ishiguro, 2006). Often this can be beneficial, with the uncanny sound valley purposefully being used to induce feelings of discomfort and fear in horror films and video games (MacDorman, 2006).

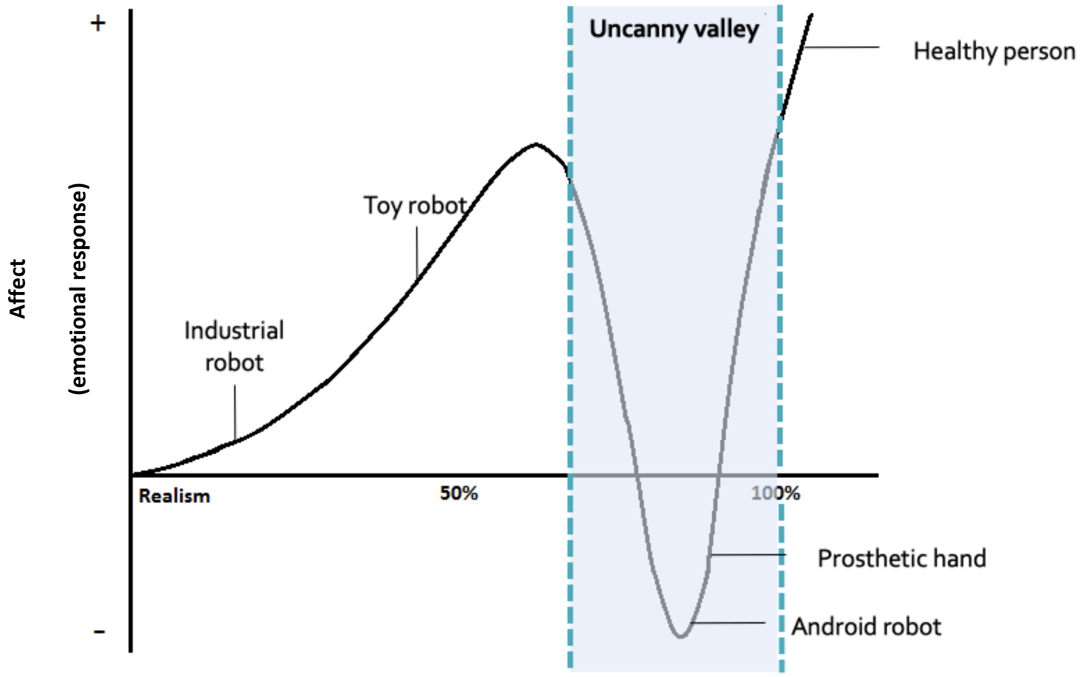


Figure 4. The Uncanny Valley graph, as proposed by Mori et al. (2012), depicting the relation between the realism of an object and an individual's emotional response to it. Adapted with permission from Mori et al., 2012, © 2012 IEEE.

Sounds that fall within the uncanny valley are known to induce negative feelings such as uneasiness, apprehension, and even terror, much in the same way that tinnitus does; as such, we hypothesise a similar effect to the uncanny sound valley in tinnitus matching and replica generation. In this study a variety of tinnitus replicas, ranging in complexity, were evaluated based on their ability to successfully replicate and reflect a participant's true tinnitus experience, as well as the degree of affect along a simple dimension of how much the individual disliked the matched sound.

It was hypothesised that:

1. A tinnitus avatar generated by matching frequency, intensity and spatial location would be the more similar to participant's tinnitus than a pure tone match.
2. Addition of the 3D spatial component would increase replica similarity.
3. The closer a sound came to replicating the tinnitus experience, without exactly matching, the more unpleasant the participant will find it.

5.3. Methods

This study was approved by the University of Auckland Human Participants Ethics Committee (UAHPEC; project reference UAHPEC1496). All participants gave written consent in accordance with the Declaration of Helsinki.

5.3.1 **Participants: recruitment and demographics**

Invitations were sent to 42 individuals recruited from a 'tinnitus volunteer database' that was composed following a tinnitus seminar to the general public. Twenty-two participants (12 male, 10 female, mean age = 54.4 years, *SD* = 12.5) responded and met recruitment criteria. The inclusion criteria were: adults aged 18 years or older, who suffered from chronic tinnitus (>6 months duration), and could communicate fluently in English. Participants who did not meet the eligibility criteria were excluded from the study; this included individuals who were under 18 years of age, those who experienced a fluctuating tinnitus or one that has been present for less than 6 months, those incapable of providing reliable subjective feedback on their tinnitus perception, and those with a hearing loss that is too severe for audible but safe levels of sound to be presented.

5.3.2 **Assessments: Tinnitus Functional Index and Tinnitus Sample Case History Questionnaire**

The Tinnitus Functional Index (TFI) and Tinnitus Sample Case History Questionnaire (TSCHQ) were administered to participants prior to conducting any psychoacoustic measurements. The TFI was used to assess the impact of tinnitus on daily life (Meikle, Henry, Griest, et al., 2012), while the TSCHQ offered information about patient's tinnitus histories and physical characteristics of their tinnitus (Langguth et al., 2007). The mean TFI score of participants was 48.1 (*SD* = 20.2), consistent with moderate-severe tinnitus (Meikle et al., 2012). The standardised instruments were completed online using REDCap® (web platform for generating, managing, and collating online surveys, www.redcap.fmhs.auckland.ac.nz).

5.3.3 **Audiological tinnitus assessment: Tinnitus Tester**

Custom LabView-based Tinnitus Testing software (Searchfield et al., 2015) was used for participant's tinnitus assessment. The LabView software used: simple, environmental, and virtual (3D) sounds to help characterise a participant's tinnitus and in turn build a more accurate, individualised tinnitus profile. The software contained a number of assessment interfaces which enabled the user to gain a detailed profile of the subjective tinnitus experience, including: audiometer function, tone/band noise pitch match, environmental sound match, and tinnitus location (3D).

Audiometer function

This function was used to perform the audiometric assessment (0.25 – 16 kHz), generate an audiogram, and determine whether a participant has a potential hearing loss that might contribute to tinnitus awareness.

Tone/Band noise pitch match

The *Tone/Band noise pitch match* interface was used to pitch-match tinnitus using tonal or noise stimuli. The interface used a 2-alternative forced-choice (2AFC) method to determine the pitch match. It enabled the user to select either a ‘pure tone’ or ‘uniform white noise’ sound for presentation, before adjusting the frequency and intensity of the sound using sliders. Once the type of sound, its pitch and loudness were determined, the sound was presented to the participant for evaluation.

Environmental sound match

The *Environmental sound match* allowed the user to generate a tinnitus match using environmental sounds. The user was able to select sounds from a pre-loaded library or chose to import sounds externally from the internet or an altogether different source. This sound could then be adjusted in terms of frequency and intensity (according to participant feedback) to determine a subjective tinnitus match.

Tinnitus location (3D)

The *Tinnitus location (3D)* function enabled the user to locate a participant’s tinnitus (derived from previous interfaces) in virtual 3D space for a spatial match of tinnitus percept.

5.3.4 **Study design/procedures**

Audiometry

Participants were seated in a sound-proof booth and fitted with Sennheiser HDA 200 circumaural headphones which were used throughout the session for both audiometric testing and sound presentation for tinnitus replica creation. Auditory thresholds were measured using the modified Hughson-Westlake procedure via the *Audiometer* function on the tinnitus testing software.

Creating the tinnitus replica

Eight tinnitus replicas were then generated for each participant and labelled: *pure tone* (PT), *noise*, *environmental* (Env), *environmental and pure tone* mix, *environmental and noise* mix, *pure tone and localisation* (PT + loc), *noise and localisation* (Noise + loc), and the tinnitus *avatar* (most complex copy of the tinnitus experience). The order in which each of the replicas was made and presented to the participants differed; for half of the participants, the replicas were generated in an order of increased sound (replica) complexity (namely *pure tone, noise, environmental, environmental and pure tone mix, environmental and noise mix, pure tone and localisation, noise and localisation, avatar*), while for the other half of the participants, the replicas were generated in a randomised order of sound complexity (*pure tone, noise, noise and localisation, environmental, environmental and pure tone mix, avatar, pure tone and localisation, environmental and noise mix*). The more complex sounds were formed using the simple replicas (i.e., *pure tone/noise*) as a foundation; if a participant perceived more than one tinnitus sound, they were asked to focus on replicating the most prominent (dominant) and/or debilitating tinnitus sound. Generation of the sounds is as follows:

Pure tone and Noise match

Using the *Tone/bandnoise pitch match* interface of the tinnitus testing software, a starting frequency and intensity was selected based on the participants audiogram and subjective description of their tinnitus experience. Selecting the 'sine' command on the interface allowed the user to present a pure tone sound, while selecting the 'uniform white noise' command enabled presentation of noise. The tinnitus testing software would present a 5 second sample of the sound to the participant, and feedback was received in terms of the participants opinion of the sound and how well they felt it reflected their tinnitus. Subsequent adjustments were made to the center frequency of the sound according to participant feedback, and a two-alternative forced choice method was implemented until a sound was generated that the participant was satisfied with and felt was as similar as possible to their tinnitus.

Environmental sound match

Using the *Environmental sound match* interface of the tinnitus testing software, an environmental sound similar to the participants tinnitus was selected based on participant's descriptions of their tinnitus (e.g., 'cicada-like', 'hissing', etc.). The sound was either selected from a royalty-free sound library that was pre-loaded onto the software, or if none of the sounds were found to match a participant's tinnitus, online sources were used to find a more suitable sound. Once a satisfactory environmental sound was obtained, it was adjusted using either the tinnitus testing software, Adobe Audition (audio editing software by Adobe Inc.), Audacity (free open-source digital audio editing software by The Audacity Team, www.audacityteam.org), or a mixture of the three audio-processing programs to achieve an environmental replica as similar to the participants tinnitus as possible. This often included adjusting the frequency, intensity, or tempo of the environmental sound.

Environmental sound with pure tone/Environmental sound with noise match

Using the *Environmental sound match* interface of the tinnitus testing software, it was possible to combine and present two sounds simultaneously. This was done for *environmental sound with pure tone and environmental sound with noise mixes.* If necessary, the resultant replica was exported from the tinnitus testing software and further modified according to patient instruction using either Adobe Audition or Audacity to obtain a replica as representative of the tinnitus as possible.

Pure tone with localisation/Noise with localisation match

The participant undertook a 3D spatial matching task using the established tonal or noise match. Matching the spatial location of a participant's tinnitus was conducted using a spatial matching task in the testing software and/or a 3D audio plugin function (anaglyph, www.anaglyph.dalembert.umpc.fr) in Adobe Audition. The selected sound was presented in 30° steps going from central (equal in both ears), to the right ear, toward the back of the head, around to the left ear, and back to center, all in a clockwise direction. Participants were asked to indicate when they felt the sound overlapped with their tinnitus in 3D space. For participants who reported a central tinnitus, standard stereo presentation was sufficient to reflect where they perceived their tinnitus. If necessary, the resultant replica was further modified according to patient instruction using either Adobe Audition or Audacity to obtain a replica as representative of the tinnitus as possible.

Tinnitus avatar match

Using the *Tinnitus location (3D)* interface of the tinnitus testing software, the tinnitus avatar was generated by combining several components of participant's tinnitus (pure tone or noise, environmental sound, and localisation). One of the two simple replicas (pure tone or noise) previously generated for the participant was chosen based on participant preference and similarity/affect scores and was 'blended' with their environmental replica. Once a satisfactory 'blended' sound was achieved, the resultant copy was presented at the exact location where the participant perceived their tinnitus (using the spatial matching protocol described above under '*Pure tone and localisation/Noise and localisation*'). The avatar was presented to the participant and, if necessary, further modified according to patient instruction using either Adobe Audition or Audacity to obtain a replica as representative of the tinnitus as possible.

Rating scales: similarity and affect

Once the final version of the tinnitus replica was obtained, the participant was asked to rate the sound based on two factors: 1. how similar they felt the sound was to their true tinnitus on a scale of 0 (completely dissimilar) to 10 (exact match), and 2. how much they liked the sound being presented on a scale of -5 (extremely dislike) to 5 (really like). The participant was instructed to once again listen to the sound presented and consider these factors before awarding the sound a final rating. All ratings (and any additional notes/comments) were recorded using REDCap®.

5.3.5 **Statistical analysis**

Responses obtained for the TFI, TSCHQ, and tinnitus replica ratings were auto-collated via REDCap® and were imported directly into Microsoft Excel for data refinement and analysis (descriptive statistics). Of the 22 responses obtained, two were excluded from data analysis; one as a result of failing to understand and follow instructions (P1), and one as a result of technical difficulties leading to incomplete data collection (P12). Only demographic data obtained from the TFI and TSCHQ was retained from these participants.

As the data failed to meet parametric assumptions (i.e., not normally distributed, ordinal data) the non-parametric Friedman Test was undertaken to investigate differences in similarity and affect ratings across the eight replicas using IBM® SPSS® Statistics 27 Software (SPSS Inc., Chicago, IL). In the case that the Friedman Test results indicated a statistically significant difference in ratings, post-hoc testing using individual Wilcoxon Signed Rank Tests with a Bonferroni correction were used.

5.4. Results

5.4.1 **Participant characteristics**

All participants had experienced bothersome tinnitus over a period of 6 months, with an average onset time of 14 years (*SD* = 17.0) (Table A1). Six out of the 22 participants (27.3%) experienced a unilateral tinnitus (22.7% left ear, 4.6% right ear), 11 participants (50%) had bilateral tinnitus (31.8% both but worse in left, 4.6% both but worse in right, 13.6% both ears equally), and 5 participants (22.7%) perceived their tinnitus as being inside their head. Tinnitus quality was most commonly described as tonal (27.3%), followed by cicadas (22.7%), hissing (13.6%), ringing or whooshing (9.1%), and other (18.4%). Seven out of the 22 participants (31.8%) related the initial onset of tinnitus to loud noise exposure, 6 participants (27.3%) to stress, one participant (4.6%) to head trauma, and one participant (4.6%) to a change in hearing. The remaining 7 participants (31.8%) felt there were other causes to the onset of their tinnitus. Out of the 22 participants, 54.5% had not tried any form of tinnitus treatment, while 22.7% had tried one treatment and 22.7% had tried several tinnitus treatments. Stress played a substantial role in modifying the tinnitus percept, with 72.7% of participants finding that it worsens their tinnitus. The remaining 27.3% of participants found it had no effect on their tinnitus. Ninety-one percent of participants did not wear hearing aids (only two participants wore hearing aids, one in their right ear, the other in their left). Measured tinnitus pitch was matched between 0.2kHz to 16kHz in participants, with 45% of participants matching their tinnitus to a pitch greater than 9kHz. Interestingly, 55% of participants matched their tinnitus to one pitch using a pure tone sound, and an altogether different pitch using noise.

5.4.2 **Tinnitus similarity matches**

The results of the Friedman Test indicated that there was no statistically significant difference in similarity ratings across the eight different tinnitus replicas, $\chi^2(2) = 8.54$, $p > 0.05$.

Overall, there appeared to be little agreement in similarity ratings among participants, as evidenced by the heterogeneous distribution of ratings across the scale (Figure 5A). The *pure tone and localisation* match obtained the highest median similarity rating (9), closely followed by the tinnitus *avatar* (most complex replica) and *environmental and noise* replicas, both of which had a median score of 8.5 (Figure 5A). While the *pure tone and localisation* replica had a higher median similarity rating, the tinnitus *avatar* was comparatively assigned higher scores by more participants (75% of ratings were between 7.25 and 10 for the *pure tone and localisation* replica while 75% of ratings sitting between 8 and 10 for *avatar*). The lowest median score was obtained by the *environmental and pure tone* and *noise and localisation* combinations (7.5).

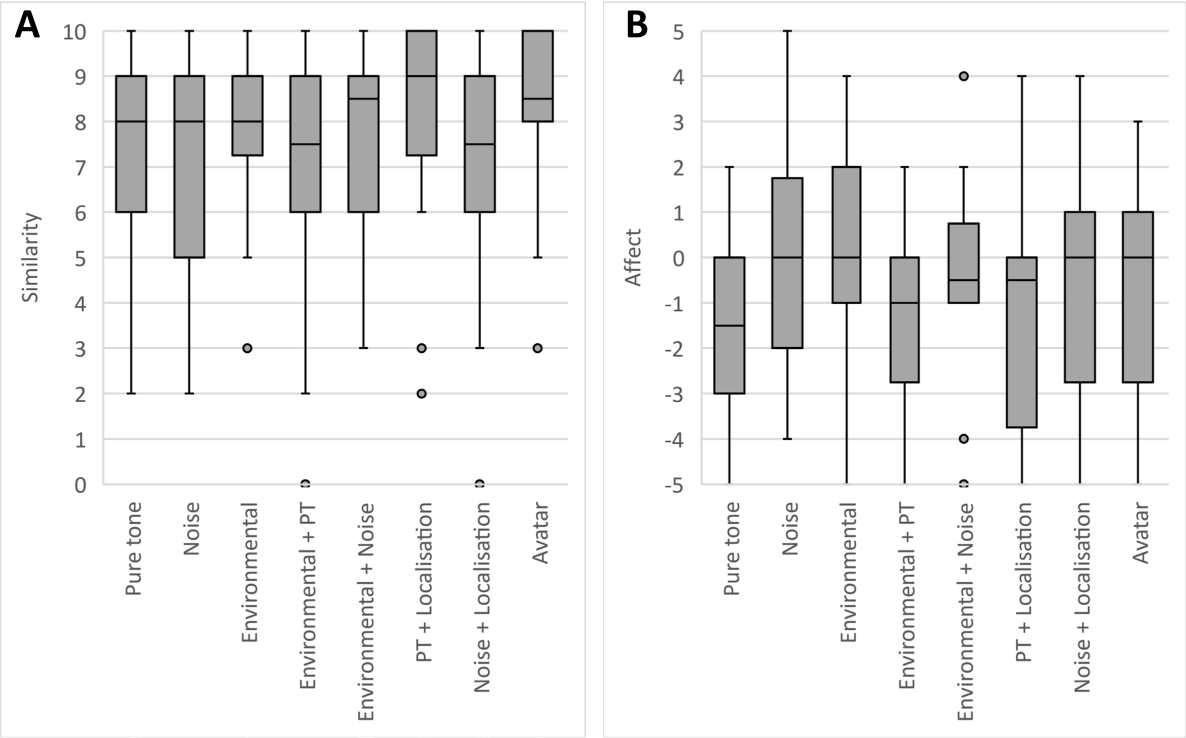


Figure 5. **(A)** Similarity and **(B)** affect ratings assigned to each of the eight different tinnitus replicas. The horizontal line within each box represents the median value of the replica scores, and the lower and upper boundaries reflect the 25th and 75th percentiles respectively. Lines (whiskers) extend to the most extreme values within 1.5 box-lengths from the upper and lower quartiles. Circles denote observations outside of this range (outliers). (PT: pure tone).

The majority of participants found the *environmental* replica to be a satisfactory representation of their tinnitus, with 75% of ratings sitting between a score of 7.25 and 10. Additionally, there is a high level of agreeability in similarity ratings for the *environmental* copy (IQR = 1.75). Comparatively, *noise* was experienced differently by participants resulting in variable ratings (IQR = 4) and was generally found to be a weaker match, with a quarter of participants finding the sound to be ‘poorly’ or only ‘somewhat’ representative of their tinnitus. Upon breaking replica ratings into ‘all pure tone versus all noise’ and ‘localisation versus no localisation’, no notable difference in ratings between sounds was observed.

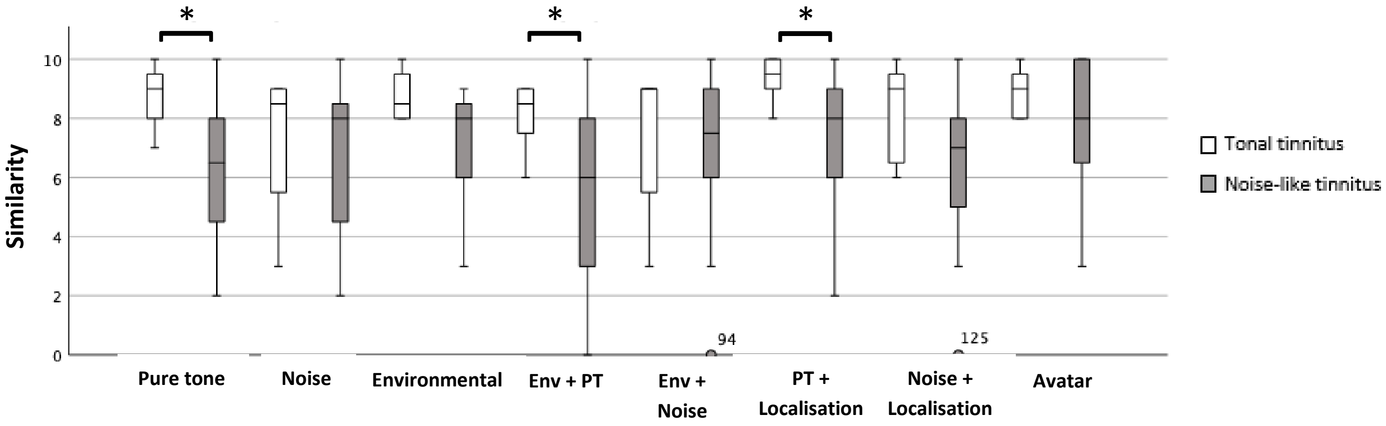


Figure 6. Similarity ratings for each of the tinnitus replicas subdivided/segregated by participants description of either tonal or noise-like tinnitus. Boxplot ranges defined as described in Figure 5. * $p < 0.05$. (PT: pure tone, Env: environmental).

Differences in similarity ratings were observed between participants who experienced tonal versus those who describe a noise-like tinnitus (Figure 6). A Mann-Whitney U test revealed that the distribution of replica similarity is the same across categories of tonal tinnitus vs. non-tonal tinnitus for all but three sounds: *pure tone*, *environmental and pure tone*, and *pure tone and localisation*. The *pure tone* similarity rating was greater for tonal tinnitus participants (Md = 9, n = 8) than for non-tonal tinnitus participants (Md = 6.5, n = 12), U = 19, z = -2.26, p = 0.025, r = -0.51. The *environmental and pure tone* similarity rating was greater for tonal tinnitus participants (Md = 8.5, n = 8) than for non-tonal tinnitus participants (Md = 6, n = 12), U = 22, z = -2.05, p = 0.047, r = -0.46. The *pure tone and localisation* similarity rating was greater for tonal tinnitus participants (Md = 9.5, n = 8) than for non-tonal tinnitus participants (Md = 8, n = 12), U = 20.5, z = -2.18, p = 0.031, r = -0.49.

The number of times each rating was awarded to the eight possible sounds offers insight into the rating distribution for a particular replica (Figure 7). The tinnitus *avatar* and *pure tone and localisation* replicas were awarded the most ‘exact match’ responses by participants and were also found to be the most satisfactory tinnitus replicas, with 90% of participants scoring the respective sounds a rating of 6 and above (Figure 7A).

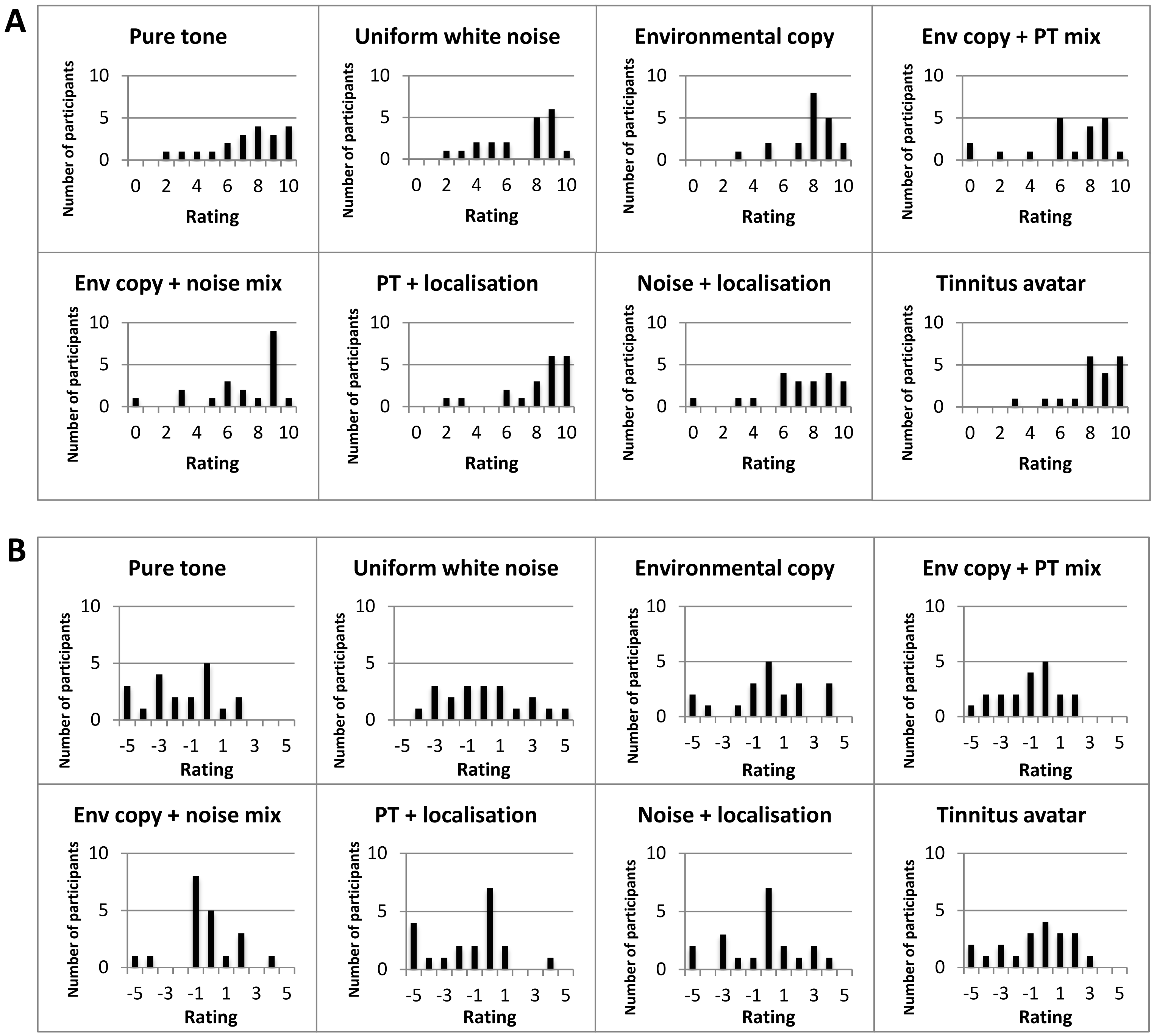


Figure 7. The number of participants that assigned a certain **(A)** similarity and **(B)** affect rating to each of the eight different sounds. The similarity data appears to be skewed to the right, with a tendency towards higher ratings.

All of the environmental replicas were highly rated, the addition of other factors to the environmental sound itself (i.e., pure tone or noise) resulted in a reduction in sound similarity to participant's tinnitus (Figure 7A). Furthermore, the *environmental and pure tone* and *environmental and noise* copies were the only sounds that received scores of zero, being found by some participants to be ‘completely dissimilar to their tinnitus’.

Differences in similarity ratings were observed between participants who were presented tinnitus replicas in an order of increasing complexity (termed ‘increasing order’) versus those who were exposed to the replicas in a random order of complexity (termed ‘random order’). A Mann-Whitney U test revealed that the distribution of replica similarity is the same across categories of sound presentation order for all but two sounds: *environmental and noise* and *avatar*. Participants who were presented sounds in a random order of complexity awarded higher ratings to both *environmental and noise* (Md = 9, n = 10) and *avatar* (Md = 9.5, n = 10) replicas when compared to participants in the increasing order group (*environmental and noise*: Md = 6, n = 10, U = 88.5, z = 3.06, p = 0.002, r = 0.68; *avatar*: Md = 8, n = 10, U = 85, z = 2.73, p = 0.007, r = 0.61). In general, participants in the random order group assigned higher ratings to replicas than those in the increasing order group. No significant trend was observed in terms of increasing level of similarity with increasing degree of sound complexity for either group.

5.4.3 **Affect**

The results of the Friedman Test indicated that there was no statistically significant difference in affect ratings across the eight different tinnitus replicas, $\chi^2(7) = 13.33, p > 0.05$.

The affect ratings for each sound are widely distributed, with almost all replicas obtaining scores spanning the entire rating range (Figure 5B). The *environmental and noise* combination was the exception to this, demonstrating a high level of agreeability among participants (IQR = 1.75). All sounds with the exception of *noise* and *environmental and noise* received a minimum affect score of -5. *Noise* was the only replica to reach the maximum score of 5 (really like). *Pure tone* was the most disliked copy (Md = -1.5), however it appears that in general the pure tone replicas were not highly rated for pleasantness by participants (*environmental and pure tone*: Md = -1, *pure tone and localisation*: Md = -0.5). Interestingly, adding the spatial element increased affect for the *pure tone* replica, and conversely decreased it for the *noise* replica.

