Masking tinnitus using three-dimensional sound processing

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Abstract

Introduction: Tinnitus is a debilitating condition in which a sound is perceived without an external sound being present. In New Zealand 207,000 people suffer from any degree of tinnitus, making it an important public health problem. Although some therapies have yielded promising results, there is no universal treatment that benefits all patients. A common treatment option for tinnitus is sound therapy. Sound therapy is the use of sound to reduce tinnitus in some way. Covering perception of tinnitus using a distracting "masker" noise is a common sound therapy approach. The effect of presenting the masker noise at different spatial locations has largely been unexplored.

Aims: The study explored: 1. The use of three-dimensional digital sound processing software to localise tinnitus in space and confirm whether this method's results are similar to the location self-reported by participants. 2. Whether presenting masker noises at different locations in a virtual sound field (spatial masking) would affect masker effectiveness. 3. Whether tinnitus functional index scores or other participant characteristics could predict masking effectiveness for different individuals

Methods: Nineteen chronic tinnitus patients were recruited for the study. Adobe Audition with Anaglyph plugin altered the three-dimensional location of a white-noise noise virtually. Tinnitus was localised using two methods: (i) the tester-guided method which moved the masker noise around in space and participants were asked to pick the location the masker noise was perceived closest to the tinnitus, and (ii) the self-report method where participants reported their tinnitus location on a physical grid. The effectiveness of masking was measured using the minimum masking level that was recorded when the masker sound was presented at three different azimuths (0, +45 and -45 degrees) and four different distances (0, 0.5, 1, 2 metres) away from tinnitus location obtained using the tester-guided method. Predictors of masking effectiveness were explored using correlation analyses with the MML. Potential predictors were based on outcomes by the tinnitus functional index and the tinnitus sample case history questionnaire.

Results: There were three main findings. First, we found that the tester-guided tinnitus location corresponded well with the perceived tinnitus location self-reported by participants. Second, increased virtual distance resulted in higher minimum masking levels when the masker-tinnitus distancer was at least 2 metres, whereas the desired masking level, on average, showed no

significant changes at different spatial positions. Third, tinnitus severity, as measured by the tinnitus functional index, does not predict masking effectiveness well. However, some patient characteristics such as age, duration of tinnitus since onset and hearing levels can be used as potential predictors. Incidental findings were also found, which showed that the minimum masking levels and the desired masking levels (where the participant was most comfortable in regard to their tinnitus and masking sound presented) were different for each patient when recorded at the varying spatial locations. On average, the minimum masking level was significantly higher than the desired level.

Conclusions: The findings from the current study provides strong evidence that spatial masking serves as novel way to augment the benefits of sound therapy that can be used to personalise this treatment on a case-by-case basis.

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Glossary

NZAS	New Zealand Audiological Society
MML	Minimum Masking Level
DML	Desired Masking Level
dB	Decibel
dB HL	Decibel Hearing Loss
dB SL	Decibel Sensation Level
AVCN	Anteroventral cochlear nucleus
PVCN	Posteroventral cochlear nucleus
DCN	Dorsal cochlear nucleus
LL	Lateral lemniscus
LSO	Lateral superior olive
MSO	Medial superior olive
SOC	Superior olivary complex
MNTB	Medial nucleus of the trapezoid body
IC	Inferior colliculus
MGB	Medial geniculate body
NZ	New Zealand
TSI	Tinnitus Severity Index
THQ	Tinnitus Handicap Questionnaire
TFI	Tinnitus Functional Index

TSCHQ	Tinnitus Sample Case History Questionnaire
fMRI	Functional Magnetic Resonance Imaging
3D	Three-dimensional

Chapter 1: Literature Review

The following literature review is structured based on the principle of iterative knowledge. First, a brief introduction to tinnitus will be given. This will be followed by some epidemiology, stating the burden of tinnitus on the public health system, and the effects tinnitus has on different aspects of life. Because the current study is largely based on the spatial aspect of tinnitus, the concept of tinnitus location will also be introduced. Then, an interlude providing a brief summary of the human auditory system will be discussed to supplement the further sections needing a basic understanding of the system. Sound localisation will be reviewed, followed by an in-depth discussion of the neurophysiological mechanisms of tinnitus generation. Finally, and perhaps the most important to the study, sections on tinnitus assessment and management will be discussed. The latter sections will provide a clear gap in research that formed the basis of the present study.

1.1 Tinnitus: definition and epidemiology

1.1.1 Tinnitus definition

Tinnitus, derived from the Latin word "*tinnire*" (to ring), describes the involuntary perception of a sound that has no external source (Bauer, 2018). The location of the perceived tinnitus can be inside or outside the head and predominantly be in one ear or both ears. As such, tinnitus can be divided into two groups: objective and subjective tinnitus. Although other methods for standard and practical tinnitus classifications have been suggested, the most popular one remains as the one that distinguishes between subjective and objective tinnitus (Cianfrone et al., 2015).

1.1.2 Objective tinnitus

Objective tinnitus has a physical sound source and usually stems from the body's internal physiology that can sometimes be heard by other individuals as well (Han et al., 2009). The common causes of objective tinnitus include cardiovascular issues such as high blood pressure

or glomus tumours, as well as Eustachian tube dysfunction, wax build-up and other muscle spasms within the Ear (Dobie, 2004). Notably, objective tinnitus is relatively rare and is reported to account for less than 1% of all tinnitus cases (Chari & Limb, 2018).

1.1.3 Subjective tinnitus

Subjective tinnitus does not have a physical sound source and its origins are typically psychological or neurological where there is an abnormal activity within the human auditory system. The development of this abnormal activity is worsened by the absence of input from the cochlea (Jastreboff, 1990). Further, this type of tinnitus is exclusively heard by the patient and is therefore referred to as a type of phantom auditory perception. The frequency of subjective tinnitus can also be constant or intermittent and have a wide range of sound types, including ringing, buzzing, hissing, roaring to rushing (Cederroth et al., 2019). For the remainder of this thesis, the emphasis will remain on subjective tinnitus.

The nature of tinnitus, usually subjective tinnitus, makes it difficult for others to understand the degree of debilitation this disorder inflicts on the patient. It is often misunderstood and under-empathised as a condition. Therefore, it is worthwhile mentioning that even though tinnitus is seldom associated with an insidious pathology, the loudness can cause severe disruptions in hearing and communication, as well as general health and quality of life (Hallberg & Erlandsson, 1993). For very severe cases, this can also have a detrimental effect on sleep quality, attention span, interpersonal relationships and other social interactions (Budd & Pugh, 1995).

1.1.4 Tinnitus epidemiology

In the population of New Zealand (NZ), 207,000 people suffer from any degree of tinnitus, making it an important public health problem (Wu et al., 2015). In comparison, a global systematic review and meta-analysis of over 700 publications revealed a prevalence of 14%, which is considerably higher than the 6% of the NZ population (Jarach et al., 2022; Wu et al., 2015). Although, it is essential to note that some studies cited in the meta-analysis use prevalence data not standardised to any single population, which may explain the large difference seen between NZ and global prevalence rates.

The severity of tinnitus amongst the epidemiological literature has a large variation because of the lack of standardised techniques measuring tinnitus severity. Moreover, there are currently no NZ studies reporting the degree of tinnitus severity amongst the population. However, owing to the findings of other studies, it is possible that out of the total NZ tinnitus sufferers,

only a small number of patients suffer to a degree that adversely affects their quality of life (clinically significant tinnitus) (Hoekstra et al., 2014; Jarach et al., 2022; Wu et al., 2015). For example, in a large European multi-country cross-sectional population study with a sample size of over 11 thousand adults, it was found that out of the 14% of tinnitus sufferers, only 1-2% of them were classified as severe (Biswas et al., 2022). Surprisingly, this is in contrast to American tinnitus studies, which state that out of the 42 million chronic tinnitus patients, 10 million are considered clinically significant (Newman et al., 2011). Nevertheless, despite the large diversity of clinically significant prevalence rates, it is known that they are increasing (Henry, Dennis, et al., 2005; Hoffman, 2004), and therefore it is important that successful management options are developed.

1.1.5 Tinnitus risk factors

Tinnitus has multiple risk factors. The main risk factor is hearing loss, however, the relationship between the loss of hearing and tinnitus is complex; some people with poor hearing do not have tinnitus, and conversely, some with tinnitus do not have hearing loss (Davis & El Refaie, 2000; Nondahl et al., 2011). The second most common risk factor is exposure to excessive noise, where people reporting high levels of recreational and occupational noise have a considerably higher chance of developing tinnitus (Nondahl et al., 2011). Other risk factors include smoking, obesity, alcohol consumption and hypertension (Davis & El Refaie, 2000), and a small genetic component has also been suggested (Kvestad et al., 2010). There are also pathology-related risk factors such as cochlear damage, meningitis, mastoiditis, head or neck injuries and recurrent middle ear infections (Baguley et al., 2013). That being said, tinnitus can also be considered a separate condition that shares common risk factors with other otologic diseases. This idea was supported by a 2015 study done by Kim et al. with 19,290 Korean participants, showing that the adjusted odds ratio for tinnitus was greater for participants with abnormal tympanic membranes, hearing loss and noise exposure.

Some of the important predisposing factors for tinnitus will be discussed in further depth in the following sections.

1.1.5.1 Hearing loss and tinnitus

Tinnitus is prevalent in 20% of patients with hearing loss, but the degree to which hearing loss affects the suffering caused by tinnitus is unclear (Pinto et al., 2015). This is because even though there are several lines of evidence that suggest associations between the characteristics of hearing loss with tinnitus severity and psychoacoustics, they cannot explain the large number

of patients that experience tinnitus without any hearing impairment (Nondahl et al., 2011). Regardless, these associations will be discussed, and tinnitus in the absence of hearing loss will be explored.

There is considerable debate about whether tinnitus pitch can be predicted by looking at the shape of an audiogram. There are three arms to this debate; (i) tinnitus pitch cannot be predicted by the audiogram, (ii) tinnitus pitch is related to the frequency that has the worst threshold, or (iii) the frequency at which the configuration of the hearing loss sharply slopes – also known as the edge frequency – can be used to predict the tinnitus pitch. Pan et al. (2009) conducted a study that refutes the ideas of tonal tinnitus correlating well with hearing loss edge frequency or the frequency with the worst threshold. They found that the average edge frequency for 195 of their participants was 2237 Hz, but the average tinnitus pitch match was strikingly higher at 4968 Hz. In fact, for seventy-five participants, the pitch match was over 8000 Hz. No significant relationships were found between tinnitus pitch and edge frequency or the frequency at which the hearing loss was maximal. In the same study, some participants did have pitch matches close to the edge frequency of hearing loss, but the authors could not find any characteristics about them that separated them from the rest. There are also studies that found significant relationships between tinnitus pitch and frequency with maximal hearing loss but not edge frequency (Henry & Meikle, 1999; Norena et al., 2002; Schecklmann et al., 2012). However, these studies do not account for participants making octave errors where octaves lower or higher than the actual pitch of the tinnitus will sound similar to the participants undergoing tinnitus pitch match testing. Accordingly, when octave errors were accounted for (by administrating octave error training), Moore et al. 2010 found a clear relationship between edge frequency and tinnitus pitch ($r = 0.94$). These findings were recently corroborated by another study (Jain et al., 2021).

Further, it has been suggested that the pitch of the hearing loss can also predict tinnitus severity. A 2004 study showed that high-frequency hearing loss, which has a steeper slope, tends to correlate with severe tinnitus (Weisz et al., 2004). However, another study also states that low-frequency hearing losses were correlated with higher tinnitus annoyance as measured by the scores of the Tinnitus Handicap Questionnaire (THQ) (Searchfield et al., 2007). In the same study, the tinnitus severity index (TSI) scores were not correlated with any audiometric findings. These ambiguous and contradictory findings between papers suggest that patients with tinnitus have heterogeneous characteristics, and multiple factors are involved in defining the effect of tinnitus on an individual (Pinto et al., 2015).

In audiology, it is a common fear that as the hearing loss becomes worse, the tinnitus will also become louder and more annoying (Aazh & Salvi, 2019). There are clear problems when trying to investigate this claim. First, there are no robust methods to measure tinnitus loudness objectively. Some researchers have attempted to design objective measurements of tinnitus intensity using functional near-infrared spectroscopy and machine learning but the use of this method needs further verification (Shoushtarian et al., 2020). As such, it is difficult to measure any changes in the intensity of tinnitus for patients with varying degrees of hearing loss. Second, even if objective measures can be created for the degree of tinnitus intensity, there is no universal way of linking tinnitus loudness with tinnitus severity because the concept of tinnitus annoyance is subjective to each patient with different sound sensitivities (McFerran et al., 2019). Third, because tinnitus severity can increase with other confounding factors like anxiety and depression that are also impacted by hearing loss degree, it is hard to distinguish whether the degree of hearing loss is directly linked to tinnitus severity or if the confounding factors indirectly exacerbate tinnitus loudness (Jarach et al., 2022; McKinney et al., 1999). Considering the third problem, studies showing direct and indirect relationships have been published. McKinney et al. 1999 showed that clinically significant hearing loss results in anxiety and depression that act to worsen the degree of tinnitus severity indirectly. A recent regression model also found that there was a statistically significant relationship between the standard audiometric frequencies and tinnitus loudness, annoyance and effect on quality of life; that is, higher hearing thresholds are associated with worse outcomes for tinnitus patients. However, this regression model only explained 52% of the variance of tinnitus loudness and the relationship found was very weak (Aazh & Salvi, 2019). Further, direct associations between the psychoacoustic loudness measures of tinnitus (minimum masking level and matched loudness) and audiometric thresholds of hearing with stronger correlations ($r > 0.5$) have also been reported (Yakunina & Nam, 2021). Therefore, treatments for hearing loss should (somewhat) decrease the psychoacoustic measures of tinnitus loudness, but tinnitus treatment in whole should consider improving the patient's quality of life in general.

Tinnitus can also occur without any peripheral hearing loss. In 2000, Simpson & Davies found that 85% of tinnitus patients also suffer from hearing loss, but 10% to 15% of the patients with tinnitus have normal audiometric thresholds across 250 Hz to 8000 Hz frequency range. A common hypothesis states that tinnitus usually arises from cochlear dysfunction, which later manifests as a symptom of abnormal activity within the auditory pathway (Jastreboff, 1990). For that reason, tinnitus without hearing loss could represent cochlear damage that was not

sufficient to cause clinically significant hearing loss but enough to elicit the symptom of tinnitus (Granjeiro et al., 2008). Results supporting this theory were found by Granjeiro et al. 2008, where distortion product otoacoustic emissions (DPOAEs) and transient evoked otoacoustic emissions (TEOAEs) measuring cochlear function were both significantly diminished in normal hearing tinnitus participants compared with normal hearing participants without any tinnitus (control group). Similar results were seen elsewhere (Liu et al., 1996). Interestingly, a 10 year follow-up was performed on the same participants of Granjeiro's study, and it was found that there were now no differences between the normal hearing tinnitus and control groups in terms of DPOAE abnormalities (Kehrle et al., 2022). These findings were combined with the discovery that 29% of the tinnitus group had now developed some degree of high-frequency sensorineural hearing loss whereas the control group retained their normal hearing. Considering this discovery, it is possible that the tinnitus group could have had a loss in the extended high-frequency range (above 8000 Hz) that may have confounded the results of the initial study in 2008. These results indicate that cochlear damage might not be the only determinant for the initiation of tinnitus and hearing loss. Moreover, prospective studies must overcome the limitations of these studies, and investigate the differences between normal hearing participants with and without hearing loss whilst taking into account hearing threshold above the standard frequency range.

1.1.5.2 Ageing and tinnitus

The prevalence of tinnitus is variable across different age groups (Yenigün et al., 2014). Generally, the number of people with chronic tinnitus increase as they age, with people between 60 to 69 years of age having the highest prevalence of 14% (Shargorodsky et al., 2010). Although, there are many confounding factors that complicate investigation into the relationship between ageing and tinnitus. First, tinnitus is a subjective symptom, whose severity is dependent on one's psychological state (Lockwood, 2005). It is possible that as we age, our tolerance for dealing with tinnitus lessens and we are more susceptible to the negative effects of tinnitus (Al-Swiahb & Park, 2016). In line with this hypothesis, Sharma et al. 2021 found that tinnitus had a significantly higher impact on daily life, stress, emotional and general wellbeing for patients aged between 56 to 65 years of age than younger patients of 15 to 25 years of age. So, the question becomes: is the prevalence of tinnitus truly higher in the elderly, or are the elderly overrepresented because they have a different psychological state that makes them more prone to the negative impacts of tinnitus? Second, given that tinnitus is normally associated with hearing loss, age-related hearing loss (presbycusis) can be one of the biggest

confounding factors when trying to delineate the sole effects of ageing on tinnitus prevalence amongst different age groups.

The lowest prevalence of tinnitus is observed in in normal hearing children. Unlike in adults, tinnitus in childhood is usually associated with treatable ear disease (Mills et al., 1986). Rosing et al. 2016 published a systematic review of 25 studies exploring the epidemiology of tinnitus in young people. In this study, they found that among the general paediatric population (with and without hearing loss) the estimated prevalence of tinnitus was 6% to 41.9%, whereas it was 3.2% to 62.2 % for hearing impaired children. In particular, children with sensorineural hearing loss have a greater risk for developing tinnitus than conductive losses (Mills et al., 1986). However, predicting tinnitus prevalence in children is not clear-cut. Multiple studies have given variable results, as demonstrated by the large data ranges shown in Rosing's study. For example, the tinnitus prevalence in South Korean adolescents was 32.3% in one study (Kim et al., 2015), while it was 17.5% in another (Lee & Kim, 2018). Further, a finding from a different study which included Danish children, aged 10 to 16 years, stated a tinnitus prevalence of 66.9% (Nemholt et al., 2020). The variability of these results can be attributed to: different tinnitus defining criteria, different age ranges used for the including children, large variety of tinnitus questionnaires used, different study protocols and statistical analyses (Raj-Koziak et al., 2021). Therefore, it is essential to develop routine tinnitus questions for paediatric appointments that can inform the management of the condition.

1.1.5.3 Sex and gender differences

Sex is a prevailing risk factors for almost all health conditions, and it serves as powerful prognostic marker (Mauvais-Jarvis et al., 2020). Here, "sex" is assumed as a biological classification encoded by the genetic makeup of a person. In a 2016 systematic review of thirty-nine papers, representing sixteen different countries, a common pattern revealed was that males tend to have a higher tinnitus prevalence than females (McCormack et al., 2016). These sex differences are likely present because of general lifestyle and employment differences amongst males and females. For example, male employment usually involves louder environments, predisposing them to noise-induced hearing loss that is a significant risk factor for developing tinnitus (Wang et al., 2020). When the sex-differences were probed further, Basso et al. 2020 found that females tend to have a higher prevalence for bothersome tinnitus when compared to males. In particular, the bothersome tinnitus in females was commonly associated with cardiovascular diseases, thyroid disease, fibromyalgia and burnout, whereas in males it was

often paired with heightened anxiety, alcohol consumption and the presence of conditions like panic disorders and Meniere's disease. The exact direction of these correlations is yet to be determined. Finally, sex-specific contribution on the characteristics of tinnitus has also been explored. These include tinnitus laterality and severity. For a full review, refer to Maas et al. (2017) and Trpchevska et al. (2020).

1.1.5.4 Mental state and tinnitus perception

The most common non-auditory factors that affect tinnitus perception are anxiety, depression and stress (Stobik et al., 2005). Sullivan et al. 1988 found that there is a higher rate of incidence for depression in patients that have tinnitus as their primary symptom, compared to those that report hearing loss as their primary complaint. Although, in the same study, the authors did recognise that these results cannot be extrapolated to all tinnitus sufferers. Instead, it is likely that these findings only represent those that experience disabling tinnitus. Nevertheless, these factors can interact and cause a vicious cycle where tinnitus is not always the first to occur i.e. a poor mental state can be present before tinnitus suffering (Folmer et al., 2001). Some postulate that people that already suffer from conditions such as anxiety disorder, depression or somatisation find it more difficult to cope with tinnitus and therefore experience greater severity (Lockwood, 2005). In fact, studies suggest that the above-mentioned emotional and psychological factors are key catalysts in the transition from acute to chronic tinnitus that is bothersome and severe (Biehl et al., 2019; Wallhäusser-Franke et al., 2017).

In lieu of the above studies, perhaps it is not important to determine the exact cause and effect relationship between tinnitus, depression and anxiety. Instead, in a clinical setting, the aim should be to answer whether depression and anxiety are playing a causative role in exacerbating the disabling effect of tinnitus on an individual's life. As depression can sometimes be better managed than tinnitus, it is thus important to identify when it is present (Sullivan et al., 1988).

Tinnitus perception also has significant associations with an individual's locus of control (Budd & Pugh, 1995). In psychology, locus of control describes how an individual perceives the control of events (Ribolsi et al., 2022). For example, people with an internal locus of control will have the belief that outcomes from events are the result of their own personal efforts. Conversely, an external locus of control refers to individuals believing that there are external sources of control that dictate the outcomes of life events. Patients with an internal locus of control tend to have less disabling tinnitus than those with an external locus of control (Budd & Pugh, 1995). One theory explaining this finding is that those with an internal source of

control are better equipped to manage their tinnitus in a more effective way and thus, are less susceptible to becoming depressed or anxious (Moring et al., 2016). Opposingly, those with an external locus of control believe that they have no control over their tinnitus which only aggravates depression and anxiety, which increases tinnitus severity. Interestingly, when the effects of anxiety and depression were accounted for, the correlation between the locus of control and tinnitus perception became non-significant (Budd & Pugh, 1995). Although more research with larger samples sizes regarding this relationship needs to be performed, these findings further emphasise the importance of considering depression and anxiety when managing patients with tinnitus.

The implications of the studies exploring the relationships between tinnitus, locus of control, depression, anxiety and stress are clear. First, it is crucial to recognise when tinnitus is present with comorbidities such as anxiety disorder, somatisation and depression. If these other conditions are present, they must be treated first, or alongside, any treatment specific to tinnitus. Second, the patient's psychological state must be considered when a tinnitus management plan is made. Simply put, tinnitus is both a medical and a psychological condition that requires a multidisciplinary management plan to achieve desirable clinical outcomes.

1.2 Tinnitus Location

The location of tinnitus is an important characteristic that is often overshadowed by other descriptors such as tinnitus pitch and loudness. As such, this attribute has been under-researched within the field of tinnitus research (Searchfield et al., 2015). Therefore, considering the aims of the thesis and the gap in research, this section has been dedicated to the introduction of some epidemiology related to the localisation of tinnitus, as well as factors that influence where tinnitus is perceived in space.

1.2.1 Epidemiology

The location of perceived tinnitus has been investigated in many studies. Bilateral tinnitus tends to be more common than unilateral tinnitus (Reiss & Reiss, 2001). Interestingly, cases that suffer from unilateral tinnitus, or have a more bothersome side, report that the sound lateralises to the left ear more commonly than the right (Searchfield et al., 2015). Stouffer & Tyler (1990) administered a questionnaire-based study performed on 528 tinnitus patients asking *"Where is your tinnitus?",* alongside other tinnitus-related questions. Similar results were found for both males and females, where 21.4% lateralised to the left ear, 20.3% said it was the same

bilaterally, 15.9% stated it was worse in the right ear, and 16.3% said they had tinnitus in both ears but it was worse on the left. A smaller number of participants also reported that their tinnitus could not be localised to either ear and was coming from within the head. In these cases, there seemed to be a slight bias to which side the tinnitus was originating from within the head; 3% stated that the tinnitus was in-head with a right-side bias, 3% had a left-side bias, and 2.5% said their tinnitus seemed to be omnipresent within the head with no defined location. The smallest number of patients (0.6%) were those that perceived tinnitus to have an external source. In total, bilateral tinnitus had a larger prevalence (52.3%) than unilateral tinnitus (37.3%). When unilateral cases were combined (either within head with single-sided bias or bilateral with tinnitus worse on one side), it was found that 54% perceived their tinnitus on the left and 46% on the right (Stouffer & Tyler, 1990).

However, despite most studies stating a left dominant tinnitus (Davis & El Refaie, 2000; M. Meikle & Griest, 1992; Stouffer & Tyler, 1990), Budd & Pugh (1995) found that only 17% had tinnitus lateralised to the left side, 26% of their study participants perceived tinnitus on the right side, 51% had bilateral tinnitus, and 6% localised tinnitus within the head. A notable limitation of the reporting with this study was that within the group of participants that had bilateral tinnitus, it was not asked whether there was a left or right bias.

Tinnitus location is not fixed throughout the life of the condition and is susceptible to change. This was made apparent by a data collected on 1630 tinnitus patients attending The Oregon Hearing Research Centre (Meikle et al., 2012). In this data set, out of 873 responders, 16.3% of the responders experienced a change in tinnitus location since onset. Out of those that noticed a change, 11.8% of patients perceived their tinnitus transiting from unilateral to bilateral, and 2% noticed a change in location e.g. from left to right or vice-versa. The finding that unilateral tinnitus often becomes bilateral, if a change is to occur, was also corroborated by (Tyler, 2000).