A Mann-Whitney U test revealed no significant difference in affect ratings between increasing order and random order participants, as well as no significant difference in affect ratings between tonal tinnitus participants and non-tonal tinnitus participants. Comparing all pure tone copies (*pure tone, environmental and pure tone,* and *pure tone and localisation*) with all noise replicas (*noise, environmental and noise,* and *noise and localisation*), a Wilcoxon Signed Rank Test revealed that the noise ratings were significantly better rated in terms of affect (i.e., more likable) compared to pure tone replicas, $z = -3.14$, $p < 0.05$ (0.002), with a small effect size ($r = 0.29$). The median affect score for pure tone replicas was -1 compared to 0 for noise replicas. The most frequent affect rating assigned to almost all replicas was a neutral affect rating of 0, with the exception of the *noise* (-3, -1, 0, 1) and *environmental and noise* (-1) replicas (Figure 7B).

The *noise* replica was the only tinnitus copy that was awarded a high affect rating of 5, albeit by a single participant (Figure 7B). In general, the most common affect rating awarded was zero, with the exception of the *environmental and noise* copy (most common rating = -1). The *noise*, *environmental*, *noise and localisation*, and tinnitus *avatar* copies were almost equally liked and disliked; for instance, 45% of participants assigned *noise* replicas a score of -1 or less while 40% awarded the sound a score of 1 or more (*environmental* replica: 35% rated the sound -1 or less, while 40% rated the copy 1 or more, *noise and localisation* replica: 35% rated the sound -1 or less, while 30% rated the copy 1 or more, tinnitus *avatar*: 45% rated the sound -1 or less, while 35% rated the copy 1 or more). Comparatively, all of the remaining tinnitus replicas were more frequently disliked than liked; a score of 1 or more was assigned by only 25% of participants in the case of *environmental and noise* copies, 20% for the *environmental and pure tone* replica, and 15% for the *pure tone* and *pure tone and localisation* replicas. The *pure tone* and *pure tone and localisation* replicas in general appear to be the most disliked sounds.

5.4.4 **Replica ratings and the uncanny valley**

There was a large degree of variability among individuals in terms of replica ratings. The median similarity rating assigned by the group was 8, and the median affect rating was 0. Ratings were widely distributed across the entire scoring range. Most replicas were found to have some degree of similarity to the tinnitus percept, with few participants awarding the sounds scores at the ‘completely dissimilar’ end of the spectrum. Additionally, the majority of the replicas were found to be reasonably representative of the tinnitus sensation, with most of the group awarding scores of 6 and above for replica similarity. However, an increase in similarity corresponded to an increase in the variability of affect ratings, with replicas of a similarity of 6 and above generally being awarded affect scores across the entire rating spectrum (i.e., from -5 to 5). Replicas that were found to be an ‘exact match’ to the tinnitus sensation were most commonly found to be tolerable, with more than half of the participants awarding a score of 0.

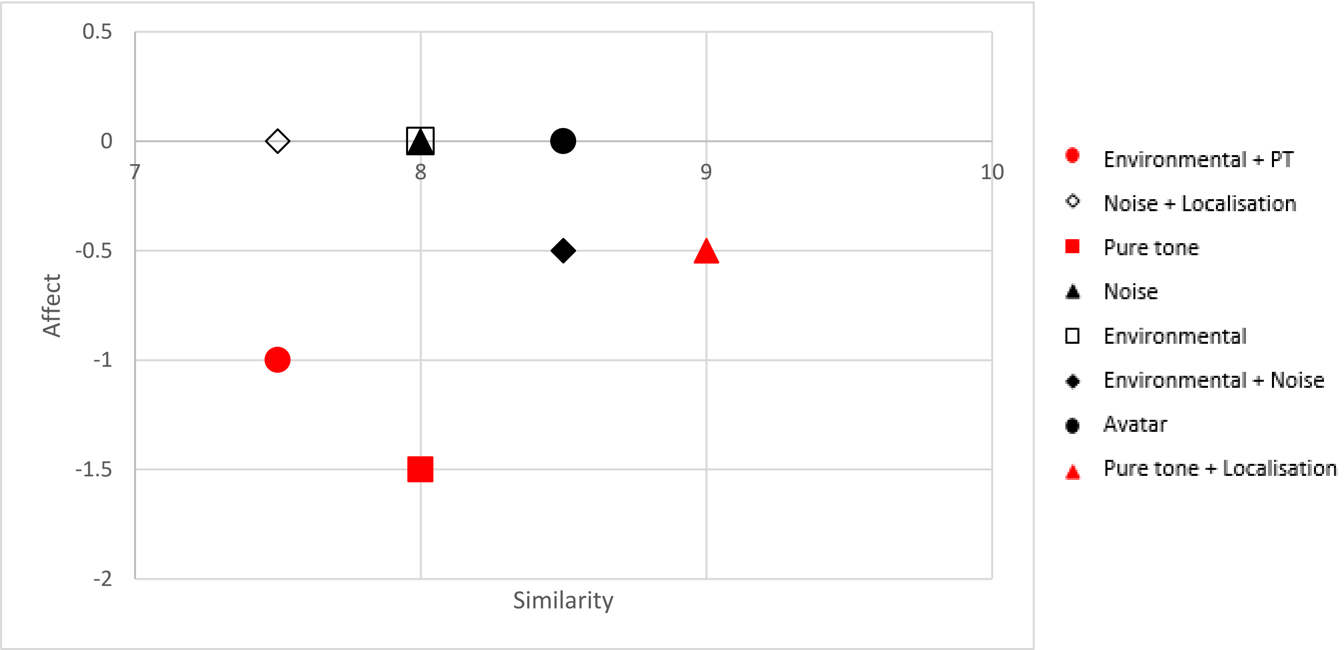


Figure 8. Interpretation of the similarity and affect ratings within the context of the uncanny valley. Each point along the continuum represents the combined similarity and affect rating for a given sound as determined by the median similarity and affect scores. Pure tone based replicas are depicted in red.

Contemplating the presence of an uncanny valley effect within each individual sound, there is no clear ‘valley’ that can be observed (Figure 8). While the *pure tone and localisation* replica offered the most accurate representation of participant’s tinnitus, it stands that in comparison to their non-tonal counterparts, pure tone based replicas are in general more poorly received by individuals (as evidenced by their negative affect scores). Interestingly however, while the tonal replicas display a response pattern where there is an increase in affect with an increase in similarity, the opposite is seen in the noise replicas.

5.4.5 **Case-by-case scenarios**

Considering the ratings assigned to each of the eight different tinnitus replicas, it is evident that there is a substantial amount of variability between participants (Figure 9). Participant P6 described experiencing a whistling tinnitus, and had their tinnitus completely matched using pure tone (10) and pure tone and localisation (10) replicas. The participant felt that none of the other replicas truly encompassed their experience, least of all noise-based replicas. The replicas which best matched P6’s tinnitus were the most disliked sounds, receiving a likability rating of -5 (really dislike).

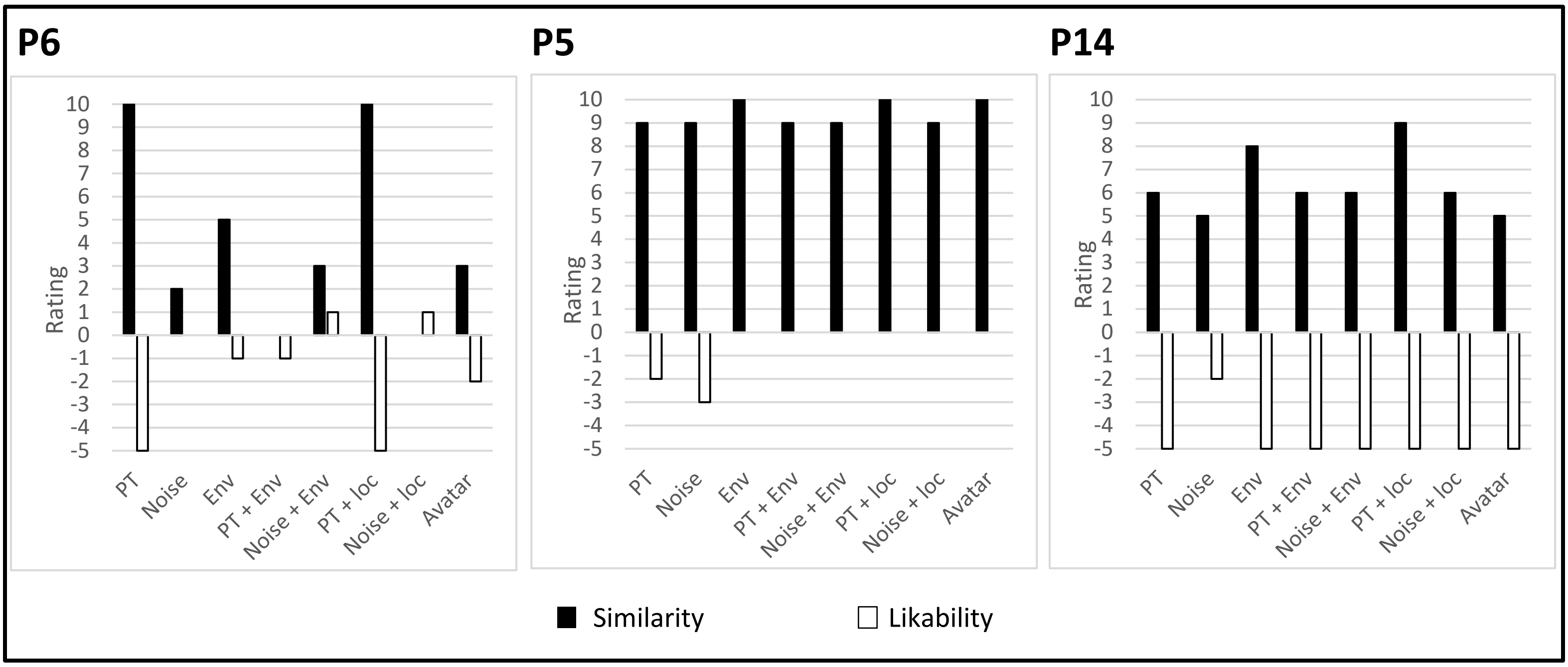


Figure 9. Similarity and likability ratings assigned to each of the eight different tinnitus replicas by three participants: P6, P5, and P14. A considerable degree of response variability can be observed between the three individuals. P6 had a ‘whistling tinnitus’ which was completely matched by the pure tone and pure tone + localisation replicas; these replicas were also the most disliked sounds. P5 had a tonal tinnitus which was satisfactorily replicated by all eight sounds. The majority of the sounds were found to be tolerable by P5, apart from the pure tone (-2) and noise (-3) copies. P14 had a cicada-like tinnitus which failed to be completely matched by any of the eight sounds, however was closely matched by the pure tone + localisation replica (9). All of the sounds were very much disliked by P14. (PT: pure tone; Env: environmental; loc: localisation).

P5 had a tonal tinnitus that was completely matched using environmental (10), pure tone and localisation (10), and tinnitus avatar (10) replicas (Figure 9). Despite their obvious differences, the participant felt that all of the sounds presented reflected their tinnitus to a relatively high degree (i.e., all sounds received a rating of 9 or above). Furthermore, the majority of the sounds were found to be tolerable by P5, apart from the pure tone (-2) and noise (-3) copies.

P14 described experiencing a cicada-like tinnitus that failed to be exactly replicated using any of the available sounds (Figure 9). While participant P14's tinnitus was closely matched using the pure tone and localisation replica (9), none of the sounds were found to be successful in matching what the participant truly experienced. All of the replicas (with the exception of noise, -2) were highly disliked by P14, receiving a likeability rating of -5.

5.4.6 **Uncanny valley in single case data**

Observing the affect of a sound as it gets closer to reflecting the tinnitus experience reveals different response patterns among individuals (Figure 10). It is evident that there is a large degree of variability in ratings, both within and between each case. P6 reflects a participant who increasingly dislikes the replicas presented as they become more similar to the tinnitus percept (confirmed by a decelerating trend). The greatest level of dislike (-5) is reached when an 'exact match' (10) is obtained. The mean affect rating (level) for the replicas is -1.5, with the ratings ranging from -5 to 1. In contrast, P13 portrays the responses of a participant who initially dislikes the tinnitus replicas, before finding them more likable as they increasingly reflect the tinnitus experience, and then perceiving them as tolerable when they reflect the tinnitus in its entirety (affect 0, similarity 10). The mean affect rating (level) for participant P13 is 0, with the ratings ranging from -5 to 3. P15 reflects a participant who has an increasingly positive response to sounds as they become more representative of their tinnitus (i.e., the better a replica reflects their tinnitus, the more they like it). This observation is confirmed by an accelerating trend. The mean affect rating (level) awarded by participant P15 is 1.6, with their ratings ranging from -2 to 4.

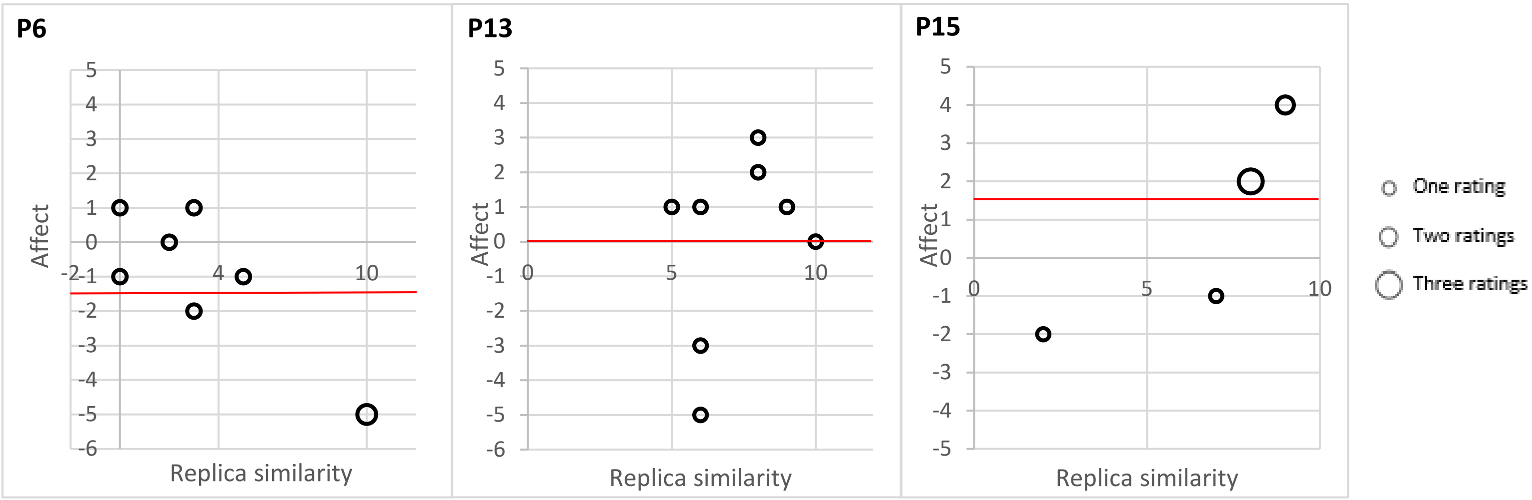


Figure 10. Interpretation of the similarity and affect ratings within the context of the uncanny valley for three individual participants: P6, P13, and P15. Size of marker reflects number of replicas assigned the same rating. Participant P6's results suggest that as the replica became more representative of their tinnitus, they disliked it more. Conversely, P13's ratings indicate an initial dislike of replicas that failed to reflect the tinnitus sensation in its entirety, followed by an increase in affect as the degree of similarity to the tinnitus is increased, before returning to a affect score of 0 at the exact match replica. P15's ratings indicate an increase in affect as the degree of similarity to the tinnitus sensation increases. Red line represents the mean affect rating (level) for each participant.

Stability analyses conducted on the data indicate a high degree of variability in the ratings awarded to each of the eight sounds by the three participants, suggesting that sounds of different similarities generally received different affect ratings and that most of the ratings were not clustered around the mean. Assessing the percentage of non-overlapping data, there is a high level of overlap between participant P6-P13, and P13-P15, suggesting that the range within which the participants rated the replicas is similar. Cases P6-P15 had a low level of overlap, indicating comparatively variable rating ranges between the two participants.

5.5. Discussion

This study evaluated the ability of several tinnitus replicas to match the true tinnitus experience as well as their affect in an attempt to discern whether a perceptual valley exists in the context of tinnitus. No statistically significant differences in ratings were found across the eight tinnitus replicas for both the similarity and affect ratings. There was a large degree of variability among the scores awarded to each sound, making it difficult to infer how participants feel about a particular replica and why this might be. Insufficient evidence was obtained to support the hypotheses of this study: 1. A tinnitus avatar generated by matching frequency, intensity and spatial location would be the more similar to participant’s tinnitus than a pure tone match, 2. Addition of the 3D spatial component would increase replica similarity, and 3. The closer a sound came to replicating the tinnitus experience the more unpleasant the participant will find it. There are several noteworthy findings which should be explored in more depth in the future.

The findings of this study build on our current understanding of tinnitus replicas and their synthesis, offering insight into avenues worth investigating. Individuals experiencing a tonal tinnitus rated pure tone based replicas as being significantly more similar to their tinnitus in comparison to individuals with non-tonal tinnitus. Furthermore, there was a trend for stronger negative affect to pure tone based sounds. The results emphasise the importance of personalisation in tinnitus therapy and implore researchers/clinicians to consider the trade-off between replica similarity and affect when creating tinnitus replicas. The following discussion will evaluate and contemplate these outcomes more thoroughly.

5.5.1 **Tinnitus replicas: from simple copies to avatars**

The generation of realistic tinnitus replicas is a difficult process. There is also a trade-off between the benefit in detail versus time invested, where generation of simple tinnitus copies is easier and faster but less likely to reflect the tinnitus experience, while generation of complex tinnitus copies is likely to encompass tinnitus to a greater degree, but is more taxing and time consuming (Vajsakovic, Maslin, & Searchfield, 2021). Considering the median similarity ratings, it appears that the pure tone and localisation match offers the most accurate representation of the tinnitus experience (Figure 5A). Additionally, the success of the avatar in recreating the tinnitus experience is also evidenced by 75% of participants awarding the replica a score between 8 and 10 (cf. 75% of scores sitting between 7.25 and 10 for the pure tone and localisation copy). The avatar was considered to be the most complex copy of the tinnitus sensation, incorporating several features (e.g. pitch, loudness, spatial localisation, sound texture) to generate the most accurate representation of a participant’s tinnitus (Searchfield, 2014). In our sample less complex replicas such as pure tone and localisation offered an equally effective means of capturing the tinnitus sensation. Additionally, the pure tone and localisation copy was most frequently awarded ratings between 9 and 10 for sound similarity, representing 60% of all pure tone and localisation ratings (vs only 35% of all pure tone ratings. Bertet et al. (2013) evaluated three different methods of tinnitus synthesis: two semi-automated protocols based on a participant’s auditory threshold, and a simple manual ‘single pitch match’ method, reporting similar outcomes to those found in this study. The researchers noted that while the manual method failed to capture the complex nature of tinnitus and only reflected the dominant pitch of tinnitus, it performed comparatively better than the more advanced semi-automated methods. It may be that in striving to make more complex copies, we lose the basic aspects and features of the tinnitus sensation.

Although more than half of the participants described their tinnitus sensation as being non-tonal (i.e., variations of descriptors such as hissing, crickets, static, etc.), the majority appeared to be satisfied with the pure tone and localisation replica regardless of how they perceived their tinnitus, with 90% of participants scoring the match a rating of 6 and above. Unsurprisingly, individuals who described having a tonal tinnitus rated pure tone based sounds (i.e., pure tone, environmental and pure tone, and pure tone and localisation) as being statistically more similar to their tinnitus than persons with non-tonal tinnitus (Figure 6). This is to be expected, as the psychoacoustic properties of the pure tone replicas is fundamentally more similar to tonal tinnitus than noise-like tinnitus, and as such should be able to capture the experience more accurately for tonal tinnitus participants than their non-tonal counterparts. This stands in favour of a ‘tailored-therapy’ approach and highlights the need for personalisation in tinnitus management as necessitated by the heterogeneous nature of the disorder; given that no two individuals experience tinnitus in the same manner, we cannot realistically expect to find a ‘one size fits all’ replica or treatment (Cederroth et al., 2019).

While the pure tone and localisation replica offered the most accurate representation of a participant’s tinnitus, it had negative affect. The pure tone replicas were in general poorly received by participants, obtaining significantly lower affect scores compared to the noise replicas (Figure 5B). The fact that participants demonstrated a more positive response toward noise-like sounds than their tonal counterparts comes as no surprise; noise has been used for tinnitus masking for decades (Sandlin & Olsson, 1999; Vernon & Meikle, 2000). Masking could explain why matching to noise and environmental sound based stimuli had the least negative affect. Most therapeutic strategies do not require the treatment sound to be an accurate representation of participant’s tinnitus, so the inability of noise to appropriately capture the tinnitus experience is not concerning. Choosing the level of replica complexity may depend on the purpose of the replica: what it is going to be used for, what it is trying to achieve, the duration of its application.

5.5.2 **Spatial component**

While the spatial element of tinnitus is a relatively unexplored component of the percept (cf. pitch/loudness), presenting the sound in the same 3D location where the participant experiences their tinnitus enables generation of a more personalised and accurate replica (Searchfield et al., 2015). Building on basic pitch-matched copies by incorporating the spatial element of the percept gives rise to a replica that not only offers more information about the individual's tinnitus experience, but is also closer to replicating the sensation in its entirety (Searchfield et al., 2015).

Although no significant difference in either similarity or affect scores was identified following the addition of the spatial component, similarity ratings revealed that introduction of the spatial element increases the degree to which a sound reflects the tinnitus experience in the case of the pure tone replicas, and conversely decreases similarity in the case of noise replicas. It is unclear as to why this might be; perhaps the broadband nature of noise-like sounds makes it difficult for them to be localised appropriately. It is thought that providing an appropriate 3D representation of tinnitus might allow the sensation to be perceived as a normal sound, in turn making the tinnitus more 'real' (Searchfield, 2014; Searchfield et al., 2015). This notion is appealing as it means that tinnitus localisation matches could have a potential use in tinnitus management by supplementing counselling and/or as a novel method of sound therapy.

5.5.3 **Interindividual variability: no 'one size fits all' replica**

It is clear that there was a large degree of variability in the ratings assigned to each of the eight sounds across the 20 participants (Figure 5). A replica that captured the tinnitus in its entirety for an individual describing tonal tinnitus completely failed to replicate the sensation of a different individual reporting tonal tinnitus. Similarly, some participants were easily pleased with all replicas, awarding them high scores, while others failed to be satisfied by any of the replicas. An example of this was observed comparing participants P5 and P14 (Figure 9); P5 assigned scores of 9 or above to all sounds despite their obvious differences. Additionally, this participant found all the sounds to be tolerable, with the exception of pure tone (-2) and noise (-3). Conversely, P14 felt that none of the sounds captured the tinnitus experience in its entirety, and completely disliked all of the replicas presented. Even at an individual level there is no predicting the outcome of sound rating; a participant might find that the *pure tone* replica sounds exactly like their tinnitus, but feel that the *pure tone and* *localisation* replica is completely dissimilar to it. It is not obvious as to why this is; it would make sense that if localisation is achieved, the replica should be *more* similar as it mimics both the psychoacoustic properties of tinnitus as well as its spatial aspect. The same observation applies in terms of affect; P5 disliked the *noise* replica, awarding it a -3 on the affect scale, however found the replica tolerable once the spatial aspect was added (*noise and localisation* = 0) (Figure 9). Perhaps there is a unique form of interaction between the tinnitus and the spatially-matched sound that alters its perception; efforts should be made to better understand these findings in the future.

5.5.4 **Uncanny valley**

According to Mori's uncanny valley theory (Mori et al., 2012), sounds that come close but fail to resemble real-world sounds in their entirety are perceived in a negative manner. Some individual participants demonstrated what might be expected according to the uncanny valley theory; with an increase in replica similarity came a decrease in affect (Figure 10). Sounds which had the highest similarity score (namely *pure tone* and *pure tone and localisation*) also gained the lowest affect scores. This can also be noted when observing the similarity and affect ratings within the context of the uncanny valley; P6 increasingly dislikes the replica as it becomes more representative of the tinnitus sensation, awarding the 'exact match' sound a 'completely dislike' score of -5. There were three repeated patterns of response toward the tinnitus replica (Figure 10). One, a reduction in affect with increasing similarity, has already been mentioned. The remaining two are: an increase in sound tolerability with an increase in tinnitus similarity, and an increase in affect concurrent with an increase in similarity. Participant P13 reflects an increase in sound tolerability as the replica becomes more representative of the tinnitus (Figure 10). Initially there is a reduction in affect around the 'neither similar nor dissimilar' point of the similarity spectrum, before an increase in affect around a similarity score of 8. However, as the similarity approaches the 'exact match' score, there is a reduction in sound affect to a score of 0. P13 represents a subset of participants who feel that the closer the sound is to their tinnitus, the more they 'don't care for it'. A similar finding was reported by Pineda et al. (2008) who noted that applying a tinnitus replica in a customised sound therapy approach actually minimised discomfort and was well tolerated by their participants. This increase in sound tolerability that comes about with an increase in tinnitus replica similarity might be indicative of a learned tolerance toward tinnitus by individuals. Participant P15 is an example of a steady increase in sound affect with an increase in similarity. P15 represents a subset of participants who increasingly like sounds that are more reflective of their tinnitus sensation as they are familiar with their tinnitus and as such are more comfortable with listening to sounds that share similar features to it. While it is possible that there are three common patterns of response – not unlike what has been observed with tinnitus masking (Feldmann, 1971) – further work using a greater study population is required to determine if this indeed is the case, and if so how it might inform tinnitus synthesis.

The issue that arises when considering the role of the uncanny valley in tinnitus is the notion that perhaps the reduction in sound affect that is seen as the sound becomes more representative of the tinnitus might not actually be a reflection of the uncanny valley phenomenon; rather, it might reflect the fact that tinnitus is negatively perceived in the first instance. Tinnitus is often described as a ringing, hissing, static, screeching, or cicada-like sound (Meikle et al., 2004); these sensations are not commonly regarded as being pleasant or relaxing. As such, perhaps what might be interpreted as the uncanny valley is in fact simply the case of an aversion toward a generally unpleasant sound, and distraction or masking from noise like sounds.

Considering the overall group results for the similarity and affect ratings within the context of the uncanny valley, it is difficult to make concrete statements and observations given the lack of an obvious trend and large degree of variability among individual scores. What is clear is that the resulting graph (Figure 8) is far from having an 'uncanny' resemblance to the trends described by Mori et al. (2012). Most replicas were found to have some degree of similarity to the tinnitus percept, with few participants awarding the sounds scores at the 'completely dissimilar' end of the spectrum (Figure 7). Additionally, the majority of the replicas were found to be reasonably representative of the tinnitus sensation, with most of the group awarding scores of 6 and above for replica similarity. This suggests that an 'exact match' for tinnitus is not necessarily reflected by one single replica, but rather is a status that can be held by several replicas which, in their own ways, reflect the sensation to a high degree. More specifically, replica generation does not have to be an 'all or nothing, hit or miss' process where hours are invested in tweaking and producing a single ideal tinnitus copy; rather, there is enough 'wriggle room' to generate several replicas that equally appropriately reflect the experience.

It seems that an increase in similarity leads to an increase in the variability of affect ratings, with replicas of a similarity of 6 and above generally being awarded affect scores across the entire rating spectrum (i.e., from -5 to 5). Perhaps the more similar a replica is to the participant's tinnitus, the more their response reflects their psychological reaction to their tinnitus (as shaped by the individual's personality traits, safety behaviours, and beliefs (Brüggemann et al., 2016; Durai & Searchfield, 2016; McKenna et al., 2014), rather than their opinion of the particular sound. Namely, if a sound is dissimilar to an individual's tinnitus, the individual will likely judge the affect of the sound solely on the basis of the sound itself (i.e., how pleasant it is to listen to); however, if the sound increasingly resembles the individual's tinnitus, the individual's affect rating of the sound is likely influenced by their own view of their tinnitus and the relationship they foster with it. This finding underlies psychoacoustical models such as the adaptation level theory of tinnitus proposed by Searchfield et al. (2012) which posits that stimuli do not act as singular entities, but instead interact with and influence each other (Helson, 1964). According to Searchfield and colleagues (2012), tinnitus intensity as perceived by an individual is dictated by several factors, not the least of which being their personality. The experiences, ideals, interpersonal relations, learning, attitudes, and emotional and intellectual behaviour of a patient shape their 'frame of reference', which in turn governs their response to stimuli.

An increase in sound similarity does not necessarily translate to a decrease in sound affect (Figure 10). Replicas that were found to be an 'exact match' to the tinnitus sensation were most commonly found to be tolerable, with more than half of the participants awarding a score of 0; this reflects one of the three profiles mentioned earlier in the discussion. Generally, replicas sitting between the 4-6 point of similarity tended to receive more negative affect scores (i.e., were more disliked). It might be that sounds that are neither reflective of the tinnitus nor completely dissimilar to it give rise to negative feelings as they are hard to place; the replicas sitting at this point along the spectrum are neither distinct from the tinnitus, nor are they indistinguishable from the sensation. As such, they may induce feelings of confusion and discomfort, a dislike for the 'unfamiliar'. Additionally, the more complex a sound becomes, the more difficult it becomes to manipulate its properties without distorting the replica. This issue was noted with the generation of environmental replicas, where real-world natural sounds had to be adjusted in pitch and/or tempo to match the participants tinnitus. These changes in pitch or tempo can seriously disfigure the sound, resulting in the generation of a sound that is not only very much dissimilar to the tinnitus, but also strange and somewhat uncanny. The resulting replica would often be extremely distorted, sounding electronic and being very disturbingly unpleasant. Even in cases where it would reflect the tinnitus, it would not be ‘quite right’, sounding unnatural. Perhaps this is the ‘uncanny valley’ or, more accurately, ‘uncanny region’ of tinnitus, suggesting that the uncanny valley relates not to sound complexity/similarity but rather sound quality.

Unlike the Mori et al. (2012) graph, there is no obvious increase in affect for simple but familiar sounds followed by a decrease in affect denoting the uncanny valley, where the replica is reflective of the tinnitus signal. This might reflect the fact that sounds aimed at mimicking the tinnitus experience are ‘set up to fail’ in the sense that they are likely to be perceived in a negative manner from the very beginning. Tinnitus is not a pleasant experience; therefore, any replica, irrespective of its level of complexity and similarity to the tinnitus, is likely to receive a negative response. Perhaps this highlights the need for restructuring the uncanny valley graph and modifying it so that it is more appropriate for evaluating the uncanny valley in tinnitus. Rather than measuring the replicas using an ‘affect’ scale, it might be more sensible to use something like a ‘tolerability’ or ‘comfort’ scale; in other words, assessing how tolerable the presented sound is or how comfortable the participant feels listening to the sound.

5.6. Summary

Although insufficient evidence was obtained to support the existence of an uncanny valley in tinnitus matching, the findings build on our current understanding of tinnitus replicas and their synthesis, offering insight into avenues worth investigating. Further work is required to confirm the observations mentioned in this study and in turn inform tinnitus synthesis and, as an extension, tinnitus profiling. The tinnitus experience can be appropriately replicated to a high degree using both complex (avatar) and simple (pure tone and localisation) replicas. Pure tone based replicas had greater negative affect when compared to their noise-like counterparts; we hypothesise that this response to pure tone based replicas reflected the dislike of pure tone sounds, while the less negative affect to noise-like replicas is due to tinnitus masking. The high degree of variability in participant ratings is reflective of the heterogenous nature of tinnitus disorder which necessitates a tailored, personalised approach to management. While it is evident that tinnitus and its replicas give rise to strong psychological responses, whether these responses are indicative of a low point in the perception of sound or are simply a reaction to generally unpleasant sounds remains unclear. Future studies should consider the effects of matching sounds in modifying tinnitus, confounding the matching process; objective measures of perceptual processing should be used to explore these possibilities.

Chapter 6. Electrophysiological and behavioural evidence of the effects of white noise and a progressive re-categorisation sound therapy on tinnitus

6.1. Chapter Introduction

The auditory categorisation training study (n = 29) presented in this chapter is a randomised tinnitus sound therapy trial comparing the effects of an effortless auditory categorisation training paradigm to conventional sound therapy using white noise. Theories forming the basis of this study were described by the auditory categorisation review (Chapter 4), and the methods used were informed by the pilot study (Chapter 5). The purpose of this study was to elucidate whether there are any differences and/or benefits in the implementation of a personalised effortless categorisation training approach relative to conventional sound therapy using broadband noise (BBN). White noise sound therapy resulted in significant improvements in tinnitus impact, severity, and negative emotionality independent of counselling. Categorisation training did not give rise to statistically significant changes in tinnitus impact. Nine participants from the white noise group and three from the categorisation training group achieved a clinically meaningful improvement in tinnitus severity (determined by a 13-point reduction in TFI score). Acute sound therapy using white noise gave rise to changes within the default mode network (specifically within the angular gyrus), while acute effortless auditory categorisation training led to an overall reduction in activity at the level of the prefrontal cortex, as well as a decrease in gamma-band activity within the auditory cortex. The study posits that the different neural changes observed using white noise sound therapy relative to auditory categorisation training indicates that the two modes of sound therapy potentially work through different mechanisms or neural pathways, in turn targeting different neural structures. An artificial intelligence Spiking Neural Network (SNN) machine learning efficiently identified and differentiated between therapeutic responders and non-responders with a high level of accuracy (overall classification accuracy was 89.44% for responders and 93.57% for non-responders). While these findings are encouraging, further work is required to discern the optimal design and method of application of simple (BBN) and complex (categorisation) modes of sound therapy, and understand long-term treatment-related neural changes.

6.2. Introduction

Despite decades of research, complete understanding of the pathophysiology and treatment of chronic subjective tinnitus has eluded researchers. Over 740 million adults experience tinnitus globally, with more than 120 million individuals considering it to be a major problem (Jarach et al., 2022). Davis and El Refaie (2000) conducted one of the largest (n = 48,313) and most reliable tinnitus prevalence studies and found tinnitus prevalence to sit at 10.1%, with 2.8% of respondents reporting a moderately annoying tinnitus experience, 1.6% describing a severely annoying tinnitus experience, and 0.5% claiming it severely affected their ability to lead a normal life. It is clear that while a considerable portion of the population hear tinnitus, only a subset of individuals experience tinnitus that causes emotional distress, cognitive dysfunction, and/or autonomic arousal - in what has been described as “tinnitus disorder” (De Ridder, Schlee, et al., 2021). The difficulty researchers and clinicians have faced when understanding tinnitus disorder is its heterogeneity in perceptual characteristics, etiological factors, and comorbidities (Cederroth et al., 2019; De Ridder, Schlee, et al., 2021). It is difficult to design and implement a treatment strategy when treatment response varies a great degree between patients. As such, it is no surprise that tinnitus has accumulated a diverse repertoire of management options throughout the years (see *Chapter 2.2 Phantom sound: An overview of tinnitus and tinnitus disorder* for a detailed review of tinnitus management strategies). While there is no gold standard for tinnitus management, current practice recommendations involve prescribing sound therapy (and hearing aids/amplification where required) in combination with counselling (Bauer & Brozoski, 2011; Cuesta et al., 2022; Hyun et al., 2022; Makar et al., 2017; Searchfield et al., 2010; Tyler et al., 2020; Zenner et al., 2017).

Sound therapy for tinnitus has a very long history (Stephens, 2000), and has been possible in a wearable form since the late 1970s (Vernon, 1977, 2000) primarily with the aim of alleviating tinnitus distress. Sound therapy action may be by reducing audibility through masking the tinnitus percept either fully (Vernon, 1977) or partially (Jastreboff, 2015; Jastreboff & Hazell, 1993; McKinney et al., 1995), promoting habituation (Jastreboff, 2000; Jastreboff & Hazell, 1993), altering aberrant cortical activity (Eggermont & Tass, 2015; Noreña & Eggermont, 2005; Tass et al., 2012), or offering a sense of relaxation and relief through managing emotional response (Dineen et al., 1997; Handscomb, 2006). While a recent study found sound therapy to be successful in tinnitus management irrespective of counselling (Tyler et al., 2020), there is currently no consensus in terms of the most appropriate and therapeutically effective auditory stimuli for sound therapy, and questions have been raised with regards to whether benefits of the therapy are truly independent of psychological effects (Brennan-Jones et al., 2020; Hobson et al., 2012; Li et al., 2019). Regardless of these caveats, sound therapy remains one of the most prevalent means of tinnitus management due to its accessibility, usability, and cost-effectiveness (Hoare et al., 2013; Hoare, Gander, et al., 2012). Many sounds have been trialled in sound therapy paradigms including broadband noise (BBN) and narrowband noise (NBN) (Kim et al., 2014; Pienkowski, 2019; Searchfield et al., 2022), fractal tones (Simonetti et al., 2018; Sweetow & Jeppesen, 2012), music (Davis et al., 2008; Hann et al., 2008; Okamoto et al., 2010; Stein et al., 2016), and real-world natural sounds (Aydin & Searchfield, 2019; Barozzi et al., 2016; Durai, Doborjeh, et al., 2021; Durai & Searchfield, 2017). However, white noise tends to be the preferred treatment sound and is often implemented in masking strategies for tinnitus (Henry et al., 2008; Hoare, Gander, et al., 2012; Hoare, Searchfield, et al., 2014; Hobson et al., 2012; Wang et al., 2020). While a recent review discouraged the use of white noise for tinnitus therapy on the basis of it potentially inducing maladaptive neuroplastic changes throughout the auditory system (Attarha et al., 2018), there is little evidence to support this hypothesis, and a plethora of research and clinical experience suggests otherwise (Folmer, 2019; Searchfield, 2021).

Although white noise might not be detrimental to hearing health or tinnitus severity, studies contrasting its efficacy against other sound therapy stimuli have shown mixed results. Kim et al. (2014) compared the therapeutic effects of white noise (BBN), NBN, and mixed-band noise on tinnitus patients undergoing tinnitus retraining therapy (TRT) and found that white noise provided a significantly greater degree of relief from their tinnitus. Other studies have failed to identify significant differences in therapeutic success between white noise and alternative – both simple and complex – types of sounds (Barozzi et al., 2017; Barozzi et al., 2016; Mondelli et al., 2021). While the lack of consistency across the literature makes it difficult to discern the most appropriate sound for implementation in sound therapy paradigms, there is some evidence that static sounds (i.e., auditory stimuli of a fixed intensity) such as white noise fall short in their therapeutic potential when compared to adaptive sounds that vary temporally (Durai et al., 2018; Handscomb, 2006; Henry, Rheinsburg, et al., 2004; Reavis et al., 2012). Henry, Rheinsburg, et al. (2004) compared the efficacy of several custom sounds on their ability to provide tinnitus relief and discovered that while all trialled sounds were "soothing" and offered some degree of alleviation with regards to tinnitus annoyance, the two sounds which provided the greatest level of relief were dynamic real-world 'tinnitus-relief' sounds (namely 'E-water' and 'E-nature'). Similarly, use of customised music in concert with counselling embedded in the Neuromonics Tinnitus Treatment method of management resulted in significantly greater alleviation of tinnitus symptoms and better user acceptability relative to the application of BBN/counselling combination, or counselling alone (Davis et al., 2008). While it was initially thought that these outcomes might reflect the unpredictable temporal properties of adaptive signals, several subsequent papers have either failed to demonstrate greater therapeutic potential of dynamic sounds over white noise (Barozzi et al., 2016), or have found white noise to offer more benefit (Durai & Searchfield, 2017). Durai and Searchfield (2017) undertook a randomised cross-over study examining the effects of adaptive nature sounds relative to constant BBN and found that while the presence of sound had a positive effect on tinnitus in general, a more meaningful reduction in TFI was observed with the BBN. Considering the results within an adaptation level theory (ALT) framework, the researchers posited that the uniform and predictable nature of BBN possibly allowed for an easier shift of the internal 'adaptation level' away from the tinnitus signal, in turn reducing overall tinnitus magnitude, while the more complex and unpredictable nature sound likely requires more time to reach peak adaptation (Durai & Searchfield, 2017). This notion supports previous recommendations of BBN implementation for sound therapy due to its tolerability, neutrality, and superiority in facilitating habituation when compared to NBN or tones (Henry et al., 2002; Jastreboff, 1999; Jastreboff & Hazell, 2008; Kim et al., 2014).

The current conflicting evidence does not diminish the need to continue to innovate and evaluate more complex signals, such as nature sounds. In concert with several other studies (Barozzi et al., 2016; Schreitmüller et al., 2013), Durai and Searchfield (2017) found that nature sounds influenced residual emotion pathways and were more pleasant, advising that a combination of nature and BBN, or a staged application from BBN to nature sounds be explored. Building on their earlier work, Durai, Doborjeh and colleagues (2021) trialled an adaptive approach modelled on the concept of auditory categorisation, attempting to alleviate tinnitus severity by recategorizing the phantom percept as a real-world natural sound (either ‘cicadas’, ‘water sound/rain’, ‘birds’, ‘fan’, and ‘water + birds’ combination), consequently reducing ambiguity surrounding the sound and relieving cognitive resources. The recategorisation training led to a significant reduction in the degree to which tinnitus impacts participant’s lives (as defined by Tinnitus Functional Index (TFI) scores), as well as the level of intrusiveness and ability to ignore tinnitus (Durai, Doborjeh, et al., 2021). Utilising an artificial intelligence (AI) based Spiking Neural Network (SNN) architecture to map, learn, visualise, and classify meaningful brain patterns, the study identified recategorisation training-specific changes in neural activity. The activity changes observed include altered activation of tinnitus neural networks and increased level of bilateral hemispheric involvement as the training sound morphed from the tinnitus replica (avatar) into the real-world environmental sound (particularly in regions concerning discriminatory judgements and attention, i.e., ventral anterior network, precentral gyrus, dorsal attention network) (Durai, Doborjeh, et al., 2021). While the results of the study highlighted the potential for recategorisation training to be implemented as a powerful tinnitus management tool, the study did not have a control group; as such further work is required to determine how the perceptual training method performs relative to conventional sound therapy (i.e., using BBN).

Perceptual training paradigms such as categorisation may have important clinical implications for disorders whose pathophysiology is rooted in neural hyperactivity, such as tinnitus (for a detailed review on categorisation as a tool for tinnitus management, see *Chapter 2.4 A Narrative Review of Auditory Categorisation and Its Potential Role in Tinnitus Perception*) (Jepsen et al., 2010; Vajsakovic et al., 2022). Neuronal hyperexcitability and increased spontaneous firing rates are neural correlates of tinnitus; a consequence of aberrant changes in cortical activation that occur following insult to the auditory periphery (Eggermont & Tass, 2015; Noreña & Eggermont, 2003; Roberts, 2018). By reducing the volume of cortical representation for training stimuli that are representative of the tinnitus experience (i.e., tinnitus avatar), categorisation training might offer a practical and cost-effective means of tinnitus management. In the case that the training is successful, the expected outcome would be a reduction in neuronal activity within the auditory cortex. Such changes are expected to oppose or even reverse tinnitus-related changes. This study expands and builds on the work undertaken by Durai, Doborjeh et al. (2021) to further evaluate the ability of the tinnitus sensation to be categorised as a real-world environmental sound using effortless auditory categorisation training. Effortless perceptual training paradigms are appealing as they are easily implemented and do not require sustained mental effort and/or cognitive control to achieve therapeutic outcomes (cf. effortful training) (Tang et al., 2022). Studies investigating effortless nature exposure have found that listening to nature sounds improves working memory (Schertz & Berman, 2019) and cognitive performance (Van Hedger et al., 2019). This study will compare the effects and mechanisms of categorisation training using a natural sound against a conventional sound therapy (white noise). The methods aimed to generate an appropriate and convincing tinnitus replica (avatar) that was representative of participant's tinnitus experience and could be morphed over time and categorised to a familiar broadband environmental sound (rain). Rain was chosen as the categorisation sound for three primary reasons; 1) it is considered as being soothing and has been found to interact with the tinnitus signal (Durai et al., 2017), 2) it is a sound which is broadband in nature and as such is likely to contain the tinnitus frequency – or aspects of it – and 3) poses a 'neutral medium' in terms of an auditory stimuli that is of real-world origin but closely resembles white noise in its spectral quality (Tian et al., 2020). Rain can be considered a middle ground between a constant, emotionally neutral sound such as noise, and a dynamic complex nature sound (such as cicadas/ocean/surf sounds). It was hypothesised that 1) a tinnitus avatar generated using the parameters pitch, loudness, and spatial location would reflect participant's true tinnitus experience to a high level of satisfaction (as determined using similarity rating scales), 2) categorisation training, whereby the tinnitus avatar is morphed over time to the rain sound (broadband environmental sound) which it is to be categorised to, results in a reduction in tinnitus severity and related distress, and 3) behavioural and perceptual changes resulting from the categorisation training may correlate with changes in neural activation.

6.3. Methods

This study was approved by the Auckland Health Research Ethics Committee (AHREC; project reference AH22843). All participants gave written informed consent in accordance with the Declaration of Helsinki.

6.3.1 **Participant eligibility and recruitment**

Participants were recruited from several platforms: The University of Auckland Hearing and Tinnitus Clinic, private audiology clinics Auckland-wide, via advertisement, and through a 'tinnitus volunteer database' that was composed following a tinnitus seminar to the general public. Those participants that could be contacted via email were sent a formal expression of interest invitation. In total, 73 individuals expressed interest in the study; these potential participants were sent a Participant Information Sheet (PIS) (see Appendix 1) which outlined the purpose of the study, what participation would involve/mean for the participant, and how to get in touch with the researchers should they wish to discuss the study, ask questions/raise concerns, and/or register their interest in participating (Figure 11). Individuals interested in participating were sent a consent form (CF) clearly detailing both the responsibilities of the individual as a participant in the study (i.e., what is required of them), as well as reiterating participant confidentiality and informing the participant of their rights in terms of voluntary involvement and the notion that withdrawal from the study could occur at any time up to two months after testing without any consequences. Participants were required to read and sign the consent form prior to proceeding with the study. Those individuals that were interested in taking part in the study were emailed a link to a set of questionnaires (Tinnitus Sample Case History Questionnaire (TSCHQ), Tinnitus Functional Index (TFI), Tinnitus Severity Numeric Scale (TSNS), and Positive Negative Affect Schedule (PANAS)) to complete online using REDCap® (web platform for generating, managing, and collating online surveys, www.redcap.fmhs.auckland.ac.nz). Participants who met the eligibility criteria were contacted and booked in to attend the three-hour study session.

Twenty-nine participants (14 male, 15 female, mean age = 56.9 years, *SD* = 12.7, range 30-75) met the eligibility criteria and were recruited into the study. The inclusion criteria were: adults aged 18 years or older, who were fluent in English, had consistent chronic tinnitus (>6 months duration), only a single tinnitus sound, tinnitus sufficiently severe (as determined using a tinnitus impact of life score calculation (Tinnitus Functional Index score of at least 25)), and had normal middle ear function with a moderate-severe degree of hearing loss or less (i.e., <90 dB hearing loss on average across the frequency range of 125-8000 Hz). Three participants (one male, two female, mean age = 56, *SD* = 4.3, range 50-60) did not complete the training regime; in these cases, only electrophysiological data was useable.

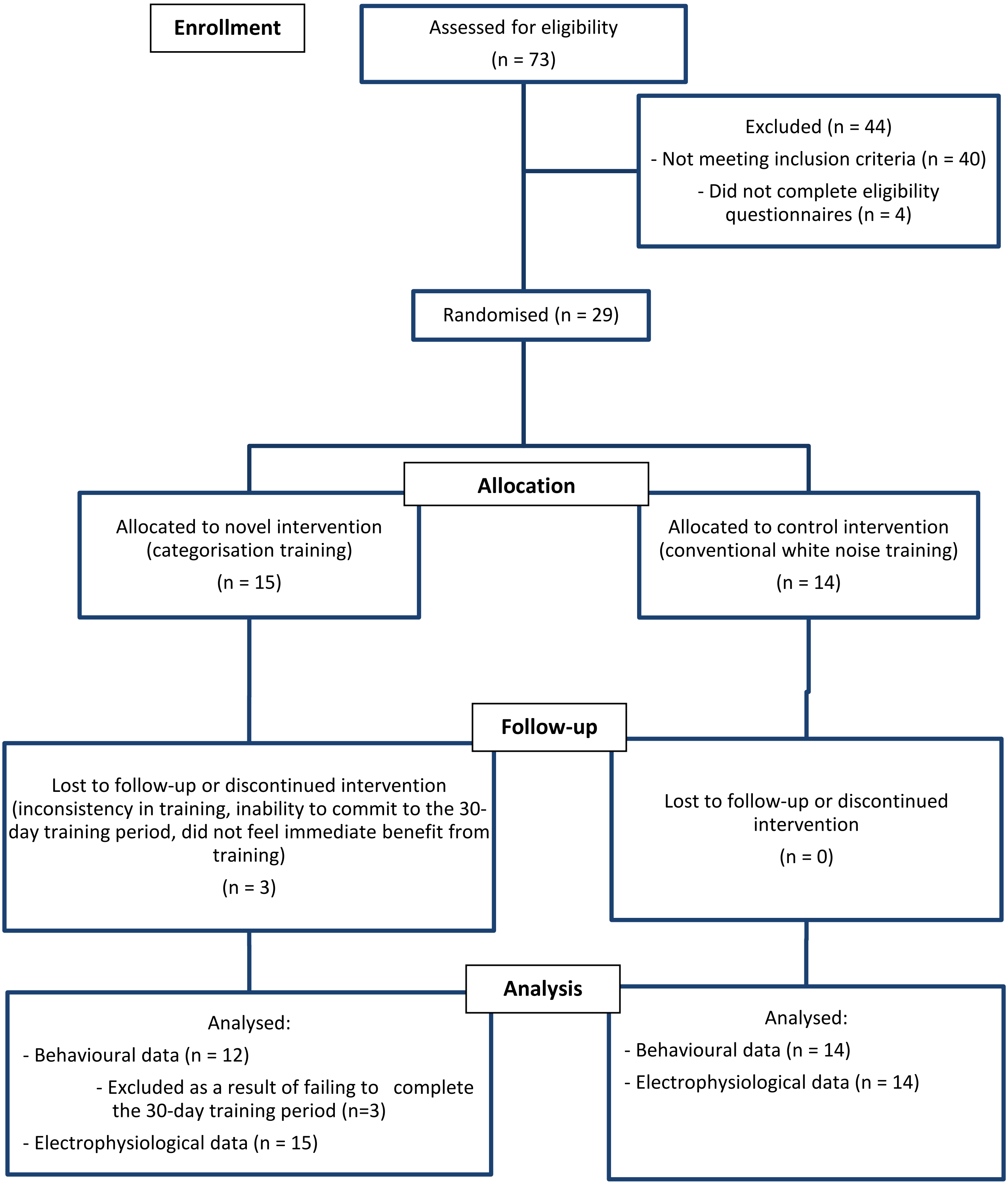


Figure 11. Consolidated Standards of Reporting Trials (CONSORT) diagram outlining the study.

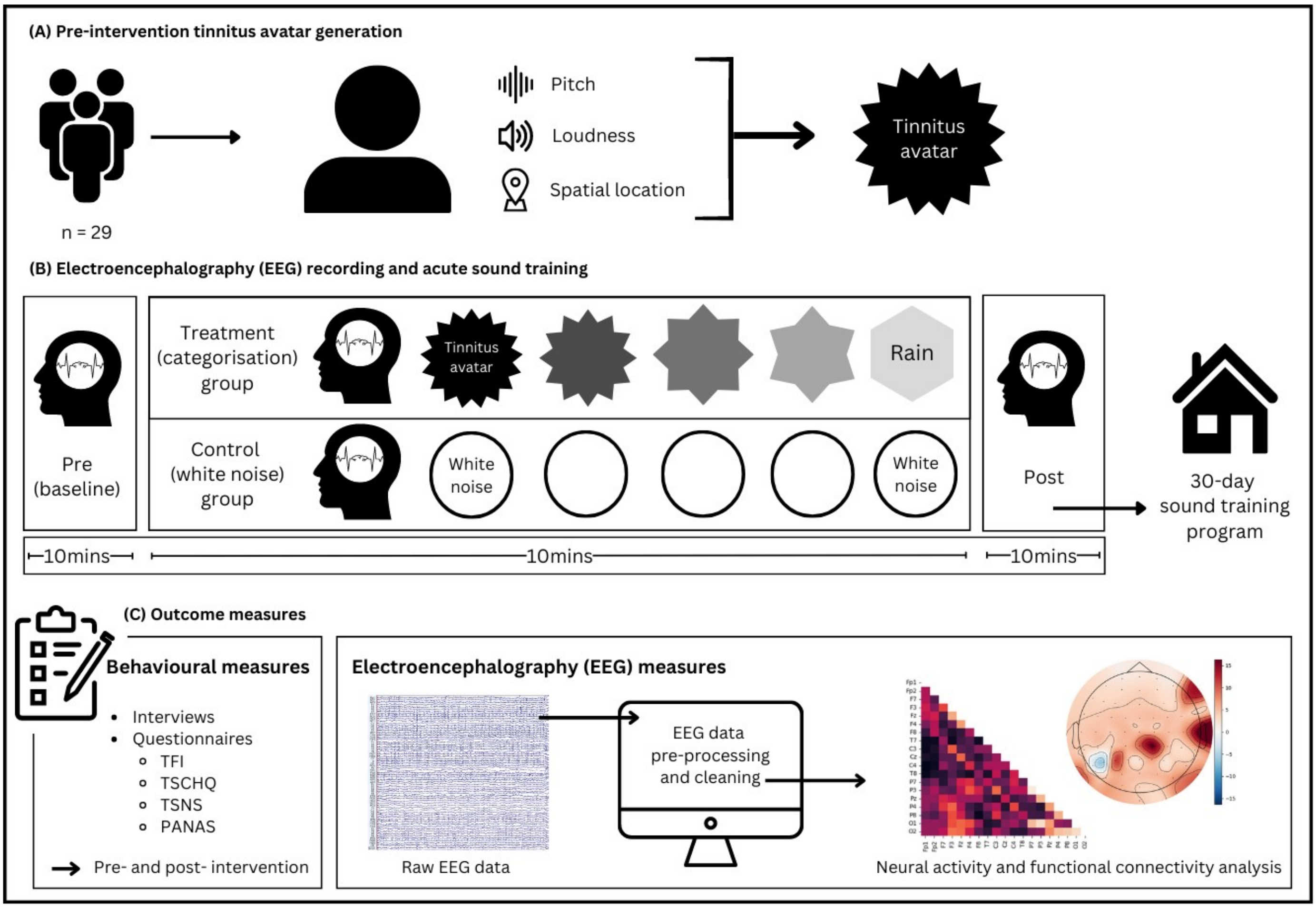


Figure 12. Summary of the study protocol. **(A)** Tinnitus avatars (complex replicas of the tinnitus experience) were generated for 29 chronic tinnitus patients using psychoacoustic parameters of pitch, loudness, and 3D location. **(B)** 10-minute electroencephalography (EEG) measures were taken at baseline (pre-intervention) with the participant sitting in silence, during acute exposure to the training sound (tailor-made categorisation sound or white noise), and following the sound training (post-intervention), again sitting in silence. Participants were supplied with 30-day's worth of training tracks and instructed to listen to the specified training tracks every day consecutively for 30-minutes. **(C)** The outcome measures used to evaluate treatment-related changes in tinnitus were behavioural measures (interviews and questionnaires, undertaken prior to and following the 30-day training period), as well as EEG measures (assessing potential changes in neural activity and functional connectivity).

6.3.2 **Study design and procedures**

Study protocol

Prior to attending the three-hour session, participants were asked to complete a battery of pre-intervention questionnaires (TSCHQ, TFI, TSNS, and PANAS) aimed at assessing tinnitus impact on participants and their quality of life; their study session was booked within a one-week window following questionnaire completion. Upon arriving to the study session, participants completed the subsequent tasks in the following order: 1) an initial pre-intervention interview, 2) audiometric testing, 3) tinnitus matching (tinnitus avatar synthesis)

(Figure 12A), and 4) electroencephalography (EEG) measures under three conditions (pre-intervention, during perceptual sound training, and post-intervention) (Figure 12B).

Following completion of the aforementioned measures, participants were provided with either white noise (control) or tailor-made categorisation (test) training tracks (depending on the treatment they were randomised to) and instructed to listen to the tracks daily for 30-minutes over the one-month period using the Z8 bone conduction headphones they were supplied with. The tracks were uploaded onto their personal Google Drive accounts for easy and remote access, with each participant receiving 30-tracks (one for each day of the 30-day training period) labelled appropriately for ease of use (e.g., Day 1 (date)).

Once the 30-day sound training regime was complete, participants were sent a series of post-intervention interview questions and a set of follow-up questionnaires (TFI, TSNS, PANAS) to assess any training-related changes in tinnitus.

Participant case history: Tinnitus Sample Case History Questionnaire (TSCHQ)

The Tinnitus Sample Case History Questionnaire (TSCHQ) offered information about patient's tinnitus histories and physical characteristics of their tinnitus (Langguth et al., 2007). It consisted of 35 questions which focus on several domains useful to researchers and clinicians, including patient background and tinnitus history, perception and experience of tinnitus, and assessment of comorbidities common to tinnitus (e.g., hearing impairment, vertigo, temporomandibular disorder). The format of the TSCHQ included multiple-choice questions (e.g., *Does the loudness of the tinnitus vary from day to day*? Available options: *YES* or *NO*), items which required a numerical value (e.g., *What percent of your total awake time, over the last month, have you been aware of your tinnitus?*), questions which necessitate a rating from 1-100 (e.g., *Describe the loudness of your tinnitus using a scale from 1-100, 1 = very faint; 100 = very loud*), and questions that require free-writing answers (e.g., *Please describe in your own words what your tinnitus usually sounds like*).

Audiological assessment

Pure-tone audiometry was conducted using the modified Hughson-Westlake procedure (Carhart & Jerger, 1959) in a sound-proof booth (ISO 8253-1) with an audiometer. Air conduction thresholds were recorded for 125-8000 Hz using insert earphones (ER-3A) or supra-aural (TDH-39P) transducers. Air conduction thresholds at high frequencies (9000, 10,000, 12,500, 14,000, and 16,000 Hz) were tested using Sennheiser HDA 200 circumaural headphones (Sennheiser electronic GmbH & Co. KG).