1.2.2 Factors influencing tinnitus location

A commonly accepted theory is that tinnitus usually lateralises to the ear with poorer hearing (Tsai et al., 2012). In a data set consisting of 1,033 tinnitus subjects from the Tinnitus Clinic at Oregon Health and Science University (i.e. OSHU Tinnitus Arhcive), it was found that bilateral tinnitus patients perceived their tinnitus to be louder in the poorer hearing ear with thresholds 5 to 10 dB HL worse than the other ear. In comparison, unilateral tinnitus subjects had an average threshold was 10 to 20 dB HL worse in the poorer hearing ear than the better ear (Nuttall et al., 2004). Similarly, for patients with no asymmetrical hearing thresholds, tinnitus

was present bilaterally or within the head with no left or right dominance (Meikle & Griest, 1992). Opposingly, some authors did find that even though their study population had no interaural hearing differences between 1000 and 4000 Hz, the tinnitus still tended to be localised to the left (Stouffer & Tyler, 1990). Although, this study is noticeably limited as the hearing asymmetry could be present at pitches above 4000 Hz or below 1000 Hz which were not considered. Indeed, it is common that asymmetrical hearing at or above 3000 Hz is often associated with asymmetrical tinnitus localisation (Meikle & Griest, 1992).

Another explanatory factor affecting the localisation of tinnitus is noise exposure (Wang et al., 2020). Particularly, many of those with left-sided tinnitus are proposed to have the laterality because of a history of gun shooting (Davis & El Refaie, 2000). During shooting, the left ear is predominantly exposed to high levels of noise from the gun barrel, while the right ear is somewhat protected by the head shadow effect caused by the face leaning towards the shoulder (Prosser et al., 1988). The protection of the right ear is more common than the left because most people are right handed (Papadatou-Pastou et al., 2020). Indeed, in the aforementioned OSHU Tinnitus Archive, a large number of participants were occupational (e.g. military) or recreational (e.g. hunting) shooters (Meikle et al., 2012). The association between noise exposure and the onset of tinnitus was further studied by Meikle & Griest (1992) by dividing the tinnitus patients into low, medium and high gunshot noise-exposure groups. Those patients that had been exposed to high levels of noise were significantly more likely to have a left-sided tinnitus than the other two groups. On average, this group had an 18.4% higher prevalence for left-sided tinnitus than right-sided. Comparatively, those that were in the medium and low noise exposure groups had only a 5.2% and 3.3% difference, albeit still statistically significant. The authors saw a clear downward trend of the differences between left- and right-sided tinnitus prevalence going from high to low noise exposure. As such, they were able to claim that asymmetrical tinnitus, in part, was due to gunshot noise-exposure. Notably, in the same study, patients that were not exposed to any noise still had a slightly higher prevalence for left-sides tinnitus. The authors attributed this to chance. Conversely, there are also other studies that refute this claim by showing no significant influence of noise exposure on tinnitus location (Coles & Hallam, 1987; Folmer et al., 2001; Sullivan et al., 1988). Therefore, more research needs to be done before claiming a causal relationship between noise exposure and perceived tinnitus location.

Other factors that are commonly thought to influence the location of tinnitus include handedness and asymmetries within the processing of the central nervous system (CNS).

Currently, there are no definitive studies showing any differences between left and right-handed people with the laterality of tinnitus (Meikle et al., 2012; Meikle & Griest, 1992). However, asymmetries within the lower brainstem (Decker & Howe, 1981, 1982), and upper cortical areas (Stouffer & Tyler, 1990; Ward, 1957), do show significant correlations with tinnitus location. The exact neurophysiology that underpins these tinnitus asymmetries will be discussed in later sections of the thesis.

1.2.3 Limitations of current research

One of the methodological limitations of cross-study comparisons for tinnitus localisation is that there are currently no universal standards that are able to describe tinnitus anywhere in space (Genitsaridi et al., 2020). Instead, current research in this field relies on self-report questionnaires that limits responses to whether tinnitus is heard in one or both ears. Indeed some studies extend response options to; right side, left side, both sides equally, both sides with left bias, both sides with right bias, and inside or outside head (Langguth et al., 2007; Nuttall et al., 2004). However, the challenge here becomes how to combine such responses to create meaningful subgroups. Another limitation of having such strict boundaries is that participants of studies cannot give an accurate enough account of their tinnitus location. Therefore, high-resolution standards that can map tinnitus location along three-dimensional space are needed to encourage more research within this field. The current thesis synthesises such a method using a polar coordinate grid to achieve its aims.

Hearing asymmetry in different studies has been defined using different criteria. This makes comparisons between studies investigating tinnitus spatial perception and hearing asymmetries difficult. For example, interaural threshold differences can be based on an average value across a specific frequency range, the value of the maximum difference between two interaural frequencies, or a combination of the two (Cahani et al., 1984; Caldera & Pearson, 2000; Cheng & Wareing, 2012; Ftouh et al., 2018). Similar assortment of differing criteria is seen in a clinical setting as well. In fact, Caldera & Pearson (2000) performed a study with 1490 audiograms and showed that the degree of hearing asymmetry can vary up to 100-fold depending on which criteria was used. To further complicate cross-study comparisons, there is a disconnect between the frequency ranges tested in clinical data (standard audiometric octaves up to 8 kHz) and research data (inter-octaves and the extended high frequency range above 8 kHz) (Genitsaridi et al., 2020). Two potential workarounds have been suggested for these limitations. First, an individual's audiogram can be represented by the area under the curve once the inter-octave frequencies have been interpolated (König et al., 2006). Second, an

optimum hearing asymmetry metric can be defined that strongly predicts tinnitus laterality. Tsai et al. (2012) proposed that the maximum interaural hearing thresholds difference averaged by the second maximum of at least 15 dB is one such metric. However, when these workarounds were assessed, neither of the studies considered extended high-frequency thresholds.

1.3 A brief overview of the human auditory system

The human auditory system is responsible for achieving the complex task of hearing. Hearing involves identifying, characterising and localising the sounds in our environment, so that the listener can respond accordingly in a timely manner (Pérez-González & Malmierca, 2014).

The auditory (or hearing) system can be structurally subdivided into a peripheral and central component. The peripheral system, located inside the densest part of the temporal bone, consists of the outer, middle and inner ear, as well as the portion of the vestibulocochlear nerve (cranial nerve VIII) that communicates with the central auditory system. This system is designed to collect, filter, amplify and convert the mechanical energy carried in sound pressure waves into electrical neural impulses that can be transmitted to the central system (Musiek & Baran, 2018; Rowe & O'Leary, 2014). These neural signals then flow upstream through multiple relay centres of the central system, which include the cochlear nucleus, the superior olivary complex, the lateral lemniscus, the inferior colliculus, the medial geniculate body and the additory cortex, in that order (Fowler & Leigh-Paffenroth, 2007). Other downstream pathways are still being discovered (Schofield, 2011). With other brain structures, the central system functions to discern target sounds in backgrounds of noise and integrate them with other sensory modalities. And at the cortical level, recognition and meaning are attached to these sounds. The human hearing system analyses sounds via multiple parallel and bidirectional processing streams especially at the level of brainstem and beyond. This allows hearing to be efficient and near-instantaneous, giving humans the ability to rapidly adapt and respond to their acoustic environments (Thompson et al., 1992).

1.3.1 Peripheral Auditory System

1.3.1.1 Outer Ear

Sounds entering the auditory system initially travel through the outer ear which consists of the pinna and the external auditory canal (EAC). The pinna is a cartilaginous protrusion from the side of the head that acts as a sound collector and directs the sound energy into the external auditory canal. Owing to the unique pattern of ridges and grooves on the pinna surface, high frequency sounds (around 5000 Hz) are differentially enhanced before entering the ear canal. This resonance pattern is thought to assist in vertical-plane sound localisation that will be discussed later (see section 1.4).

The EAC brings the sounds collected by the pinna and transfers it towards the tympanic membrane. Owing to its shape that resembles an open-ended tube, the EAC acts as a resonator of sounds between 3000 to 4000 Hz. The presence of this resonance is responsible for giving a natural perception to incoming sound (Dempster & Mackenrie, 1990).

1.3.1.2 Middle Ear

The middle ear is an air-filled space embedded within the temporal bone that houses three ossicles essential for transferring sound from the tympanic membrane to the inner ear (Musiek & Baran, 2018). These ossicles are the malleus, incus and stapes, in that order, and are sometimes referred as the ossicular chain. The distal end of the ossicular chain is attached to the tympanic membrane via the manubrium of the malleus and the proximal portion attaches to the fluid-filled inner ear via the stapes footplate resting within the cochlear oval window. The main function of this anatomical configuration is to increase the sound energy imparted into the inner ear and therefore overcome the impendence difference between the air of the outer ear and fluid of the inner ear (Purves et al., 2001).

1.3.1.3 Inner Ear

The inner ear consists of the cochlea and the balance organs of the vestibular system. Located within the petrous part of the temporal bone, the bony cochlea is a completely enclosed fluid-filled structure responsible for converting the mechanical energy imparted by the vibrations of sound waves into electro-chemical energy that is carried in the form of neural impulses (Ekdale, 2016). Initially, the energy into the cochlea (specifically the scala vestibuli compartment of the cochlea) enters through the oval window by the movement of the stapes footplate, and a travelling wave is generated across the cochlear basilar membrane. According to cochlear fluid

mechanics, the travelling wave begins at the base of the of the cochlea and travels apically where the maximal amplitude occurs at a frequency-dependent place (Brugge & Howard, 2002). During this movement, the outer and inner hair cells seated on the basilar membrane have apical stereocilia that bend backwards and forwards as they brush against the overlaying tectorial membrane (Musiek & Baran, 2018).

The shearing force caused by the interaction of the outer hair cell and the tectorial membrane open mechanoelectrical transduction channels situated at the tip of each stereocilia. Depending on the direction of the stereocilia movement, these channels open or close and allow a flow of potassium and calcium ions down their electrochemical gradient. The influx of these ions causes the outer hair cells to depolarise which results in an voltage-dependent shortening and lengthening of the cell body (Ricci et al., 2006). The changes in outer hair cell length acts to amplify the vibratory movement of the basilar membrane where the mechanical energy created increases the amplitude of the travelling wave. This active process is called reverse mechanoelectrical transduction and it evolved to enhance the inner hair cell response (Fettiplace & Kim, 2014; Ricci et al., 2006).

The cochlea has certain regions that respond better to specific sound frequencies. This frequency specificity is owed to the resonance properties of the basilar membrane and the cellular apparatus that sits upon it, collectively referred to as the organ of Corti. Resultingly, the cochlea is organised tonotopically where the base responds maximally to high frequency sounds and the apex reacts the most to low frequency sounds. This tonotopic map is also preserved throughout the auditory pathway (Dick et al., 2017; Koops et al., 2020).

1.3.1.4 Cochlear Nerve

The cochlear nerve has both efferent and afferent fibres (Liberman & Liberman, 2019). Approximately 95% of the afferent fibres innervate with inner hair cells, whereas the remaining 5% synapse with outer hair cells (Spoendlin, 1972). The inner hair cell efferent fibres are the main output neurons of the cochlea. These afferent fibres carry auditory information from the cochlea to the cochlear nucleus of the brainstem (Musiek & Baran, 2018). Fibres that carry low frequency information are located within the core of the nerve and the high frequency fibres are situated closer to the surface (De Ridder et al., 2004).

1.3.2 Central Auditory System

The following sections are arranged in the order in which the ascending auditory information is transmitted from the brainstem to higher order centres located in the thalamus and the cortex. Together, these form the central auditory pathways.

1.3.2.3 Cochlear Nucleus Complex

The cochlear nucleus is the first relay centre that receives ipsilateral input from the excitatory fibres of the cochlear nerve (K. A. Davis, 2005). Although predominantly thought of as a monaural nucleus, the cochlear nucleus also receives some input from fibres descending from binaural nuclei, as well as commissural fibres from the contralateral nucleus (K. A. Davis, 2005). The cochlear nucleus complex (CNC) consists of three nuclei; the anteroventral cochlear nucleus (AVCN), the posteroventral cochlear nucleus (PVCN) and the dorsal cochlear nucleus (DCN) (Harrison & Feldman, 1970). Each of these nuclei send upstream projections to different nuclei along the central auditory pathway. The AVCN sends projections to (i) the lateral superior olive (LSO) of the superior olivary complex (SOC) in the brainstem, (ii) the medial superior olive (MSO) of the SOC bilaterally, and (iii) the contralateral trapezoid body that acts as an intermediate before sending projections to the ipsilateral LSO. The PVCN chiefly sends upstream fibres to the bilateral SOC and inferior colliculus (IC) of the midbrain. The DCN sends fibres contralaterally to the IC via the lateral lemniscus (LL) (Middlebrooks, 2015). Like the cochlear nerve and the cochlea, the CNC is also tonotopically mapped in a way where low frequency information is culminated ventrolaterally and high frequency input is processed along the dorsomedial aspect (Hackett, 2015).

1.3.2.4 Superior Olivary Complex

The SOC is a collection of brainstem nuclei and the three primary subdivisions include the MSO, the LSO, and the medial nucleus of the trapezoid body (MNTB) (Kulesza, 2007). Each of these process slightly different information. For example, the MSO and LSO have a tonotopic preference where the LSO is mostly responsive to high frequency sounds and the MSO responds most to low frequencies (Oliver et al., 2003). The inputs these nuclei receive is also different. Notably, the SOC is the first relay centre along the central pathway that receives binaural information (Tollin, 2003). Within the SOC, the LSO neurons are of the EI-type, where they are excited by ipsilateral projections from the CNC but inhibited by contralateral projections. Conversely, the EE-type are excited by both contralateral and ipsilateral projections (Couchman et al., 2010; Tollin, 2003). Together, the EI- and EE-type of neurons

process interaural time and interaural intensity differences, respectively. Therefore, these neurons within the SOC allow sound localisation to occur as both of these interaural cues are critical for sound localisation (Tollin, 2003).

1.3.2.5 Lateral Lemniscus

The lateral lemniscus (LL) is an auditory tract in the brainstem that connects the axons of the cochlear nucleus to the inferior colliculus (IC) in the midbrain. The LL is subdivided into three major nuclei including the dorsal, ventral and intermediate nuclei (Henkel, 2018). Together these nuclei provide differing innervation patterns and projections bilaterally to both inferior colliculi. Specifically, the dorsal LL receives bilateral auditory input and can project to either the ipsilateral or contralateral IC. However, the ventral LL mostly obtains ipsilateral innervation but projects only to the ipsilateral IC (Schofield, 2005). The LL also has a tonotopic map, where low frequency sounds stimulate the dorsal region, and the high frequencies stimulate the ventral LL (Brugge & Howard, 2002).

1.3.2.6 Inferior Colliculus

The inferior colliculus is a major relay centre along the auditory pathway, where essentially all ascending auditory information culminates before entering thalamic processing. As such, the IC is an important site for binaural integration of all sounds (Adams, 1979). Most IC neurons are responsive to binaural sounds, where contralateral and ipsilateral inputs are generally excitatory and inhibitory, respectively (Semple & Aitkin, 1979). The IC neurons are also sensitive to sound localisation cues such as interaural intensity and time differences (Yost & Zhong, 2014).

The IC receives, mainly the central IC nucleus, receives innervation from the LSO and LL bilaterally; MSO, MNTB and LL ipsilaterally; and CNC contralaterally. The only nucleus that does not innervate the IC is the ventral LL nucleus. The IC then has bilateral ascending projections to the medial geniculate body (MGB) of the thalamus (Oliver, 2005). Once again, the tonotopic map is preserved in the IC as well, where lower sound frequencies are processed along the dorsal aspect, and the higher frequencies are processed along the ventrolateral aspect (Baumann et al., 2011). High-resolution imaging also shows a laminar tonotopic map along the depth of the IC that has a heterogenous and patchy appearance (Ress & Chandrasekaran, 2013).

1.3.2.7 Medial Geniculate Body of the Thalamus

The MGN of the thalamus has three nuclei: ventral, medial and dorsal MGB. The neurons of the ventral MGB have a preference to contralateral input, but ipsilateral auditory simulation also stimulates the ventral MGB, albeit to a lesser degree (Middlebrooks, 2015). Moreover, the ventral MGB has a tonotopic map where high frequency sounds are represented along the lateral aspects of the MGB, and progressively higher frequencies are represented towards the medial aspects (Standring, 2021). Some neurons of the MGB also have the ability to encode interlay intensity differences (Edeline, 2011).

The circuitry of the MGN is as follows. All three nuclei receive input from the IC, with the medial and dorsal nuclei also receiving projections from the SOC, LL and the somatosensory regions. The ventral MGN then projects to the auditory cortex, whereas the dorsal and medial MGB regions project to the auditory association areas including the basal ganglia and the amygdala (Jenison, 2001).

1.3.2.8 Auditory Cortex

The primary auditory cortex, sometimes known as Herschl's gyrus, is located within the temporal lobe (Musiek & Baran, 2018). There are two streams that provide input to the auditory cortex, referred as the primary and nonprimary auditory pathways. The primary auditory pathway is exclusively dedicated to the processing of auditory information and involves the central IC, the ventral MGB and the primary auditory cortex. The nonprimary pathway, also called the reticular sensory pathway, involves the IC, dorsal MGB and medial MGB. The function of this pathway is to join all other sensory information with auditory information to allow the selection of which sensory information needs to be prioritised first (Ahveninen et al., 2006). For example, when we are reading a book whilst listening to music, this nonprimary pathway will allow us to attend alternately to prioritise the most important task.

1.3.3 Descending Auditory Pathway

The pathways discussed above have long been accepted as the classical view of the central auditory system. In recent years, however, a nonclassical view involving the role of descending projections is also becoming prevalent (Kraus, 2021). These include projections from the IC to the LL, SOC and CNC, as well as neurons originating from the periolivary and preolivary nuclei of the SOC to the cochlear nerve directly (Schofield, 2010).

A perhaps better studied descending auditory pathway is the one located within the peripheral auditory system. In this, efferent fibres descending from the SOC synapse bilaterally with the outer hair cells of the cochlea. Although these fibres originate bilaterally from the MSO, a stronger input is received from the contralateral side. There are also a small number of efferent fibres (approximately 5%) that synapse at the inner hair cells (Spoendlin, 1972). In addition to the MSO-related descending control, the LSO also sends inhibitory descending fibres that synapse with the buttons of afferent fibres. In turn, the LSO is able to control the afferent neuronal response transmitted from the hair cells via the cochlear nerve (Ciuman, 2010; Spangler et al., 1987). The exact function of these descending pathways remains elusive, however noise protection, mediation of selective attention and enhancing the signal-to-noise ratio, seem to be the defining roles (Ciuman, 2010).

1.4 Sound localisation

The ability to localise sound is an important capability that has been pivotal in the survival of the species. In the present-day, sound source localisation contributes greatly to the enhancement of speech comprehension especially in the presence of noise (Risoud et al., 2018). There are three cues that enable sound source localisation to occur: two of which are monaural cues (interaural time difference and interaural intensity difference) and one monaural spectral cue (Middlebrooks, 2015). Together, these cues allow localisation to occur in three dimensions, where two of the dimensions are angular (azimuth in the horizontal plane or elevation in the vertical plane), and one is depth (i.e. the distance the sound is away from the head). These three dimensions are shown in Figure 1. The following review will only focus on how the azimuth is determined in the horizontal plane (using binaural cues) and how depth distance is determined monaurally, because elevation is not considered in the study.

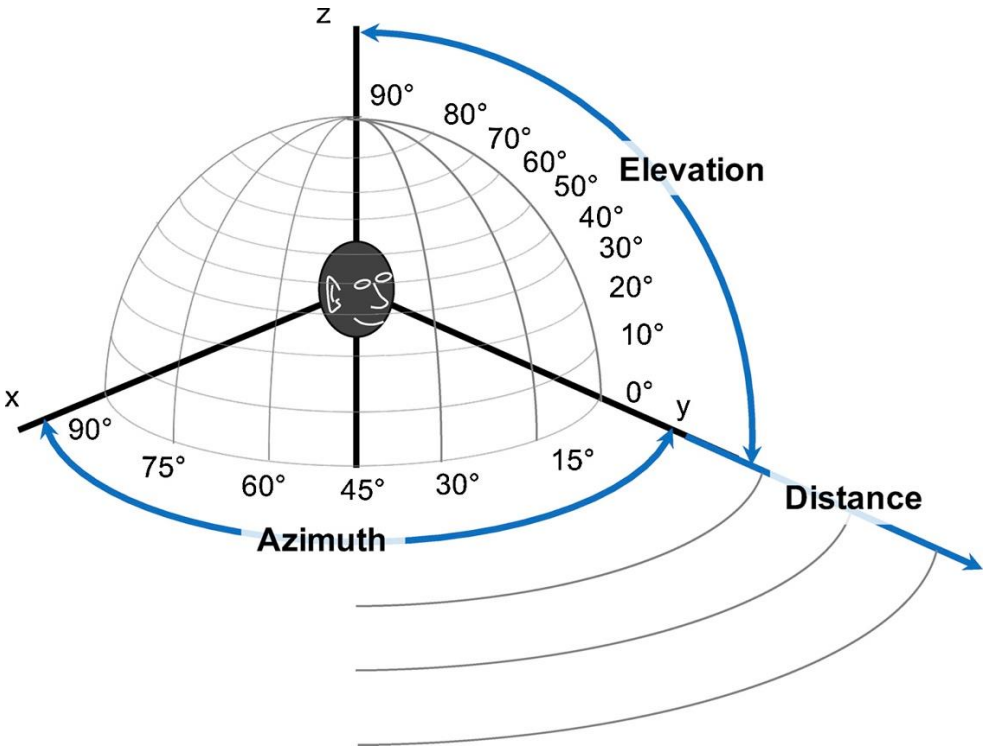

Figure 1. Three dimensional polar coordinates used for sound source localisation. Cited in Risoud et al. (2018).

1.4.1 Horizontal localisation

Localisation of sound within the horizontal plane (azimuthal) requires the interaural time difference (ITD) and interaural intensity difference (IID) cues. These cues are also frequency dependent, where ITD cues operate well for low frequency components of sound, and IID operates within the high frequency ranges. Middle frequency sounds (centred on 2000 Hz) are therefore the hardest to localise as neither ITD or IID are dominant (Simmons, 2006). The frequency spectrum width also affects the accuracy of horizonal sound localisation, where the highest accuracy occurs for white-noise, followed by broadband noise, narrowband noise, and pure-tones, in that order (Yost & Zhong, 2014).

1.4.1.1 Interaural Time Difference

ITD is defined as the difference in the time of arrival of a sound between the two ears (Risoud et al., 2018). This not only causes a difference in the arrival time for the sound waves in both ears, but the incident sound wave seen by either ear is different in phase and amplitude/intensity (Van Opstal, 2016). It has been mathematically proposed that the maximum frequency of sound that can carry the ITD cue is 1525 Hz (Risoud et al., 2018), and this has also been confirmed experimentally (Mills et al., 1986). The reasoning behind this upper limit is that for sound wave frequencies above 1500 Hz, phase-shift becomes irrelevant because several high-frequency

and small-wavelength sound waves may have followed one another by the time they reach the farther ear (Risoud et al., 2018).

1.4.1.2 Interaural Intensity Difference

IID refers to the amplification or attenuation of the sound signal depending on which path the incidence wave takes to each ear (Middlebrooks, 2015). The closer ear, ipsilateral to the sound wave, provides amplification to the sound pressure level (SPL) by the collecting properties of the pinna, whereas the contralateral ear experiences attenuated SPLs owing to the head shadow effect (obstruction of the sound waves by the head) (Risoud et al., 2018). Opposite to ITD, the IID cue operates best in higher frequencies because the pinna's amplification effect is optimal for frequencies around 4 kHz which increases the difference in SPL received by the two ears (Musiek & Baran, 2018). Further, the difference is increased because higher-frequencies have shorter-wavelengths that are more susceptible to the shadow effect (Risoud et al., 2018).

1.4.2 Sound depth perception

The ability to judge to the depth of sound is not as well understood as sound localisation on the vertical and horizontal planes. In general, sound depth perception chiefly uses monoaural cues which is considerably more accurate with familiar sounds compared to unfamiliar ones (Coleman, 1962) and tends to overestimate long distances whilst underestimating short distances (Zahorik, 2002).

There are four auditory cues that influence the ability of humans to perceive depth: direct-to-reverberant energy ratio, level, spectral characteristics and binaural cues (especially interaural level difference (ILD)) (Risoud et al., 2018). First, the direct-to-reverberant energy ratio is based off the principle that direct incident sound waves dominate for closer sounds, whereas reflected sound waves predominate for incident sound waves coming from farther away sources (e.g. gunshot in a farm) (Garas, 2012). In turn, the ratio between these two types of sound waves gives, in part, the perception of auditory depth (Hartmann, 1997). Second, the level of the incident sound waves also is an important distance cue, where farther sound waves will lose energy as they propagate towards the listener i.e. each time the distance is doubled, there is 6 dB level drop in sound (Coleman, 1962). Third, the spectrum of the incident sound waves changes as it travels towards the listener. Generally, spectral cues for distance perception are mostly operative in the higher frequency ranges because high-frequency sounds are more prone to become "muffled" by the air particles (Coleman, 1962). Finally, some information about the distance of a sound source can also be gained by the binaural ILD cue. This is because

sounds located nearby (< 1.5m) have a significant difference between ears than those that are farther away (Brungart et al., 1999). There are also some visual cues that aid in the perception of sound depth but that is outside the scope of this review (Middlebrooks, 2015).