Tinnitus matching: Defining the psychoacoustic properties of the participant's tinnitus

MedRx Tinnometer (MedRx Inc.) and Adobe Audition Software (Adobe Inc.) installed on a DELL Latitude E6400 laptop computer (Dell Inc.) was run with the participants in the soundproof booth using circumaural Sennheiser HDA 200 transducers (Sennheiser electronic GmbH & Co. KG). These two programmes were used to conduct tinnitus psychoacoustic matching and define the pitch, loudness, and location of participant's tinnitus. The pitch of tinnitus was assessed with the participant responding to a 2-alternative forced-choice method of pitch matching presented at 15 dBSL (Sensation Level). To ensure there is no octave confusion, the matched pitch was re-presented to the participant and compared to tones that will be one octave above, and one octave below. Loudness matching in dBSL was performed in two steps: 1. the threshold level was determined for the pitch of tinnitus as per standard audiometry; 2. intensity was increased from threshold until the participant indicated a good match to the subjective loudness of their tinnitus. The site of the participants' tinnitus was located through a virtual 3D space interface available in the Adobe Audition software (Adobe Inc.) (using a Head-Related Transfer Function).

The psychoacoustic parameters were manipulated as follows:

- Tinnitus pitch: adjusted in half-octave steps between 250-16000 Hz
- Tinnitus spatial location: a 3D audio plugin 'anaglyph' (Poirier-Quinot & Katz, 2018) was used to change the perceived elevation of the sound in space in 30^0 steps as well as the auditory delay between the left and right ears
- Tinnitus loudness: adjusted in 2dB steps

Tinnitus matching and training sound generation

Comprehensive psychoacoustic mapping of each participant's current tinnitus was undertaken by playing sounds using Adobe Audition software (Adobe Inc.) in order to generate the tinnitus avatar (complex replica of tinnitus). The participants were instructed to listen to sounds being presented to them through Z8 bone conduction headphones (Shenzhen JEDI Technology Co., Ltd.) and engage with the experimenter to generate a replica of their tinnitus (tinnitus avatar). The experimenter presented and adjusted a pure tone sound (defined by a single frequency component and intensity) according to the participant's feedback until a sound was reached that was as representative of the patient's tinnitus as possible based on three parameters: frequency (pitch), intensity (loudness), and spatial location. Once the participant was happy with the sound, they were asked to rate the sound based on two features: 1) how well it reflected their true tinnitus sound, and 2) how much they liked the sound. The rating was conducted using a Likert scale: 1-10 for how well the sound reflects the tinnitus, with 0 = completely dissimilar and 10 = exact match, and 1 to 10 for sound likability, with 1 = really disliked sound and 10 = really liked sound. Following the rating, the sound was saved and used as the starting point for the categorisation training. All sounds were played at a comfortable listening level and the final sound stimuli for all participants was adjusted for individual hearing thresholds using Adobe Audition (Adobe Inc.) or Audacity software (Audacity®).

Sound training: categorisation training group

For participants randomised to the 'categorisation training' group, Adobe Audition (Adobe Inc.) or Audacity software (Audacity®) were used to design and generate the categorisation training sound using “crossfade” functions. The sound therapy stimulus (i.e., categorisation training sound) was generated by integrating the tinnitus avatar and an audio file of rain into a 'cross fade' audio clip, which gradually morphed from the avatar to the rain sound over the 30-day training period. Rain was used as the sound with which we wish to categorise the tinnitus as it is both a real auditory object, and one that has a broad frequency spectrum within which tinnitus is likely to fall and be categorised to. Additionally, it is generally found to be a pleasant sound and is commonly used in conventional sound therapy (masking) approaches. The sound therapy stimulus was adjusted in stages to facilitate shifts towards the real auditory object (rain). For the first two days, the “avatar” of tinnitus sound was played so that the participant learns to associate this sound with his or her own tinnitus. For the next 26 days, the sound gradually morphed with 13-step stages of change from the “avatar” to the real auditory object (rain) sound (i.e., the participant listened to a new stage of the morphed sound every two days as it gradually progresses from the avatar to the rain sound). The last two days (day 29 and 30) the participant only listened to the fully morphed sound (i.e., the sound matched all the auditory characteristics of the real auditory object (rain)).

Sound training: white noise group

Participants randomised to the 'white noise' group were provided with conventional sound therapy (white noise) and instructed to listen to the file for at least 30 minutes a day for 30 days.

6.3.3 **Outcome measures: Electrophysiological and behavioural measures**

Electroencephalography (EEG)

Electroencephalography (EEG) was used to investigate whether administration of categorisation training stimuli 1) alters the representation of sound within the auditory cortex itself, and/or 2) changes functional networks and strength of connections in the brain. Three sequential 10-minute EEG recordings were taken: 1. baseline recording prior to exposure to training sound (i.e., pre-intervention), 2. acute exposure to training sound (categorisation track or white noise), and 3. acute post sound training recording (i.e., post-intervention).

Setup

The experiment was run in a dimly lit sound attenuating room. Participants were seated comfortably in an armchair and recordings were made in an awake state in a passive condition. Participants' scalp under the electrode was cleaned with alcohol swabs and a cap with inbuilt sockets for electrodes was placed on the head and electrodes were connected to those sockets. EEG measures were undertaken using 66 active surface electrodes (Biosemi ActiveTwo system, www.biosemi.com) placed on the scalp according to the international 10-10 system array through attachment to an appropriately sized Biosemi 64 electrode head cap with SignaGel electrode gel (Figure 13). An additional electrode was placed on each mastoid. EEG signals were recorded continuously at a sampling rate of 8192

Hz and downsampled to 512 Hz. Impedances were checked to remain below 25 kohms. Off-line analysis was conducted using Brain Electrical Source Analysis (BESA) Research 6.0 ® Software (www.besa.de). Electrodes were re-referenced to an average reference montage if needed for clarity of recordings. Each EEG recording was corrected for eye blink and movement artefacts using the adaptive model approach in BESA.

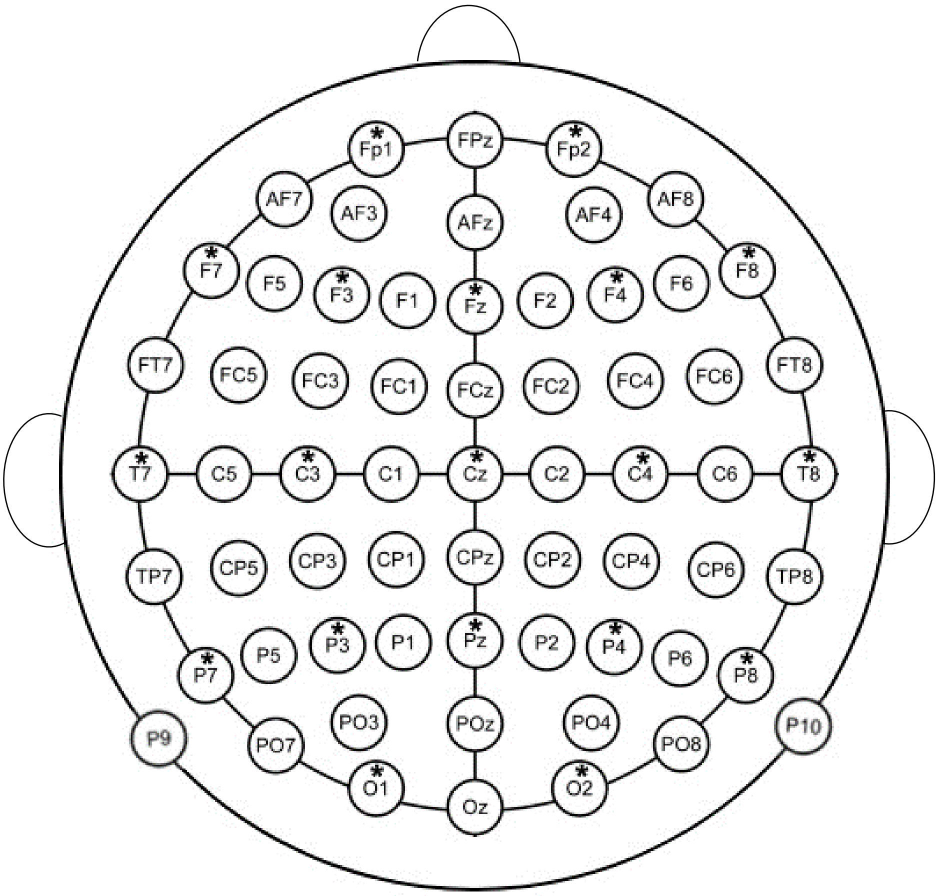


Figure 13. Electrode setup according to the international 10-10 arrangement. Asterisk signifies selected channels of the 10-20 arrangement.

Recording procedure

EEG was continuously recorded while the participant sat quietly in a soundproof booth staring at a grey cross on a computer screen for 10 minutes. EEG was recorded under three different conditions:

1. Baseline recording (following interview and hearing test completion, but prior to generating the tinnitus replica and training sound exposure)
2. Sound training recording (EEG recorded while participant is acutely exposed to training sound, either categorisation track or white noise)
3. Post-intervention (EEG recorded immediately following cessation of sound training)

The baseline recording was compared to the post-intervention EEG recording to investigate changes in activation of neural tinnitus networks, particularly relating to attention and discriminatory judgments (e.g., dorsal attention network, precentral gyrus, ventral anterior network) following categorisation training. Participants in both groups received the exact same instructions and were treated in the exact same manner; the only difference being the type of sound training they received.

Electroencephalography: data pre-processing

EEG data was recorded continuously at a sampling rate of 8192 Hz and down sampled to 512 Hz for analysis. Each file was pre-processed and cleaned using EEGLAB (Delorme & Makeig, 2004), a MATLAB toolbox designed for processing electrophysiological data. A high-pass finite impulse response (FIR) filter was applied at 1 Hz to remove slow artifacts, as well as a 50 Hz notch filter to mitigate electrical noise. The independent component analysis (ICA) was performed using the runica.m (Infomax ICA) decomposition algorithm and used to remove commonly detected artifacts such as eye movements/blinks and cardiac, muscular, and respiratory artifacts. Bad channels were interpolated, and any additional artifacts (e.g., from movement of electrode cables) were manually rejected upon visual inspection of the data. Data was saved as .set and .fdt files prior to exporting into Microsoft Excel.

Electroencephalography: data analysis

Modelling of EEG data using brain-inspired spiking neural networks (SNN) architecture

Computational modelling of EEG data was performed according to the steps outlined in Doborjeh et al. (2019). EEG signals were converted into spikes where changes in the signal above a spike threshold gave rise to a positive spike, while a signal below the threshold resulted in the encoding of a negative spike. Signals which did not rise above or fall below the threshold were not encoded (i.e., no spike was generated). Data were subsequently mapped onto the Talairach brain atlas (a 3D SNN reservoir consisting of 1471 neurons) (Talairach, 1988) with the 64 electrode inputs being positioned according to their respective (x, y, z) coordinates within the Talairach brain template. Following spatial mapping of the data, the model was trained in an unsupervised learning mode using the Spike Timing Dependent Plasticity (STDP) learning rule (Masquelier et al., 2009). In this study, two separate models were trained for therapeutic responders and non-responders at pre-intervention (baseline) and post-intervention (following perceptual sound training) for the categorisation and white noise groups. Neuronal interactions were computed and visualised using a Feature Interaction Network (FIN) based on the total input interaction between the 64 input neurons (EEG channels), in turn giving rise to average one-to-one interaction between the input neurons. Pattern classification was conducted by training an output layer classifier in supervised learning mode to learn the association between the SNN connectivity and class label information (i.e., responder vs. non-responder). Prediction analyses were performed to determine whether participants in either sound training group were likely to respond to therapy.

Neural activity: Power spectral density

Electroencephalography (EEG) data were imported into MNE Python 1.4.2 (Gramfort et al., 2013), an open-source python package that enables analysis and visualisation of neurophysiological data. Power spectral density (PSD) was computed to explore the distribution and patterns of neural activity among categorisation and white noise participants under the different conditions (namely baseline, sound training, post sound training). PSD was averaged across each condition in the following manner: across the entire 10-minute recording for the pre- and post-training conditions, and across three 3-minute segments of the sound training recording. More specifically, the training recording was split into a ‘first three minutes’, ‘second three minutes’, and ‘last three minutes’ giving rise to training time 1 (T1), training time 2 (T2), and training time 3 (T3); this was done to preserve and document any changes in neural activity that might have occurred over the duration of the training sound morphing from the tinnitus avatar to the rain sound in the categorisation group, and to maintain comparability between the white noise and categorisation groups for purposes of data analysis.

The frequency range of the power spectrum was segregated into five frequency bands of interest: delta (1-3 Hz), theta (4-7 Hz), alpha (8-12 Hz), beta (13-30 Hz), and gamma (31-49 Hz). Changes in PSD were evaluated for these frequency bands given their role in active brain processing and theories surrounding their aberrant activity being a neural correlate of tinnitus manifestation and propagation. Changes in PSD were explored for the full 10-10 electrode arrangement, as well as the more conservative 10-20 electrode setup and potential regions of interest: Auditory Cortex (AC), Limbic System (LS), Dorsal Attention Network (DAN), Default Mode Network (DMN), Ventral Anterior (VA), Precentral Gyrus (PrG), Postcentral Gyrus (PoG), Frontal lobe (FL), Temporal lobe (TL), Fronto-central lobe (FCL), Centro-parietal lobe (CPL), OPL = Occipito-parietal lobe (OPL), Left Hemisphere (LH), Right Hemisphere (RH). Topographic plots were generated in MNE python; power spectrum differences between post- and pre-intervention neural activity (i.e., ‘difference’ plots) were observed by subtracting the pre-intervention power spectra from the post-intervention power spectra.

Functional connectivity: Phase locking value

Changes in functional connectivity were explored by using the phase locking value (PLV) to estimate the degree of connectivity between electrode pairs. PLV measures the degree of phase locking (synchrony) between two or more EEG signals over time by evaluating how consistent the phase difference between them is within a time-series (Choi & Kim, 2018). PLV values range from 0-1; a PLV value of 1 indicates a high level of synchrony between the two signals, while a value of 0 suggests a lack of phase synchronisation (i.e., no/poor connectivity). In order to conduct PLV analyses, data was split into 20 second epochs. PLV were computed using MNE Python 1.4.2 (Gramfort et al., 2013) for the 10-20 electrode arrangement (in the interest of conserving time and resources) for the categorisation and white noise groups for pre- and post-intervention conditions, as well as for the ‘difference’ between pre- and post-intervention (calculated by subtracting the pre-intervention (baseline) PLV from the post-intervention PLV). Absolute differences of ≥0.1 were highlighted in an ‘absolute difference’ PLV plot.

Behavioural measures: TFI, TSNS, and PANAS questionnaires

Tinnitus Functional Index (TFI)

The Tinnitus Functional Index (TFI) (Meikle et al., 2012) was used to detect whether there were any changes in the impact of tinnitus on life pre- versus post- sound training. It consists of 25 items assessing the level of tinnitus severity across eight domains: cognition, emotion, sleep, intrusiveness, sense of control, interference with relaxation, auditory difficulties, and quality of life. The items are scored from 0-10 on an 11-point Likert scale, with the exception of questions 1 and 3 which are expressed in percentages (0-100%). The overall score is a reflection of the severity and level of negative impact of tinnitus: tinnitus is considered as either ‘not a problem’ (0-17), ‘small problem’ (18-31), ‘moderate problem’ (32-53), ‘big problem’ (54-72), or ‘very big problem’ (73-100). The TFI has been validated for test-retest reliability and internal consistency in New Zealand (Chandra et al., 2015). As such, it is the primary outcome measure of this study. A score reduction of 13 points is considered clinically relevant (Meikle et al., 2012). The mean TFI score of participants was 50.8 (*SD* = 17.6), consistent with moderately severe tinnitus (Meikle et al., 2012).

Tinnitus Severity Numeric Scale (TSNS)

The Tinnitus Severity Numeric Scale (TSNS) (The Tinnitus Research Initiative, 2009) was used to assess initial tinnitus severity and detect any possible treatment-related changes in tinnitus severity. It consists of one main question assessing the degree to which tinnitus is perceived as a problem, as well as five questions (tinnitus severity numeric scales) evaluating: 1) how unpleasant tinnitus is, 2) how uncomfortable tinnitus is, 3) how annoying tinnitus is, 4) how loud tinnitus is, and 5) how intrusive tinnitus is. The rating scale ranges from 1 (not at all/little severity) to 10 (extremely/greatest possible severity).

Positive and Negative Affect Schedule (PANAS)

The Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988) was used to detect treatment-related changes in emotional state. The PANAS consists of 20 items; 10 items concerned with assessing positive affect (determining the extent to which an individual felt excited, enthusiastic, strong, interested, proud, inspired, alert, active, determined, and attentive) and 10 items directed at evaluating negative effect (defining the degree to which an individual felt nervous, scared, upset, stressed, hostile, guilty, jittery, afraid, ashamed, and irritable). All items are rated on a scale from one (‘very slightly or not at all’) to five (‘extremely’).

Behavioural measures: Interviews

A pre-intervention interview was conducted by the researcher at the beginning of the study session following participant arrival (see Appendix 2 for interview questions/prompts). A verbatim transcription of participant responses was conducted by the researcher during the session; this was done by the researcher typing participant’s answers directly into REDCap® in real-time as they were being interviewed. Any incidental observations made by the researcher were also recorded in REDCap® as a ‘Note’. Following the 30-day sound training period, participants were sent a link via email to a post-intervention exit interview consisting of several questions evaluating the participant’s experience with the sound training, any changes in tinnitus, and an opportunity for participants to voice any questions, concerns, and suggestions/opinions (see Appendix 3 for exit interview questions/prompts).

Interview responses were managed and analysed using the framework method described by Gale and colleagues (2013) which employs five steps: interview familiarisation, thematic coding and categorising, indexing, charting, and finally mapping and interpretation (Gale et al., 2013). Noteworthy and/or interesting observations were labelled and assigned codes: common themes were identified (by author DV) and data were arranged according to the common themes into categories. Codes that were conceptually related were grouped together under an overarching category (see Appendix 4). The analytical framework method was applied to each interview prior to charting the data and identifying meaningful patterns both within and between participants (DV in consultation with GDS). Thematic analysis and notable quotations were included in the results following standard qualitative methodology practice.

6.3.4 **Statistical analyses**

SPSS Statistics (IBM, SPSS Inc.) and Graphpad Prism 9.3.1 (GraphPad Software, Inc.) were used for the analysis of behavioural (questionnaire) results. A two-way repeated measures analysis of variance (ANOVA) was used to investigate significant differences in TFI/TSNS/PANAS scores from pre- to post-training for the white noise and categorisation groups. The TFI data failed to meet the assumption of normality (according to the Kolmogorov-Smirnov test); as such, a logarithmic transformation was applied for appropriate statistical analysis. Qualitative interviews (detailed above) were undertaken pre sound training to give insight into participant's relationship with their tinnitus, define their perceived tinnitus experience, and outline their views on tinnitus management, and post sound training to detect possible changes in the tinnitus sensation or incidental observations, evaluate how well the sound training was received, and note any limitations and/or flaws of the training paradigm. Interviews were collated, thematically organised, and analysed according to the framework method described by Gale and colleagues (2013).

RStudio (Posit, PBC) was used for analysis of EEG results. Data met all parametric assumptions except the assumption of homogeneity; as such, a logarithmic transformation was applied (and supported by a residual coefficient of 1.15) so as to normalise data for analysis and ensure accuracy of results (values displayed in bar graphs represent back-transformed data). Application of a logarithmic transformation was also supported by the notion that EEG frequency bands naturally follow a logarithmic scale (Burgess, 2019). A mixed-methods repeated measures analysis of variance (ANOVA) was applied to investigate significant changes in neural activity (represented/measured as power spectral density (PSD)) both within and between groups (categorsiation/white noise) across the five different conditions (baseline, sound training (T1, T2, T3), and post), as well as for each of the five frequency bands of interest (delta, theta, alpha, beta, and gamma).

6.4. Results

6.4.1 **Participant hearing and tinnitus characteristics**

All participants experienced a chronic, bothersome tinnitus with an average onset of 11 years (SD = 11.0) (Table 7). Tinnitus was primarily described as being bilateral (60.7%), with the left ear being more affected than the right (28.6% bilateral tinnitus worse in left ear vs. 7.1%

bilateral tinnitus worse in right ear). A quarter of the group experienced tinnitus ‘inside the head’, while only 10.7% claimed their tinnitus was unilateral. For the most part participants did not know the cause of their tinnitus (46.5%); those who had an idea of a presumed cause related initial onset to head trauma (14.3%), loud blast of sound (14.3%), change in hearing (7.1%), stress (7.1%), whiplash (7.1%), and exposure to noisy environments (7.1%). Most commonly tinnitus was described as tonal (35.7%), followed by hissing (28.6%), cicadas (14.3%), ringing (14.3%), whining (3.6%), and static (3.6%). The majority of participants described having a ‘high’ to ‘very high’ pitched tinnitus (53.6% high, 25% very high), with fewer participants experiencing a medium-pitched tinnitus (21.4%), and no participants having a low-pitched tinnitus. Half of the 29 participants had not tried any form of tinnitus treatment, while 35.7% had tried one treatment, 10.7% had tried several treatments, and only 3.6% had tried many treatments.

Table 7. Participant characteristics measured at baseline for the entire study population (‘General’), and the two experimental groups (‘White noise’ and ‘Categorisation’). Values represent *Mean* (*standard deviation*).

		General	**White noise**	**Categorisation**
Demographics	Gender	Male: 14 Female: 15	Male: 7 Female: 7	Male: 7 Female: 8
	Age	56.8 (12.9)	54.21 (13.4)	59.43 (12.5)
Tinnitus characteristics	Duration (years)	11.0 (11.0)	10.2 (11.0)	11.9 (11.5)
	Presumed cause	Head trauma: 14.3% Loud blast of sound: 14.3% Change in hearing: 7.1% Stress: 7.1% Whiplash: 3.6% Other: 53.6% • Noisy environment: 13.3% • Don’t know: 86.7%	Head trauma: 14.3% Loud blast of sound: 21.4% Change in hearing: 7.1% Stress: 7.1% Other: 50% • Noisy environment: 14.3% • Don’t know: 85.7%	Head trauma: 14.3% Loud blast of sound: 7.1% Change in hearing: 7.1% Stress: 7.1% Whiplash: 7.1% Other: 57.1% • Noisy environment: 12.5% • Don’t know: 87.5%
	Location of tinnitus perception	Both ears, worse in left: 28.6% Both ears, worse in right: 7.1% Both ears equally: 25% Inside the head: 28.6% Left ear:7.1% Right ear: 3.6%	Both ears, worse in left: 21.4% Both ears, worse in right: 7.1% Both ears equally: 28.6% Inside the head: 21.4% Left ear:14.3% Right ear: 7.1%	Both ears, worse in left: 35.7% Both ears, worse in right: 7.1% Both ears equally: 21.4% Inside the head: 35.7%
	Description of tinnitus sound	Tone: 35.7% Hiss: 28.6%	Tone: 42.9% Hiss: 35.7%	Tone: 28.6% Hiss: 21.4%

		Cicada: 14.3% Ringing: 14.3% Whining: 3.6% Static: 3.6%	Cicada: 14.3% Ringing: 7.1%	Cicada: 14.3% Ringing: 21.4% Whining: 7.1% Static: 7.1%
	Tinnitus pitch:	Medium: 21.4% High: 53.6% Very high: 25%	Medium: 21.4% High: 57.1% Very high: 21.4%	Medium: 21.4% High: 50% Very high: 28.6%
	Number of treatments undergone for tinnitus	None: 50% One: 35.7% Several: 10.7% Many: 3.6%	None: 28% One: 42.9% Several: 21.4% Many: 7.1%	None: 71.4% One: 28.6%
	Perceived hearing problem	Yes: 42.9% No: 57.1%	Yes: 50% No: 50%	Yes: 35.7% No: 64.3%
	Hearing aids	Yes (both): 14.3% No: 85.7%	Yes (both): 14.3% No: 85.7%	Yes (both): 14.3% No: 85.7%
Tinnitus Functional Index*	Total TFI score	50.8 (17.6)	53.4 (17.3)	47.8 (17.4)
Tinnitus Severity Numeric Scale*	Perceived problem	Small: 7.1% Moderate: 53.6% Big: 21.4% Very big: 17.9%	Small: 7.1% Moderate: 50% Big: 21.4% Very big: 21.4%	Small: 7.1% Moderate: 57.1% Big: 21.4% Very big: 14.3%
	Loudness rating (1-10)	7.1 (1.7)	7.1 (1.9)	7.1 (1.6)
	Discomfort rating (1-10)	6.9 (2.3)	7.4 (1.9)	6.4 (2.6)
	Annoyance rating (1-10)	7.5 (1.9)	7.6 (1.8)	7.4 (2.0)
	Ability to ignore tinnitus (1-10)	7.1 (2.1)	7.8 (1.8)	6.4 (2.1)
	Pleasantness rating (1-10)	7.1 (1.7)	7.4 (1.2)	6.9 (2.2)
Emotional/psychological*	Positive emotionality	34.2 (6.0)	33.9 (5.8)	34.5 (6.1)
	Negative emotionality	20.6 (7.3)	21.4 (7.7)	19.7 (6.7)

*Three participants removed from any before-after measures (i.e., TFI, TSNS, PANAS) as a result of not completing the training.

While a substantial proportion of the group felt they had a hearing problem (42.9%), only 14.3% of participants wore hearing aids (both ears). Average hearing thresholds of participants shows symmetrical hearing with normal low-frequency hearing, moving to mild hearing loss from 1500 Hz to 6000 Hz before gently sloping to moderate hearing loss between 8000 Hz to 10,000 Hz and entering a moderate-severe degree of hearing loss from 12,000 Hz onwards (Figure 14).

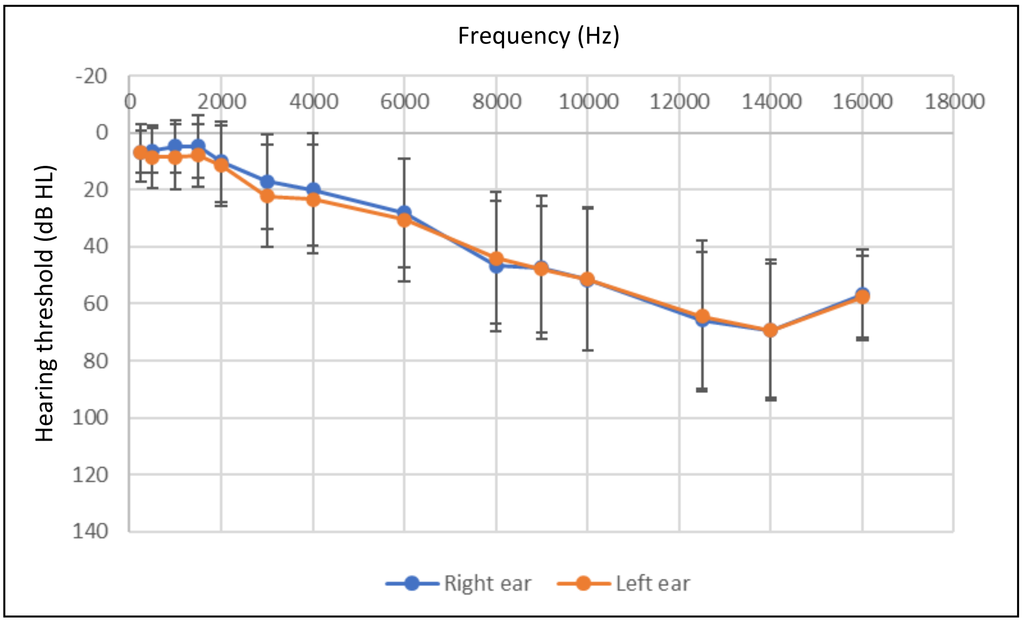


Figure 14. Average hearing thresholds of participants for the right and left ear across conventionally tested frequencies. Error bards represent ± 1 SD.

6.4.2 **Questionnaire outcomes**

Tinnitus Functional Index

There was a statistically significant decrease in total TFI score for the white noise group from pre-training (M = 53.4, SD = 18.0) to post-training (M = 39.0, SD = 9.9), *F* (1, 24) = 1.33, $p < 0.01$ (Figure 15A). The mean decrease in TFI scores was 14.4, with 95% confidence interval ranging from 4.42 to 24.44. Statistical significance did not persist following multiple comparisons with corrections; only a main effect was observed, no significant differences were observed upon breaking the TFI scores into their respective subscales. Nine participants in the white noise group and three participants in the categorisation group achieved clinically meaningful reductions in tinnitus severity (determined by a 13-point reduction in TFI score). No significant differences were observed for the categorisation group. Interestingly however, the categorisation group demonstrated increased TFI scores following the 30-day training regime for the ‘Control’, ‘Relaxation’, and ‘Emotional’ subscales suggesting a worsening of the negative tinnitus impact on these domains following long-term auditory categorisation training (see Figure A1 in Appendix 5). No significant difference between white noise and categorisation TFI scores was identified.