1.5 Mechanisms underlying tinnitus generation

Tinnitus is a multifaceted condition and because of its diverse nature, there are multiple theories that have been proposed for its aetiology. The predominant view of tinnitus is that it is a symptom of an underlying disease instead of being a disease on its own. These causative diseases could include, but are not limited to, otosclerosis, Meniere's disease and middle ear conditions (Esmaili & Renton, 2018). However, there are several instances where tinnitus is idiopathic (Savage et al., 2009), which highlights the importance of understanding the symptom outside the context of the underlying disease. Despite the advancements in tinnitus research, there is still controversy regarding the exact mechanisms underlying the condition, and resultingly, the same applies for tinnitus treatments. To date, the attempts at settling this contention range from explaining the pathophysiological mechanisms at a cellular level for tinnitus generation, to tinnitus perception at the system level (Saeed & Khan, 2021). In more recent years, however, the focus has shifted to understanding tinnitus at a system level that explores complex brain networks and the interactions between auditory and non-auditory structures for tinnitus generation. The following sections will discuss these levels in more depth.

1.5.1 Cellular level

1.5.1.1 Increased neural synchrony and hyperactivity

Perhaps the most studied explanations for tinnitus generation are increased neuronal synchrony (i.e. increased firing rates of a neuronal population in a simultaneous manner) and cortical hyperactivity (Saeed & Khan, 2021). Together, these theories are also termed the "central gain control" theory across literature. The initiation of these mechanisms begin with the loss of hearing input from the periphery, but can manifest in different ways when viewed at a central level. The causes can include a number of hearing losses, but those that are noise-induced in nature tend to be the leading factors (Auerbach et al., 2014). The decreased processing within the cochlea, with decreased cochlear nerve activity, downregulates the inhibitory processes within the central areas responsible for sound processing. In turn, this downregulation leads to increased cortical hyperactivity, especially within the primary auditory cortex (Norena et al., 2002). Other mechanisms by which this hyperactivity occurs include, in addition to the

aforementioned decreased inhibition, increased excitatory synaptic response or upregulated intrinsic neural excitability (Auerbach et al., 2014; Illing et al., 2005). Although this theory is well-accepted, whether it underlies the sensation of tinnitus is unknown. The changes causing cortical hyperactivity occur hours to days after high noise exposure, which does not explain the observation that most sufferers experience tinnitus immediately after exposure (Norena & Eggermont, 2003).

Increased neural synchrony is another potential mechanism. The temporal firing synchrony of multiple cortical neuronal populations is reported to increase immediately after noise induced damage to the cochlea, particularly those connected to the tonotopic region of the damaged cochlea (Norena & Eggermont, 2003; Seki & Eggermont, 2003). Notably, this is different from increased firing rates observed due to loss of peripheral inhibition; in this case there is an increase in neural synchronicity that occurs immediately, alongside a general increase in cortical activity that is delayed. These neuronal populations that experience an increase in synchrony also tend to be the ones that undergo a change in their frequency tuning properties (Seki & Eggermont, 2003).

The location along the auditory pathway where these changes occur is debated. Increased spontaneous firing rates (SFRs), or hyperactivity, was observed in the primary output neurons of the DCN, called the fusiform cells, after noise-exposure (Brozoski et al., 2002; Koehler & Shore, 2013). These increases in SFRs was close to the frequencies of the noise and the behaviourally-determined pitch of the tinnitus (Brozoski et al., 2002). Other animal studies showed that there was higher neuronal activity in the MGB of the thalamus for animals with tinnitus than those without, but similar changes were not seen in the DCN (Shore et al., 2016; Takeuchi & Izumi, 2012). The reason for these discrepancies could underly the diversity by which tinnitus is experienced by suffers.

1.5.1.2 Dysregulation of synaptic neurotransmission

Changes in neurotransmission is another tinnitus mechanism that occurs at the cellular level. The processes that underlie these changes are intrinsically linked to the above-mentioned theory of central gain control. Pilati et al. (2012) performed a study on tinnitus rat models and found that after intense noise exposure, the DCN fusiform cells showed a downregulation of high voltage-gated potassium channels within the synapses. These channels are responsible for mediating synaptic potassium currents that are largely inhibitory i.e. reducing excitability (Gu et al., 2007; Rudy & McBain, 2001). As a result, the downregulation of these channels create

a bursting pattern (i.e. high firing rate) within the DCN neurons (Pilati et al., 2012). Another study demonstrates a decrease in a presynaptic enzyme, glutamic acid decarboxylase (GAD), that also acts to increase firing rates within the high-frequency region of the auditory cortex (Yang et al., 2011). Overall, these pathological mechanisms create an unbalanced system where the loss of neuronal inhibition leaves excitatory processes unmatched, resulting in hyperexcitability that is perceived as tinnitus (Richardson et al., 2012).

There are also other studies that provide evidence for the association of neurotransmission changes and tinnitus generation. Brozoski et al. (2010) showed that supplementing taurine, an agonist of the inhibitory GABA receptor, provided reductions in tinnitus. The mechanism highlighted was that taurine specifically acts to increase the inhibitory processes within the MGB, which reduces neuronal hyperactivity and thus, tinnitus perception (Brozoski et al., 2010). These findings were confirmed by (Richardson et al., 2012), who showed similar results when NO-711 (GABA reuptake inhibitor) and vigabatrin (GABA receptor agonist) were given in combination. Similar mechanisms have also been observed in the central nucleus of the IC, where exposure to intense sounds caused a decrease in GABAergic inhibition, increased hyperactivity and thus, tinnitus (Berger & Coomber, 2015). Together, the studies detailed in this section show a decrease of an inhibitory drive that allows the excitatory drive to remain unchecked along multiple structures of the auditory pathway, including the DCN, MGB, IC and the primary auditory cortex. As a result, this hyperactivity is perceived as tinnitus.

1.5.1.3 Maladaptive plasticity

Neuroplasticity is the process of by which the nervous system reorganises itself to adapt and change in response to new stimuli (Cramer et al., 2011). The phenomenon of neuroplasticity was first discovered in 1966, and was solely used in the context of memory formation (Livingston, 1966). However, in the last decade, the connection between tinnitus and neuroplasticity has also been explored. In the context of neuroplasticity, both tinnitus initiation, as well as the maintenance of chronic tinnitus have been described (Guitton, 2012). For example, the NMDA receptor's sub-unit, 2B is involved in memory consolidation (a neuroplastic process) (Zhao et al., 2005). When this subunit is blocked by an NMDA antagonist specific to the cochlea, tinnitus is abolished in noise-induced tinnitus models (Guitton & Dudai, 2007). This finding illustrates that the alteration of neuroplasticity is a mechanism that is present at the onset of tinnitus (Saeed & Khan, 2021). Further, subjective chronic tinnitus has similarities to neuropathic pain, where pain is not life threatening but still has severe

consequences on an individual's quality of life (Møller, 2011). The reason behind this could be attributed "misdirected" learning, where the patient starts associating, or learning, that the phantom sound is a trigger for distress (Møller, 2016). This has been suggested to occur through prolonged maladaptive plasticity within auditory and non-auditory structures (Vanneste et al., 2014).

1.5.2 System level

1.5.2.1 Auditory structures involved in tinnitus generation

1.5.2.1.1 Dorsal cochlear nucleus

One of the first auditory nuclei implicated with tinnitus generation was the DCN and accordingly the DCN was sometimes referred as the "tinnitus generator" (Shore et al., 2016; Zwieten et al., 2019). Many lines of evidence converged stating that the main pathological change that occurred in the DCN was an increase in neural synchrony (Baizer et al., 2012; Dehmel et al., 2012; Martel et al., 2019; Shore et al., 2016; Wu et al., 2016). There are multiple related mechanisms underlying this change that were found using animal models: (i) increased synchronicity in spontaneous firing rates in response to blocked NMDA receptors, (ii) increased overall firing rates in salicylate-induced tinnitus models, and (iii) increased stimulus timing dependent plasticity in other tinnitus animals models (Martel et al., 2019; Stefanescu & Shore, 2015). Although the increased activity is seen in both the DCN and the IC, the IC seems to have a lower degree of hyperactivity than the DCN (Olsen et al., 2018; C. Wu et al., 2016). Therefore, these findings elucidate that there must be independent changes that occur in the DCN causing relatively higher levels of hyperactivity than the IC (Manzoor et al., 2013). More research must be done to explore the interrelationship between the DCN and IC to better understand the contribution they have towards tinnitus generation. Nevertheless, when combined with the studies discussed in the previous section on cellular change, it is indisputable that the DCN plays a key role in the pathogenesis of tinnitus.

1.5.2.1.2 Inferior colliculus

The connection between the IC and tinnitus generation is formed on the basis of neural hyperactivity (Palmer & Berger, 2018). In salicylate-induced animals models for tinnitus, it is demonstrated that IC neurons show increased excitability and gap detection thresholds (representing an objective measure for tinnitus presence) (Berger & Coomber, 2015). Contradictory to these findings, a study has also shown no significant differences in hyperactivity between animals models with and without tinnitus (Coomber et al., 2014).

Further, human studies show that complete excision of the DCN reduces IC hyperactivity in tinnitus animal models, elucidating that the DCN, in part, responsible for driving the pathological changes in the IC (Manzoor et al., 2013). However, functional MRI, using blood flow as a proxy for measuring neuronal activity, found no significant differences in the IC activity of tinnitus and control groups (Lanting et al., 2014). This finding has been referenced in another study stating that the overactivation of the IC could be due to abnormal tolerance to sound instead of tinnitus (Boyen et al., 2014). As opposed to the DCN, the role of the IC is not straightforward and more research is required to confirm its contribution.

1.5.2.1.3 Medial geniculate body of the thalamus

The MGB has been implicated to have tinnitus generative mechanisms. These include changes such as increased astrocyte activation and microglia proliferation within the MGB in animal models of tinnitus (Xia et al., 2020). However, the research done in this area is extremely limited (Saeed & Khan, 2021). In fact, some studies are also contradictory, where one states that there is increased hyperactivity in tinnitus models (Kalappa et al., 2014), while another showed decreased excitability of the MGB neurons after tinnitus was induced (Su et al., 2012).

Perhaps the more interesting role of the MGB in tinnitus generation involves its connections with the amygdala. These connection is a major component of the limbic system that processes negative emotions like those stirred by tinnitus (Caspary & Llano, 2017). However, this topic will be reserved for the upcoming section explaining the link between the emotional centre (amygdala), the MGB and the emotional component to tinnitus.

1.5.2.1.4 Auditory cortex

The auditory cortex is the final structure in which auditory information is processed and has a well-established role in tinnitus generation. There are multiple studies that make this claim. First, a study showed that the intensity of tinnitus increased with gamma band activity within the auditory cortex opposite to the side of tinnitus (Loo et al., 2009). Second, a functional near-infrared spectroscopy (fNIRS) approach, that measures blood-oxygenation, showed that there was an increased haemodynamic flow to the auditory cortex indicating increased neuroplasticity in tinnitus models (Zhai et al., 2021). Third, a similar approach was used to demonstrate that there is an increase in baseline neuronal activity within the auditory cortex in tinnitus patients (San Juan et al., 2021). Fourth, similar to the DCN and IC, salicylate-induced tinnitus rat models showed neuronal hyperexcitability within the auditory cortex as well (Yi et

al., 2016). Therefore, the auditory cortex is probably involved in tinnitus pathology, likely through pathological increases in neuronal activity (C. Wu et al., 2018; Yi et al., 2016).

1.5.2.2 Other proposed models for tinnitus generation

There are several models for tinnitus that have been proposed. These include: (i) the peripheral models that explains tinnitus is caused by cochlear dysfunction (Mulders & Robertson, 2009); (ii) subcortical hyperactivity models that propose tinnitus occurs due to excessive neural activity (Auerbach et al., 2014); (iii) neural synchrony models that postulate an increase in synchronicity of neuronal firing underlies tinnitus; (iv) filling-in models that state the auditory cortex that lacks input will reorganise to receive non-auditory input from adjacent areas that can wrongly be perceived as tinnitus; and (v) the predictive coding model that hypothesises that tinnitus is the result of the mismatch between predictions created by higher centres of the brain and actual auditory information flowing via bottom-up projections (termed 'evidence') (Noda et al., 2018). Noticeably, models (i), (ii) and (iii) have been extensively highlighted in the previous sections. Collectively, these models are problematic because, except for the predictive coding model, there are large discrepancies between neural changes underpinning each model and there are contradictions with the connectivity between cortical and sub-cortical areas involved. For a full review of each model, refer to Sedley et al. (2016).

1.6 Mechanisms underlying tinnitus perception.

Chronic tinnitus has two components: a phantom sound and one that causes distress and suffering. Delineating these two components is important because not everyone that experiences the phantom sound is distressed (Wu et al., 2018; Yi et al., 2016). As such, mechanisms behind both need to be understood to form specific treatments addressing the two components separately. This section will focus on the latter, which falls under the *perception* of tinnitus, just as the previous sections focussed on the *generation* of the phantom sound.

1.6.1 Distress and depression networks

There has been one study aiming to separate the neural circuits underpinning tinnitus-caused distress and depression. Here, distress is defined as a transient phase that negatively affects a person's ability to deal with stressors, whereas stress is considered more of a constant emotional state (Folkman, 2013; Muscatell et al., 2009). In the study, electroencephalogram (EEG) activity showed a direct relationship between scores of tinnitus-induced distress (as measured by a the Dutch version of the Tinnitus Questionnaire) and neural activity within the

orbitofrontal cortex, anterior cingulate cortex, and other auditory association areas (Joos et al., 2012). Another finding from the same study stated a positive correlation between the Beck Depression Inventory (questionnaire evaluating depressive symptoms) and the activity of cortical regions. Previous studies have implicated the role of the anterior cingulate gyrus in tinnitus distress networks, whereas the orbitofrontal cortex has been proposed as a site for depressive networks for tinnitus (Saeed & Khan, 2021). Therefore, the parahippocampal areas such as the orbitofrontal cortex and the anterior cingulate gyrus, are likely to be involved in tinnitus-related stress and depression.

1.6.2 Auditory-limbic networks

The connections between auditory and limbic areas, responsible for defining emotional and attentional states to sound, have long been proposed by the neurophysiological model of tinnitus (Jastreboff, 1990). Evidence to this proposition has also been gathering, where a study using blood oxygenation level dependent (BOLD) measures, found that the functional connectivity of the brain was altered for patients with distressing and depressive tinnitus, when compared with patients that had non-bothersome tinnitus (Burton et al., 2012). Moreover, in another study it was found that the during the pathogenesis of chronic tinnitus, functional connectivity of the brain transitions from specific sites within the auditory areas to more diffuse sites including the limbic system (Rauschecker et al., 2010). For example, it was found that the limbic system has the ability to downregulate the processing of unwanted sounds by sending inhibitory top-down signals that prevents such sounds from entering the auditory cortex (termed the 'noise cancelling' function of the limbic system). The breakdown of this top-down inhibition was reported in tinnitus patients, where the unwanted sound enters the auditory cortex and causes cortical reorganisation that translates into tinnitus perception (Rauschecker et al., 2010). Therefore, it is likely that tinnitus perception is guided by maladaptive cortical plasticity within the auditory-limbic networks of the brain.

1.7 Tinnitus assessment

Despite tinnitus being subjective in nature, there are multiple forms of quantifiable assessments that have been developed to assess certain psychoacoustical features of an individual's tinnitus. These tests are not 'objective' per se, but they do allow tinnitus characteristics such as pitch, loudness, spatial location and minimum masking level (MML), to be measured in a standardised manner (Meikle et al., 2008). Some of these test batteries have existed for 25 years,

while others are more recent (Henry, 2016). In addition to tinnitus-specific assessments, researchers also gain an understanding of a person's hearing status by administering tests such as pure-tone audiometry with an extended frequency range, speech audiometry, immittance measures, and otoacoustic emissions. The results of these further assessments, in turn, can aid in explaining various tinnitus characteristics (Vernon & Meikle, 2003).

Another benefit of psychoacoustic tinnitus measures is that they are quick to administer and they can accurately produce an informative summary of the tinnitus characteristics in a research setting (Meikle et al., 2008). In comparison, the administration of subjective questionnaires if often time consuming and is not appropriate for some patients that are unable to complete such them due to language barriers, trouble reading or other disabilities that are sometimes associated with tinnitus (Henry, 2016; Kennedy et al., 2004; Newman et al., 2011). There is no clear-cut evidence of a causal relationship between psychoacoustic measure outcomes and tinnitus severity (Andersson, 2002; Dineen et al., 1997). As such, these should not be used instead of tinnitus questionnaires to determine the degree to which a person suffers from tinnitus. The main use of psychoacoustical methods is strictly to quantify treatment trials and measure the success of research endeavours (Henry, Dennis, et al., 2005; Henry, Zaugg, et al., 2005). In addition, they can be used in a clinical setting to inform tinnitus patients of their condition, which serves as an effective strategy for patients to gain a sense of control over the condition through diminishing the fear of the unknown (Henry, Zaugg, et al., 2005). However, despite these benefits, psychoacoustics tinnitus assessment has been suggested to be underutilised in tinnitus therapy because of the time it takes to administer in a fast-paced clinical setting (Meikle et al., 2008).

1.7.1 Psychoacoustic measures

1.7.1.1 Pitch match

From subjective reports of tinnitus patients, the pitch of the tinnitus can vary from a low-pitch buzz to a high-pitch screeching noise (Tyler, 2000). In a research setting, the 'tinnitus pitch' is defined as the acoustic tone that is the most similar to the predominant pitch of the tinnitus, where it is not necessary that the acoustic tone mimics the sound of the tinnitus completely (Tyler & Conrad-Armes, 1983). As such, patients during pitch matching are required to identify the narrowband pitch that is most similar to the pitch of their perceived tinnitus. Although most individuals are able to select narrowband noises that are the most similar to their tinnitus, some find it extremely difficult owing to the complex sound characteristics of their tinnitus compared

to the simple puretone digitally produced by most tinnitus-matching computer software (Tyler, 2000). There is a clear trend of tinnitus being pitch-matched to higher frequencies, where a study showed that the average pitch-match obtained across 1630 sufferers was 5970 Hz, with most tinnitus patients falling in the 8000 to 9900 Hz range (Meikle et al., 2004). These distributions of tinnitus pitch-matches overlap strongly with the hearing loss pitches, and therefore, can be used as a counselling tool to prevent the onset of tinnitus by promoting the protection of one's hearing (Henry, Zaugg, et al., 2005).

1.7.1.2 Loudness match

The loudness of the tinnitus is another important descriptor for understanding an individual's tinnitus. In research, loudness-matching is often performed after pitch-matching, where the narrowband frequency that is obtained from pitch-matching is incrementally increased in intensity until the patient deems it to be the same loudness as their tinnitus. The term, sensation level (SL), is given to the difference between the loudness-matched intensity of the narrowband noise and the threshold of hearing for a particular frequency (Andersson, 2002). In older studies, the loudness-match was routinely performed using a 1000 Hz narrowband noise, however, in recent years, the individual's pitch-match frequency is used instead (Meikle et al., 2008). In the same study mentioned above, it was found that out of 1630 tinnitus sufferers, more than 95% of the participant obtained a loudness match of under 15 dB SL (Meikle et al., 2004).

1.7.1.3 Location match

The psychoacoustic measures of tinnitus such as pitch, loudness and MML, often overshadow the measure of perceived location. As mentioned in previous sections, questionnaires about broad categories of location have been well-established in research but these are often binary (e.g. left or right ear localisation) and lack the multi-dimensional quality of tinnitus location (Searchfield, 2014). The only study to date that has aimed to match the tinnitus location in space at a greater resolution was performed by Searchfield et al. (2015). This study was done in two phases. The first phase tested whether a sound being moved around in space could overlap the exact location of the tinnitus percept. And the second phase was intended to develop a reliable software that could allow localisation of perceived tinnitus across the vertical and horizontal planes. The results of this seminal study revealed that tinnitus patients were indeed capable of matching the perceived location of their tinnitus to an externalised sound that was played digitally via 3D sound processing software. One of the further developments suggested as a result of the findings revealed in the study, was the investigation into the distance cue.

That is, where do sounds need to be played in the 3D space for patients with tinnitus inside their heads to localise it.

1.7.1.4 Minimum masking level and desired masking level

The minimum masking level (MML) describes the intensity at which a distracting noise needs to be played for the perception of tinnitus to be completely obscured (Henry & Meikle, 2000). However, 'masking' in the context of tinnitus has been suggested as misleading. This is because, in traditional sense, 'masking' requires multiple sounds to interact at the level of the basilar membrane of the cochlea, whereas tinnitus masking only has the masker sound stimulating the cochlea whilst the tinnitus phantom sound originates more centrally (Jastreboff & Jastreboff, 2001). In the context of tinnitus, as opposed to diagnostic audiology, the masking sound can be thought to 'suppress' the tinnitus sound from coming into the attention of the patient (Durai et al., 2021). This definition of masking relates not to cochlear mechanism or suppression, but rather cognitive load.

Masking can also be partial, where the masker will reduce the perception of tinnitus but not completely obscure it. Partial masking is often stated in Tinnitus Retraining Therapy and a common term associated in this context is 'mixing point' (Phillips & McFerran, 2010). Mixing point refers to the threshold at which the masker signal begins to interfere with the perception of tinnitus (Henry, Zaugg, et al., 2005). The concept of partial masking is clinically important because tinnitus does not have to be completely masked to alleviate the bothersome symptoms of tinnitus perception. In line, another psychoacoustic measure for tinnitus is the desired masking level (DML) which is less strict with its definition and can be achieved when two patient-reported outcomes are met: (i) the tinnitus is masked to the extent where the patient cannot hear it or can hear it very weakly, and (ii) the masker signal is perceived as being less noxious than the tinnitus. The DML is needed because it is sometimes the case that the masking sound itself can be presented at such a level that it becomes overbearing and more bothersome than the tinnitus itself.

In addition to loudness matches, MML has been shown to reduce after tinnitus treatment, thus the use of these psychoacoustical measures as a way to gauge treatment success has been proposed (Jastreboff et al., 1994). Specifically, after a form of tinnitus treatment had been administrated, the study showed an average of 5.3 dB decrease in MML for 74% of the tinnitus patients reporting improvements (Jastreboff et al., 1994). Similarly, an increase of 4.9 dB was reported amongst those participants that experienced no change or worsening of their tinnitus.

Therefore, these finds further provided the proof of using MML as measure for treatment effectiveness.

1.7.2 Questionnaires

Numerous tinnitus questionnaires have been created and they share a common aim to indirectly measure the effects of tinnitus, such as difficulty concentrating and sleeping, and negative emotions such as distress, depression and anxiety (Henry, 2016). By proxy of these measurements, the severity of tinnitus, effects of tinnitus on person's quality of life, and the effectiveness of treatments can be assessed over time (Goebel & Hiller, 1994). The selection of tinnitus questionnaire ultimately depends on the specific needs of the researcher or clinician. Perhaps the most well-established questionnaire is the Tinnitus Handicap Inventory (THI) which is a self-report questionnaire that assesses the functional and emotional consequences of tinnitus (Newman et al., 1996). But the THI was not designed as an outcome measure. However others also exist that are used routinely in different specific populations. For example, the Beck depression inventory (BDI) that is the most used questionnaire to measure tinnitus-caused depression, the visual analogue scale (VAS) that uses a visual scale to determine the disturbance caused by tinnitus, the tinnitus functional index (TFI) and the tinnitus sample case history questionnaire (TSCHQ) (Karatas & Deniz, 2012). The present study uses the TFI and TSCHQ and these will be the focus of the following two sections.

1.7.2.1 Tinnitus Functional Index

The tinnitus functional index (TFI) is a self-report questionnaire that measures the degree of impact tinnitus has caused on an individual's life. The questionnaire was first developed by Meikle et al. (2012) and it consists of 25 items that span across eight domains: intrusiveness, sense of control, cognitive interference, sleep disturbance, auditory difficulties, relaxation, quality of life, and emotional distress. Each domain has an associated score whose sum can averaged across eight domains to give an overall TFI score representing a valid and reliable measure assessing tinnitus severity in both clinical and research settings (Fackrell et al., 2016; Meikle et al., 2012).

The intrusiveness domain of the TFI assesses the degree to which tinnitus restricts a person from focussing on daily life activities. The sense of control domain describes the extent to which a person can manage their tinnitus. The cognitive interference domain refers to the disturbances tinnitus causes to a person's ability to concentrate and remember. The sleep disturbance domain looks at the effects of tinnitus on sleep quality. The auditory difficulties

domain assesses how tinnitus effects speech comprehension and hearing. The relaxation domain measures how easily the person can relax whilst coping with tinnitus. The quality-of-life domain is perhaps the most holistic and gives information about tinnitus' overall influence on a person's life. Lastly, the emotional distress domain assesses the emotional response to tinnitus, like anxiety and depression (Meikle et al., 2012)

Another use of the TFI is that it evaluate the effectiveness of various tinnitus treatments. Fackrell et al. (2016) used the TFI to assess the efficacy of mindfulness-based cognitive therapy, where they found that there was a significant difference in overall TFI scores for patients who received the therapy with control patients (no therapy). Therefore, the TFI is a useful tool to not only evaluate the effects of tinnitus on person's different life domains, but also an effective tool to monitor changes related to tinnitus treatments.