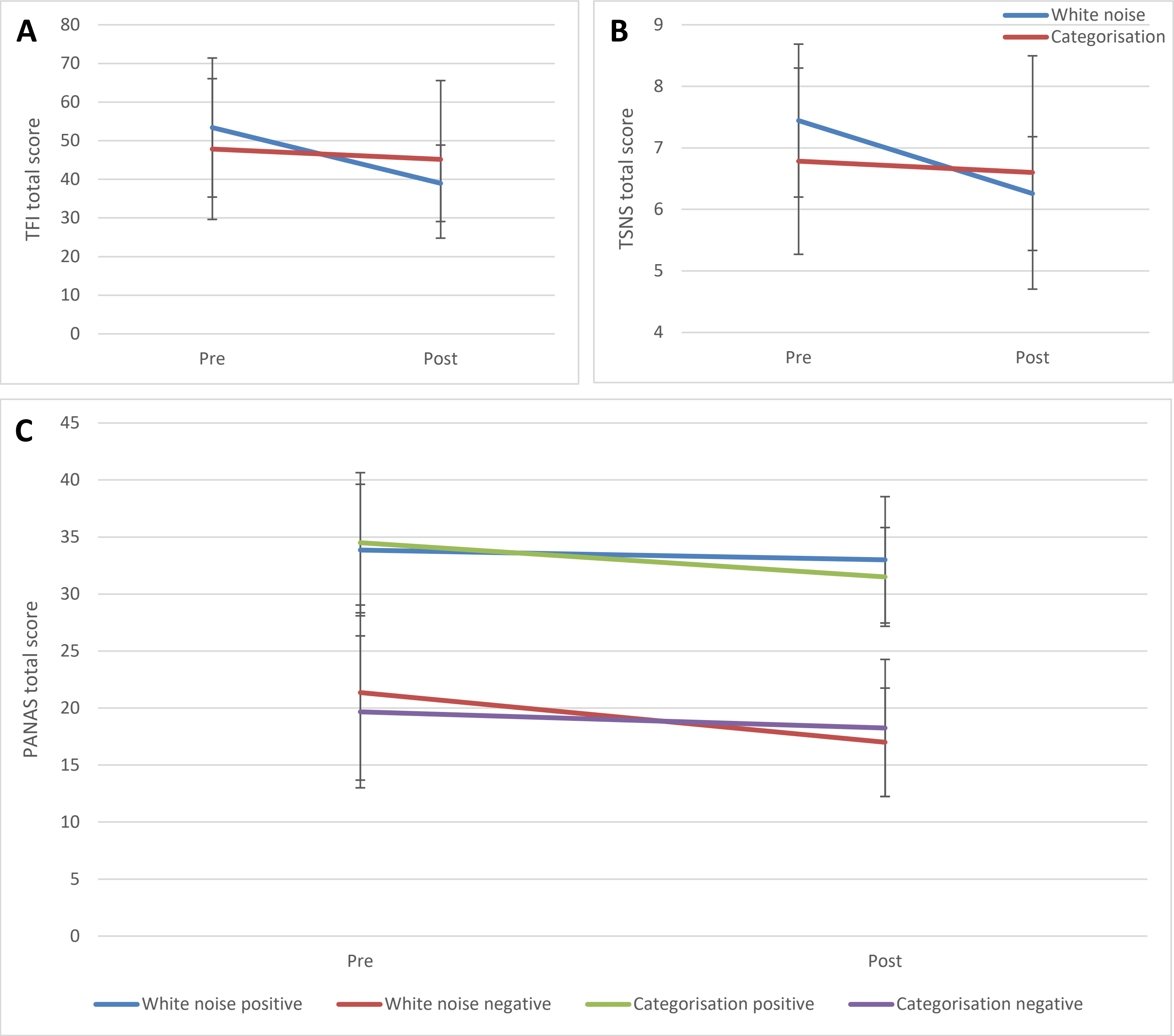


Figure 15. Changes in total score for the **(A)** Tinnitus Functional Index (TFI), **(B)** Tinnitus Severity Numeric Scale (TSNS), and **(C)** Positive and Negative Affect Schedule (PANAS) for the white noise and categorisation groups. There was a statistically significant decrease in the total TFI and total TSNS scores for the white noise group from pre-training (TFI M = 53.4, SD = 18.0; TSNS M = 7.4, SD = 1.3) to post-training (TFI M = 39.0, SD = 9.9; TSNS M = 6.3, SD = 1.0). The Negative Emotionality subscale of the PANAS was significantly lower following the 30-day training for the white noise group (post-training M = 17.0, SD = 4.9; pre-training M = 21.4, SD = 8.0). There were no significant differences in the total score across either of the three behavioural measures (i.e., TFI, TSNS, PANAS) for the categorisation group. Error bars represent ± standard deviation (SD). Note: ‘positive’ and ‘negative’ denote the subscales of the PANAS (i.e., Positive Emotionality, Negative Emotionality).

Tinnitus Severity Numeric Scale

There was a statistically significant decrease in the total TSNS score for the white noise group from pre-training (M = 7.4, SD = 1.3) to post-training (M = 6.3, SD = 1.0), F (1, 24) = 9.13, $p < 0.002$ (Figure 15B). The mean decrease in total TSNS scores was 1.1, with 95% confidence interval ranging from 0.61 to 1.76. There was no significant difference in TSNS scores for the categorisation group, nor were there any significant differences between the white noise and categorisation groups for TSNS scores. Statistical significance did not persist following multiple comparisons with corrections for either group (i.e., no significant differences in subscale ratings were observed).

Positive and Negative Affect Schedule

There was a statistically significant decrease in the Negative Emotionality subscale of the PANAS for the white noise group from pre-training (M = 21.4, SD = 8.0) to post-training (M = 17.0, SD = 4.9), F (1, 24) = 8.05, $p < 0.009$ (Figure 15C). The mean decrease in PANAS scores was 4.4, with 95% confidence interval ranging from 1.23 to 7.48. There was no significant difference in PANAS scores for the categorisation group, nor was there a significant difference in PANAS scores between white noise and categorisation groups.

Tinnitus synthesis: generation of the avatar

Overall, the resulting avatar was found to be an appropriate and satisfactory reflection of participant’s tinnitus experience (Table 8). Several participants (P27, P33, and P53) mentioned that the pitch and loudness were appropriate, but the sound itself failed to capture their tinnitus regardless of how much the replica was modified. One participant (P48) randomized to the white noise group struggled to have their tinnitus replicated during the tinnitus synthesis procedure and so did not provide any replica similarity/likability ratings. Participants generally appeared to have a neutral reaction to the avatar, neither strongly liking the replica nor entirely detesting it (Table 8). Additionally, participants in the white noise group assigned higher similarity and likability ratings relative to those in the categorisation group.

Table 8. Average tinnitus avatar similarity and likability (affect) ratings for the entire study population (‘General’), and the two experimental groups (‘White noise’ and ‘Categorisation’). Values represent *Mean* (*standard deviation*).

	General	**White noise**	**Categorisation**
Avatar similarity	7.0 (1.7)	7.4 (0.9)	6.7 (2.1)
Avatar likability	4.8 (1.9)	5.0 (1.7)	4.5 (2.1)

Qualitative analysis (participant interviews)

Pre-intervention interviews were obtained and analysed for all 29 participants, however post-intervention interview data was only collected and analysed for 26 participants (three participants were excluded from analysis as a result of failing to complete the training protocol).

Pre-intervention interviews

Participant’s tinnitus experience: relationship with and perception of tinnitus

Perception of the tinnitus sensation was generally described as being constant, loud, high-pitched sound that is annoying and intrusive. Awareness was found to vary depending on mood and external factors, with distraction reducing awareness:

It’s pretty much the same the whole time – the annoyance/bothersomeness comes and goes, it depends on external factors, mood, quietness, etc. At the moment it’s quite annoying as I’m thinking about it. [Participant #14, categorisation]

It’s always the same but I’m less stressed by it today and not as fixated on it as I usually am…It can vary due to stress and sleep, mental state can affect how I experience it, the level is always the same it’s just whether I notice it or not. [Participant #20, white noise]

Individuals generally fostered a negative view of tinnitus, with descriptors such as ‘frustrating, agitating, stressful, debilitating’ commonly being used to describe their tinnitus experience. Notwithstanding that most individuals felt that they were used to their tinnitus or can/have learned to cope with it (with many mentioning that distraction reduces awareness of their tinnitus), their relationship with their tinnitus was not a good one:

I hate it...It sounds like a constant pressure cooker going off. [Participant #10, categorisation]

A lot of the time I just ignore it...But particularly when it's quiet I'm always conscious of it, it's annoying but it's been there for so long I've grown used to it. [Participant #19, categorisation]

[My relationship with my tinnitus is] resigned reluctant. 'It's there, I can't do anything about it' kind of relationship. [Participant #15, white noise]

It's gotten better over time, obviously I hate it, rather it wasn't there, I learn every day to try and live with it, some days are easier than others. [Participant #20, white noise]

It's a delayed losing battle. It always wins, I've reached a stalemate with it. [Participant #23, categorisation]

It is having a huge effect on my quality of life, it's made me a lot more stressed, high level of anxiety which comes and goes without any notice...I've accepted it but it's still debilitating. [Participant #26, categorisation]

I don't like it – it's good if I'm busy but as soon as it's quiet or in a room like this it's annoying, it's annoying at night, it's annoying in the middle of the night, not annoying as I'm falling asleep as I'm quite tired but I do wake up with my tinnitus...I have to do something so as not to hear it like an activity or having music on. [Participant #27, categorisation]

Overall, most participants felt that their tinnitus is worsened or exacerbated by emotional states such as tiredness, anger, and stress, as well as drinking alcoholic beverages and being in quiet environments. Being in loud/busy environments, listening to music or water sounds (rain/shower/etc.), and concentrating/being distracted by a task was typically found to provide momentary tinnitus relief. Interestingly, a number of participants held hearing loss beliefs associated with their tinnitus, feeling that the tinnitus interferes with their hearing:

I'd prefer not to have it, it stresses me out a bit, not so much the tinnitus itself as more around what it means...Is [my tinnitus] going to get worse? Am I going to go deaf? It's a point of frustration and agitation. [Participant #19, categorisation]

Tinnitus management

A number of participants explored conventional means of tinnitus management in an attempt to reduce or altogether eradicate their tinnitus sensation. The most commonly used management strategy involved some form of tinnitus masking, typically through playing music/noise/audiobooks via headphones/radio/hearing aids. Several participants mentioned using mindfulness/meditation and/or distraction techniques to alleviate their tinnitus sensation. One participant claimed to receive benefit from CBT, while another mentioned using paroxetine as a form of tinnitus management. Furthermore, 11 participants did not use any management strategy to mitigate their tinnitus.

I use CBT and have tried Bose sound earphones, I play either crackling fire, or ocean, or wind sounds. It only helps when I've got [the headphones] on, doesn't stop the tinnitus but does detract from it. [Participant #26, categorisation]

Just acknowledging that it's there makes a difference. I think about it like schizophrenia – if those people can learn to ignore the voices and label them as being 'safe' then so can I. [Participant #18, white noise]

Post-intervention interviews

Participant's tinnitus experience: treatment-related changes in tinnitus perception

In general, participants felt that their tinnitus sensation remained the same (i.e. 'unchanged') as it had been prior to – and throughout – the study. Terms frequently used to describe tinnitus included 'constant', 'annoying', and 'loud', remaining largely unchanged from those used before intervention implementation. Interestingly, one participant felt that they experienced increased sensitivity to their tinnitus following the training:

[My tinnitus is] loud and clear. Obviously I've spend a lot of time over the last month concentrating on it, and I have a feeling that this has caused me to be a bit more sensitive to it. [Participant #19, categorisation]

Perceptual sound training paradigm: feedback and improvements

Overall, participants in both the white noise and categorisation groups were of the opinion that the sounds were pleasant, soothing/relaxing, and easy to listen to, claiming that the sounds were a 'soothing distraction' and 'nice break from tinnitus':

I've found it quite soothing. I've looked forward to listening to the track, it's been a nice distraction. The track was ambient sound with a tone similar to my tinnitus. Over the month, I felt as though the tone disappeared. [Participant #5, categorisation]

I did like the treatment. It was relaxing and a welcome break from hearing the tinnitus. Would continue to use purely for the relaxation. [Participant #20, white noise]

Furthermore, participants in the categorisation group noted that the sound was non-intrusive, of good quality, and easy to ignore:

I found them non-intrusive and helped in drowning out the sounds. I was able to ignore the tinnitus more easily while playing them. [Participant #3, categorisation]

It was easy to ignore the sounds after a while. A couple of times I didn't notice when the track had finished. [Participant #17, categorisation]

Only one participant felt that their training track was annoying and unpleasant:

My treatment frequency was very like how I feel about my own tinnitus frequency, annoying, but able to be ignored largely, but so very good that it could be turned off after 30 minutes! It was never any problem, I was also so hopeful that it might improve my own tinnitus, to no avail, but you would never call it "pleasant". [Participant #12, categorisation]

Participant's experience of the overall training method was a positive one, with most participants finding the training regime interesting and easy to follow and stick to. A few participants mentioned enjoying the routine of completing the training and in fact even looking forward to the sessions, however a couple of participants mentioned that they felt the training had increased their awareness of their tinnitus:

I found the experience interesting. In a way made me more conscious of my tinnitus as you knew you need to factor the 30mins listening in each day and what effect it may be having. [Participant #1, white noise]

[The training regime was] not onerous overall, I could fit it in reasonably well. I'm not overall convinced that it's changed anything however, my feeling is that it has caused me to concentrate on my tinnitus, thus become more aware of it. [Participant #19, categorisation]

Considering recommendations for how to improve the tinnitus training tracks, the most common suggestions included increasing the duration of the training track, offering the ability to listen to different sounds, and providing a more accurate tinnitus replica:

Identifying the correct pitch of your tinnitus is probably a really important part of creating an effective treatment. I certainly found it a challenge to confidently match my tinnitus as part of the consultation and wonder if potentially my results are as a consequence of this? It might be beneficial if prior to the assessment there is a way for individuals to identify the sound of the tinnitus themselves using an at home app or to have the opportunity to do this *themselves in the consultation. I have attempted doing this before at home and found the ability to adjust the sounds myself up or down really useful in refining the exact tone I am hearing. I am also curious as to whether extending the treatment improves results or combining the treatment with other methods such as meditation would make it more effective. [Participant #20, white noise]*

In general, participants in both groups felt that they would be interested in using the treatment sound in the future for tinnitus relief, with only a few not expressing interest or having some doubts and hesitations. A couple of participants mentioned that they would be interested in continuing with using the treatment sounds if they were adjusted according to their suggestions (i.e., providing a more appropriate tinnitus replica or modifying the training sound in some way).

Training-related changes in tinnitus

Overall there were only a few more people that experienced a change in their tinnitus compared to those who felt that their tinnitus remained unchanged. Changes experienced by participants in response to perceptual training were both positive and negative; participants either claimed that their tinnitus was more noticeable and felt louder than prior to starting the trial, or they felt that their tinnitus was less intrusive and had gotten quieter following the trial. Participants who claimed that their tinnitus was more noticeable were those who underwent white noise sound training:

I think it may have changed to be more noticeable or the experience has made me more conscious of it. The 'hiss' seems louder when I am in a quiet environment but the pitch is constant. The tinnitus maybe a bit more intense. [Participant #1, white noise]

Whilst the sounds played did have a masking quality, my perception was the tinnitus was more noticeable afterwards. [Participant #2, white noise]

I don't really think it has changed much, though my sensitivity to it has probably increased due to the trial requiring me to think about it rather more than normal. Certainly I notice it a lot more in quiet environments (home-office, quiet car, at night). [Participant #9, white noise]

However, there were also a number of participants in the white noise group which felt that their tinnitus became softer following the training:

Yes, [my tinnitus has changed since the start of the trial], the right ear is a lot quieter. [Participant #11, white noise]

I'd say [my tinnitus] is somewhat better, mainly the volume seems less, have longer periods in the day where I don't notice it. [Participant #25, white noise].

Those in the categorisation group also exhibited mixed responses to the training, with some feeling it became fractionally quieter, and others largely finding that there was no change. Only one participant felt their tinnitus might have worsened:

Unfortunately, I think it may have gotten slightly worse. Either that or it has stayed the same. It does not appear to have improved. [Participant #28, categorisation]

There were a few participants who, whilst reporting no change to their tinnitus, felt benefit from the training nevertheless:

No, it's the same as at the start but feels more manageable. It's more noticeable in quieter environments. At work, in the office, it's not as apparent. It's less apparent when exercising. [Participant #5, categorisation]

No I don't think it has changed, but at least when the rain sound is playing I get some respite from it, which I previously did not have. I appreciate being included in the trial and I feel that I have a significant benefit from the experience. [Participant #13, categorisation]

Interestingly, one participant experienced a change in the spatial location of their tinnitus:

[My tinnitus] is still present but it feels like it has moved a little far from ears/head. [Participant #24, categorisation]

There was a large amount of variation in the changes experienced by the participants in both groups; the majority of participants felt that there was no change, however some found their tinnitus to be more tolerable and/or less noticeable, while others felt an increased level of awareness of their tinnitus. While some felt their tinnitus got louder, more participants claimed to experience a small reduction in their tinnitus loudness. No obvious trends among participants or treatment groups was observed. Most participants did not experience – or were aware of – any interactions between the treatment sounds and their tinnitus. Only one participant felt that their tinnitus interacted with the training sound, in that it blended with the tinnitus then ‘overwhelmed’ it (except when the participant was feeling stressed). While most participants did not experience any circumstantial changes which may have influenced their tinnitus sensation and the perceptual training experience, a few participants became sick (flu or COVID) during the trial, and a couple expressed experiencing extreme stress for a brief period during the 30-days, with these participants noting that these factors might have affected the way in which they responded to the training. One participant trialled nortriptyline.

6.4.3 **Electroencephalography measures**

Power spectral density: training-related changes in neural activity

There was a significant difference in median power spectral density (PSD) across time for both the categorisation and white noise groups (Figure 16). The overall trend appeared to be an increase in activity across all frequency bands as the condition changed from baseline, to training (T1, T2, T3), through to post sound exposure. In the categorisation group there was a significant increase in median PSD from T1 to post (for all frequency bands apart from beta), T1 to T3 (for the alpha, beta, and gamma bands), and T2 to T3 (for the gamma band) (see Table A1 in Appendix 6).

Additionally, there was a significant decrease in median PSD from baseline to T1 for the gamma band; it appears that in general for the categorisation group the baseline median PSD was higher, dropping at T1, followed by subsequent increases in average PSD as time went on, sometimes going back to the same level as baseline, in other cases exceeding the baseline value. The white noise group experienced similar differences in neural activity, demonstrating a significant increase in median PSD from baseline to post (for the delta and gamma bands), T1 to T2 and T1 to post (for the alpha, beta, and gamma frequency bands), T1 to T3 (for the beta and gamma bands), and baseline to T3 (for the gamma band). In contrast to the categorisation group, there is no general pattern that can be noted in terms of neural activity over time.

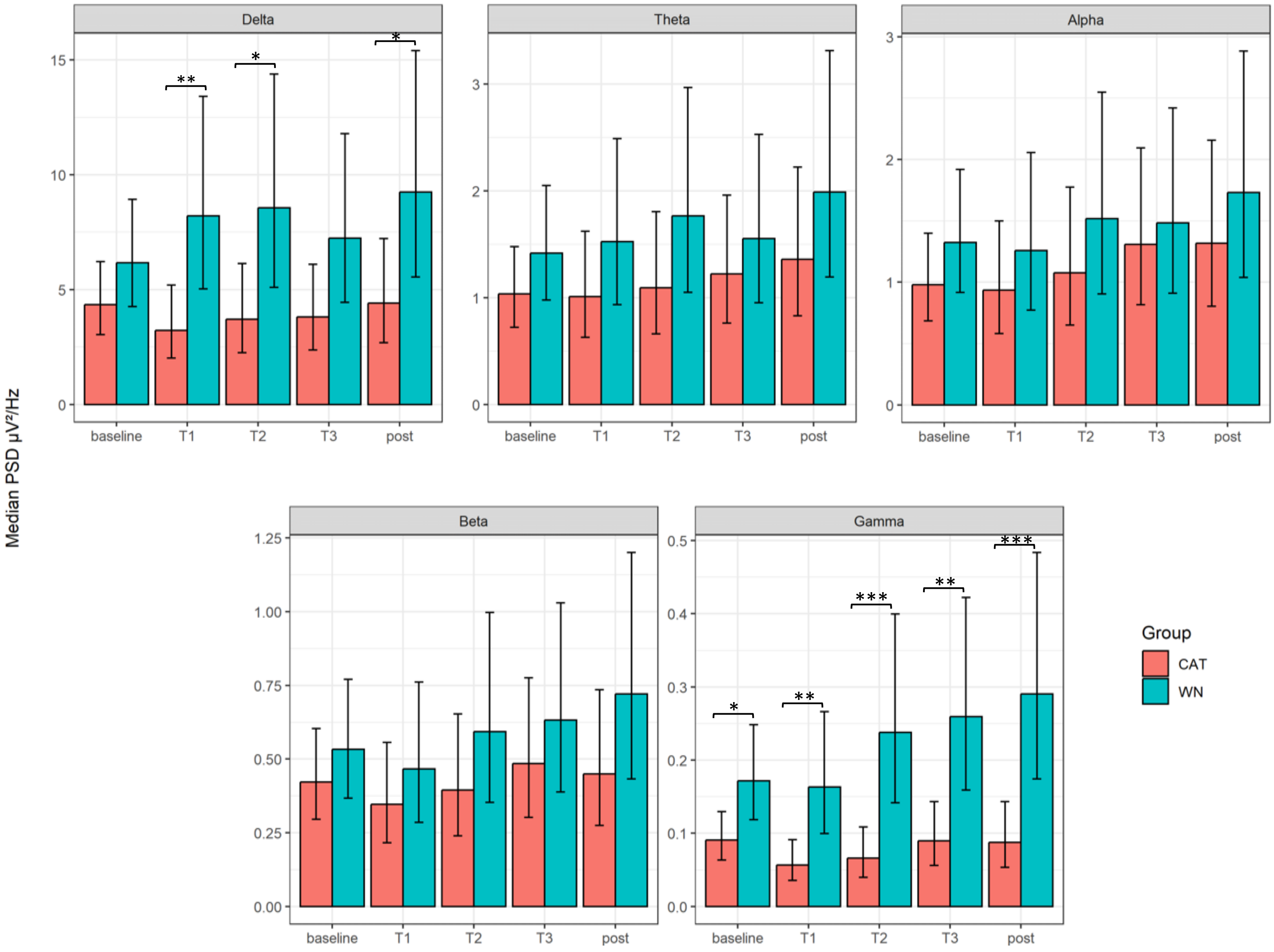


Figure 16. Differences in median PSD across time (baseline, sound training (T1, T2, T3), and post) per frequency band for the white noise and categorisation groups. While the white noise group demonstrated comparatively elevated PSD values in general, the median PSD was significantly higher for T1, T2, and post conditions of the delta band and all time points for the gamma band relative to the categorisation group. Error bars represent ± standard error (SE). Asterisk signifies the significance level (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

There was a significant difference in median PSD between the categorisation and white noise groups at the level of the delta and gamma frequency bands (Figure 16). Overall, there is a greater level of activity seen within the white noise group relative to the categorisation group. There was a significant difference in median PSD at T1 (WN Md = 8.21, CAT Md = 3.23, $p < 0.01$), T2 (WN Md = 8.56, CAT Md = 3.72, $p < 0.05$), and Post (WN Md = 9.25, CAT Md = 4.41, $p < 0.05$) for the delta band, and for all time points for the gamma band: baseline (WN Md = 0.17, CAT Md = 0.09, $p = 0.01$), T1 (WN Md = 0.16, CAT Md = 0.06, $p < 0.01$), T2 (WN Md = 0.24, CAT Md = 0.07, $p < 0.001$), T3 (WN Md = 0.26, CAT Md = 0.09, $p < 0.01$), and Post (WN Md = 0.29, CAT Md = 0.09, $p < 0.001$). Additionally, there was a significant difference in median PSD between the categorisation and white noise groups at the level of the postcentral gyrus (CAT Md = 0.52, WN Md = 0.99, $p < 0.05$) and centroparietal lobe (CAT Md = 0.64, WN Md = 1.26, $p < 0.05$).

6.4.4 **Connectivity analysis: Neural activity and functional connectivity**

General trends in neural activity

To spatially compare and contrast the effects of categorisation and white noise training on neural activity, topographic plots were computed of the power spectral density ($\log_{10}\mu V^2/Hz$) averaged over the five frequency bands investigated for the baseline and post-intervention conditions, as well as for the post-baseline difference (Figure 17). The categorisation group demonstrated an overall reduced level of activity relative to the white noise group, specifically following sound training (Figure 17). At baseline, the categorisation group exhibited a general reduction in activity, especially when compared to the white noise group (Figure 17). The categorisation group experienced a mild increase in activity within the dorsolateral prefrontal cortex (DLPFC; BA46), orbitofrontal cortex (OFC; BA10), and parahippocampus (PHC; BA37). Comparatively, the white noise group displayed a high level of activity at the level of the PHC and angular gyrus (AG; BA39), as well as elevated activity across the frontal lobe, specifically within structures such as the DLPFC, OFC, and inferior frontal gyrus (IFG; BA45).

There was a notable change in neural activity following sound training for both groups: the categorisation group demonstrated a mild reduction in activity centrally, however had a hotspot of increased activity within the primary visual cortex (PVC; BA17). Conversely, the white noise group experienced a global increase in activity with hotspots of activity confined to the IFG, medial temporal gyrus (MTG; BA21), and superior parietal sulcus (SPS; BA05). Additionally, elevated neural activity was also detected at the PHC, AG, and inferior temporal gyrus (ITG; BA20).

Overall looking at the activity difference (pre-training (baseline) minus post-training (post-intervention)), the categorisation group demonstrated a notable increase in activity within the PVC, as well as a mild increase in activity within the secondary somatosensory cortex (SSC;

BA02), supramarginal gyrus (SMG), and mixed activity at the level of the SPS. The categorisation group also demonstrated reductions in activity at the level of the DLPFC. In contrast, the white noise group exhibited an overall increase in activity globally, with hotspots of high activity localized to the MTG, IFG, and SPS, with milder elevations in neural activity within the ITG and mixed activity within the AG and PHC.

Neural activity: band-specific trends

Investigating the effect of sound training on neural activity further, the average PSD was broken down according to the frequency bands of interest (delta, theta, alpha, beta, and gamma) and visualized using topographic brain maps (Figures 18 & 19). Again, there are notable differences in activity both between the categorisation and white noise groups, as well as between the different frequency bands.

Delta

Both groups demonstrated elevated levels of activity for the delta band; specifically, a considerable hotspot of increased activity was observed at the PHC for both groups. Additionally, the categorisation group exhibited a mild increase in activity at the DLPFC, while the white noise group showed increased activity within the AG. Both groups showed an increase in overall activity post sound training, with the categorisation group displaying hotspots of increased activity within the region of the PVC while the white noise group showed increased neural activity within the AG, SPS, MTG, and IFG. Considering the difference in activity between baseline to post-intervention, the categorisation group saw an increase in activity surrounding the SSC and SMG, with a hotspot of increased activity localized to the PVC. The categorisation group experienced a reduction in activity at the level of the DLPFC, and mixed activity was observed within the SPS. Comparatively, the white noise group demonstrated a hotspot of increased activity confined to the MTG and SPS, with a milder increase in activity within the IFG, and mixed activity within the AG. Decreased activity was detected within the PHC for the white noise group.

Theta

The categorisation and white noise groups differ in their theta activity at baseline not only in the neural structures implicated, but also in the general pattern of activity; the categorisation group demonstrated a lower level of activity globally compared to the white noise group, with a marginal increase in activity at the DLPFC and PHC. In contrast, the white noise group experienced hotspots of increased activity within the AG and PHC, with a less noticeable increase in activity within the IFG and OFC. The categorisation group exhibited a mild increase in activity globally following sound training, with a specific hotspot of increased activity at the PHC and PVC. Conversely, the white noise group demonstrated a notable increase in activity across the IFG and inferior temporal gyrus (ITG, BA20). Furthermore, milder increases in activity were observed at the AG, PVC, PHC, and MTG. Considering the difference in activity between baseline to post-intervention, the categorisation group exhibited a mild increase in neural activity at the level of the PHC and PVC, as well as a mild reduction in activity at the DLFPC. The white noise group showed a notably different pattern of activity, demonstrating a mild increase in activity throughout, with hotspots at the IFG, ITG, SPS, PVC and PHC. A milder increase in activity was observed within the MTG, as well as mixed activity within the AG.

Alpha

Activity at baseline differs between the categorisation and white noise groups; the categorisation group exhibited a marginal reduction in activity localized to the fronto-parietal lobe with a mild increase in activity across the DLPFC and PHC, while the white noise group showed a mild increase in activity globally with hotspots of increased activity at the IFG, PHC, and AG. Following sound training, the categorisation group demonstrated a mild increase in activity globally in addition to a marginal increase in activity confined to the PVC. Comparatively, the white noise group also saw increased activity throughout the occipitoparietal lobe, in addition to a substantial increase in activity at the IFG and milder elevation within the AG, ITG, and PHC. Considering the difference in activity between baseline to post-intervention, the categorisation group demonstrated a marginal increase in activity across the occipital lobe, as well as a decrease in activity at the DLPFC. The white noise group showed a visible increase in activity at the IFG and ITG, as well as milder increases in neural activity within the PHC and PVC, and mixed activity within the AG.