1.7.2.2 Tinnitus Sample Case History Questionnaire

The tinnitus sample case history questionnaire, simply called TSCHQ, is a clinical tool to gather general information on patient's tinnitus, medical history and lifestyle (Sørensen et al., 2020). The TSCHQ asks questions regarding the onset, duration and laterality of tinnitus, the characteristics of the phantom sound, and any associated balance and auditory conditions e.g., vertigo or hearing loss. The questionnaire also includes questions regarding any previous medical diagnose, medications, patient's lifestyle like occupation and exposure to loud noises (Sørensen et al., 2020). This wholistic questionnaire is used more in a clinical setting than a research one, where it helps clinicians select appropriate treatments for managing their tinnitus patients (Kojima et al., 2017). For example, sometimes underlying medical conditions can be identified that may be contributing towards tinnitus, as well as any ototoxic medications that the patient might be taking that could exacerbate tinnitus symptoms. Moreover, it can also help understand that other exacerbating factors like high stress or exposure to loud noises in a patient's lifestyle that must be reduced for them to better cope with their tinnitus.

Due to the large clinical success of the TSCHQ, it has been made in multiple versions and languages (Sørensen et al., 2020). Owing to the same wide-established use, this questionnaire has been shown to be a reliable and valid measure for tinnitus severity across multiple studies (Kojima et al., 2017; Langguth et al., 2007; Müller et al., 2016). Therefore, clinicians and researchers can choose from several validated questions to gather information about the patient's tinnitus and the impact it has on their lives.

1.8 Tinnitus Management

Tinnitus treatments have come a long way over the last decade. Nevertheless, the complex nature of tinnitus has prevented the development of any treatments that can completely remove its perception (Kleinjung & Langguth, 2020). Multiple psychology-based therapies have been attempted, where the most popular is Cognitive Behavioural Therapy (CBT) that has shown to alleviate some negative outcomes of tinnitus (Landry et al., 2020). In recent years, the need for more accessible and affordable options has given way to the creation of internet-based CBTs (Aazh & Danesh, 2021). These act to minimise time-consuming visits to a therapist and allows individuals to gain the benefits in a self-help format (Rodrigo et al., 2022). CBT can be categorised as a therapy to habituate a patient to the reaction of tinnitus i.e. to reduce the negative psychological effects caused by tinnitus. Opposingly, sound therapy, which is another common arm of tinnitus management, is based on the goal of habituating an individual to the perception of the phantom sound itself (Hobson et al., 2012). Some of these sound therapies act to reverse synchronised pathological brain activity underlying tinnitus (Hall et al., 2022), while others are designed in a self-help format motivated by the same intentions that were behind the development of internet-based CBTs (Sereda et al., 2015). A new direction for sound therapy has been to personalise it to better match the heterogeneity of the psychoacoustical properties of tinnitus sounds that people experience (Searchfield et al., 2019, 2021). Tinnitus retraining therapy (TRT) borrows specific principles from both CBT and sound therapy, and has been shown to have significant benefits for tinnitus reduction when implemented digitally (Searchfield & Sanders, 2022).

Other treatment options such as cochlear implants (Van de Heyning et al., 2008), pharmacotherapy, brain stimulation (Elgoyhen & Langguth, 2010), and alternative therapies (Meehan et al., 2004) also exist, but the evidence for the success of these therapies is poor (Hoare et al., 2011). The problem behind assessing the clinical efficacy of these treatments is three-fold: (i) the properties of tinnitus are highly diverse, (ii) the results of the studies are prone to placebo effects, and (iii) many treatment trials have low-quality methodology (Han et al., 2009; Landgrebe et al., 2012). Therefore, the following review will focus on the formerly introduced CBT and sound therapy, that can be combined to yield maximal benefits for tinnitus patients.

1.8.1 Cognitive behavioural therapy (CBT)

CBT is an encompassing term that combines multiple concepts from cognitive and behavioural therapies that aims to reduce the effects of tinnitus perception rather than diminish its loudness (Fuller et al., 2020). The behavioural component of such therapies (e.g. relaxation) tend to disrupt learned associations between tinnitus and counter-productive responses like avoiding activities that exacerbate the tinnitus sound. On the other hand, the cognitive component focusses on the associations individuals create between thoughts and emotions, and the goal here is to correct the errors within these associations to improve patient's emotions surrounding tinnitus perception (Beck, 1979; Ellis & Grieger, 1986).

Many interventions for tinnitus are labelled under the 'CBT' category, but they cannot be assumed equivalent. Even though they all consist of the same elements, CBT options are diverse in regards to: method of administration (e.g. internet-mediated, via phone, or in-person); the number and frequency of sessions (e.g. daily, weekly, fortnightly), duration of the session; the type of clinician managing the sessions (e.g. nurse, doctor, psychologist, therapist, computer-based); setting of the session (e.g. private clinic or hospital); or whether the therapy is delivered in a group or one-to-one (Fuller et al., 2020).

The most recent meta-analysis to-date has been performed by Fuller et al. (2020), which includes 28 studies with 2733 participants overall. In the review, the CBTs included were mostly performed in an in-person or online setting and had a duration between 3 to 22 weeks. Findings stated that there was significant, but low-certainty, evidence that CBT was better than no intervention for improving tinnitus patient's quality of life. CBT was also found to reduce depression and anxiety but these results were very uncertain. Finally, the author's stated that it is also uncertain whether CBT improved one's negative emotional interpretations of tinnitus. Interestingly, the greatest improvements in perceptions of tinnitus were found for groups given CBT in combination with other therapies such as sound therapy (e.g. tinnitus retraining therapy). It is important to note, however, that some author's suggest that the adverse effects associated with these therapies due to their challenging nature is underreported, especially when the results are statistically significant (Pitrou et al., 2009).

1.8.2 Sound therapy

Sound therapy has a mechanism of action based on the principle of habituation, which is a learned process that aims to reduce the perception of tinnitus, or reduce its perception, by regarding the phantom sound non-threatening or irrelevant (Hobson et al., 2012). One form of

sound therapy is based on the concept of sound enrichment, where soothing sounds are produced to distract the individual from the bothersome and annoying phantom sounds of tinnitus (Han et al., 2009). Although, a far more common form is sound masking, which distracts the listener from their tinnitus by producing masking sounds through hearing aids, sound machines, or smartphone devices (Searchfield et al., 2019). Masking sound therapy has been shown to reduce the intensity and frequency of tinnitus sounds, improve sleep and decrease ancient and depression related to tinnitus (Laura et al., 2015). It is important to note that if the patient cannot hear their tinnitus (complete masking) then they cannot habituate to it. Instead, it is important to prescribe a masking level that achieves down-regulation of the tinnitus, instead of complete removal, to facilitate habitation (Jastreboff, 1995; McKinney et al., 1999).

1.8.2.1 Physiology and psychoacoustical properties of tinnitus masking

Two physiological theories for masking have been suggested by Delgutte. (1990). The first, so-called "busy telephone-line effect", explains that when a masker sound is played, the auditory system becomes preoccupied with its processing and is unable to process any other probe signals (e.g. tinnitus). The second is termed the "suppressions effect", which states that a masker sound is able to mechanically interfere with the probe sound at the level of the basilar membrane within the cochlea (Delgutte, 1990). A seminal finding that suggests that tinnitus, which is not an external sound, is masked though the former theory is that unilateral tinnitus can be effectively masked through contralateral masking that has a pitch remotely different from the tinnitus pitch (Feldmann, 1971). This observation thus shows that successful tinnitus masking relies on the interference patterns created centrally (i.e. at the site of tinnitus generation) rather than peripherally (i.e. within the cochlea). Central masking is referred as "informational masking", whereas the latter describes "energetic masking" which follows the mechanics of the cochlea (e.g. tonotopic) (Searchfield, 2014; Searchfield et al., 2012).

In comparison with the masking of external sounds where the masker signal needs to be at the same centre frequency as the signal, tinnitus masking requires no such prerequisite (Henry et al., 2002). This could be explained by the broader psychophysical tuning curves observed for tinnitus (Tyler & Conrad-Armes, 1983). Further, tinnitus masker sounds also exhibit non-linearity in regards to the intensity they need to overcome and successfully mask the tinnitus sound (Feldmann, 1971; Penner & Zhang, 1996). That is, it is often the case that the presentation of a masker elevates the loudness perception of the tinnitus. This observation can

be explained through the adaptation level theory (ALT) of tinnitus that was first formalised in the context of tinnitus by Helson. (1964). ALT has somewhat been alluded to in previous sections, but formally stated, it describes tinnitus perception as adaptive where the psychoacoustical properties (e.g. loudness) can be altered based on the background noise it presents itself in (Coren et al., 2004; Searchfield et al., 2012). Therefore, the concepts of ALT need to be considered as the presentation of a masker can cause adaptive changes and psychologically alter the perception of tinnitus.

1.8.2.2 Types of tinnitus masker sounds

Tinnitus sound therapy can use many different types of masker sounds, including broadband noise narrowband noise, music, or environmental sounds (e.g. rain, flowing river, chirping of birds) (Henry et al., 2002). The selection of masker sounds is difficult because each patient has different reactions to specific sounds. The clinical goal is to choose a type of sound that effectively masks the tinnitus whilst being careful that the masker sound is not associated with any annoyance as this could hinder habituation. A study has shown, by comparing annoyance ratings, that narrowband noise was the least annoying with annoyance increasing with wider bandwidths of sound (Sandlin & Olsson, 1999). The same study also found that a continuous sound was better tolerated than intermittent presentation of the masker signal. On the contrary, the *effectiveness* of tinnitus maskers increases with the bandwidth of noise, where wideband noise (e.g. white noise) was more effective at masking tinnitus than narrowband noise centred around the tinnitus frequency or pure tones pitch matched to the tinnitus (Kemp & George, 1992). Therefore, the most common type of masker noise is white noise that has a spectra where each frequency has the same level of sound energy which leads to maximal informational masking of the tinnitus (Terry & Jones, 1986).

1.8.2.3 Presentation location of masker sounds

In addition to masker type, the effectiveness of masking is also determined by the spatial distance between the external sound and masker (Kidd et al., 1998). When maskers and signals are placed further apart, the signal-to-noise (SNR) ratio increases and the signal becomes easier to detect. Opposingly, when the masking sound is moved in close proximity to the unwanted signal, the SNR decreases and the signal becomes significantly harder to perceive (Arbogast et al., 2005; Dubno et al., 2002; Kidd et al., 1998). Kidd et al. (1998) also observed that this phenomenon is more pronounced within the higher frequencies. However, the effect of this masker-signal separation has mostly been studied with external sounds, and scarcely in the

context of tinnitus signals which are likely to be internally produced and perceived. The only study to date that has attempted to verify the effects of spatial masking has been performed by Kubota et al. (2022) and Searchfield et al. (2016). In Searchfield's proof-of-concept study, it was demonstrated that when the masker sound is placed in the same spatial position as the tinnitus, the masking noise had a lower MML i.e. better effective masking. In the same study, the authors also found that there was a significant improvement in masking effectiveness by 3D masking compared to 2D making (i.e. unilateral or bilateral masking). These findings were further researched by Kubota and colleagues who hypothesised that although spatial 3D masking is more effective, if a masker signal is placed away from the tinnitus sound, then the perception if tinnitus is mitigated due to the "attention grabbing" effect of the farther placed masker sound. The hypothesis was proven correct by the results of the study, where 71% of the participants showed lower MMLs for the sound placed away from the tinnitus than when it was placed closer to it. However, a major limitation of this study was that it simulated participant's tinnitus by presenting a high-pitched 4 kHz tone through headphones. Although this tone was similar to tinnitus in the sense that it was placed within the head by the use of 3D sound processing, it still acted as an externally produced sound and it is unclear whether the same results will be observed if true tinnitus patients were used. There is also no current research investigating how the distance of the masker signal from the tinnitus impacts the masking effectiveness. The current study will try to fill this gap in knowledge to further progress the topic of spatial tinnitus masking and will use true tinnitus sufferers as participants.

Chapter 2: Aims and Hypotheses

2.1 Aims

The study had three aims. The first was to spatially localise participant's tinnitus with the assist of the Anaglyph Adobe Audition plug-in and to investigate whether the tinnitus location match obtained through self-report was different from that obtained with the use of Anaglyph. This will answer whether the presence of a masking noise (presented through anaglyph) changes the position of participant tinnitus. The second was to determine whether presenting tinnitus maskers at different angles and distances away from the participant's perceived tinnitus has any effect of masking effectiveness. In this case, nine different locations away from the tinnitus were assessed. Finally, the third investigated whether any tinnitus functional index scores or other participant characteristics could predict the masking effectiveness for different individuals. Masking effectiveness was assessed by using minimum masking levels and desired masking levels.

2.2 Hypotheses

Based on the three aims present in the study, it is hypothesised:

1. That the tinnitus location indicated by the self-reported method will correspond well with the location of the tinnitus obtained by presenting a masker sound using the Anaglyph software.

2. The minimum masking level of masking sounds presented further away from the perceived tinnitus in a virtual sound field is larger, indicative of less effective masking.

3. There is a correlation between masking effectiveness and the degree of tinnitus severity (measured by the tinnitus functional index) i.e.participants with more severe tinnitus will require a greater level of masking.

Chapter 3: Methods

The methods used in this study were approved by the University of Auckland Health Research Ethics Committee (AHREC) on the 24th November 2022 for 3 years (reference number AH25266). Funding was provided by the University of Auckland School of Population Health Postgraduate Fund.

3.1 Participants

A total of 19 participants took part in this study, aged between 23 to 79 years. The mean age of the participants was 54. Participants were predominantly recruited through the University of Auckland Hearing and Tinnitus Clinic database; those that resided in Auckland were sent an email invitation and study advert (Appendix D). The average (mean) length of time between tinnitus onset and study participation was 12 years.

3.1.1 Inclusion Criteria

Participants were included based on their age, degree of audiometric hearing thresholds, and their tinnitus. Eligible participants needed to (i) be aged over 18 years, (ii) have hearing thresholds no greater than 40 dB HL across the standard audiometric frequencies (octaves between 250 to 8000 Hz) when pure-tone audiometry was performed, and (iii) have constant tinnitus experienced for at least 6 months prior to the study.

3.2 Equipment

All testing was conducted at the University of Auckland's Audiology Teaching Clinic in a sound-treated room (ANSI S2.01-1997). Each study session with a participant lasted up to two hours in length and no follow-up sessions were required. A Welch Allyn™ otoscope was used to check that no abnormalities of the external ear canal (e.g. outer ear infections or obstructions) were present at the time of testing.

Pure-tone air-conduction hearing thresholds were obtained using a MedRx™ AVANT A2D+ audiometer connected with a RadioEar® DD450 circumaural headset. Tinnitus pitch- and level-matching was performed using the MedRx™ Tinnometer® module with the same headset. The MedRx™ Avant Software was installed on a Dell Latitude 5410 which allowed control over the audiometer and Tinnometer®.

A Dell OptiPlex 7040 MT computer installed with Adobe® Audition (version 22.2) was then used to present all sounds for tinnitus location matching. To obtain the location match for the perceived tinnitus, the Adobe Audition Anaglyph plug-in was used which allowed digital control over output sound location (i.e. three-dimensional sound processing) and level. For more details on the Analgyph plugin refer to http://anaglyph.dalembert.upmc.fr/index.html.

3.3 Sounds Used

All sounds used in the experiment were digitally produced. Audiometry assessing participant's hearing thresholds used pure-tones within the standard (octaves between 250 Hz to 8 kHz) and the extended (10, 12 and 16 kHz) that were generated by the MedRx™ Avant Software. Tinnitus pitch and level matching used narrowband noise with a centre frequency that was altered based on participant's tinnitus. Once tinnitus pitch had been matched, a sound with the same central frequency was generated (by Adobe® Audition) to determine the location match of the tinnitus. Finally, a white masking noise was digitally generated by Adobe® Audition (fig. 1) to study the effects of changing masker distance and angle on masking effectiveness.

Notably, the computer's volume controls were kept consistent for each participant, and the gain was only adjusted by using digital dials within the Adobe® Audition software.

3.4 Procedures

Prior to any testing, each participant was required to read the information sheet provided and sign the consent form (Appendix A).

3.4.1 Questionnaires

Two questionnaires were completed by each participant before any testing commenced. If participant arrived late to their scheduled session, the questionnaires were sent via email to be completed at participant's earliest convenience. The questionnaires were the Tinnitus Functional Index (TFI), and the Tinnitus Sample Case History Questionnaire (TSCHQ) (Appendix B). Only questions 1, 2, 16 and 17 were used from the TSCHQ, whereas all questions were used from the TFI to calculate the TFI scores. The instructions used for scoring the TFI can be found on www.dva.gov.au/about-us/dva-forms/tinnitus-functional-index-questionnaire-and-scoring-instructions.

The TFI, developed by (Sørensen et al., 2020), provided a self-report measure of the severity and negative impact of tinnitus for each participant. It has been validated for clinical and research purposes for the New Zealand population (Chandra, 2013).

The TSCHQ provided general- and tinnitus-specific characteristics about the participants, and is routinely used for research and clinical purposes at The University of Auckland Hearing and Tinnitus Clinic. Questions covered age, gender, tinnitus duration (from onset to study date), tinnitus loudness, awareness of tinnitus, distress caused by tinnitus, and other descriptors. Refer to Appendix B for a complete list of questions.

3.4.2 Pure-tone Audiometry

Hearing thresholds were obtained for each participant, unless they provided a recent audiogram completed no longer than 6 months prior to the study session by a NZAS audiologist.

Pure-tone audiometry used the modified Hughson-Westlake ascending test method (Carhart & Jerger, 1959) with a step-size of 5 dB HL. Testing for air-conduction thresholds (in dB HL) began with the better hearing ear (if known), otherwise the right Ear was tested first if symmetrical hearing was presumed. Standard audiometric frequencies were tested, these included octaves between 250 Hz and 8000 Hz. Inter-octave frequencies of 750, 1500, 3000 and 6000 Hz were only tested if the adjacent octaves had a difference in thresholds of greater than 15 dB. Extended high frequency thresholds for 10000, 125000, 14000 and 16000 Hz were also obtained using this method.

3.4.3 Tinnitus Pitch Matching

Tinnitus pitch matching was performed using the two-alternative forced-choice (2AFC) procedure. In this procedure, the participant was presented with two example sounds, in which they have to pick the example sound that is more similar in pitch to their subjectively perceived tinnitus. Once the decision has been made, the participant was presented with another pair of example sounds where they would again have to decide which example sound is closer to their tinnitus. A pitch match was obtained once the participant had selected the same example sound twice (with 1/8 octave spacing). To reduce the number of reversals needed before a pitch match was obtained, the first pair of example sounds were chosen to be inside a frequency range that was predicted to be close to the person's perceived tinnitus, that is, where the person had their worst hearing thresholds.

Each sound was played 10 dB SPL higher than their hearing threshold at the corresponding frequency to ensure audibility. For participant's with unilateral tinnitus, sounds were presented into the Ear contralateral to the side with the worse tinnitus. In cases where tinnitus was equal bilaterally, sounds were presented into the Ear with better hearing thresholds.

3.4.4 Tinnitus Loudness Match

The tinnitus loudness match was obtained by presenting a tone that was pitch matched to participant's perceived tinnitus. Sound level was increased in a 1 dB step size until the participant believed the loudness matched that of their perceived tinnitus. This procedure was repeated twice and the sound level (in dB SPL) for each trial was recorded. The loudness match was calculated as the mean sound level obtained from the two trials.

3.4.5 Tinnitus Location Match

Participant's perceived tinnitus was subjectively localised on a two-dimensional (2D) horizontal plane through a self-report and a tester-guided method.

Self-reported localisation was performed by asking the participant to indicate where their tinnitus was located on a provided room diagram. The room diagram was overlayed with a polar grid which allowed coordinates to be recorded once the participant had indicated where their tinnitus was located (see Figure 2A). Twelve equally distanced speakers were also placed 1-meter from participant to help them visualise the room diagram provided in real-space (see Figure 2B). If more than one tinnitus sound was heard, then the participants were asked to select the more severe one and focus on that for the rest of the experiment. However, if two or more equally severe tinnitus sounds were heard, then the participant was asked to select only one tinnitus sound for the experiment randomly.

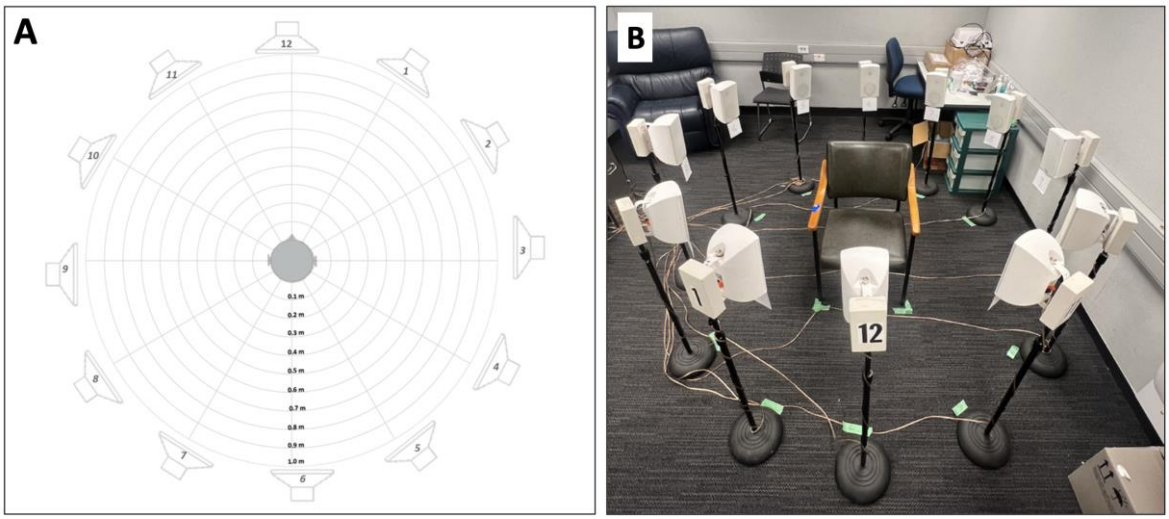

Figure 2. Room diagram corresponding to room set-up. Panel A shows a polar grid used for self-reported localisation of participant's perceived tinnitus. Panel B shows the corresponding twelve-speaker room set-up.

Tester-guided localisation of perceived tinnitus used three-dimensional (3D) sound processing performed by Anaglyph (see Figure 3). The Anaglyph plugin is capable of presenting sound in 3D space using an average head-related transfer function (HRTF). In this case, the default HRTF (pre-loaded) was used for the current study. The stereo-sound used for this experiment was a digitally generated (through Adobe Audition) white-noise track. First, the sound was moved circumferentially around the head at an equal distance; starting from the front, then moving clockwise from 0° to 360° azimuth at ear level. Each participant was asked to confirm whether the tone was continuously audible throughout the circumferential movement. Adjustments to the sound level were made if necessary.

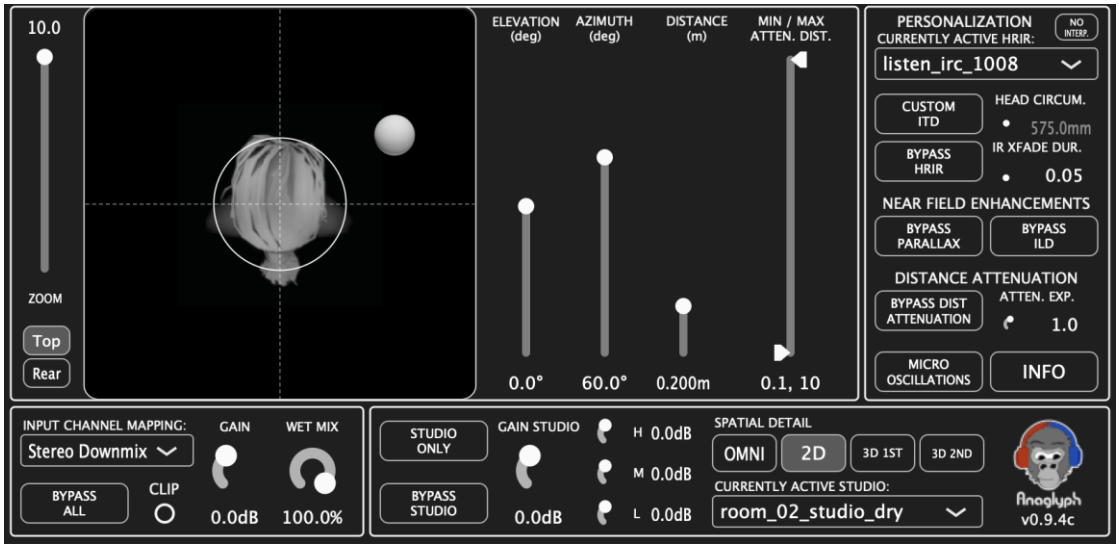

Figure 3. Anaglyph's Guided User Interface (GUI). Example shows point source (white circle) with a distance of 0.2 m from head at an azimuth of 60°.

Next, the circumferential motion of the sound around the head was repeated but in this instance, the participant was asked to tell the presenter to stop when they best believed that the angle of the sound was close to that of their perceived tinnitus. Once the angle (or, azimuth) was determined, then the sound was slowly moved away from their head and the participant was asked to indicate when the sound seemed to overlap their tinnitus in space. In sum, this tester-guided procedure produced an azimuth and distance value for each participant's perceived tinnitus, which is similar to the spatial coordinates acquired through the self-reported method. For the following masking study, these tester-guided spatial coordinates were used as an origin where masker distance and angle deviations were made from these coordinates.

3.5 Comparison of Different Spatial Masking Conditions

All masking for the remainder of the experiment was done using a white noise generated by Adobe Audition, as opposed to the tinnitus pitch-matched tone. This was chosen because as stimulus bandwidth increases, there is a greater degree of accuracy when localising sound along the horizontal plane, where maximal localisation accuracy occurs with wideband white noise (Yost & Zhong, 2014). Producing the same white noise for all participants also controlled for the variability caused by each participant having a different pitch match.

Measurements used to compare the different masking conditions were done at twelve different positions in space. These included four different distances (0, 0.5, 1 and 2 m) and at three different angles (-45°, 0°, +45°) away from participant's perceived tinnitus located using the tester-guided method. At each of these positions, three dial level measurements were taken; the participant's hearing threshold for the white noise, the minimum masking level (MML) and the desired masking level (DML). The threshold was obtained by a modified Hughson-Westlake method similar to pure-tone audiometry, but with a step-size of 0.3 dB. Once the threshold was determined, the MML was determined by increasing the white noise in 0.3 dB steps and asking the participant to indicate when the white noise was loud enough to distract them completely from their tinnitus. Similarly, the DML was also obtained by increasing the level of the white noise in 0.3 dB steps above threshold. However, in this case, the level was increased until the participant believed the white noise was just distracting enough for their tinnitus to become non-bothersome.

The dial values for MML and DML were corrected for each participant's hearing ability by subtracting the threshold dial value from the MML and DML. These produced two corrected

measurements, the corrected MML in dB SL and DML in dB SL. All further mention of "MML" and "DML" will refer to the corrected measurements.

3.6 Experimental Design

The experimental design is a repeated measures design. This was used to determine the effects of changing the masker distance and angle from perceived tinnitus for each participant and across participants.

3.7 Data and Statistical Analysis

The raw data for each participant was recorded using Microsoft Office Excel 2021. All statistical analyses were performed using GraphPad Prism version 9.4.1 for MacOS, GraphPad Software, San Diego, California USA, www.graphpad.com.

Kolmogorov-Smirnov normality test was used and, unless stated otherwise, evidence of non-normality was not obtained. Based on this outcome, parametric tests were used for variables that had evidence for being normally distributed. To investigate the effects of different masking presentation locations, a linear mixed mathematical model was used to account for the within-participant variation. The repeated-measures undertaken were the MML and the DL.

A two-way ANOVA (analysis of variance) was used to answer whether any masker presentation locations significantly differed in terms of the outcomes measured (i.e. DMLs and MMLs). This was followed by a Tukey's multiple comparisons test to examine where the differences occurred. A two-tailed paired t-test was then used to find any significant differences between the outcome measures DML and MML. When comparing the tester-guided and self-reported methods for tinnitus localisation, the two variables concerned were the azimuth and distance. Due to non-normality the non-parametric Wilcoxon matched-pairs signed rank test was used. A one-way ANOVA, followed by Tukey's multiple's comparisons test was used to compare the sole-effects of masker distance and angle on the MML. A Pearson's correlation analysis was performed to investigate whether the effectiveness of masking (as measured by MML and DML) can be predicted by participant characteristics (e.g. tinnitus functional indices, age, tinnitus duration, tinnitus loudness, awareness of tinnitus, etc). A significance criterion of .05 was used for all analyses.

Chapter 4: Results

4.1 Participant Characteristics

4.1.1 Tinnitus Sample Case History Questionnaire Responses

The nineteen participants recruited for this study had a mean age of 54; 8 were female and 11 were male. Approximately half of the participants had known hearing problems (n = 10) but only one of them wore hearing aids. Sixteen participants also experienced some form of hyperacusis where they found loud sounds problematic to deal with, where 4 of them stated that loud sounds made their tinnitus worse.

A large familial component of tinnitus was discovered where 79% of the participants had family history of tinnitus complaints (n = 15). The average duration since tinnitus onset was 11.8 years (142 months), but there was considerable amount of variability with the maximum being 62 years and the minimum being 7 months. Eight participants experienced a sudden onset of tinnitus whereas the other 11 had a gradual onset. In some cases (n = 5) the cause of tinnitus was unknown to the participant, but the other 14 knew the event that their tinnitus onset was related to (e.g. whiplash, loud blast of sound, stress or head trauma). There was large bias towards left-dominant tinnitus (n = 10) and only 4 participants had right-sided tinnitus. The remaining 5 had tinnitus that was perceived as being in the centre of their head. The majority of participants experienced tinnitus that was intermittent throughout the day (79%), whereas for the others it was constant (21%). Ten individuals experienced tinnitus as a constant tone, whereas the remaining 9 either perceived it as a "cricket-like" sound (n = 5). Some also stated that their tinnitus resembled another complex sound (n = 4).

Out of the nineteen individuals, only 2 of them had undergone any form of tinnitus treatment and only 4 stated that their tinnitus was improved in the presence of background noise (e.g. music, white-noise, or environmental sounds). Out of these participants, none of them reported that any if these background noises completely removed the presence of tinnitus.

4.1.2 Hearing Status

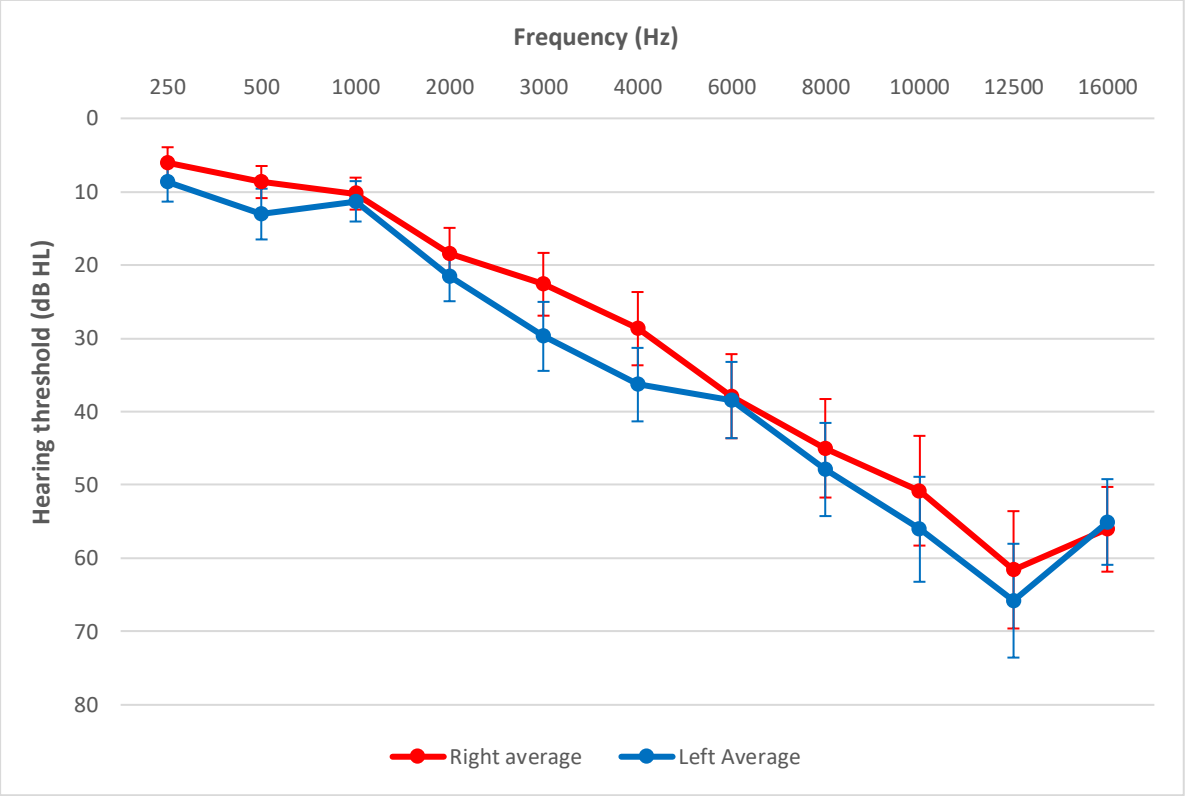

Figure 4. Average audiogram of all participants. The red and blue lines show the average (mean) hearing thresholds for the right and left ears, respectively. The error bars represent the standard error of mean (SEM). Higher hearing thresholds (i.e. lower on the page) can be interpreted as poorer hearing threshold at that frequency. The step-size for testing was 5 dB HL. In total there were 19 participants that had their air conduction thresholds obtained.

On average, participants have a gradually sloping hearing loss that becomes worse in the higher frequencies. According the NZAS guidelines, the hearing loss can be classified as a mild loss at the lower pitches, gradually worsening to a moderate loss in the middle pitches, then finally reaching moderate-severe hearing loss levels in the high pitches. There was a12500 Hz notch where the hearing loss is the greatest, but some recovery can be observed at 16000 Hz. The variation amongst the hearing thresholds of participants is lowest in the lower and middle frequencies but increased in the higher frequency regions. This can particularly be seen in the frequencies 3000 Hz and beyond. On average, the greatest asymmetry also occurred within the 2000 to 6000 Hz frequency range, and a slighter asymmetry occurred in the extended frequency range of 10000 to 12500 Hz. However, these asymmetries were not clinically significant as per NZAS clinical guidelines.

4.1.2 Tinnitus Pitch Match

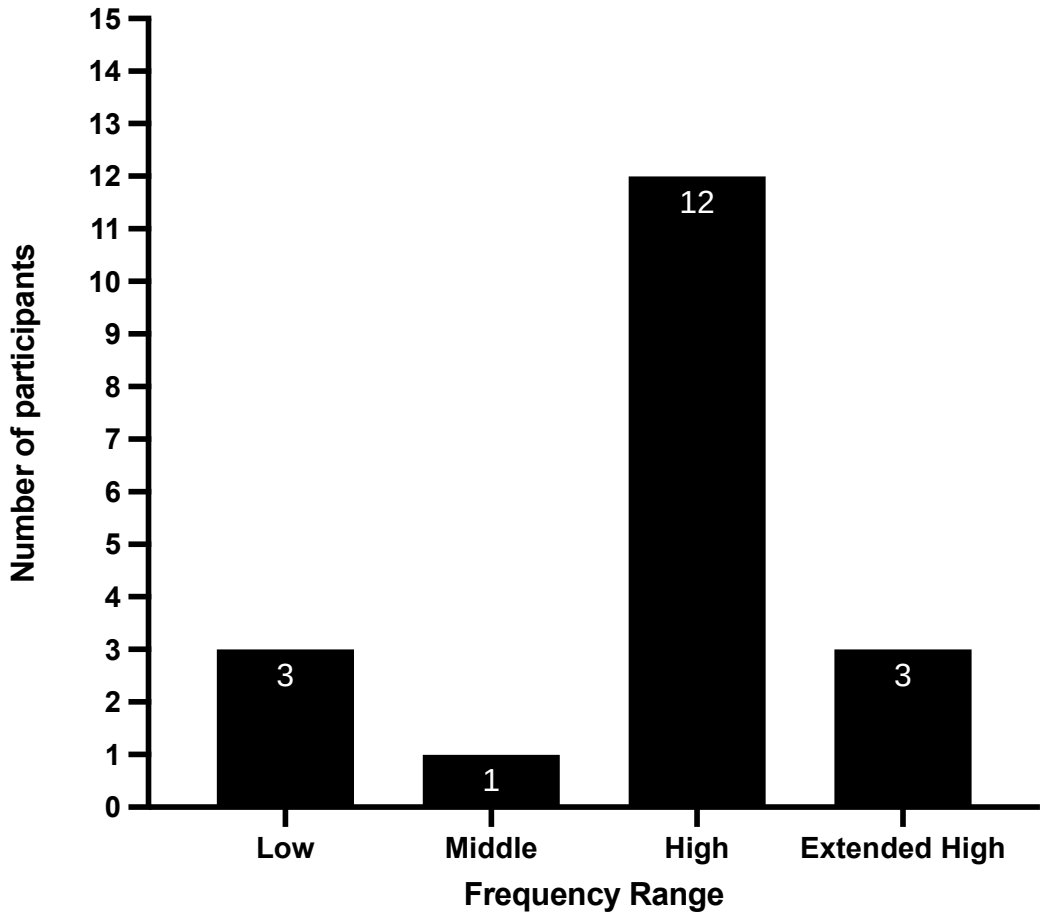

Figure 5. Tinnitus pitch matches for all participants. The x-axis refers to frequency ranges that the tinnitus pitch was matched to. Low frequencies are defined as 0 to 750 Hz; middle as 751 to 3000 Hz; high as 3001 to 8000 Hz; and extended high frequencies are 80001 to 16000 Hz. The number on top of the bars refer to the corresponding y-axis value that describes the number of participants that were counted to have tinnitus pitches within the stated frequency ranges. In total, there were 19 participants that were pitch matched.

Most participants (n = 12) had a tinnitus pitch that was in the higher frequency region. There were equal number of participants (n = 3) that had a tinnitus pitch that was similar to sounds in the extended frequency and low frequency region. The lowest occurrence of tinnitus pitch was in middle frequencies, with only one participant stating that their tinnitus sound was within the 751 to 3000 Hz range. The average (mean) pitch match for this group of participants was 5222 Hz. Overall, there was no clear trend that tinnitus pitch match followed in terms of frequencies that had the greatest hearing loss.

4.2 Comparing tester-guided and self-report methods for tinnitus localisation

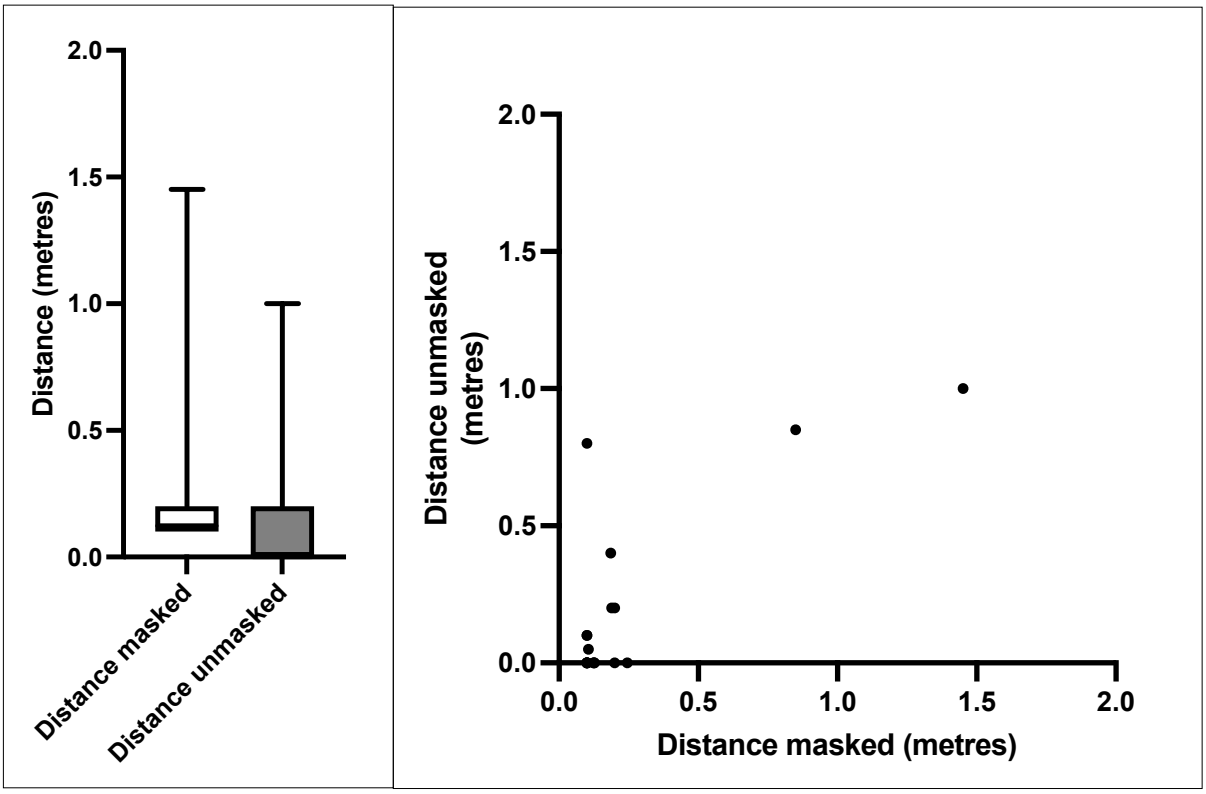

Figure 6. Perceived Tinnitus distance with masker and without masker. The correlation scatter plot (right) and box-and-whiskers plot (left) show the distance of the tinnitus for all nineteen participants when measured via the tester-guided (masker on or 'masked') method and the self-reported (masker off or 'unmasked') method. These are represented by the x- and y-axes on the correlation plot, respectively. The grey boxes on the left panel describe the interquartile range, with the horizontal line within it being median distance value. The distance effect of the masker for the tester-guided method was simulated by the Anaglyph software.

The box and whiskers showed the median value for distance of perceived tinnitus from head was 0.124m when measured via the tester-guided (with masker) method, and was 0m for the self-reported method (left panel). The range of distance values obtained was high for both of the methods. Wilcoxon matched-pairs signed rank test indicated that there was no statistically significant difference between the tinnitus distance measured with and without masker ($p = .0715$). Correlation analysis also revealed no significant correlations between the two measurement methods of distances ($r = 0.38$, $p = .1081$), where the scatter was quite high in the correlation plot (right panel).

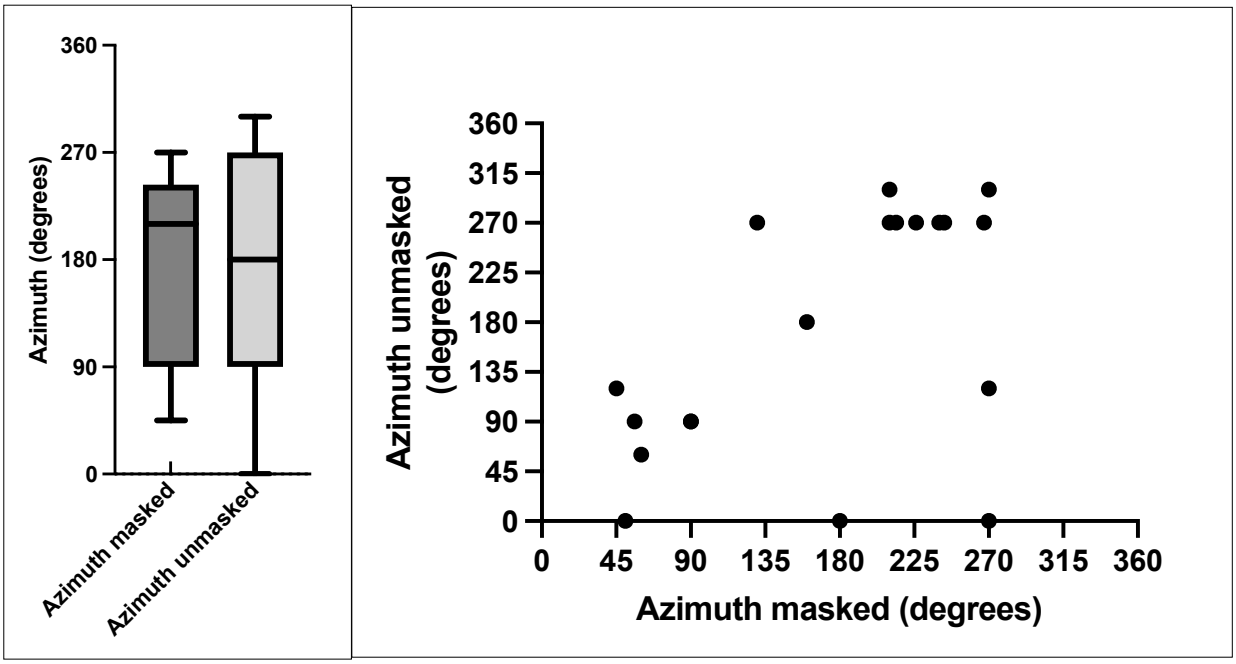

Figure 7. Perceived Tinnitus angle with masker and without masker. The correlation scatter plot (right) and box-and-whiskers plot (left) show the angle of the tinnitus for all nineteen participants when measured via the tester-guided (masker on or 'masked') method and the self-reported (masker off or 'unmasked') method. These are represented by the x- and y-axes on the correlation plot, respectively. The grey boxes on the left panel describe the interquartile range, with the horizontal line within it being distance median value. The angle effect of the masker for the tester-guided method was simulated by the Anaglyph software.

The box and whiskers showed the median value for the azimuth of perceived tinnitus was 210 degrees when measured via the tester-guided (with masker) method and was 180 degrees for the self-reported method (left panel). The minimum azimuth obtained with the self-reported method was 0 degrees, whereas it was 45 degrees for the tester-guided method. Wilcoxon matched-pairs signed rank test indicated that there was no statistically significant difference between the tinnitus distance measured with and without masker ($p = .4559$). However, correlation analysis revealed a statistically significant moderate association between the two measurement methods of perceived tinnitus azimuth ($r = 0.46$, $p = .0496$). The scatter plot (right panel) also showed a slight grouping of participants in the higher angles of azimuth (approximately 225 to 270 degrees) for both methods for determining tinnitus location.

4.3 Identifying most effective and desired masking locations for study participants

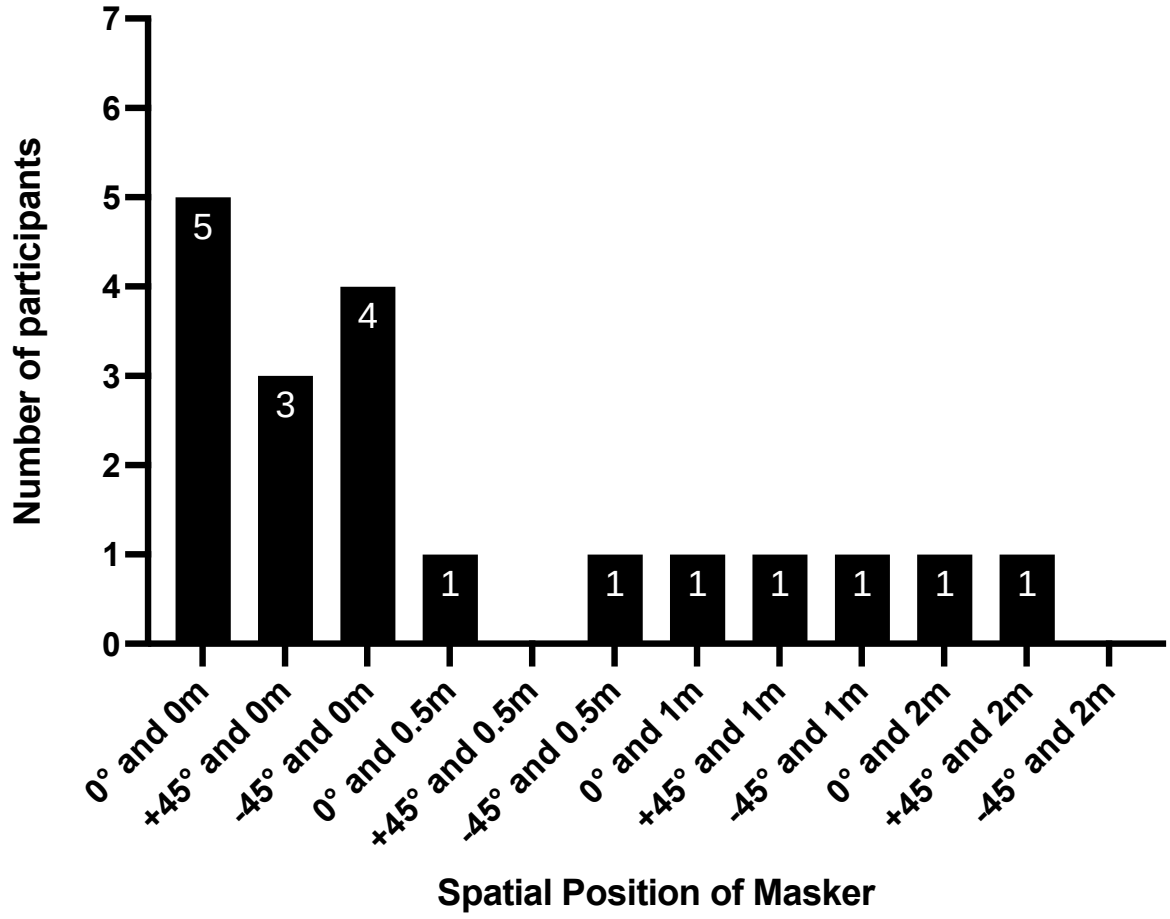

Figure 8. Number of lowest MMLs at different spatial positions. Each bar refers to the number of participants that had the lowest MML at a particular spatial location where the masker was presented. The spatial positions are labelled along the x-axis. The number of participants are also labelled at the tip of each bar that correspond to the y-axis value. The spatial position is named in reference to the participant's location match. For example, the first bar represents the number of participants that had lowest MMLs when the masker was presented 0m and 0 degrees away from the tinnitus location match (obtained from the tester-guided method).