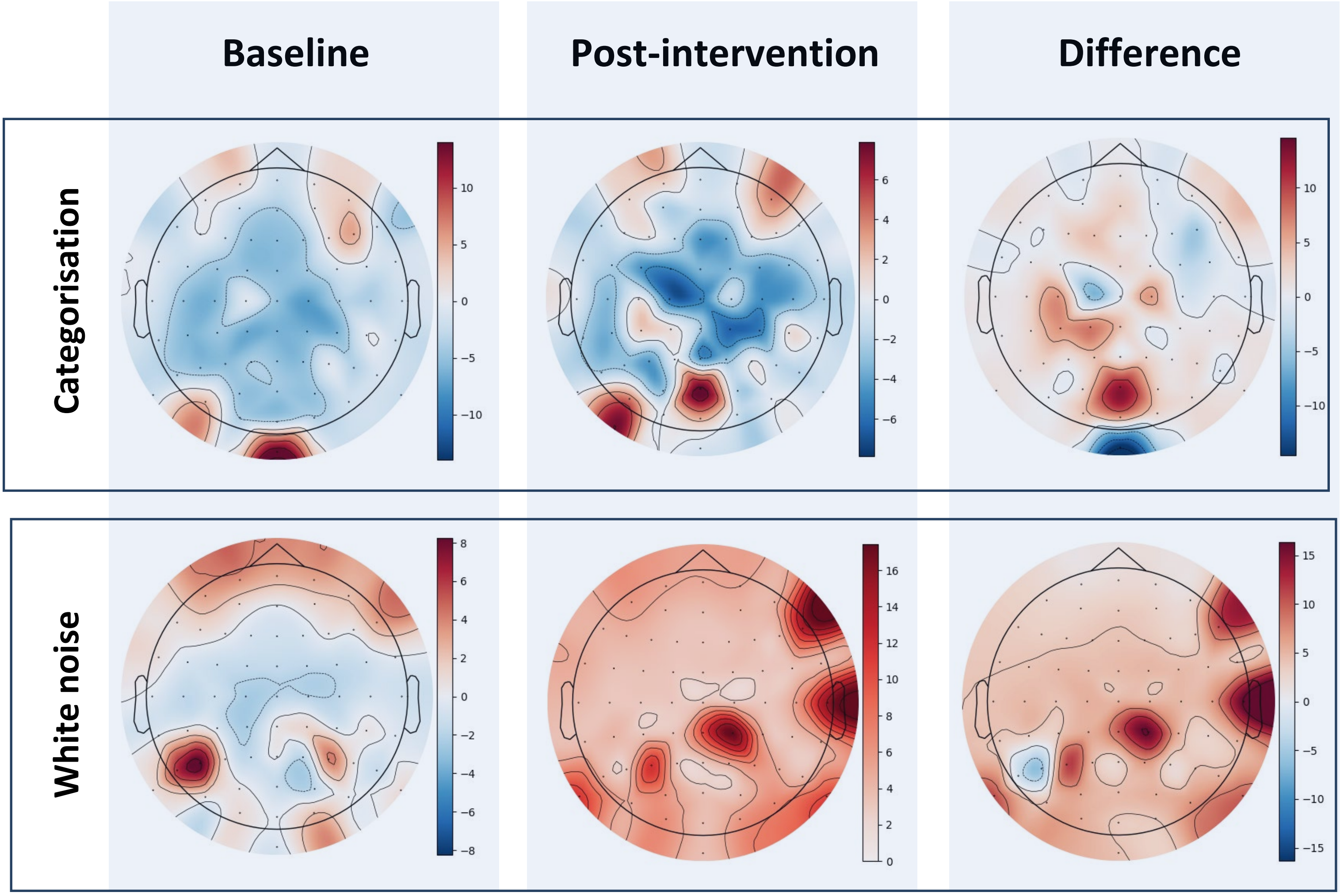


Figure 17. Topographic maps of the power spectral density ($\log_{10}\mu V^2/Hz$) averaged over the five frequency bands (delta, theta, alpha, beta, and gamma) for the categorisation and white noise groups at baseline and post-intervention conditions, as well as for the post-baseline difference. The power range is shown in the corresponding colour bars, where red indicates an increase in activity and blue depicts a decrease in activity.

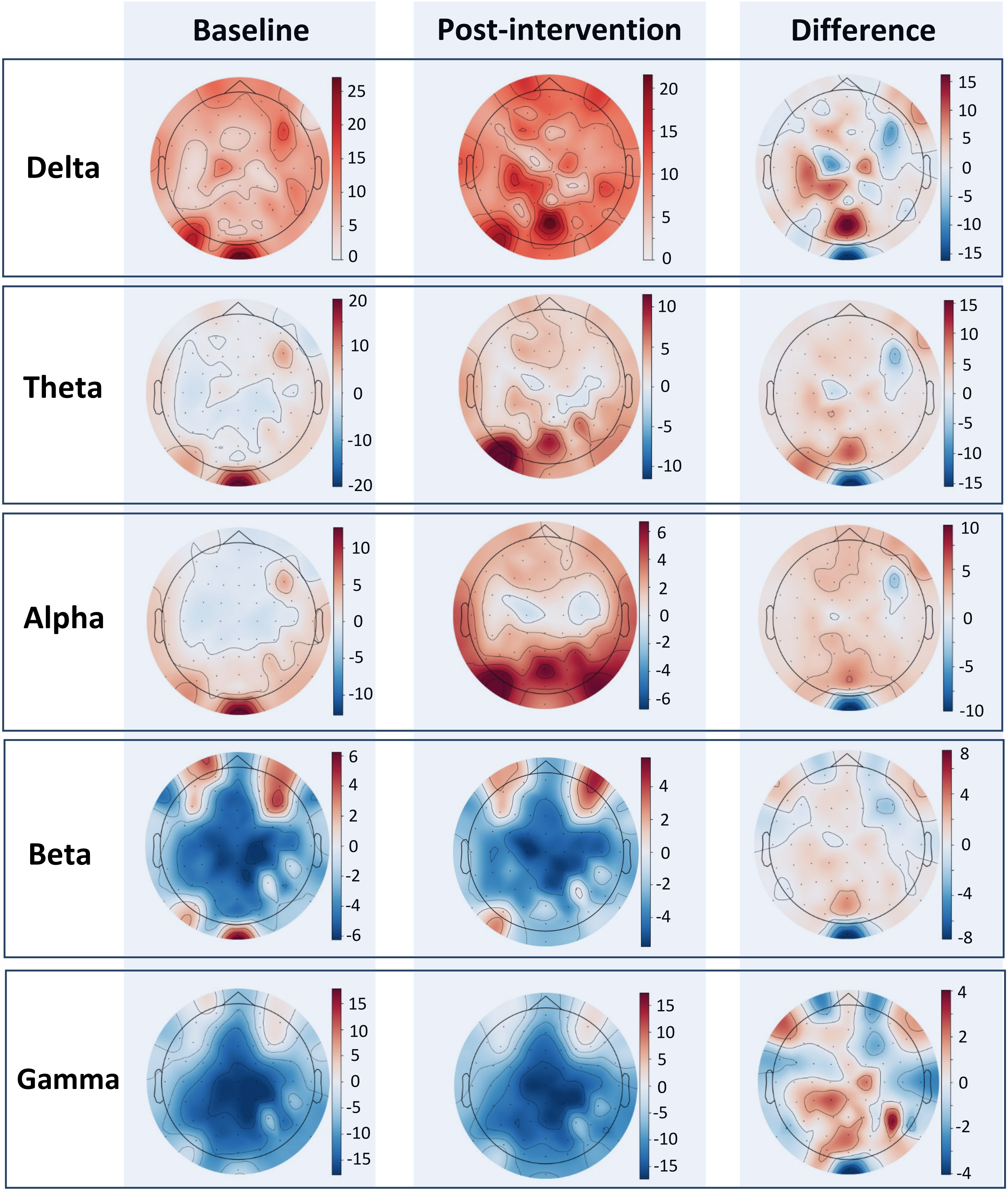


Figure 18. Categorisation group topographic maps of the power spectral density ($\log_{10}\mu V^2/Hz$) decomposed into each of the five frequency bands (delta, theta, alpha, beta, and gamma) at baseline and post-intervention conditions, as well as for the post-baseline difference. The power range is shown in the corresponding colour bars, where red indicates an increase in activity and blue depicts a decrease in activity.

Beta

Both categorisation and white noise groups demonstrated a general reduction in activity globally, with specific hotspots of increased activity; categorisation group had increased activity surrounding the OFC and pre-supplementary motor cortex (pSMC), while the white noise group exhibited increased activity within the IFG, AG, and secondary visual cortex (SVC). Both groups experienced elevated activity at the level of the DLPFC and PHC. Patterns of neural activity following sound therapy are like those seen at baseline for the categorisation group; comparatively, the white noise group saw an increase in activity in the occipitoparietal region, with a hotspot of increased activity within the AG and IFG. Considering the difference in activity between baseline to post-intervention, both groups had mildly elevated neural activity throughout following sound training. Additionally, there was a slight increase in neural activity within the occipital lobe for the categorisation group, as well as a mild reduction in activity within the DLPFC and pSMC. Conversely, the white noise group revealed a hotspot of increased activity within the IFG, as well as a mild increase in activity within the right PHC. Moreover, a mild reduction in neural activity was observed within the left PHC, along with mixed activity localized to the AG.

Gamma

The categorisation group experienced a global decrease in activity at baseline with a mild increase in activity within the DLPFC that can also be observed post-intervention; however, looking at the difference in activity between baseline to post-intervention, there is a hotspot of increased activity within the AG, in addition to mildly elevated activity at the DLPFC, IFG, SSC, and visual cortices. Furthermore, the categorisation group experienced a reduction in activity within several meaningful structures including the primary auditory cortex (PAC), OFC, and MTG, with milder reductions in neural activity within the PHC and ventrolateral prefrontal cortex (VLPFC). Considering the white noise group, baseline activity demonstrates a general decrease in activity throughout, specifically within the PHC, with hotspots of mild increased activity within the AG, DLPFC, and SVC. Post-intervention for the white noise group saw a preservation of the general decreased activity however with several hotspots of increased activity showing up at the IFG, SMG, and AG, as well as mild elevation within the PHC, SVC, and DLPFC. Examining the difference in activity between baseline to post-intervention for the categorisation group, there was a notable increase in the IFG, SMG, PHC, and right AG, as well as a mild increase in activity at the MTG and PAC, and mild decrease within the left AG.

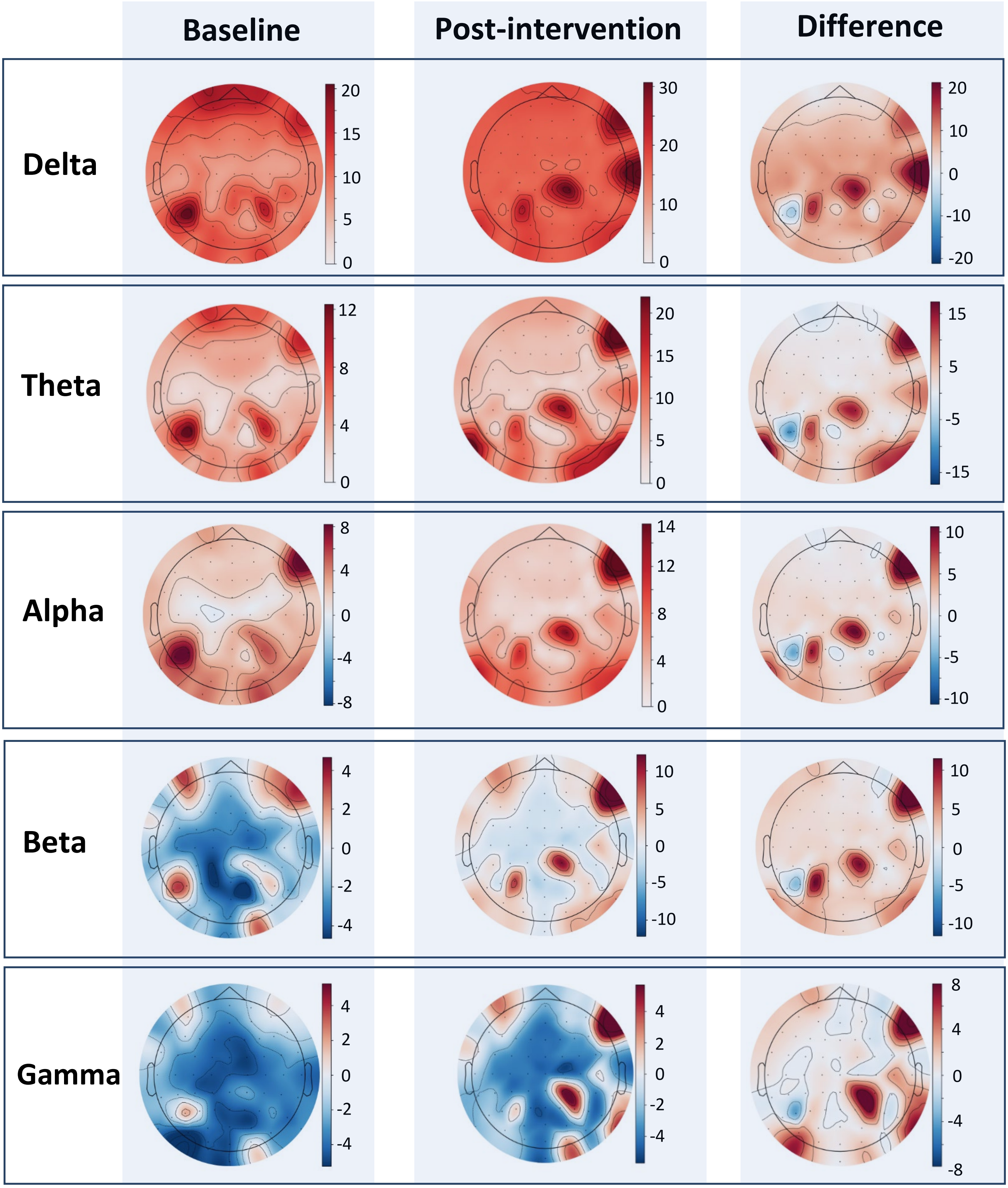


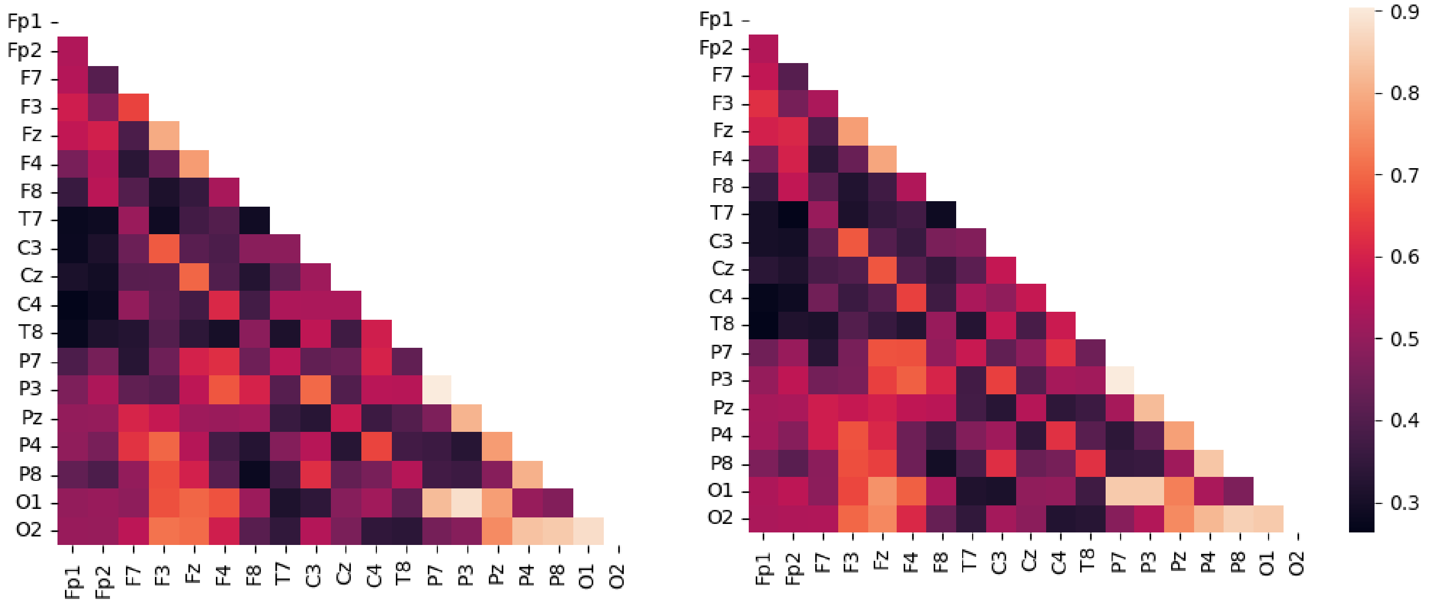
Figure 19. White noise group topographic maps of the power spectral density ($\log_{10}\mu V^2/Hz$) decomposed into each of the five frequency bands (delta, theta, alpha, beta, and gamma) at baseline and post-intervention conditions, as well as for the post-baseline difference. The power range is shown in the corresponding colour bars, where red indicates an increase in activity and blue depicts a decrease in activity.

Functional connectivity: phase locking value versus novel SNN methods

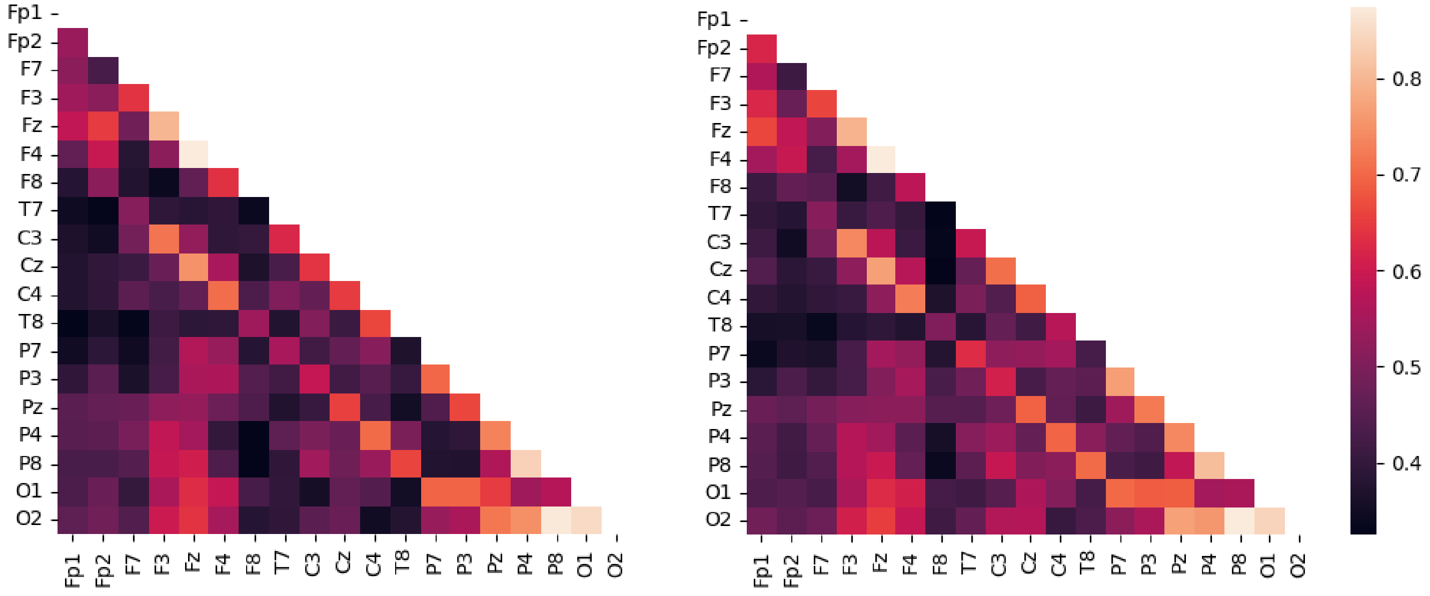
Functional connectivity was examined using 1) a conventional phase locking value (PLV) method of connectivity analysis in which changes in the connectivity network (increase/decrease) were identified by measuring the correlation between two pairs of EEG channels, and 2) a novel SNN architecture based cluster analysis in which the total temporal interaction (in terms of spike communication) between 64 input neurons is calculated during STDP learning to generate an average one-to-one interaction between the input neurons (EEG electrodes), with thicker lines indicating stronger interactions. Interestingly, the two methods gave rise to different outcomes.

Phase locking value

Observing the PLV connectivity network at baseline and post-intervention for both the categorisation and white noise groups reveals similar patterns in connectivity form baseline to post sound training (Figure 20). Overall, both the categorisation and white noise group demonstrated a higher level of connectivity between the O1-O2 (SVC) electrodes; additionally, the categorisation group also showed increased connectivity between the P3-P7 (AG and PHC respectively) and P3-O1 (AG and SVC respectively) electrodes, while the white noise group exhibited an increase in connectivity between the F4-Fz (pSMA) and P8-O2 (PHC and SVC respectively) pairs of electrodes.



(A) Categorisation baseline **(B) Categorisation post-intervention**

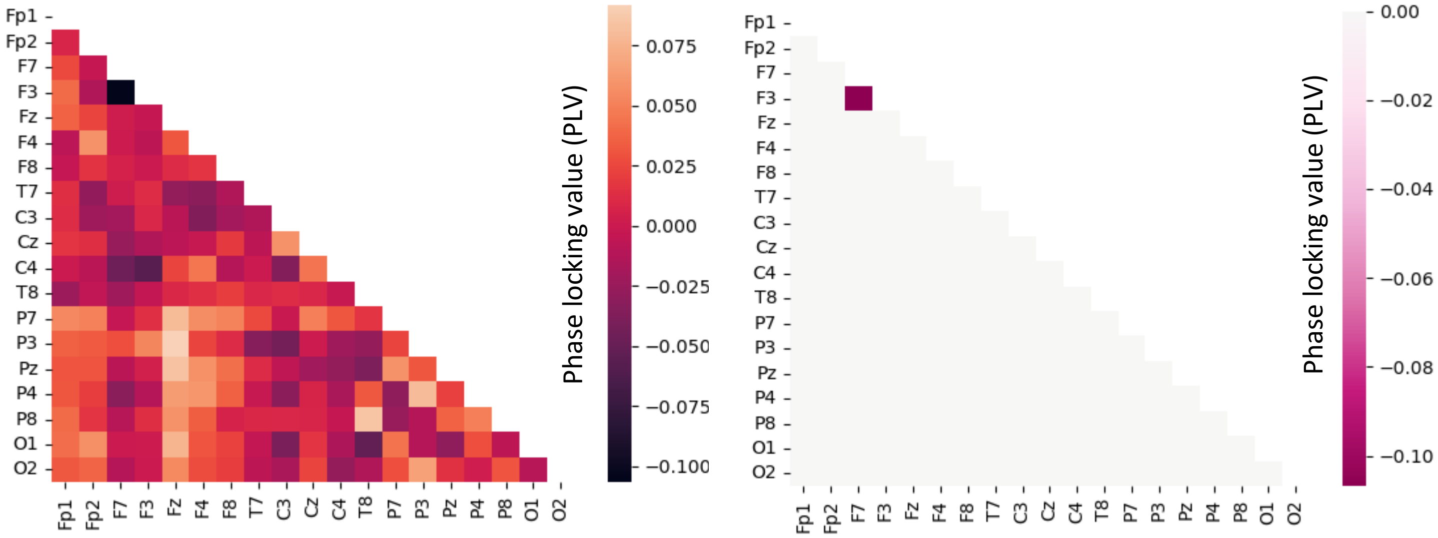


(C) White noise baseline **(D) White noise post-intervention**

Figure 20. Phase locking value (PLV) connectivity estimates for EEG channel pairs across both baseline and post-intervention conditions for the categorisation **(A, B)** and white noise **(C, D)** groups. The degree of connectivity is shown in the corresponding colour bars; the darker the colour, the weaker the functional connectivity.

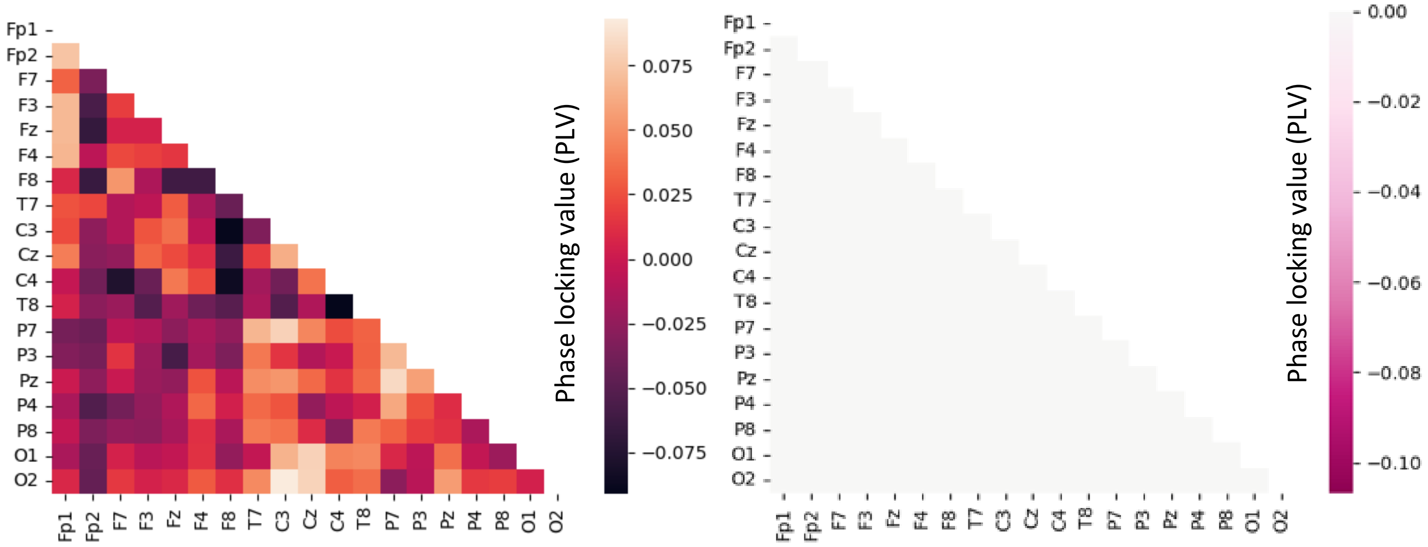
Differences in connectivity were computed to investigate potential changes in connectivity as a result of sound training for both categorisation and white noise groups (Figure 21). Connections that demonstrated the greatest degree of change from baseline to post-intervention (defined as an inter-channel connectivity with an absolute difference of at least

0.1) are highlighted in Figure 21. The darker the shade of pink on the colour bar of the absolute difference matrix, the greater the decrease in functional connectivity post-intervention compared to baseline (pre-intervention); there were no cases in which an increase in connectivity was observed. Considering the absolute difference between the baseline and post-intervention connectivity matrix, it appears that the only notable difference in activity is a decrease in connectivity at the level of the F3-F7 (pSMA and VLPFC respectively) electrodes in the categorisation group (Figure 21B).



(A) Categorisation difference

(B) Categorisation absolute difference



(C) White noise difference

(D) White noise absolute difference

Figure 21. Baseline to post-intervention differences in phase locking value (PLV) connectivity estimates for EEG channel pairs for the categorisation (**A**, **B**) and white noise (**C**, **D**) groups. Absolute difference plots (**B** and **D**) highlight inter-channel connectivity with an absolute difference of at least 0.1. Changes in connectivity can be examined using the absolute difference colour bar; the darker the shade of pink, the greater the reduction in functional connectivity. Note: no increase in functional connectivity was observed going from baseline to post-intervention conditions in either group.

Spiking Neural Networks cluster analysis

None of the regions identified by the PLV method as having significant levels of connectivity were confirmed as having a high level of connectivity upon using the SNN-based method of analysis. Neuronal interaction lines formed between the input neurons following sound training differed slightly between the categorisation and white noise groups (Figure 22).

While both groups showed thick lines indicative of a strong interaction between PO7-PO8 (PHC), TP8-P10 (MTG and PHC), and FC6-C6 (IFG and PAC) pairs of electrodes, the categorisation group also revealed an increased level of connectivity between FPz-FP1 (OFC), FT8-C6 (VLPFC and PAC), and AFz-T7 (DLPFC and secondary auditory cortex (SAC)). Comparatively, strong interactions have been observed between AFz-FP1 (DLPFC and OFC), AFz-FT7 (DLPFC and VLPFC), and again at the F8-C6 (IFG and PAC) electrodes for the white noise group.