When the masker was presented 0 degrees and 0 metres away from the tinnitus location match, most number of participants (n = 5) were found to have the lowest MML recorded when compared to other spatial positions. The second most effective masking position was when the masker was presented 45 degrees counter-clockwise to the tinnitus location match, where four participants showed lowest MMLs. This was followed by the spatial position where the masker was presented 45 degrees in the clockwise direction of the tinnitus location match (n = 3). All other spatial positions had an equal number of participants that had the lowest MMLs in these particular locations (n = 1). The exception was when the masker was presented 0.5 m away and at an angle of 45 degrees clockwise from the tinnitus location match, in which no participant demonstrated effective masking.

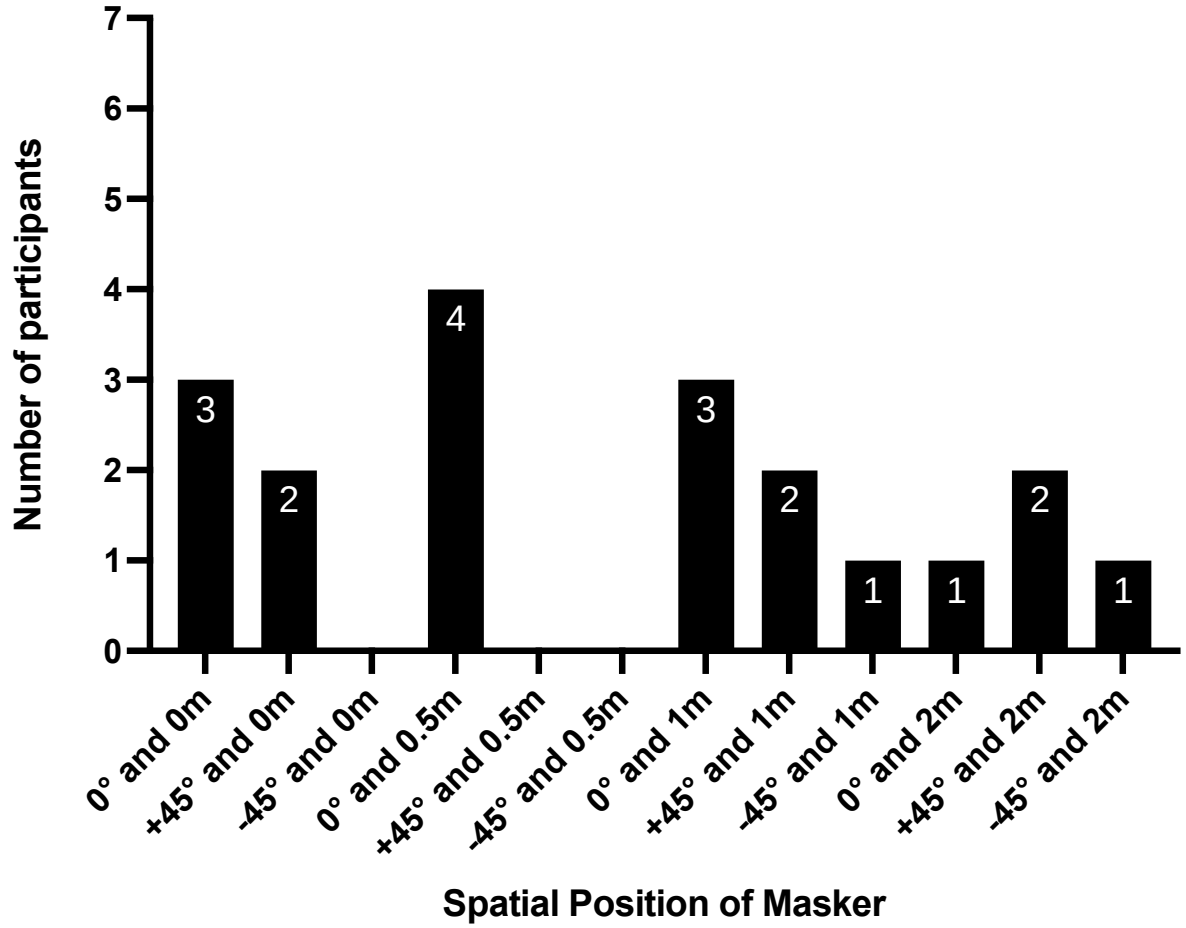

Figure 9. Number of lowest DMLs of masking at different spatial positions. Each bar represents the number of participants that chose the lowest desired level of masking at a particular spatial location where the masker signal was presented. The x-axis represents the twelve different spatial locations where the masking sound was presented at. The number at the tip of each bar corresponds to the value on the y-axis. The spatial position is named in reference to the participant's location match. A total of 19 participants are represented in this graph.

The greatest number of participants (n = 4) found that there tinnitus was masked most desirably when the masker signal was presented 0 degrees and 0.5 metres away from their tinnitus location match. The most notable finding was that there was considerable variability in which spatial location the participants reported most desirable tinnitus masking, with other spatial positions having similar number of participants. Some spatial locations of tinnitus masking were not selected by any participant to be the most desirable; these included when the masker signal was 0.5 metres and 45 degrees away from the tinnitus location match in both the counter-clockwise and clockwise direction, as well as when the masker signal was 0m and 45 degrees away in the counter-clockwise direction.

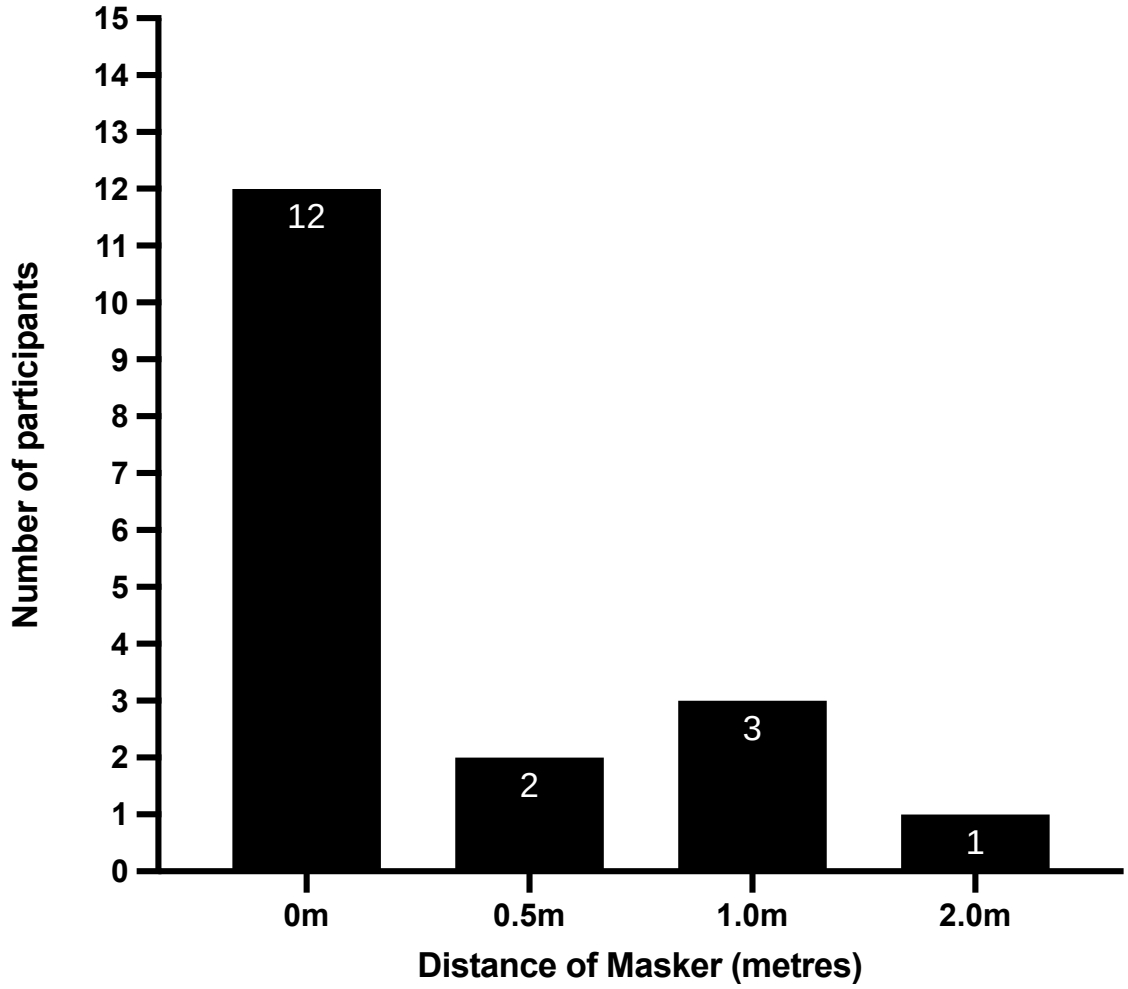

Figure 10. Lowest MMLs at different masker distances. This bar graph is similar to figures 5 and 6, but shows spatial positions with the same distances away from the tinnitus location match in a collapsed format. This graph aims to isolate the distance effects on masking. Each bar represents the number of participants that had the lowest MML when the masker was presented at particular distances away from the location match (x-axis). The number at the tip of each bar corresponds to the value on the y-axis. A total of 19 participants are represented in this graph.

The is a discernible preference for masker sounds being played 0 metres away from the location of the tinnitus match. A total of 12 participants, which constitute to 83% of the current study's sample size, showed lowest MMLs when the masking signal was played on top of their tinnitus. The least effective masking distance was when the masker signal was presented 2 metres away from the tinnitus location match. Overall, the closer the masker signal is presented, in terms of distance away from the tinnitus location match, the more effective the masking is for most people in this study.

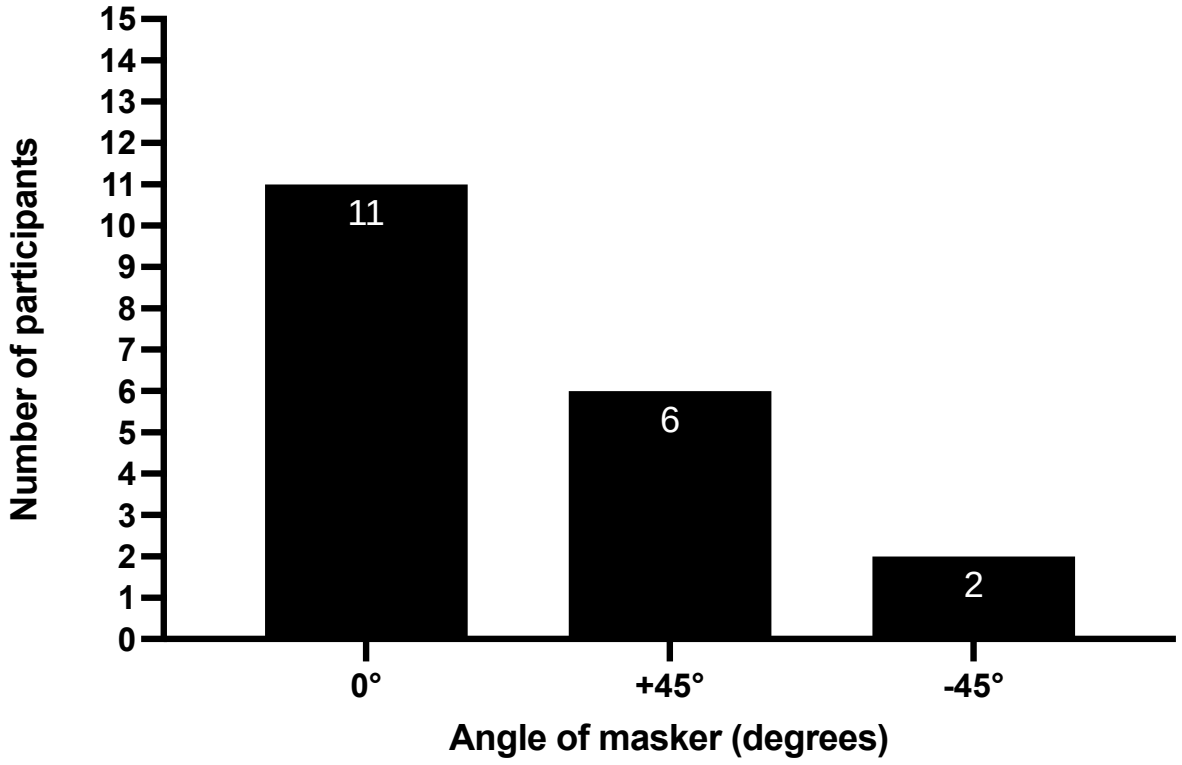

Figure 11. Lowest MMLs at different masker angles. This bar graph is similar to figures 5 and , but shows spatial positions with the same angles away from the tinnitus location match in a collapsed format. This graph aims to isolate the angle effects on masking. Each bar represents the number of participants that had the lowest MML when the masker was presented at particular distances away from the location match (x-axis). The number at the tip of each bar corresponds to the value on the y-axis. A total of 19 participants are represented in this graph.

Most of the participants (57%) showed the lowest MMLs when the masker signal was presented 0 degrees away from the tinnitus location match. This was followed by 6 participants showing the most effective masking when the masker signal was presented 45 degrees away from the location match in the clockwise direction, and only 2 participants showing the same 45 degrees in the counter-clockwise direction. Overall, although there are 11 participants that had lowest MMLs in the 0 degree position, there were also 8 participants that had lowest MMLs when the angle was deviated by 45 degrees.

4.4 Masker location effects on MML and DML

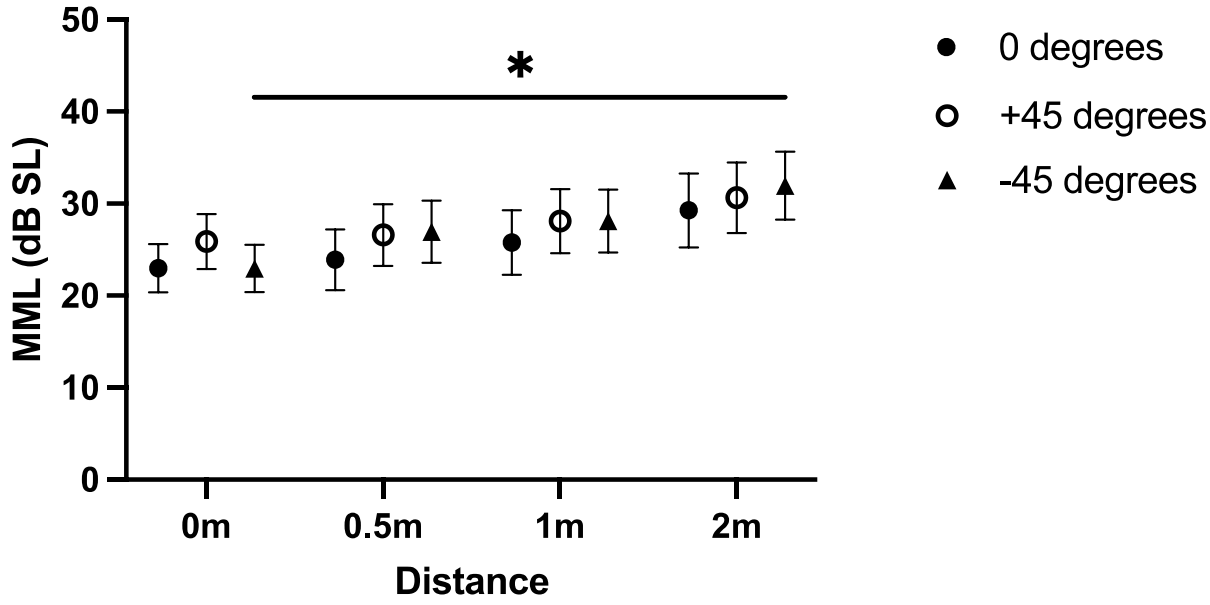

Figure 12. MMLs at different masker locations. This scatter plot shows how the MML is changed when the masker signal is presented at different spatial locations from the tinnitus location match. The distance away from the location match is shown on the x-axis, and the angle deviated from the location is shown by the legend on the right. The y-axis represents the corrected MML in decibels sensation level. The error bars show the SEM in the positive and negative direction. The asterisk represents significant differences between a pair of groups ($p < 0.05$).

The two-way ANOVA revealed that there was no statistically significant interaction between the effects of masker distance and angle on the MML ($F(3.272, 58.90) = 1.074$, $p = .3703$). Simple main effects analysis showed that the angle deviation of the masker signal from the location match did not have a significant effect on MML ($F(1.512, 27.21) = 1.214$, $p = .3016$). However, the simple main effects analysis showed that the distance away of the masker signal had statistically significant effects on the MML ($F(1.139, 20.51) = 8.389$, $p = .007$). In particular, the pairwise comparison revealed that, on average, the MML was 9 dB SL lower when the masker signal was 0m and 45 degrees (counter-clockwise) away from the location match than when it was 2m and 45 degrees (counter-clockwise) away from the location match ($p = .0341$).

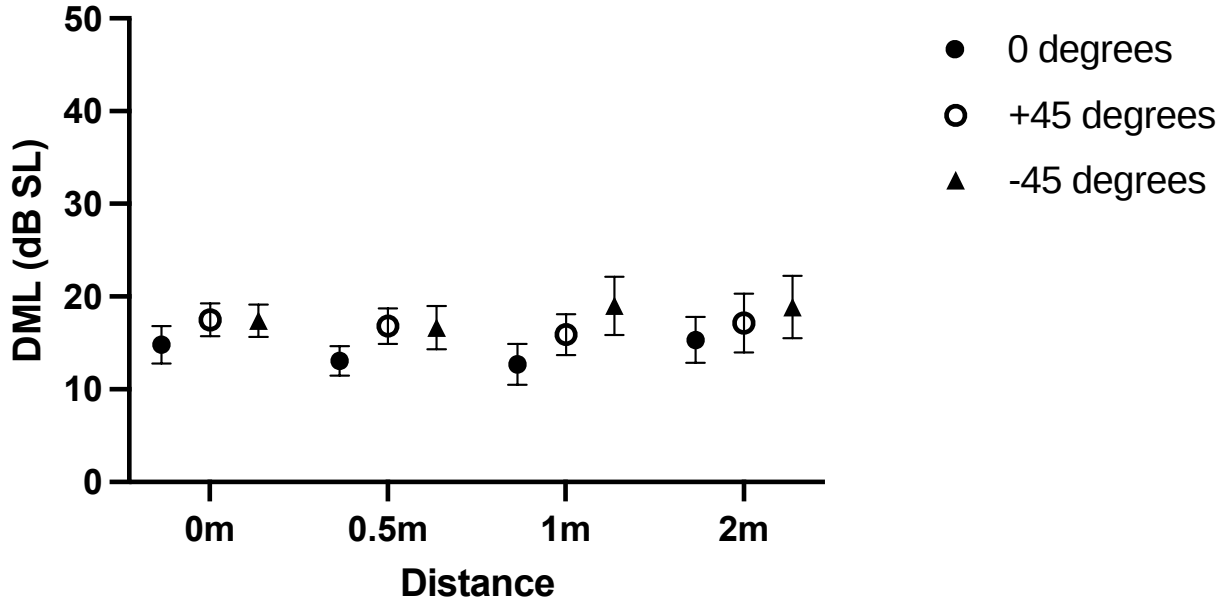

Figure 13. DMLs at different masker locations. This scatter plot shows how the DML is changed when the masker signal is presented at different spatial locations from the tinnitus location match. The distance away from the location match is shown on the x-axis, and the angle deviated from the location is shown by the legend on the right. The y-axis represents the corrected DML in decibels sensation level. The error bars show the SEM in the positive and negative direction.

The two-way ANOVA revealed that there was no statistically significant interaction between the effects of masker distance and angle on the DML $F(3.781, 68.07) = 0.6841$, $p = .5875$). Simple main effects analysis showed that the distance of the masker signal from the location match did not have a significant effect on DML ($F(1.290, 23.22) = 0.6272$, $p = .4755$). However, the simple main effects analysis showed that the angle of deviation of the masker signal from the tinnitus location had statistically significant effects on the DML ($F(1.685, 30.33) = 5.194$, $p = .0152$).

4.5 Isolating masker distance and angle effects on MML

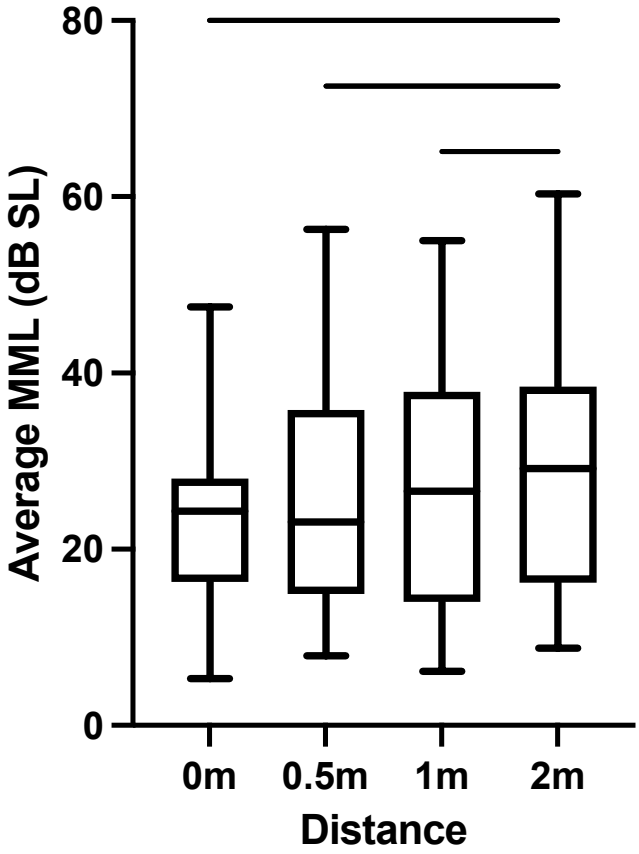

Figure 14. Masker distance effect on MML. These box-and-whiskers plots show the spread of MMLs for when the masker is presented at distances 0, 0.5, 1 and 2m away from the tinnitus location match (x-axis) irrespective of the masker angle deviation. The y-axis shows the corrected average MML in decibel sensation level, which represents the mean MML at each distance. The range of the MMLs for each distance is shown by the thin vertical line. The median MML is shown the horizontal line within the interquartile range box. The number of asterisks represent the strength of statistical significance for the differences between a pair of groups. $p \leq 0.05$ (*), $p \leq 0.01$ (**), $p \leq 0.001$ (***).

The one-way ANOVA revealed that the distance of the masker signal from the tinnitus location match had an significant effect on the MML ($F(1.645, 29.61) = 8.373$, $p = .0.0023$). On average: (i) when the masker signal is placed 2m away from the tinnitus, the MML is 6.7 dB SL higher than when it is placed 0m away from the tinnitus (adjusted $p = .0207$), (ii) the MML is 4.8 dB SL higher when masker is presented 2m away from tinnitus than 0.5m away (adjusted $p = .006$), and (iii) the MML is 3.3 dB SL higher when masker is presented 2m away from tinnitus than 1m away (adjusted $p = .0.0267$). The lowest median MML was found for when the masker was 0.5m away from the tinnitus, and the highest median MML was when the masker was 2m away. The variation in MML values were similar for all masker distances.

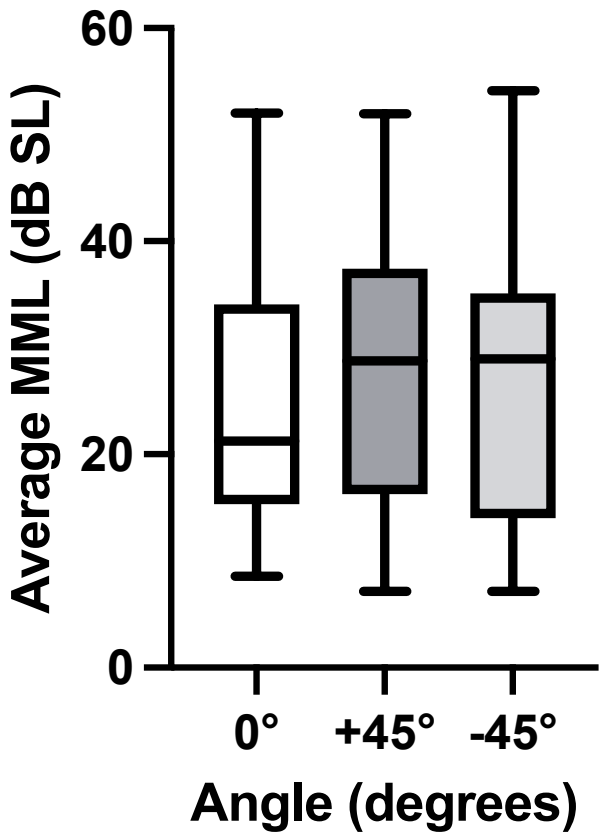

Figure 15. Masker angle effect on MML. These box-and-whiskers plots show the spread of MMLs for when the masker is presented at angles 0 and 45 degrees away from the tinnitus location match (x-axis) irrespective of the masker distance. The negative and positive angles on the x-axis represent angle deviations in the counter-clockwise and clockwise direction, respectively. The y-axis shows the corrected MML in decibel sensation level. The range of the MMLs for each distance is shown by the thin vertical line. The median MML is shown the horizontal line within the interquartile range box.

The one-way ANOVA revealed that the angle deviation of the masker signal from the tinnitus location match had no significant effects on the MML ($F(1.512, 27.21) = 1.214$, $p = .0.302$). The median MML was lowest for when the masker signal was presented 0 degrees away from the tinnitus location match but was similar for when it was presented 45 degrees in either the clockwise or counter-clockwise direction. The variability of MMLs for each angle was similar.

4.6 Comparing MML with DML

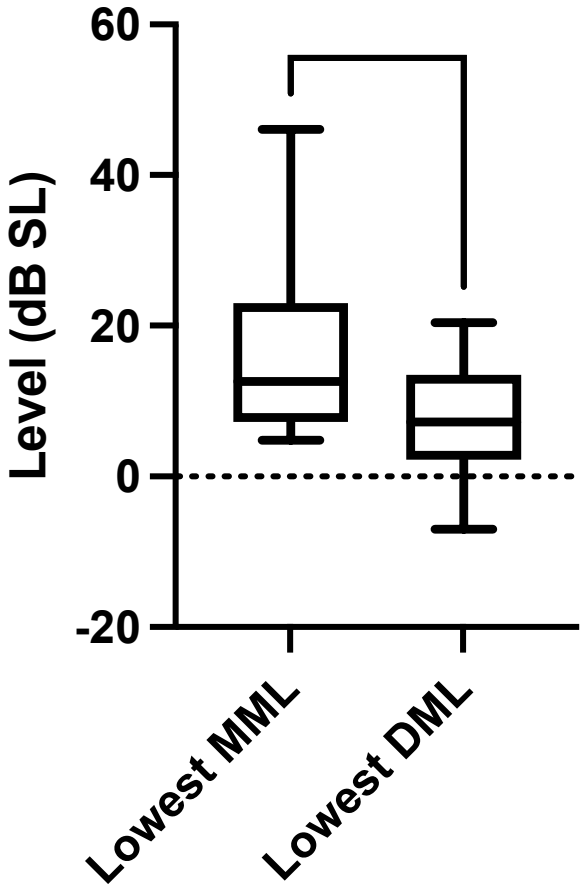

Figure 16. Comparing MML with DML. These box-and-whiskers plots show the distribution of lowest MML and DML values across all nineteen study participants. The horizontal dotted line shows 0 dB SL. The range of both lowest MMLs and DMLs is represented by the vertical thin solid black lines of the plots, whereas the horizontal solid black line within the interquartile range box represent the median. The y-axis shows the corrected level in decibel sensation level. The number of asterisks represent the strength of statistical significance for the differences between a pair of groups. $p \leq 0.05$ (*), $p \leq 0.01$ (**), $p \leq 0.001$ (***).

The median value for the lowest MML across all participants was 12.6 dB SL, and the median value for the lowest DML was 7 dB SL. The two-tailed paired t-test revealed that, on average, the lowest MML is 9.7 dB SL below lowest MML ($T(18) = 3.158$, $p = .00542$). However, this difference could be as high as 16.2 dB SL, or as low as 3.2 dB SL.

4.8 Predictors for masking effectiveness

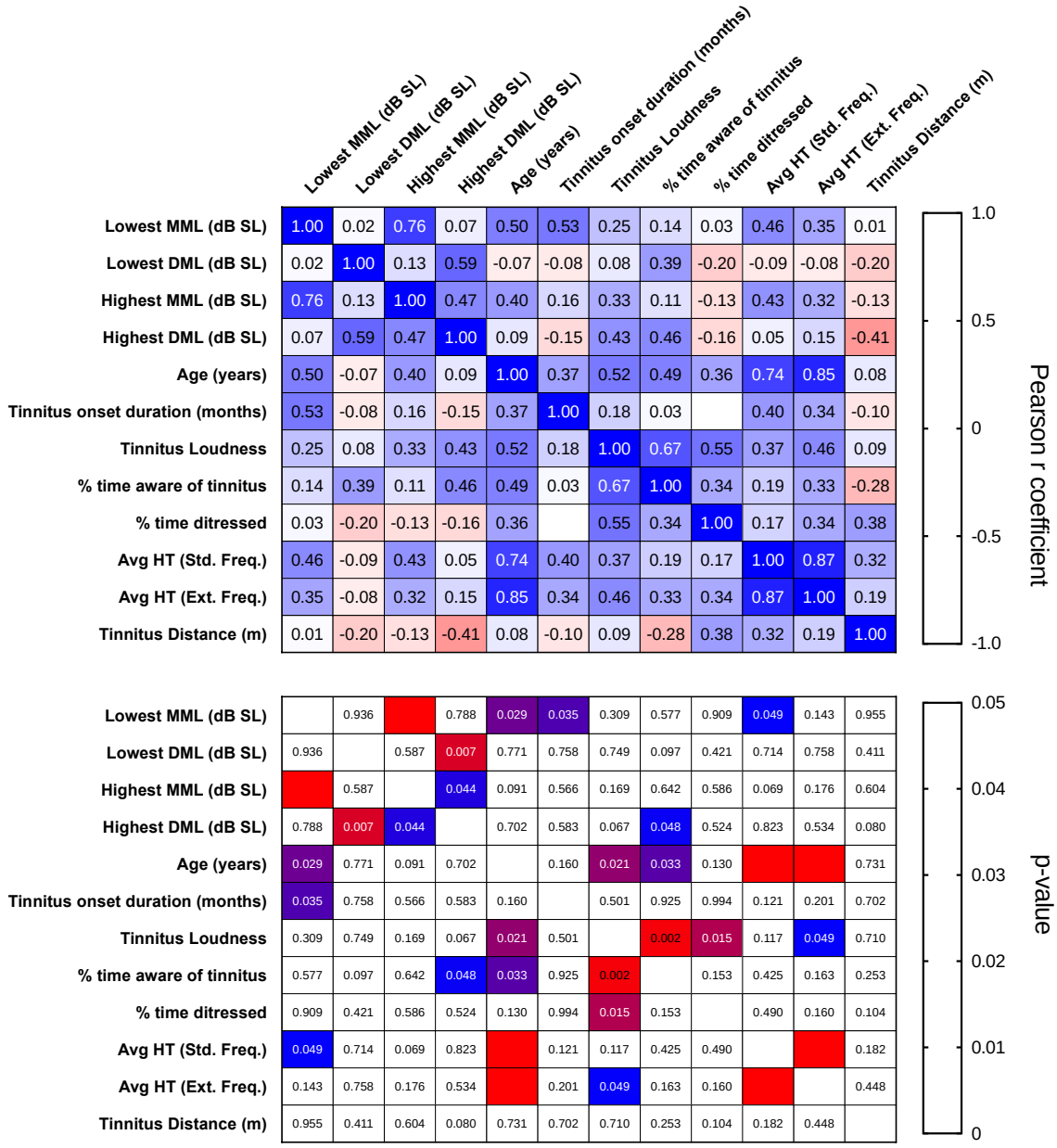

Figure 17. Potential predictors of MMLs and DMLs based on different patient attributes. The top panel shows a correlation heat map showing the associations between patient attributes (such as age, tinnitus and hearing characteristics) and the MMLs and DMLs measured. The numbers within each box are the Pearson's correlation coefficients (r). Blue represents a positive correlation, whereas red represents a negative correlation. The strength of the correlations is shown by the shades of blue and red; with the darker shades representing stronger associations, and lighter shades representing weaker correlations. The bottom panel shows the same associations as the top panel, but the values within the boxes represent the p-values or the statistical significance of the above associations. All boxes that are coloured in the bottom panel indicate significant association, with blue colours referring to strong evidence for the association and red colours referring to weaker evidence. Tinnitus loudness was measured on a scale of 0 to 100; % time aware of and distressed by tinnitus was defined in terms of the previous month from study; the 'average HT' referred to the mean hearing threshold of participants in both the standard frequency range (250 Hz to 8000 Hz) and the extended range (8000 Hz to 16000 Hz); 'tinnitus distance' here refers to the distance of perceived tinnitus measured by the tester-guided method.

There were three patient attributes that had a statistically significant association with the lowest MML, which could be used to predict the lowest MML. These included a moderate association between lowest MML and participant age ($r = 0.50$, $p = .029$), the duration of tinnitus since onset ($r = 53$, $p = 0.035$) and the average hearing threshold within the standard frequency range ($r = 0.46$, $p = .049$). There were no significant associations between the lowest DML and any of the patient attributes, however, there was one significant and moderate association which was between the highest DML and the time aware of tinnitus ($r = 0.46$, $p = .048$), albeit this had a low evidence for significance. Surprisingly, there were no significant associations the DML and MML measures, with perceived tinnitus loudness.

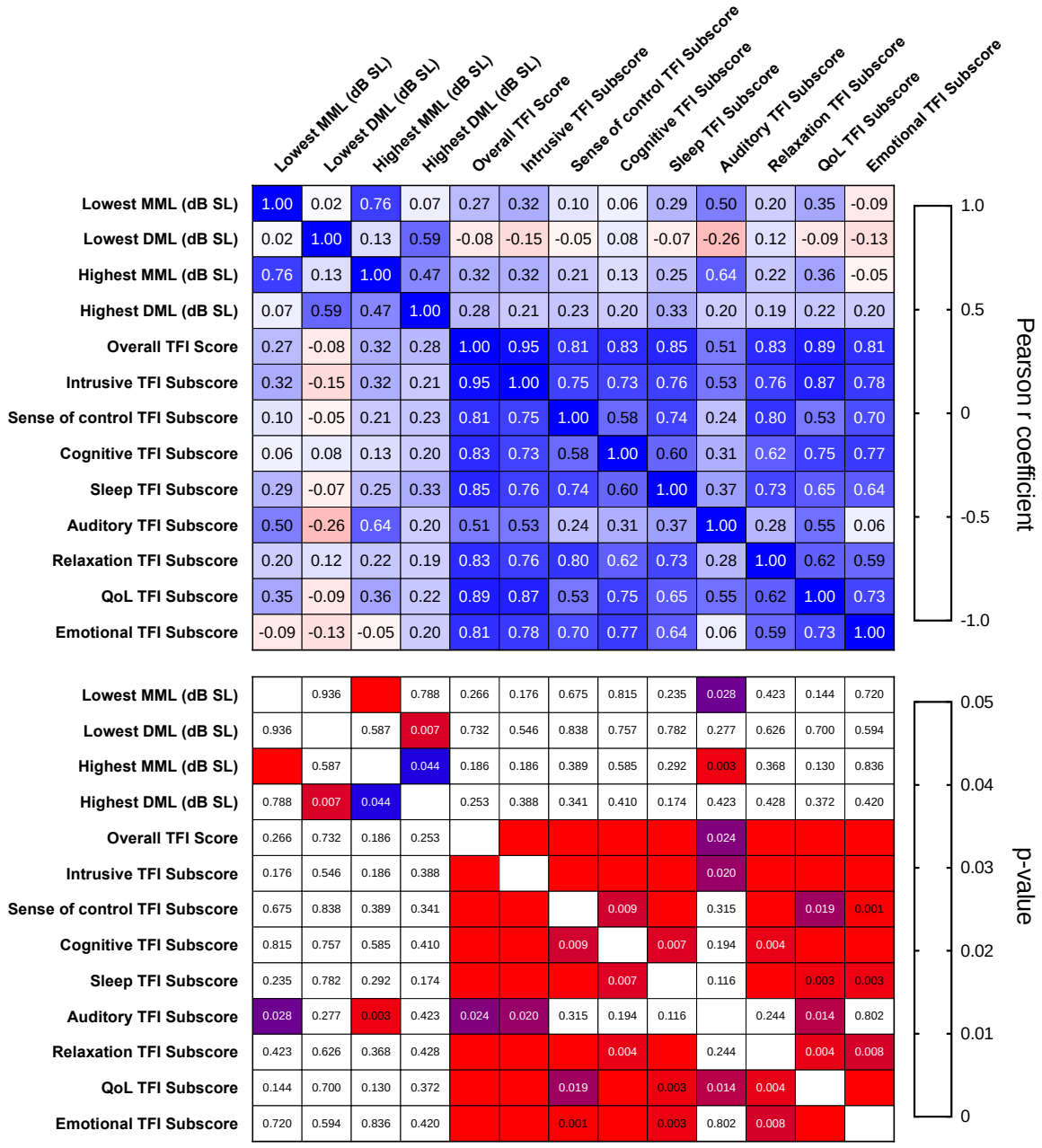

Figure 18. Potential predictors of MMLs and DMLs based on different domains of the TFI questionnaire. The top panel shows a correlation heat map showing the associations between the TFI domains and the MMLs and DMLs measured. The numbers within each box are the Pearson's correlation coefficients (r). Blue represents a positive correlation, whereas red represents a negative correlation. The strength of the correlations is shown by the shades of blue and red; with the darker shades representing stronger associations, and lighter shades representing weaker correlations. The bottom panel shows the same associations as the top panel, but the values within the boxes represent the p-values or the statistical significance of the above associations. All boxes that are coloured in the bottom panel indicate significant association, with blue colours referring to strong evidence for the association and red colours referring to weaker evidence. All blank and coloured boxes refer to extremely strong evidence for the association with the p-value being close to 0.

There were little associations between the outcome measures DML and MML with the TFI questionnaire. The only two significant associations were between the lowest MML and the auditory domain of the TFI (r = 0.50, p = .0.028), and the highest MML with the auditory

domain of TFI (r = 0.64, p = .0.003). The highest MML had a statistically significant and a strong association with the auditory domain of the TFI, whereas the lowest MML had a moderate association. Both these associations had strong statical evidence. Notably, the correlation analysis did not find any statistically significant associations between the DML and any of the TFI domains, especially the overall TFI score.

Chapter 5: Discussion

The present study had three aims: to investigate whether there was any difference in the spatial location of participant tinnitus that is self-reported compared to the tinnitus location obtained via a spatially moving masker sound (processed via the sound processing software Anaglyph); to determine if there was any effect on masker effectiveness when tinnitus maskers are played at different distances and azimuth along the horizontal plane; and to explore whether tinnitus functional index scores or other participant characteristics could predict the masking effectiveness for different individuals. The hypotheses generated for this study were that (i) there will be no difference in the self-reported tinnitus location and the location found through playing a moving masker signal, (ii) the effectiveness of masking will decrease as the masker signal moves farther from the tinnitus location in terms of azimuth and distance along the horizontal plane, and (iii) tinnitus severity and some patient hearing and tinnitus characteristics will be able to predict the effectiveness of a masking-based treatment such as sound therapy.

These three hypotheses were tested by recording the outcome measures minimum masking level (MML) and desired masking level (DML), as well as the coordinates at which the tinnitus was localised using self-report and tester-guided methods. Results were also compared to general hearing and tinnitus characteristics gathered by the Tinnitus Sample Case History Questionnaire (TSCHQ), and tinnitus severity scores calculated from the Tinnitus Functional Index (TFI).

5.1 Main Finding I: Tinnitus location is similar when measured with and without masking sound

The current study showed that the perceived location of tinnitus self-reported by the patient was similar to the location found using a moving masking sound (i.e. tester-guided method). In particular, there was no significant difference between the horizontal azimuth of the tinnitus (Figure 7) or the horizontal distance of the tinnitus from head (Figure 6) when comparing the two localisation approaches (i.e. self-reported with no masker versus tester-guided with masker). These findings complete the first aim of the study and support the first hypothesis stating that the tinnitus location obtained from moving a masker sound produced by the 3D sound processing software, Anaglyph, will correspond well with the self-reported location of tinnitus. This is a novel finding within the literature as there are currently no studies

investigating the influence a masker sound has on obtaining tinnitus location, especially in a spatial plane. The only studies reporting changes in tinnitus location during masking have been in terms of tinnitus laterality, which is an over-simplistic way of defining tinnitus location. For example, Meikle (1997) reported that out of the 1630 tinnitus patients tested in the OSHU Tinnitus Archive, 84% of them had no changes in tinnitus laterality and had undergone some sort of sound therapy (i.e. masking therapy). However, it must be noted that this tinnitus data set was collected over the span of thirteen years, whereas the results observed in the current study are concerned with a much shorter time-window where the tinnitus location was recorded during the masker presentation instead of months or years afterwards. Therefore, it is difficult to ascertain whether tinnitus location will stay constant during masking sound presentation when investigated in a much larger sample sizes like the ones reported within the OSHU Archive.

The finding at hand can also be discussed in the context of neurophysiological changes. Studies have shown that following the administration of sound therapy, many neuroanatomical changes can occur (Liu et al., 2018). Particularly, the dorsal cochlear nucleus and the thalamus had increased brain volume (Wei et al., 2020). It was interesting to note that these studies showed symmetrical alterations within these prominent anatomical tinnitus generators (Caspary & Llano, 2017; Shore et al., 2016; Xia et al., 2020). Because sound therapy (i.e. exposure to masking sounds) causes similar changes on both sides of the auditory structures implicated in tinnitus generation, then the effects it has on psychoacoustical properties of tinnitus (such as location) will also be similar bilaterally. However, for this postulation to be investigated, research must be done on finding the exact functional and anatomical mechanisms that underly tinnitus location, and then how these are impacted by the presentation of masker sounds.

5.2 Main Finding II: Masking effectiveness is influenced by masker-tinnitus proximity

5.2.1 Finding the optimal masker location on the horizontal plane

The current study also provided evidence for the idea that masking effectiveness is impacted by the location of the masker relative to the location of perceived tinnitus. The outcome measure recorded to test the degree of masking effectiveness was the MML. When the masker signal was moved further away from the perceived tinnitus location within the virtual sound field, the MML increased which indicated that the masking effectiveness became worse. In

particular, there was a significant decrease in masking effectiveness (characterised by higher MML) when comparing a masker sound presented 2 metres away from the tinnitus location match, than when it was presented 0 metres away; both 45 degrees counter-clockwise direction (Figure 12). This completes the second aim and supports the hypothesis stating that the MML of masking sounds presented further away from the perceived tinnitus in a virtual sound field is larger, indicative of less effective masking. To the author's knowledge, these are the first findings in literature assessing the effects of changing the azimuth and distance away from tinnitus location on masking effectiveness. Further studies will need to be done, especially with larger sample sizes, for these findings to be confirmed.

Furthermore, the findings stated here refute the conclusions drawn by Kubota et al. (2022), that the further away a masker is played from the tinnitus, the more effective it will be due to its greater attention-diverting capability. In fact, the furthest position that was tested, in terms of distance (2 metres away from the location of tinnitus), was the only position that gave a significantly lower masking effectiveness measure. This can be attributed to multiple factors. First, the testing paradigm used in Kubota's study utilised simulated tinnitus that, being an externally produced sound, might have different masking interactions compared to the internally produced real tinnitus used in the current study. Second, only one distance of 1.8 metres was assessed in Kubota's study, which was not assessed in the present study. Finally, Kubota's study used an external speaker to produce the masking noise that allows the participant to use visual cues for sound depth perception (Middlebrooks, 2015). In comparison, our study used masking produced in a virtual sound field that does not allow the visual cue to be used to judge the distance of the masker from the participant. Therefore, the distances used in Kubota's study might not be directly comparable to our study.

5.2.2 The most effective masking position on an individual basis

The MML was shown to be lowest at specific tinnitus masker positions for each individual i.e. each participant had a spatial position where the masker proved to be most effective. For example, five participants out of the nineteen experienced the lowest MML when the masker sound was spatially overlapping the location of their perceived tinnitus (i.e. 0 metres away in distance and 0 degrees away from the tinnitus location match) (Figure 8). There were also some participants that showed more effective masking at locations other than their tinnitus, such as those reporting lowest MMLs at different azimuth angles and distances away from the tinnitus location match. Similar findings were published by Searchfield et al. (2016) stating that, for

those that tinnitus location can be obtained, presenting a 3D masker was more effective than the commonly used binaural masking. Although our study did not make direct comparisons to binaural masking, the critical concept that was highlighted is that *spatial location matters* when the goal is to mask most effectively, and it is different for each individual.

5.2.3 Isolating distance and azimuth effects on masker effectiveness

The above findings were also observed by isolating distance and azimuth effects separately. It was found that 63% of our study population (n = 12) experienced lowest MMLs when the masker was 0 metres away from their tinnitus location match, whereas only one participant had lowest MMLs at 2 metres away (Figure 10). However, the same degree of discrepancy in the counts of participants was not seen when the masker azimuth was concerned; 57% (n = 11) had lowest MMLs at 0 degrees azimuth, but 42% (n = 8) participants also had lowest MMLs at 45 degrees azimuth from location match (Figure 11). This shows that for our study population, the distance effect on MML was greater than the azimuth effect. To further this point, results also showed that on average, when the masker sound is presented 2 metres away from the tinnitus location match, it is less effective than presenting a masker at 1, 0.5 and 0 metres away (Figure 14). This is in comparison to the azimuth positions tested that, on average, had similar degrees of masking effectiveness (Figure 15).

The fact that the masker distance is more important than the masker azimuth for determining masking effectiveness, can perhaps be explained by the mechanics of sound localisation. For distance to be perceived, a decrement of 6 dB in sound level is perceived as doubling of the distance (e.g. the difference between the levels of sounds 2m versus 0m away will be 12 dB) (Coleman, 1962); whereas for azimuth to be perceived, an ILD of only 3 dB needs to be applied to perceive sounds having a 45 degrees azimuth difference (Smith & Price, 2014). Therefore, due to the greater sound level-attenuating capability of the level cue used in depth perception compared to the ILD cue used in azimuth localisation, it may be possible that the MMLs were attenuated more when comparing the masking distance effect than with the azimuth effect. Hence, explaining the significant differences seen in MMLs recorded at different distances but not at different azimuth angles. Though it must be considered that most studies explaining these localisation cues use pure-tones, whereas masker sounds that are broadband white-noises may behave differently.

5.3 Main Finding III: Masking effectiveness is predicted by some patient characteristics and tinnitus severity measures

Our study showed that some participant characteristics recorded by the TSCHQ, as well as some domains of the TFI, can be used to predict masking effectiveness for different patients undergoing tinnitus sound therapy. The investigation into these predictors used correlation analysis, where several pieces of information gathered by the TFI and TSHQ were correlated with the lowest and highest MMLs recorded across the twelve spatial positions. The magnitude of these lowest values reflected how easy it was to mask an individual's tinnitus i.e. lower values were indicative of greater ease of masking. The analyses showed that although there were some TSCHQ and TFI outcomes that could be used to predict masking effectiveness, most of the outcomes were not significantly associated with the lowest or highest MMLs recorded. This completed our third and final aim of the study, and provided evidence for our hypothesis that there is a correlation between masking effectiveness and the degree of tinnitus severity (measured by the tinnitus functional index), where participants with more severe tinnitus will require a greater level of masking. The following two sections will discuss these associations in more depth.

5.3.1 TSCHQ-measured patient characteristic predictors

Our study shows that the only three patient characteristics acquired by the TSCHQ that predicted how easily an individual's tinnitus can effectively be masked was their age, duration of tinnitus since onset, and the average standard frequency-range hearing threshold. Correlation analysis between the lowest MML and TSCHQ outcomes revealed that the MML predictor that had the strongest evidence for an association was age, followed by duration of tinnitus onset, and then hearing thresholds within the standard frequency ranges (Figure 19). More specifically, all three of these associations were positive which is indicative of a direct correlation, where the increase in lowest MML was paired with an increase in the three predictors. This partially completed our third aim of the study that had the goal of investigating whether any patient characteristics or TFI scores could predict masking effectiveness.

First, in the context of age and duration of tinnitus onset, it is hard to state what exactly underlies the correlation between these factors and the ease of tinnitus masking. However, literature suggests that older patients with longer durations of tinnitus might respond less effectively to masking sound therapy (Anwar, 2013; Martinez-Devesa et al., 2010; Searchfield

et al., 2021). Theoretically, this could be because older tinnitus patients have a lowered tolerance for dealing with tinnitus and are more susceptible to its negative effects (Al-Swiahb & Park, 2016; Sharma et al., 2021); and thus, find it harder to minimise its effects by the distracting masker noise presented i.e. higher MMLs.

Second, when discussing the association of lowest MML and hearing thresholds, it must be restated that the MML values reported within this study were adjusted for the participant's hearing threshold. Therefore, given that each MML value already accounted for the hearing thresholds, there must be other independent factors associated with hearing loss that act to decrease the ease of effective masking. A potential reason behind this association might be based on the fact that because tinnitus patients with worse hearing thresholds (i.e. hearing losses) also have increased tinnitus severity (Aazh & Salvi, 2019; McKinney et al., 1999). Someone with more severe tinnitus will need a louder masker signal to divert their attention from their tinnitus sound. A similar concept is seen in cognitive health research, where annoying sounds tend to force the listener to attend to them, whereas less annoying sounds are more easy to be distracted from (Andringa & Lanser, 2013).