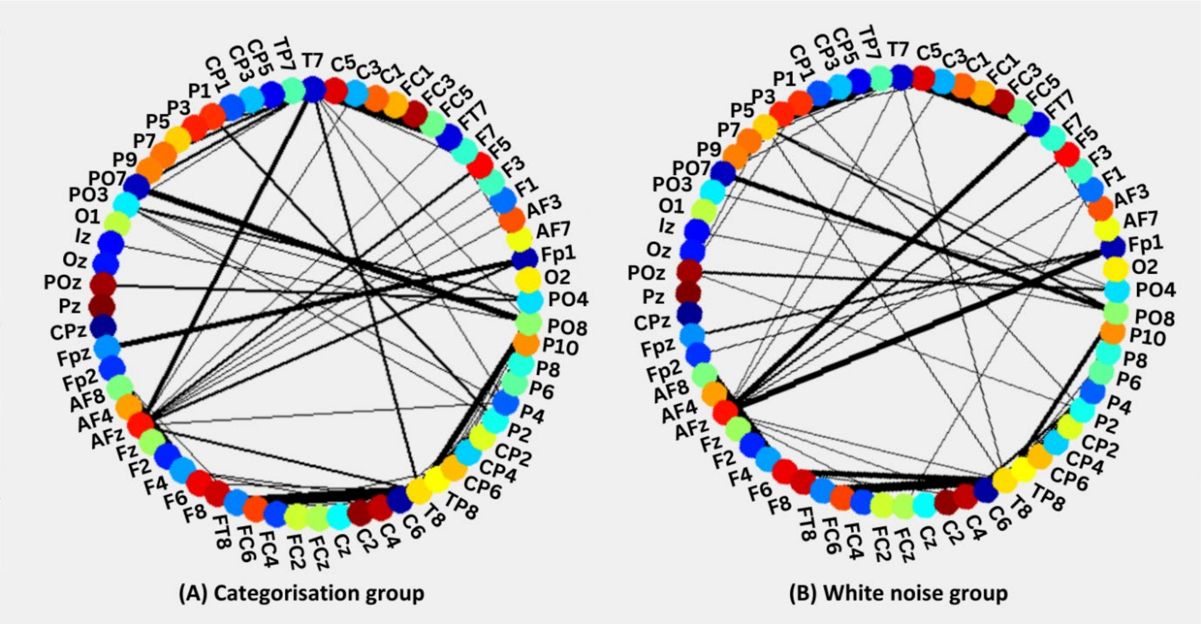


Figure 22. Feature Integration Network (FIN) demonstrating the average one-to-one interaction between the 64 input neurons (electrode sites) based on the total input interaction for the (A) categorisation and (B) white noise groups post sound training. FIN nodes denote input neurons (electrode sites), and the lines connecting the nodes represent connectivity weights between them (thicker lines indicate greater causal interaction bewteen neural areas corresponding to the respective electrodes).

Brain-inspired spiking neural networks: using AI to predict therapeutic success

A SNN model was trained using EEG data collected at baseline (pre-intervention) to predict output classes post sound training (post-intervention) so as to determine whether the SNN architecture can reliably be used to predict patient’s response to sound therapy. The predictive outcomes were the two groups of participants (i.e., therapeutic responders and non-responders) as defined by a 13-point improvement in TFI scores. The leave-one-out cross-validation (LOOCV) method was implemented for pattern classification, with the model having an overall accuracy of 91.67%, classifying non-responder samples with 93.57%

accuracy, and responder samples with 89.44% accuracy. Furthermore, running the classification on the categorisation and white noise groups separately, the model had an overall accuracy of 93.89% for the categorisation group and 96.43% for the white noise group. The SNN model classified non-responder samples in the categorisation group with 98.89% accuracy and the white noise group with 98% accuracy, and classified responder samples with 78.89% accuracy in the categorisation group and 95.56% in the white noise group.

6.5. Discussion

This study investigated the effects and neurophysiological mechanisms of categorising tinnitus to a familiar broadband environmental sound (rain) using a passive perceptual training approach. It was hypothesised that 1) a tinnitus avatar generated using several psychoacoustic parameters (pitch, loudness, spatial location) would accurately reflect participant's tinnitus experience, 2) passive auditory categorisation training would offer greater tinnitus relief (reduced tinnitus severity and related distress) than standard practice white noise and 3) categorisation training related alterations in tinnitus perception might be reflected in changes in neural activity and functional connectivity. Generation of an appropriate tinnitus avatar representative of participant's tinnitus experience was achieved in this study. While both groups experienced benefit from the passive sound training, only the white noise group saw significant reductions in tinnitus severity and related distress (Figure 15). Though this is contrary to the hypothesis of this study, the acute training-related changes in neural activity within regions associated with tinnitus distress (specifically at the level of the prefrontal cortex) that were observed following categorisation training offer promising implications for the use of categorisation training for tinnitus management, and support the further investigation of auditory perceptual training paradigms of sound therapy. Moreover, differences in neural activity between the white noise and categorisation training groups allude to the involvement of different pathways or modes of action, suggesting that perhaps the application of only one or the other in isolation might be an oversimplified approach to tinnitus management.

The study aimed to gain a better understanding of tinnitus avatars and their role in sound therapy, as well as to discern whether there are benefits in opting for more complex modes of sound therapy over conventional broadband noise (BBN). Overall, the behavioural, qualitative, and electrophysiological results of this study are encouraging and support further exploration of passive sound therapy for tinnitus management. The following discussion will evaluate and consider these outcomes more thoroughly, teasing out their implications for passive sound therapy and its place in tinnitus management.

6.5.1 **Tinnitus avatar and its implementation in sound therapy**

Overall, participants in both groups were satisfied with the similarity of the avatar to their tinnitus in terms of how accurately and completely it captured the sensation in its entirety (Table 8). Participants had a neutral reaction to the tinnitus replica, neither liking nor particularly disliking the sound. This was encouraging as it meant that the replica could be used as a starting point in the perceptual training paradigm. The avatar was reflective of the tinnitus (in its pitch, loudness, and spatial location), but was also tolerable enough to be listened to by participants without inducing feelings of distress and discomfort commonly associated with tinnitus. Furthermore, qualitative findings support the application of the tinnitus avatar within a sound therapy mode of tinnitus management; participants generally found the training sound to be soothing/relaxing, non-intrusive, and easy to ignore. Only one participant felt that the training sound was annoying and unpleasant, largely due to it reflecting their own tinnitus sensation, and two participants mentioned the avatar failed to reflect their tinnitus at some point along the training period. Categorisation training is based on perceptually re-categorising one sound to another (Durai, Doborjeh, et al., 2021; Guenther et al., 1999; Guenther et al., 2004); as such, it is imperative that an accurate tinnitus avatar is generated to ensure that the sound being recategorised to the broadband environmental sound (rain) is in fact the participant's tinnitus and not a sound distinct from it (i.e., a poorly matched replica). Inaccurate tinnitus avatars could compromise the efficacy of auditory categorisation training. These findings highlight the need to allow for personalisation and real-time remote adjustment of tinnitus therapeutics; perhaps enabling participants to adjust their avatar to match their tinnitus via a mobile phone app (Mahboubi, Ziai, & Djalilian, 2012; Searchfield & Sanders, 2022). Such real-time adjustment would allow for better categorisation training efficacy as it would ensure that the tinnitus replica remains representative of the tinnitus being categorised. Additionally, it would be useful for clinicians/researchers to have access to participant data so as to monitor any changes in tinnitus and ensure participants are following treatment plans accordingly. Participants in this study were instructed to listen to their training tracks at the same loudness level as their perceived tinnitus – no louder or quieter. It is possible that the level of sound presentation affected treatment results; while white noise can typically be presented at or above the minimum masking level (MML), the categorisation training track was to be played at the same loudness level as the tinnitus so as to not be perceived as a sound distinct from the tinnitus itself and allow for ease of integration and categorisation to the rain sound. While participants were instructed and reminded of the level of sound presentation, follow-up remarks indicate that perhaps some individuals played their training tracks at a level greater than their tinnitus. Further work is required to determine the optimal level of sound presentation for use within a categorisation training paradigm.

6.5.2 **Psychological versus physiological impact of passive sound therapy**

Sound therapy related behavioural changes

Participants who were prescribed white noise sound therapy experienced a statistically significant decrease in tinnitus impact and severity (as evidenced by reductions in TFI and TSNS scores respectively), as well as a reduction in negative emotional affect (reduced negative emotionality score of the PANAS) following the 30-day training regime (Figure 15). The categorisation group also demonstrated reductions in TFI, TSNS, and PANAS scores, however changes in these behavioural measures were not significant enough to imply a meaningful improvement in tinnitus with categorisation training. The two groups were well matched for age, sex, and tinnitus duration, however the white noise group was comprised of more distressed individuals (as evidenced by higher baseline scores across the behavioural measures, i.e. TFI, TSNS, and PANAS). This is not the first study to demonstrate that treatment respondents reflect a subset of individuals whose lives and quality of living is severely impacted by tinnitus (Lehner et al., 2012; Maxwell et al., 2021; Searchfield et al., 2023; Theodoroff et al., 2017). While it is not clear whether the greater tinnitus severity of the white noise group at baseline influenced their response to the conventional sound therapy, it is possible that this higher level of tinnitus distress meant that individuals belonging to the white noise group had more room for improvement and as such were more susceptible to therapeutic benefit (Maxwell et al., 2021). On the other hand, one might argue that greater tinnitus severity could conversely pose a barrier to improvement; however, it seems reasonable that individuals who are not as bothered by their tinnitus experience less benefit from therapy. Future studies are encouraged to stratify randomisation to ensure an appropriate balance in baseline scores across behavioural measures (specifically the TFI) between treatment groups.

Sound therapy related neural changes

There was a clear difference in both the amount of cortical activity observed between the two groups, as well as the neural structures implicated following sound training. While the categorisation group displayed a reduced level of neural activity relative to the white noise group in general, a significantly lower degree of activity was identified for the delta and gamma frequency bands (Figure 16). While it is not clear as to why the two groups differed so prominently in their neural activity at baseline, it is hypothesised that this might reflect the elevated degree of tinnitus distress and severity experienced by the white noise group (as determined by the behavioural measures, i.e., TFI, TSNS, and PANAS scores). Differences in neural activity and functional connectivity have been identified in the transition from acute to chronic tinnitus (Lan et al., 2021; Vanneste, van de Heyning, et al., 2011). Additionally, different patterns of neural connectivity were observed between non-bothered (Wineland et al., 2012) and bothered (Burton et al., 2012) tinnitus patients relative to healthy controls. It is possible that the neural structures involved in tinnitus and the degree to which they are affected increase to reflect the worsening of tinnitus symptoms, or perhaps illustrate the progression from tinnitus-to-tinnitus disorder. However, there is insufficient evidence in the results of this study to lend support to such notions and/or draw conclusions on what the neural differences between the two groups represent.

Both groups demonstrated an increase in activity at the level of the PHC, DLPFC, and OFC at baseline (Figure 17). These findings offer support to previous studies reporting maladaptive neural changes in the frontal, temporal, and parietal areas of individuals with bothersome tinnitus (Cheng et al., 2020; Han, Na, et al., 2019; Schecklmann et al., 2013; Shulman & Goldstein, 2002; Ueyama et al., 2013). These areas are each thought to play a role in the manifestation, propagation, and maintenance of tinnitus. Aberrant parahippocampal activity is thought to prevent habituation to the tinnitus signal (De Ridder et al., 2006; Vanneste, van de Heyning et al., 2011), while the DLPFC and OFC are involved in the emotional processing and interpretation of tinnitus, often believed to be associated with tinnitus-related distress (Golm et al., 2016; Vanneste & De Ridder, 2012a; Vanneste et al., 2010). The prefrontal cortex has been described as a "candidate for the integration of sensory and emotional aspects of tinnitus" (Jastreboff, 1990), with studies reporting that bothersome tinnitus is correlated with elevated activity within structures such as the DLPFC and medial prefrontal cortex (Golm et al., 2013). At baseline, the white noise group also experienced a high level of activity within the AG, as well as elevated activity within the IFG. The AG (along with the precuneus, posterior cingulate cortex, medial prefrontal cortex, and inferior parietal cortical regions) belongs to the default mode network (DMN), a resting-state functional network of tinnitus (Husain & Schmidt, 2014; Mantini et al., 2007). The function of the DMN, along with several other neural networks including the auditory, limbic, visual, saliency, and attention networks (specifically the dorsal attention network (DAN) comprised of the intraparietal sulcus and frontal eye fields, and the ventral attention network (VAN) consisting of the temporoparietal junction and ventral frontal cortex) is compromised in tinnitus (Vanneste & De Ridder, 2012a); as such, reversal of aberrant activity in these networks via perceptual auditory training may result in tinnitus improvement.

Following acute exposure to the training sounds, the categorisation group experienced an increase in activity at the level of the PVC, SSC, and SMG and a reduction at the DLPFC, while the white noise group showed an increase in activity globally, particularly at the level of the MTG and IFG, with mixed activity at the AG and PHC. Additionally, both groups experienced a high level of functional connectivity in the visual cortices (Figure 17). Passive auditory stimulation has previously shown reductions in neural activity within the visual cortex through the recruitment of local inhibitory circuitry within the PVC (Amaral & Langers, 2015). This was not observed in this study this study, however Durai, Doborjeh et al. (2021) suggest that activation of regions involved with visual categorisation and recognition might reflect the brain's attempt at identifying visual information for the corresponding training sound. Furthermore, the reduction of DLPFC activity achieved using the categorisation training is an encouraging result as it suggests that the training might interfere with processes that play an active role in tinnitus distress (Vanneste et al., 2010).

The DLPFC contains auditory memory cells, has a bilateral facilitatory effect on auditory memory storage, and is associated with auditory attention and early inhibitory modulation of input to the PAC (Shekhawat & Vanneste, 2018; Vanneste & De Ridder, 2012a). Patients with bothersome tinnitus experience a greater level of activity in the DLPFC relative to individuals with mild tinnitus (Golm et al., 2013); occlusion or reversal of the maladaptive activity within the structures of the prefrontal cortex, specifically the DLPFC, could in turn alleviate tinnitus severity and related distress. Additionally, the categorisation group saw a reduction in gamma band activity within the auditory cortex following perceptual sound training; given that gamma activity in the auditory cortex reflects tinnitus intensity (De Ridder, Elgoyhen, et al., 2011; Van Der Loo et al., 2009; Vanneste et al., 2017), this finding offers supplementary support to the potential benefit of categorisation training for tinnitus management.

In contrast to the categorisation group, the mixed activity at the level of the AG and PHC seen post-intervention for the white noise group might reflect the ability of broadband noise to divert attention from the tinnitus and aid habituation (Henry et al., 2006a; Searchfield, 2021). Furthermore, stimulation of the hyperactive AG has been found to eliminate tinnitus (Plewnia, Reimold, Najib, Brehm, et al., 2007); as such, the ability of white noise to alter its neural activity is an encouraging result. The white noise group also demonstrated a high level of functional connectivity between the AG and PHC (Figure 17). While this has not previously been demonstrated in the literature, it may reflect the shared role of the AG and PHC in auditory memory (Li et al., 2022; Shulman, 1995; Vanneste & De Ridder, 2012a), however further work is required to investigate the significance of this result. It is evident that the two treatment sounds appear to act through different mechanisms, targeting different cortical structures. The reduction in the DLPFC following perceptual training is a common finding among the categorisation group, with the trend being maintained even when breaking neural activity down according to the frequency bands of interest (Figure 18). Comparatively, while the white noise group did not demonstrate such consistent changes at the level of the DLPFC, it saw the reoccurring involvement of the AG throughout. This stands as another point of difference between the two groups; the categorisation group predominantly recruited the DLPFC while the white noise group saw greater engagement of the AG. While this might be a treatment-specific effect, it is also possible that elevated activity of these regions at baseline is indicative of different tinnitus subtypes or personality profiles (Mohan et al., 2022; Simoes, 2021; Song et al., 2015). It would be useful to compare the resting state activity of the two groups relative to non-tinnitus subjects so as to gain a better understanding of the dimensions across which the groups differ, and whether they might inform response to treatment.

The fact that the auditory categorisation training and white noise sound therapy target distinct, yet equally therapeutically significant neural structures is a valuable and informative finding of this study. It might be that the implementation of categorisation training or white noise in isolation (as was done in this parallel treatment design) is perhaps an oversimplified approach to tinnitus management, in turn limiting therapeutic success. While the neural structures affected by the two modes of sound therapy commonly overlapped, the reduction in activity at the prefrontal cortex was only seen following categorisation training, and comparatively the change in AG activity was only achieved using white noise. This suggests that there is room for an improved approach to therapy, perhaps by presenting the two sounds simultaneously or adopting a staged mode of treatment (Figure 23). This would theoretically reflect a ‘two birds, one stone’ means of sound therapy, where neural structures involved in tinnitus can simultaneously be targeted through auditory training stimuli acting via different neural pathways or mechanisms to offer the greatest chance of relief. Future studies are encouraged to implement a factorial and/or cross-over trial design as outlined in Figure 23 to discern whether there is any added benefit to combining and/or staggering the white noise/categorisation sound therapies.

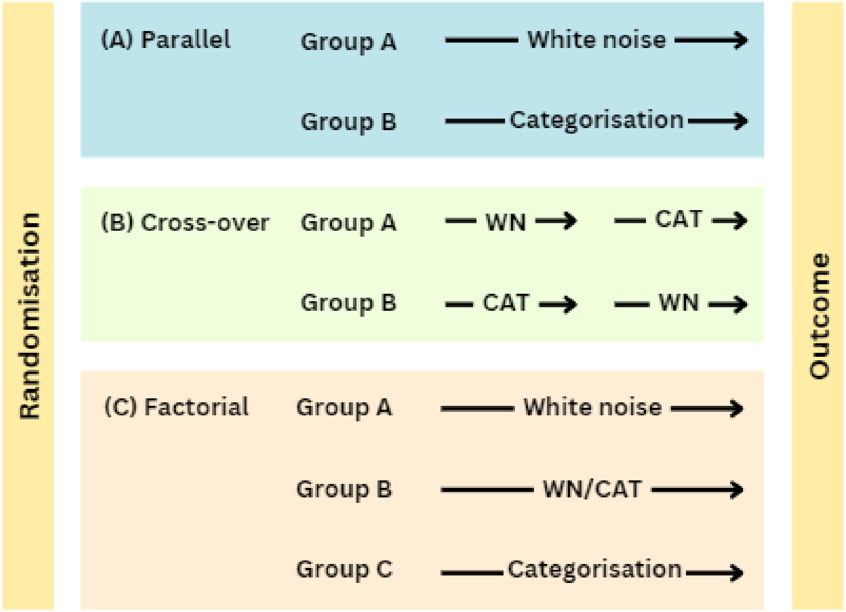


Figure 23. Schematic proposal of different trial designs that could be applied in the future to determine whether there is any additional benefit to combining and/or staggering conventional white noise sound therapy with novel passive categorisation training for tinnitus therapy. **(A)** A classic parallel design was used in this study whereby participants were randomised to either the white noise or categorisation training group and received the single therapy they were assigned to for the duration of the trial. Future studies are encouraged to investigate the benefits of using either a **(B)** cross-over design, in which participants are randomised to either the white noise or categorisation group at the start of the trial, before subsequently swapping to the alternative treatment at the midway point of the trial, or **(C)** factorial trial in which participants are randomised to a white noise group, categorisation group, and mixed group in which the white noise and categorisation are administered simultaneously. Note: WN = white noise, CAT = categorisation.

The results of this study propose a reconsideration of current 'single auditory stimuli' methods of sound therapy and encourage the shift to a more polytherapeutic approach to treatment. While neural changes were observed for both groups, clinically significant improvements in tinnitus severity were only observed with the white noise group. Considering these findings within an adaptation level theory (ALT) (Searchfield et al., 2012) framework of tinnitus, it is possible that this is a reflection of the fact that white noise likely acts through a different mode compared to the categorisation training sound (Durai & Searchfield, 2017). The ALT posits that the overall perceived magnitude of tinnitus can change from moment to moment, adapting based on changes in cochlear outflow, context, emotion, and attention. Namely, the interaction of several factors – including the tinnitus signal itself, background/contextual stimuli, and residual/social factors – act to shape an individual's 'frame of reference' and determine how any given individual experiences and reacts to their tinnitus (Searchfield et al., 2012; Searchfield et al., 2019). Durai and Searchfield (2017) hypothesised that broadband noise acted through a 'presence of sound effect’, whereby a reduction in tinnitus is achieved by shifting the individual’s internal adaptation level away from their tinnitus and towards the background noise stimulus, while nature sounds offer relief through a ‘valence of sound effect’ based on the neutralisation of tinnitus-related negative emotions, stress, anxiety, and depression. Durai and Searchfield (2017) suggest that the dynamic quality of nature sounds means that they perhaps require more time to reach peak adaptation, in turn offering a delayed tinnitus benefit. The results of this study support this notion; auditory perceptual training using broadband nature sounds interferes with neural pathways associated with tinnitus perception and related distress. It is possible that while white noise offers immediate relief through its masking quality, more complex auditory stimuli such as that applied within a categorisation training paradigm require more time to alleviate tinnitus symptoms and achieve relief as they are not designed to be applied as ‘maskers’ and likely act through more long-term pathways. Further work is required to define and contrast the mechanisms of action of simple versus complex sounds in sound therapy, as well as to determine the most appropriate method of application.

Functional connectivity: comparison of conventional and novel neural connectivity measures

The two methods of functional connectivity analysis gave rise to different results, however there was some agreement with regards to the regions impacted by the sound training. According to the PLV, only the categorisation group experienced a change in functional connectivity following sound exposure. Passive auditory sound training resulted in a reduction in functional connectivity between the left pSMA and the left VLPFC for the categorisation training group (Figure 21B). While functional connectivity between the pSMA and prefrontal areas is not a novel finding (Johansen-Berg et al., 2004; Lima et al., 2016), the significance of this change in neural connectivity within the context of tinnitus is not well understood. The role the pSMA plays in tinnitus perception is obscure, however there is evidence to suggest that it is involved in modulating auditory-motor interactions (Lima et al., 2016) and filling in missing auditory input (Shahin et al., 2009). If tinnitus is propagated or maintained by abnormal increases in gain within the central auditory pathway (as per the central gain theory of tinnitus), it is possible for there to be recruitment and increased involvement of the pSMA. In contrast to the pSMA, the VLPFC was initially believed to have a role in tinnitus control (Vanneste & De Ridder, 2012c), however this function has not been substantiated further in the literature and subsequent studies have instead proposed the involvement of the VLPFC in nonspatial auditory cognition and congruity (Song et al., 2012). Considering this in the context of the current findings, we propose that a reduction in functional connectivity in these regions might reflect a change in the spontaneous motor response to the categorisation training stimuli and/or tinnitus signal, however additional efforts are required to further investigate these networks and their role in tinnitus.

In contrast to these findings, the SNN cluster analysis identified increased functional connectivity in neural attention networks and several cortical regions associated with emotional and auditory processing following sound therapy for both groups (Figure 22). Tinnitus is known to be associated with increased functional connectivity between the auditory and limbic systems (Chen, Xia, et al., 2017; Kim et al., 2012; Maudoux et al., 2012); it is believed that tinnitus distress is likely correlated to this enhanced connectivity between the auditory and emotional centres, and that treatments that poses the ability to reduce this connectivity are likely to provide therapeutic benefit to tinnitus. This study did not identify a reduction in connectivity within these structures. Moreover, the study found that the categorisation group demonstrated greater connectivity between the attention networks and auditory cortices, while the white noise group saw increased connectivity between the attention networks and areas involved in emotional processing of sound. Sound therapy is believed to alter the tinnitus experience by interfering with its audibility or perception, changing the individual's reaction to sound, and/or providing context and reality to the phantom auditory signal (Searchfield et al., 2019). These results might reflect the differential processing and interpretation of the two auditory stimuli by the brain: categorisation training stimuli likely requires attentional auditory resources to evaluate and give context to the dynamic categorisation training stimuli as it morphs from the avatar to the rain sound, and conversely the involvement of emotional networks could illustrate the presence of sound effect of white noise. Further work is required to understand the effects of passive perceptual training versus white noise effects on functional connectivity. It is important to reflect on the fact that non-auditory regions – such as those involved in attention and emotion – also play important roles in tinnitus, and are often targets of therapies such as CBT which aim to mitigate the attentional and emotional dimensions of the tinnitus experience (Durai, Sanders, et al., 2021). This perhaps suggests that while therapeutic benefit has been observed using sound therapy alone (in the case of the white noise group), the application of CBT or personalised counselling would have acted to reduce the elevated functional connectivity observed in this study and in turn enabled greater therapeutic success. This again demonstrates the potential benefit of a personalised polytherapeutic approach to tinnitus management and offers encouragement for its exploration in future tinnitus research.

The variation in the functional connectivity observed likely reflects the fact that PLV and SNN cluster analysis methods work through different mechanisms. PLV computes differences in connectivity by calculating the consistency in the phase difference between two electrodes (Lachaux et al., 1999; Mormann et al., 2000), while the SNN architecture computes the number of spatiotemporal interactions between EEG variables using a Feature Interaction Network (FIN) (Durai, Sanders, et al., 2021). While the PLV offers information on ‘snippets’ of EEG data (epochs), the SNN architecture-based approach accounts for temporal dynamics and as such is considered as an appropriate method for the processing of spatio-temporal brain data (STBD) (Doborjeh et al., 2019; Kasabov, 2014). Although there was no obvious consistency in the functional connectivity findings between the two methods (other than the involvement of the PHC), the neural structures implicated typically appeared to reflect regions which were found to exhibit changes (increases or decreases) in neural activity across the different conditions (baseline, sound training, post) for the two groups: namely, the AG, DLPFC, VLPFC, MTG, IFG, OFC, and PAC. Further work is required to better understand the benefits to using different modes of connectivity analyses, as well as to determine their place in tinnitus research.

The changes in neural activity and functional connectivity observed in this study reflect only the acute effects of effortless sound training. It is possible that long-term training would have sustained these changes or perhaps seen the involvement of different neural structures and networks. Durai, Doborjeh et al. (2021) found that long-term (3-month) exposure to a stepped morphing sound preserved the resting state decrease in activity in the right parietal regions close to temporal sites that was observed following acute exposure (30-minutes) to the sound, but also gave rise to an increase in activity within right parietal regions close to centro-parietal regions and central sites. The authors posit that this might reflect the recruitment of attentional networks in diverting attention away from the tinnitus following long-term administration of the sound therapy (Durai, Doborjeh, et al., 2021). Given that the present study identified acute changes in attentional networks, the sustained involvement of this network reported by Durai, Doborjeh and colleagues (2021) is promising as it suggests that these alterations are likely to persist with long-term sound therapy. Several studies have reported an increase in tinnitus relief concurrent with the duration of sound therapy (Jin et al., 2022; Jin et al., 2021; Li et al., 2019). Sound therapy administered for 3-hours a day over a 6-month period found significant and consecutively increasing improvements in patient's tinnitus at the 3-month and 6-month follow-ups (as defined by visual analogue scale tinnitus loudness and annoyance ratings and the Korean version of the Tinnitus Primary Function Questionnaire scores) (Jin et al., 2021). Comparatively, a clinical trial conducted by Henry et al. (2006b) comparing the efficacy of tinnitus masking and tinnitus retraining therapy found that although both management strategies considerably improved patient's tinnitus, tinnitus masking effects remained constant over time, while tinnitus retraining therapy effects improved incrementally. It is possible that differential changes in both the neural and behavioural observations are seen following long-term exposure to either of the two sound therapies trialled in this study. Perhaps the level of relief offered by the white noise sound therapy plateaus over time, given the static nature of the sound, while the dynamic sounds used in auditory categorisation training give rise to slow but incremental benefit. The effects of chronic effortless categorisation training cannot however be discerned from this study; the electroencephalographic results presented act as a pilot for future studies which are necessary to firstly define the neural sites affected by long-term auditory categorisation, secondly establish whether there are added benefits to chronic sound therapy, and lastly contrast the efficacy of long-term application of conventional sound therapy using white noise to categorisation training.

6.5.3 **Artificial intelligence based tools for the prediction of therapeutic success**

In addition to applying the SNN architecture for the investigation of functional connectivity, the model was also used to predict patient's response to sound therapy by processing EEG data and learning patterns of spiking that could discern therapeutic responders to non-responders. The overall classification accuracy was 89.44% for responders and 93.57% for non-responders. The high classification accuracy is also evident even upon running the model on categorisation and white noise groups separately. This result suggests that the model can efficiently identify and differentiate between responders and non-responders with a high level of accuracy, offering support to the notion that SNN-based methods serve as powerful tools for the prediction of patient response to sound therapies (Durai, Sanders, et al., 2021). Development and implementation of non-invasive tools for the prediction of therapeutic success could revolutionise current modes of tinnitus management as well as potentially aid in tinnitus subtyping and participant profiling by illuminating both behavioural and neurophysiological differences between responders and non-responders.

6.5.4 **Strengths, limitations, and future directions**

This study was able to successfully generate tinnitus avatars and implement them for use within a passive perceptual training paradigm for tinnitus. Additionally, it is one of the few studies to find therapeutic benefit of white noise in the absence of counselling. The differential findings of this study with regards to the efficacy of white noise versus more complex categorisation training in offering tinnitus relief, as well as the different neural changes observed, suggest that the two modes of sound therapy likely work through different mechanisms, targeting different neural structures. In turn, the findings of this study support the application of sound therapy within a personalised polytherapeutic method of tinnitus management.

While this study has built on current understanding regarding the use of different modes of sound therapy for tinnitus management, there are several limitations worth considering and addressing in the future. This study was one of many that suffered the consequences of the COVID-19 pandemic; lockdowns meant that recruitment had to be postponed and given that the predominant tinnitus demographic consists of individuals deemed as vulnerable to the virus (i.e., adults >65 years of age), it was at times difficult to plan recruitment. Furthermore, follow up electroencephalographic measures (i.e., following the 30-day sound training) which were initially planned as part of the study could not be executed due to lockdown-associated time and resource constraints. This meant that only acute neurophysiological changes could be observed and discussed. Future studies should apply one of the different trial designs discussed, and should investigate the longitudinal differences in neural activity and functional connectivity with categorisation training.