Surprisingly, our correlation analysis found no significant association with lowest MML and perceived tinnitus loudness (Figure 19). In fact, the highest MML recorded for each participant was also not associated with tinnitus loudness (Figure 19). This seems counterintuitive because, in principle, louder tinnitus should require a higher level of masking sound to remove its perception (Jastreboff, 1990; Jastreboff et al., 1994). Perhaps our counterintuitive results can be explained by the diversity in tinnitus perception. Generally, patients that have louder tinnitus sound also require more masking because their tinnitus requires a greater degree of distraction to overcome the bothersome nature of the sound (Dauman & Tyler, 1992). However, we know that different patients have different coping strategies; thus some with perceivably louder tinnitus are less bothered, whereas some who have relatively quieter tinnitus find it harder to cope with (Mancini et al., 2020). Therefore, it may be possible that the participants in the current study had diverse coping strategies for their tinnitus, which could underly the non-correlation observed between tinnitus loudness and ease of masking i.e. lowest MML.

5.3.2 TFI-measured tinnitus severity predictors

Overall, we found that the TFI was not a good predictor of effective tinnitus masking. This was shown by the insignificant correlation between DMLs and MMLs with the overall TFI score indicative of the degree of tinnitus severity. In concert with the TSCHQ outcome associations,

this completed the third aim of the study and provided evidence that did not support our hypothesis that participants with more severe tinnitus will require a greater level of masking. Although no research has been done correlating TFI outcomes with psychoacoustical measures of tinnitus such as MML, there have been studies indicating that there is low correlation between other severity-assessing tinnitus questionnaires such as the THQ (tinnitus hearing questionnaire) or THI (tinnitus handicap index) with MMLs (Figueiredo et al., 2010; Mancini et al., 2020; Nyenhuis et al., 2013). These findings suggest that a tinnitus treatment such as sound therapy should be evaluated by measuring tinnitus itself (like MML), rather than questionnaire outcomes measuring the reaction to tinnitus.

The only TFI-reported measure that was moderately correlated with the highest and lowest MMLs, was the auditory TFI sub score that assessed how tinnitus impacted speech comprehension and hearing (Figure 20). Both these correlations were positive, which was expected because if there is a true correlation between the auditory TFI domain with the MML, it should not only impact the lowest MML but also the highest MML i.e. as the auditory TFI sub score increases, so should the undeniably interlinked lowest MML and the highest MML values. Given that the lowest MML values were significantly correlated with hearing thresholds discussed in the above section (Figure 19), it is perhaps unsurprising that participants who scored higher on the auditory domain of the TFI also showed a significant correlation (considering higher auditory domain TFI scores reflect poorer hearing performance).

5.4 Other findings relating to the desired masking level (DML)

The DML was a more subjective measure of masking sound efficacy in diminishing the adverse effects of tinnitus. Although the DML does not always reflect the level at which complete masking of tinnitus is achieved, it does indicate when a patient feels most comfortable with their tinnitus sound therapy. Therefore, if the goal of tinnitus treatment is to remove the annoyance of tinnitus, the outcome measure used should be DML. Opposingly if the goal is to remove the perception of tinnitus completely, then MML is a better measure for treatment success. Our study found that, on average, the DML tends to be 9.7 dB lower than the MML value (Figure 16). This is expected as there are many participants that find the masking noise presented during sound therapy to be more irritating than the tinnitus itself, and thus reach a satisfactory result when the tinnitus is partially masked where the masker sound level is relatively lower than what would be needed to reach complete masking. These findings highlight the importance of patient-centric tinnitus treatments where measures of treatment

success do not always need to be defined by removal of the condition (as is the case when trying to reach complete masking), but the removal of negative impacts of the condition on patient's life.

We found that each participant of the current study had a specific location of masking where the lowest DML was achieved (Figure 9). Notably, however, the spatial location at which the lowest MML was recorded (Figure 8) did not always correspond with the location of lowest DML. This was shown by the difference in participant counts for lowest MML and DML values at each position given in Figures 8 and 9, respectively. This finding is critical when trying to implement spatial masking in a clinical setting, where the clinician needs to realise that if the goal of treatment is to remove tinnitus perception then the best location of masker signal will be different than if the goal was to remove the annoyance of tinnitus.

There was no significant interaction between the effects of masker distance and angle on the DML (Figure 13). However, when the distance and azimuth effects were isolated, a simple mains effect analysis did show a significant effects of masker azimuth on DML (Figure 13). This finding is opposite to the one found in context with MML, where there were no significant interactions between masker azimuth and MML, but there were for masker distance and MML (Figure 11). The exact reasoning for these opposing results is hard to postulate, however, they do indicate that when trying to achieve the goal of removing tinnitus annoyance, the azimuth of the masker is more important than the distance along the horizontal plane.

5.4 Significance of Research

On average, the current study reports that a specific distance needs to be reached between the masker and tinnitus location, for the merits of spatial masking to apply. However, when observed at an individual level, there is evidence in the current study that suggests personalised spatial masking can benefit every tinnitus patient as all current study participants had a specific location in auditory space where they find the most benefit from masking. Therefore, sound therapy may benefit by applying a more tailored approach, where not only the best type of masker sound type is considered for the individual, but also the most optimal masker location in the auditory field.

5.5 Limitations and Future Research

The simulation of sound localisation was foundational for the current study. The 3D processing that occurs to virtualise spatialisation of a sound source, in this case the masker noise, uses multiple binaural cues including ITD and IID for azimuth perception, as well as monoaural cues like incident sound level to infer sound depth. These spatial cues are severely disrupted by the presence of hearing loss which, in turn, leads to poorer spatial-discrimination of sound (Häusler et al., 1983). Therefore, given that our study population had a considerable amount of hearing loss (Figure 4), the location match of tinnitus obtained in the current study could be inaccurate. However, considering that most participants with tinnitus also have associated hearing losses (Pinto et al., 2015), and given that a greater degree of loss relates to louder and easier-to-localise tinnitus; it was difficult to obtain participants without any hearing losses that could also localise their tinnitus in space. Moreover, the tinnitus location obtained via the tester-guided method did correspond well with the self-reported method. Which suggests that the localisation ability of our study participants was not impaired. Nevertheless, future research can consider restricting the inclusion criteria further for lower degrees of hearing loss to investigate whether the findings differ from the current study.

Changes in the location of tinnitus, particularly laterality, is a common occurrence in clinical studies (Meikle & Griest, 1992). However, the time-course in which this change occurs is not well-defined, let alone the time-course for changes in 3D spatial localisation of tinnitus. For the present study, we assumed that throughout testing, the location of tinnitus remained constant with the location match initially obtained via the tester-guided method. However, if the tinnitus location were to change, then the present results obtained would be difficult to interpret because the twelve different spatial positions defined assumed a static tinnitus location match as a reference. Therefore, it would be interesting to see if the same results can be obtained during follow-up testing sessions of the same study population.

The present study did not compare spatial masking with the commonly used binaural masking (equal masking noise in both ears) used in sound therapies currently. This was because Searchfield et al. (2016) had already previously shown that spatial masking is more effective than binaural masking. However, Searchfield only investigated this claim when the masker

sound was presented in the same spatial location as the tinnitus location match. It would be interesting to know whether the same finding would be reported when masker distance and azimuth changes are made as we did in the present study. This could be a potential aim to include for future spatial masking studies.

The current study had a sample size of nineteen participants. Although this was a lower sample study, the repeated-measures design used allowed sufficient statistical power for an effect to be observed. Furthermore, there were some results, particularly those of location tester-guided matches (Figure 17), that showed extreme azimuth and distance values. Given that most tinnitus patients experience tinnitus internally or externally but close-to-head (Meikle et al., 2004), it was difficult to ascertain whether these distant location matches were an artefact of the small sample size or showed true tinnitus locations i.e. not outliers. To explore this further, future studies can opt for a larger sample sizes to incorporate more patients with distant tinnitus locations.

Summary and Conclusion

The present study's main goal was to explore whether altering the distance and azimuth during spatial masking can provide a benefit in terms of masking effectiveness. Strong evidence was found stating that, on an individual basis, presentation of maskers at positions other than the spatial location of tinnitus provides more effective masking. There is also some evidence stating that patient characteristics such as age, time since tinnitus onset, and hearing sensitivity can serve as predictors for how easily the tinnitus can be masked. Therefore, spatial masking of tinnitus in sound therapy can be beneficial clinical tool that can be personalised to patient tinnitus and increase its therapeutic potential.

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APPENDIX A

Participant information Sheet

SCHOOL OF POPULATION HEALTH – AUDIOLOGY
Faculty of Medical & Health Sciences

THE UNIVERSITY OF AUCKLAND
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Participant Information Sheet

Study title: Masking tinnitus using three-dimensional sound processing

Principal investigator: Dr Grant Searchfield (Associate Professor, Section of Audiology).
Master of Audiology Research Student: Kanav Singh (Audiology Intern).

To individuals interested in participating as a research participant:

Project Description

Tinnitus can be a debilitative condition that can cause persistent anxiety, lack of sleep, depression and loss of concentration in daily activities. The perception of tinnitus is not correlated with the presence of any external sound and is only heard by the sufferer. Sound therapy, which masks the tinnitus by the presentation of other sounds, is based on the principle of distraction. This study aims to better our understanding of sound therapy by determining whether the presenting the masking sound at different points in space can alter the perception of tinnitus.

The research project is under the supervision of the principal investigator, Grant Searchfield (Associate Professor, Section of Audiology) as a part of the Master's of Audiology degree for Kanav Singh. The data collection will be undertaken by Kanav Singh (second year Master of Audiology).

You are invited to participate in our study at the University of Auckland Hearing and Tinnitus Clinics, building 507, Grafton Campus. Testing will take up to 2 hours of your time to complete in a one-off session. You will be reimbursed with a $20 Westfield voucher for your participation in the research. Parking is not provided, however, there is free public parking at the Auckland Domain across the University campus. There is also paid on-street parking on Park Avenue which is directly adjacent to the building 507.

In order to be eligible for this study, you must: be aged over 18, be fluent in English, have constant tinnitus (minimum 6 months duration) that must be present on the day of the study session, and no more than a mild hearing loss. This will be confirmed during the audiometric test of hearing during the study session. A mild loss is defined as hearing threshold no greater than 40 dB HL (decibel hearing loss).

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266.

Project Procedures

Interested participants will be requested to complete a consent form before the study session if they have not already sent a signed consent form via email.

Audiological Examination:

This involves:

1. Brief otological history, including two tinnitus questionnaires
2. Otoscopy (examination of the ear canal using a hand-held light)
3. Audiometric testing of hearing

Tinnitus Assessment:

You will first be asked to estimate the position of your tinnitus in a room diagram given. Then a set of headphones will be given and a white noise will be played coming from different positions within the room. The noise will also be of varying volumes and the volume will be decreased to identify the lowest level that your tinnitus is masked at.

Risks and Benefits, Incidental Findings

There are no specific risks associated with taking part in this study. As a benefit, you can choose to receive a free detailed copy of your hearing/audiological testing results.
It is not anticipated but there is a possibility that you may come to realise that your tinnitus is of high concern and impacting various aspects of your daily life, or of unanticipated hearing loss. For any concerns, you can get in touch with the primary investigators both during and after the study to discuss. Dr. Grant Searchfield is a qualified audiologist 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 time without providing a reason and withdraw your data for up to two months after the date of testing. This can be done by contacting Kanav Singh (ksin899@aucklanduni.ac.nz).

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 researchers (Kanav Singh and Dr. Grant Searchfield) will be the only ones with access to the data at any point throughout the entirety of the project. Each participant will be assigned a number at the beginning of the project and all test assessment data will bear this number and no other identifiable information. The list of numbers linking participant data will be kept in a locked file on university premises throughout the duration of the project. All personal information which may identify individuals will be destroyed immediately after completion of the project; the only information to be retained is that necessary for analysis of the results.

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266.

separately from the data by the Dr. Grant Searchfield in a locked cabinet on university premises for a period of 6 years, after which they will be destroyed. Written material will be disposed in confidential bins for further destruction (shredding and incineration). All digitally coded information not being kept for analysis and all identifying data will be permanently wiped from computer storage. De-identified digital information will be retained for potential future use (i.e. analysis).

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.
- You are allowed to bring your your whanau/family, or support person to the study session if desired.
- 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. If you wish to take part, please contact Kanav Singh or Dr Grant Searchfield (details below). A consent form will be sent to you via email and you will have the option of signing it digitally or signing it on the day of the study.

Contact Details

Further questions regarding the research project may be directed to:

1. Kanav Singh (Audiology Intern)
   Email: ksin899@aucklanduni.ac.nz
2. Dr. Grant Searchfield (Head of Audiology)
   Phone: 3737599 ext. 86316
   E-mail: g.searchfield@auckland.ac.nz
3. 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 ext. 83711, or at Auckland Health Research Ethics Committee, The University of Auckland, Private Bag 92019, Auckland 1142.

Compensation

If you were injured in this study, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266.

Consent Form

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

MEDICAL AND HEALTH SCIENCES

Consent Form

This form will be retained for 6 years in secure storage by the researchers before being destroyed.

Study title: Masking tinnitus using three-dimensional sound processing

Principle investigator: Dr Grant Searchfield (Associate Professor, Section of Audiology).
Master of Audiology Research Student: Kanav Singh (Audiology Intern)

I have read the Participant Information Sheet and have understood the explanation of this research project and my role as a participant. I have had the opportunity to ask questions of the investigators, to consult my whanau, hapu, or iwi, or a family member/friend. I have had time to consider whether to take part. I am satisfied with the answers I have been given. I know who to contact if I have further questions about the study.

- I have read and understand the Participant Information Sheet for volunteers taking part in this study.
- I understand that taking part in this study is voluntary and that I may withdraw from participation at any time up to two months after I have been tested without providing a reason. If I do withdraw, this will not affect my relationship with the University and Clinic in any way and all data pertaining to me will be destroyed safely.
- I understand that participation in this study is confidential and that no material that could identify me will be used in any reports relating to this study. The data from this research (including the questionnaires and other details) will be stored confidentially.
- I understand that consent forms will be kept for 6 years, after which they will be securely shredded.
- I understand that de-identifiable collective data will be kept indefinitely for potential future use. If you do not wish for your de-identified data to be retained for future use, please indicate this below.

I agree to take part in this research during which I will be asked to undergo detailed hearing and tinnitus assessment (otoscopy, pure tone audiometry, questionnaires, tinnitus testing).

I **wish / do not wish** to receive a summary of findings (circle one).
I **wish / do not wish** for my de-identified data to be retained for future use (circle one).

Email: _____

I, (please print full name) _____ hereby consent to take part in this study.

Signature: _____ Date: _____

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266.

APPENDIX B

Tinnitus Functional Index (TFI) Questionnaire

TINNITUS FUNCTIONAL INDEX

Today's Date _____ (Month / Day / Year) Your Name _____ (Please Print)

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

I **Over the PAST WEEK...**

1. What percentage of your time awake were you consciously **AWARE OF** your tinnitus?

Never aware ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *Always aware*

2. How **STRONG** or **LOUD** was your tinnitus?

Not at all strong or loud ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely strong or loud*

3. What percentage of your time awake were you **ANNOYED** by your tinnitus?

None of the time ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *All of the time*

SC **Over the PAST WEEK...**

4. Did you feel **IN CONTROL** in regard to your tinnitus?

Very much in control ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Never in control*

5. How easy was it for you to **COPE** with your tinnitus?

Very easy to cope ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to cope*

6. How easy was it for you to **IGNORE** your tinnitus?

Very easy to ignore ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to ignore*

C **Over the PAST WEEK how much did your tinnitus interfere with...**

7. Your ability to **CONCENTRATE**?

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

8. Your ability to **THINK CLEARLY?**

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

9. Your ability to **FOCUS ATTENTION** on other things besides your tinnitus?

Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

SL **Over the PAST WEEK...**

10. How often did your tinnitus make it difficult to **FALL ASLEEP** or **STAY ASLEEP**?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

11. How often did your tinnitus cause you difficulty in getting **AS MUCH SLEEP** as you needed?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

12. How much of the time did your tinnitus keep you from **SLEEPING** as **DEEPLY** or as **PEACEFULLY** as you would have liked?

None of the time ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *All of the time*

08.15.08

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

A	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*									*Completely interfered*
13.	Your ability to **HEAR CLEARLY**?	0	1	2	3	4	5	6	7	8	9	10
14.	Your ability to **UNDERSTAND PEOPLE** who are talking?	0	1	2	3	4	5	6	7	8	9	10
15.	Your ability to **FOLLOW CONVERSATIONS** in a group or at meetings?	0	1	2	3	4	5	6	7	8	9	10
R	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*									*Completely interfered*
16.	Your **QUIET RESTING ACTIVITIES**?	0	1	2	3	4	5	6	7	8	9	10
17.	Your ability to **RELAX**?	0	1	2	3	4	5	6	7	8	9	10
18.	Your ability to enjoy **"PEACE AND QUIET?"**	0	1	2	3	4	5	6	7	8	9	10
Q	**Over the PAST WEEK, how much has your tinnitus interfered with...**	*Did not interfere*									*Completely interfered*
19.	Your enjoyment of **SOCIAL ACTIVITIES**?	0	1	2	3	4	5	6	7	8	9	10
20.	Your **ENJOYMENT OF LIFE**?	0	1	2	3	4	5	6	7	8	9	10
21.	Your **RELATIONSHIPS** with family, friends and other people?	0	1	2	3	4	5	6	7	8	9	10

22. How often did your tinnitus cause you to have difficulty performing your **WORK OR OTHER TASKS**, such as home maintenance, school work, or caring for children or others?

Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

E **Over the PAST WEEK....**

23. How **ANXIOUS** or **WORRIED** has your tinnitus made you feel?

Not at all anxious or worried ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely anxious or worried*

24. How **BOTHERED or UPSET** have you been because of your tinnitus?

Not at all bothered or upset ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely bothered or upset*

25. How **DEPRESSED** were you because of your tinnitus?

Not at all depressed ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely depressed*

08.15.08

Tinnitus Sample Case History Questionnaire (TSCHQ)

Section of Audiology
Level 3, Bldg. 730, School of Population Health
Faculty of Medical and Health Sciences
261 Morrin Road
Glen Innes
Auckland 1072

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES
School of Population Health

TINNITUS SAMPLE CASE HISTORY QUESTIONNAIRE

Last Name:
First Name(s):

1	**Date of birth:** Click here to enter a date.
2	**Gender:** Choose an item.
3	Handedness: ○ Right ○ Left ○ Both sides
4	Family history of tinnitus complaints ○ Yes If YES: ☐ Parents ☐ Siblings ☐ Children ○ No
5	Initial onset: When did you first experience your tinnitus? Click here to enter a date.
6	How did you perceive the beginning? ○ Gradual ○ Abrupt
7	Was the initial onset of your tinnitus related to: ☐ Loud blast of sound ☐ whiplash ☐ Change in hearing ☐ Stress ☐ Head trauma ☐ Other: _____
8	Does your tinnitus seem to PULSATE? ☐ YES, with heart beat ☐ YES, different from heart beat ☐ No
9	Where do you perceive your tinnitus? ☐ Right ear ☐ Left ear ☐ Both ears, worse right ☐ Both ears, worse left ☐ Inside the head ☐ Elsewhere
10	How does your tinnitus manifest itself over time? ○ intermittent ○ Constant
11	Does the LOUDNESS of the tinnitus vary from day to day? ○ Yes ○ No
12	Describe the LOUDNESS of the tinnitus using a scale from 1 – 100. 1 = VERY FAINT; 100 = VERY LOUD _____

13	Please describe in your own words what your tinnitus usually sounds like*: * The following list gives examples of some possible sensations, feel free to use other terms as well: hissing, ringing, pulsing, buzzing, clicking, cracking, tonal (like a dial tone or other kinds of tones) humming, popping, roaring, rushing, typewriter, whistling, whooshing.
14	Does your tinnitus more sound like a tone or more like noise: ☐ Tone ☐ Tone ☐ Crickets ☐ Other
15	Please describe the PITCH of your tinnitus: ☐ Very high frequency ☐ High frequency ☐ Medium frequency ☐ Low frequency
16	What percent of your total awake time, over last month, have you been aware of your tinnitus? For example, 100% would indicate that you were aware of your tinnitus all the time, and 25% would indicate that you were aware of your tinnitus ¼ of the time. _____% (Please write a single number between 1 and 100)
17	What percent of your total awake time, over the last month, have your been annoyed, distressed or irritated of your tinnitus? _____% (Please write a single number between 1 and 100)
18	How many different treatments have you undergone because of your tinnitus? ○ None ○ None ○ Several ○ Many
19	Is your tinnitus reduced by music or by certain types of environmental sounds such as the noise of a waterfall or the noise of running water when you are standing in the shower? ○ Yes ○ No ○ I don't know
20	Does the presence of loud noise make your tinnitus worse? ○ Yes ○ No ○ I don't know
21	Does any head and neck movement (e.g. moving the jaw forward or clenching the teeth), or having your arms/hands or head touched, affect your tinnitus? ○ Yes ○ No
22	Does taking a nap during the day affect your tinnitus? ○ Worsens my tinnitus ○ Reduces my tinnitus ○ Has no effect
23	Is there any relationship between sleep at night and your tinnitus during the day? ○ Yes ○ No ○ I don't know

24	Does stress influence your tinnitus? ○ Worsens my tinnitus ○ Reduces my tinnitus ○ Has no effect
25	Does medication have an effect on your tinnitus? Medication: Effect/Details: (4 rows)
26	Do you think you have a hearing problem? ○ Yes ○ No
27	Do you wear hearing aids? ○ Right ○ Right ○ Left ○ None
28	Do you have a problem tolerating sounds because they often seem much too loud? That is, do you often find too loud or hurtful sounds which other people around you find comfortable? ○ Never ○ Rarely ○ Sometimes ○ Usually ○ Always
29	Do sounds cause you pain or physical discomfort? ○ Yes ○ No ○ I don't
30	Do you suffer from headache? ○ Yes ○ No
31	Do you suffer from vertigo or dizziness? ○ Yes ○ No
32	Do you suffer from temporomandibular disorder? ○ Yes ○ No
33	Do you suffer from neck pain? ○ Yes ○ No
34	Do you suffer from other pain syndromes? ○ Yes ○ No
35	Are you currently under treatment for psychiatric problems? ○ Yes ○ No

APPENDIX D

Study Advert

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

MEDICAL AND HEALTH SCIENCES

RESEARCH PARTICIPANTS NEEDED

Want to contribute to hearing & tinnitus research?
FREE hearing test included!

About the research:

I am seeking people with tinnitus to participate in a study assessing the effects of playing distractor (masking) noise on the perception of tinnitus. I will test your hearing and tinnitus masking by producing white noise at different spatial locations and volumes. In doing so, the validity of using tinnitus sound therapy personalised to the individual's spatial perception of tinnitus will be tested.

I will be undertaking this project as part of my Master of Audiology degree at the University of Auckland, which will be supervised by Dr. Grant Searchfield (Associate Professor, Audiology).

The study session will take place at The University of Auckland (Grafton Campus) and is expected to take up to 2 hours. **For your time, a $20 Westfield voucher will be given.**

Eligibility criteria:

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

- Be aged **over 18**,
- Have **constant tinnitus** (minimum 6 months duration) that must be present on the day of the study,
- Have **normal hearing** OR **no more than a mild hearing loss.**

For further information and to take part in the study, please feel free to contact Kanav Singh (ksin899@aucklanduni.ac.nz).

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266..

Email Invitation

Kia ora,

My name is Kanav and I am the student researcher involved in this project who will be conducting the testing. I will be supervised by Dr. Grant Searchfield, who is an associate professor and the Head of Audiology.

The location of the testing room will be at The University of Auckland at the Grafton campus, and the testing is expected to take 2 hours. During the first hour, you will fill out two tinnitus questionnaires and we will check your hearing. In the second hour, your tinnitus will be mapped spatially and we will try mask it using white noise. There will be breaks between the two sessions, giving you the opportunity to grab something to eat or drink.

Please see attached for the Consent Form (CF) and Participant Information Sheet (PIS). Please note that you will be required to sign the CF on the day of the study, prior to any testing, if you have read, understood, and are happy to participate in this project. If you wish, you may also sign the CF attached and send it back to us through email. As a thank you for your time and participation, you will be compensated with a gift/koha of a $20 Westfield voucher.

The date and time can be arranged according to the your availability as I am quite flexible. Please reply to this email with a suggested date and time and I will try my best to schedule you in. If you are unable to make it on the time we have scheduled please let me know via email (ksin899@aucklanduni.ac.nz).

If you have any questions or concerns, please do not hesitate to reach out to either myself or my supervisor. His contact email is: g.searchfield@auckland.ac.nz

Kind regards,

Kanav Singh

Approved by the Auckland Health Research Ethics Committee on 24/11/2022 for three years. Reference number AH25266.