A few participants reported having COVID-19 during their training period and contemplated whether this affected their response to therapy; a recent systematic review by Beukes, Ulep, et al. (2021) reported that participant’s tinnitus was found to be more problematic after

COVID-19 (and the general circumstance of the pandemic). Given that the majority of participants did not experience COVID-19 related health issues, we believe that the integrity of the study results are likely unaffected; it is however interesting to consider the broader effects of the pandemic, and whether auditory training in concert with counselling – or counselling alone – would have seen greater improvements in tinnitus in light of the stress and anxiety caused by the circumstances surrounding the pandemic.

6.5.5 **Conclusion**

Tinnitus heterogeneity poses a hurdle to treatment as it means that a ‘one-size-fits-all’ approach to management is not possible. The tinnitus avatar is able to accurately capture and reflect the tinnitus experience to a high level of satisfaction. While white noise sound therapy offered clinically meaningful improvement in tinnitus severity, distress, and negative emotionality, differential neural changes obtained using the two different modes of sound therapy suggest even greater benefit could potentially be achieved using a personalised polytherapeutic approach. Neural changes at the level of the prefrontal cortex (following passive auditory categorisation training) and within the default mode network (following white noise sound therapy) are encouraging as they are directly correlated with tinnitus distress. Future studies should elucidate the best design and method of application of simple (BBN) and complex (categorisation) modes of sound therapy, and should examine long-term treatment-related neural changes.

Chapter 7. General Discussion and Conclusions

7.1. Chapter introduction

The studies in this thesis examined the use of different sounds for the generation of convincing tinnitus replicas and effortless personalised categorisation training. This chapter will provide a summary of the overall findings of this project, discussing the results presented in the preceding chapters with respect to the aims of the thesis, and contemplating their implications for wider clinical use and tinnitus research.

7.2. Tinnitus synthesis: informing the creation of tinnitus replicas

Tinnitus replicas form an important component of both tinnitus assessment and management; they offer insight into the tinnitus sensation itself (i.e., psychoacoustic characteristics) in turn demonstrating what the participant is experiencing, and can often be applied in sound therapy and/or sound-based treatments (Durai, Doborjeh, et al., 2021). The narrative review presented in Chapter 3 demonstrated that most tinnitus replicas are simplistic copies generated by matching tinnitus pitch and loudness to a pure tone. Given that tinnitus is such a varied experience and is not necessarily perceived as a tonal stimuli, the review stressed the need to investigate the use of more complex sounds for tinnitus synthesis. The pilot study outlined in Chapter 5 explored the use of different auditory stimuli for tinnitus synthesis, assessing the ability of these sounds to capture an individual's tinnitus sensation and emotional impact. Although the study hypothesised that a tinnitus avatar (most complex replica of tinnitus) would serve as a superior tinnitus match relative to a simple pure tone replica, the results indicated less complex replicas such as the pure tone and localisation copy offered an equally appropriate representation of participant's tinnitus experience. Considering emotional affect however, the study found that pure tone based replicas were in general not well received by participants and had negative affect, particularly when compared to their noise-like counterparts. This is likely a reflection of the fact that noise is known to offer tinnitus relief through its masking ability (Sandlin & Olsson, 1999; Vernon & Meikle, 2000), as was observed in the subsequent auditory categorisation study (Chapter 6). Additionally, the pilot study investigated the concept of an uncanny valley effect (Mori et al., 2012) in tinnitus matching. It was hypothesised that sounds replicating the tinnitus experience in its entirety would be perceived by the participant as being unpleasant. Insufficient evidence was obtained to substantiate the presence of an uncanny valley in tinnitus matching. While it is clear that tinnitus and its replicas induce strong psychological responses, it is unclear whether this is indicative of a low point in the perception of sound or simply a reaction to generally unpleasant sounds. Further work is required to clarify these findings.

The authors posit that replica complexity should reflect its intended use and overall purpose: if a replica is required for simple tinnitus matching, it seems feasible to generate simpler, less time/resource consuming replicas such as the pure tone and localisation copy. The replica offers an accurate representation of tinnitus and does not necessarily need to be pleasant as the participant will not be exposed to it for long durations. Conversely, if a replica is required for use in sound therapy (such as in the auditory categorisation study in Chapter 6), the avatar would be more suitable. Although the avatar was more difficult to generate, it was perceived as being more pleasant and as such likely to be appropriate for long-term implementation within sound therapy. Moreover, the auditory categorisation training study (Chapter 6) accurately replicated participants' tinnitus using the tinnitus avatar. A strong theme throughout this thesis is the notion of tinnitus heterogeneity; the fact that the tinnitus experience is extremely variable in every dimension of the symptom, not only from person to person, but also within a given individual (Cederroth et al., 2019). The heterogeneous nature of tinnitus was reflected in the high degree of variability in both similarity and affect ratings assigned to the tinnitus replicas (Chapter 5). The auditory categorisation study reported cases where participants felt their avatar failed to reflect their tinnitus experience at some point along the 30-day training period. These findings emphasise the need for personalised and real-time remote adjustment of tinnitus replicas for use in sound therapy paradigms, supporting the overall importance and benefit of implementing a personalised approach to tinnitus management. Both studies (pilot study, Chapter 5, and auditory categorisation study, Chapter 6) highlighted the need to move away from 'one-size-fits-all' approaches of tinnitus assessment and management, and adopt more tailor-made personalised methods.

7.3. Tinnitus management: personalised polytherapeutic applications of sound therapy

Sound therapy is a common form of tinnitus management, often used in combination with counselling (Bauer & Brozoski, 2011; Cuesta et al., 2022; Hyun et al., 2022; Makar et al., 2017; Searchfield et al., 2010; Tyler et al., 2020; Zenner et al., 2017). The narrative review of auditory categorisation (Chapter 4) evaluated the presence of a perceptual magnet effect in audition and considered its implications within the context of tinnitus sound therapy. While the neuroplastic changes observed as a result of auditory categorisation training were deemed as being potentially beneficial to tinnitus therapy, the review demonstrated the relative dearth of tinnitus research on categorisation and emphasised the need to explore the concept further. The auditory categorisation study (Chapter 6) compared and contrasted the effects of conventional white noise sound therapy to an alternate putative sound therapy employing auditory perceptual training. The study is also one of the few to explore the use of white noise independent from counselling (Tyler et al., 2020). It demonstrated the ability of achieving therapeutic benefit solely using sound presentation, offering support to the use of sound therapy for tinnitus management.

While clinically significant improvements in tinnitus severity, distress, and negative emotionality were observed using the white noise sound therapy only, the two modes of sound therapy targeted different tinnitus neural networks (auditory attention, memory, and default mode networks). Sound therapy using white noise gave rise to changes within the default mode network (specifically within the AG), while passive auditory categorisation training led to an overall reduction in activity at the level of the prefrontal cortex, as well as a decrease in gamma-band activity within the auditory cortex. The altered neural activity seen following effortless sound therapy is encouraging as these regions are directly associated with tinnitus perception and distress; targeting these neural structures through the application of auditory training stimuli that appear to act via different neural pathways/mechanisms could offer the greatest chance of relief. Future studies should explore the benefit of applying white noise and passive auditory categorisation within a polytherapeutic paradigm by implementing either a staggered or factorial treatment design.

The narrative review presented in Chapter 2 found that machine learning and modelling techniques may support researchers and clinicians move towards tailor-made tinnitus therapy. One predictive tool (the Spiking Neural Network (SNN) methodology) applied and evaluated in the auditory categorisation training study (Chapter 6) was able to identify and distinguish between therapeutic responders and non-responders with a high level of accuracy. This finding stands in concert with several other studies (Doborjeh et al., 2015; Doborjeh et al., 2019; Durai, Sanders, et al., 2021) and lends support to the use and development of these SNN-based methods for the prediction of therapeutic success and identification of the behavioural and neurophysiological characteristics that determine and differentiate responders from non-responders.

7.4. Clinical implications of findings

The findings of this thesis will inform the future development of tinnitus replicas and perceptual training paradigms for the management and mitigation of tinnitus symptoms. Findings relating to methods and parameters of tinnitus synthesis suggest that simple 'cartoon-like' replicas of tinnitus remain appropriate for clinical use, however considerations of the emotional impact of such replicas should be made when applying the sounds over an extended period of time. Implementation of tinnitus avatars should be considered when moving away from short-term tinnitus psychoacoustic matching purposes of tinnitus synthesis towards more long-term therapeutic applications (i.e., sound therapy). Generation of realistic and accurate tinnitus avatars is essential for sound therapies rooted in perceptual training paradigms such as auditory categorisation training. Moreover, the findings of different modes of sound therapy to bring about changes within distinct – yet therapeutically relevant – neural sites is promising. While further work is required to validate these results, this thesis has been successful in demonstrating the benefit of sound therapy independent of counselling. The thesis supports and encourages the adoption of a personalised, tailor-made approach to tinnitus management, utilising a polytherapeutic design adapted to each individual patient, informed and guided by AI-based prediction methods such as the SNN architecture.

7.5. Limitations and future considerations

Replication is required to confirm the observations mentioned in this thesis. Further efforts are required to build and evaluate tinnitus replicas. Additionally, efforts should be made to restructure the uncanny valley testing. A real-world sound should be included in the sound presentation and evaluation process to establish a clear anchor point for comparisons. This will in turn bring clarity to the question of whether or not an uncanny valley phenomenon exists for tinnitus, and what it might mean in terms of sound-based management.

This thesis was affected by the COVID-19 pandemic. The frequent lockdowns and uncertainty surrounding the projection of the pandemic meant that recruitment for the auditory categorisation study (Chapter 6) was difficult, particularly considering that the predominant tinnitus demographic consists of COVID-vulnerable individuals (i.e., adults >65 years of age). Moreover, lockdown-associated time and resource constraints meant that follow-up electroencephalographic measures (i.e., following the 30-day sound training) originally planned as part of the auditory categorisation study could not be performed, leading to a focus and interpretation of acute neurophysiological changes only. Future work is required to investigate the longitudinal differences in neural activity and functional connectivity with categorisation training. Three participants contracted the virus during their training period, however given the majority of participants were unaffected by COVID-19 at the time of the trial, we believe that this did not affect the results of the study. The narrative review outlined in Chapter 2 reflected upon and considered the impact of COVID-19 on tinnitus management strategies, drawing on the need to adapt therapies for remote application with the aim of reducing barriers to healthcare services and increasing accessibility to tinnitus therapy. It is interesting to contemplate the broader impact of the pandemic on tinnitus management and whether auditory training in combination with counselling (or counselling alone) would have resulted in greater improvements in tinnitus given the stress and anxiety brought about by the circumstances surrounding the pandemic.

7.6. Summary and conclusions

This thesis explored the use of different auditory stimuli for tinnitus synthesis and investigated whether there were any differences and/or benefits in the application of a personalised passive categorisation training approach compared to conventional sound therapy using broadband noise (BBN). The findings of the thesis highlight the heterogeneous nature of tinnitus that necessitates a shift in tinnitus management strategies away from a ‘one-size-fits-all’ or ‘gold standard’ approach, towards more personalised, tailor-made polytherapeutic methods of therapy. Simplistic tinnitus replicas based on the presentation of a spatially-matched pure tone stimuli are sufficient for simple tinnitus matching purposes. The use of complex tinnitus avatars should be reserved for circumstances that require more long-term exposure to sound, such as in sound therapy paradigms.

Sound therapy using conventional white noise offers tinnitus relief independent of counselling. Moreover, neural changes observed within the default mode network following white noise sound therapy and at the level of the prefrontal cortex following passive auditory categorisation training are encouraging as they are directly correlated with tinnitus distress. The notion that simple (BBN) and complex (categorisation) modes of sound therapy act at these different neural sites is a promising finding that requires further investigation; targeting these areas through the application of both strategies within a polytherapeutic approach should be explored.

Appendix: Auditory Categorisation Training Study

Appendix 1: Participant Information Sheet (PIS) for the auditory categorisation training study outlined in Chapter 6.

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES
SCHOOL OF POPULATION HEALTH

Participant Information Sheet

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Passive sound training as a means of tinnitus management

Investigators

Associate Professor Grant Searchfield (Principal Investigator/Supervisor)
Dunja Vajsakovic (Researcher/PhD student)
Boen Deng BBIOMEDSC (HON) student

The mechanisms of tinnitus (phantom sound) perception are still poorly understood and ways to most efficiently suppress tinnitus are being investigated. Dr. Grant Searchfield, Associate Professor in the Audiology Section and director of the University of Auckland

Hearing and Tinnitus Clinic, and Dunja Vajsakovic, PhD candidate, are conducting an intervention study to investigate the effectiveness of a passive perceptual training paradigm as a means of tinnitus management.

You are invited to participate in our novel tinnitus sound training trial at the University of Auckland Hearing and Tinnitus Clinics, Grafton.

In this trial, we will attempt to create a copy of your tinnitus (your tinnitus avatar) using computer software to gain a better understanding of your tinnitus experience. A treatment sound will be created based on your tinnitus profile; this sound will be loaded onto an MP3 player which you can take away to use. You will be asked to listen to this sound daily for a minimum of 30 minutes over a period of 30 days (this can be done while doing other tasks). It is anticipated that exposure to the treatment sound will result in the brain passively learning to alter tinnitus perception and thereby reducing tinnitus audibility and distress.

In addition to measuring changes in tinnitus characteristics, we will also measure changes in psychological well-being (measured with emotion questionnaires) between the start and end of the trial.

This study will use EEG (brain wave) measurements to measure underlying changes in brain networks relating to tinnitus loudness and distress change following administration of passive perceptual training. Past studies have shown that several networks (involving both auditory and non-auditory regions) may contribute towards final tinnitus perception.

In order to be eligible for this study, you must:

- ✓ Be aged 18 years or older
- ✓ Be fluent in English
- ✓ Have chronic tinnitus (minimum 6 months duration)
- ✓ Have tinnitus which is sufficiently severe as determined (using a tinnitus impact of life score calculation)
- ✓ Have no more than a moderately-severe hearing loss and no middle ear issues
- ✓ Have a tonal tinnitus (i.e., one that sounds like a pure tone and is not hissing/crackling in nature)
- ✓ Have tinnitus which **DOES NOT**:
    - o Fluctuate (i.e., is constant)
    - o Consist of more than one tinnitus sound
- ✓ Have a smartphone (android/iPhone)

As a token of our appreciation for your time and effort in participating in this study, you will be provided with your very own set of bone conduction headphones which you can keep following the study.

If during the screening tests in the first session you are found to not meet the inclusion criteria and proceed further for the study (e.g., too severe a hearing loss, tinnitus is not severe enough) you will still be given the opportunity to ask any questions regarding your tinnitus and provided general informational counselling.

Please find below an outline of the study.

Prior to the appointment: Questionnaires (15 minutes)

Before the initial appointment, you will be asked to fill in the following questionnaires measuring tinnitus history and impact on life (Tinnitus Case History Questionnaire, Tinnitus Functional Index, Tinnitus Severity Numeric Scale) and psychological impact (Positive and Negative Affect Schedule). The questionnaires will take approximately 15 minutes to complete. You will receive access to these questionnaires through a link that will be emailed to you. The link will take you to a website that will allow you to complete and submit the questionnaires at a time that is convenient for you.

If you meet the eligibility criteria for the study, you will be invited to the following appointment. The appointment consists of **one session lasting approximately 2.5-3h** and is split up into several parts as outlined below:

Part one (approximately 60 minutes total): Hearing and tinnitus screening/assessment, baseline EEG measurements

In this part of the appointment, we will discuss your tinnitus and conduct a full diagnostic hearing test:

A. Initial interview (10 minutes)

At the initial appointment, you will take part in an interview with the investigator where you will be asked to discuss your tinnitus. This will be an opportunity for us to assess your tinnitus, gain a better understanding of your experience, and offer appropriate counselling.

B. Pure Tone Audiometry (10 minutes):

You will be played a variety of sounds through a pair of headphones. These sounds will be short beeps at different pitches and volumes. You will be asked to respond by pressing a button when you hear a beep.

C. Generation of Tinnitus Avatar (15-25 Minutes):

Psychoacoustical measurement (how the tinnitus sounds) will be taken using tinnitus testing software for tinnitus pitch, loudness, maskability and location in space. The measurements will be used to generate a sound file which is an avatar of your tinnitus, and you will make fine adjustments until the sound best matches your tinnitus.

You will be asked to rate the pleasantness of the sounds you listened to and asked a few questions regarding whether you believe the sounds should be used in longer-term tinnitus interventions.

If you meet the eligibility criteria for the study, you will carry on with the following task:

Part two: Electroencephalography (EEG) recordings (60 minutes)

EEG is a non-invasive technique to measure the brain activity by electrodes placed on the head. Participants' scalp under the electrode will be cleaned with alcohol swabs and a cap with inbuilt sockets for electrodes will be placed on the head and electrodes will be connected to those sockets. EEG is a painless technique for recording brain activity and will require washing head/hair after the testing.

In this part of the session, you will be asked to sit still while your brain activity is being measured. Three recordings will be taken while you:

1. Sit in silence in a dimly lit room and watch a grey cross presented in the center of a computer monitor screen for 10 minutes. During this time, we will observe your baseline (resting-state) EEG (brain waves).
2. Sit listening to your custom-made training sound. During this time, you will watch a grey cross presented in the center of a computer monitor screen for a further 10 minutes.
3. Once again sit in silence in a dimly lit room and watch a grey cross presented in the center of a computer monitor screen for a final 10 minute period.

The EEG will be recorded with participants sitting in a comfortable chair, in a sound treated room. Our research team will be happy to talk through the procedure (EEG) if you need further clarification, before consent is given.

Part three: Intervention (one month)

During the final part of this session, the training sound clip will be loaded onto your personal device. The sound will be set at a comfortable and safe listening level as determined by both you and the investigator. You will be encouraged to listen to this for a **minimum of 30 minutes per day** over the following **one-month period** (you can do quiet activities while listening to the sounds, e.g., reading, gardening, etc.).

Part four: Follow-up (one month after your initial session)

One month following your initial appointment, you will once again be asked to complete the battery of questionnaires (a link will be sent to you via email giving you access to the questionnaires). The link will take you to a website that will allow you to complete and submit the questionnaires at a time that is convenient for you.

You will also receive some questions about your tinnitus and how you feel the perceptual training may or may not be influencing it, the situations in which you are using the sound clip, and any other incidental observations or fine fittings which need to made.

Part four will be completed remotely – you will not have to come in to the clinic.

We will submit a report for publication at the end of this research.

Risks and Benefits, Incidental Findings

There are no specific risks associated with taking part in the research. As a benefit, you can choose to receive a free detailed copy of your hearing/audiological testing results or take away the treatment sounds.

It is not anticipated, but in cases you may come to realise that tinnitus is of high concern or is impacting various aspects of your daily life. For any concerns, you can get in touch with the primary investigators both during and after the study in order to discuss concerns. All of the investigators are qualified audiologists with relevant tinnitus training, and can hence address your queries appropriately.

Consent, Participation and Withdrawal

Completing the consent form will indicate your consent to participate. Participation is entirely voluntary. You have the right to withdraw from the study at any stage without stating a reason and withdraw your data up to two months after the date of testing.

Summary of Findings

You can also request for a summary of study findings by entering in your details on the consent form. This information will be stored separately from the experimental data, in a secure electronic folder on the primary investigator’s computer and destroyed after all research reports are sent out.

Data Storage, Retention, Destruction

The data obtained from this experiment will be stored to disc for a period of up to six years and will be used for publication in a scientific journal. The consent forms will be stored in a separate folder to study data. After six years, your data will be deleted from disc and your consent form and all related paperwork put through a shredder. No material that could personally identify you will be used in any reports in this study. The information and data collected from you will be stored securely, in locked cabinets and on secure computer networks. Only the investigators will have access to this information, and your data will be made confidential by assigning a unique code to it.

Summary of Your Rights

- Your participation is entirely voluntary.
- You may withdraw from the project at any time without stating a reason.
- You may have your data withdrawn from the study within **two months** of your participation.
- You may obtain results regarding the outcome of the project from the experimenters upon completion of the study.
- Your identity will be kept strictly confidential throughout the study. You will not be identified in any publications arising from the work.
- After six years, your data will be deleted from disc and your consent form and all related paperwork put through a shredder.
- You are encouraged to consult with your whanau/family, hapu or iwi regarding participation in this project.
- For some people discussing their tinnitus may be distressing. Support is available through the University of Auckland clinics.

Thank you for reading this Participant Information Sheet and considering our study.

Contact Details

If you have any questions, concerns, or complaints about the study at any stage, please contact:

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If you require Māori cultural and health support, talk to your whānau in the first instance. Alternatively, you may contact the Eisdell Moore Centre, Māori Hearing Research Co-ordinator via email: Alehandrea.Manuel@auckland.ac.nz.

For concerns of an ethical nature, you can contact the Chair of the Auckland Health Research Ethics Committee at ahrec@auckland.ac.nz or at 373 7599 x 83711, or at Auckland Health Research Ethics Committee, The University of Auckland, Private Bag 92019, Auckland 1142.

APPROVED BY THE AUCKLAND HEALTH RESEARCH ETHICS COMMITTEE on 16/09/2021 for three years. Reference Number AH22843

Appendix 2: Pre-intervention interview questions and prompts.

1. How is your tinnitus at the moment?
2. What is your relationship with your tinnitus?
3. Have you found any management strategies that help with your tinnitus?
4. Are there any sounds that your tinnitus interacts with? I.e., are there any sounds that:
    a. Alter the way in which you perceive/hear your tinnitus
    b. Perhaps sounds that change what your tinnitus generally sounds like, how loud it is, where you hear it, its pitch, etc.?
    c. Or sounds that perhaps suppress your tinnitus?
5. Are there any situations which you might feel exacerbate your tinnitus? Or conversely make it less prominent?
6. Is there anything else you think I should know about your tinnitus?

Appendix 3: Post-intervention (exit) interview questions and prompts.

1. How is your tinnitus at the moment?
2. Has your tinnitus changed since the start of the trial? If yes, how has it changed? If no, why do you think it hasn't changed? (I.e., characteristics of your tinnitus such as the pitch, duration, fluctuation, intensity in different environments, etc.)
3. What did you think about the treatment sound(s)? (E.g., Quality, Annoyance, Pleasantness)
4. How did you experience/find the training?
5. What environments have you been using the sounds in?
6. Do you feel like the sound has been interacting with your tinnitus since the last appointment? How?
7. Overall, do you feel like listening to the treatment sound(s) have resulted in a change in your tinnitus? How/Why or why not?
8. How can the treatment sound(s) be improved and why would this be an improvement?
9. Would you be interested in using the treatment sound(s) in the future for tinnitus relief?
10. Are there any major changes in your life circumstances or incidents since the last appointment, which you believe may have had an influence on your tinnitus?

Appendix 4: Codes developed and used following the framework method for analysis of the interviews in the auditory categorisation training study (Chapter 6).

PRE-INTERVENTION INTERVIEW CODES	
CODE	**DESCRIPTION**
Tinnitus experience	
Perception	*Perception of the tinnitus sensation*
View of tinnitus	*Tinnitus experience, beliefs surrounding tinnitus, relationship with tinnitus*
Management/therapy	
Tinnitus management	*Methods/strategies used with the aim of reducing or eliminating tinnitus perception*
Psychoacoustic properties/tinnitus 'behaviour'	
Change/alterations in tinnitus sensation	*Changes in tinnitus as a result of interactions with other sounds, emotional states, specific environments, etc.*

POST-INTERVENTION (EXIT) INTERVIEW CODES	
CODE	**DESCRIPTION**
Tinnitus experience	
Perception	*Perception of the tinnitus sensation*
Perceptual training	
Experience/thoughts on the training sound	*Participant's experience of the sound used for the perceptual training*
Experience/thoughts on training regime	*Participant's experience of the overall training method*
Training environments	*Environments in which the participant completed the training*
Improvement of training sound (suggestions)	*Any improvements the participant feels are necessary*
Usefulness of treatment sounds	*Would the participant be interested in using the treatment sound in the future for tinnitus relief*
Psychoacoustic properties/tinnitus 'behaviour'	
Change/alterations in tinnitus sensation from training	*Changes in tinnitus as a result of perceptual training*
Change/alterations in tinnitus sensation	*Changes in tinnitus as a result of interactions with other sounds, emotional states, specific environments, etc.*
Interactions	*Any noted/observed changes in tinnitus as a result of the training sound interacting with the tinnitus*
Life circumstances	*Major changes in life circumstances or incidents since the last appointment which may have had an influence on participants tinnitus*

Appendix 5: Worsening of tinnitus severity across 'Control', 'Relaxation', and 'Emotional' domains of TFI for the categorisation group following 30-day effortless auditory categorisation training.

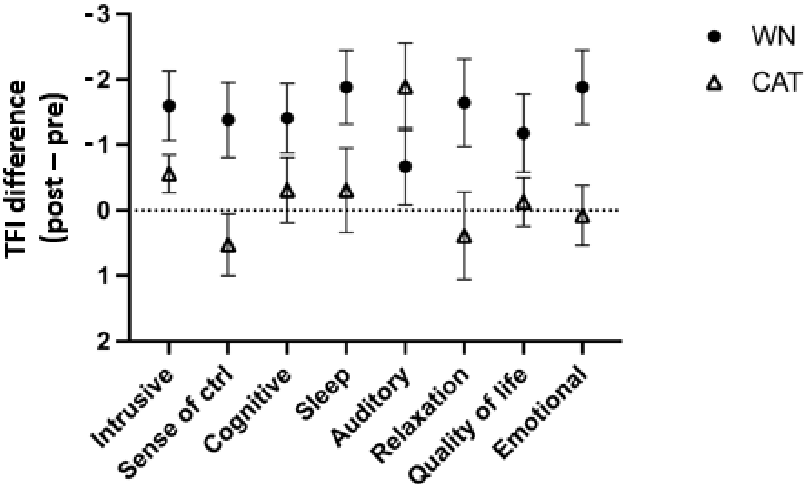

Figure A1. Difference (post-intervention minus pre-intervention) in TFI subscale scores for the white noise and categorisation groups. A negative difference indicates an improvement in tinnitus for the corresponding domain. The categorisation group demonstrated increased TFI scores following the 30-day training regime for the ‘Control’, ‘Relaxation’, and ‘Emotional’ subscales suggesting a worsening of the negative tinnitus impact on these domains following long-term auditory categorisation training.

Appendix 6: Mixed-methods ANOVA significance (p-value) output for the auditory categorisation training study (Chapter 6).

Table A1. Within-group statistical significance (p-value) output from the mixed-method analysis of variance (ANOVA) assessing significant differences in median power spectral density (PSD) between conditions within each test group. Significant results ($p \leq 0.05$) are highlighted in orange.

		Categorisation					**White noise**				
Band	Condition	Baseline	T1	T2	T3	Post	Baseline	T1	T2	T3	Post
Delta	Baseline	1.00	0.06	0.37	0.44	0.94	1.00	0.08	0.08	0.37	0.02
	T1	0.06	1.00	0.13	0.19	0.02	0.08	1.00	0.66	0.34	0.40
	T2	0.37	0.13	1.00	0.84	0.26	0.08	0.66	1.00	0.21	0.62
	T3	0.44	0.19	0.84	1.00	0.40	0.37	0.34	0.21	1.00	0.17
	Post	0.94	0.02	0.26	0.40	1.00	0.02	0.40	0.62	0.17	1.00
Theta	Baseline	1.00	0.87	0.76	0.33	0.11	1.00	0.65	0.23	0.60	0.06
	T1	0.87	1.00	0.38	0.13	0.03	0.65	1.00	0.12	0.88	0.06
	T2	0.76	0.38	1.00	0.38	0.15	0.23	0.12	1.00	0.33	0.45
	T3	0.33	0.13	0.38	1.00	0.54	0.60	0.88	0.33	1.00	0.17
	Post	0.11	0.03	0.15	0.54	1.00	0.06	0.06	0.45	0.17	1.00
Alpha	Baseline	1.00	0.77	0.59	0.09	0.08	1.00	0.76	0.46	0.52	0.13
	T1	0.77	1.00	0.12	0.01	0.01	0.76	1.00	0.05	0.21	0.02
	T2	0.59	0.12	1.00	0.13	0.18	0.46	0.05	1.00	0.87	0.40
	T3	0.09	0.01	0.13	1.00	0.97	0.52	0.21	0.87	1.00	0.39
	Post	0.08	0.01	0.18	0.97	1.00	0.13	0.02	0.40	0.39	1.00
Beta	Baseline	1.00	0.21	0.71	0.42	0.72	1.00	0.42	0.56	0.33	0.09
	T1	0.21	1.00	0.15	0.01	0.06	0.42	1.00	0.01	0.02	0.00
	T2	0.71	0.15	1.00	0.11	0.40	0.56	0.01	1.00	0.63	0.21
	T3	0.42	0.01	0.11	1.00	0.66	0.33	0.02	0.63	1.00	0.46
	Post	0.72	0.06	0.40	0.66	1.00	0.09	0.00	0.21	0.46	1.00
Gamma	Baseline	1.00	0.00	0.07	0.93	0.83	1.00	0.76	0.07	0.02	0.00
	T1	0.00	1.00	0.11	0.00	0.00	0.76	1.00	0.00	0.00	0.00
	T2	0.07	0.11	1.00	0.02	0.06	0.07	0.00	1.00	0.51	0.20
	T3	0.93	0.00	0.02	1.00	0.90	0.02	0.00	0.51	1.00	0.53
	Post	0.83	0.00	0.06	0.90	1.00	0.00	0.00	0.20	0.53	1.00

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